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Incident hypercholesterolemia in relation to changes in vigorous physical activity

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Abstract

Purpose—Test whether changes in vigorous exercise affect the risk for hypercholesterolemia.

Methods—Incident physician-diagnosed hypercholesterolemia was compared in recreational runners whose weekly distances run increased > 0.5 km/day (4034 men, 1897 women), remained constant (± 0.5 km/d; 4685 men, 1904 women), or decreased > 0.5 km/d (15,678 men, 6224 women) during 7.8 yr of prospective follow-up.

Results—Relative to those whose distance was maintained or reduced, the odds ratio (OR) (95% confidence interval) for hypercholesterolemia for those whose running increased was significantly less than 1 for men {OR: 0.82 (0.72–0.93), $P = 0.0006$ }, women {OR: 0.71 (0.54–0.92), $P = 0.01$ }, and men and women combined adjusted for sex {OR: 0.80 (0.72–0.89), $P < 0.0001$ }. The significance of the odds ratios was somewhat diminished when adjusted for baseline and follow-up BMI in men {OR: 0.89 (0.79–1.01), $P = 0.06$ }, women {OR: 0.71 (0.54–0.92), $P = 0.08$ }, and the adjusted sexes combined {OR: 0.88 (0.79–0.98), $P = 0.02$ }. When average distance run {i.e., (baseline + follow-up) / 2} was compared with incident hypercholesterolemia in the 6589 runners whose distance remained constant, each kilometer-per-day increment in average running distance was associated with an odds ratio significantly less than 1 in men {OR: 0.90 (0.86–0.93)}, women {OR: 0.91 (0.84–0.98)}, and the adjusted sexes combined {OR: 0.90 (0.87–0.93)}, which was also attributable in part to BMI in men {OR: 0.94 (0.90–0.97), $P = 0.0005$ }, women {OR: 0.96 (0.89–1.04), $P = 0.35$ }, and the adjusted sexes combined {OR: 0.94 (0.91–0.97), $P = 0.0003$ }.

Conclusions—The odds for hypercholesterolemia: 1) decrease in runners who increase their running mileage and 2) decline in association with the higher dose of vigorous activity even in the absence of any change in exercise. These effects are associated in part to the runners' BMI.

Keywords

high cholesterol; prevention; running; epidemiology

INTRODUCTION

It is estimated that 100 million American adults have total blood cholesterol values ≥ 200 mg/dl and 34.5 million ≥ 240 mg/dl (11). Reducing plasma cholesterol concentrations substantially reduces the risks for cardiovascular disease (11).

Aerobic training is reported to produce modest reductions in plasma total and LDL-cholesterol. In their review of 51 training studies, Leon and Sanchez (10) estimated that aerobic training reduced LDL-cholesterol concentrations by approximately 5% ($P < 0.05$) and total cholesterol concentrations by 1% (NS). Other meta-analyses conclude that aerobic exercise decreases LDL-cholesterol by 5% but not total cholesterol concentrations in patients with type II diabetes (3) and that aerobic exercise decreases plasma total and LDL-cholesterol by 2% and 3%, respectively, in women (4). Four percent reductions in plasma concentrations of non-HDL-cholesterol are reported for meta-analyses of walking-based interventions (5). The limited sample size and narrow activity ranges produced in these studies preclude the derivations of dose-response relationships between changes in physical activity and plasma total cholesterol or LDL-cholesterol concentrations or hypercholesterolemia.

To better understand the effects of vigorous physical activity on hypercholesterolemia, we compared changes in vigorous physical activity (km/d) to incident hypercholesterolemia in runners surveyed at baseline and after 7.7 yr. Specific hypotheses tested were as follows: 1) whether men and women who increase their activity are at lower risk for becoming hypercholesterolemic than those who maintain or reduce their activity, 2) whether average distances run affects the odds for becoming hypercholesterolemic in the absence of any change in exercise, and 3) whether body weight mediates the effects of vigorous exercise on hypercholesterolemia.

