Published in final edited form as:

Metabolism. 1994 July ; 43(7): 917–924.

The Effects of Weight Loss by Exercise or by Dieting on Plasma High-Density Lipoprotein (HDL) Levels in Men With Low, Intermediate, and Normal-to-High HDL at Baseline

Paul T. Williams, Marcia L. Stefanick, Karen M. Vranizan, and Peter D. Wood

Stanford Center for Research in Disease Prevention Stanford University School of Medicine
Stanford

Life Sciences Division Lawrence Berkeley Laboratory Berkeley

Abstract

To assess whether baseline plasma high-density lipoprotein (HDL) cholesterol levels affected the HDL response to weight loss, we examined lipoprotein changes in overweight men aged 30 to 59 years who were randomized to lose weight by exercise training (primarily running, N = 46) or by caloric restriction (ie, dieting, N = 42) or to remain sedentary, nondieting controls (N = 42) in a 1-year study. In exercisers, absolute increases in HDL (mg/dL) were greatest in men with normal-to-high baseline HDL and least in men with low baseline HDL. Specifically, when divided into groups of low (≤ 37 mg/dL), intermediate (38 to 47 mg/dL), and normal-to-high HDL cholesterol (≥ 48 mg/dL) at baseline, the exercisers increased HDL cholesterol by 2.3 ± 1.9 , 4.9 ± 1.1 , and 7.0 ± 1.3 mg/dL, respectively; HDL₂ cholesterol by 0.8 ± 1.6 , 2.3 ± 1.2 , and 5.1 ± 1.3 mg/dL; and HDL₂ mass by 2.8 ± 5.1 , 9.5 ± 8.9 , and 31.7 ± 11.0 mg/dL. Relative increases in HDL cholesterol were more similar in the low ($7.1\% \pm 6.1\%$), intermediate ($12.4\% \pm 3.9\%$), and normal-to-high men ($13.2\% \pm 4.0\%$). Regression analyses were performed to assess whether baseline HDL cholesterol was related to the amount of absolute HDL change per unit of weight loss. In exercisers, the increase in HDL₃ cholesterol concentrations was significantly greater in men with low HDL than in those with normal-to-high HDL at entry (2.0 ± 0.8 v 0.2 ± 0.8 mg/dL per kg/m² lost). In contrast, the increase in HDL₂ cholesterol was nearly four times greater in men with normal-to-high HDL than in those with low HDL at entry (3.7 ± 0.7 vs. 1.0 ± 0.7 mg/dL per kg/m² lost). In dieters, weight loss significantly increased HDL cholesterol, HDL₂ cholesterol, and HDL₂-mass after 1 year, but the absolute increases were unrelated to baseline HDL cholesterol level. Thus, exercise-induced weight loss, but not diet-induced weight loss, affects HDL cholesterol concentrations in men differently depending upon their entry level.

Low plasma concentrations of high-density lipoprotein (HDL) cholesterol are associated with increased risk of coronary heart disease (CHD) in men [1,2]. HDL cholesterol includes two major subfractions, HDL₂ and HDL₃. The HDL₂ subfraction has a higher cholesterol content and is of lesser density than HDL₃. Elevated concentrations of either subfraction may provide protection from CHD [2]. The National Cholesterol Education Program has identified low HDL cholesterol (≤ 35 mg/dL) as an important CHD risk factor [3]. Hygienic measures have been suggested for increasing HDL levels, yet it remains to be determined whether such measures will be effective in the very population that most needs the increase.

We have previously shown that weight loss through exercise or through dieting produces favorable changes in HDL cholesterol and HDL₂ concentrations [4,5]. Metabolic, behavioral, or genetic factors that produce low baseline HDL cholesterol could affect the HDL response to weight loss. This report extends our original findings by considering the influence of baseline HDL cholesterol levels on the HDL response to weight loss in 130 men who participated in a 1-year controlled trial of weight loss by increased exercise alone or by caloric restriction (dieting) alone without change in diet composition [4,5]. Our objective is to assess whether weight loss by exercise or by dieting is as effective at increasing HDL in men with low HDL as in men with higher HDL cholesterol. Characterizing men by initial HDL status may also reveal differences in the effects of weight loss by exercise or by dieting.

SUBJECTS AND METHODS

Subjects and Experimental Design

Data were obtained from a randomized, controlled clinical trial of exercise and weight loss in sedentary middle-aged men who were nonsmokers, not taking medication that might affect lipid metabolism or blood pressure, normotensive, and normolipidemic [4]. The men were aged 30 to 59 years and were 20% to 60% over Metropolitan ideal weight. They were assigned at random to one of the following three experimental conditions: control (no change in diet or exercise); exercise (supervised physical activity, primarily brisk walking and running, with no change in diet); and calorie restriction (ie, dieting without increased exercise). The exercisers were asked to begin calisthenics and to walk, jog, or run for 25 minutes three times per week at 60% to 80% of maximal heart rate. We recommended that the periods of continuous jogging be increased to 40 to 50 minutes 4 days or more per week. The dieters were given individual prescriptions designed to reduce total body fat by one third over a 9-month period, assuming that a 7,762-kcal reduction in energy intake would produce a 1-kg fat loss [4]. The dieters met regularly with a nutritionist, either individually or as a group, for instructions on dieting and reinforcement of behavioral strategies. The training staff was unaware of the participants' HDL levels. The participants were therefore prescribed the same dietary intervention and training assistance, without regard to their initial HDL levels. Making changes in dietary composition was discouraged in all groups. During a final 6-week stabilization period, the dieters adjusted food intake and the exercisers adjusted exercise level to keep weight stable [4].

