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## Factors Associated with Age-related Declines in Cardiorespiratory Fitness from Early Adulthood through Midlife: CARDIA

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### Abstract

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**Purpose:** To describe maximal and submaximal cardiorespiratory fitness from early adulthood to midlife and examine differences in maximal fitness at age 20 and changes in fitness over-time by sub-categories of socio-demographic, behavioral, and health-related factors.

**Methods:** Data include 5,018 Coronary Artery Risk Development in Young Adults participants [mean (SD) age 24.8 (3.7) years, 53.3% female and 51.4% Black participants] who completed at least one maximal graded exercise test at baseline and/or the Year 7 and 20 exams. Maximal and submaximal fitness were estimated by exercise duration and heart rate at the end of stage 2. Multivariable adjusted linear mixed models were used to estimate fitness trajectories using age as the mechanism for time after adjustment for covariates. Fitness trajectories from ages 20 to 50 in 5-year increments were estimated overall and by sub-groups determined by each factor after adjustment for duration within the less favorable category.

**Results:** Mean (95% confidence interval) maximal fitness at age 20 and 50 years was 613 (607, 616) and 357 (350, 362) seconds; submaximal heart rate during this period also reflected age-related fitness declines [126 (125, 127) and 138 (137, 138) beats per minute]. Compared to men, women had lower maximal fitness at age 20 ( $p<0.001$ ), which persisted over follow-up ( $p<0.001$ ); differences were also found by race within sex-strata (all  $p<0.001$ ). Differences in maximal fitness at age 20 were noted by socio-economic, behavioral, and health-related status in young adulthood (all  $p<0.05$ ), which persisted over follow-up (all  $p<0.001$ ) and were generally consistent in sex-stratified analyses.

**Conclusions:** Targeting individuals experiencing accelerated fitness declines with tailored intervention strategies may provide an opportunity to preserve fitness throughout midlife to reduce lifetime cardiovascular disease risk.

## Keywords

EXERCISE TEST; FOLLOW-UP STUDIES; YOUNG ADULT; MIDDLE LIFE

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## INTRODUCTION

Substantial evidence accumulated over the past several decades has informed the inverse association of cardiorespiratory fitness (henceforth: fitness) with risk of premature mortality and non-fatal and fatal cardiovascular disease (CVD) (1–9). Age-related declines in fitness have also been documented (10–17) and have been attributed to changes in heart structure and function that are mediated by reductions in cardiac output and/or arteriovenous oxygen difference (18). The association of age with fitness is further influenced by hereditary factors and underlying disease, as well as potentially modifiable risk factors including physical activity and body composition (12, 18).

However, much of the evidence cited for age-related declines in fitness comes from cross-sectional studies, which suggests a 5–10% lower fitness level per decade increase in age across adulthood (10–16). Evidence from longitudinal studies is significantly more limited and includes small, homogenous samples including endurance-trained athletes (19–25). A study by Fleg et al. (17) using the Baltimore Longitudinal Study of Aging (BLSA) cohort expanded this evidence by documenting age-related declines in a population-based sample and found that the rate of decline in peak oxygen uptake ( $\text{VO}_2$ ) ranged from 3–6% per

decade in the second and third decade of life to 20% per decade in the seventh decade and beyond. Study findings also suggested that the rate of decline per decade was higher in men than women after the fourth decade (17). Similar to prior work, the BLSA sample was largely homogeneous; primarily comprised of White and affluent participants. Additional limitations of prior longitudinal studies documenting age-related declines in fitness include relatively short follow-up periods and limited assessments (<10 years; n≈2 assessments), which is not ideal given adulthood lasts several decades (17, 24).

Given the importance of fitness across the life course to optimize cardiovascular health, additional research is also needed to examine early adult factors that are associated with lower concurrent fitness and accelerated age-related fitness declines. Early adulthood may be a particularly important period of the life-course given it is when a greater appreciation of, and value is placed on, healthy lifestyle behaviors (26), but it is also when there is a perception of invincibility to future risk of disease (27). Early adulthood is also a period when a number of important life events occur that can potentially impact intentions to engage in healthy lifestyle behaviors (28). Given potential differences in fitness by sex (29), it is also important to examine the role of socio-economic, behavioral, and health-related factors on age-related declines in fitness in women and men, separately.

