Inactivity, exercise training and detraining, and plasma lipoproteins. STRRIDE: a randomized, controlled study of exercise intensity and amount

Cris A. Slentz,1 Joseph A. Houmard,3 Johanna L. Johnson,1 Lori A. Bateman,1 Charles J. Tanner,3 Jennifer S. McCartney,3 Brian D. Duscha,1 and William E. Kraus1,2
1Division of Cardiology and 2Duke Center for Living, Duke University Medical Center, Durham; and 3Department of Exercise and Sports Science and Human Performance Laboratory, East Carolina University, Greenville, North Carolina

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Inactivity, exercise training and detraining, and plasma lipoproteins. STRRIDE: a randomized, controlled study of exercise intensity and amount. J Appl Physiol 103: 432–442, 2007. First published March 29, 2007; doi:10.1152/japplphysiol.01314.2006.— Exercise has beneficial effects on lipoproteins. Little is known about how long the effects persist with detraining or whether the duration of benefit is effected by training intensity or amount. Sedentary, overweight subjects (n = 240) were randomized to 6-mo control or one of three exercise groups: 1) high-amount/vigorous-intensity exercise; 2) low-amount/vigorous-intensity exercise; or 3) low-amount/moderate-intensity exercise. Training consisted of a gradual increase in amount of exercise followed by 6 mo of exercise at the prescribed level. Exercise included treadmill, elliptical trainer, and stationary bicycle. The number of minutes necessary to expend the prescribed kilocalories per week (14 kcal·kg·body wt−1·wk−1 for both low-amount groups; 23 kcal·kg·body wt−1·wk−1 for high-amount group) was calculated for each subject. Average adherence was 83–92% for the three groups; minutes per week were 207, 125, and 203 for sessions per week were 3.6, 2.9, and 3.5 for high-amount/vigorous-intensity, low-amount/vigorous intensity, and low-amount/moderate-intensity groups, respectively. Plasma was obtained at baseline, 24 h, 5 days, and 15 days after exercise cessation. Continued inactivity resulted in significant increases in low-density lipoprotein (LDL) particle number, small dense LDL, and LDL-cholesterol. A modest amount of exercise training prevented this deterioration. Moderate-intensity but not vigorous-intensity exercise resulted in a sustained reduction in very-low-density lipoprotein (VLDL)-triglycerides over 15 days of detraining (P < 0.05). The high-amount group had significant improvements in high-density lipoprotein (HDL)-cholesterol, HDL particle size, and large HDL levels that were sustained for 15 days after exercise stopped. In conclusion, physical inactivity has profound negative effects on lipoprotein metabolism. Modest exercise prevented this. Moderate-intensity but not vigorous-intensity exercise resulted in sustained VLDL-triglyceride lowering. Thirty minutes per day of vigorous exercise, like jogging, has sustained beneficial effects on HDL metabolism.

Address for reprint requests and other correspondence: C. A. Slentz, Division of Cardiology, Dept. of Medicine, P.O. Box 3022, Duke Univ. Medical Center, Durham, NC 27710 (e-mail: cris.slentz@duke.edu).

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prescriptions required for sustained health benefits. Therefore, the main purposes of the present analysis were to determine whether the training-induced benefits in serum lipids and lipoproteins are sustained over 5 and/or 15 days of exercise cessation and to determine if either exercise amount or exercise intensity impact the duration of these benefits.

METHODS

A complete description of the Studies of a Targeted Risk Reduction Intervention Through Defined Exercise (STRRIDE) study design is published elsewhere (16). The research protocol was reviewed and approved by the relevant institutional review boards at Duke University and East Carolina University.

Subjects. After providing written, informed consent, subjects who were 40 to 65 yr old, sedentary, overweight, or mildly obese (body mass index 25–35 kg/m²) and dyslipidemic (either LDL-cholesterol of 130–190 mg/dl, or HDL-cholesterol <40 mg/dl for men or <45 mg/dl for women) were randomly assigned to one of three training groups or a nonexercising control group. Subjects for this cohort were recruited continuously between January 1999 and June 2002, with exercise training completed by April 2003. Subjects with complete lipid data (n = 240) were used in the analysis.

