MINIREVIEW

Effects of Exercise on Plasma Lipids and Lipoproteins of Women (43644)

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Abstract. **This review summarizes the cross-sectional and training studies (acute and chronic) that have examined the relationship between exercise and plasma lipid and lipoproteins in women. Because women experience major fluctuations in reproductive hormones throughout the life cycle, the effects of the endogenous sex steroid status on the association between exercise and plasma lipoproteins also are addressed. In general, cross-sectional studies report a positive association between exercise and high density lipoprotein-cholesterol (HDL-C) in both pre- and postmenopausal women. Women on hormone replacement therapy who report exercising have higher HDL-C than sedentary women on hormone replacement therapy. Results from longitudinal training studies have been inconsistent because of experimental design, i.e., inadequate type, duration, and intensity of exercise intervention, lipid measurements made across the menstrual cycle, and studies carried out in women with high baseline HDL-C. Since lipids vary approximately 10–25% throughout the menstrual cycle, menstrual phase should be controlled when determining lipid changes after an exercise intervention. In approximately half of the intervention studies, an increase in HDL-C was demonstrated; the magnitude of the response that can be expected is ≈10%. The responsiveness of pre- versus postmenopausal women to an exercise intervention is unknown. Studies are needed to clarify the interactive effects of exercise and sex hormones on plasma lipoproteins in women of all ages. This information will be useful in developing intervention programs to reduce the risk of coronary heart disease in women.**

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Cardiovascular disease is the leading cause of death in the United States. The most serious and common form of cardiovascular disease is coronary heart disease (CHD) (1). Approximately 50% of cardiovascular disease deaths in women are the result of CHD (2). Estimates indicate that about 100,000 of these CHD-related deaths in women occur before they reach their projected life expectancy (3). Contrary to public perception, CHD is a disease that afflicts a major proportion of both men and women.

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In comparison to men, women are somewhat protected against CHD during the premenopausal years (Fig. 1). Thereafter, the incidence of myocardial infarction, one manifestation of CHD, increases. Women, 45–64 years of age, have one third the rate of CHD seen in men of the same age. After age 65, the rate of CHD for women increases and approximates that observed for men 45–64 years of age (4). In general, women develop CHD 10 years later than men. Despite this, the morbidity associated with CHD is much greater for women than men (5).

Along with age and gender, other CHD risk factors have been identified. It is well established that both an elevated low density lipoprotein-cholesterol (LDL-C) and a low high density lipoprotein-cholesterol (HDL-C) are powerful risk factors for the development of

CHD (6, 7). HDL-C was the strongest predictor of CHD in women in the Framingham (8), Lipid Research Clinics (9), and Donolo-Tel Aviv studies (10). Other CHD risk factors for women include diabetes (11), hormonal status (12–14), simultaneous use of oral contraceptive agents and cigarettes (15), and education level (16).

The hormonal changes that occur as a result of menopause affect the risk of CHD. For example, the incidence of CHD is higher in postmenopausal women compared with premenopausal women. This relationship exists even after controlling for age and other risk factors (8, 10, 12–14). The change in CHD risk that occurs with menopause is associated with a reduction in HDL-C and an elevation in LDL-C (17, 18). Since population studies have shown that HDL-C (8–10) and triglyceride levels (19) are the best predictors of CHD in women, interventions that alter these plasma lipids can potentially decrease CHD risk. Data from the Lipid Research Clinics Follow-up Study suggest that increasing HDL-C with hormone replacement therapy is associated with a decrease in cardiovascular mortality (9).

A sedentary lifestyle is another significant risk factor for CHD (20). Using 1988 Behavioral Risk Factor Surveillance System data, the Centers for Disease Control assessed the prevalence of a sedentary lifestyle at 58%, which is higher than smoking (25%), obesity (22%), hypertension (17%), and diabetes (5%) (21). In the 13 states studied, the percentage of CHD deaths that were attributed to a sedentary lifestyle ranged between 29% and 40% (21). An estimated 38% of all women ages 19 and older engage in regular physical activity (22). Moreover, despite a recent emphasis on exercise, the level of physical activity has not changed in women from 1978 to 1985 (22).

The association between lack of physical activity and the incidence of CHD has been recognized since the 1950s (23). More recently, many epidemiological investigations have reported significant relationships between (i) physical activity and CHD risk factors (24–28), (ii) physical activity and all-cause mortality (29, 30), and (iii) physical fitness levels and CHD mortality (29, 31, 32). These studies suggest that an increase in the level of physical activity could reduce the incidence of CHD.

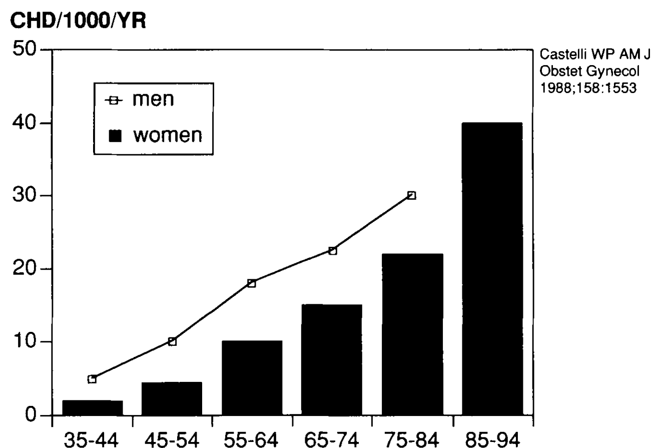

Figure 1. The relationship between age and the incidence of coronary heart disease in men and women (annual rate in Framingham study).

Physical activity or exercise may reduce CHD mortality by favorably altering the plasma lipoprotein profile. Numerous investigators have examined the effects of exercise on plasma lipoproteins. Although the majority of studies have been done with men, some have been conducted with women. However, the effects of exercise in women are less clear because there are fewer studies and the results are more variable. Thus, the purpose of this Minireview is to summarize the studies that have examined the effects of exercise on plasma lipids and lipoproteins, especially HDL-C, in women. The central question is whether exercise can favorably modify plasma lipoprotein profiles and thereby reduce the risk of CHD in women. This information will be useful in developing effective intervention strategies to reduce CHD risk in women.