METHODS

The survey instruments and the baseline characteristics of the National Runners' Health Survey are described elsewhere (14–27). Briefly, a two-page questionnaire, distributed nationally at races and to subscribers of a popular running magazine (Runners' World, Emmaus, PA), solicited information on demographics, running history, weight history, smoking habits, prior history of heart attacks and cancer, and medications for blood pressure, thyroid conditions, high cholesterol, and diabetes. Recruitment took place between 1991 and 1994 (primarily 1993) and follow-up was between 1999 and 2002. We estimate that approximately 15% of the participants who received questionnaires responded to our survey (the percentage is not exactly known due to uncertainty in the actual number of questionnaires distributed at footrace events and the proportion of participants who received multiple questionnaires). All applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research. The study protocol was approved by the University of California Committee for the Protection of Human Subjects, and all participants signed committee-approved informed consents.

Physical activity was reported as usual miles run per week and was converted into kilometers per day for the purpose of analysis. Self-reported distance run has been found to be highly reliable (test-retest correlations of $r = 0.89$ [15]). Although other leisure-time physical activities were not recorded for this cohort, data from runners recruited after 1998 (when the survey question was introduced) show that running represents a majority of all vigorously intense activity in those men and a majority of their total leisure-time physical activity.

Follow-up questionnaires were sent by mail requesting information on current running levels, body weight, and medical conditions. Multiple follow-up survey questionnaires were sent and telephone calls made until a priori determined response rate of 80% of participants provided follow-up information or were known deceased. Participants reported whether a physician had told them they had high cholesterol since their baseline questionnaire and whether they took medications for high cholesterol at baseline and the end of follow-up. Incident hypercholesterolemia is defined as physician diagnosis or starting medications for the condition after their baseline survey. Self-reported high cholesterol has been demonstrated by others as generally reliable using repeated surveys and confirmed diagnosis from medical records (1).

Statistics

We used logistic regression analyses to test whether changes in distance run per week were related to the incidence of hypercholesterolemia (JMP version 5.1; SAS Institute, Cary, NC). All results (except the sample description of Table 1) include adjustment for the mean age during follow-up (age and age²), follow-up duration, and weekly intakes of alcohol, meat, fish, and fruit at baseline and end of follow-up. The ANOVA of Table 1 is primarily descriptive and presents the means $\pm$ SD for this purpose, with post hoc group comparisons using t-test and Bonferroni correction for the three group comparisons. Means are presented $\pm$ SD (for descriptive results) or $\pm$ SE (for representing the error in estimation) as noted, and differences and odds ratios that are $P < 0.05$ are designated as statistically significant. The results are presented as follows: 1) adjusted simultaneously for BMI at baseline and end of follow-up (BMI_{exercise} adjustment); and 2) adjusted for their BMI when they first began running 12 miles/wk (BMI_{preexercise} adjustment). Throughout this article, average running distance refers to the average of the baseline and the follow-up survey values. We also used logistic regression analyses to estimate the incidence of hypercholesterolemia within five age intervals of 18–34, 35–44, 45–54, 55–64, and 65–74 yr (17).

RESULTS

There were 24,397 men and 10,025 women who were nonsmokers, nonvegetarian, nondiabetic, and nonhypertensive at baseline who provided running distance, height, and weight at both baseline and follow-up. Relative to the entire baseline cohort, those who were excluded ran similar weekly baseline distances as those used in the analyses (mean $\pm$ SE of excluded vs included: males = 3.27 ± 0.03 vs 3.37 ± 0.01 km/d, females = 3.37 ± 0.04 vs 3.20 ± 0.01 km/d) but were significantly older (males = 48.5 ± 0.1 vs 44.2 ± 0.1 yr, females = 42.1 ± 0.2 vs 38.3 ± 0.1 yr), heavier (males = 24.01 ± 0.04 vs 23.84 ± 0.02 kg/m², females = 21.50 ± 0.05 vs 21.25 ± 0.02 kg/m²), and had run more year prior to baseline (males = 13.9 ± 0.1 vs 13.1 ± 0.1 yr, females = 10.4 ± 0.1 vs 9.9 ± 0.1 yr). Incident hypercholesterolemia was reported by 3054 (12.5%) men and 519 (5.2%) women.

Table 1 presents the characteristics of the sample by change in running distance. The majority of men (64.3%) and women (62.1%) decreased their running distance by >0.5 km/d, 19% of men and women maintained their running distance within ± 0.5 km/d, and 16.5% of men and 18.9% of women increased their running distance more than 0.5 km/d

between baseline and follow-up. Those that increased their running distance ate more fruit, ran further, were leaner, and gained less weight between baseline and follow-up than other runners and were younger and drank less alcohol if male.