Laboratory Procedures

At baseline and 1 year, the men reported to our clinic in the morning after having abstained for 12 to 16 hours from all food and any vigorous activity. Weight and height were determined in light clothing without shoes on a standard beam balance. Two separate measurements of HDL cholesterol levels were obtained from plasma drawn at the baseline visit. The first HDL cholesterol level was determined in our laboratory by dextran sulfate-magnesium precipitation followed by enzymatic determination of cholesterol [6,8]. This measurement was consistently in a state of control, as monitored by the Lipid Standardization Program of the Centers for Disease Control and the National Heart, Lung, and Blood Institutes. Plasma HDL cholesterol, HDL₂ cholesterol, and HDL₃ cholesterol concentrations were also determined at the University of Washington by enzymatic methods following precipitation by dextran sulfate-magnesium [6,7]. Reference samples were used to ensure that HDL₂ cholesterol measurements had a coefficient of variation less than 7.7% and that HDL₃ cholesterol measurements had a coefficient of variation less than 4.4%. Plasma HDL₂ and HDL₃ total mass concentrations were determined by analytic ultracentrifugation [9]. The reproducibility of lipoprotein mass concentrations as determined by measurements within individuals at different visits shows that repeated measurements of HDL₂ mass and HDL₃ mass are correlated at $r = 0.78$ and $r = 0.75$, respectively [10]. Dietary nutrient intakes were estimated by computer analysis of food records maintained by the participants over a 7-day diet period [11]. Body mass index was calculated

as a person's weight (kg) divided by the square of their height (m). Self-reported physical activity level was estimated from a 7-day physical activity questionnaire [12]. Additionally, the runners recorded exercise durations and frequencies in diaries. The entries were verified by the training staff.

Statistical Analyses

We used regression analyses to test whether baseline HDL cholesterol levels are related to the HDL response to weight loss by exercise or by dieting. A regression line was drawn for the 1-year change in HDL (the dependent variable, plotted along the y-axis) versus baseline HDL (the independent variable, plotted along the x-axis) in exercisers, dieters, and controls separately. The difference between the exercisers' and controls' or between the dieters' and controls' regression lines represents the effect of the intervention for a given baseline value of HDL cholesterol. If the two regression lines are parallel, then the effect of the intervention on HDL is constant for all baseline concentrations. If the slopes of the regression lines are significantly different from each other, then the intervention effect depends on baseline HDL cholesterol concentrations. Separate baseline HDL cholesterol measurements were used for the independent variable (Stanford measurement) and for calculating the change in HDL cholesterol between baseline and 1 year (University of Washington measurement), thereby minimizing the effect of regression to the mean (see Discussion). We also used t tests to test for differences in changes between exercisers, dieters, and controls when the data were stratified by their entry plasma HDL cholesterol concentration. Again, to minimize the effects of regression to the mean, we used separate HDL cholesterol measurements for stratifying the sample and for computing the HDL change from baseline to 1 year. The cut-points were chosen before analysis. The low group in this sample of overweight men was defined by the lowest HDL quartile, between 24 and 37 mg/dL, the intermediate group was defined by the interquartile range of HDL, between 38 and 47 mg/dL, and the normal-to-high HDL group was defined by the highest HDL quartile, between 48 and 78 mg/dL. We chose the upper and lower quartiles because they provide a wide separation between the high and low group while maintaining adequate sample size for parameter estimation. Regression analyses were used to test whether entry HDL cholesterol levels affected the HDL response to weight loss. All significance levels are two-tailed.

RESULTS

Table 1 displays baseline characteristics for men with low, intermediate, and normal-to-high HDL cholesterol. At baseline, entry HDL cholesterol correlated negatively with plasma triglyceride concentrations and carbohydrate intake and positively with alcohol intake. Tables 2 and 3 show that the intakes of alcohol, carbohydrate, and fat showed little mean change during the trial and were unrelated to baseline HDL cholesterol, except for fat intake in controls. Distances subsequently run during the trial correlated significantly and positively with baseline HDL cholesterol ($r = 0.34$, $P = 0.02$), even when adjusted for baseline body mass index ($r = 0.32$, $P = 0.03$).

Figure 1 displays the changes in HDL in exercisers and sedentary controls by their baseline HDL cholesterol levels. The difference between the regression lines for the exercisers and controls becomes larger as the baseline HDL cholesterol is increased. The positive difference between the regression line slopes of the exercisers (β_E) and controls (β_C) is significant ($\beta_E - \beta_C = 0.26 \pm 0.10$, $P = 0.02$), suggesting that the increase in HDL cholesterol is significantly greater for exercisers with initially higher HDL cholesterol. Baseline HDL cholesterol is also related to the increase in the exercisers' HDL₂ cholesterol ($\beta_E - \beta_C = 0.27 \pm 0.07$, $P = 0.0005$) and HDL₂ mass ($\beta_E - \beta_C = 1.4 \pm 0.5$, $P = 0.006$). The results remain significant when adjusted for any changes in nutrient intake. Baseline HDL cholesterol was not significantly related to

changes in the exercisers' HDL₃ cholesterol ($\beta_E - \beta_C = -0.01 \pm 0.08$, $P = 0.88$) and HDL₃ mass ($\beta_E - \beta_C = 0.11 \pm 0.67$, $P = 0.88$; results not displayed).