To date, while there have been a number of studies that have examined the relationship between exercise and plasma lipoproteins in women, few of these have evaluated hormonal influences. In particular, the studies that have been conducted have not examined (i) the effects of the menstrual status, e.g., presence of menstruation (premenopausal) versus absence of menstruation (postmenopausal or amenorrheic), and (ii) the effects of menstrual phase, i.e., the time during the menstrual cycle when blood samples are collected. Because of the relationship between menstrual status and plasma lipoproteins, this will be addressed first in our Minireview.

Relationship Between Menstrual Status and Plasma Lipids and Lipoproteins

Premenopausal Women. Designing studies to evaluate the effects of exercise on plasma lipids of women presents a unique problem. Unlike men, premenopausal women have cyclical changes in serum lipids that have been attributable to fluctuations in endogenous sex steroid levels. Most investigators have found that plasma total cholesterol concentrations begin to rise through the menstrual phase, then peak in the late follicular or ovulatory phase (Fig. 2). After ovulation, plasma total cholesterol concentrations continue to decline until the late luteal or menstrual phase (33–38). In the follicular phase, plasma total cholesterol concentrations are 8–10% higher than in the luteal phase (33, 35, 36).

HDL-C has been shown to increase at ovulation (39), be higher in the luteal phase compared with the

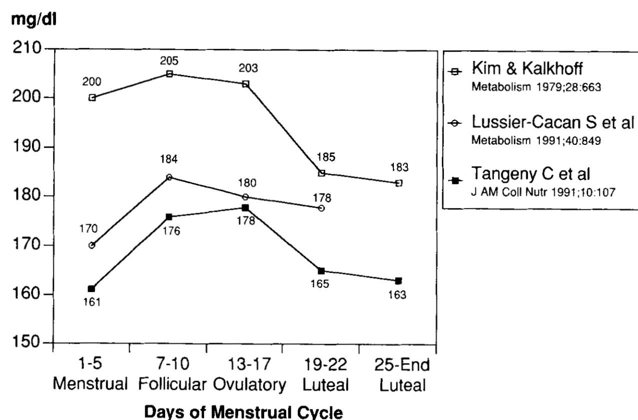

Figure 2. The relationship between stage of menstrual cycle and total cholesterol levels. The numbers on the horizontal axis refer to days of the menstrual cycle.

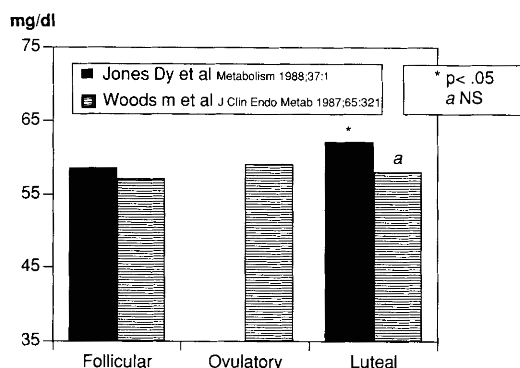

Figure 3. The effects of menstrual cycle on HDL-C levels.

follicular phase (35), or remain constant across phases (Fig. 3) (33, 40). Apolipoprotein (apo) A-I, the major apolipoprotein in HDL, is significantly higher in the follicular, ovulatory, and luteal phases compared with the menstrual phase (36). Triglyceride concentrations have been shown to increase at ovulation (33, 40), be lower in the late luteal versus early luteal phase (34), be higher in the midfollicular phase only when subjects are on a low fat diet (35), or not change throughout the cycle (36). Other investigators, however, have not observed any significant change in lipids and lipoproteins during the menstrual cycle (41–43). The variable results from these studies could be due to (i) the method used to characterize the menstrual cycle and time of measurement within a phase, (ii) differences in laboratory methods for estimating lipoproteins, (iii) a small sample size with insufficient power to detect differences, and (iv) only measuring lipoproteins during one menstrual cycle even though intraindividual variability is high. More studies are needed to confirm the magnitude of change in lipids across the menstrual cycle and how these changes can be modified by an exercise program.

Postmenopausal Women. At menopause, women experience a change in their lipoprotein profile that increases their risk of CHD: plasma total cholesterol and LDL-C increase and HDL-C decreases (12). In a prospective study, Matthews *et al.* (17) demonstrated that natural menopause was associated with a reduction in HDL-C concentrations and an increase in LDL-C concentrations after controlling for age, smoking, and adiposity. It appears that the hypoestrogenemic status of surgical or natural menopause may adversely affect lipid metabolism. The question remains of whether exercise intervention programs that improve the lipid profile will offset the atherogenic lipoprotein profile observed postmenopausally. When conducting studies in women, both the phase of the menstrual cycle and the menopausal status should be controlled.

Physical Activity and Plasma Lipids and Lipoproteins

Cross-Sectional Studies. Whether relationships are observed in cross-sectional studies can simply reflect the sensitivity of the methods used to collect the data. For example, various methods can be used to assess activity and fitness levels. Activity logs, questionnaires, and motion sensors can be used to measure physical activity, while fitness levels can be determined by more objective measures, such as maximal oxygen consumption (44). Cauley *et al.* (45) found that the method used to assess activity affected the activity/HDL-C relationship. Physical activity as determined by motion sensors was positively related to HDL-C and HDL_2-C ($r = 0.22$ and $r = 0.19$, respectively) and unrelated to HDL_3-C. However, the number of kilocalories expended/week as determined by the Paffenbarger Index was only related to HDL_3-C ($r = 0.15$) (45).

Many cross-sectional studies with women have shown that the level of exercise, fitness, or activity is associated with higher HDL-C and lower LDL-C levels in both pre- and postmenopausal women (Table I). Female runners consistently have higher HDL-C levels than controls (46, 50, 52, 53) or joggers (49). Overall, LDL-C is 9–24% lower and HDL-C levels are 17–36% higher in women who report high activity or fitness levels. In the Lipid Research Clinics Program Prevalence Study, HDL-C was approximately 5 mg/dl higher in active women (classified by treadmill test and self-reported strenuous physical activity) ages 20–39 years, and 5.4 mg/dl higher in active women ages 40–59 years (47). Menopausal status was not controlled in this study.