Exercise training. The exercise groups were assigned as follows (30 : 1) high-amount/vigorous-intensity exercise, the caloric equivalent of ~20 miles of jogging per week for a 90-kg person at 65–80% peak oxygen consumption (V̇O₂); 2) low-amount/vigorous-intensity exercise, the caloric equivalent of ~12 miles of jogging per week at 65–80% peak V̇O₂; and 3) low-amount/moderate-intensity exercise, the caloric equivalent of ~12 miles of walking per week at 40–55% peak V̇O₂. For the high-amount/vigorous-intensity group, the specific prescription was to expend 23 kcal/kg body wt⁻¹·wk⁻¹. For the two low-amount groups, energy expenditure was 14 kcal/kg body wt⁻¹·wk⁻¹. For example, if a subject weighed 100 kg, and was randomly assigned to one of the low-amount groups (14 kcal/kg body wt⁻¹·wk⁻¹), then their prescribed weekly caloric expenditure was 14 kcal × 100 kg = 1,400 kcal/wk. The number of minutes of exercise needed per week then depended on their fitness level. If, for example, their peak V̇O₂ was 4 liters of oxygen per minute (4 l/min) and they were assigned to the vigorous exercise group, then their exercise work rate was set at a level that required 3 l/min of oxygen consumption (3 l/min is 75% of 4 l/min). The work rate was verified by a submaximal test. The submaximal test involved exercising at increasing work rates until a work rate that required an oxygen consumption of 3 l/min was obtained. The exercise intensity was then maintained at that level by exercising within a heart rate range that corresponded to this initial work rate. The work rate was adjusted at the end of the ramping up period via another maximal and submaximal test. The calculation of caloric expenditure was based on each liter of oxygen consumed during exercise being equivalent to 5 kcal (this was not corrected for respiratory exchange ratio). So, in the above example, an exercise prescription of 1,400 kcal/wk divided by 15 kcal expended/min of exercise at 75% would be obtained by 93 min of exercise per week [(1,400 kcal/wk)/15 kcal expended/min] = 93 min of exercise/wk.

Details about the prescribed and actual exercise training are included in Table 1. The average weekly exercise frequency for each group is given in Table 1.

Table 1. Baseline subject characteristics and characteristics of exercise training program

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (n = 55)</th>
<th>Low Amount/Moderate Intensity (n = 54)</th>
<th>Low Amount/Vigorous Intensity (n = 65)</th>
<th>High Amount/Vigorous Intensity (n = 66)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>51.9 ± 7.2</td>
<td>53.6 ± 5.4</td>
<td>52.0 ± 6.9</td>
<td>51.2 ± 6.1</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>85.9 ± 14.5</td>
<td>87.1 ± 15.4</td>
<td>86.9 ± 13.5</td>
<td>87.6 ± 13.7</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>29.7 ± 3.2</td>
<td>29.7 ± 3.0</td>
<td>29.9 ± 3.0</td>
<td>29.6 ± 2.7</td>
</tr>
<tr>
<td>Peak V̇O₂, ml·kg⁻¹·min⁻¹</td>
<td>27.4 ± 6.0</td>
<td>27.2 ± 5.9</td>
<td>29.3 ± 6.1</td>
<td>28.3 ± 5.1</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>28 (51)</td>
<td>25 (46)</td>
<td>29 (45)</td>
<td>28 (42)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>27 (49)</td>
<td>29 (54)</td>
<td>36 (55)</td>
<td>38 (58)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>White, n (%)</td>
<td>41 (75)</td>
<td>44 (82)</td>
<td>51 (78)</td>
<td>56 (85)</td>
</tr>
<tr>
<td>Black, n (%)</td>
<td>14 (25)</td>
<td>10 (18)</td>
<td>11 (17)</td>
<td>6 (9)</td>
</tr>
<tr>
<td>Other, n (%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>3 (5)</td>
<td>4 (6)</td>
</tr>
<tr>
<td>Prescribed intensity, kcal/kg body wt⁻¹·wk⁻¹</td>
<td>14</td>
<td>14</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Prescribed amount, miles/wk</td>
<td>12</td>
<td>12</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Prescribed average kcal expended/wk</td>
<td>1,220 ± 215</td>
<td>1,216 ± 188</td>
<td>2,014 ± 314</td>
<td>83.2 ± 15.3</td>
</tr>
<tr>
<td>Adherence, %</td>
<td>88.3 ± 14.1</td>
<td>90.7 ± 11.9</td>
<td>16.7 ± 3.1</td>
<td>10.5 ± 1.7</td>
</tr>
<tr>
<td>Actual kcal/wk</td>
<td>1,075 ± 254</td>
<td>1,104 ± 226</td>
<td>1,681 ± 245</td>
<td>1,055 ± 254</td>
</tr>
<tr>
<td>Actual time, min/wk</td>
<td>203 ± 39</td>
<td>125 ± 28</td>
<td>207 ± 45</td>
<td>207 ± 45</td>
</tr>
<tr>
<td>Frequency, session/wk</td>
<td>3.5 ± 0.7</td>
<td>3.9 ± 0.5</td>
<td>3.5 ± 0.8</td>
<td>3.6 ± 0.8</td>
</tr>
</tbody>
</table>