Table 4 describes these changes in HDL in exercisers and controls when the men are divided into groups defined by low, intermediate, and normal-to-high entry HDL cholesterol concentrations. In each case, the difference between exercisers and controls (column 4) represents the treatment effect. Exercise-induced weight loss significantly increased total HDL cholesterol and the percent increase in HDL cholesterol in the intermediate and normal-to-high men. Plasma HDL₂ cholesterol and HDL₂ mass concentrations increased significantly in the normal-to-high exercisers only. The exercisers' increases in HDL₂ cholesterol and HDL₂ mass were significantly greater in the normal-to-high HDL men than in the low HDL men.

Weight Loss Versus HDL Change in Exercisers

Regression analyses were used to examine whether entry HDL cholesterol levels affected the amount of HDL change per unit of weight loss in the exercisers. Separate regression lines were fitted to the low, intermediate, and normal-to-high exercisers for changes in HDL (dependent variable, plotted along the y-axis) versus change in body mass index (independent variable, plotted along the x-axis). Negative regression slopes signify that a decrease in body mass index was associated with an increase in HDL.

Figure 2 displays the regression lines for changes in HDL versus changes in body mass index for low and normal-to-high HDL men. Significance levels in the figure are for the difference between slopes. Significance levels in the text below are for the individual regression slopes. Per unit of weight loss (kg/m^2), the increase in HDL cholesterol was the same in the low and normal-to-high HDL men. The regression slopes were as follows: low $\beta = -3.0 \pm 0.8 \text{ mg/dL per } \Delta\text{kg/m}^2$ ($P < 0.001$), intermediate $\beta = -2.4 \pm 0.7 \text{ mg/dL per } \Delta\text{kg/m}^2$ ($P < 0.001$), and normal-to-high $\beta = -3.9 \pm 0.8 \text{ mg/dL per } \Delta\text{kg/m}^2$ ($P < 0.001$).

Although there were no differences in the change in HDL cholesterol per kilogram of weight loss in the intermediate-to-high versus low HDL men, there were significant differences for changes in HDL subfractions. The increase in HDL₃ cholesterol was significantly greater in the low HDL men ($\beta = -2.0 \pm 0.8 \text{ mg/dL per } \Delta\text{kg/m}^2$, $P = 0.02$) than in the normal-to-high HDL men ($\beta = -0.2 \pm 0.8 \text{ mg/dL per } \Delta\text{kg/m}^2$, $P = .78$). In contrast, the increase in HDL₂ cholesterol was nearly four times greater in the normal-to-high HDL men ($\beta = -3.7 \pm 0.7 \text{ mg/dL per } \Delta\text{kg/m}^2$, $P = 0.0001$) as in the low HDL men ($\beta = -1.0 \pm 0.7 \text{ mg/dL per } \Delta\text{kg/m}^2$, $P = 0.15$). The increase in HDL₂ mass per kilogram lost was more than four times greater in the normal-to-high HDL men ($\beta = -19.6 \pm 4.1 \text{ mg/dL per } \Delta\text{kg/m}^2$, $P = 0.001$) than in the low HDL men ($\beta = -4.5 \pm 4.2 \text{ mg/dL per } \Delta\text{kg/m}^2$, $P = 0.29$). Men with intermediate HDL had regression slopes that fell between the high and low HDL men for HDL₃ cholesterol ($\beta = -0.7 \pm 0.7 \text{ mg/dL per } \Delta\text{kg/m}^2$, $P = 0.28$), HDL₂ cholesterol ($\beta = -1.7 \pm 0.6 \text{ mg/dL per } \Delta\text{kg/m}^2$, $P = 0.004$), and HDL₂ mass ($\beta = -9.7 \pm 3.4 \text{ mg/dL per } \Delta\text{kg/m}^2$, $P = 0.007$). There were no significant associations between changes in body mass index and plasma HDL₃ mass concentrations in men with low, intermediate, or normal-to-high HDL at entry.

Weight Loss by Dieting

Figure 3 displays the 1-year change in HDL cholesterol in dieters by baseline HDL cholesterol. Dieters and controls are represented by the two parallel lines; there is no difference in the regression slopes of the dieters (β_D) and controls ($\beta_D - \beta_C = 0.03 \pm 0.12$, $P = 0.84$). Thus, changes in the dieters' HDL cholesterol appear to be independent of entry HDL cholesterol levels. There were also no significant differences between the dieters' and controls' regression slopes for HDL₂ cholesterol, HDL₃ cholesterol, HDL₂ mass, HDL₃ mass, or % Δ HDL cholesterol (analyses not displayed). Although changes in HDL cholesterol, HDL₂ cholesterol,

and HDL₂ mass were all significantly associated with changes in weight [4], the increase was not significantly different in men with low, intermediate, or normal-to-high entry HDL cholesterol (analyses not displayed).

