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Fatness, fitness, and cardiometabolic risk factors in middle-aged white men

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ABSTRACT

The objective was to test the hypothesis that traditional and novel cardiometabolic risk factors would be significantly different in groups of men of different fatness and fitness. Total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, glucose, insulin, high-sensitivity C-reactive protein, alanine aminotransferase, aspartate aminotransferase, γ-glutamyltransferase, leptin, adiponectin, tumor necrosis factor–α, interleukin-6, interleukin-10, fibrinogen, and insulin resistance were assessed in 183 nonsmoking white men aged 35 to 53 years, including 62 who were slim and fit (waist girth ≤90 cm and maximal oxygen consumption [VO_2max] above average), 24 who were slim and unfit (waist girth ≤90 cm and VO_2max average or below), 39 who were fat and fit (waist girth ≥100 cm and VO_2max above average), and 19 who were fat and unfit (waist girth ≥100 cm and VO_2max average or below). Seventy-six percent gave blood on 2 occasions, and the average of 1 or 2 blood tests was used in statistical tests. Waist girth (centimeters) and fitness (milliliters of oxygen per kilogram of fat-free mass) were associated with high-density lipoprotein cholesterol, leptin, and insulin resistance after adjustment for age, saturated fat intake, and total energy intake. High-density lipoprotein cholesterol, triglycerides, alanine aminotransferase, and insulin resistance were significantly different in men who were fat and fit and those who were fat and unfit. These data suggest that differences in lipid and lipoprotein concentrations, liver function, and insulin resistance may explain why the risks of chronic disease are lower in men who are fat and fit than those who are fat and unfit.

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1. Introduction

Obesity is associated with increased risk of cardiovascular disease and type 2 diabetes mellitus [1,2]; however, the risks of chronic disease are lower in obese men with moderate to high levels of aerobic fitness [3,4]. Total cholesterol concentration, blood pressure, and other traditional risk factors may not explain why the risks of chronic disease are lower in men who are fat and fit than men who are fat and unfit [3]. Therefore, we assessed traditional [5] and novel [6,7] cardiometabolic risk factors in the present study, including adipokines [7], markers of inflammation [6-9], and markers of liver damage [10-12]. We hypothesized that fatness and fitness would be related to cardiometabolic risk factors, and we hypothesized that traditional and novel risk factors would be significantly different in groups of different fatness and

Contributions: O'Donovan designed the study and collected the data. O'Donovan, Kearney, and Sherwood analyzed the data. All authors contributed to the manuscript.

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fitness. There are several cross-sectional studies of fatness and fitness [13], but the present study was unusually robust. The within-subject variation in blood-borne cardiometabolic risk factors is considerable [14], so we took blood on 2 occasions to obtain a better indication of participants' average levels. The available evidence suggests that fitness does not reduce all-cause mortality in sedentary men [15], so we only included active men in the slim and fit group and the fat and fit group.

2. Methods

2.1. Participants

A total of 183 white men took part in this study from January 2006 to July 2007. Health and fitness tests took place at Brunel University, and most volunteers were recruited from local employers that e-mailed recruitment literature on our behalf. Volunteers were also recruited via leaflets at health and fitness clubs and adverts in health and fitness magazines. We excluded volunteers aged less than 35 or more than 55 years, those who had smoked in the last 2 years, those taking medication that might affect cholesterol or blood pressure, and those with symptoms of angina or intermittent claudication [16]. An institutional review board approved this study, and all participants gave written informed consent.