Because incident hypercholesterolemia was similar in those that maintained and those that decreased their usual running distance (Table 1) and was similar for different levels of change in kilometers per day within the declining exercise group (analyses not displayed), we compared incident hypercholesterolemia for those whose running increased to all other runners (Figure 1). Men and women who reported increasing their running distances > 0.5 km/d had significantly lower odds for being diagnosed with high cholesterol. There was no significant difference in the odds reduction for men and women in these analyses ($P = 0.29$ for difference in odds reduction), so sex-adjusted analyses were included for men and women combined. Adjustment for their pre-exercise BMI (i.e., when first began running 12 miles/wk) had little affect on the odds ratios in men {odds ratio (95% confidence interval): 0.80 (0.71– 0.90), $P = 0.001$ }, women {0.70 (0.53–0.92), $P = 0.01$ }, or the combined sexes {0.80 (0.72–0.89), $P = 0.0001$ }; however, the significance levels were made marginal by adjusting for BMI_{exercise} in men ($P = 0.06$) and women ($P = 0.08$). An odds ratio significantly less than 1 was obtained when the sample of men and women were combined and adjusted for both sex and BMI_{exercise} ($P = 0.02$).

Table 2 compares the baseline and follow-up running distances with respect to the odds for incident hypercholesterolemia. Two models are presented, which differ in whether the baseline and the end-of-follow-up running distances are entered separately (Model 2) or re-expressed as their difference and average (Model 1). There were no significant differences in the odds reduction between men and women ($P > 0.80$), and therefore the results were also presented for their combined results adjusted for sex. Under Model 1, change in kilometers-per-day run was significantly related to the odds of developing hypercholesterolemia in men and for the sexes combined with or without adjustment for BMI_{preexercise} but became nonsignificant when adjusted for BMI_{exercise}. Higher average running distance significantly reduced the odds for becoming hypercholesterolemic in both men and women, even when adjusted for BMI_{exercise}.

Under Model 2, significance levels refer to the significance of the end of follow-up kilometers-per-day run when adjusted for baseline distance and the significance of the baseline kilometers-per-day run when adjusted for the end of follow-up distance. In both sexes, the incidence of hypercholesterolemia was inversely and independently related to distance run at both baseline and follow-up. The end-of-follow-up distance had a stronger effect on incident hypercholesterolemia than the baseline distance, and although unaffected by adjustment for BMI_{preexercise}, its significance was diminished by adjusting for BMI_{exercise}. The weaker baseline association was also significant and was unaffected by BMI_{exercise} or BMI_{preexercise} adjustment. Figure 2 (left) displays the runners' odds ratios for the baseline distance adjusted for end-of-follow-up distance and for end-of-follow-up distance adjusted for the baseline distance. The odds of men and women becoming hypercholesterolemic were significantly lower for those who ran ≥ 2 km/d than < 2 km/d at the end of follow-up survey and declined thereafter through ≥ 8 km/d. In both sexes, the odds

were 50% lower at 8 km/d than < 2 km/d. Baseline running distances were more weakly predictive of the odds for becoming hypercholesterolemic than the follow-up distances.

In Table 2, the significance level for the change in kilometers-per-day run in Model 1 is mathematically identical with the significance level for testing whether separate effects for the baseline and follow-up running distances (i.e., Model 2) produce a better fit than their average effect. When there is no adjustment for BMI_{exercise}, the baseline and follow-up running distances have significantly different relationships to incident hypercholesterolemia (significant km/d in Model 1). However, this difference is entirely attributable to BMI_{exercise}. Specifically, when adjusted for BMI_{exercise} there is no improvement for the separate effects over the average kilometers per day in accounting for incident hypercholesterolemia (nonsignificant km/d in Model 1).

The sample included 4034 men and 1897 women whose running distances remained constant between baseline and follow-up (± 0.5 km/d). The logistic regression analyses of these stable runners (Table 3) show that the men and women's odds ratios for incident hypercholesterolemia declined in proportion to their running distance, even in the absence of any change in distance. Adjusting for BMI_{preexercise} produced little change in the odds ratios, whereas adjusting for BMI_{exercise} reduced their effect in both sexes, causing the women's ratio to become nonsignificant. Figure 2 (right) shows that men who consistently ran between 4 and 6, between 6 and 8, and >8 km/d had odds for becoming hypercholesterolemic that were 32%, 57%, and 57% lower, respectively, than men who consistently ran < 2 km/d. The odds for women becoming hypercholesterolemic were 47% lower if they consistently ran between 2 and 4 km/d ($P = 0.02$), 43% lower between 4 and 6 km/d ($P = 0.03$), and 68% lower if they consistently ran 6–8 km/d ($P = 0.02$) compared with those < 2 km/d. Adjustment for BMI_{exercise} eliminated the significance of the women's results.

