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Lifestyle Changes and 14-year Change in High-Density Lipoprotein Cholesterol in a Cohort of Male Physicians

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Abstract

Background—While cross-sectional studies have identified lifestyle factors associated with high-density lipoprotein cholesterol (HDL-C), no studies have examined the association between changes in lifestyle factors and long-term changes in HDL-C.

Methods—We examined the association between changes in lifestyle factors and changes in HDL-C over a 14 year period in a cohort of 4,168 U.S. male physicians followed between 1982 and 1997 and with HDL-C measured at both time points. Using linear regression, we examined the association between HDL-C change and categorized changes in alcohol consumption, physical activity, body mass index (BMI), and smoking, adjusting for age, baseline HDL-C, and other covariates.

Results—Stable BMI of <25 kg/m² or BMI reduction from ≥25 kg/m² to <25 kg/m² were associated with increases in HDL-C of 3.1 to 4.7 mg/dL over 14 years. Alcohol consumption of ≥1 drink daily or increase in alcohol consumption from <1 to ≥1 drink daily were associated with increases in HDL-C of 2.4 to 3.3 mg/dL over 14 years. Adopting a sedentary lifestyle was associated with decreases in 14-year decreases in HDL-C.

Conclusion—These findings suggest that reductions in BMI and increases in alcohol consumption are associated with 14-year increases in HDL-C, while decreases physical activity are associated with 14-year decreases in HDL-C.

Previous studies have shown that lifestyle factors including moderate alcohol consumption, regular physical activity, maintaining a healthy body mass index (BMI), and abstinence from smoking, are associated with higher single measurements of HDL-C in men and women (1-11). However, the potential association between composite lifestyle factors and long-term changes in HDL-C remains unexamined. In a cohort of U.S. male physicians followed prospectively starting in 1982, the authors examine associations between baseline and updated lifestyle factors and changes in HDL-C, adjusting for age, baseline

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comorbidities, baseline HDL-C and non-HDL cholesterol, and medications. In additional analyses, the authors compare subgroups of the cohort stratified by the magnitude of increase of HDL-C. Finally, to determine whether high or low baseline HDL-C levels modify the effect of lifestyle changes on subsequent HDL-C changes, the authors examine relationships between lifestyle factors and HDL-C change in sub-groups stratified by baseline HDL-C levels.

METHODS

Population

The Physicians' Health Study I (PHS I) is a prospective cohort of 22,071 US male physicians aged 40 to 84 years who were initially free of cancer and CVD in 1982 when they were randomized into a trial of aspirin and beta-carotene. At baseline, information regarding self-reported risk factors and comorbidities were collected, with updates collected 6 months after enrollment and annually thereafter via mailed questionnaires. Detailed descriptions of the methods of PHS I has been published previously (12-15).

At baseline, all PHS participants were mailed blood kits which consisted of Vacutainer tubes containing EDTA, instructions for blood draws, and cold packs. Bloods were returned from 15,127 men via overnight carrier during enrollment between August 1982 and August 1983, and stored at -80°C . Among those returning a baseline blood sample, 9,520 also returned a follow-up blood sample between December 1995 and January 1998, of whom 4,593 men had both baseline and follow-up lipids measured. Total and HDL cholesterol were measured by the Lipid Research Laboratory of Brigham & Women's Hospital, which participates in the standardization program for total and HDL cholesterol of the Centers for Disease Control and the National Heart, Lung, and Blood Institute. Briefly, cholesterol in whole plasma and HDL-C were measured using a Hitachi 911 analyzer (Roche Diagnostics) and reagents manufactured by Roche Diagnostics and Genzyme (14). Further details regarding laboratory techniques have been previously described (12-15).

The authors excluded 72 of men who developed coronary heart disease (CHD) between the baseline and follow-up blood sample collections. 252 men were excluded due to missing data on baseline or follow-up hypertension, diabetes mellitus, lifestyle factors, cholesterol, or parental history of MI. Men with missing data on cholesterol medication during follow-up ($n=101$) were also excluded, however men with missing data on baseline cholesterol modifying therapy remained in the analysis and are reported in Table I. For this study, our baseline population therefore consisted of 4,168 male physicians. Our primary outcome was change in HDL-C, defined as the difference between each subject's follow-up (collected between December 1995 and January 1998) levels and baseline (collected between August 1982 and August 1983), approximately 14 years apart.

