Longitudinal Associations of Aerobic Activity, Muscle-Strengthening Activity, and Adiposity with Cardiorespiratory Fitness

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ABSTRACT

MEERNIK, C., M. SCHEINOWITZ, D. LEONARD, C. E. BARLOW, T. LEONARD, K. PETTEE GABRIEL, A. PAVLOVIC, J. D. BERRY, L. F. DEFINA, and K. SHUVAL. Longitudinal Associations of Aerobic Activity, Muscle-Strengthening Activity, and Adiposity with Cardiorespiratory Fitness. *Med. Sci. Sports Exerc.*, Vol. 57, No. 2, pp. 345–354, 2025. **Purpose:** Cardiorespiratory fitness (CRF) declines with age, and greater declines increase the risk for adverse health outcomes. Understanding factors that attenuate age-related decreases in CRF can help extend healthy life. We sought to determine the longitudinal associations of aerobic physical activity, muscle-strengthening activity (MSA), and adiposity with CRF. **Methods:** Study participants were enrolled in the Cooper Center Longitudinal Study and had three or more preventive medical examinations at the Cooper Clinic (Dallas, Texas) during 1987–2019. Aerobic activity and MSA were self-reported, and three measures of adiposity were clinically assessed: body mass index (BMI), body fat percentage, and waist circumference. CRF, expressed as metabolic equivalents (METs), was estimated by a maximal treadmill test. The longitudinal associations of aerobic activity, MSA, and adiposity with CRF were estimated using multivariable mixed linear regression models. **Results:** The study included 6105 participants who were followed for a median of 7.1 yr. Most participants were men (83.6%), and their average age at baseline was 47.0 (SD = 8.7) yr. Mean CRF at baseline was 12.2 (SD = 2.3) METs. Increasing aerobic activity (per 500 MET·min·wk^{-1}, $\beta = 0.069$, 95% confidence interval = 0.064–0.074 METs) or MSA (per days per week, $\beta = 0.066$, 95% confidence interval = 0.058–0.073 METs) was associated with increased CRF over time. Increasing BMI, body fat percentage, or waist circumference were each associated with decreased CRF over time. **Conclusions:** These data offer longitudinal evidence on how changes in aerobic activity, MSA, and various measures of adiposity (beyond BMI) independently correlate with CRF over time. Healthy lifestyle behaviors that include increasing aerobic and MSA and limiting adiposity may positively influence the retention of fitness with age and improve downstream health outcomes. **Key Words:** ADIPOSITY, CARDIORESPIRATORY FITNESS, EXERCISE, HEALTHY LIFESTYLE

EPIDEMIOLOGY

Low cardiorespiratory fitness (CRF) is a risk factor for various chronic health conditions and premature death, with associations similar to those observed for other strong risk factors such as smoking, diabetes, or coronary artery disease (1–11). Low CRF is also an important marker of frailty, contributing to more functional limitations and disability in older age (12). Notably, CRF often declines with healthy aging, particularly after middle age (13–15), but steeper declines in CRF increase the risk for adverse health outcomes, including hypertension, metabolic syndrome, hypercholesterolemia (16), frailty (17), and all-cause and cardiovascular disease (CVD) mortality (18). Identifying modifiable factors that can minimize age-related declines in CRF—or contribute to stable or improving CRF with age—is thus critical to extend healthy years of life.

Aside from age, CRF is influenced by genetic, sociodemographic, behavioral, and health-related factors (19,20). Physical activity is one of the more frequently studied modifiable determinants of CRF, demonstrating a dose–response relationship in longitudinal studies: increasing the frequency of activity is associated with increased CRF over time among adults (15,19,21–25). However, the majority of studies have only assessed aerobic physical activity or have analyzed all forms of physical activity together (19), which precludes more specific guidance regarding

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the effectiveness of aerobic activity or muscle-strengthening activity (MSA) in minimizing CRF declines with age (14).

Clinical studies have primarily focused on aerobic activity to increase CRF (26), but MSA may also affect CRF, as demonstrated in randomized controlled trials and intervention studies (27–31). MSA—particularly dynamic and high-intensity MSA—can lead to physiological adaptions that contribute to increases in CRF (29,32). Although mechanistic evidence remains relatively scarce, data suggest that adaptations span metabolic, molecular, cardiovascular, and musculoskeletal responses and include improved oxidative capacity associated with increased mitochondrial activity, increased leg strength and Type IIa muscle fibers (less fatigable), increased muscle capillary growth, and increased cardiac output (29,32–34). However, the quality of evidence regarding the effect of MSA on CRF remains low (27). Existing studies investigating the effect of MSA on CRF have had short durations (most ≤6 months) and inclusion criteria has often been narrow (e.g., physical inactive adults or clinical populations with existing morbidity), so it is unclear how findings translate over years or decades among a general population.