Values are means ± SD. Peak oxygen consumption (peak V̇O₂) is the highest amount of oxygen consumed per minute during a maximal graded exercise test. *Actual prescribed amount of exercise was in kcal per kg of body weight per week. This was done in order to make the exercise stimulus amount equivalent for men and women and individuals of all body weights. †Prescribed amount in miles per week is the approximate miles of walking or jogging that is calorically equivalent to 14 kcal/kg body wt⁻¹·wk⁻¹ for the low-amount groups and 23 kcal/kg body wt⁻¹·wk⁻¹ for the high-amount group. Adherence was calculated as the number of minutes of exercise performed at the appropriate exercise intensity each week divided by the number of minutes prescribed per week. Actual amount in calorically equivalent miles per week is equal to adherence times 12 miles/wk for the low-amount groups and times 20 miles/wk for the high-amount group. ‡At the beginning of the study the kcal expended per week for the 3 groups was 1,075, 1,104, and 1,681, respectively, for the low-amount/moderate-intensity, low-amount/vigorous-intensity, and high-amount group. By the end of the study, correcting for the increased fitness level (absolute V̇O₂ increases were 0.129, 0.278, and 0.392 l/min for each group, respectively) but with no change in minutes done, the average increase in kcal/wk was +65 (6%) for the low-amount/moderate-intensity group; +130 (11.7%) for the low-amount/vigorous-intensity group; and +304 (18%) for the high-amount group. The resulting kcal expended per week for each group was 1,140, 1,234, and 1,985, representing 93.4%, 101.5%, and 98.6% of the originally prescribed exercise amounts, respectively. Adherence was significantly different between the 2 vigorous-intensity groups (P < 0.01). ‡High-amount group completed a significantly greater exercise amount per week than the low-amount groups (P < 0.0001). †Low-amount/vigorous-intensity group required significantly fewer minutes per week and a significantly lower number of days of exercise per week (P < 0.0001).
group is also shown in Table 1. In Table 1 and elsewhere, we describe the amount (defined as kcal of energy expenditure per week) and intensity of exercise as being calorically equivalent to an approximate number of miles of walking or jogging. This was done to help the reader easily understand both the intensity and the amount of exercise prescribed. In fact, very few subjects jogged. Rather, they walked briskly up a moderate to steep grade to achieve the correct intensity (similar to jogging) and/or they exercised on an elliptical trainer or, less often, a stationary bicycle. The low-amount/moderate-intensity and the high-amount groups both averaged ~58 min/session for an average of 3.5 or 3.6 times each week, respectively. The low-amount/vigorous-intensity group averaged 43 min per exercise session and 2.9 sessions/wk. Importantly, neither exercise frequency nor exercise duration per session was prescribed but was, within reason, left up to the subject. Rather, the total number of minutes for each subject was prescribed. For example, if a subject was prescribed 200 min/wk, they could choose to do this in four sessions of 50 min each, or five sessions of 40 min each. However, for safety concerns, they were essentially not allowed to choose to do three sessions of 67 min each per week.

There was an initial ramp period of 2–3 mo followed by 6 mo at the appropriate exercise prescription, so that the total duration was 8–9 mo of training. All exercise sessions were verified by direct supervision or by heart rate monitors that provided recorded data (Polar Electro, Woodbury, NY).

**Crossover controls.** In the present study, to minimize the negative effect of randomization to the control group, all participants were assured that if they were in the control group that, after the control period, they would be randomized into one of the three exercise groups. This had the added benefit of increasing the statistical power when exercise detraining analyses were conducted, as in the present study. In previous studies from the STRRIDE trial, the exercise training results were not used from the control crossover subjects as this would violate the independence of groups in statistical procedures comparing the four groups. However, in the present study and for all detraining analyses, all data from subjects that completed the exercise-training period are included in the analysis (for the present report, that included 240 subjects with complete assay data), and the control data were essentially not allowed to choose to do three sessions of 67 min each per week.