In epidemiological studies, HDL-C concentrations have been correlated with the level of leisure activity expressed as caloric expenditure. Owens and co-workers (57) reported that premenopausal women (n = 533) who expended at least 1000 kcal/week on leisure activities had a significantly higher HDL-C and a lower body mass index (BMI) than women who reported fewer

Table I. Relationship Between Exercise and Lipoproteins in Women: Cross-Sectional Studies

Author (ref.)	Subjects	*n*	Age (yr)	Study design	Results (mg/dl)			
						LDL-C		HDL-C
Menopausal status not mentioned								
Wood et al., 1977 (46)	Runners	43	42	Runners: Ran at least 15 miles/wk for an average of 3 yr	Runners	113 ± 33[a]		75 ± 14[a]
	Controls	101	42	Controls: Sedentary women	Controls	124 ± 34[b]		56 ± 14[b]
Haskell et al., 1980 (47)	Inactive/ active	2067	20–69	Treadmill tests: Self-reported activity levels				
						HDL-C		
						Inactive		Active
					20–29 yr	54 ± 14[a]		58 ± 14[b]
					30–39 yr	55 ± 13[a]		58 ± 15[b]
					40–49 yr	58 ± 15		63 ± 21
					50–59 yr	61 ± 17		62 ± 14
					60–69 yr	58 ± 15		75 ± 26
Gibbons et al., 1983 (48)	Women with varying fitness level	1700	18–65	Physical fitness categories were:		HDL-C (adjusted values)		
				0–15% = very poor;		56		
				15–35% = poor;		54		
				35–65% = fair;		57		
				65–85% = good;		58		
				85–95% = excellent;		59		
				95–100% = superior		60		
					Using multiple linear regression modeling to control for the effects of age, weight, and year of exam, physical fitness was independently and significantly associated with HDL-C			
						TC	HDL-C[1]	LDL-C
Premenopausal women								
Moore et al., 1983 (49)	Long distance runners	45	39	Runners: Ran ≥26 miles/week 6 mo before study	Runners	185 ± 28	78 ± 17[a]	95 ± 22
	Joggers	49	39	Joggers: Jogged ≥6 miles/wk 6 mo before study	Joggers	182 ± 28	70 ± 22[b]	97 ± 13
	Controls	47	39	Inactive	Control	179 ± 32	62 ± 13[b]	101 ± 28
						TC	LDL-C	HDL-C
Stamford et al., 1984 (50)	Chronic joggers or runners	42	35	Fitness level determined by a modified Balke physical work capacity test	High activity	198 ± 7[a]	114 ± 7[a]	70 ± 3[a]
	Sedentary	66	35		Low activity	204 ± 5[a]	126 ± 5[b] ($P < 0.10$)	60 ± 2[b]
						TC[2]		HDL[2]
Upton et al., 1984 (51)	Middle-aged marathoners (MAM)	42	38	MAM: Subjects had been running for 6 yr, with an average of 74 km/wk for the previous 6 mo	MAM	176 ± 26[a]		64 ± 8[a]
	Young marathoners (YM)	25	9	YM: Subjects had been running an average of 5 yr, 89 km/wk for previous 6 mo	YM	169 ± 24[a]		66 ± 5[a,b]
	Middle-aged 10-km runners (MAR)	33	10	MAR: Subjects had never raced distances greater than 10 km; women had been running 3.5 yr, averaging 40 km/wk	MAR	166 ± 24[a]		55 ± 8[a,b]
	Middle-aged sedentary women (MAC)	39	37	MAC: Subjects had not performed any regular aerobic exercise for at least the past 5 yr	MAC	206 ± 38[b]		56 ± 14[b]
						TC	LDL-C	
Hartung et al., 1986 (52)	Runners	18	42	Runners: Currently jogging 34 miles/wk and at least 20 miles/wk for 6 mo before the study	Runners	175 ± 34[a]	88 ± 24[a]	
	Controls	18	39	Controls: Sedentary women	Controls	192 ± 46[a]	116 ± 50[b]	

—Table I continues

Table I. —Continued

Author (ref.)	Subjects	*n*	Age (yr)	Study design	Results (mg/dl)			
						HDL-C	HDL_2C	apoA-1
					Runners	74 ± 21[a]	34 ± 17[a]	158 ± 26[a]
					Controls	60 ± 14[b]	19 ± 12[b]	150 ± 43[a]
						TC		HDL-C
Morgan et al., 1986 (53)	Runners	9	36	Runners: Ran 38 miles/wk during the preceding year	Runners	182 ± 24[a]		72 ± 12[a]
	Weight trainers	19	27	Weight trainers: Trained 3 times/wk; duration varied from 60 to 224 min	Weight trainers	180 ± 20[a]		56 ± 5[b]
	Controls	9	34	Controls: Sedentary women	Controls	183 ± 21[a]		58 ± 14[b]
Meilahn et al., 1988 (54)	Premenopausal women	541	47	Leisure time physical activity was estimated using the Paffenbarger questionnaire Women were categorized into quartiles based on cal expended/week on physical activity: 0–499 kcal; 500–999 kcal; 1000–1999 kcal; ≥2000 kcal	Using stepwise multiple regression analysis, physical activity was not independently associated with the lipid parameters measured (LDL-C, HDL_2-C, and HDL_3-C)			
							TC	
Lamon-Fava et al., 1989 (55)[3]	Amenorrheic runners (AR)	9	25	AR: Ran 36 miles/wk and had no menses during the prior 12 months	AR ER C		4.8 ± 0.9[a] 4.4 ± 0.7[a] 4.8 ± 0.8[a]	
							apoA-1	
	Eumenorrheic runners (ER)	16	29	ER: Ran 40 miles/wk and were normally menstruating	AR ER C		1.4 ± 0.2[a] 1.6 ± 0.2[a] 1.5 ± 0.3[a]	
						ApoB		apoA-1:apoB
	Controls (C)	36	28	Inactive	AR ER C	0.6 ± 0.2[a] 0.5 ± 0.1[a] 0.7 ± 0.2[b]		2.6 ± 0.7[a] 3.2 ± 0.5[b] 2.2 ± 0.8[c]
						LDL-C		HDL-C
Kaiserauer et al., 1989 (56)	AR	8	27	AR: Ran 39 miles/wk	AR	89 ± 1[a]		64 ± 4[a]
	ER	9	26	ER: Ran 31 miles/wk	ER	67 ± 5[b]		61 ± 4[a]
	C	7	22		C	79 ± 4[a,b]		48 ± 4[b]
Owens et al., 1990 (57)	Same subjects as Ref. 54	541	47	Same study design as Ref. 54	Using univariate analysis, there was a threshold effect of exercise reported. Women who reportedly expended ≥1000 kcal/wk on physical activity had a higher HDL-C (57 vs 61 mg/dl). Women who reported ≥2000 kcal/wk of physical activity had a significantly lower TC (~4%) and LDL-C (~9%) and a higher HDL_2-C (~26%)			
Postmenopausal women								
Cauley et al., 1986 (45)	Postmenopausal women	255	58	Using the Large Scale Integrated Activity Monitor, subjects were categorized into 5 different quintiles of physical activity	Total HDL-C and HDL_2-C were higher (~8 mg/dl for each) only in the group with the highest activity level			
				Using the Paffenbarger Harvard Alumni Survey, subjects were categorized into tertiles for activity level	Physical activity was a significant predictor of HDL_3-C			
						TC	HDL-C[4]	LDL-C
Reaven et al., 1990 (58)	Exercise/no exercise	1273	70	Risk factor screening survey part of LRC Prevalence Program; Self-reported exercise	Regular exercise	232	72[a]	137
					No regular exercise	228	68[n]	138