To address these research gaps, we leverage Coronary Artery Risk Development in Young Adults (CARDIA), a diverse and well-characterized prospective cohort study that conducted a symptom-limited graded exercise treadmill test (GXT) protocol at baseline and year 7 and 20 follow-up exams. The objectives of this study are to: 1) describe maximal and submaximal fitness from early adulthood to midlife and 2) examine differences in estimated maximal fitness at age 20 and changes in fitness through midlife by sub-categories of socio-demographic, behavioral, and health-related factors in the entire cohort and by sex.

## METHODS

### Design Overview and Study Participants

The CARDIA cohort includes 5,115 adults aged 18 to 30 years enrolled at baseline (1985–86) at four clinics across the United States (U.S.), including Birmingham, Alabama; Chicago, Illinois; Minneapolis, Minnesota, and Oakland, California, to provide approximately equal representation within each clinic by race (Black or White), sex (male or female), age (18–24 or 25–30 years), and education (high school or less or more than high school). Community-based sampling was performed at three clinics (Birmingham, Chicago, and Minneapolis), while Oakland participants were sampled from the membership of a large integrated health care program (Kaiser Permanente Northern California). Approximately 50% of those invited were successfully enrolled. Participants have been re-examined approximately every 2 to 5 years. At the year 20 follow-up exam (2005–06), 72% of the surviving cohort was examined (30). All CARDIA participants provided informed consent at each examination and the institutional review boards at each participating center approve the study annually.

## Data Collection

Standardized questionnaires and protocols were used to assess age and early adult factors associated with concurrent fitness levels and fitness change, which included socioeconomic (sex assigned at birth, self-defined race, education and financial strain), behavioral (physical activity, alcohol and tobacco use), and health-related [body mass index (BMI); based on measured height (m) and weight (kg) and self-rated health] factors. All data collection measures and protocols are publicly available through the CARDIA website (see Exam Materials under Scientific Resources) (30).

Factors associated with early adult fitness levels and fitness change from early adulthood through midlife were organized as time-invariant or time-varying measures and selected a priori based on literature review and/or biological plausibility for confounding the main associations of interest. Time-invariant measures included: sex assigned at birth (male or female), self-identified race (Black or White), and enrolling CARDIA clinic to account for U.S. regional differences. Time varying measures included: education [high school (or equivalent) degree or less or Associate's degree or more), financial strain (difficulty paying for basics like food, medical care and heating: somewhat hard, hard, very hard or not very hard), physical activity (not meeting or meeting physical activity guidelines based on a threshold of <300 or ≥300 exercise units (i.e., unit of expression for summary estimates), respectively (31), as reported on the CARDIA Physical Activity Questionnaire), alcohol use (yes or no in the past year), tobacco use (former/current or never tobacco user), BMI [overweight/obese ( $\geq 25 \text{ kg/m}^2$ )] or underweight/normal ( $<25 \text{ kg/m}^2$ )] and self-rated health from the Short Form 12 Health Survey® (SF-12) (32) (poor/fair or good/excellent). Baseline measures were used to infer early adult factors associated with concurrent fitness and fitness change from early adulthood to midlife. To account for the effect of measures that could change during the 20 years of follow-up, the cumulative number of years classified within the less favorable category was estimated using data collected at the Year 0, 2, 5, 7, 10, 15, and 20 exams. Specifically, beginning with the baseline exam, each of the early adult factors were defined by the number of years a participant reported (or was): 1) having less than or equal to a high school degree or equivalent; 2) having it be at least somewhat hard to pay for basics; 3) not meeting physical activity guidelines; 4) using alcohol or tobacco products; 5) having overweight or obese; and/or 6) having fair or poor health.