Dietary evaluations and body weight control. Nutrient intakes of each subject were determined before and after training using a 3-day food record and a 24-h dietary recall interview. To minimize the confounding effects of weight loss, subjects were counseled to maintain diet and body weight. Subjects were recruited with the knowledge that this was an exercise, not a weight loss, study, and as such, if their intent was to lose weight, they should not participate. This was emphasized during the phone screening, during the initial consent meeting, and at the baseline dietary interview. Before written consent was obtained, subjects were informed that if they lost or gained 2.5% or more of their body weight, a nutrition counselor would collect and analyze their recent nutrient intake and suggest methods to maintain or increase their body weight. Body weight was monitored weekly throughout the study.

**Lipid and lipoproteins.** Fasting plasma samples were analyzed by LipoScience (Raleigh, NC) for lipoprotein profiling by nuclear magnetic resonance spectroscopy (26). Each measurement provides concentrations of six VLDL, four LDL (including intermediate-density lipoprotein [IDL]), and five HDL subclasses and calculated weighted-average VLDL, LDL, and HDL particles sizes, LDL particle concentration, and estimates of total cholesterol, triglycerides, LDL-cholesterol (LDL-C) and HDL-cholesterol (HDL-C). All samples sent for lipid and lipoprotein analysis were anonymous with respect to treatment group.

**Statistical methods.** Baseline measures are presented as means and SDs. Baseline differences between the four groups were evaluated via ANOVA with Fisher’s post hoc test used to determine significant differences between groups. Pre- to posttraining (within 24 h of the last training session) changes in lipoproteins were determined independently for each group by one-tailed t-tests. Five-day and 15-day detraining effects were also evaluated by one-tailed t-tests on the change between baseline samples and samples obtained at each of the detraining time points. One-tailed t-tests were chosen as exercise and lipid reviews suggest that an exercise training intervention would either lead to beneficial effects or no change. We are not aware of data that would suggest that an exercise intervention in sedentary overweight subjects would lead to negative effects on lipids or lipoproteins. Pre- to post control group changes were also evaluated with one-tailed t-tests, in this case with the hypothesis that continued sedentary living would likely lead to either no effects or negative effects on lipids and lipoproteins. Again, we are not aware of any data that would suggest that continued inactivity in overweight sedentary individuals would be expected to lead to improvements in lipids. P values of less than or equal to 0.05 were considered statistically significant. The main purpose of the detraining data analysis was to determine which of the statistically significant acute effects of exercise was still significantly elevated above baseline (i.e., which benefits were sustained) over 5 and/or 15 days of exercise cessation.

**RESULTS**

Baseline characteristics for each group and the characteristics of the exercise training programs are shown in Table 1. There were no differences between groups for any baseline characteristics. The high-amount group had significantly lower adherence than the low-amount/vigorous-intensity group but not significantly lower than the moderate-intensity group. Despite the lower overall adherence, the high-amount group averaged ~50% more total exercise amount than the two low-amount groups (P < 0.0001). The low-amount/vigorous-intensity group had fewer total exercise minutes per week and a lower weekly exercise frequency than the other two exercise groups (P < 0.0001), as expected.

The baseline values for lipids and lipoproteins are presented in Table 2. There were no significant group differences at baseline for any variable with the exception of VLDL size. VLDL size was significantly larger in the moderate-intensity exercise group compared with both the inactive control group and the high-amount exercise group. Outlier analysis revealed four subjects (2 in the moderate-intensity group and 2 in the high-amount group) that were greater than three SDs above the mean. When these subjects were removed from the analyses, no significant group differences remained at baseline. However, as this had essentially no effect on the overall results presented herein, we have chosen to present data from the entire data set, including these subjects.