2.2. Fatness, fitness, and activity

Height and weight were measured with minimal clothing and without shoes, and body mass index (BMI) was expressed as kilograms per meter squared. Skinfold thicknesses were measured at the triceps, biceps, subscapular, and suprailiac regions; and percentage body fat was estimated [17]. Fat-free mass (FFM) was estimated as total body weight minus fat weight. Waist girth was measured with an inelastic tape in a horizontal plane at the narrowest part of the torso [18]; and values less than or equal to 90 cm were used to identify slim men, and values greater than or equal to 100 cm were used to identify fat men. Aerobic fitness was assessed during an incremental cycling test, and oxygen consumption was measured using an automated gas analyzer that was periodically validated against the Douglas bag technique (Oxycon Pro; Viasys Healthcare, Hoechberg, Germany). Exercise tests were terminated at 80% of age-predicted maximum heart rate in 25 (14%) of 183 volunteers to reduce the risk of cardiovascular injury [19], and maximal oxygen consumption (VO_2max) was estimated by extrapolating submaximal heart rate and oxygen uptake values. Maximal oxygen consumption was expressed in absolute terms (liters per minute) to identify fitness categories: men who scored "very poor," "poor," "fair," or "average" were deemed unfit; and men who scored "good," "very good," or "excellent" were deemed fit in relation to age-specific norms [20]. Fitness categories were derived from absolute values because heavier individuals are penalized when VO_2max is expressed relative to body weight. The VO_2max was expressed as milliliters of O_2 per kilogram FFM per minute in regression models because FFM is a reflection of metabolically active tissue. Physical activity was assessed using the Five-City Project Physical Activity Recall Questionnaire [21, 22].

2.3. Cardiometabolic risk factors

Participants were asked to visit the laboratory on 2 occasions separated by 3 to 10 days to minimize the confounding effect of biological variation [14]. Participants sat in a chair for at least 5 minutes at the start of each visit to the laboratory, and systolic (SBP) and fifth phase diastolic (DBP) blood pressures were measured twice at the right arm using a mercury sphygmomanometer. 44 men (24%) gave blood on 1 occasion, and 139 men (76%) gave blood on 2 occasions; and the average of 1 or 2 blood tests was used in statistical tests. Venous blood was drawn in the morning following a 12-hour fast and at least 24 hours of abstinence from vigorous-intensity activity. Blood samples were frozen at –80°C before being tested in the same analyzer run. Total cholesterol concentration, high-density lipoprotein cholesterol (HDL-C) concentration, low-density lipoprotein cholesterol (LDL-C) concentration, triglyceride concentration, glucose concentration, insulin concentration, high-sensitivity C-reactive protein (hsCRP) concentration, alanine aminotransferase (ALT) activity, aspartate aminotransferase (AST) activity, and γ-glutamyltransferase (GGT) activity were measured using an Abbott Architect cs8200 analyzer (Abbott Laboratories, Abbott Park, IL). Enzyme-labeled immunosorbent assay was used to quantify leptin (DRG Instruments, Marburg, Germany), adiponectin, tumor necrosis factor (TNF)–α, interleukin (IL)-6, and IL-10 (R & D Systems, Abingdon, UK). Fibrinogen level was estimated using the STA-Fib(2) kit and STA-R Evolution analyzer (Stago, Asnieres, France). The coefficient of variation of each assay was less than or equal to 5%. Insulin resistance was estimated from the homeostasis model assessment of insulin resistance (HOMA), which correlates well with the euglycemic-hyperinsulinemic clamp technique [23]. Participants were asked to complete a 7-day food diary, and nutrient intake was analyzed using CompEat software (Nutrient Systems, Banbury, UK). Socioeconomic status was assessed during an interview in accordance with the Office for National Statistics manual [24].

2.4. Statistical methods

Sample size was determined using the standardized difference, which is the ratio of the clinically relevant difference and the standard deviation of the primary outcome variable [25]. Low-density lipoprotein cholesterol was chosen as the primary outcome variable, and cross-sectional data suggest that LDL-C concentration is around 0.8 mmol·L^{-1} lower in habitual exercisers than sedentary men [26, 27] and that the standard deviation in LDL-C concentration is around 0.96 mmol·L^{-1} [28]. Thus, the standardized difference is 0.8/0.96 = 0.83. When this value is used in Altman's nomogram [25], there is around a 98% probability at the 5% level of significance of detecting differences in LDL-C of 0.8 ± 0.96 mmol·L^{-1} with 45 subjects in each group. Because it is difficult to recruit fat and unfit men [26], we decided to recruit more slim and fit men. This strategy reduces power compared with a 1:1 ratio, but gives a 90% probability of detecting a 0.8 ± 0.96-mmol·L^{-1} difference in LDL-C with 60 slim and fit men (the reference