**Maximal Graded Exercise Test**—The CARDIA GXT was designed to estimate maximal, symptom-limited performance and utilized a modified Balke protocol (33), consisting of up to nine 2-minute stages of increasing difficulty (increase in treadmill speed and/or grade), beginning at an estimated workload of 4.1 metabolic equivalent of task (MET)s and ending at 19.0 METs (34). The testing procedure at Years 0, 7, and 20 was identical and included the following components: screening for medical eligibility using American College of Sports Medicine criteria (35); participant preparation for electrocardiogram (ECG); resting (supine) 12-lead ECG; pre-exercise (standing) 3-lead ECG and blood pressure; exercise on the treadmill; recovery following exercise; and participant discharge. Participant disposition at each of the exams when the GXT was offered has been previously reported (36).

Resting heart rate [beats per minute (bpm)] was obtained as part of the core exam after sitting quietly at rest for five minutes. Pulse, blood pressure, and a 12-lead ECG were obtained on each participant at rest, and heart rate, blood pressure, and a three-lead ECG obtained during the last 30 seconds of each 2-minute stage, at peak effort (immediately prior to stopping), and every minute for 3 minutes post-exercise. A rating of perceived exertion (RPE; 6–20 scale) was obtained near the end of each stage and at maximal exercise (37).

Peak  $\text{VO}_2$ , defined as the highest value of  $\text{VO}_2$  attained during a staged GXT (38), was used to estimate maximal fitness based on exercise duration on the treadmill (in seconds) among those achieving 85% of age-predicted maximal heart rate using the CARDIA formula, which considers the quadratic association of age with maximal heart rate (39). Submaximal fitness was estimated based on heart rate at the end of stage 2, with higher values indicative of lower submaximal fitness. The workload for stage 2 was: 3.4 mph treadmill speed, 6% grade or 6.4 METs. A protocol deviation occurred at one clinic during the Year 7 follow-up exam by allowing use of the treadmill handrails (39) during exercise, which resulted in inflated (longer) exercise duration estimates (i.e., maximal fitness indicator). The exercise duration values were corrected using a calibration equation that utilized information collected at the baseline and year 20 exams (see Supplemental Text, SDC 5). For these tests, a rating of perceived exertion threshold of 15 or “hard” (37), rather than 85% of age-predicted maximal heart rate, was used to infer maximal effort (85% age-predicted maximal heart rate for mean cohort age of 31 years at Year 7 = 150.8 bpm). A sensitivity analysis, excluding these tests (n=926) was conducted.

### Statistical Analysis

Analyses were conducted using R version 4.0.1, and the code used to complete these analyses is publicly available at: <https://github.com/bcjaeger/CARDIA---GXT-duration>. Initial statistical analyses involved data cleaning, variable derivation, and a descriptive content analysis that included univariate summaries of primary analysis variables at the Year 0, 7, and 20 exams, overall and by groups defined by race and sex.

Linear mixed models were fit to estimate maximal and submaximal fitness over-time using age as the mechanism for time. The association of age with fitness indicators was modeled using restricted cubic splines with five knots at the 10<sup>th</sup>, 25<sup>th</sup>, 50<sup>th</sup>, 75<sup>th</sup>, and 90<sup>th</sup> age percentiles. All models included participant-specific random intercepts to account for correlation in repeated assessments and were adjusted for sex (in models including the entire cohort), race (in models not examining differences by race), education, and CARDIA clinic. Models were further adjusted for sociodemographic, behavioral, and health-related factors that may influence maximal fitness at baseline and during the follow-up. Factors influencing maximal fitness during the follow-up period included the cumulative number of years within the less favorable category. To assess whether there was a difference in maximal fitness over follow-up, we tested for interaction between age and each factor listed above. All models were fitted to the entire cohort and to male and female participants, separately.

The percent change in fitness for each successive 5-year increment was also calculated using estimated maximal and submaximal fitness by race within sex strata [(mean fitness at given 5-year age increment – mean fitness at immediately prior age increment) / mean

fitness at immediately prior age increment \* 100]. Five-year, rather than 10-year (17), increments were used to provide more granular estimates of fitness change during this important life-course transition. We also estimated the difference in fitness between sub-groups determined by baseline status of sociodemographic, behavioral, and health-related factors. These differences were estimated from age 20 to 50 in 5-year increments. Bootstrap resampling was applied to generate 95% confidence intervals (CI) for the differences in estimated fitness described above.

