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Decline in Cardiorespiratory Fitness and Odds of Incident Depression

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Abstract

Background—Studies of physical activity and incidence of physician-diagnosed depression have been limited to a single estimate of self-reported physical activity exposure, despite follow-up periods lasting many years.

Purpose—To examine longitudinal change in cardiorespiratory fitness, an objective marker of habitual physical activity, and incident depression complaints made to a physician.

Methods—Cardiorespiratory fitness assessed at four clinic visits between 1971 and 2006, each separated by an average of 2–3 years, was used to objectively measure cumulative physical activity exposure in cohorts of 7936 men and 1261 women, aged 20–85 years, from the Aerobics Center Longitudinal Study who did not complain of depression at their first clinic visit in 1971–2003. Data were analyzed in August 2010.

Results—Across subsequent visits, there were 446 incident cases in men and 153 cases in women. After adjustment for age, time between visits, BMI at each visit, and fitness at Visit 1, each 1-minute decline in treadmill endurance (i.e., a decline in cardiorespiratory fitness of approximately 1 half-MET) between ages 51 and 55 years in men and ages 53 and 56 years in women, increased the odds of incident depression complaints by approximately 2% and 9.5%, respectively. The increased odds remained significant but were attenuated to 1.3% and 5.4% after further adjustment at each visit for smoking, alcohol use, chronic medical conditions, anxiety, and sleep problems.

Conclusions—Maintenance of cardiorespiratory fitness during late middle-age, when decline in fitness typically accelerates, helps protect against the onset of depression complaints made to a physician.

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Introduction

The projected burden of depression on public health worldwide is second to only cardiovascular disease,¹ but only half of U.S. adults with major depressive disorder receive healthcare treatment, which is often not adequate.^{2,3} RCTs have shown that exercise training reduces depression symptoms among depressed^{4–6} and chronically ill⁷ patients. Less is known about whether regular physical activity protects against the onset of depression symptoms.

At least 11 prospective observational studies suggest that there is a reduction in physician-diagnosed incident depression among people who were active at baseline.^{8–18} After adjustment for baseline risk factors, including age, gender, BMI, race, education, income, smoking, alcohol use, and medical conditions, the average odds were 27% lower among active people (OR=0.73 [95% CI=0.66, 0.81]). Only two studies reported results for both men and women.^{12,17} Those studies relied on self-reports of physical activity and used approaches to classify people into activity groups that were not equivalent across studies. None of the studies assessed change in physical activity exposure; included sequential measures of outcome; or discounted residual confounding by fluctuating traits common to physical inactivity and depression risk, including psychiatric comorbidities such as anxiety and sleep problems.²

Cardiorespiratory fitness (CRF) provides an objective, surrogate measure of physical activity exposure. The decline in CRF seen in healthy adults aged 40–60 years is best explained by reduced moderate-to-vigorous physical activity, after accounting for age, BMI, and smoking.¹⁹ In a prior prospective analysis of the Aerobics Center Longitudinal Study (ACLS) cohort, there was an inverse relationship between a single measure of CRF and subsequent depression symptoms.²⁰ Here, it was hypothesized that steeper declines in CRF among men and women from the ACLS cohort would be associated with higher odds of incident depression complaints made to a physician at four clinic visits, each separated by an average of 2–3 years.

Methods

Study Population

The ACLS is a prospective epidemiologic study investigating health outcomes associated with physical activity and CRF at the Cooper Clinic, Dallas TX.²¹ Participants elected to come to the clinic for periodic preventive medical examinations and for counseling regarding health and lifestyle behaviors, including diet and physical activity. The clinic broadly markets its services via mass media and among occupational groups and serves patients from all 50 states. Many participants were sent by their employer, some were referred by their physicians, and others were self-referred. At the time of their first clinic examination, the ACLS was described to patients who then provided written informed consent (nearly 100% of patients examined) for enrollment in the follow-up longitudinal study. The study protocol was approved annually by the Cooper Institute's IRB.