—Table I continues

Table I. —Continued

Author (ref.)	Subjects	*n*	Age (yr)	Study design		Results (mg/dl)	
						HDL-C	LDL-C[5]
Comparing premenopausal to postmenopausal							
Hartung et al., 1984 (59)	Premenopausal inactive (PI)	31	34	Level of jogging/running was not specifically defined	PI	67[a]	94
	Premenopausal joggers (PJ)	34	38		PJ	70[b]	96
	Premenopausal long distance runners (PL)	34	37		PL	72[b]	100
	Postmenopausal inactive (I)	14	50		I	62[a]	108
	Postmenopausal joggers (J)	13	46		J	74[b]	100
	Postmenopausal long distance runners (L)	10	47		L	80[b]	94
						TC	HDL-C
Rainville and Vaccaro, 1984 (60)	Premenopausal runners (pre-R)	10	44	Pre-R: Ran 25–75 miles/wk for a minimum of 3 yr	Pre-R	188 ± 19[a]	74 ± 16[a]
					Pre-C	206 ± 46[a]	62 ± 11[a]
	Premenopausal controls (pre-C)	10	46	Pre-C: Did not participate in any form of regular exercise		[6]	
	Postmenopausal runners (post-R)	10	56	Post-R: Ran 25–65 miles/wk for minimum of 3 yr	Post-R	216 ± 39[a]	74 ± 18[a]
					Post-C	241 ± 43[a]	56 ± 14[b]
						LDL-C	
	Postmenopausal controls (post-C)	10	57	Post-C: Did not participate in any form of regular exercise	Pre-R	115 ± 18[a]	
					Pre-C	144 ± 21[b] [6]	
					Post-R	141 ± 40[a]	
					Post-C	185 ± 41[b]	

Note. Means sharing different superscripts differ at the $P < 0.05$ level unless otherwise noted.
[1] Significantly different from joggers and controls, $P < 0.001$.
[2] NS after covariance for body mass index.
[3] Lipid values are mmol/liter; apoA-1 is g/liter.
[4] Significantly different at $P < 0.001$, remained after adjustment for age, alcohol, cigarettes, estrogen and WHR.
[5] There was a significant effect of menopausal status across all exercise groups.
[6] $P < 0.05$ post-C versus pre-C.

activities. Women who reported expending 2000 kcal/week had the additional benefit of significantly lower total cholesterol, triglyceride, and LDL-C levels and a higher HDL_2-C level. Similarly, Meilahn *et al.* (54) found that women with the highest reported caloric expenditure (>2000 kcal/week) had an HDL_2-C concentration that was approximately 4 mg/dl higher ($P < 0.001$), an LDL-C concentration that was 10 mg/dl lower ($P < 0.01$), and similar HDL_3-C concentrations as less active women. In the multivariate analyses, however, energy expended on activities was not an independent predictor of the HDL subfractions, perhaps because activity level was highly confounded with BMI, which remained a significant predictor. Upton *et al.* (51), using covariate analysis, reported that differences in BMI accounted for the significantly higher HDL-C in female marathon runners compared with sedentary control subjects.

In contrast, three other investigators have shown that the exercise-HDL-C relationship is maintained between sedentary and physically active subjects after adjusting for differences in body weight and body composition. Moore *et al.* (49) reported that HDL-C concentrations were significantly higher in long distance runners (78 mg/dl) versus joggers (70 mg/dl) or inactive controls (62 mg/dl). Both distance run and percentage body fat were independent predictors of HDL-C in all of the groups. When the data were adjusted for these variables, the association between HDL-C and activity level remained. Similarly, Haskell *et al.* (47) found that HDL-C concentrations were higher in active women even after covariate adjustment for BMI. Cauley *et al.* (45) also noted that BMI and sport activity were independent predictors of HDL-C. In this large cohort study, however, BMI was the strongest predictor of HDL-C. Taken together, these studies suggest that there is, in fact, an independent effect of exercise on HDL-C; however, this relationship may not be as strong as that observed between body weight and HDL-C. This likely accounts for the inconsistencies in the cross-sectional studies that have examined the independent relationship between exercise and HDL-C. These find-

ings underscore the limitations of cross-sectional studies in establishing the independent effects of exercise on plasma lipids and lipoproteins. Longitudinal studies are necessary to clarify the causal relationship between exercise and HDL-C without the confounding effects of body weight.

Several cross-sectional studies (45, 49–60) have examined the relationship among menstrual status, exercise, and plasma lipids, lipoproteins, and apolipoproteins. In premenopausal women, both exercise level and menstrual status affect plasma lipids and apolipoproteins. Lamon-Fava *et al.* (55) found that normally menstruating runners had plasma cholesterol and triglyceride concentrations that were 7.6% and 25.4% lower, respectively, than control women. Amenorrheic runners had lipid profiles comparable to the controls except that apoB was 20% lower. The apoA-I to apoB ratio was significantly lower in the amenorrheic runners than the eumenorrheic runners. Thus, the adverse effects of amenorrhea on the apoA-I to apoB ratio were not improved by high activity levels. Kaiserauer *et al.* (56) also found that amenorrheic runners had higher LDL-C than the regularly menstruating group. HDL-C was similar in the amenorrheic and eumenorrheic groups. Regardless of menstrual function, runners had higher HDL-C than eumenorrheic sedentary controls.

In postmenopausal women, "sport activity" (45) or "regular exercise" (58) was associated with higher HDL-C concentrations. Reaven *et al.* (58) found that women who reported engaging in strenuous exercise had significantly higher HDL-C than nonexercisers after controlling for age, alcohol, cigarettes, estrogen use, and BMI. Using exogenous estrogens shifted the HDL-C curve upward (see Fig. 4). However, there still appears to be a response to exercise because HDL-C concentrations were higher in those reporting light or moderate exercise compared with sedentary controls. For women who were not taking estrogen, the increase in HDL-C was greatest between the sedentary and light activity categories; increasing activity from light to moderate or heavy was not associated with any incremental change in HDL-C.