group) and 20 men in any other group [25]. Group comparisons only included unfit men who reported no regular moderate-intensity (~4 metabolic equivalents [METs]) or vigorous-intensity (≥6 METs) activity in the last 2 years and fit men who reported taking part in at least 60 minutes of vigorous-intensity aerobic activity per week in the last 2 years, which is the minimum amount recommended to develop and maintain cardiorespiratory fitness (1 MET is equivalent to the energy expended at rest) [19]. Multiple linear regression was used to investigate if fatness (waist girth, centimeters) and fitness (VO_2max, milliliters of O_2 per kilogram FFM per minute) were associated with cardiometabolic risk factors. Model 1 contained age and fatness or age and fitness. Model 2 contained age, fatness, and fitness. Model 3 contained age, fatness, fitness, saturated fat intake, and total energy intake. Residuals were regarded as normally distributed if results of Shapiro-Wilk tests were not significant ($P > .05$); and log10 transformation normalized triglyceride, hsCRP, ALT, and leptin data. General linear model analysis of variance was used to investigate group differences. Hochberg GT2 and Gabriel post hoc tests were used when sample sizes were different, and the Games-Howell post hoc test was used when the result of Levine test of equality of error variance was significant ($P < .05$) [29]. All data were analyzed using SPSS for Windows, version 15.0 (SPSS, Chicago, IL). All P values presented are 2-tailed.

3. Results

Table 1 shows participants' characteristics. The average age was around 40 years, and around 80% of participants were employed in managerial and professional occupations. Fatness, fitness, and activity varied widely; and the sample of 183 men included 62 who were slim and fit (waist girth ≤90 cm, VO_2max above average in relation to age-specific norms, and at least 60 minutes of vigorous-intensity activity per week in the last 2 years), 24 who were slim and unfit (waist girth ≤90 cm, VO_2max average or below, and no regular moderate- or vigorous-intensity activity in the last 2 years), 39 who were fat and fit (waist girth ≥100 cm, VO_2max above average, and at least 60 minutes of vigorous-intensity activity per week in the last 2 years), and 19 who were fat and unfit (waist girth ≥100 cm, VO_2max average or below, and no regular moderate- or vigorous-intensity activity in the last 2 years). Waist girth was not significantly different in men who were slim and fit and those who were slim and unfit (84 ± 5 and 84 ± 5 cm), but was higher in men who were fat and fit and those who were fat and unfit (109 ± 7.5 and 105 ± 6 cm, $P < .001$ vs slim groups). Maximal oxygen consumption was not significantly different in men who were slim and fit and those who were fat and fit (3.8 ± 0.5 and 4.0 ± 0.5 $L \cdot min^{-1}$), but was lower in men who were slim and unfit and those who were fat and unfit (2.7 ± 0.3 and 2.9 ± 0.7 $L \cdot min^{-1}$, $P < .001$ vs fit groups). Body mass index and body fat were in keeping with group classifications (Table S1, online supplement).

Table 1 – Participants' characteristics (n = 183)

	Mean ± SD (range)
Age, y	42 ± 5 (35-53)
Weight, kg	89.9 ± 16.5 (60-141)
BMI, $kg \cdot m^2$	28.1 ± 4.9 (19.1-45.3)
Body fat, %	22 ± 6 (7-33)
Waist girth, cm	93.8 ± 11.7 (67.2-129.0)
Maximal oxygen consumption, $L \cdot min^{-1}$	3.55 ± 0.71 (1.93-5.49)
Maximal oxygen consumption, mL $O_2 \cdot kg_{FFM}^{-1} \cdot min^{-1}$	51.3 ± 9.1 (28.8-79.7)
Years of exercise	14 ± 11 (0-39)
Socioeconomic status	
Managerial and professional occupations, %	79
Intermediate occupations, %	15
Routine and manual occupations, %	5
Other, %	0.5