CRF is also affected by adiposity, which demonstrates an inverse relationship with CRF in longitudinal studies (19,23) (although individuals can be both overweight/obese and fit and at similar risk of death as normal weight and fit individuals (35)). However, many previous studies only assessed adiposity using body mass index (BMI), which lacks sensitivity in identifying excess body fat (36,37). Longitudinal studies that use adiposity measures other than BMI are lacking (19), limiting the strength of evidence regarding how changes in adiposity within individuals affect CRF over time.

In the current study, we sought to examine changes in CRF within individuals over time while controlling for between-participant effects, thereby isolating time-varying behavioral and health-related factors from non–time-varying genetic and sociodemographic determinants of CRF. Specifically, this study extends previous research—including research within the Cooper Center Longitudinal Study (CCLS) (15,38)—by assessing aerobic activity and MSA separately in relation to CRF, as well as assessing measures of adiposity beyond BMI. The aims of the study were to estimate the longitudinal associations of 1) aerobic activity and MSA with CRF and 2) BMI, body fat percentage, and waist circumference with CRF.

METHODS

Study sample. Aerobic physical activity, MSA, adiposity measures, and CRF were measured among adults who visited the Cooper Clinic (Dallas, Texas) for a preventive medical examination during 1987–2019 and were enrolled in the CCLS after providing informed consent. Baseline clinic visits occurred between 1987 and 2017. At each clinic visit, study participants underwent fitness assessment, physical examination, and laboratory testing and completed a medical history questionnaire. The CCLS is approved annually by the Institutional Review Board at The Cooper Institute.

Among 59,501 CCLS participants with a clinic visit between 1987 and 2019, we excluded participants who did not have at least three clinic visits over the study period (n = 46,784); participants with missing covariates (n = 459); those who did not perform a modified Balke treadmill test (n = 16); those who did not reach at least 85% of their age-predicted maximal heart rate during the treadmill test (n = 53); those <20 yr old (n = 3) or >80 yr old (n = 4); those with a history of myocardial infarction (n = 22), stroke (n = 9), or cancer (n = 278); or those who were underweight (BMI <18.5 $kg \cdot m^{-2}$) (n = 33). After the exclusion criteria above were considered, 5735 additional individuals were excluded because they no longer had at least three qualifying visits. The final analytic cohort included 6105 apparently healthy CCLS participants. Subgroup analysis was limited to included participants with complete data on body fat percentage and waist circumference (n = 2984). Supplemental Table 1 (Supplemental Digital Content, http://links.lww.com/MSS/D96) provides descriptive statistics comparing included participants with those who had no other exclusions except for having only one or two clinic visits during the study period. Included participants (i.e., those with at least three clinic visits) were more likely to be men, White, nonsmokers, meet national guidelines for aerobic activity and MSA, have lower BMI and body fat, and have higher CRF.

Aerobic physical activity and MSA. The primary exposures were changes in aerobic physical activity and MSA over time. Detailed leisure-time aerobic activity during the prior 3 months were self-reported at each clinic visit, including the type, frequency, and duration of activity, as previously described (39). Metabolic equivalent (MET) values for aerobic activity intensity were assigned using the Compendium of Physical Activities (40); moderate-intensity aerobic activities were those from 3 to <6 METs, whereas vigorous-intensity aerobic activities were those ≥6 METs. MET values were multiplied by the activity's weekly frequency and duration and summed across activities as MET-minutes per week. MSA was self-reported using two questions: "Are you currently involved in a muscle-strengthening program?" and "How many days per week do you do these exercises?" Corresponding to the units of current national guidelines (41), aerobic activity was analyzed as MET-minutes per week, and MSA was analyzed as days per week.

Adiposity measures. Three measures of adiposity were examined in relation to CRF over time: BMI, body fat percentage, and waist circumference among a subgroup of participants with complete information. All were assessed at each clinic visit by trained staff. BMI was calculated as a participant's weight in kilograms divided by height in meters squared; weight was measured using a standard clinical scale and height was measured using a stadiometer. Body fat percentage was estimated with the Jackson–Pollock equation using the sum of seven skinfold sites (42), which were assessed with calipers. Waist circumference was measured at the umbilicus level with a cloth tape measure (43).

Covariates. Additional participant characteristics were assessed at each clinic visit, including age, sex, and self-reported

EPIDEMIOLOGY

current smoking status, which were identified *a priori* as confounders of the relationship between physical activity or adiposity and CRF based on previous literature (14,15,44,45). Importantly, age, sex, and smoking—together with physical activity, adiposity, and genetics—account for the majority of variability in CRF among generally healthy adults (14,15,46–48).

CRF: Outcome. CRF, expressed as METs, was estimated at each clinic visit by a maximal treadmill test using a modified Balke protocol, as previously described (49). Briefly, treadmill speed and grade were systematically increased until volitional exhaustion or termination due to medical reasons (49). Based on the final treadmill speed and grade, CRF was estimated (50) and converted to METs (1 MET = 3.5 mL O_2 uptake·kg^{-1}·min^{-1} (51)). The time on the treadmill using this method is strongly correlated with $\dot{V}O_{2max}$ in both men (r = 0.92) (52) and women (r = 0.94) (53).