All PHS I participants gave written, informed consent to participate in the study at enrollment. The PHS I has been approved by the Institutional Review Board of the Brigham & Women's Hospital, Boston, MA.

Baseline and follow-up characteristics

For these analyses, we considered 4 self-reported lifestyle factors collected at baseline and follow-up as potential predictors of change in HDL-C: BMI, alcohol consumption, exercise, and smoking. BMI (in kg/m^2) was converted from height (inches) and weight (pounds) collected at baseline and at PHS II enrollment (approximate date of follow-up HDL-C measurement). BMI was dichotomized into normal BMI ($<25 \text{ kg}/\text{m}^2$) or overweight/obese ($\geq 25 \text{ kg}/\text{m}^2$). The cohort was divided into 4 groups: those who maintained a BMI of $\geq 25 \text{ kg}/\text{m}^2$ throughout the study (reference), increased from $<25 \text{ kg}/\text{m}^2$ to $\geq 25 \text{ kg}/\text{m}^2$ during the

study, decreased from ≥ 25 kg/m² to < 25 kg/m², and maintained a BMI of < 25 kg/m². Alcohol consumption documented at baseline and follow-up was dichotomized into “moderate” intake (≥ 1 drink/day) or less than moderate intake (< 1 drink/day). Subjects were then categorized: those who consumed < 1 drinks /day throughout the study (reference), increased consumption from < 1 to ≥ 1 drinks/day, decreased consumption from ≥ 1 to < 1 drinks/day during the study, or those who maintained an alcohol consumption of < 1 drinks/day. Smoking status was categorized as either currently smoking or not. Subjects were then categorized: smoking throughout the study (reference), quitting smoking, initiating smoking, or never smoking. Finally, regular physical activity was defined as exercise to sweat at least once per week, and was documented at baseline and 9-years follow-up, in 1991. Previous researchers have defined “physically active” in this way in PHS (16-17). Subjects were characterized as exercising to sweat < 1 times/week (reference), increasing exercise from < 1 to ≥ 1 times/week, decreasing exercise from ≥ 1 to < 1 times/week, or exercising ≥ 1 times/week throughout the study.

Other relevant covariates

Age (in years), race, history of diabetes (no/yes), history of hypertension (defined as having either past/current treatment, systolic blood pressure > 140 mmHg, or diastolic blood pressure of > 90 mmHg; no/yes), and early parental history of myocardial infarction (MI) < 60 years of age (no/yes), were collected on baseline and follow-up questionnaires. Non-HDL cholesterol was calculated at baseline and follow-up by subtracting the HDL-C value from the total cholesterol value at each time point. Information on whether cholesterol modifying therapy (CMT) was initiated was collected at baseline, 7-month follow-up, and near the time of the second blood draw. Other lipid parameters including triglycerides and glucose levels were not available in the database.

Data analyses

First, coronary risk factors at baseline and follow-up were compared along with changes in HDL-C over the approximate 14-year period. Associations between baseline characteristics of the cohort and baseline HDL-C were examined. The association between each 4-category lifestyle change factors and corresponding 14-year change in HDL-C was then examined using linear regression. Multivariate models included race, non-HDL cholesterol, hypertension and diabetes at baseline or diagnosed during follow-up, CMT initiated during the study, parental history of MI, and all 4-category lifestyle change factors, paralleling the approach examining predictors of change in total cholesterol/HDL-C ratio in PHS I (16). Multivariate parameter estimates and p-values for the association between each lifestyle factor and HDL-C change, along with mean (SD) HDL-C in 1997 for co-morbidity and lifestyle change sub-groups, were determined. To further examine the relationship between HDL-C change and BMI change (as BMI in 1997 minus BMI in 1982), a plot of predicted change in HDL-C with 95% confidence interval was generated. In sensitivity analyses, we repeated the analyses in a subgroup of participants not administered CMT during the 14 year interval.

In secondary analyses, we compared men with HDL-C increases of ≥ 12.5 mg/dL versus an HDL-C increase of < 12.5 mg/dL or decrease in HDL-C, with 12.5 mg/dL approximating the standard deviation in observed change in HDL-C in this cohort and providing clinically meaningful increments of HDL-C change. The 4-category lifestyle factors were compared between these two HDL-C change subgroups, using t-tests to compare continuous variables and Cochran-Mantel-Haenszel tests to compare categorical variables.