Cardiometabolic risk factors also varied widely, and the number of participants who provided at least 1 valid blood sample ranged from 119 for IL-10 to 183 for glucose (Table S2, online supplement). Interleukin-10 data were not analyzed because of the loss of statistical power. SPSS was coded to ignore other missing values; and the observed power of group comparisons at the 5% level of significance was 0.31 for fibrinogen, 0.36 for IL-6, 0.41 for TNF-α, 0.5 for AST, 0.63 for total cholesterol, and greater than or equal to 0.9 for HDL-C, LDL-C, triglycerides, glucose, insulin, HOMA, hsCRP, ALT, GGT, adiponectin, and leptin.

Table 2 shows the relationships between fatness (waist girth, centimeters), fitness (VO_2max, milliliters per kilogram FFM per minute), and cardiometabolic risk factors. Standardized regression coefficients are not dependent on the units of measurement and are presented to facilitate interpretation. In model 1, for example, the standardized regression coefficient indicates that as waist girth increases by 1 standard deviation, triglyceride concentration increases by 0.29 standard deviations. The standard deviation for waist girth is 11.7 cm (Table 1), and the standard deviation for triglyceride concentration is 0.66 $mmol \cdot L^{-1}$ (Table S2, online supplement). Therefore, for every 11.7-cm increase in waist girth, there is a 0.19-$mmol \cdot L^{-1}$ increase in triglyceride concentration (0.29 × 0.66 = 0.19). Fatness was associated with blood pressures, HDL-C, triglycerides, glucose, insulin, HOMA, hsCRP, ALT, AST:ALT, GGT, leptin, and IL-6 after adjustment for age (model 1) and after adjustment for age and fitness (model 2). Fitness was associated with blood pressures, HDL-C, triglycerides, glucose, insulin, HOMA, hsCRP, ALT, AST:ALT, adiponectin, and leptin after adjustment for age (model 1) and with HDL-C, triglycerides, insulin, HOMA, and leptin after adjustment for age and fatness (model 2). One hundred two participants completed 7-day food diaries; and the relationships between fatness, fitness, and cardiometabolic risk factors were not markedly changed after adjustment for age, saturated fat intake, and total energy intake (model 3, data not shown).

Systolic blood pressure was not significantly different in men who were slim and fit and those who were slim and unfit (114 ± 11 and 117 ± 13 mm Hg), but was higher in men who were fat and fit and those who were fat and unfit (130 ± 14 and 131 ± 14 mm Hg, $P < .01$ vs slim groups). Diastolic blood pressure followed a similar pattern (Table S1, online supplement). High-density lipoprotein cholesterol was not significantly different in slim and fit, slim and unfit, and fat and fit

Table 2 – Relationships between fatness, fitness, and cardiometabolic risk factors in regression models

	Model 1		Model 2	
	Waist girth, cm	VO_2max, mL·kg$^{-1}_{FFM}$·min^{-1}	Waist girth, cm	VO_2max, mL·kg$^{-1}_{FFM}$·min^{-1}
SBP, mm Hg	.56‡	−.25†	.55‡	−.03
DBP, mm Hg	.53‡	−.19*	.55‡	.04
TC, mmol·L^{-1}	.07	−.06	.06	−.04
HDL-C, mmol·L^{-1}	−.32‡	.33‡	−.22†	.25 (.05)†
LDL-C, mmol·L^{-1}	.10	−.12	.06	−.10
Triglycerides, mmol·L^{-1}	.29‡	−.26†	.22†	−.17 (.02)*
Glucose, mmol·L^{-1}	.33‡	−.20†	.29‡	−.08
Insulin, μU·mL^{-1}	.49‡	−.41‡	.39‡	−.26 (.05)‡
HOMA	.49‡	−.41‡	.38‡	−.26 (.06)‡
hsCRP, mg·L^{-1}	.44‡	−.22†	.42‡	−.05
ALT, U·L^{-1}	.32‡	−.17*	.30‡	−.05
AST, U·L^{-1}	.13	.02	.17	.08
AST:ALT	−.35‡	.27†	−.29†	.15
GGT, U·L^{-1}	.26†	−.09	.27†	.02
Fibrinogen, g·L^{-1}	.10	−.14	.05	−.11
Adiponectin, ng·mL^{-1}	−.36‡	.22†	−.33‡	.09
Leptin, ng·mL^{-1}	.67‡	−.44‡	.57‡	−.22 (.04)†
TNF-α, pg·mL^{-1}	−.06	−.05	−.10	−.09
IL-6, pg·mL^{-1}	.19*	−.04	.21*	.05