The acute (16–24 h after the last training session) and sustained (5 and 15 days after the last training session) effects of different amounts and intensities of exercise training, as well as the effects of continued inactivity on variables of high-density lipoproteins (HDL-C, large HDL, and HDL size), are presented in Fig. 1. The data are presented as change scores of the specific time point value minus the baseline value. The high-amount exercise training group experienced significant improvements in all three HDL-related variables at 24 h postraining, and these beneficial effects were sustained for 5 and 15 days after the last training session. HDL-C levels increased 24 h postraining in both of the low-amount exercise training groups. However, only the increase in the vigorous-intensity group was significant (P < 0.03). In all exercise groups, whatever increase was observed at 24 h postraining...
appeared to be maintained throughout the detraining period. However, in the low-amount/moderate-intensity training group, HDL particle size was not changed significantly within 24 h posttraining, but at both 5 and 15 days after the last session, it was significantly increased. The mechanism or significance of this is not clear, although in this group, there may be a lag time from the end of the training period before the maximal effects of training on HDL metabolism occur. In the control group, no changes were observed.

The 24-h posttraining and sustained effects of exercise amount and intensity on VLDL particles are presented in Fig. 2. VLDL-triglyceride (VLDL-TG) concentrations were significantly reduced below baseline levels in all exercise groups at 24 h posttraining. However, the magnitude of the lowering effect was much smaller in both vigorous-intensity compared with the moderate-intensity training groups. The triglyceride levels were lowered by 37 mg/dl (22%) in the lower-intensity training group [and were reduced by 16 mg/dl (11%) and 18 mg/dl (12%) in the low- and high-amount/vigorous training groups, respectively]. Particularly interesting was that the moderate training intensity group was the only group that experienced sustained lowering in VLDL-TG levels at all detraining time points. VLDL-TG levels returned to baseline after only 5 days of detraining in both of the vigorous-intensity training groups. These results were essentially identical with those observed for serum triglycerides (data not shown). The change in large VLDL and VLDL size followed a similar pattern. The lower exercise training intensity resulted in a larger reduction in large VLDL concentration and VLDL size than in the two vigorous-intensity training groups. In these lipoprotein variables, the effects were still significantly reduced at 5 days in the lower-intensity group (with levels of significance at the margins).

In Fig. 3, the effects of different amounts and intensities of exercise training on low-density lipoproteins (LDL-C, LDL particle number, and LDL particle size) are presented. There were no significant acute effects that were maintained at 5 or 15 days after the last exercise session for any LDL-related measure. There was a significant posttraining increase in LDL size at 24 h for both of the vigorous-intensity training groups and a small but nonsignificant increase in the moderate-intensity group. However, LDL size returned to baseline values during the detraining period. In the high-amount group, there was a decrease in the LDL particle number ($P < 0.05$), but this early effect was also not maintained during the detraining period. The predominant findings in the LDL-related variables were observed in the inactive, control group, which experienced detrimental increases in LDL particle number ($P < 0.01$), small dense LDL ($P < 0.05$; data not shown), and LDL-C ($P < 0.05$), along with a decrease in LDL particle size ($P < 0.05$). Surprisingly, in the low-amount/vigorous-intensity group, there was a significant decrease in both LDL-C and LDL particle number ($P < 0.01$) after 5 days of detraining, but not 24 h after the last session and not after 15 days of detraining. The significance of this, if any, is not clear. In Table 3, all lipoprotein change scores (means and SDs) are presented.

Table 4 presents data on the percent change values for body weight, peak $V_{\text{O}2}$, visceral fat, and abdominal subcutaneous fat before and after training. Body weight increased in the inactive control group, while decreasing in a dose-response fashion in the exercise groups. Peak $V_{\text{O}2}$ decreased in the control group and increased 6.3%, 12.3%, and 17.9% in the low-amount/moderate-intensity, low-amount/vigorous-intensity, and high-amount groups, respectively. The inactive controls experienced a large and significant increase in visceral fat, whereas the two low-amount groups prevented this increase. The high-amount group had a significant decrease in visceral fat. Abdominal subcutaneous fat was unchanged in all but the high-amount group, where it decreased by 6%.

**DISCUSSION**

The beneficial effects of regular exercise on lipids and lipoproteins are well documented (20). For example, we have published data demonstrating that regular exercise results in widespread beneficial effects on the lipoprotein profile, with the majority of improvements being related to amount, not intensity, of exercise (15). However, whether the effects are only acute, lasting 1–3 days, as is a consistent finding with...
regard to insulin sensitivity, or whether the effects of regular exercise on lipids are more sustained is not well-studied. This is important information as the well-described robust but short-lived effect of exercise on insulin sensitivity has been helpful from both a practical point of view (i.e., for optimal exercise prescription, the short-lived benefit suggests that daily or near daily exercise is best) and for mechanistic purposes, (e.g., hundreds of experiments have been conducted to investigate the mechanisms responsible for the large increase in insulin sensitivity, as well as for the short-term nature of this effect). Conversely, the number of time-course studies on the sustainability of exercise-induced lipid benefits is quite limited. The purpose of the present study was to determine the effects of regular exercise on lipids at 16–24 h, 5 days, and 15 days after the last training session of exercise. Additionally, we were interested in investigating whether the early versus sustained nature of these effects was related primarily to exercise training amount and/or exercise intensity.