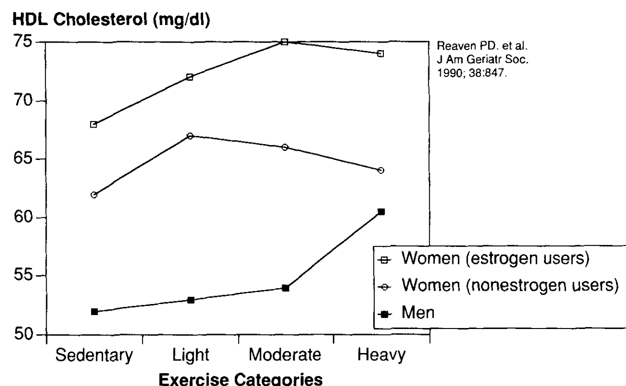

Figure 4. The relationship between exercise intensity and HDL-cholesterol levels in men and women.

Two studies compared plasma lipid and lipoproteins with menopausal status in female runners (59, 60). Hartung *et al.* (59) found that HDL-C was higher in both exercising (long distance runners or joggers) premenopausal and postmenopausal women compared with inactive women. Furthermore, there was no difference in HDL-C between premenopausal and postmenopausal women who exercised. There was, however, a significant interaction between menopausal status and exercise and the HDL-C to LDL-C ratio. In premenopausal women, exercise had no effect on the ratio (0.71–0.73 between groups), whereas in postmenopausal women, the ratio improved as the level of exercise increased (from 0.57 in inactive women to 0.85 in runners, $P < 0.01$). Because of this interaction, it has been suggested that postmenopausal women exhibit a greater response to exercise (61); this hypothesis warrants further investigation. In a study conducted by Rainville and Vaccaro (60), postmenopausal trained runners had higher HDL-C (74 mg/dl vs 56 mg/dl), lower LDL-C (141 mg/dl vs 185 mg/dl), and a higher HDL-C to LDL-C ratio (0.57 mg/dl vs 0.32 mg/dl) than sedentary postmenopausal women. In premenopausal runners, only LDL-C was significantly different from control subjects (115 mg/dl vs 144 mg/dl, respectively). Hence, exercise appeared to attenuate the age-related increase in LDL-C and prevent the age-related decrease in HDL-C (Table I).

Taken together, the cross-sectional studies suggest that premenopausal and postmenopausal women who choose a more active lifestyle can have a less atherogenic plasma lipoprotein profile. The differences observed are of sufficient magnitude to beneficially affect CHD morbidity and mortality in women of all ages. These findings are potentially important and provide a strong basis for longitudinal studies that identify the most appropriate exercise regimen for women of all ages.

Exercise Training Studies. Because of the lack of experimental control in cross-sectional studies, well-designed longitudinal studies are essential to increase our understanding of how exercise affects plasma lipids and lipoproteins in women. These studies have provided important information about the chronic effects of exercise of varying intensity and duration on the plasma lipids and lipoproteins of different female populations. Some investigators also have examined the acute effects of exercise on plasma lipids and lipoproteins of women. Perhaps the greatest benefit of acute studies is that they increase our understanding of the mechanism(s) that regulates the lipoprotein response to exercise. A better understanding of the effects of acute

exercise on plasma lipids may help explain the reasons for the long-term benefits of exercise on CHD mortality.

Acute Studies. Several studies have been conducted to examine the acute effects of exercise on plasma lipids and lipoproteins in women. These investigations were designed to examine the plasma lipid and lipoprotein response to a single bout of exercise. In general, they have been done using trained athletes who participate in a high intensity event of long duration. Adjustments were made for changes in plasma volume that occur during exercise. Most of the studies reported some lipid/lipoprotein effect (Table II). Acute exercise increased HDL-C from 4% to 23%, with an average increase of 11%. The plasma total cholesterol responses were more variable; some studies observed an increase, whereas others reported a decrease.

The focus of the research conducted to date has differed, with some investigators (62, 65) studying the temporal pattern of the lipoprotein response to exercise and others (63, 64) looking at the compositional change in HDL in response to exercise. Inconsistent results have been reported in the studies that have examined temporal changes in lipids and lipoproteins that occur both during and after a period of intense exercise (62, 65, 66). Despite an increase in HDL-C during an exercise bout, Lennon *et al.* (62) did not note a 15-min, postexercise sustained increase. Swank *et al.* (65) reported a 5-min, postexercise increase in HDL-C that was not sustained by 96 hr after exercise. The increase in HDL-C was due to an increase in HDL_3-C subfraction. Both Lennon *et al.* (62) and Swank *et al.* (65) measured lipids after a short bout of exercise, i.e., 40 minutes. After a marathon, runners have an increase in HDL-C immediately after the event (64) or 1 day after the race (66). By Day 3 after exercise, HDL-C had returned to baseline levels (66). Compositional changes in the HDL particle after intense exercise have been reported. Schriewer *et al.* (63) found that HDL-C and apolipoprotein A-I were increased and HDL phosphatidylcholine decreased after a 100-km run. Thus, there may be postexercise compositional changes in the HDL particle, but increases in HDL-C appear to be transient.

In summary, acute exercise does affect plasma lipids and lipoproteins and, specifically, HDL-C of women. These studies show that HDL-C transiently increases in response to acute exercise. There are inconsistent results, however, with respect to the temporal response of the HDL-C increase, the subfraction affected, and the compositional status of the particle. While the acute exercise effects are interesting and can provide some information about the dynamics of plasma cholesterol changes and lipoprotein metabolism in response to exercise, chronic exercise is more important for determining long-term changes in the lipoprotein profile.