Values are standardized β coefficients. Model 1 contained age and waist girth or age and VO_2max. Model 2 contained age, waist girth, and VO_2max. ΔR^2 is shown in parentheses in model 2 if the addition of VO_2max made a significant contribution to the change in the amount of variance that could be explained, $P < .05$. Triglycerides, hsCRP, ALT, and leptin were log transformed. Number of observations is 171, except SBP, DBP, and glucose (183); HOMA (169); fibrinogen (151); adiponectin (182); leptin (174); and TNF-α and IL-6 (181). TC indicates total cholesterol.
* $P < .05$.
† $P < .01$.
‡ $P < .001$.

groups, but was lower in men who were fat and unfit (Fig. 1). Triglyceride concentration was not significantly different in slim and fit, slim and unfit, and fat and fit groups, but was higher in men who were fat and unfit (Fig. 1). Homeostasis model assessment of insulin resistance was not significantly different in slim and fit and slim and unfit groups, higher in the fat and fit group, and higher still in the fat and unfit group (Fig. 1, with glucose and insulin concentrations in Table S1 in the online supplement). High-sensitivity C-reactive protein was not significantly different in men who were slim and fit and those who were slim and unfit (0.93 ± 1.12 and 1.06 ± 0.93 mg·L^{-1}), but was higher in men who were fat and fit and those who were fat and unfit (2.61 ± 2.75 and 2.00 ± 1.12 mg·L^{-1}, $P < .05$ vs slim groups). Alanine aminotransferase was not significantly different in slim and fit and slim and unfit groups, higher in the fat and fit group, and higher still in the fat and unfit group (Fig. 1). Aspartate aminotransferase was not significantly different in groups of different fatness and fitness, but the ratio of AST to ALT was lower in the fat and fit group and lower still in the fat and unfit group (Table S1, online supplement). γ-Glutamyltransferase was not significantly different in men who were slim and fit and those who were slim and unfit (23.69 ± 12.56 and 23.24 ± 8.12 U·L^{-1}), but tended to be higher in men who were fat and fit and those who were fat and unfit (38.32 ± 33.30 and 40.68 ± 22.71 U·L^{-1}, $P \leq .09$ vs slim groups). Adiponectin was not significantly different in slim groups, but was lower in fat groups (Fig. 1). Leptin was not significantly different in slim groups, but was higher in fat groups (Fig. 1). Total cholesterol, LDL-C, fibrinogen, TNF-α, and IL-6 concentrations were not significantly different in groups of different fatness and fitness (Table S1, online supplement).

4. Discussion

Fatness and fitness were independently related to several cardiometabolic risk factors in the present study, and some traditional and novel risk factors were significantly different in groups of different fatness and fitness. Differences in HDL-C concentration, triglyceride concentration, ALT activity, and HOMA may explain why the risks of chronic disease are lower in men who are fat and fit than those who are fat and unfit. Our study of men who were fat, fit, and active is in keeping with the notion that physical activity and the pursuit of physical fitness reduce the risks associated with obesity [30].