DISCUSSION

This report has assessed the differential effects on HDL concentrations of weight loss by exercise (primarily running) and by dieting, according to initial HDL cholesterol levels in 130 men who participated in a 1-year randomized clinical trial [4]. In exercisers, regression analyses suggest that the exercise-induced increases in absolute levels (mg/dL) of HDL cholesterol, HDL₂ cholesterol, and HDL₂ mass were greatest in the men with the highest entry HDL cholesterol (Fig 1). These results were further supported when the exercisers were then stratified into three groups by their plasma HDL cholesterol concentrations at entry, ie, a low group consisting of the lowest HDL quartile, an intermediate group consisting of the interquartile range, and a normal-to-high group consisting of the highest HDL quartile. Increases in HDL₂ cholesterol and HDL₂ mass in the exercise group were significantly greater in the initially normal-to-high HDL men than in the low HDL men (Table 4).

We also examined the relationship between HDL change and weight loss within each stratum. Figure 2 shows that in exercisers, per kilogram/meter² of weight loss, the increase in HDL cholesterol was similar in the normal-to-high and low HDL men. However, the increase involved HDL₃ in the low group and HDL₂ in the normal-to-high group. As compared with low HDL men, increases in HDL₂ cholesterol and HDL₂ mass were four-fold greater in the normal-to-high HDL men per kilogram of weight loss.

In contrast to exercisers, the increases in the dieters' HDL cholesterol, HDL₂ cholesterol, and HDL₂ mass concentrations were unrelated to their entry HDL cholesterol (Fig 3). When HDL response to weight loss was examined by regression analyses, the changes in HDL cholesterol, HDL₂ cholesterol, and HDL₂ mass per kilogram/meter² of weight loss were the same regardless of entry HDL cholesterol. Baseline HDL cholesterol did not predict compliance to a reduced-calorie diet.

Regression to the mean occurs when measurement error induces a negative correlation between a baseline measurement and the difference between the baseline and follow-up measurement. We have attempted to minimize the effects of regression to the mean by using different baseline HDL cholesterol measurements for the independent (predictor) variable and for the calculation of HDL change (the dependent variable). Baseline HDL cholesterol measurements were assayed at different laboratories from plasma samples collected at the same baseline visit. Although an inverse correlation between the dependent and predictor variables is unlikely to emanate from laboratory measurement error, one could arise from measurement error from biological variation (ie, variation between clinic visits). Figure 1, however, shows that the controls' regression slope is essentially flat for the change in HDL cholesterol versus baseline HDL.

Etiology

The etiology of the low HDL in these men is in fact not known. Consistent with other reports [13–15], we found that low baseline levels of HDL cholesterol were related to higher plasma triglycerides and greater carbohydrate consumption when compared with those in overweight men with normal-to-high baseline levels. Adjustment for these baseline factors did not eliminate the influence of initial HDL cholesterol concentrations on the HDL response to exercise. HDL cholesterol levels may be in part genetically determined [16,17]. Hasstedt et al [18] report that a dominant major gene may cause low HDL cholesterol in some individuals. Perova et al [19] report that incubation with cholesterol-loaded fibroblasts produced increases

in HDL_{2b} in normolipidemic sera, but not in hypoalphacholesterolemic sera. When incubated with hepatoma cell, HDL₂ decreased in normolipidemic sera and increased in hypoalphacholesterolemic sera. These differences may reflect defective HDL_{2b} in low HDL men [19]. Genetic deficiencies in factors that regulate HDL (eg, hepatic or lipoprotein lipase activity, lecithin cholesterol acyltransferase, cholesteryl-ester transfer activity) or structural defects in the HDL particles themselves might limit the HDL response to exercise-induced weight loss in men with low HDL. However, to be consistent with our data, these deficiencies must somehow affect the HDL response to weight loss by exercise (Fig 1) without affecting the HDL response to diet-induced weight loss (Fig 3).

The low HDL exercisers in this trial also ran less total distances and lost somewhat less weight than the high HDL men, and this may account in part for their smaller increases in HDL. This is the second study from our group to show that baseline HDL cholesterol levels in sedentary men predicted weekly distance run during exercise training [20]. Higher HDL cholesterol levels at baseline may be a marker for men genetically endowed with muscle fiber types that make running easier and thereby facilitate weight loss [21]. Specifically, the association between the initial HDL cholesterol levels at baseline and the distance run during the study may be due to (1) a greater ease of adopting long-distance running in men with a higher proportion of slow-twitch red muscle fibers [22,23]; (2) a higher concentration of lipoprotein lipase activity in slow-twitch red muscle fibers [24]; (3) a positive correlation between baseline HDL cholesterol concentrations and baseline postheparin lipoprotein lipase activity (which includes both adipose and muscle tissue lipase activity) [25,26]. Thus, baseline HDL cholesterol may predict compliance to weight loss by exercise. The increases in HDL cholesterol during the trial may be due to increased adipose tissue lipoprotein lipase activity [27], decreased hepatic lipase activity [28], decreased plasma free fatty acid levels [29,30], or decreased cholesteryl ester triglyceride exchange [31]. To our knowledge, muscle fiber composition is unlikely to affect the ease of restricting caloric intake and therefore should respond to diet-induced weight loss.