Statistical analysis. In primary analysis, multivariable mixed linear regression models were fit to estimate beta (β) values and 95% confidence intervals (CI) for the longitudinal associations of aerobic activity and MSA with CRF. CRF at each time point was regressed on the baseline values of the exposures and the corresponding changes from baseline to separate the between-participant (i.e., cross-sectional) and within-participant (i.e., longitudinal) estimates. The longitudinal association reported for any exposure is the estimated slope of the within-participant CRF versus exposure graph, adjusted for baseline values and changes in covariates. The models included random intercept and time effects to account for the correlation of repeated measurements and repeated changes in measurements within participants. Age-group at baseline (20–44, 45–64, and 65–80 yr) was used as the between-participant timescale and time since baseline was used as the within-participant timescale. The rate of change of CRF within participants at different baseline ages was estimated using an age-group–time interaction. Change in aerobic activity from baseline (per MET-minute per week) and change in MSA from baseline (per day per week) were analyzed as continuous exposures, adjusting for sex (men, women), current smoking (yes, no; at baseline and change from baseline), BMI (at baseline and change from baseline), and baseline aerobic activity and MSA.

To improve interpretability, we multiplied the regression coefficient and SE for the change in aerobic activity by 500 so that estimates are reported per 500 MET·min·wk^{-1} (rather than per 1 MET·min·wk^{-1}), which aligns with the current recommended level of aerobic activity in the United States (54). Thus, the estimate can be interpreted as the change in CRF associated with transitioning from being inactive to meeting guidelines for aerobic activity. Additionally, we estimated longitudinal associations between duration (h·wk^{-1}) and volume (MET·min·wk^{-1}) of aerobic activity intensity (moderate vs vigorous) with CRF, overall and by sex.

In the subgroup of participants with complete data on BMI, body fat percentage, and waist circumference, changes from baseline in each adiposity measure were assessed in relation to CRF in separate models using the same methods as described above for changes in physical activity over time; models adjusted for age-group at baseline, sex, current smoking (at baseline and change from baseline), aerobic activity (at baseline and change from baseline), MSA (at baseline and change from baseline), adiposity measure of interest at baseline, and time since baseline. Adiposity measures were standardized to mean zero and unit SD (based on all observations) before entering the models to enable comparisons (i.e., estimates reflect a change in CRF per SD change in adiposity measure). Additionally, the association between the change in each adiposity measure and CRF was assessed using within-person explained variance (calculated as 1 minus the ratio of random slope variance estimates in which the numerator was estimated from the model described above, and the denominator was estimated from a random intercept and slopes model without BMI, body fat percentage, or waist circumference) (55).

Effect modification of the associations of aerobic activity, MSA, and adiposity with CRF by sex was examined using stratified analysis. Separate analyses were also conducted among participants 50 yr and older at baseline (n = 3,240 overall; n = 1,513 with complete adiposity data) to assess whether associations differed among older adults compared with the overall sample; this age cut point was used to align with the typical onset of age-related changes in skeletal muscle (56). This analysis adjusted for the same covariates as analysis of the overall sample, although the categorization of age-groups now had a lower bound of 50 yr (i.e., 50–64 yr, 65–80 yr). Lastly, to estimate unadjusted time trends and intraclass correlations (ICC) in the exposure variables, we fit sex-specific models in which aerobic activity, MSA, and adiposity measures at each time point were regressed separately on time since baseline with random intercepts but no other effects. Analyses were initiated in 2023 using SAS/STAT®, version 9.4 (SAS Institute, Inc., Cary, NC).

RESULTS

Sample characteristics. Among 6105 CCLS participants with a median follow-up of 7.1 yr (quartile 1, quartile 3: 4.3, 12.2), most were men (83.6%) and identified as White (94.9%) (Table 1). Participants had an average of 4.9 (SD = 2.3) clinic visits (range, 3–19 visits), which were a mean of 2.3 (SD = 2.0) yr apart. At baseline clinic visit, the average age of study participants was 47.0 (SD = 8.7) yr, a minority of participants were current smokers (8.7%), and the mean BMI was 25.8 (SD = 3.6) kg·m^{-2}. Participants' mean CRF at baseline was 12.2 (SD = 2.3) METs, and it was higher among men (12.5 METs, SD = 2.2) compared with women (10.4 METs, SD = 2.0) (Table 1).

Among men, the rate of change of CRF declined significantly faster with increasing age at baseline; similarly, among women, the rate of change of CRF declined faster with increasing age at baseline, although differences were not statistically significant (Fig. 1). Time trends and ICC for aerobic activity, MSA, and adiposity measures are presented in Table 2. In the full sample, aerobic activity tended to decline slightly over time among women and remain stable among men. MSA and BMI increased over time among both men and

TABLE 1. Characteristics at baseline clinic visit (1987–2017) among participants with three or more clinic visits in the CCLS (n = 6105), overall and by sex.