This study was robust because we reduced the confounding effects of biological and analytical variation and we carefully identified men who were fat, fit, and active to avoid misclassification. The within-subject variation in total cholesterol (6%), HDL-C (7%), triglycerides (21%), and other blood-borne risk factors is considerable [14]; and we took blood on 2 occasions to obtain a better indication of participants' average levels. Blood samples were stored at −80°C and tested in the same analyzer run to minimize analytical variation. A waist girth of greater than or equal to 100 cm was used to define fat men because it is associated with the accumulation of visceral adipose tissue [31], and a waist girth of less than or equal to 90 cm was used to define slim men to avoid misclassification. Maximal oxygen

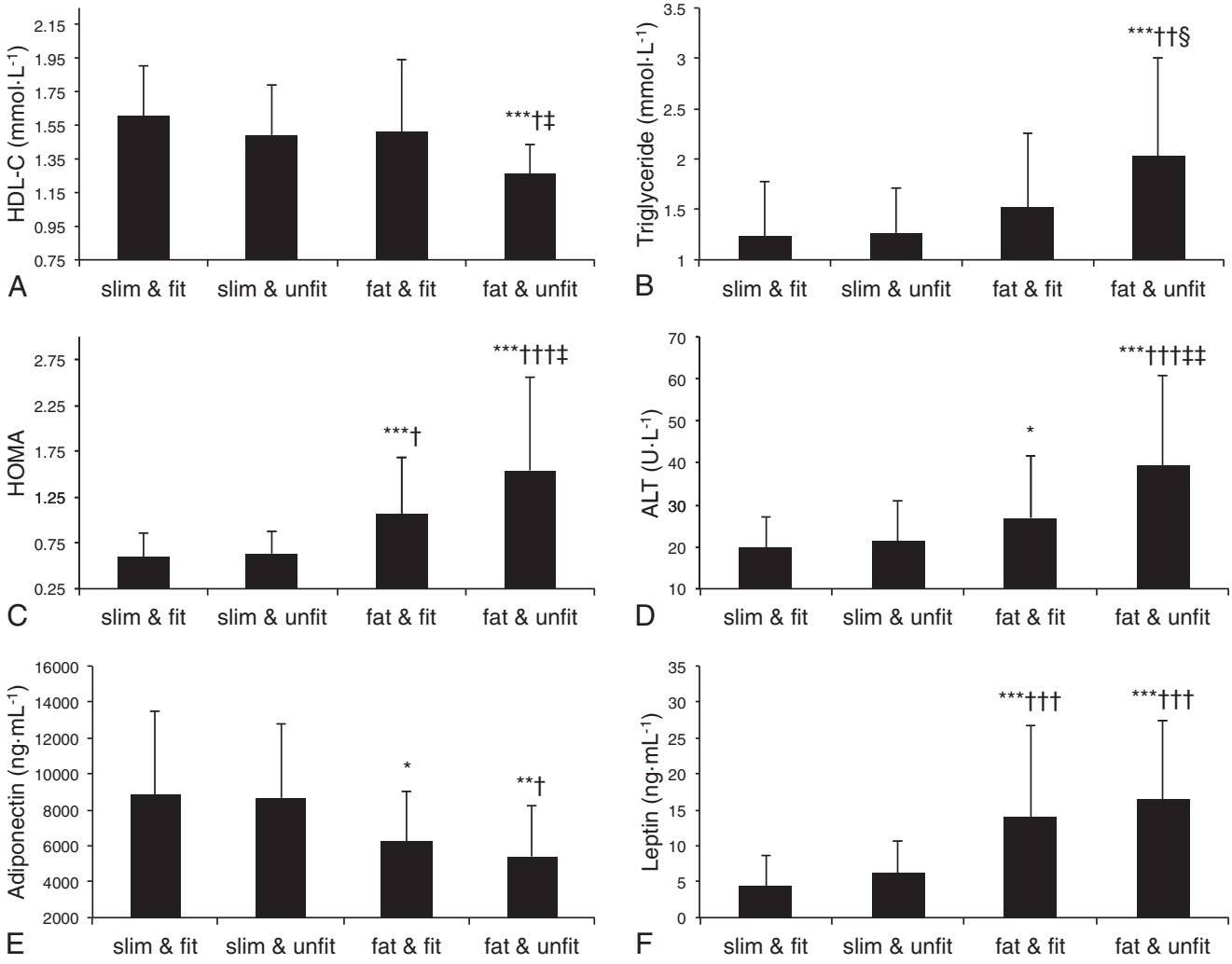

Fig. 1 – High-density lipoprotein cholesterol concentration (A), triglyceride concentration (B), HOMA (C), and ALT activity (D) in 58 men who were slim and fit, 23 who were slim and unfit, 38 who were fat and fit, and 17 who were fat and unfit. Adiponectin concentration in 61 men who were slim and fit, 24 who were slim and unfit, 39 who were fat and fit, and 19 who were fat and unfit (E). Leptin concentration in 54 men who were slim and fit, 23 who were slim and unfit, 39 who were fat and fit, and 19 who were fat and unfit (F). Bars are means, and error bars are standard deviations. $^{*}P < .05$, $^{**}P < .01$, $^{***}P < .001$ vs slim and fit. $^{\dagger}P < .05$, $^{\dagger\dagger}P < .01$, $^{\dagger\dagger\dagger}P < .001$ vs slim and unfit. $^{\ddagger}P < .05$, $^{\ddagger\ddagger}P < .01$, $^{\S}P = .06$ vs fat and fit.

consumption is the criterion measure of aerobic fitness, and "fit" and "unfit" men were defined with reference to untrained men of the same age [20]. The norms were largely derived from cycling tests, and VO_2max was expressed independent of body weight to avoid penalizing heavier individuals. For example, a 110-kg man of 40 years of age has an excellent score of 4.0 $L \cdot min^{-1}$ when VO_2max is expressed independent of body weight and a below average score of 36 $mL \cdot kg^{-1} \cdot min^{-1}$ when VO_2max is expressed relative to body weight [20]. Blair and colleagues have concluded that