Summary

Our results suggest that exercise-induced weight loss but not diet-induced weight loss affects HDL cholesterol concentrations in men differently depending on their entry level. Although all participants received the same intervention without regard to their initial HDL, the adherence to the prescribed training regimen in the exercise group appeared to be affected by the exercisers' baseline HDL cholesterol levels. The hygienic treatment of low HDL by diet-induced weight loss provides an alternative for men who may not be able to increase HDL cholesterol through exercise alone.

Acknowledgments

We wish to thank Dr Richard Terry, Barbara Frey-Hewitt, Nancy Ellsworth, and Dr Darlene Dreon for their help in completing the study. Analytic ultracentrifugation was performed under the direction of Dr Frank Lindgren (Lawrence Berkeley Laboratory), and precipitation of HDL cholesterol subfractions was performed under the direction of Dr John Albers (University of Washington).

Supported in part by Grants No. HL-24462, HL-02183, and HL-49828 from the National Heart, Lung, and Blood Institute of the National Institutes of Health, and conducted at Stanford University and Lawrence Berkeley Laboratory (Department of Energy DE-ACO3-76SF00098 to the University of California).

REFERENCES

1. Miller GJ, Miller NE. Plasma high density lipoprotein concentrations and the development of ischaemic heart disease. *Lancet* 1975;1:16–19. [PubMed: 46338]

2. Stampfer MJ, Sacks FM, Salvini S, et al. A prospective study of cholesterol, apolipoproteins and risk of myocardial infarction. *N Engl J Med* 1991;315:373–381. [PubMed: 2062328]
3. National Cholesterol Education Program. Report of the Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults. Washington DC: US Department of Health and Human Services. Public Health Services, National Institutes of Health. US Government Printing Office 234-6211/00222; p. 78
4. Wood PD, Stefanick ML, Dreon D, et al. Changes in plasma lipid and lipoproteins in overweight men during weight loss through dieting as compared with exercise. *N Engl J Med* 1988;319:1173–1179. [PubMed: 3173455]
5. Williams PT, Krauss RM, Vranizan KM, et al. Changes in lipoprotein subfractions during diet-induced and exercise-induced weight loss in moderately overweight men. *Circulation* 1990;81:1293–1314. [PubMed: 2317911]
6. Altain CC, Peons LS, Chan CS, et al. Enzymatic determination of total serum cholesterol. *Clin Chem* 1974;20:470–475. [PubMed: 4818200]
7. Warnick GR, Benderson J, Albers JJ. Dextran sulfate-Mg₂ precipitation procedure for quantitation of high-density-lipoprotein cholesterol. *Clin Chem* 1982;28:3379–3388.
8. Warnick GR, Benderson J, Albers JJ. Quantitation of high-density-lipoprotein subclasses after separation by dextran sulfate and Mg²⁺ precipitation. *Clin Chem* 1982;28:1574. abstr.
9. Lindgren, FT.; Jensen, LC.; Hatch, FT. The isolation and quantitative analysis of lipoproteins. In: Nelson, GJ., editor. *Blood Lipids and Lipoproteins: Quantitation, Composition and Metabolism*. Wiley-Interscience; New York. NY: 1972. p. 181-774.
10. Williams PT, Krauss RM, Vranizan KM, et al. Effects of exercise-induced weight loss on low-density lipoprotein subfractions in healthy men. *Arteriosclerosis* 1989;9:623–632. [PubMed: 2783076]
11. Nutrition Coordinating Center. Reference Food Table. University of Minnesota; Minneapolis, MN: 1986.
12. Blair SN, Haskell WI, Ho P, et al. Assessment of habitual physical activity by seven-day recall in a community survey and controlled experiments. *Am J Epidemiol* 1985;122:794–804. [PubMed: 3876763]
13. Miller NE, Bolton CH, Hayes TM, et al. Associations of alcohol consumption with plasma high density lipoprotein cholesterol and its subfractions: The Caerphilly and Speedwell Collaborative Heart Disease Studies. *J Epidemiol Community Health* 1988;42:220–225. [PubMed: 3251002]
14. Haskell WL, Camargo C, Williams PT, et al. The effect of cessation and resumption of moderate alcohol intake on serum high density lipoprotein subfractions. *N Engl J Med* 1984;310:805–810. [PubMed: 6366553]
15. Williams PT, Krauss RM, Wood PD, et al. Associations of diet and alcohol intake with high-density lipoprotein subclasses. *Metabolism* 1985;34:524–530. [PubMed: 3999973]
16. McGue M, Rao DC, Iselus I, et al. Resolution of genetic and cultural inheritance in twin families by path analysis: Application to HDL-cholesterol. *Am J Hum Genet* 1985;37:999–1014.
17. Williams PT, Vranizan KM, Austin MA, et al. Familial correlations of high-density lipoprotein subclasses based on gradient gel electrophoresis. *Arteriosclerosis* 1992;12:1467–1474.
18. Hasstedt SJ, Ash KO, Williams RR. A reexamination of major locus hypotheses for high density lipoprotein cholesterol levels using 2170 persons screened in 55 Utah pedigrees. *Am J Med Genet* 1986;24:57–67. [PubMed: 3706413]
19. Perova NV, Shakhov Yu A, Serdjuk AP, et al. Interconversions of HDL subfractions in normolipidemic and hypoalphacholesterolemic sera incubated with fibroblasts and hepatoma cell lines Hep-G2. *Biochem Int* 1988;17:1029–1038. [PubMed: 2854464]
20. Williams PT, Wood PD, Haskell WL, et al. The effects of running mileage and duration on plasma lipoprotein levels. *JAMA* 1982;247:2614–2619.
21. Williams PT. High density lipoproteins and lipase activity in runners. *Atherosclerosis* 1993;98:251–252. [PubMed: 8457264]
22. Costill DL, Fink WJ, Pollock M. Muscle fiber composition and enzyme activities of elite distance runners. *Med Sci Sports* 1976;8:96–100. [PubMed: 957938]
23. Tikkanen HO, Harkonen M, Naveri H, et al. Relationship of skeletal muscle fiber type to serum high density lipoprotein cholesterol and apolipoprotein A-I levels. *Atherosclerosis* 1991;90:47–51.