Chronic Studies. Since 1979, a number of studies have been conducted to examine the effects of an exercise training program on the plasma lipids and lipoprotein levels of women of varying ages. The results reported are inconsistent, with some investigators demonstrating varying beneficial effects and others noting no favorable effects on plasma lipids and lipoproteins (Table III). Approximately half of the studies observed some beneficial effect of exercise on plasma lipids and lipoproteins in women. Only three of these studies reported increases in HDL-C between 11% and 27% ($\bar{X}$ = 18% increase in HDL-C). Interestingly, one of the successful training studies (74) was designed to produce a weekly caloric expenditure of 1500–2000 kcal, the same levels that were correlated with HDL-C in the cross-sectional studies (54, 57). Some investigators (67, 68, 71, 75) reported a modest reduction in plasma total cholesterol (5%) in women who participated in an exercise training program. Negative lipid changes ob-

Table II. Acute Effects of Exercise on Plasma Lipids and Lipoproteins in Women

Author (ref.)	n	Age (yr)	Exercise program	Plasma lipid response[a] (mg/dl)			
				Total cholesterol		HDL-C	
				Pre	Post	Pre	Post
Studies reporting an effect							
Lennon et al., 1983 (62)	7 Moderately trained	26	40-min bicycle ergometer session at 55% VO_2max	178*	165†	64	65[b]
Schriewer et al., 1984 (63)[c]	12	29–54	100-km race	5.5*	5.1†	1.6*	1.8†
Skinner et al., 1987 (64)	12	21–41	42-km marathon	160*	177†	52*	64†
Swank et al., 1987 (65)	9	25	40-min run at 70% VO_2max	Not presented		62*	66†
Goodyear et al., 1990 (66)	12	25	42-km race	197	187	72*	76†,[d]
Studies not reporting an effect							
Lennon et al., 1983 (62)	7 Well trained	25	40-min bicycle ergometer session at 55% VO_2max	196	183	54	53

[a] Means sharing different symbols (*, †) differ at the $P < 0.05$ level.
[b] Despite no HDL-C postexercise effect, there was a significant increase during the exercise bout.
[c] Values are mmol/liter.
[d] Ten minutes after exercise, there was no increase in HDL; however, on Day 1 after exercise, there was a significant increase.

Table III. Effect of an Exercise Training Program on Plasma Total and HDL-C in Women

Author (ref.)	n	Age (yr)	Exercise program: Description	Exercise program: Duration	Total cholesterol[a] (mg/dl): Pre	Total cholesterol[a] (mg/dl): Post	HDL-C[a] (mg/dl): Pre	HDL-C[a] (mg/dl): Post	Body wt
Studies reporting an effect									
Moll et al., 1979 (67)	14	22–26	Jogging 5 days/wk, 70% VO_2max for 30–45 min	6 wk	171*	161†	63	58	No change
Shephard et al., 1980 (68)	65	34	Fitness program 3 days/wk; 30 min 60–70% VO_2max for 15–17 min	6 mo	204*	189†	73	71	No change
Allison et al., 1981 (69)	11	20	Jogging 3 times/wk, 85% maximal heart rate for 45 min	8 wk	169	170	66*	62†	No change
Bassett-Frey et al., 1982 (70)	16	19–29	Bicycle ergometer 3 days/wk, 70% maximal heart rate reserve for 30 min	10 wk	167*	179†	62	62	No change
Brownell et al., 1982 (71)	37	20–57	Aerobic exercise program 3–4 times/wk, 70% maximal heart rate for 15–20 min	10 wk	187*	179†	59	58	−1 kg[b]
Rotkis et al., 1984 (72)	19	24–37	Progressive running 5–6 days/wk to 65 miles/wk	8–15 mo	185	185	60*	69†	No change
Hardman et al., 1989 (73)[c]	28	45	Progressive program of brisk walking 155 min/wk, 60% of predicted maximal oxygen uptake	12 mo	5.4	5.0	1.2*	1.5†	Not reported
Hill et al., 1989 (74)	9	22–45	3–4 training sessions/wk progressed from 20 min to 60 min/session, 70% of predetermined maximal heart rate	10 wk	179	179	55*	61†	No change
Blumenthal et al., 1991 (75)	25	45–55 Postmenopausal	Walking/jogging 3 days/wk, 70% maximal heart rate reserve for 35 min	12 wk	231*	220†	61*	57†	−1 lb[b]
Duncan et al., 1991 (83)[c]	59	20–40	Aerobic walker (8.0 km/hr)	2–4 wk	4.6	4.9	1.4*	1.5†	No change
			Brisk walker (6.4 km/hr)		4.9	4.8	1.5	1.6	No change
			Strollers (4.8 km/hr)		4.8	4.7	1.3*	1.4†	No change
			Controls		4.4	4.6	1.4	1.5	No change
			Walking intervention: 4.8 km/day, 5 days/wk						
Studies not reporting an effect									
Franklin et al., 1979 (76)	13	29–47	Walking and jogging 4 days/wk, 75% VO_2max for 15-25 min	12 wk	205	206	Not reported		No change
Cauley et al., 1987 (77)	105	58	Walking 7 miles/wk	2 yr	225*	230†	61*	62†	No change
Juneau et al., 1987 (78)	60	47	Walking or slow jogging 5 days/wk, 65–77% of peak heart rate for 55 min	6 mo	218	223	63	68	No change
McNaughton and Davies, 1987 (79)[c]	5	19–43	Aerobic dance program 2 days/wk, 70% maximal heart rate for 1 hr	16 wk	4.9	5.1	1.5	1.4	No change
Williford et al., 1988 (80)	10	23 ± 6	Aerobic dance training 3 days/wk, 60–90% of maximal heart rate reserve	10 wk	177	179	51	53	No change
Sedgwick et al., 1988 (81)[c]	110	20–65	3-5 training sessions/wk, 65% maximal heart rate for ~1 hr	5 yr	5.5	5.4	Not reported		−0.4 kg[d]
Merrill and Friedricks, 1990 (82)	16	22	Self-selected exercise 3 days/wk for 30–45 min to elevate heart rate 50% above baseline	14 wk	172	176	51	53	Not reported
Blumenthal et al., 1991 (75)	25	45 Premenopausal	Walking/jogging 3 days/wk, 70% maximal heart rate reserve for 35 min	12 wk	197	190	65	64	−1 lb[b]

[a] Means sharing different symbols (*, †) differ at the $P < 0.05$ level.
[b] A significant weight change was observed ($P < 0.05$).
[c] Values are mmol/liter.
[d] Inactive group gained 1.4 kg.

served include a modest increase (7%) in total cholesterol (70) and slight decreases in HDL-C (7%) in response to exercise training (69, 75).