One of the primary findings in this study was that with respect to high-density lipoprotein (HDL-C, large HDL, and HDL size), the beneficial effects found at 24 h were largely sustained at both 5 and 15 days after exercise cessation. This sustained effect was most clearly observed in the high-amount exercise training group where all three variables were significantly improved at all time points after the cessation of exercise training (see Fig. 1). However, this effect was also evident in the two lower-exercise-amount groups, in which increases observed at 24 h were sustained at 5 and 15 days of detraining. Reviews and meta-analyses have previously concluded that regular exercise leads to significant improvements in HDL-C. The present investigation is the first randomized, controlled study to show that this benefit and the improvements

![Fig. 1. Initial and sustained posttraining effects of different amounts and intensities of exercise, as well as continued physical inactivity, on high-density lipoprotein (HDL) cholesterol, large HDL, and HDL size. Data are presented graphically as means and SE for the change between the time point and baseline values for the variables indicated in each panel. The 24-h time point refers to 24 h after the last exercise training session; the 5-day time point refers to 5 days of no exercise after training cessation; and the 15-day time point refers to the 15 days of no exercise after training cessation. *P < 0.05; **P < 0.01; ***P < 0.001.](image-url)
in HDL size and large HDL are sustained for up to 2 wk after exercise withdrawal. This benefit may be especially significant clinically, as HDL-C is thought to also have anti-inflammatory, antioxidative, antiaggregatory, anticoagulant, and profibrinolytic activities (25), in addition to its role in reverse cholesterol transport (39).

A second major finding was that the moderate-intensity training group reduced total triglycerides and VLDL-TG at 24 h after exercise training by twice the magnitude as in the two more vigorous exercise-training groups. Perhaps more importantly, only the lower intensity exercise training resulted in sustained total and VLDL-TG-lowering effects after 15 days. In the two vigorous-intensity training groups, total triglycerides and VLDL-TG had returned to baseline after only 5 days, indicating that there was no sustained triglyceride-lowering effect in these two groups. The greater and more prolonged triglyceride-lowering effect that occurred in the lower intensity exercise training group is best explained by the lower exercise intensity itself, as this group had a similar weekly exercise frequency and similar total number of minutes of exercise per week as the high-amount group and equal amount of exercise as the other low-amount exercise group. While the mechanism for this effect is unclear, exercise of different intensities may have tissue-specific effects on the endothelial cell anchored lipoprotein lipase (LPL), resulting in differential effects of exercise of varying intensities on triglyceride, VLDL, and HDL metabolism (12).

Low-intensity exercise equivalent to walking ∼11 miles/wk appears to reduce triglycerides by ∼25% in overweight/mildly obese, sedentary, middle-aged men and postmenopausal women (the percentage decrease was the same for normal and hypertriglyceridemic individuals; data not shown). Furthermore, a significant amount of the triglyceride-lowering effect was maintained for up to 15 days after the last session of exercise in the lower intensity group. This represents a highly statistically significant and a clinically
important acute and sustained decrease. Although this study is a relatively large, randomized controlled exercise training trial and the findings with regard to triglycerides and low-intensity exercise are important, these findings would be greatly strengthened if replicated by additional large, randomized controlled studies.

As a third major finding, in the present study, we observed that sustained physical inactivity resulted in statistically significant increases in LDL particle number, small dense LDL, and LDL-C and in significant decreases in LDL particle size. In the inactive control cohort, we have previously reported that 6 mo of maintenance of baseline physical inactivity resulted in statistically significant weight gain (36), increased levels of visceral fat (35), increased umbilical waist circumference (36), decreased cardiovascular fitness (4), and decreased insulin sensitivity (11). The increase in LDL particle number and the increase in small dense LDL in the inactive control group observed here are particularly significant indicators of increased cardiovascular risk. Research over the last two decades clearly demonstrates that these variables are better indicators of cardiovascular risk than are those measured in the traditional lipid profile (13, 17, 18, 37, 42). In our previous report on the effects of exercise amounts and intensities on lipoproteins in this cohort, the analysis was designed to look at differences between the exercise groups and the control group and not at changes within a specific group. Thus the observation herein is an important finding that extends the list of the detrimental effects of physical inactivity in humans.