24. Gollnick PD, Armstrong RB, Saubert CW, et al. Enzyme activity and fiber composition in skeletal muscles of trained and untrained men. *J Appl Physiol* 1972;33:312–319. [PubMed: 4403464]
25. Borensztajn, J. Heart and skeletal muscle lipoprotein lipase. *Lipoprotein Lipase*. Borensztajn, J., editor. Evener; Chicago, IL: 1987. p. 133-147.
26. Eckel, RH. Adipose tissue lipoprotein lipase. In: Borensztajn, J., editor. *Lipoprotein Lipase*. Evener; Chicago, IL: 1987. p. 133-147.
27. Nikkila EA, Taskinen MR, Rehunen S, et al. Lipoprotein lipase activity in adipose tissue and skeletal muscle of runners: Relation to serum lipoproteins. *Metabolism* 1978;27:1661–1671. [PubMed: 212665]
28. Stefanick, ML.; Terry, RB.; Haskell, WL., et al. Relationships of changes in post-heparin hepatic and lipoprotein lipase activity to HDL-cholesterol changes following weight loss achieved by dieting versus exercise. In: Gallo, L., editor. *Cardiovascular Disease: Molecular and Cellular Mechanisms, Prevention, and Treatment*. Plenum; New York, NY: 1987. p. 61-68.
29. Vihko V, Sarviharju J, Souminen H. Effects of endurance training on concentrations of individual plasma free fatty acids in young men at rest and after moderate bicycle ergometer exercise. *Ann Med Exp Biol Fenn* 1973;51:112–117. [PubMed: 4774080]
30. Bray, GA. Metabolic effects of corpulence. In: Howard, IA., editor. *Recent Advances in Obesity Research*. Newman; London, UK: 1975. p. 56-65.
31. Tall AR. Plasma lipid transfer proteins. *J Lipid Res* 1988;27:361–367. [PubMed: 3522782]

Fig 1.

Relationship between baseline HDL cholesterol levels and 1-year change in (A) HDL cholesterol, (B) HDL₂ cholesterol, and (C) HDL₂ mass in exercisers (squares) and controls (diamonds). Significance levels are given for the difference in the regression slopes. Independent HDL cholesterol measurements are used for baseline HDL and Δ HDL. Baseline HDL cholesterol was not significantly related to changes in the exercisers' HDL₃ cholesterol ($\beta_E - \beta_C = -0.01 \pm 0.08$, $P = 0.88$) and HDL₃ mass ($\beta_E - \beta_C = 0.11 \pm 0.67$, $P = 0.88$; results not displayed).

Fig 2. Effects of weight loss (body mass index) on HDL cholesterol, HDL₂ cholesterol, HDL₃ cholesterol, and HDL₂ mass in exercisers with initially low (diamonds) and normal-to-high HDL (squares). Significance levels are given for the difference in the regression slopes between the exercisers with low and normal-to-high HDL at entry. The regression slopes for exercisers with intermediate HDL at entry fell between the low and the normal-to-high HDL men (not displayed, see text).

Fig 3. Relationship between baseline HDL cholesterol levels and 1-year change in HDL cholesterol in dieters (squares) and controls (diamonds). Significance level is given for the difference in the regression slopes. Independent HDL cholesterol measurements are used for baseline HDL and Δ HDL.