The count and proportion of missing values was examined overall, by exam, and by race and sex groups. Based on these data, we assumed the primary analysis variables were missing at random and conducted multiple imputation to obtain valid standard errors for statistical inference. Multiple imputation with chained equations was applied, accounting for the longitudinal design of the study. Five imputed datasets were formed by fitting a random forest to each variable with missing data, separately, and then performing predictive mean matching.

As the current analysis jointly performed multiple imputation and bootstrapping, recommendations of Schomaker et al. (40) were followed to obtain bootstrapped CIs that incorporate uncertainty from missing values. That is, we imputed five datasets using each bootstrapped replicate of the current study's data and formed bootstrapped distributions of model estimates using the pooled estimates from the multiple imputed data.

## RESULTS

The analytic sample included 5,018 CARDIA participants who completed the GXT protocol at least once (n=11,108 tests), did not use beta blocker medications at the time of the GXT, and achieved 85% of their age-predicted maximal heart rate (Figure 1) (39). Table 1 shows the baseline characteristics of the entire analytic sample and after stratification by race and sex. Mean [standard deviation (SD)] age and BMI were 24.8 (3.7) years and 24.5 (5.0) kg/m<sup>2</sup>, respectively, and most were women (53.3%) and identified as Black (51.4%). Black men and White women had the highest and lowest proportion of less than or equal to a high school degree or equivalent (82% and 52%, respectively). Black and White men also had the highest and lowest proportion of financial strain (41% and 27%, respectively) and current tobacco use (37% and 27%, respectively). Black women and White men had the lowest and highest proportion of meeting physical activity guidelines (37% and 73%, respectively) and alcohol use (78% and 92%, respectively). Black and White women also had the highest and lowest proportion of fair or poor health status (16% and 6%, respectively).

Mean (95% CI) estimated maximal fitness at age 20 years was 613 (607, 616) seconds, which decreased to 357 (350, 362) seconds at age 50. These age-related declines in fitness were consistent when considering mean (95% CI) estimated heart rate at the end of stage 2 which ranged from 126 (125, 127) to 138 bpm (137, 138) bpm. Both maximal and submaximal fitness indicators supported significantly higher estimated fitness at age 20 in men compared with women [736 (732, 743) and 510 (501, 516) seconds, respectively, and 113 (112, 114) and 137 (135, 138) bpm, respectively; both p<0.001]. While men had higher fitness levels than women through age 50 years (both p<0.001), the estimated differences

attenuated over-time [435 (426, 441) and 292 (283, 297) seconds at age 50, respectively, and 127 (126, 128) and 147 (145, 148) bpm at age 50, respectively].

When comparing differences by race within sex-strata (Figure 2; Supplemental Table 1, SDC 1), Black woman had lower estimated maximal fitness levels at age 20 and the rate of 5-year fitness decline ranged from  $-6.4\%$  (ages 20 to 25) to  $-10\%$  per 5-year age increment through age 50 years compared with a more attenuated range of maximal fitness decline from  $-0.8\%$  to  $-10\%$  in White women. Black men had lower estimated maximal fitness levels at age 20 than White men and these differences increased over-time [Black men:  $-6.9\%$  (ages 20–25) to  $-11\%$  per 5-year age increment through age 50 years; White men:  $-4.2\%$  to  $-8.2\%$ ]. Among women, estimated submaximal fitness at age 20 did not significantly differ by race ( $p=0.48$ ); however, the rate of increase in heart rate at the end of stage 2 was higher in Black compared with White women ( $p<0.001$ ). In men, estimated submaximal fitness at age 20 was higher in Black men compared with White men ( $p=0.008$ ). However, differences in estimated submaximal fitness by race were not statistically supported at age 25. At each 5-year increment from age 30 and beyond, estimated submaximal fitness was lower in Black men compared with White men ( $p$  for differences in estimated submaximal fitness over follow-up  $<0.001$ ).