We tested for interactions between baseline HDL-C and the lifestyle change categories by including baseline HDL-C*ordinal lifestyle change category variables in our models. To test

whether association between lifestyle and HDL-C changes were modified by initially low or high HDL-C levels, subgroups defined by baseline HDL-C above or below median were compared.

RESULTS

There were 4,168 subjects who met inclusion criteria. Baseline and follow-up characteristics of the cohort are displayed in Table I. The mean (SD) increase in HDL-C was 0.97 (11.5) mg/dL. The prevalence of diabetes mellitus and hypertension increased in the cohort between baseline and 14-year follow-up. Of subjects who initiated CMT during follow-up, the mean (SD) increase in total cholesterol was 33.0 (46.6) mg/dL and the mean increase in HDL-C was 2.25 (11.8) mg/dL. Most subjects (55.1%) engaged in regular physical activity throughout the study and very few subjects smoked at baseline or follow-up (5.9% and 2.4% respectively). Most subjects remained categorized with a BMI of either <25 or ≥ 25 kg/m² (76.5%) throughout the study. Over half of the cohort consumed less than a moderate amount of alcohol (51.4%) throughout the study.

Table II displays the association between lifestyle factors and both baseline HDL-C and 14-year change in HDL-C. Baseline alcohol consumption, physical activity, smoking, BMI, non-HDL cholesterol, and hypertension were all significantly associated with baseline HDL-C levels. Change in HDL-C was significantly associated with baseline HDL-C and non-HDL cholesterol measured in 1997. Decreasing BMI or maintaining a stable low BMI of <25 kg/m² were both significantly associated with increases in HDL-C. Figure 1 demonstrates the relationship between change in BMI as a continuous variable and predicted change in HDL-C. Maintaining moderate alcohol consumption or increasing alcohol consumption from <1 beverage daily to ≥ 1 beverage daily was also associated with 14-year increases in HDL-C. Men who were active at baseline (exercised to sweat ≥ 1 times per week) but became sedentary (exercised to sweat <1 times per week) at follow-up had significant reductions in their HDL-C over the 14-year period. In an analysis of $n=3,253$ men who were not administered CMT during study follow-up, results were essentially unchanged (not shown). Table III displays characteristics of 554 (13%) subjects who had a 14-year HDL-C increase of ≥ 12.5 mg/dL or more, who were compared to the remainder of the cohort (men with a smaller HDL-C increase, stable HDL-C, or decrease in HDL-C).

In analyses including baseline HDL-C*ordinal lifestyle change category terms, analyses revealed significant interactions between baseline HDL-C and change in alcohol consumption (p , interaction <0.0001), baseline HDL-C and change in BMI (p , interaction <0.0001), and baseline HDL-C and change in physical activity (p , interaction = 0.0002). In analyses examining interactions between continuous BMI change and ordinal alcohol consumption or exercise categories, we found neither of these interactions to be statistically significant. Table IV examines analyses stratified by the median baseline HDL-C of 40.5 mg/dL. We found a modest alteration of the effect of lifestyle changes on HDL-C change by baseline HDL-C.

DISCUSSION

In a cohort of male physicians with measurements of HDL-C 14 years apart, the authors found that stable low BMI, decreasing BMI, moderate alcohol consumption, and increasing alcohol consumption were all associated with increases in HDL-C, while decreases in physical activity were associated with decreases in HDL-C. In analyses examining potential interactions between baseline HDL-C and lifestyle changes and analyses stratified by baseline HDL-C both demonstrated that the effect of some lifestyle changes, such as becoming sedentary, on HDL-C change varied according to baseline HDL-C.

In this study, the magnitude of HDL-C increase associated with weight loss, maintaining low BMI, maintaining moderate alcohol intake, or increasing alcohol intake varied between approximately 5 and 10%, corroborating previous studies that examined associations between these lifestyle factors and HDL-C (1-14). Unlike previous cross-sectional studies examining associations between exercise and HDL-C, these authors did not find an association between increases in physical activity and changes in HDL-C(1). These findings may reflect the fact that most subjects (54.7%) were regularly physically active over the entire 14-year period, so HDL-C response to increases or decreases in physical activity in the small number of subjects who experienced them may not have been detected.