All ACLS participants received comprehensive preventive medical examinations and maximal graded treadmill exercise tests. Between 1971 and 2006, a total of 10,290 participants aged 20–85 years (14% of the enrolled population) without a complaint of depression at their first clinic visit received at least four comprehensive medical examinations and maximal graded treadmill exercise tests at routine clinic visits. Participants were excluded from analysis if they did not achieve at least 85% of age-predicted maximal heart rate during the treadmill test ($n=322$) or had missing data on any covariate other than BMI ($n=771$).

Thus, 1261 women and 7936 men were included for analysis. The median (interquartile range) of the duration between Visit 2 and Visit 1, Visit 3 and Visit 2, and Visit 4 and Visit 3 was 1.13 (1.08), 1.18 (1.11), and 1.33 (1.51) years, respectively. Most participants were non-Hispanic whites, relatively well-educated, with middle and upper SES.

Measures

Cardiorespiratory fitness—CRF was defined as the total time of a symptom-limited maximal treadmill exercise test, using a modified Balke protocol. The treadmill speed was 88 meters per minute for the first 25 minutes. The grade was 0% for the first minute, 2% for the second minute, and then increased 1% each subsequent minute until 25 minutes had elapsed. After 25 minutes, the grade remained constant while the speed increased 5.4 meters each minute until test termination. Patients were encouraged to give a maximal effort, and the test endpoint was volitional exhaustion or termination by the physician for medical reasons.

The mean (SD) percentage of age-predicted maximal heart rate achieved during exercise was 101.5% (6.6%). Total time of the test using this protocol correlates highly with measured maximal oxygen uptake in both men ($r=0.92$) and women ($r=0.94$). Thus, CRF in this study is analogous to maximal aerobic power defined as METs when estimated from the final treadmill speed and grade.²² Each minute of maximal treadmill test time reported here predicted 0.49 maximal METs (SEE=0.27, $r=0.993$) for men and 0.46 maximal METs (SEE=0.15, $r=0.997$) for women.

The exam included measurement of ECG during rest and exercise. Abnormal exercise ECG responses were broadly defined as rhythm and conduction disturbances or ischemic ST-T wave abnormalities. Trained laboratory technicians, with physician supervision, administered the exercise tests and other procedures according to a standardized manual of operations. At Visit 1, maximum heart rate ($M\pm SD$, bpm) was 175 ± 13 for women and 176 ± 14 for men. Maximum heart rate at subsequent visits did not differ ($p>0.10$) between incident depression cases and noncases, respectively, at subsequent visits.

Depression—Depression complaints were obtained from archived physician charts by the medical staff after follow-up to patient responses on a standardized medical history questionnaire that asked patients to indicate (yes or no) whether they had ever had a problem with depression (“Please indicate whether you have ever had a significant problem with any of the symptoms or conditions listed below”) and whether depression was a current problem (“Is this still a problem?”). Complaints of anxiety and sleep problems were assessed the same way.

Other measures—Height and weight were measured on a standard physician’s balance-beam scale and stadiometer. BMI was computed as Quetelet’s index. Random missing BMI observations (because of manual recording omissions of either height or weight) were 12.9% of all observations and were replaced by the mean of 10 imputations using a maximum-likelihood estimator.²³ Resting blood pressure was measured using standard auscultation methods after a brief period of quiet sitting.

Blood chemistry was analyzed for lipids and glucose using standardized automated bioassays. Hyperlipidemia was defined as fasting total cholesterol ≥ 6.2 mmol/L (240 mg/dL) or triglyceride ≥ 2.26 mmol/L (200 mg/dL). Individuals who reported a history of physician-diagnosed hypertension or who had blood pressures $\geq 140/90$ mmHg at the examination were classified as having hypertension. Diabetes was defined as a fasting glucose level ≥ 7.0 mmol/L (126 mg/dL), physician diagnosis, or treatment with insulin. Information on smoking habits (current smoker or not), alcohol intake (drinks per week),

and other medical conditions (yes or no) was obtained from a standardized medical history questionnaire. Number of medical conditions was the sum of the seven medical conditions (heart attack, stroke, cancer, diabetes, hypertension, hyperlipidemia, and abnormal resting or exercising ECG).