Characteristic	n (%)		
	Overall	Men	Women
N	6105	5101 (83.6)	1004 (16.4)
Age-group (yr)			
20–44	2537 (41.6)	2111 (41.4)	426 (42.4)
45–64	3393 (55.6)	2834 (55.6)	559 (55.7)
65–80	175 (2.9)	156 (3.1)	19 (1.9)
Race or ethnicity[a]			
White	5021 (94.9)	4182 (95.4)	839 (92.6)
Black	60 (1.1)	46 (1.0)	14 (1.5)
Hispanic	125 (2.4)	98 (2.2)	27 (3.0)
Other race or ethnicity	85 (1.6)	59 (1.3)	26 (2.9)
Missing	814	716	98
Current smoker	531 (8.7)	493 (9.7)	38 (3.8)
Aerobic activity (MET·min·wk^{-1})			
0	741 (12.1)	634 (12.4)	107 (10.7)
>0 to <500	791 (13.0)	652 (12.8)	139 (13.8)
≥500 (meeting national guidelines)	4573 (74.9)	3815 (74.8)	758 (75.5)
MSA (d·wk^{-1})			
0	3326 (54.5)	2813 (55.1)	513 (51.1)
1	202 (3.3)	168 (3.3)	34 (3.4)
2–7 (meeting national guidelines)	2577 (42.2)	2120 (41.6)	457 (45.5)
		Mean (SD)	
Age (yr)	47.0 (8.7)	47.1 (8.8)	46.6 (8.6)
Moderate aerobic activity (min·wk^{-1})	64.1 (106.5)	55.2 (99.4)	109.3 (128.0)
Vigorous aerobic activity (min·wk^{-1})	126.3 (162.2)	128.3 (153.4)	115.8 (200.6)
Total aerobic activity (MET·min·wk^{-1})	1330.1 (1346.7)	1325.0 (1290.1)	1356.1 (1604.6)
MSA (d·wk^{-1})	1.4 (1.7)	1.4 (1.7)	1.4 (1.6)
BMI (kg·m^{-2})	25.8 (3.6)	26.3 (3.3)	23.2 (3.5)
Body fat (%)[b]	21.6 (5.6)	20.9 (5.3)	25.0 (5.8)
Waist circumference (cm)[b]	90.0 (11.3)	92.4 (9.3)	74.3 (10.4)
Maximal CRF (METs)	12.2 (2.3)	12.5 (2.2)	10.4 (2.0)

[a]Percentages exclude missing observations.
[b]Characteristics contain missing data (body fat: 9.2% missing overall; waist circumference: 11.4% missing overall).

women. In the subsample with complete data on the adiposity measures, aerobic activity tended to decline slightly over time among men and increase slightly among women. MSA and all measures of adiposity increased over time among men and women. In both samples, correlations of adiposity over time were higher than those of aerobic activity and MSA as indicated by ICC.

Descriptive statistics for the subgroup of participants who had nonmissing data on all adiposity measures (n = 2984) are presented in Supplemental Table 2 (Supplemental Digital Content, http://links.lww.com/MSS/D96). The subgroup had a higher proportion of men compared with the full sample (88.7% vs 83.6%, respectively) but was otherwise similar.

Aerobic physical activity and MSA. On average, participants reported approximately 1 h of moderate-intensity aerobic activity per week and approximately 2 h of vigorous-intensity aerobic activity per week at baseline clinic visit (Table 1). Men reported less moderate- and more vigorous-intensity activity compared with women. Participants reported an average of 1330 (SD = 1347) MET·min·wk^{-1} of aerobic activity, with 74.9% of participants achieving recommended physical activity guidelines of at least 500 MET·min·wk^{-1} (41) (Table 1); 12.1% reported no aerobic activity at baseline. Additionally, participants reported an average of 1.4 (SD = 1.7) d·wk^{-1} of MSA, with 42.2% of participants reporting MSA at least 2 d·wk^{-1} per guidelines (41) and 54.5% reporting no MSA (Table 1). The prevalence and the weekly duration of physical activity types reported at the baseline clinic visit are described in Supplemental Table 3 (Supplemental Digital Content, http://links.lww.com/MSS/D96). The most frequently reported activities overall were walking (36.8% overall, 33.2% among men, 54.6% among women), jogging (35.6% overall, 38.8% among men, 19.3% among women), and weight machine (32.3% overall, 31.9% among men, 34.5% among women).

Longitudinal associations of aerobic physical activity and MSA with CRF. In longitudinal multivariable analysis estimating β coefficients, an increase of 500 MET·min·wk^{-1} of aerobic activity over time was associated with 0.069 (95% CI = 0.064–0.074) METs increase in CRF, and an increase of 1 d·wk^{-1} of MSA over time was associated with 0.066 (95% CI = 0.058–0.073) METs increase in CRF. Associations were similar, although of slightly lower magnitude, among participants 50 yr and older at baseline: an increase of 500 MET·min·wk^{-1} of aerobic activity over time was associated with 0.048 (95% CI = 0.041–0.054) METs increase in CRF, and an increase of 1 d·wk^{-1} of MSA over time was associated with 0.055 (95% CI = 0.045–0.065) METs increase in CRF.