Data were also analyzed to assess the effects of running distance on the age-related increase in hypercholesterolemia. Figure 3 displays the incidence rates per 1000 person-years. Regardless of age, the incidence of hypercholesterolemia decreased with average reported distance run (marginally for 65–74 yr, $P = 0.06$). Compared with 35- to 44-yr-old men who ran < 2 km/d, men who ran >6 km/d had a lower probability for becoming hypercholesterolemic regardless of their age. The decrease in incidence above 65 yr may be due to most men having been diagnosed before entering this age group and the small sample size for the group.

DISCUSSION

These analyses show that changes in men's and women's running distance were significantly related to the incidence of hypercholesterolemia, which is consistent (but not proof) of a causal relationship. Previously, we have reported that men's distances were inversely related to their prevalence of LDL-cholesterol-lowering medications cross-sectionally (14, 22) and that baseline running distance predicted the rate of incident hypercholesterolemia prospectively (21), but these observations do not necessarily imply causality, that is, both associations could simply reflect an innate preference for individuals

with low LDL-cholesterol to choose to run longer distances. Self-selection on the basis of low cholesterol has not been previously reported; however, other lipoproteins (i.e., high HDL-cholesterol concentrations) have been shown to affect the propensity to run longer distances (24, 27). Self-selection is less likely to account for a decrease in hypercholesterolemia in men and women who increase their running distance, that is, when change is involved. The current results, in conjunction with our two prior reports, are clinically important because vigorous exercise is not currently recognized as a generally effective hygienic approach to the prevention of high cholesterol (11).

The runners' BMI accounted for significant portions of the differences in hypercholesterolemia associated with change in running distance. The effects of weight loss on plasma cholesterol concentrations are well documented (11), and greater body weight seems to increase the risk for hypercholesterolemia even among ostensibly healthy weight individuals (23). In western societies, men and women generally gain weight as they age (2, 13). Running promotes leanness in two ways: 1) the attenuation of the age-related weight gain in proportion to the exercise dose (17) and 2) the acute weight change after increases or decreases in exercise due to changing energy expenditure (25, 26). Exercise consistency may also affect body weight, that is, we have reported that the amount of weight lost by increasing running distance is less than the weight gained by decreasing distance (16). Thus, repeated bouts of increasing and decreasing activity could lead to accumulated weight gain.

The leanness of runners is also due, in part, to lean men and women choosing to run. Pre-exercise BMI accounts for approximately 26% of the BMI difference between high-mileage and low-mileage men and 58% of this difference was in women (18). However, self-selection does not seem to explain the attenuation of the hypercholesterolemia-running relationship when adjusted for BMI_{exercise}. Specifically, the odds for developing hypercholesterolemia were not appreciably affected by adjustment for BMI_{preexercise} (i.e., BMI when the runners began running 12 km/wk).

Not all of the association between vigorous exercise and lower hypercholesterolemia risk was attributable to the runners' leanness. Specifically, adjustment for BMI_{exercise} did not eliminate the significant association between distance run and hypercholesterolemia: 1) when comparing the combined sample of men and women who increased their running > 0.5 km/d with other runners (Fig. 1); 2) when calculating the odds ratio per kilometers per day of average distance run in men, women, and the sexes combined (Table 2; Model 1); 3) when calculating the odds ratios per kilometers per day for baseline and follow-up running distance (Table 2; Model 2); and 4) when calculating the odds ratio per kilometers per day in stable runners (Table 3).