a physically active lifestyle can increase aerobic fitness and reduce all-cause mortality, with [32] and without [3,33] assessing habitual activity. It might be appropriate to assume that aerobic fitness is a reflection of habitual activity in large studies because "naturally fit" men are rare [15] and misclassification is unlikely to bias toward the null. Any misclassification is more likely to bias toward the null in small studies. Therefore, we only included active men in the slim and fit group and the fat and fit group.

This study has a number of limitations. The selection of waist girth thresholds was somewhat arbitrary; however, the results were similar when the International Diabetes Federation [34] threshold of greater than or equal to 94 cm was used to identify fat men (Table S3, online supplement). There were more men in each group when the single threshold was used, and the similar results may reflect the conflicting forces of greater sample size (which tends to increase power) and greater misclassification (which tends to bias toward the null). The use of submaximal fitness tests might introduce bias because they tend to overestimate VO_2max. However, extrapolation only produced unrealistic values in 6 inactive men; and one was allocated to the slim and unfit group, and 5 were allocated to the fat and unfit group. Physical activity was self-reported, but vigorous-intensity activity is recalled with some

accuracy [21]. Eighty-one (44%) of 183 participants did not complete food diaries, but saturated fat intake and total energy intake explained little of the variance in cardiometabolic risk factors. Sample size was sufficient to detect several statistically significant results; but a larger study might reveal more about the relationships between fatness, fitness, fibrinogen, IL-6, IL-10, TNF-α, and AST; however, it is noteworthy that IL-10 was often undetectable in the present study and other studies of healthy men [35,36]. The results of the present study may not be observed when other measures of fatness and fitness are used and may not be generalizable to groups of substantially different fatness, fitness, and activity. Our study of white men cannot help explain why fitness may reduce the risks of chronic disease in overweight and obese women [30].