In sex-stratified analysis, changes in aerobic activity over time had a greater positive association with CRF among men compared with women: an increase of 500 MET·min·wk^{-1} was associated with 0.073 (95% CI = 0.067–0.078) METs increase in CRF in men compared with 0.045 (95% CI = 0.034–0.057) METs increase in CRF in women (Fig. 2).

In analysis of aerobic activity intensity, among men, increases in the duration (per hour per week) of vigorous-intensity activity were associated with approximately two times the increase in CRF compared with increases in the duration of moderate-intensity activity (β = 0.065, 95% CI = 0.060–0.070 vs β = 0.031, 95% CI = 0.024–0.038, respectively) (Supplemental Table 4, Supplemental Digital Content, http://links.lww.com/MSS/D96). However, increases in the volume (per 500 MET·min·wk^{-1}) of either vigorous- or moderate-intensity activity were associated with similar increases in CRF. A different pattern was observed among women; increases in the duration of aerobic activity were associated with similar increases in CRF, regardless of intensity, whereas increases in the volume of moderate-intensity activity had a stronger association with CRF compared with increases in the volume of vigorous-intensity activity.

Longitudinal associations of adiposity with CRF. In three separate longitudinal models, 1 SD increase in BMI (β = −1.028, 95% CI = −1.070 to −0.986 METs), body fat percentage (β = −0.617, 95% CI = −0.645 to −0.589 METs), or waist circumference (β = −0.691, 95% CI = −0.726 to −0.655 METs) over time was associated with a decrease in CRF. In assessing the explanatory power of each adiposity measure, body fat percentage explained 22.2% of the within-person variance, followed by waist circumference (17.3%) and BMI (14.9%).

Similar to associations with physical activity among the older-aged sample, associations with each adiposity measure were of slightly lower magnitude among participants ≥50 yr old at baseline (per SD increase: BMI, β = −0.873, 95%