Data Analyses

Latent transition and class analysis—Participants in the cohort were classified as incident cases and noncases at a subsequent clinic visit using latent transition analysis (LTA) on observed cases and noncases performed by *Mplus* 6.1.²³ LTA provided Bayesian probability estimates of people being classified as depressed or not at Visits 3 and 4 given their depression status at preceding Visits 2 and 3. The number of classes for incident cases (i.e., patterns of change) was tested by a significant chi-square change ($\chi^2 \Delta$) estimated by a bootstrapped likelihood-ratio test.²³

Latent growth modeling—Trajectories of change in treadmill test duration in minutes were estimated using latent growth modeling (LGM)²⁴ in *Mplus* 6.1 after multivariate adjustment of treadmill time for between-participant differences in the covariates measured at each visit (simultaneous adjustment of the time-varying covariates in LGM would not converge because of low within-participant variation in the covariates). The following covariates were included in two models: (1) age, time between visits, and BMI, (2) those variables plus smoking (yes/no), alcohol use, number of medical conditions, and anxiety and sleep problems. The change latent variable was modeled twice – first, using just a linear change function, and second, using both linear and quadratic change functions. Robust maximum-likelihood parameters and their SEs were estimated for initial status (i.e., mean at baseline), change (i.e., slope of differences across the four clinic visits), and the variances (i.e., inter-individual differences) of initial status and change.

Baseline status and change in CRF were compared between the two classes (i.e., cumulative incident cases vs noncases) using χ^2 difference tests ($\chi^2 \Delta$) between a freely estimated baseline model and a nested model in which parameters were constrained to be equal between the groups. Model fit was evaluated with multiple indices, including the comparative fit index (CFI), Tucker Lewis index (TLI), the root mean-square error of approximation (RMSEA), and standardized root mean-square residual (SRMR).²⁵

Logistic regression analysis—Logistic regression analysis using maximum-likelihood estimation was performed in SPSS 18.0 to determine the odds that initial values and change functions (i.e., orthogonal contrasts for linear or quadratic trends) identified by the LGM for adjusted CRF across visits could accurately predict cases of incident depression (i.e., classes of cumulative cases and noncases defined the binary dependent variable). The group that never complained of depression symptoms (i.e., noncases) was the reference for all logistic ORs. Significance of likelihood ratios and goodness of model fit were tested by χ^2 tests. Sensitivity analysis tested the models while excluding first incidence cases at Visits 2 and 3 to help rule out a selection bias of early depression preceding the decline in fitness.

Results

Latent Transition and Class Analysis

Prevalence of depression complaints was 1.7%, 2.8%, and 3.8% of the cohort of men and 3.8%, 5.2%, and 7.8% of the cohort of women at Visits 2–4 (Table 1). At Visit 2, there were 132 incident depression cases in men and 48 incident cases in women. Over all three follow-up visits, there were 446 incident cases in men and 153 in women (Table 2). Cumulative incident rates were 5.6% in men and 12.1% in women. Fit of the LTA model was good for

men ($\chi^2(46)=60.2$, $p=0.078$) and women ($\chi^2(46)=12.2$, $p=1.00$). Probabilities of incident cases at Visits 3 and 4 were 2.0% and 2.3% in men and 3.8% and 5.3% in women.

Conversely, probabilities that people who were diagnosed with depression symptoms at the preceding visit did not complain of depression at the next visit were 47.7% and 42.4% in men and 58.3% and 47.0% in women, respectively. The best-fitting models indicated two classes of cases (i.e., observed cumulative cases and noncases) between Visits 2 and 4 for both men ($\chi^2 \Delta (4)=997.7$, $p<0.001$) and women ($\chi^2 \Delta (4)=177.8$, $p<0.001$). Three-class models were not supported ($p>0.50$).