It is interesting that we did not find significant differences in the primary outcome variable, despite sufficient statistical power. Significant differences in LDL-C have been observed in other cross-sectional studies [26,37]; but we found no relationships between fatness, fitness, and LDL-C in 113 men in a previous study [26] or 171 men in the present study. Exercise interventions rarely bring about reductions in LDL-C [37]; however, exercise training can increase lipoprotein lipase activity and, thus, improve HDL-C and triglyceride concentrations [37-39]. Fatness (waist girth, centimeters) and fitness (VO_2max, milliliters per kilogram FFM per minute) were independently related to HDL-C and triglycerides in the present study, and the available evidence suggests that exercise training may improve HDL-C and triglyceride concentrations with or without weight loss [40-42]. The reported changes in HDL-C were modest, but the quality of most interventions was poor.

It is increasingly apparent that insulin resistance is central to cardiovascular disease and type 2 diabetes mellitus [6]. The effect of exercise on insulin sensitivity is also well documented [43], and it is plausible that men who are fat and fit have a greater capacity than men who are fat and unfit to store excess fat in insulin-sensitive adipose tissue rather than the viscera or the liver. Indeed, fatness (waist girth, centimeters) and fitness (VO_2max, milliliters per kilogram FFM per minute) were independently associated with insulin resistance (HOMA) in the present study; and we have previously reported that visceral fat and liver fat were lower in men who were fat and fit than those who were fat and unfit [44]. Visceral fat is associated with dyslipidemia [9], and it is noteworthy that HDL-C and triglycerides were significantly different in men who were fat and fit and those who were fat and unfit. Steatosis is associated with nonalcoholic fatty liver disease [10], and it is also noteworthy that ALT and AST:ALT were significantly different in men who were fat and fit and those who were fat and unfit. Insulin resistance and hyperinsulinemia are associated with endothelial dysfunction [6], and insulin concentrations may have been sufficient to impair endothelial function and raise blood pressure in men who were fat and fit and those who were fat and unfit. Obesity per se may also raise blood pressure [45], and BMI and waist girth were correlated with SBP and DBP independent of insulin concentration (eg, the partial correlation between waist girth and SBP was 0.5, $P < .001$).

Fitness is often associated with adipokines and markers of inflammation independent of fatness [13]. Adiponectin increases insulin sensitivity and has anti-inflammatory properties [6,7], but fitness was not associated with adiponectin after adjustment for waist girth. Fitness also explained little of the variance in proinflammatory cytokines; and we found no significant differences in hsCRP, leptin, TNF-α, and IL-6 in men who were fat and fit and those who were fat and unfit. Age is associated with inflammation, and participants in the present study were relatively young and had relatively low concentrations of proinflammatory cytokines [46,47]: 3% of men who were slim and fit, 26% of men who were slim and unfit, 50% of men who were fat and fit, and 41% of men who were fat and unfit had an elevated CRP concentration of greater than or equal to 2.00 $mg{\cdot}L^{-1}$. The prevalence of elevated CRP in overweight (BMI 25.0-29.9 $kg{\cdot}m^2$) and obese (BMI ≥30 $kg{\cdot}m^2$) men decreased across low-, moderate-, and high-fitness groups in a study of 722 men aged around 50 ± 10 years [47]. The prevalence of elevated fibrinogen (>2.97 $g{\cdot}L^{-1}$) in overweight and obese men also decreased across fitness tertiles [48]. Obesity is associated with leptin resistance [7,49], which may explain why leptin concentrations were similar in men who were fat and fit and men who were fat and unfit.

The “fitness vs fatness” issue has provoked heated debate in recent years [50], partly because fitness is more influential than activity in reducing the morbidity and mortality associated with obesity [30]. This discrepancy may occur because objectively measured fitness is a better reflection of habitual activity than self-reported activity [51]. This discrepancy may also occur because fitness reflects time spent in vigorous-intensity activity [52], which is probably more beneficial to health than moderate-intensity activity [53,54]. The present study of cardiometabolic risk factors suggests that fitness reduces the risks associated with obesity; however, it is possible that fitness reduces all-cause mortality independent of cardiometabolic risk factors [33]. More experimental research is required to determine the independent effects of exercise training on cardiometabolic risk factors in obese adults.

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Conflicts of Interest

None.

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