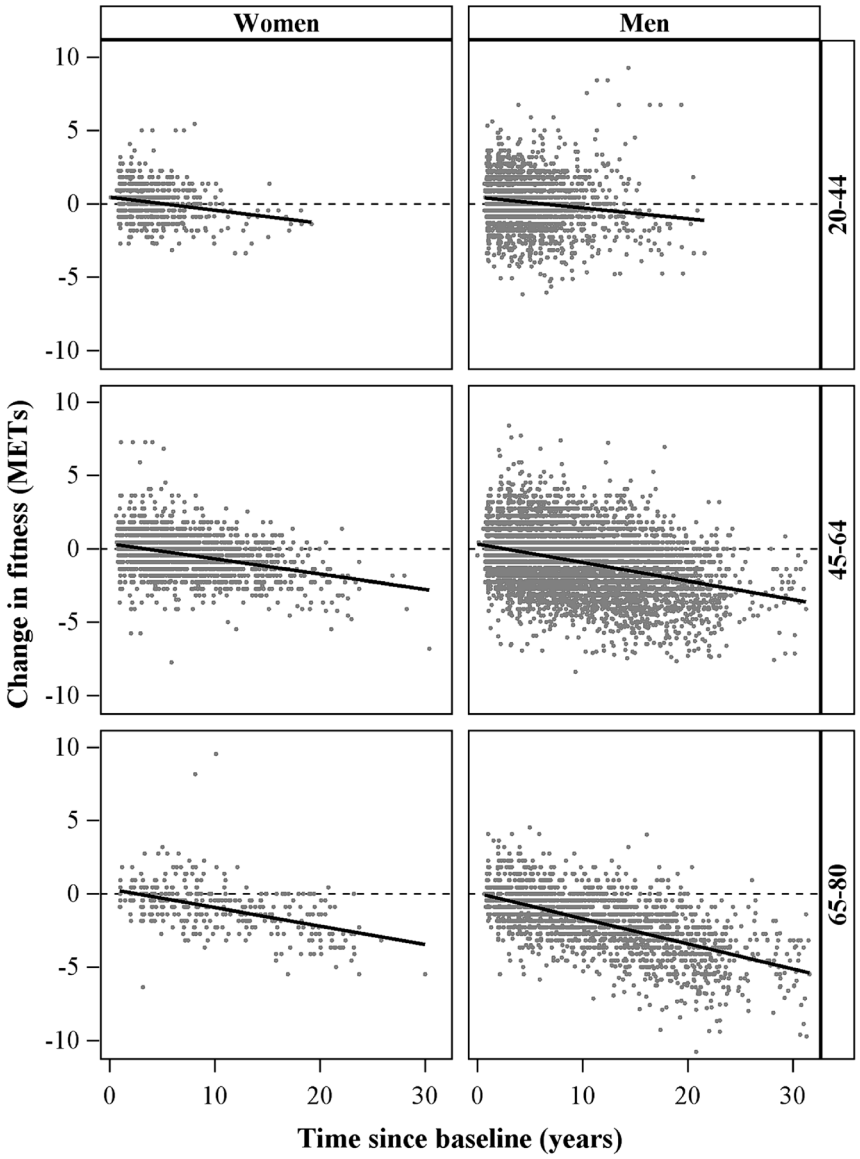

FIGURE 1—Change in CRF (METs)[a] versus time since baseline clinic visit (yr) among CCLS participants, by age at baseline (yr) and sex (n = 6105). [a] Unadjusted slopes (METs per year) among women: ages 20–44 yr at baseline: −0.06; ages 45–64 yr at baseline: −0.08; ages 65–80 yr at baseline: −0.13 (time–age interaction P = 0.051). Unadjusted slopes (METs per year) among men: ages 20–44 yr at baseline: −0.08; ages 45–64 yr at baseline: −0.13; ages 65–80 yr at baseline: −0.19 (time–age interaction P < 0.0001).

CI = −0.933 to −0.813 METs; body fat percentage, β = −0.457, 95% CI = −0.495 to −0.420 METs; waist circumference, β = −0.546, 95% CI = −0.592 to −0.500 METs). In sex-stratified analysis, changes in all three measures of adiposity (BMI, body fat percentage, waist circumference) had greater inverse associations with CRF among men compared with women, such that increasing adiposity over time was associated with greater decreases in CRF among men (Fig. 3). The same patterns were observed using unstandardized coefficients (Supplemental Table 5, Supplemental Digital Content, http://links.lww.com/MSS/D96).

DISCUSSION

Among a large sample of apparently healthy adults with multiple preventive medical exams during 1987–2019, increasing aerobic activity or MSA within individuals over time was associated with increased CRF. Conversely, increasing adiposity over time (as measured by BMI, body fat percentage, or waist circumference) was associated with decreased CRF. Associations were consistent among both men and women and among participants 50 yr and older at baseline. Among adiposity measures, body fat percentage explained the most within-person variance in CRF, followed by waist circumference and BMI. These data offer longitudinal evidence that changes in aerobic activity, MSA, and adiposity (beyond BMI) within individuals independently correlate with changes in CRF—a strong, clinically relevant predictor of chronic disease and mortality (2).

Previous research within this cohort observed that midlife aerobic activity and BMI were related to longitudinal changes in CRF across at least two clinic visits (15), but the relation between changes in those exposures and changes in CRF over time was not examined—a key limitation given age-related

TABLE 2. Unadjusted time trends and ICC in measures of physical activity and adiposity among participants with three or more clinic visits in the CCLS.

		Mean at Baseline		Mean Change Per Year		
Exposure	Sex	Estimate	SE	Estimate	SE	Intraclass Correlation
Full sample (n = 6105)						
Aerobic activity (MET·min·wk^{-1})	Men	1368.04	15.59	0.41	1.33	0.48
	Women	1379.83	35.04	−4.81	3.71	0.41
MSA (d·wk^{-1})	Men	1.46	0.02	0.03	0.00	0.47
	Women	1.49	0.04	0.04	0.00	0.45
BMI (kg·m^{-2})	Men	26.23	0.05	0.07	0.00	0.90
	Women	23.15	0.11	0.09	0.00	0.89
Subsample with complete adiposity data (n = 2984)						
Aerobic activity (MET·min·wk^{-1})	Men	1431.73	20.58	−3.91	1.58	0.49
	Women	1385.91	57.18	3.83	5.08	0.47
MSA (d·wk^{-1})	Men	1.48	0.03	0.04	0.00	0.47
	Women	1.65	0.07	0.03	0.01	0.40
BMI (kg·m^{-2})	Men	25.81	0.06	0.07	0.00	0.89
	Women	23.06	0.17	0.06	0.01	0.89
Body fat (%)	Men	20.19	0.09	0.16	0.00	0.77
	Women	24.08	0.29	0.03	0.01	0.78
Waist circumference (cm)	Men	91.36	0.16	0.13	0.01	0.81
	Women	72.74	0.45	0.24	0.03	0.75

changes in physical activity and adiposity (57,58). Our study extends beyond changes in aerobic activity and BMI to additionally assess the role of changing MSA, abdominal obesity (waist circumference), and body composition (body fat percentage) on CRF change. Data regarding the influence of MSA on CRF throughout the life course are particularly needed given the primary focus to date on aerobic activity as a means of increasing CRF and improving health outcomes (26). The mechanisms linking MSA to CRF are not as well understood but may be related to metabolic, molecular, cardiovascular, and musculoskeletal adaptations (29,32–34). When possible, future longitudinal studies should analyze the independent and joint effects of aerobic activity and MSA on CRF to inform more targeted interventions and physical activity recommendations that optimize improvements in CRF.