The authors identified a subgroup of n=554 subjects who achieved an increase in HDL-C of ≥ 12.5 mg/dL during follow-up. There are several potential explanations why these men may have had their large increases in HDL-C. CMT use was initiated in 26.0% of this subgroup during the study period. Many of these men may have made favorable lifestyle changes simultaneously, such as reducing BMI, as reflected in Table III. These 554 men were older and more likely to have baseline hypertension and diabetes, which may have provided impetus for these and additional, unmeasured lifestyle changes (diet, for instance) to promote higher HDL-C. Alternatively, this group may represent “strong responders” in whom genetic factors may be responsible for these larger HDL-C increases that resulted from lifestyle changes. Previous authors examining whether genes modify the impact of lifestyle on HDL-C levels have had mixed results (18).

Updated lifestyle parameters over time and 2 available measurements of HDL-C levels taken 14 years apart PHS I make this cohort ideal for examining associations between changes in lifestyle parameters and changes in lipids. However, some limitations should be noted. First, this study was underpowered to evaluate the impact of smaller incremental changes in lifestyle factors (such as increasing from weekly to daily exercise) on HDL-C change. Using the broad definitions of changes in lifestyle used here, the analysis had a power of $\geq 80\%$ to detect an HDL-C increase of 5% for many the activity, BMI, and alcohol consumption category comparisons. Although a large number of subjects (626) had missing data regarding baseline CMT use, a small number of men for whom baseline CMT use was available used CMT (5), so it is unlikely that missing baseline CMT data could have biased our findings. We did not examine lifestyle impact on HDL-C subclasses as this data is available on a small number of PHS participants; examining whether lifestyle variably impacts HDL-C subclasses represents a potentially important area of future research (19). We did not find significant associations between race and HDL-C change, however the number of non-white participants in PHS is very small. Examining associations between lifestyle changes and HDL-C change in persons of varying racial background, in women, in persons of varying geographic background, or subjects with known co morbidities such as heart disease, represents an important area of future research. Residual confounding, such as the impact of fluctuating dietary factors on HDL-C change, may be a concern and remains an area of important future research.

Sources of variation in our measurement of HDL-C change for which we could not account include regression to the mean, within-individual variation, differences in laboratory technique, or other unobserved predictors of HDL-C (20-21). We would expect, however, that these sources of measurement error would impact the sample in a uniform fashion and thus influence our results toward the null. Thus the magnitude of significant lifestyle-HDL-C change associations that we found is likely to be underestimated in this study.

This study demonstrates that adopting or maintaining favorable lifestyle habits are associated with increases HDL-C, while adopting or maintaining unfavorable may result in decreases in HDL-C over time in a cohort of male physicians. Although more questions

regarding the relationships between lifestyle modification and HDL-C change remain, our results provide further support for the promotion of maintaining a low BMI, pursuing a physically active lifestyle, and other beneficial lifestyle factors.

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FIGURE 1.
Predicted HDL-C change by 14-year BMI change (blue) and upper (green) and lower (red) 95% confidence intervals.

Table I

Baseline and follow-up characteristics of 4,168 U.S. male physicians with high-density lipoprotein cholesterol levels measured in 1982 and 1997.

Characteristic	Baseline, 1982	1997
Age, mean (SD), years	48.9 (6.8)	63.1 (6.8)
Race, no. (%)		
White	3948 (94.7)	3958 (94.7)
Asian	123 (3.0)	123 (3.0)
Hispanic	58 (1.4)	58 (1.4)
Black	19 (0.5)	19 (0.5)
American Indian	1 (0.02)	1 (0.02)
Other	8 (0.2)	8 (0.2)
Multiple answers	11 (0.3)	11 (0.3)
BMI [*] , mean (SD), kg/m ² *	24.5 (2.6)	25.6 (3.2)
Non-HDL cholesterol, mean(SD), mg/dL [*]	171.6 (41.1)	163.4 (36.2)
HDL cholesterol, mean (SD), mg/dL	42.2 (14.8)	43.2 (15.0)
Change in HDL cholesterol (SD), mg/dL	-	0.97 (11.5)
Alcohol consumption, no. (%)		
<1 drink weekly	1044 (25.1)	825 (19.8)
1-6 drinks weekly	2221 (53.3)	1474 (35.4)
1 or more drinks weekly	903 (21.7)	1869 (44.8)
Diabetes, no. (%)	49(1.2)	166 (4.0)
Hypertension, no. (%)	670 (16.1)	1508 (36.2)
Parental history of MI [*] , no. (%)	430 (10.3)	430 (10.3)
Currently smoking, no. (%)	244 (5.9)	98 (2.4)
Past smoker, no. (%)	1527 (366)	1768 (42.4)
Regularly physically active, no. (%) [†]	3155 (75.7)	2644 (63.4)
BMI ≥25 kg/m, no. (%)	1564 (37.5)	2241 (53.8)
CMT [*] used at baseline, no.(%)		
Yes	5 (0.12)	
No	3537 (84.9)	
Missing	626 (15.0)	
CMT begun during study period, no.(%)	-	915 (22.0)
Activity change, no. (%)		
Sedentary during study	-	667 (16.0)
No longer sedentary at follow-up	-	346 (8.3)
Sedentary at follow-up	-	857 (20.6)
Active during study	-	2298 (55.1)
BMI change, no. (%)		
Stable ≥25 kg/m throughout	-	1412 (33.9)
Gained weight to ≥25 kg/m	-	829 (19.9)