Three ancillary analyses were presented in addition to the primary findings of Figure 1. First, in Table 2, the difference and the average of the baseline and follow-up running distances are considered simultaneously (Model 1). The analyses suggest that there is a greater odds reduction associated with a 1- km/d increment in average running distance (11% reduction) than a 1- km/d increment in the change in running distance (2% reduction). In part, this difference could be the consequence of the greater measurement error for the change variable than the average, in that measurement error will bias the estimates toward

the null hypothesis (12). Second, the baseline and follow-up running distances were included simultaneously as predictors of incident hypercholesterolemia (Model 2), which suggest a somewhat stronger effect of the follow-up distance than the baseline distance. These results differ from those of incident diabetes (19) and hypertension (20) in this cohort, which showed that running distances at baseline were unrelated to the odds for the disease when adjusted for distances at follow-up. The analyses suggested that there are at least two components to the effect of running distance on hypercholesterolemia, one mediated by BMI_{exercise} that has a more immediate effect on elevating cholesterol and one producing a more long-term effect on elevating cholesterol that is independent of BMI_{exercise} . This second component could reflect long-term effects of prior vigorous exercise, other genetic, behavioral, or environmental factors that remain relatively constant during the follow-up, which affect both distance run and cholesterol levels (e.g., high-fat or high-cholesterol diet), or effects due to self-selection. Third, we restricted the analyses to runners who did not change their running distance during the study to show that the dose of exercise affected the odds for becoming hypercholesterolemic independent of exercise change. The consistent runners represent the idealized prospective cohort design in which the exposure to the risk factor does not change over time.

Caveats

There are important limitations of these analyses that warrant recognition. Men and women who run regularly may differ from others genetically, socioeconomically, psychologically, and with respect to other health behaviors. However, we expect that the biological processes that relate hypercholesterolemia to changes in exercise and adiposity to be similar in runners and non-runners. Although we adjusted for weekly servings of meat, fish, fruit, and alcohol, these outcome measures do not adequately characterize dietary cholesterol, saturated fat, or total fat intake, which are known to influence cholesterol levels (11). The analyses are based on self-reported running distances and physician diagnosis of hypercholesterolemia, which, despite their validation and use in other epidemiological studies (1), could bias the results. Participants did not report the month of their high-cholesterol diagnoses at follow-up, and therefore it is not known whether seasonal variations in cholesterol levels contributed to the differences in incident hypercholesterolemia with running distance (6). We do not believe that the decline in hypercholesterolemia with increasing distance is due to fewer opportunities for diagnosis in the more athletic men. The Health Professionals Study reported that their more vigorously active participants had more routine medical checkups than less active men (8), and there was no difference in routine medical checkup by activity level in the Nurses' Health Study (9).

In summary, these data suggest that promoting vigorous exercise may be more efficacious in preventing hypercholesterolemia than currently acknowledged by the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). It recommends moderate amounts of moderate-intensity physical activity as part of a therapeutic lifestyle change to favorably affect metabolic syndrome, lower triglycerides, and increase high-density lipoproteins (11). The report states that the efficacy of LDL-cholesterol lowering by exercise is limited to some individuals. Our data suggest that increases in vigorous physical activity may postpone

or eliminate the need for LDL-cholesterol-lowering medications thereby both improving the person's quality of life and reducing the economic cost to society. Moreover, vigorous physical activity can be advocated and more readily embraced at a much earlier age than medications. This is important because LDL-cholesterol lowering produces substantially greater CHD risk reductions when started earlier in life (7). The prevention of hypercholesterolemia by vigorous exercise is in part due to the prevention of the tendency for men and women to gain weight as they age, particularly when begun during early adulthood.

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FIGURE 1.

Odds ratio for incident hypercholesterolemia in 4035 men and 1897 women who increased their running distance >0.5 km/d compared with 20,363 men and 8128 women whose running distance-remained constant or decreased during 7.7 yr of follow-up. Odds ratios adjusted for the mean age, follow-up duration, and reported intakes of meat, fish, fruit, and alcohol. Additional adjustment for BMI_{exercise} (both baseline and end-of-follow-up BMI) as indicated.

FIGURE 2.

Odds ratio for incident hypercholesterolemia by baseline and follow-up running distance in all 24,397 men and 10,025 women (left) and by average running distance in 4685 men and 1904 women whose running distance remained within ± 0.5 km/d between baseline and follow-up (right). Odds ratios adjusted for the mean age, follow-up duration, and reported intakes of meat, fish, fruit, and alcohol. Additional adjustment as indicated. Brackets represent 95% confidence intervals. Significant odds reductions relative to the least active runners ($< \text{km/d}$) are coded as follows: *P 0.05, †P 0.01, ‡P 0.001, §P 0.0001.

FIGURE 3.