Our study is among the first to demonstrate longitudinal improvements in CRF associated with an increasing number of days per week of MSA and declines in CRF associated with varying measures of increasing adiposity. Notably, changes in all measures of adiposity were more strongly related to CRF in men compared with women. Conversely, a study within the Coronary Artery Risk Development in Young Adults (CARDIA) cohort found generally consistent longitudinal associations between BMI and CRF by sex (23); differences in findings may be related to differences in the age of study populations. To inform clinical advice, future studies should explore how changes in adiposity affect changes in CRF across the lifespan and whether these associations are modified by sex.

Our findings align with other longitudinal studies that have examined changes in various measures of physical activity and adiposity on CRF over time (21–23,59). For instance, in the CARDIA cohort, the cumulative number of years not meeting physical activity guidelines (aerobic activity and MSA grouped as total physical activity) over a 20-yr follow-up was associated with lower CRF in early adulthood and over time in both men and women (n = 5018), as was the cumulative number of years being overweight or obese (as measured by BMI) (23). Additionally, CARDIA participants with the greatest declines in physical activity, or the greatest increases in weight, over a 7-yr period experienced the greatest declines in CRF (59).

In our study, the increases in CRF related to aerobic activity or MSA appeared to be of lower magnitude than the decrease

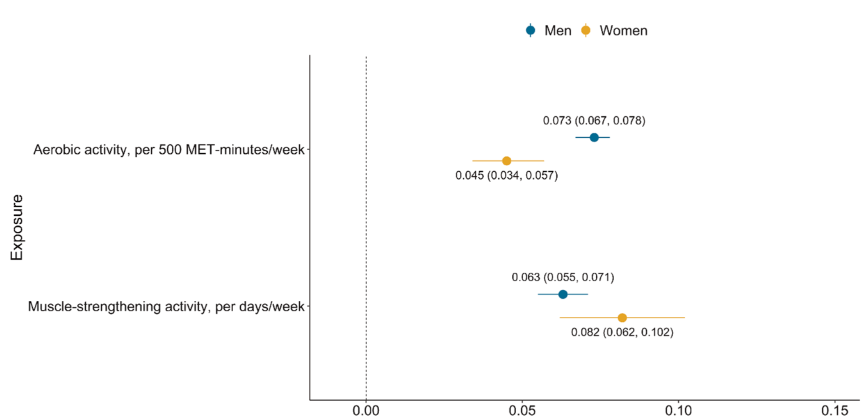

FIGURE 2—Estimated beta coefficients for longitudinal associations between physical activity and CRF (METs) in the CCLS[a]. [a] Estimates reflect the change in CRF associated with a change in the exposure over time. Exposures were included in the same model and were adjusted for age-group at baseline, sex, current smoking (at baseline and change from baseline), BMI (at baseline and change from baseline), aerobic activity at baseline, MSA at baseline, and time since baseline.

EPIDEMIOLOGY

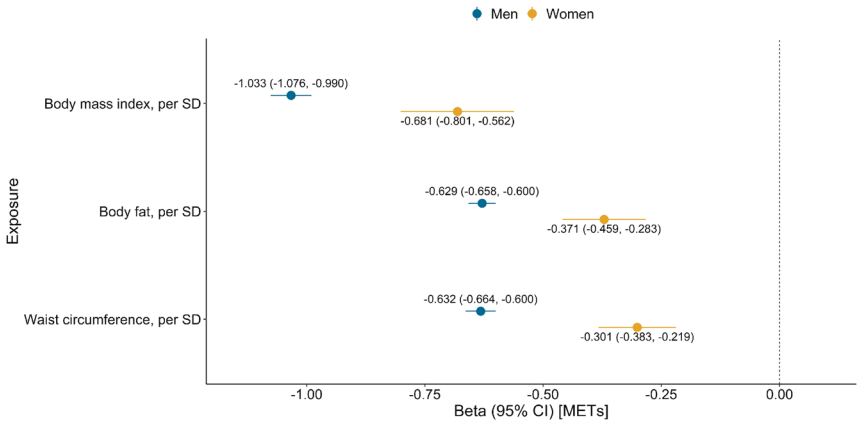

FIGURE 3—Estimated beta coefficients for longitudinal associations between standardized adiposity measures and CRF (METs) in the CCLS[a]. [a] Estimates reflect the change in CRF associated with a change in the exposure over time. Only participants with complete data on all adiposity measures were included (*n* = 2984). Each adiposity measure was evaluated in a separate model. Models adjusted for age-group at baseline, sex, current smoking (at baseline and change from baseline), aerobic activity (at baseline and change from baseline), MSA (at baseline and change from baseline), adiposity measure of interest at baseline, and time since baseline.