Both the acute and sustained effects of exercise amount and intensity were markedly different with respect to their effects on HDL and VLDL-TG lipoproteins. Generally there is a significant inverse correlation between HDL and triglyceride levels. Indeed, some suggest that decreasing triglycerides play a major role in increasing HDL-C levels(40). However, the lower intensity exercise training was found to have substantial triglyceride-lowering effects that were both acute and sus-
Table 3. Lipid and lipoproteins change scores 24 h, 5 days, and 15 days after the last training session

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 55)</th>
<th>Low Amount/Moderate Intensity</th>
<th>Low Amount/Vigorous Intensity</th>
<th>High Amount/Vigorous Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>24 h (n = 54)</td>
<td>5 day (n = 51)</td>
<td>15 day (n = 52)</td>
<td>24 h (n = 65)</td>
</tr>
<tr>
<td>Cholesterol, mg/dl</td>
<td>5.0 (23)</td>
<td>−1.3 (22)</td>
<td>−3.8 (23)</td>
<td>−4.2 (23)</td>
</tr>
<tr>
<td>LDL-C, mg/dl</td>
<td>4.7 (19)</td>
<td>0.3 (19)</td>
<td>−3.3 (21)</td>
<td>1.7 (25)</td>
</tr>
<tr>
<td>LDL particles, nmol/l</td>
<td>96.9 (289)</td>
<td>1.4 (233)</td>
<td>−2.8 (21)</td>
<td>2.1 (29)</td>
</tr>
<tr>
<td>Small dense LDL, mg/dl</td>
<td>7.7 (33)</td>
<td>1.4 (23)</td>
<td>−2.8 (21)</td>
<td>2.1 (29)</td>
</tr>
<tr>
<td>LDL size, nm</td>
<td>−0.12 (0.47)</td>
<td>0.06 (0.45)</td>
<td>0.03 (0.48)</td>
<td>0.04 (0.47)</td>
</tr>
<tr>
<td>HDL-C, mg/dl</td>
<td>0.0 (6.1)</td>
<td>−0.6 (5.5)</td>
<td>0.7 (5.3)</td>
<td>1.1 (6.2)</td>
</tr>
<tr>
<td>Large HDL-C, mg/dl</td>
<td>0.4 (7.1)</td>
<td>−0.3 (7.4)</td>
<td>1.1 (5.9)</td>
<td>2.1 (9.7)</td>
</tr>
<tr>
<td>LDL size, nm</td>
<td>−0.01 (0.26)</td>
<td>0.04 (0.20)</td>
<td>0.08 (0.22)</td>
<td>0.09 (0.27)</td>
</tr>
<tr>
<td>Triglycerides, mg/dl</td>
<td>6.7 (48)</td>
<td>−36.5 (75)</td>
<td>−21.5 (66)</td>
<td>−16.2 (59)</td>
</tr>
<tr>
<td>VLDL-triglycerides, mg/dl</td>
<td>6.8 (46)</td>
<td>−33.6 (66)</td>
<td>−18.8 (62)</td>
<td>−16.2 (51)</td>
</tr>
<tr>
<td>Large VLDL, mg/dl</td>
<td>0.1 (34)</td>
<td>−30.6 (70)</td>
<td>−13.7 (50)</td>
<td>−10.2 (49)</td>
</tr>
<tr>
<td>VLDL size, nm</td>
<td>0.66 (8.6)</td>
<td>−5.2 (10.9)</td>
<td>−2.4 (9.2)</td>
<td>−2.0 (12.5)</td>
</tr>
<tr>
<td>IDL-C, mg/dl</td>
<td>−0.2 (3.7)</td>
<td>−1.1 (4.5)</td>
<td>−0.7 (5.3)</td>
<td>0.0 (4.7)</td>
</tr>
</tbody>
</table>

Values are means (SD).

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of vigorous-intensity exercisers, thereby resulting in a “rebound” in serum VLDL and triglycerides in these groups.