Table 1

Baseline characteristics for men with normal-to-high, intermediate, and low HDL cholesterol concentrations

	HDL cholesterol (mg/dL)			Correlation with Baseline HDL cholesterol All (24–78 mg/dL)
	Low (≤ 37)	Intermediate (38–47)	Normal-to-High (≥ 48)	
N	34	62	34	130
HDL cholesterol (mg/dL)	32.5 $\pm$ 3.6 ^{*†}	40.3 $\pm$ 3.9 [†]	52.3 $\pm$ 7.8	0.94 [‡]
HDL ₂ cholesterol (mg/dL)	3.4 $\pm$ 1.6 ^{*†}	5.5 $\pm$ 2.5 [†]	11.9 $\pm$ 5.4	0.82 [‡]
HDL ₃ cholesterol (mg/dL)	29.1 $\pm$ 2.9 ^{*†}	34.8 $\pm$ 3.7 [†]	40.4 $\pm$ 4.4	0.82 [‡]
HDL ₂ mass (mg/dL)	7.4 $\pm$ 8.4 ^{*†}	19.0 $\pm$ 14.5 [†]	52.2 $\pm$ 31.1	0.80 [‡]
HDL ₃ mass (mg/dL)	182.9 $\pm$ 31.6 ^{*†}	211.5 $\pm$ 25.4 [†]	243.9 $\pm$ 36.1	0.67 [‡]
Triglycerides (mg/dL)	165.0 $\pm$ 63.8 [†]	130.8 $\pm$ 66.7 [†]	98.5 $\pm$ 42.7	−0.41 [‡]
Alcohol intake (% of total calories)	6.0 $\pm$ 6.5	5.7 $\pm$ 5.6	7.4 $\pm$ 7.6	0.17
Carbohydrate intake (% of total calories)	39.2 $\pm$ 8.4 [†]	38.1 $\pm$ 6.2 [†]	37.0 $\pm$ 7.4	−0.21 [‡]
Fat intake (% of total calories)	39.1 $\pm$ 6.2	40.4 $\pm$ 5.0	40.0 $\pm$ 6.2	0.11
Body mass index (kg/m ²)	29.6 $\pm$ 1.9	29.7 $\pm$ 2.3 [†]	28.6 $\pm$ 2.3	−0.16
Reported physical activity (kcal/kg/d)	35.8 $\pm$ 3.6	34.6 $\pm$ 2.5	34.5 $\pm$ 1.6	−0.13

NOTE. Results are the mean $\pm$ SD. Divide by 38.6 to convert cholesterol from mg/dL to mmol/L and by 88.5 to convert triglycerides from mg/dL to mmol/L.

* Significantly different from intermediate at $P \leq 0.05$.

[†] Significantly different from high at $P \leq 0.05$.

[‡] Correlated significantly with baseline HDL cholesterol at $P \leq .05$.

Table 2

Intervention effects in men with normal-to-high, intermediate, and low HDL cholesterol Concentrations

	HDL cholesterol (mg/dL)		
	LOW (<37)	Intermediate (38–47)	Normal-to-High (≥48)
Assigned to exercise (%)	38.2	33.9	35.3
Assigned to diet (%)	23.5	32.3	41.2
Assigned to control (%)	38.2	33.9	23.5
Distance run (exercisers)	6.9 ± 4.6	10.3 ± 5.9	11.6 ± 5.5
Δ Calories/day (dieters)	−273 ± 366	−370 ± 406	−338 ± 571
Δ Percent alcohol intake [‡]			
Exercisers	0.2 ± 3.0	0.9 ± 3.3	−1.2 ± 3.3
Dieters	−0.3 ± 2.2	−0.5 ± 4.2	−0.4 ± 4.2
Controls	−1.6 ± 4.3	−0.3 ± 4.8	0.6 ± 3.5
Δ Percent carbohydrate [‡]			
Exercisers	2.3 ± 6.0	0.3 ± 5.2	2.3 ± 6.6
Dieters	1.5 ± 3.7	1.7 ± 6.4	1.3 ± 7.6
Controls	−2.5 ± 5.9	−0.8 ± 4.9	1.0 ± 3.2
Δ Percent fat [‡]			
Exercisers	−1.6 ± 6.2	−2.4 ± 4.4	−0.9 ± 6.3
Dieters	−2.5 ± 6.3	−2.2 ± 5.4	−1.6 ± 8.1
Controls	4.1 ± 3.6 [†]	1.3 ± 6.7	−1.5 ± 5.1
Δ Body mass index			
Exercisers	−1.1 ± 1.3	−1.2 ± 1.3	−1.5 ± 1.1
Dieters	−2.0 ± 0.8	−2.4 ± 1.1	−2.3 ± 1.6
Controls	0.5 ± 1.0	0.0 ± 1.5	0.1 ± 0.7

NOTE. Results are the mean ± SD.

* Significantly different from intermediate at $P \leq 0.05$.[†] Significantly different from high at $P \leq 0.05$.[‡] Expressed as the percent of total calories.

Table 3

Correlation between baseline HDL cholesterol and intervention effects

Distance run (exercisers)	0.34 [*]
Δ Calories/day (dieters)	−0.06
Δ Percent alcohol intake [†]	
Exercisers	−0.18
Dieters	0.06
Controls	0.07
Δ Percent carbohydrate [†]	
Exercisers	0.11
Dieters	0.13
Controls	0.23
Δ Percent fat [†]	
Exercisers	0.01
Dieters	−0.19
Controls	−0.31
Δ Body mass index	
Exercisers	−0.26
Dieters	−0.14
Controls	−0.13

^{*} Correlated significantly with baseline HDL cholesterol at $P \leq 0.05$.

[†] Expressed as the percent of total calories.