Latent Growth Models

The overall trajectory of CRF was identified by a quadratic model adjusted for age, time between visits, and BMI that had good fit to the data for men ($\chi^2(1)=5.52$, $p=0.019$, CFI=1.00, TLI=0.998, RMSEA=0.024, SRMR=0.000) and women ($\chi^2(1)=0.79$, $p=0.374$, CFI=1.0, TLI=1.0, RMSEA=0.000, SRMR=0.000). The mean treadmill times at Visit 1 were 19.098 minutes, SE=0.045 in men and 14.436 minutes, SE=0.107 in women. There were slight linear increases from Visit 1 to Visit 2 for men (0.226 minutes, SE=0.036, $p<0.001$) and women (0.307 minutes, SE=0.089, $p=0.001$). Thereafter, there were quadratic declines for men (−0.205 minutes, SE=0.010, $p<0.001$) and women (−0.203 minutes, SE=0.024, $p<0.001$) at Visit 4.

Figures 1a and 2a show the growth trajectories for CRF in men and women, respectively, for cumulative incident depression cases and noncases. In men, incident cases had a linear (−0.037 minutes, SE=0.158) and quadratic (−0.201 minutes, SE=0.045) decline in CRF (adjusted for age, time between visits, and BMI) that was greater than in noncases (0.242 minutes, SE=0.037; −0.205 minutes, SE=0.010; $\chi^2 \Delta=22.97$, $df=2$, $p<0.001$). In women, the linear increase (0.663 minutes, SE=0.309) and quadratic decline (−0.417 minutes, SE=0.087) in CRF each were greater for incident cases than noncases (0.256 minutes, SE=0.092; −0.173, SE=0.025; $\chi^2 \Delta 1df=7.37$, $p<0.01$ and $\chi^2 \Delta 1df=4.4$, $p<0.05$). Adjustments for the other covariates had no appreciable effects on model fit or parameter estimates for either men or women, except the linear change no longer differed between incident cases and noncases in women ($\chi^2 \Delta 1df=1.60$, $p>0.10$; Figures 1b and 2b).

Logistic Regression Analysis

The first logistic model was significant and had good fit for men (linear change: $\chi^2(1)=18.8$, $p<0.001$; goodness of fit: $\chi^2(7932)=7923$, $p=0.528$; Hosmer and Lemeshow $\chi^2(8)=1.9$, $p=0.985$) and women (quadratic change: $\chi^2(1)=12.4$, $p=0.001$; goodness of fit: $\chi^2(1257)=1275$, $p=0.358$; Hosmer and Lemeshow $\chi^2(8)=11.2$, $p=0.193$; Table 3). Odds of incident depression for a 1-minute decline in CRF across visits were 2% higher in men (OR=1.019 [95% CI=1.004, 1.021]) and 9.5% higher in women (OR=1.095 [95% CI=1.041, 1.151]). Results were attenuated but had similar fit and remained significant in the second logistic model that further adjusted for smoking, alcohol use, number of medical conditions, and complaints of anxiety or sleep problems in men (linear change, $p=0.004$) and women (quadratic change, $p=0.034$). Adjusted odds of incident depression with a 1-minute decline in CRF were 1.3% higher in men (OR=1.013 [95% CI=1.004, 1.021]) and 5.4% higher in women (OR=1.054 [95% CI=1.004, 1.106]).

The linear model had a similarly good fit when first incidence cases at Visits 2 and 3 were excluded for men (Model 1 OR=1.022 [95% CI=1.008, 1.036]; Model 2 OR=1.012 [95% CI=0.998, 1.027]) and women (Model 1 OR=1.109 [95% CI=1.028, 1.197]; Model 2 OR=1.079 [95% CI=1.001, 1.163]).

Discussion

The results extend findings of prospective studies of self-reported physical activity and depression risk by showing that the odds of incident depression were increased by 2% (1.3% adjusted) in men for each minute (i.e., about 1 half-MET) of linear decline in fitness from the second to the fourth clinic visit (between ages 51 and 55 years) and by 9.5% (5.4% adjusted) in women for each minute of decline between the third and fourth visit (between ages 53 and 56 years). Although more modest in size than reported by prior observational studies of physical activity, these odds are not biased by self-reporting of physical activity. Also, they represent multiple assessments of exposure and depression outcomes, which had previously been reported only for symptom reduction among depressed patients.²⁶