Incidence of hypercholesterolemia by age classes stratified by the average reported running distance (km/d) at baseline and the end of follow-up in men between 18 and 75 yr. Brackets represent $\pm$ SE.

TABLE 1

Characteristics of runners who increased, maintained, and decreased their reported running distance.

	Change in daily running distance (km/d) between baseline and follow-up			
	Increased (>0.05)	Maintained (0.5 to -0.5)	Decreased (-0.05)	ANOVA (P)
Males				
Sample size	4034	4685	15,678	
Incident hypercholesterolemia (%)	9.54±0.46	12.27±0.48	13.36±0.27	<0.0001
Age (yr)	42.94±9.86 ^{*†}	44.90±10.08 [†]	44.22±10.47	<0.0001
Education (yr)	16.59±2.45 ^{*†}	16.69±2.41 [†]	16.43±2.45	0.0001
Follow-up duration (yr)	7.42±1.83 [†]	7.48±1.83 [†]	8.01±1.75	0.0001
Distance run (km/d) ^a	2.28±2.06 ^{*†}	-0.04±0.24 [†]	-3.26±2.42	0.0001
Average distance run (km/d)	5.29±2.99 ^{*†}	4.06±2.87 [†]	4.52±2.77	0.0001
BMI(kg/m ²) ^a	0.44±1.40 ^{*†}	0.78±1.41 [†]	1.44±1.79	0.0001
Average BMI (kg/m ²) ^b	24.05±2.62 ^{*†}	24.44±2.73	24.50±2.78	0.0001
Meat (servings/wk) ^a	0.14±2.55 [†]	0.24±2.62 [†]	0.45±2.79	0.0001
Average meat (servings/wk) ^b	2.92±3.28	3.04±3.25	2.96±3.32	0.22
Fish(servings/wk) ^a	0.10±1.60	0.04±1.54	0.06±1.83	0.27
Average fish (servings/wk) ^b	1.56±1.26	1.56±1.27	1.55±1.32	0.95
Fruit (pieces/wk) ^a	0.21±8.70 [†]	-0.14±7.94 [†]	-1.18±8.67	0.0001
Average fruit (pieces/wk) ^b	11.05±7.97 ^{*†}	10.56±7.42	10.56±7.53	0.0009
Alcohol (mL/wk) ^a	7.77±89.95	8.20±90.48	10.20±94.35	0.20
Average alcohol (mL/wk) ^b	77.58±99.80 ^{*†}	87.57±109.23	86.50±107.40	0.0001
Females				
Sample size	1897	1904	6224	
Incident hypercholesterolemia (%)	3.53±0.42	6.09±0.55	5.40±0.29	<0.0001
Age (yr)	37.55±9.14 ^{*†}	39.70±9.71 [†]	38.02±9.95	0.0001
Education (yr)	15.92±2.34	15.98±2.36 [†]	15.88±2.35	0.27
Follow-up duration (yr)	7.33±2.02 [†]	7.22±2.05 [†]	7.71±2.02	0.0001
Distance run (km/d) ^a	2.37±1.99 ^{*†}	-0.04±0.25 [†]	-3.13±2.23	0.0001
Average distance run (km/d)	5.21±2.78 ^{*†}	4.02±2.88 [†]	4.26±2.63	0.0001
BMI (kg/m ²) ^a	0.40±1.44 ^{*†}	0.77±1.67 [†]	1.18±2.03	0.0001
Average BMI (kg/m ²) ^b	21.29±2.36 ^{*†}	21.87±2.82	21.78±2.61	0.0001
Meat (servings/wk) ^a	0.22±2.32 [†]	0.25±2.04 [†]	0.41±2.22	0.0006
Average meat (servings/wk) ^b	1.33±1.66 [*]	1.46±1.96 [†]	1.35±1.70	0.05
Fish (servings/wk) ^a	0.18±1.55	0.15±1.38	0.19±1.77	0.76

	Change in daily running distance (km/d) between baseline and follow-up			
	Increased (>0.05)	Maintained (0.5 to -0.5)	Decreased (-0.05)	ANOVA (P)
Average fish (servings/wk) ^b	1.39±1.29 [*]	1.28±1.06 [†]	1.35±1.21	0.02
Fruit (pieces/wk) ^a	-0.05±10.32 [†]	0.31±8.95 [†]	-0.93±8.17	0.0001
Average fruit (pieces/wk) ^b	11.69±7.53 ^{*†}	11.05±6.90	11.09±6.72	0.003
Alcohol (mL/wk) ^a	10.32±59.36	9.22±68.59	10.71±70.81	0.71
Average alcohol (mL/wk) ^b	49.46±65.88 ^{*†}	54.34±71.47	54.12±70.49	0.03

All values are presented as means ±SD except incident hypercholesterolemia, which is presented as percent ±SE.