Supplemental Table 2, SDC 2, shows the differences in estimated maximal fitness at age 20 and changes in fitness over-time by sub-categories of socio-demographic, behavioral, and health-related factors in the overall cohort. After multi-variable adjustment, maximal fitness levels at age 20 were lower in those with less education, with more difficulty paying for basics, not physically active, no alcohol use, former or current smokers, having overweight or obese, and in fair or poor self-rated health (all  $p<0.05$ ). Similarly, differences in age-related declines in fitness were noted over the follow-up period by sub-categories of education, financial strain, physical activity, alcohol use, smoking status, weight status, and self-rated health (all  $p<0.001$ ). Of note, differences in age-related declines in fitness by sub-categories of alcohol use attenuated and reversed direction after age 45 with those not consuming alcohol having higher estimated maximal fitness levels than those reporting alcohol use when considering the cumulative number of years reporting alcohol use.

Results were largely consistent in sex-stratified analysis, with a few differences noted. Specifically, among women (Supplemental Table 3, SDC 3), there was no evidence for a difference in estimated maximal fitness at age 20 by baseline category of financial strain or smoking status [ $-7.7$  ( $-19.0, 3.1$ ) and  $19$  ( $8.9, 34$ ) seconds, respectively]. Also, there was a lack of evidence for a difference in fitness over-time by alcohol status. While there was a lack of evidence that estimated fitness at age 20 differed by education or alcohol consumption in men [ $-25$  ( $-47, -9.9$ ) and  $8.5$  ( $-6.1, 26.0$ ) seconds, respectively; Supplemental Table 4, SDC 4), changes in fitness over-time differed by these factors (both  $p<0.001$ ).

### Sensitivity Analysis

After excluding tests ( $n=926$ ) subject to the protocol deviation at Year 7, the estimates and interpretations did not vary substantially; therefore, the corrected maximal fitness estimates obtained from this clinic were included in primary analysis (results available upon request).

## DISCUSSION

Optimizing cardiorespiratory fitness across the life-course, despite age-related anatomical and physiological changes to the cardiorespiratory system, is a critically important factor to reduce the ongoing cardiovascular disease burden. While prior exercise training and epidemiologic studies have described age-related declines in fitness, the current study contributes several novel findings to this evidence base. First, age-related declines in maximal fitness appeared to occur within the first few years of early adulthood and accelerated through midlife; declines that were mirrored when considering submaximal fitness. Second, important differences in maximal and submaximal fitness levels during early adulthood, and changes in fitness from early adulthood to midlife, were noted by race in men and women. Over the follow-up period, submaximal and maximal fitness declines were more attenuated in White men compared to Black men. Third, there were several factors present in early adulthood that were associated with both lower concurrent fitness levels and accelerated fitness declines through midlife; particularly when accounting for the cumulative number of years within the less favorable category since baseline.

While there remains limited evidence from longitudinal studies documenting age-related declines during earlier periods of adulthood, cross-sectional and longitudinal findings from the BLSA suggested a 5% per decade decline in peak  $\text{VO}_2$  starting at age 30 years (17). A rate of decline that was similar among Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) participants aged 60–77 years over 2-years [mean (SD): 23.4 (6.2) to 22.4 (6.0) ml/kg/min] (24). In contrast, findings from CARDIA suggest more accelerated declines in estimated maximal fitness per 5-year increment, ranging from 4.6% from ages 20–25 years to  $\approx 10\%$  per 5-year increment after age 30 years. This is equivalent to a reduction in estimated maximal workload from approximately 12 METs at baseline (duration just over 10 minutes) to 8 METs over the follow-up period (duration just under 6 minutes). While differences in findings between studies could be partially explained by use of estimated, rather than measured, maximal fitness in the current study, other reasons likely exist. Specifically, the limited racial diversity, smaller sample sizes of BLSA (particularly those aged  $<30$  years;  $n=105$ ) and FINGER, fewer assessment time-points, and shorter follow-up periods (7.9 and 2 years) may also contribute to the more attenuated fitness declines from early adulthood to midlife observed in prior longitudinal studies compared to CARDIA.