In evaluating these intervention studies, several confounding variables need to be addressed. First, studies reporting positive effects of exercise on plasma lipids and lipoproteins in general used exercise regimens that were of greater intensity and/or of longer duration (>12 months). Second, the effects reported are not due to changes in body weight that accompany the exercise training program since the majority of studies reviewed did not observe any weight change. Third, no one has studied the effects of exercise in women with low HDL-C levels. The majority of studies have used subjects with baseline HDL-C levels greater than 60 mg/dl. Fourth, responses observed could be related to men-

strual phase in premenopausal women and menstrual status overall. Because the phase of the menstrual cycle affects plasma lipid levels, failure to control the phase in which blood is sampled can lead to erroneous conclusions.

Recently, Duncan *et al.* (83) held menstrual phase constant for blood sampling during a dose-responsive exercise intervention in premenopausal women. A total of 102 women were randomized to one of four groups: aerobic walkers, brisk walkers, strollers, and sedentary controls. The 59 women who completed the trial walked 5 miles/day (at intensities between 3 and 5 mph), 5 days a week, for 24 weeks. All blood samples were drawn during the same phase of the menstrual cycle. At the end of the intervention, fitness levels as assessed by maximal oxygen uptake corresponded to the intensity of walking, i.e., aerobic walkers became most fit and the sedentary control group remained the least fit. However, changes in HDL-C were not related to the intensity of the exercise intervention. The strollers and aerobic walkers had significant increases in HDL-C after the intervention, while the brisk walkers did not. It is important to note that the brisk walkers began with higher HDL-C levels than the other three groups. This is one of the first studies to show that the rise in HDL-C after an exercise intervention is not related to the intensity of the exercise. Further studies are needed to establish the efficacy of low level, sustained exercise on increasing HDL-C levels of women.

Menstrual status could also affect the plasma lipoprotein response to an exercise intervention. Currently, only one group has investigated exercise training in pre- and postmenopausal women. Blumenthal *et al.* (75) randomized women to a 12-week strength or aerobic training program. The only significant changes in plasma lipids were a fall in both total cholesterol and HDL-C in postmenopausal women who were aerobically trained. No significant changes were observed in premenopausal women. This would suggest that the plasma lipid/lipoprotein response is related to the endocrine status of women.

The exercise intervention studies conducted to date have provided useful information in establishing a causal relationship between exercise and HDL-C levels. Another type of exercise paradigm has been used by several investigators to further examine the effects of exercise on plasma lipoproteins. In these studies, exercise only versus diet plus exercise effects are compared (Table IV). The major objectives of these studies have been to evaluate the interactive effects of diet and exercise on modifying the plasma lipoprotein profile and specifically to determine whether exercise augments the plasma lipid/lipoprotein effects of a lower fat diet. Because of the experimental design employed, these studies have provided a unique opportunity to clarify the benefits of exercise alone and with a fat-modified diet on plasma lipids and lipoproteins.

The most important finding reported is that the addition of exercise to a lower fat dietary intervention program favorably affects HDL-C levels in overweight and obese subjects. Two investigators (84, 85) reported that exercise attenuates the diet-induced decline in HDL-C in response to a Step-One diet that was prescribed to elicit weight loss. In contrast, Leighton *et al.* (86) did not observe an exercise effect for reasons that are unclear. Thus, these studies provide further evidence that exercise increases HDL-C despite consumption of a low fat diet, which in general reduces HDL-C. With respect to LDL-C, exercise did not augment the favorable cholesterol-lowering effect of diet in two of the three studies (Table IV). There was an effect in one study, however. In summary, exercise intervention studies alone or in conjunction with a low fat diet suggest that exercise has an independent HDL-C raising effect in women.

The plasma lipid changes that have been reported in a number of studies are clinically important. The inconsistency in the results reported to date is likely due to many confounding factors (e.g., type, intensity, duration of exercise; age; menopausal and endocrine status; and stage of the menstrual cycle) that have not been well controlled. Further studies that are designed to control for these variables are needed to gain a better understanding of the effects that exercise has on plasma lipids and lipoproteins in women. In addition, studies are needed to determine the extent to which these factors affect the exercise-induced plasma lipid/lipoprotein response. These investigations will clarify the relative significance of important confounding variables as well as their interactive effects with exercise on the CHD risk status of women.

Training Studies with Males and Females: Comparative Effects. Studies of men and women are useful in comparing the gender effects of exercise and provide some insight about the role hormones (e.g., principally endogenous sex steroids) play in regulating the lipoprotein response to exercise. The most obvious difference in the lipoprotein profile between men and women is the quantity of cholesterol transported in the LDL and HDL fractions. Before menopause, women have lower LDL-C levels and higher HDL-C levels. Despite these differences, the studies conducted to date demonstrate rather remarkable similarities between men and women in response to exercise (Table V).

There have been two approaches taken to examine the effects of exercise on plasma lipids and lipoproteins in men and women. One approach is to evaluate the effects of exercise in men and women together without distinguishing gender effects. The other, and more commonly used, approach is to examine the gender effects of exercise by comparing the responses noted for men

Table IV. Effects of Diet and Exercise on Plasma Lipids and Lipoproteins

Author (ref.)	Protocol			
	Diet		Diet + exercise	
	LDL-C	HDL-C	LDL-C	HDL-C
Leighton et al., 1990 (86)	−4%	−12%	−11%[a]	−13%[a]
Nieman et al., 1990 (84)	−12%[b]	−11%[b]	−12%[b]	0%
Wood et al., 1991 (85)	−9%	−10%	−9%	+1%

[a] Diet and diet plus exercise induced significant ($P < 0.0001$) changes in LDL-C and HDL-C when compared with baseline values (diet: LDL-C = 4.6 vs 4.4 mmol/liter and HDL-C = 1.8 vs 1.6 mmol/liter; diet and exercise: LDL-C = 4.7 vs 4.2 mmol/liter and HDL-C = 1.8 vs 1.6 mmol/liter). There were no significant differences for these lipoprotein parameters between the two treatment groups.
[b] Values were significantly different ($P < 0.05$) from baseline ($P < 0.05$). LDL-C = 3.1 and 2.7 mmol/liter (diet + exercise); 3.1 and 2.7 mmol/liter (diet). HDL-C = 1.5 and 1.5 mmol/liter (diet + exercise); 1.5 and 1.3 mmol/liter (diet).
[c] Mean values for women were significantly different ($P < 0.05$) from the control group.
[d] Mean value for women was significantly different ($P < 0.01$) from the diet-only group.

with those for women. Three studies have been conducted that have pooled data collected from men and women (87, 89, 90). All of these studies report an effect of exercise on plasma lipids and lipoproteins. However, the most notable finding is that exercise increased HDL-C levels significantly and the response was remarkably similar. These investigators all reported a 10% increase in HDL-C (the baseline HDL-C level in the studies was 51–54 mg/dl). In contrast, there was no effect of a 6-week exercise program on HDL-C in the study conducted by Lipson *et al.* (89); however, plasma total cholesterol was significantly reduced.