The fact that only high-volume, vigorous-intensity exercise resulted in acute and sustained improvements in HDL cholesterol suggests that the major modulator of HDL metabolism in response to exercise training is likely body habitus variations, such as visceral and subcutaneous fat stores and skeletal muscle mitochondrial capacity, which takes longer to regress posttraining. Conversely, changes in LDL size appear to regress fairly rapidly with cessation of exercise training in all groups. This parallels the relatively rapid reversal of insulin action in all groups. It is likely that these two metabolic parameters are functionally related although the mechanisms whereby these are linked can only be speculative at this point.

Because of the difficulty of conducting exercise detraining studies (individuals who exercise regularly are quite reluctant to stop exercising), relatively few studies have investigated the effects of exercise cessation on maintenance of changes in lipids and lipoproteins following the intentional cessation of exercise training. A literature review revealed 11 studies (7–10, 19, 21, 24, 32, 38, 41, 43) on the effects of exercise detraining or cessation on lipids. Of these 11 studies, 8 studies involved groups of 12 or fewer detraining subjects, and only 2 of the 11 studies were randomized controlled studies, with 1 of these 2 studies reporting on only five detraining subjects. Only three of these studies investigated detraining times that were between 3 and 14 days (9, 10, 21); the others investigated detraining times of 1 mo to 1 yr. These three studies reported conflicting results with regard to lipoprotein changes, perhaps due to the confounding effects as noted above. In a recent extensive review of the topic, Leon and Sanchez (20) concluded that the effects of exercise on lipids are markedly inconsistent. Partially as a result of this inconsistency, in their recommendations for future research, they emphasized the need for large, randomized, controlled studies on this topic and identified a specific need for exercise detraining studies that the present study at least partially fulfills.

There are numerous strengths and limitations to the present study. STRRIDE was a multicenter, randomized controlled study investigating different amounts and intensities of exercise training over a relatively long term of 8–9 mo with multiple detraining time points, allowing for the assessments regarding the acute and sustained effects of the different training regimens. Also, for a study of its type, i.e., with a large number of carefully measured physiological variables in each subject, this is a relatively large study, providing power to measure significant effects between group and outcome. Furthermore, the exercise stimulus was well documented as both the exercise intensity and the number of minutes assigned each week were verified by direct observation and/or recording heart rate monitors.

The results should be viewed also with some cautionary notes. First, this is the first report of its kind, and the findings will be greatly strengthened when they are replicated in other large randomized, controlled studies. Second, the time frame of this study extends only to 2 wk beyond the last training session; generalizations beyond this point, which might be of great interest, will require additional study. Third, the subjects in this study were overweight or mildly obese with mild to moderate dyslipidemia and were middle-aged men and postmenopausal women. Normal weight individuals or individuals with normal lipoproteins would likely respond differently to the exercise intervention, the inactive control period, and the extended detraining period.

In conclusion, the importance of studying the duration of exercise effects on lipoproteins is exemplified by the understanding gained from studying the robust but short-lived effect of exercise on insulin sensitivity, as the knowledge gained has improved exercise prescription (the short-lived benefit suggests daily or near daily exercise is optimal) and our understanding of mechanisms related to this effect. However, the number of time-course studies on the sustainability of exercise-induced lipid benefits is quite limited. The data presented herein show that many of the acute benefits of exercise training on lipoproteins are sustained for up to 2 wk after the cessation of the exercise-training stimulus. Additionally, the findings from this study suggest that there may well be a benefit to individualizing the exercise prescription for wellness around the particular lipoprotein abnormality in order to maximize the desired effects. Specifically, with high-amount training, the significant acute improvements in HDL-C, HDL particle size, and large HDL were sustained at significant levels above baseline for up to 2 wk of detraining. On the other hand, if the lipid abnormality involves hypertriglyceridemia, low-intensity exercise may be the best recommendation, as only the lower, more moderate exercise training intensity resulted in sustained VLDL- and total triglyceride-lowering effects. Finally, as we have reported previously, physical inactivity has numerous, statistically significant, detrimental metabolic consequences. In addition to increased body weight, waist circumference, visceral fat, insulin resistance, and reduced cardiovascular fitness, the observations from the present study are that LDL particle
number was significantly increased with significant worsening in small dense LDL, LDL-C, and LDL size over 6 mo of continued sedentary lifestyle in overweight and mildly obese individuals. Notably, all exercise regimens prevented the deterioration in the LDL profile observed in the inactive group, and this beneficial effect was maintained even through 15 days of exercise detraining.

GRANTS
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REFERENCES