The analyses cannot rule out the possibility that incident depression resulted in physical inactivity and, hence, reduced CRF. However, this alternative interpretation is unlikely given the prior observation in the ACLS cohort that baseline fitness measured at the first clinic visit predicted low incident depression estimated by elevated scores on the CES-D screening test.²⁰ Also, the higher odds of depression with declining fitness held in the sensitivity analysis that excluded people with first incidence at Visit 2 or Visit 3, supporting the likelihood that early depression did not precede the decline in fitness. Finally, the similar maximum heart rate observed for incident cases and noncases at each visit, and similar treadmill times for cases and noncases at Visits 2 and 3, indicate that people were not less motivated to perform at their maximum level on the treadmill test when they were depressed.

Novel features of the study include the use of CRF as an objective, surrogate measure of repeated physical activity exposures across time in men and women from the same cohort and repeated assessment of time-varying covariates. There could be residual confounding by traits common to both physical activity and depression proneness,²⁷ but this is the first prospective report of incident depression and physical activity or fitness to assess and control for complaints of anxiety or sleep problems, which are comorbid with major depression in middle-aged U.S. adults.²

A weakness of the study is the definition of incident depression based on a complaint made to a physician rather than on the use of a standardized clinical interview or research diagnostic criteria specific to types of depressive disorder. Most physicians are not trained to administer or interpret diagnostic tests for depression, which are currently in flux²⁸ (www.dsm5.org/proposedrevision/Pages/DepressiveDisorders.aspx). Nonetheless, incident cases of a depression complaint made to a physician have clinical relevance for preventive medicine settings.²⁹ Contemporary information on medication use or antidepressant treatments, menopausal or pregnancy status, or dietary habits was not sufficient to include these factors in the analysis.

Another limitation is that the cohort is predominantly white, relatively healthy and well-educated, and of middle-to-upper SES.³⁰ As with other epidemiologic cohort studies, there is possible selection bias or lack of representativeness of the study population. However, the homogeneity of the ACLS population sample on sociodemographic factors enhances the internal validity of the current findings, which are consistent with others from cross-sectional^{31,32} and longitudinal^{33,34} analyses of self-reported physical activity in population minority groups or other nationalities.³⁵ Incidence rates in this middle-aged ACLS cohort (12% in women and nearly 6% in men) are consistent with those reported in earlier prospective studies of physical activity and physician-diagnosed incident depression^{8–18} (mean of those studies, 4% [95% CI= 0.02, 0.06]; range: 1.7%–12.7%). Prevalence rates in the ACLS cohort are similar to 12-month rates in U.S. adults aged 50–60 years.²

The decline in fitness seen here among noncases (about 6% in men and 4% in women) is consistent with that observed in the total ACLS cohort.¹⁹ Among incident cases, the linear decline across the four visits in men was nearly 8%, and the quadratic decline between Visits 3 and 4 in women was nearly 6%. Each of those declines approximates an additional loss of 0.5 minutes of maximal treadmill time, an amount easily retained in most people by modest amounts of regular, moderate-to-vigorous physical activity consistent with current recommendations for health.³⁶ A large randomized trial would be needed to determine how many incident cases might be prevented by mitigating this decline in fitness. The results reported here suggest that modest amounts of regular moderate-to-vigorous physical activity³⁶ sufficient to slow the accelerating age-related decline in cardiorespiratory fitness during late middle-age has protective benefits against the onset of depression complaints in both men and women.

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Figure 1. Decline in cardiorespiratory fitness and incident depression in men

Note: Values are adjusted for (a) age, time between visits, and BMI; (b) age, time between visits, BMI, smoking, alcohol use, number of medical conditions, and complaints of anxiety or sleep problems. Adjusted Ms and SEs at each visit are shown; SEs for male noncases (0.0465 to 0.510) are smaller than the symbol height.

Figure 2. Decline in cardiorespiratory fitness and incident depression in women

Note: Values are adjusted for (a) age, time between visits, and BMI; (b) age, time between visits, BMI, smoking, alcohol use, number of medical conditions, and complaints of anxiety or sleep problems. Adjusted Ms and SEs at each visit are shown.