Characteristic	Baseline, 1982	1997
Lost weight to <25 kg/m	-	152 (3.6)
Stable <25 kg/m throughout	-	1775 (42.6)
Change in alcohol consumption, no.(%)		
<1+/daily during study	-	2143 (51.4)
Increased to 1+/daily at follow-up	-	1122 (26.9)
Decreased to <1+/daily at follow-up	-	156 (3.7)
≥1/daily during study	-	747 (17.9)
Change in smoking status, no. (%)		
Smoked during study	-	73 (1.8)
Quit at follow-up	-	171 (4.1)
Began smoking at follow-up	-	25 (0.60)
Never smoked during study	-	3899 (93.6)

* BMI=Body Mass Index; CMT=cholesterol modifying therapy; HDL-C=high density lipoprotein cholesterol; MI=myocardial infarction; kg/m²=kilograms/square-meter; mg/dL=milligrams/deciliter; SD=standard deviation; no.=number

[†] Regular physical activity defined as exercising to sweat at least once weekly

Table II

Parameter estimates for association between patient characteristics and baseline high-density lipoprotein cholesterol (left columns) and change in high-density lipoprotein cholesterol (right columns) in 4,168 U.S. male physicians, 1982-1997

Characteristic	Baseline HDL-C		Change in HDL-C		Follow-up HDL-C
	β Coefficient	p-value	β Coefficient	p-value	Mg/dL* mean (SD)
Age	0.09	<0.007	0.034	0.28	
Non-white	-3.48	0.0002	0.75	0.30	40.3 (12.9)
Non-HDL cholesterol	-0.06	<0.0001	-0.03	<0.0001	
Hypertension	-2.33	<0.0001	-0.34	0.33	41.4 (14.8)
Diabetes	-1.21	0.53	-0.62	0.46	37.0 (14.3)
CMT*, used at baseline	4.04	0.51	N/A		
CMT, initiated during study	N/A		0.57	0.15	41.4 (13.7)
Parental history of MI*	-0.36	0.61	0.9	0.09	42.1 (13.9)
HDL-C in 1982	N/A		-0.34	<0.0001	
Alcohol consumption, baseline			N/A		
<1 drink weekly	Reference				
1-6 drinks weekly	4.15	<0.0001			
1 or more drinks weekly	9.48	<0.0001			
Currently smoking, baseline	-3.96	<0.0001	N/A		
Past smoker, baseline	0.66	0.15	N/A		
BMI*, baseline	-1.41	<0.0001	N/A		
Regularly physically active, baseline†	2.03	<0.0001	N/A		
Activity change	N/A				
Sedentary throughout study			reference		40.7 (15.0)
No longer sedentary at follow-up			0.37	0.59	42.3 (14.3)
Sedentary at follow-up			-1.31	0.02	41.2 (14.5)
Active throughout study			-0.19	0.68	44.8 (15.2)
BMI change	N/A				
Stable ≥ 25 kg/m throughout			reference		38.4 (13.5)