In CARDIA, differences in estimated submaximal fitness levels at each 5-year age increment and age-related declines by race within sex-strata mirrored those shown with maximal fitness with one exception. Specifically, estimated submaximal fitness at age 20 was higher in Black men while estimated maximal fitness at this age was higher in White men. After age 30, estimated submaximal and maximal fitness levels were consistently higher in White men compared with Black men. Regardless, the consistency in observed differences in submaximal and maximal fitness by a variety of subgroups has important research and clinical implications. For example, investigators of studies with limited financial resources to purchase necessary equipment (e.g., stress test systems, treadmills) and/or access to certified exercise testing personnel and/or medical (physician) supervisions could consider assessing fitness using submaximal test protocols. Given submaximal test



protocols often pose less risk to participants and/or patients, eligibility would likely expand to include those with prevalent conditions, functional limitations, or experience symptoms of pain and/or fatigue, which would potentially result in a less biased sample (36).

Sex-related differences in estimated fitness at age 20 years and age-related declines were expected given known biological differences in the capacity to achieve a given level of fitness. In women, greater fat mass, lower hemoglobin concentrations, and lower maximal cardiac output due to smaller heart size and lower plasma volume all contribute to lower fitness levels in women compared to men (29). Conversely, while racial differences in fitness have been previously described in the literature (34, 41–43), the underlying mechanisms remain poorly understood and are likely not due to differences in genetics or ancestry. For example, when accounting for age, sex, body size, and physical activity levels, the HERITAGE Family Study (43), found no statistically significant difference in  $VO_2\text{max}$  by race. Rather, observations of race-specific differences may instead be attributable to differences in socioeconomic, structural, or cultural inequities that are directly or indirectly associated with poorer fitness (44). Studies, including those published using prior CARDIA data (45, 46), have demonstrated the importance of habitual physical activity and maintenance of a healthy body weight to optimize fitness. As shown in the current study, Black women had a higher prevalence of inadequate physical activity and obesity in early adulthood (i.e., baseline) than other race/sex groups. Given observational data, it is not possible to isolate the factors causing or contributing to the observed racial differences in fitness from early adulthood through midlife among CARDIA participants. However, these observed differences may arise in part to health disparities associated with race including differences in access to safe places to be physically active and/or health care access and quality, including obesity prevention and management.

Perhaps the most important findings relate to the observed differences in age-related fitness declines through midlife by socioeconomic, behavioral, and health-related factors present in early adulthood. Early adulthood is a period of rapid change (47, 48), characterized by major life events including changes in relationships (e.g., marriage), family structure (e.g., birth of a child), residence, and employment, which can temporarily or permanently alter lifestyle behaviors and have subsequent implications on overall health. In the current study, participants who reported sufficient physical activity to meet guidelines, consumed alcohol, and never smoked had higher estimated fitness at age 20; a pattern that persisted for all behaviors except alcohol use after age 45. Also, individuals with overweight/obesity and fair/poor reported health had lower fitness in early adulthood and during the early adult to midlife transition. Together these findings suggest that early adulthood may serve as a critical life-course stage to intervene on unhealthy behaviors to optimize cardiovascular health to reduce risk or delay onset of subsequent disease.

Study strengths include use of the well-characterized CARDIA cohort to describe age-related changes in fitness during an earlier period of adulthood than previously described. Further, the fitness assessments in CARDIA span 20 years and this longer follow-up period was identified as a critical need for future studies (17). CARDIA is also a non-clinical sample and may provide a more accurate representation of fitness and aging in the general population, including antecedents of fitness changes using a life-course framework.

While a prior CARDIA study documented the potential biases associated when evaluating health risks only among those willing and able to perform a GXT (36), our statistical approach allowed us to include 98% of the baseline sample. Also, maximal fitness estimates originating from a single field center were corrected due to a protocol deviation with a threshold of 15 RPE used to infer peak effort. While prior studies have a priori excluded these tests, findings from the sensitivity analysis support the utility of this approach.