While these experiments have provided important information about general exercise effects, studies that have grouped men and women separately allow relative comparisons to be made. These studies also provide a perspective about the potential of exercise to modify CHD risk factors in both men and women.

The gender effects of exercise on plasma lipids and lipoproteins are presented in Table V. There are two obvious conclusions that can be made from the data reported. As observed for the studies conducted with women, the responses reported are inconsistent. Despite this, the majority of studies have reported a beneficial effect of exercise on either plasma total cholesterol or HDL-C levels. It also is interesting to note that these studies report a similar beneficial response (≈10%) for both men and women. Although there is evidence to demonstrate that exercise does have a beneficial effect on plasma lipids and lipoproteins, it is unclear why there are so many inconsistencies reported in the literature. In part, this likely is because different experimental designs have been used and the subjects studied have been heterogeneous. For example, different exercise programs of varying intensity and duration have been used and important subject characteristics (such as age, weight and adiposity, hormonal status, diet, smoking status, and alcohol consumption practices) that might affect the study outcome have not been controlled. In addition, adherence to the exercise program will affect the responses observed. Some studies failed to monitor compliance objectively. Further studies are needed to identify the important factors that account for the variation in the response noted for plasma lipids and lipoproteins in men and women who participate in a regular exercise program. These studies will be valuable in identifying effective exercise programs that beneficially affect plasma lipids and lipoproteins in both men and women and thereby reduce the risk of CHD.

Summary

Exercise has been shown to beneficially affect the plasma lipoprotein profile of women. The cross-sectional studies report a consistent relationship between exercise and HDL-C. The exercise training studies conducted both with women and with men and women report inconsistent results. Nonetheless, several studies have shown that exercise increases HDL-C and decreases plasma total cholesterol levels. The magnitude of the response is similar for both women and men and is approximately 10%. Further studies are needed to increase our understanding of how different factors such as exercise intensity and duration, age, gender, hormonal status, body weight and body composition, etc., affect the plasma lipid and lipoprotein response to exercise.

There have been few studies designed to examine exercise and lipoprotein relationships that have controlled for sex hormone status (e.g., menopausal status, hormone replacement therapy, and oral contraceptive use). Some investigators have reported different exercise effects in premenopausal and postmenopausal women. And, endogenous and exogenous sex steroid hormones have a marked effect on plasma lipoproteins. Since the use of exogenous estrogen therapy is becoming widespread, studies are needed to clarify the interactive effects of exercise and sex steroid hormones on plasma lipids. In addition, the effects of oral contraceptive (OCA) use on exercise-induced plasma lipid and lipo-

Table V. Gender Effects of Exercise on Plasma Lipids and Lipoproteins

Author (ref.)	Subjects	*n*	Age (yr)	Exercise program		Response[a] (mg/dl) TC		HDL-C		Body wt
						Pre	Post	Pre	Post	
Shephard et al., 1980 (68)	Male	41	36	Supervised aerobic physical activity for 30 min, 3 times/wk for 6 mo.	♂	208	203	58	58	−2[b]
	Female	65	34	Subjects classified as high adherers are reported	♀	204*	189†	73	71	−2[b]
						Pre	Post	Pre	Post	
Allison et al., 1981 (69)	Male	11	20	Progressive running program for 45 min, 3 times/wk for 8 wk	♂	174	176	60*	54†	No change
	Female	11	22		♀	169	170	66*	62†	No change
						Pre	Change	Pre	Change	
Brownell et al., 1982 (71)	Male	24	42	Aerobic exercise program, 30-min sessions, 3 times/wk for 10 wk	♂	207	−10[b]	42	+1.5	−1[b]
	Female	37	35		♀	187	−8[b]	59	−1	−1[b]
						Pre	Post	Pre	Post	
Goldberg et al., 1984 (88)	Male	6	33	Progressive resistance weight training for 45–60 min, 3 times/wk for 16 wk	♂	209	194	51	59	No change
	Female	8	27		♀	198*	179†	77	81	No change
						Pre	Post	Pre	Post	
Juneau et al., 1987 (78)	Male	60	49	Self-monitored, home-based exercise training, 5 times/wk, 50 min/session for 6 mo	♂	221	219	44	46	−1.5 kg[b]
	Female	60	47		♀	218	223	63	68	No change
						Pre	Post	Pre	Post	
McNaughton and Davies, 1987 (79)[c]	Male	7	40	Aerobic dance program 2 days/wk, 1 hr/session for 16 wk	♂	5.1	5.0	1.1	1.2	−5 kg[b]
	Female	5	26		♀	4.9	5.1	1.5	1.4	No change
						Pre	Post	Pre	Post	
Hill et al., 1989 (74)	Male	8	24–26	Progressive aerobic exercise program to 1 hr, 4 times/wk for 10 wk	♂	197*	172†	59	57	No change
	Female	9	22–45		♀	179	179	55*	61†	No change

Author (ref.)	Subjects	*n*	Age (yr)	Exercise program		TC Low		Moderate		High		HDL-C Low		Moderate		High		Body wt
						Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	
Merrill and Friedricks, 1990 (82)	Male	32	22	Self-selected aerobic activity for 30–45 min, 3 times/wk for ~14 wk	♂	143	149	178	176	231*	192†	38	39	42	41	43	40	Not reported
	Female	32	22		♀	144	149	172	176	214*	192†	47	44	51	53	70	52	Not reported
	Subjects were assigned to three groups on the basis of initial total cholesterol level																	

[a] Means sharing different symbols (*,†) differ at the ($P < 0.05$) level.
[b] A significant weight change was observed ($P < 0.05$).
[c] Values are mmol/liter.

protein responses need to be clarified since a recent report (91) has shown that HDL-C did not increase in a small number ($n = 7$) of exercising women taking a low-dose estrogen formulation (OCA). HDL-C increased, in contrast, by 0.14 mmol/liter in the women who did not take OCA. This recent study and others reviewed herein underscore the need for well-controlled studies that establish the role of endogenous hormones (i.e., menopausal status) and exogenous hormones (i.e., OCA and hormone replacement therapy) on the effects of exercise on plasma lipids and lipoproteins of women and consequently their risk of CHD.

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