Table 1

Participants characteristics of 1261 women and 7936 men according to follow-up visits, M (SD) or %, unless otherwise noted

Characteristics	Visit 1	Visit 2	Visit 3	Visit 4
Women				
Age, years	48.9 (10.5)	51.1 (10.2)	53.4 (10.0)	55.9 (10.1)
BMI, kg/m ²	22.4 (3.4)	22.6 (3.4)	22.9 (3.4)	23.1 (3.5)
Treadmill test duration, minutes	14.4 (4.4)	14.6 (4.4)	14.2 (4.4)	13.5 (4.4)
Maximal METs	10.0 (2.1)	10.1 (2.0)	9.9 (2.1)	9.6 (2.0)
Maximal heart rate, bpm	175 (13)	174 (13)	172 (14)	170 (14)
Resting systolic blood pressure, mmHg	114 (15)	115 (15)	117 (16)	119 (17)
Resting diastolic blood pressure, mmHg	76 (9)	76 (9)	77 (9)	78 (9)
Fasting total cholesterol, mmol/L	5.3 (1.0)	5.3 (0.9)	5.3 (0.9)	5.3 (1.0)
Fasting triglyceride, mmol/L	1.1 (0.8)	1.1 (0.7)	1.1 (0.7)	1.1 (0.7)
Fasting glucose, mmol/L	5.7 (0.8)	5.2 (0.8)	5.2 (0.9)	5.2 (0.8)
Number of medical conditions, <i>n</i> ^a	0.4 (0.5)	0.4 (0.5)	0.5 (0.5)	0.5 (0.5)
Current smoker, <i>n</i> (%)	69 (5.5)	57 (4.5)	40 (3.2)	37 (2.9)
Alcohol use (> 5 drinks per week), <i>n</i> (%)	220 (17.4)	247 (19.6)	294 (23.3)	330 (26.2)
Sleep problems, <i>n</i> (%)	76 (6.0)	117 (9.3)	145 (11.5)	190 (15.1)
Anxiety, <i>n</i> (%)	44 (3.5)	76 (6.0)	83 (6.6)	113 (9.0)
Depression, <i>n</i> (%)	0 (0)	48 (3.8)	66 (5.2)	98 (7.8)
Men				
Age, years	49.3 (10.5)	51.2 (10.2)	53.1 (10.1)	55.3 (10.0)
BMI, kg/m ²	25.8 (3.1)	25.9 (3.1)	26.1 (3.2)	26.3 (3.3)
Treadmill test duration, minutes	19.1 (4.7)	19.2 (4.6)	18.7 (4.6)	18.0 (4.7)
Maximal METs	12.2 (2.3)	12.2 (2.3)	12.0 (2.3)	11.6 (2.3)
Maximal heart rate, bpm	176 (14)	174 (14)	172 (14)	170 (15)
Resting systolic blood pressure, mmHg	122 (14)	122 (14)	123 (14)	124 (15)
Resting diastolic blood pressure, mmHg	81 (9)	81 (9)	81 (9)	82 (9)
Fasting total cholesterol, mmol/L	5.3 (1.0)	5.3 (1.0)	5.2 (1.0)	5.1 (1.1)
Fasting triglyceride, mmol/L	1.4 (1.0)	1.4 (1.0)	1.4 (1.0)	1.4 (1.0)
Fasting glucose, mmol/L	5.6 (0.8)	5.5 (0.7)	5.5 (0.8)	5.6 (1.0)

Characteristics	Visit 1	Visit 2	Visit 3	Visit 4
Number of medical conditions, ^a	0.5 (0.5)	0.5 (0.5)	0.6 (0.5)	0.6 (0.5)
Current smoker, <i>n</i> (%)	887 (11.2)	772 (9.7)	733 (9.2)	699 (8.8)
Alcohol use ($\geq$ 5 drinks per week), <i>n</i> (%)	2436 (30.7)	2562 (32.3)	2707 (34.1)	2913 (36.7)
Sleep problems, <i>n</i> (%)	466 (5.9)	572 (7.2)	681 (8.6)	810 (10.2)
Anxiety, <i>n</i> (%)	171 (2.2)	227 (2.9)	315 (4.0)	387 (4.9)
Depression, <i>n</i> (%)	0 (0)	132 (1.7)	224 (2.8)	305 (3.8)