There are also important limitations that should be considered when interpreting the findings. First, the CARDIA GXT protocol did not include collection of expired gases needed to obtain measured peak  $\text{VO}_2$ , which is considered a gold standard measure of maximal cardiorespiratory fitness. The criterion validity of treadmill duration as an estimate of measured peak  $\text{VO}_2$  is unknown in CARDIA; however, this strategy is used in other studies without gas collection (49). However, whether measured or estimated fitness assessments are obtained, maximal GXT protocols rely on the participant's intrinsic motivation to achieve a workload consistent with their maximal effort; particularly among population-based samples. Similarly, estimated peak  $\text{VO}_2$  values correspond to actual maximal heart rate that ranged within 85–100% of age-predicted maximal heart rate, depending on motivation, fatigue, pain or other symptomology. In the current analyses, we used the CARDIA formula to predict maximal heart rate based on age; however, other formulas exist. Also, heart rate at the end of Stage 2 was used to estimate submaximal fitness given the associated workload; however, it is possible that this may have represented a maximal effort in deconditioned individuals. Second, early adulthood factors associated with differences in concurrent fitness levels and fitness changes from early adulthood through midlife were participant-reported and may be subject to recall and prevarication biases. However, these data were collected every 2–5 years for 20 years, which may be more sensitive to change. Further, body composition measures (lean and fat mass) across exam years were not available and, due to limited numbers (4.56% at baseline), the underweight and normal weight BMI categories were combined. However, studies have shown that the potential health risks of having underweight increase with age (50). Also, given participant information prior to baseline are not available, estimates of cumulative number of years within the less favorable category were assigned a zero at baseline and accumulated thereafter. Finally, while models included several key covariates, the potential for residual confounding cannot be disregarded.

## CONCLUSIONS

In summary, among the well-characterized CARDIA cohort, age-related declines in fitness from early adulthood to midlife were observed. In addition, several factors present as young adults were associated with lower concurrent fitness levels and/or accelerated fitness declines over-time, including education, financial strain, physical activity, alcohol and tobacco use, BMI, and self-rated health. Since fitness provides a reflection of total body health given required integration of several anatomical systems, these novel findings support the importance of the early adult period when developing and testing strategies focused on increasing healthy life expectancy.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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The authors have no conflicts of interest to disclose. The results of the study do not constitute endorsement by the American College of Sports Medicine. Study results are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. The Coronary Artery Risk Development in Young Adults Study (CARDIA) is conducted and supported by the National Heart, Lung, and Blood Institute (NHLBI) in collaboration with the University of Alabama at Birmingham (HHSN268201800005I & HHSN268201800007I), Northwestern University (HHSN268201800003I), University of Minnesota (HHSN268201800006I), and Kaiser Foundation Research Institute (HHSN268201800004I). Additional support for this work was provided by the CARDIA Fitness Study (R01 HL078972 to BS & SS) and CARDIA Activity and Heart Failure Study (R01 HL149796 to KPG). The views expressed in this manuscript are those of the authors and do not necessarily represent the views of the National Heart, Lung, and Blood Institute; the National Institutes of Health; or the U.S. Department of Health and Human Services.