^a Follow-up minus baseline survey values.

^b Average of the baseline and follow-up survey values.

^{*} Significantly different (P = 0.05) from maintained.

[†] Significantly different (P = 0.05) from decreased

TABLE 2

Odd ratios (95% confidence intervals) of incident hypercholesterolemia by running distance.

	Model 1		Model 2	
	km/d	Average km/d	Baseline km/d	Follow-up km/d
Males				
Unadjusted for BMI	0.98 [*] (0.96–0.99)	0.89 [§] (0.87–0.90)	0.97 [§] (0.95–0.98)	0.92 [§] (0.91–0.94)
Adjusted for BMI _{preexercise}	0.98 [†] (0.97–0.99)	0.89 [§] (0.88–0.91)	0.97 [§] (0.95–0.98)	0.93 [§] (0.91–0.94)
Adjusted for BMI _{exercise}	0.99(0.98–1.01)	0.93 [§] (0.91–0.94)	0.97 [†] (0.95–0.99)	0.95 [§] (0.94–0.97)
Females				
Unadjusted for BMI	0.98 (0.95–1.02)	0.89 [§] (0.85–0.92)	0.96 [*] (0.92–1.00)	0.93 [†] (0.89–0.97)
Adjusted for BMI _{preexercise}	0.99(0.95–1.02)	0.89 [§] (0.85–0.92)	0.96 [*] (0.92–0.99)	0.93 [†] (0.89–0.97)
Adjusted for BMI _{exercise}	1.00 (0.97–1.04)	0.92 [§] (0.88–0.96)	0.96 [*] (0.92–1.00)	0.96 [*] (0.92–1.00)
Combined, adjusted for sex				
Unadjusted for BMI	0.98 [†] (0.97–0.99)	0.89 [§] (0.88–0.90)	0.96 [§] (0.95–0.98)	0.92 [§] (0.91–0.94)
Adjusted for BMI _{preexercise}	0.98 [†] (0.97–0.99)	0.89 [§] (0.88–0.91)	0.96 [§] (0.95–0.98)	0.93 [§] (0.91–0.94)
Adjusted for BMI _{exercise}	0.99 (0.98–1.01)	0.93 [§] (0.91–0.94)	0.97 [§] (0.95–0.98)	0.96 [§] (0.94–0.97)

Models 1 and 2 represent two approaches to entering the baseline and follow-up distances into the model, either separately as recorded or reexpressed as their difference and average.

Odds ratios were adjusted for the mean age, follow-up duration, and reported intakes of meat, fish, fruit, and alcohol. Additional adjustments for BMI_{preexercise} (i.e., when they began running 12 mi/wk) and BMI_{exercise} (both at baseline and end-of-follow-up BMI) are indicated.

Significance levels coded:

* P 0.05;

† P 0.01;

‡ P 0.001; and

§ P 0.0001.

TABLE 3

Odds ratio (95% confidence interval) of incident hypercholesterolemia per kilometers-per-day run in 4034 male and 1897 female runners who maintained their distance run ± 0.5 km/d between baseline and follow-up.

	Males	Females	Combined, Adjusted for Sex
Unadjusted for BMI	0.90 [§] (0.86–0.93)	0.91 [*] (0.84–0.98)	0.90 [§] (0.87–0.93)
Adjusted for BMI _{preexercise}	0.90 [§] (0.86–0.93)	0.92 [*] (0.84–0.99)	0.90 [§] (0.87–0.93)
Adjusted for BMI _{exercise}	0.94 [‡] (0.90–0.97)	0.96(0.89–1.04)	0.94 [‡] (0.91–0.97)

Adjustments for age, follow-up duration, and reported intakes of meat, fish, fruit, and alcohol are shown. Additional adjustments for BMI_{preexercise}(i.e., when they began running mi/wk) and BMI_{exercise} (both at baseline and end-of-follow-up BMI) are indicated.

Significance levels coded:

* P 0.05;

‡ P 0.01;

‡ P 0.001;

§ P 0.0001.