in CRF related to adiposity, which has been observed in previous studies as well (59,60). For context, for the average man in the United States (61), a 2.9-point increase in BMI (approximately 20-lb weight gain) over time is associated with a 1-MET decline in CRF based on our results (slightly less than a 1 SD increase in BMI). Similarly, for the average woman in the United States (61), a 4.7-point increase in BMI (approximately 27-lb weight gain) is associated with a 1-MET decline in CRF (slightly more than a 1 SD increase in BMI). Although not directly comparable, the relation between increasing aerobic activity or MSA with CRF was an order of magnitude lower. However, this may have been influenced by a study population that was fitter and more active at baseline, on average, than the general U.S. population (57,62). For instance, compared with adults ages 40–49 yr in the National Health and Nutrition Examination Survey, our sample at baseline (mean age of 47 yr) was fitter by 3.3% to 5.9% (mean CRF in men: 12.1 vs 12.5 METs, respectively; mean CRF in women: 9.8 vs 10.4 METs, respectively) (62). Additionally, among adults 18 yr and older in the National Health Interview Survey, 46.9% met recommended guidelines for aerobic activity (vs 74.9% in our sample), and 31.0% met guidelines for MSA (vs 42.2% in our sample) (57). In a sample that is less active and fit at baseline, physical activity may be associated with more pronounced gains in CRF (63,64), similar to evidence that improved CRF is associated with more pronounced health benefits in low fit individuals (6,65).

Regardless, even modest improvements in CRF may improve health. For instance, each unit increase in $\dot{V}O_{2max}$ (equivalent to 0.29 METs increase in CRF) was associated with a 45-d increase in life expectancy in the Copenhagen Male Study (66). Other studies have demonstrated that a 1-MET increase in CRF is associated with reductions in all-cause mortality (by 10%–25%) (1,8,67), CVD mortality (by 13%) (8), cancer mortality (by 7%) (8), and CVD or coronary heart disease (CHD) incidence (by 15%) (1). The health benefits of higher CRF are also observed in high-risk individuals, including those with metabolic syndrome, diabetes, or preexisting CHD (65,67,68). Improvements in CRF among inactive individuals (i.e., transitioning out of the lowest quintile of fitness) during midlife confers a similar protective association: a 44% reduction in all-cause mortality compared with individuals who remained the lowest fit over an average of 5 yr (69).

A few limitations of the study should be considered. CCLS participants are generally healthy, White, active, and have access to preventive healthcare, which improves internal validity but may limit the generalizability of findings. As mentioned, our sample may have achieved less pronounced gains in CRF associated with increases in physical activity due to high baseline levels of CRF (63,64,70). Additionally, the sample may have experienced steeper age-related declines in CRF compared with a less active sample (71–73). However, the CCLS is one of the few cohorts in the United States with even one time point of CRF; multiple time points allow for novel longitudinal analysis of CRF changes over time in relation to changes in exposures. Importantly, the same treadmill test protocol was used throughout the study period, although CRF was estimated, not directly measured. Adiposity measures were objectively measured in the clinic, whereas aerobic activity and MSA were self-reported. Self-reported physical activity is often higher compared with direct measurement (e.g., accelerometers) (74,75), which would bias estimates toward the null in instances of nondifferential misclassification. Future studies should evaluate directly measured physical activity over time in relation to changes in CRF. Aligning with previous longitudinal studies of CRF change (14,15,22,59), our analyses accounted for age, sex, and smoking status; in addition to physical activity and adiposity, these factors account for the majority of nongenetic contributors to CRF among generally healthy adults (14,15,46–48). However, changes in other lifestyle and health-related factors (e.g., diet, sleep, medication use) may also contribute to CRF changes over time and should be further explored (19).

Additionally, the aim of the study was not to distinguish the precise regimen of aerobic activity or MSA that most benefits

CRF over time. For instance, prior research has demonstrated that vigorous-intensity aerobic activity differentially influences CRF compared with moderate-intensity aerobic activity, and these associations vary based on initial fitness level (25,64,76). Similarly, among men in our study, increases in the duration of vigorous-intensity activity were associated with nearly twice the increase in CRF compared with increases in the duration of moderate-intensity activity, although patterns were different among women. Future studies in more diverse samples should further explore how different intensities (including intensity of MSA), types, and patterns of physical activity (e.g., duration of bouts; "weekend warrior" pattern) (25) protect against age-related declines in CRF and associated health outcomes in men and women.

Our study extends findings from previous research by following more than 6000 participants across at least three clinic visits, with novel longitudinal data on changes in MSA and multiple measures of adiposity. Although CRF is affected by a complex interplay of modifiable and nonmodifiable factors (e.g., age, genetics), our study demonstrated that increasing aerobic activity and MSA and decreasing adiposity are associated with improved CRF over time. These and other healthy lifestyle behaviors (e.g., not smoking (47)) may have clinically impactful effects on fitness and downstream health outcomes, thereby extending healthy lifespan.

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The Cooper Center Longitudinal Study (https://www.cooperinstitute.org/research/ccls) data are not publicly available. A scientific data request may be submitted to The Cooper Institute's Scientific Review Board Committee for review. The committee meets regularly to assess the merits of all requests.

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