Characteristic	Baseline HDL-C		Change in HDL-C		Follow-up HDL-C
	β	p-value	β	p-value	Mg/dL [*] , mean (SD)
Gained weight to ≥ 25 kg/m			-0.62	0.18	41.9 (13.8)
Lost weight to < 25 kg/m			4.67	< 0.0001	44.7 (16.1)
Stable < 25 kg/m throughout			3.05	< 0.0001	47.5 (15.4)
Change in alcohol consumption	N/A				
< 1 +/daily during study			reference		39.8 (13.7)
Increased to 1+/daily at follow-up			2.37	< 0.0001	45.6 (14.5)
Decreased to < 1 /daily at follow-up			-1.63	0.06	42.7 (15.7)
≥ 1 /daily during study			3.34	< 0.0001	49.4 (16.6)
Change in smoking status, no. (%)	N/A				
Smoked during study			reference		40.0 (17.3)
Quit at follow-up			0.38	0.79	40.6 (14.9)
Began smoking at follow-up			-0.004	0.99	39.5 (13.2)
Never smoked during study			0.64	0.6	43.4 (15.0)

* BMI=body mass index; CMT=cholesterol modifying therapy; HDL-C=high density lipoprotein cholesterol; MI=myocardial infarction; mg/dL=milligrams per deciliter

[†] Regularly physically active is defined as exercising to sweat at least once weekly.

[‡] Parameter estimates for predictors of baseline HDL-C are adjusted for age in 1982, race, non-HDL cholesterol in 1982, hypertension or diabetes at baseline, baseline alcohol consumption, baseline smoking status, parental history of MI, regular physical activity at baseline, and baseline BMI

[§] Parameter estimates for predictors of change in HDL-C are adjusted for age in 1997, race, non-HDL cholesterol in 1997, hypertension or diabetes at baseline or diagnosed during the study, CMT initiated during the study, parental history of MI, baseline (1982) HDL-C, and 4-category change in physical activity, BMI, alcohol consumption, and smoking status.

Table III

Characteristics of U.S. male physicians who achieved high-density lipoprotein cholesterol (HDL-C) increase of ≥ 12.5 mg/dL compared to those who achieved HDL-C increase of < 12.5 mg/dL over a 14 year period, 1982-1997.

Characteristic	HDL-C Change >12.5 mg/dL	HDL-C Change <12.5 mg/dL	P-value [‡]
Age in 1982, yrs, mean (SD)	49.9 (7.3)	48.7 (6.7)	0.0001
Non-white	33 (6.0)	187 (5.2)	0.44
BMI [*] in 1982, kg/m ² *	24.2 (2.4)	24.5 (2.6)	0.03
Non-HDL cholesterol on 1982, mg/dL [*] , mean(SD)	171.8 (42.1)	171.5 (41.0)	0.89
HDL-C in 1982, mg/dL	38.4 (14.8)	42.8 (14.7)	<0.0001
Baseline Alcohol intake, no.(%)			
<1 beverage weekly	117 (21.1)	927 (25.7)	0.02
1-6 beverages weekly	296 (53.4)	1925 (53.3)	0.94
≥ 1 beverage daily	141 (25.5)	762 (21.1)	0.02
Diabetes at baseline, no.(%)	14 (2.5)	35 (0.97)	0.002
Hypertension at baseline, no.(%)	119 (21.5)	551 (15.3)	0.0002
Parental history of MI [*] , no.(%)	57 (10.3)	373 (10.3)	0.98
Smoking at baseline, no.(%)	40 (7.2)	204 (5.6)	0.14
Past smoker at baseline, no.(%)	219 (39.5)	1308 (36.2)	0.13
Regularly physically active at baseline [‡] , no.(%)	405 (73.1)	2750 (76.1)	0.13
BMI ≥ 25 kg/m ² at baseline, no.(%)	189 (34.1)	1375 (38.1)	0.08
Treated with CMT [*] during study, no.(%)	144 (26.0)	771 (21.3)	0.01
Categorized change in activity, no. (%)			
Remained sedentary	94 (17.0)	573 (15.9)	0.51
Initiated regular exercise ≥ 1 weekly	55 (9.9)	291 (8.1)	0.14
Eliminated regular exercise	95 (17.2)	762 (21.1)	0.03
Remained active	310 (56.0)	1988 (55.0)	0.68
Categorized change in BMI, no. (%)			
Stable BMI ≥ 25 kg/m ²	147 (26.5)	1265 (35.0)	<0.0001
Increased BMI <25 kg/m ² to ≥ 25 kg/m ²	88 (15.9)	741 (20.5)	0.01
Decreased BMI, ≥ 25 kg/m ² to <25 kg/m ²	42 (7.6)	110 (3.0)	<0.0001
Stable BMI <25 kg/m ²	277 (50.0)	1498 (41.5)	0.0002
Categorized alcohol intake, no.(%)			
Consumed ≥ 1 beverage daily	122 (22.0)	625 (17.3)	0.007
Increased from <1 to ≥ 1 beverage daily	165 (29.8)	957 (26.5)	0.10
Decreased from ≥ 1 to <1 beverage daily	19 (3.4)	137 (3.8)	0.68
Consumed <1 beverage daily	248 (44.8)	1895 (52.4)	0.0008
Categorized smoking status, no.(%)			
Never smoked	512 (92.4)	3387 (93.7)	0.25