^aMedical conditions included heart attack, stroke, cancer, diabetes, hypertension, hyperlipidemia, and abnormal resting or exercising electrocardiogram bpm, beats per minute

Table 2

Participant baseline characteristics of 1261 women and 7936 men according to incident depression status, M (SD) unless otherwise noted

Characteristics	Women		Men	
	Never Depressed (n=1108)	Ever Depressed (n=153)	Never Depressed (n=7490)	Ever Depressed (n=446)
Age, years	49.3 (10.5)	46.6 (9.8)	47.8 (10.4)	49.4 (10.5)
BMI, kg/m ²	22.5 (3.4)	22.2 (3.0)	25.8 (3.1)	26.1 (3.5)
Treadmill test duration, minutes	14.4 (4.5)	14.8 (4.2)	19.5 (4.9)	19.1 (4.7)
Maximal METs	10.2 (2.0)	10.0 (2.1)	12.4 (2.4)	12.2 (2.3)
Maximal heart rate, bpm	175 (13)	175 (13)	176 (13)	176 (14)
Number of medical conditions, ^a	0.5 (0.7)	0.4 (0.6)	0.7 (0.8)	0.7 (0.8)
Current smoker, n (%)	62 (5.6)	7 (4.6)	838 (11.2)	49 (11.0)
Alcohol use (< 5drinks per week), n (%)	199 (18.0)	21 (13.7)	2304 (30.8)	132 (29.6)
Sleep problems, n (%)	63 (5.7)	13 (8.5)	414 (5.5)	52 (11.7)
Anxiety, n (%)	34 (3.1)	10 (6.5)	138 (1.8)	33 (7.4)

^aMedical conditions included heart attack, stroke, cancer, diabetes, hypertension, hyperlipidemia, and abnormal resting or exercising electrocardiogram.
bpm, beats per minute

Table 3

Logistic models of incident depression according to declines in CRF

	B	SE	Wald statistic	Likelihood ratio, X² (1 df)	p-value	OR (95% CI)
MODEL 1^a						
Men						
Intercept	2.964	0.251	139.390	154.410	<0.001	
Baseline CRF	-0.002	0.013	0.020	0.020	0.887	0.998 (0.973, 1.024)
Linear decline	0.019	0.004	19.183	18.808	<0.001	1.019 (1.011, 1.028)
Quadratic decline	0.015	0.014	1.227	1.219	0.269	1.015 (0.988, 1.043)
Women						
Intercept	1.977	0.357	30.741	32.095	<0.001	
Baseline CRF	0.011	0.024	0.209	0.210	0.647	1.011 (0.964, 1.061)
Linear decline	0.016	0.009	3.365	3.409	0.065	1.016 (0.999, 1.034)
Quadratic decline	0.091	0.025	12.572	12.373	<0.001	1.095 (1.041, 1.151)
MODEL 2^b						
Men						
Intercept	3.003	0.261	131.958	144.509	<0.001	
Baseline CRF	-0.006	0.014	0.220	0.220	0.639	0.994 (0.968, 1.020)
Linear decline	0.013	0.004	8.249	8.171	0.004	1.013 (1.004, 1.022)
Quadratic decline	-0.001	0.013	0.006	0.006	0.940	0.999 (0.973, 1.025)
Women						
Intercept	1.838	0.367	25.117	25.917	<0.001	
Baseline CRF	0.016	0.025	0.414	0.416	0.519	1.016 (0.967, 1.068)
Linear decline	0.011	0.009	1.735	1.752	0.186	1.011 (0.994, 1.029)
Quadratic decline	0.053	0.025	4.538	4.507	0.034	1.054 (1.004, 1.106)

^aModel 1 was adjusted for age, time between visits, and BMI at each visit.^bModel 2 was further adjusted for smoking, alcohol use, medical conditions, anxiety, and sleep problems at each visit.
CRF, cardiorespiratory fitness