Table 4

One-year change in HDL cholesterol and HDL subfractions in men with low (≤ 37 mg/dL), intermediate (38–47 mg/dL), and normal-to-high (≥ 48 mg/dL) HDL cholesterol at baseline.

	Exercisers (mean $\pm$ SD)	Dieters (mean $\pm$ SD)	Controls (mean $\pm$ SD)	Exercisers – Controls (difference $\pm$ SE)	Dieters – Controls (difference $\pm$ SE)
Δ HDL cholesterol (mg/dL) [‡]					
Low	2.9 $\pm$ 5.6	6.6 $\pm$ 8.3	0.6 $\pm$ 3.8	2.3 $\pm$ 1.9	6.0 $\pm$ 3.1*
Intermediate	3.2 $\pm$ 5.2	3.6 $\pm$ 5.8	-1.7 $\pm$ 4.7	4.9 $\pm$ 1.1*	5.3 $\pm$ 1.3*
Normal-to-high	7.2 $\pm$ 6.1	4.8 $\pm$ 5.5	0.1 $\pm$ 3.9	7.0 $\pm$ 1.3*	4.7 $\pm$ 2.3*
Δ HDL ₂ cholesterol (mg/dL) [‡]					
Low	1.0 $\pm$ 2.9	2.8 $\pm$ 2.8	0.2 $\pm$ 2.7	0.8 $\pm$ 1.6	2.5 $\pm$ 1.7
Intermediate	2.6 $\pm$ 4.7	1.8 $\pm$ 3.8	0.3 $\pm$ 3.1	2.3 $\pm$ 1.2	1.5 $\pm$ 1.1
Normal-to-high	5.5 $\pm$ 5.5	4.1 $\pm$ 4.6	0.4 $\pm$ 3.1	5.1 $\pm$ 1.3**†	3.8 $\pm$ 1.2*
Δ HDL ₃ cholesterol (mg/dL) [‡]					
Low	1.9 $\pm$ 3.5	3.9 $\pm$ 6.0	0.4 $\pm$ 2.9	1.5 $\pm$ 2.2	3.5 $\pm$ 2.0
Intermediate	0.7 $\pm$ 5.3	1.8 $\pm$ 4.3	-2.0 $\pm$ 2.9	2.7 $\pm$ 1.9	3.8 $\pm$ 1.7*
Normal-to-high	1.7 $\pm$ 4.6	0.6 $\pm$ 4.3	-0.3 $\pm$ 2.8	1.9 $\pm$ 1.7	0.9 $\pm$ 1.5
Δ HDL ₂ -mass (mg/dL)					
Low	5.1 $\pm$ 16.8	13.7 $\pm$ 16.5	2.3 $\pm$ 7.9	2.8 $\pm$ 5.1	11.5 $\pm$ 6.2
Intermediate	15.5 $\pm$ 26.4	14.1 $\pm$ 28.2	5.9 $\pm$ 30.8	9.5 $\pm$ 8.9	8.2 $\pm$ 9.5
Normal-to-high	26.5 $\pm$ 35.4	15.7 $\pm$ 22.7	-5.2 $\pm$ 11.7	31.7 $\pm$ 11.0**†	20.9 $\pm$ 7.4*
Δ HDL ₃ -mass (mg/dL)					
Low	6.3 $\pm$ 26.0	19.9 $\pm$ 25.7	-22.6 $\pm$ 30.3	28.9 $\pm$ 11.1*	42.5 $\pm$ 12.4*
Intermediate	-6.1 $\pm$ 31.1	-5.0 $\pm$ 34.3	-12.2 $\pm$ 33.1	6.1 $\pm$ 9.9	7.2 $\pm$ 10.8
Normal-to-high	1.9 $\pm$ 37.6	2.3 $\pm$ 31.8	-21.4 $\pm$ 33.7	23.3 $\pm$ 16.1	23.7 $\pm$ 14.6
$\Delta\%$ HDL cholesterol					
Low	9.4 $\pm$ 18.0	20.5 $\pm$ 24.1	2.3 $\pm$ 12.6	7.1 $\pm$ 6.1	18.2 $\pm$ 9.2*
Intermediate	8.2 $\pm$ 12.9	9.3 $\pm$ 14.1	-4.2 $\pm$ 12.1	12.4 $\pm$ 3.9*	13.5 $\pm$ 4.2*

	Exercisers (mean ± SD)	Dieters (mean ± SD)	Controls (mean ± SD)	Exercisers – Controls (difference ± SE)	Dieters – Controls (difference ± SE)
Normal-to-high	13.6 ± 11.2	9.4 ± 11.5	0.4 ± 6.7	13.2 ± 4.0 *	9.0 ± 3.9 *

NOTE. The samples sizes are as follows: 13 exercisers, 8 dieters, and 13 controls in the low HDL group; 21 exercisers, 20 dieters, and 21 controls in the intermediate HDL group; and 12 exercisers, 14 dieters, and 8 controls in the normal-to-high HDL group.

* Significantly different from controls at P < .05.

[†] The exercise minus control group difference is significantly greater in the normal-to-high men than in the low men at P ≤ 0.05.

[‡] Divide by 38.6 to convert cholesterol from mg/dL to mmol/L.