Characteristic	HDL-C Change >12.5 mg/dL	HDL-C Change <12.5 mg/dL	P- value [‡]
Quit during study	30 (5.4)	141 (3.9)	0.09
Initiated smoking during study	2 (0.36)	23 (0.64)	0.43
Smoked throughout study	10 (1.8)	63 (1.7)	0.92

* BMI=Body Mass Index; CMT=cholesterol modifying therapy; HDL-C=high density lipoprotein cholesterol; MI=myocardial infarction; kg/m²=kilograms/square-meter; mg/dL=milligrams/deciliter; SD=standard deviation; no.=number

[†] Regularly physically active is defined as exercising to sweat at least once weekly.

[‡] P-values of Cochrane-Mantel-Haenszel tests displayed for differences between the two groups for categorical variables. P-values for t-tests displayed for differences between the two groups for continuous variables.

Table IV

Parameter estimates for association between patient characteristics and change in high-density lipoprotein cholesterol (HDL-C), stratified by median baseline HDL-C of 40.5 mg/dL, 1982-1997.

	Baseline HDL-C >40.5 mg/dL		Baseline HDL-C ≤40.5 mg/dL	
	β Coefficient [†]	p-value	β Coefficient [†]	p-value
Age	0.02	0.62	0.03	0.3
Non-white	0.04	0.98	1.21	0.15
Non-HDL cholesterol	-0.05	<0.0001	-0.02	0.004
Hypertension	-0.63	0.26	0.04	0.93
Diabetes	-2.16	0.23	-0.002	0.99
CMT [*] , initiated during study	0.24	0.72	0.93	0.05
Parental history of MI [*]	1.92	0.02	-0.15	0.82
HDL-C in 1982	-0.36	<0.0001	-0.38	<0.0001
Activity change				
Sedentary throughout study	Reference		Reference	
No longer sedentary at follow-up	-1.13	0.33	1.50	0.06
Sedentary at follow-up	-3.38	0.0002	0.29	0.65
Active throughout study	-1.27	0.1	0.45	0.42
BMI [*] change				
Stable ≥25 kg/m throughout	Reference		Reference	
Gained weight to ≥25 kg/m	-1.03	0.16	0.09	0.87
Lost weight to <25 kg/m	5.01	0.0008	4.62	<0.0001
Stable <25 kg/m throughout	3.40	<0.0001	2.47	<0.0001
Change in alcohol consumption				
<1+/daily throughout	Reference		Reference	
Increased to 1+/daily at follow-up	2.20	0.0002	2.43	<0.0001
Decreased to <1+/daily at follow-up	-4.58	0.0002	2.91	0.02
≥1/daily throughout	3.63	<0.0001	2.6	<0.0001
Change in smoking status, no. (%)				
Smoked throughout study	Reference		Reference	
Quit at follow-up	-0.71	0.79	1.03	0.53
Began smoking at follow-up	0.83	0.84	-0.19	0.94
Never smoked during study	0.09	0.97	1.09	0.42

* BMI=body mass index; CMT=cholesterol modifying therapy; HDL-C=high density lipoprotein cholesterol; MI=myocardial infarction

[†] Parameter estimates for predictors of change in HDL-C are adjusted for age in 1997, race, non-HDL cholesterol in 1997, hypertension or diabetes at baseline or diagnosed during the study, CMT initiated during the study, parental history of MI, baseline (1982) HDL-C, and 4-category change in physical activity, BMI, alcohol consumption, and smoking status.