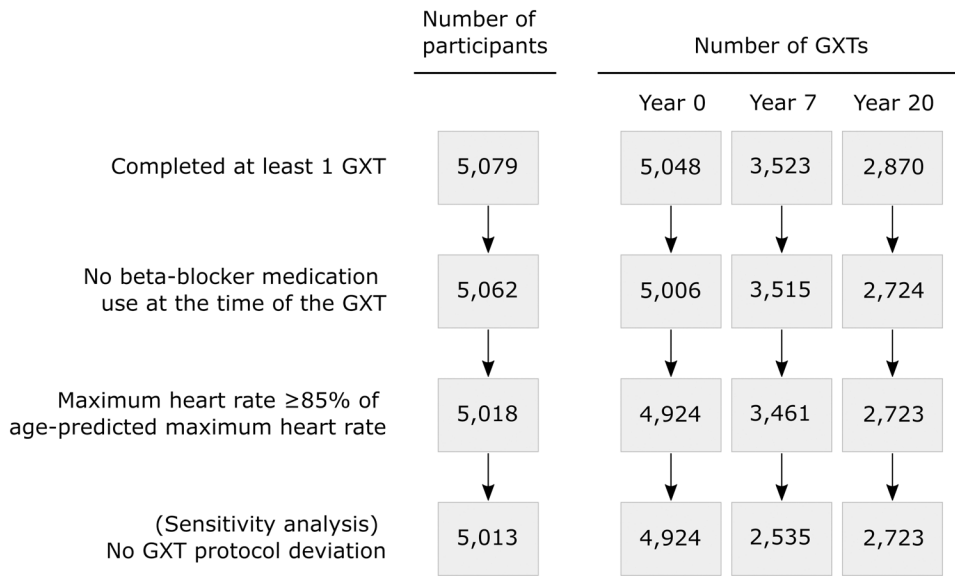
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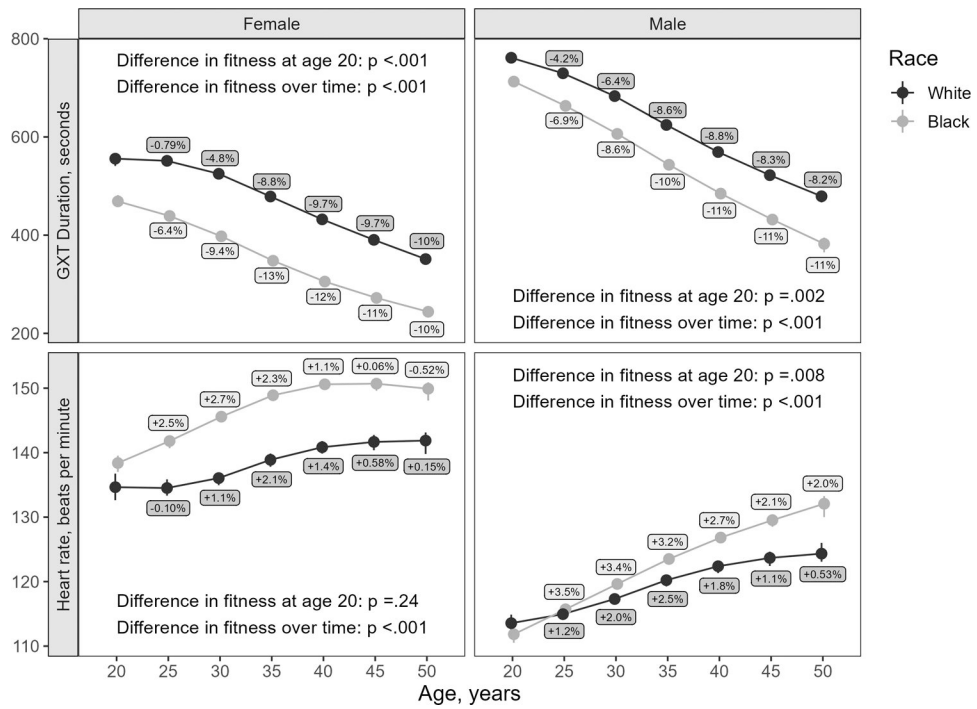
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**Figure 1.** The number of participants, and graded exercise tests at each timepoint, available for analysis with each exclusion applied.



**Figure 2.** Estimated graded exercise test duration (top row) and heart rate at the end of stage 2 (bottom row) for female (left column) and male (right column) participants with respect to age in years. Point estimates are adjusted for education and field center. Interval estimates indicate 95% confidence intervals. Differences in fitness were estimated from age 20 to 50 in 5-year increments by race within sex strata.

**Table 1.**Descriptive characteristics of the entire analytic sample<sup>\*,†</sup> and by race/sex groups.

Characteristic	Overall	Black Women	Black Men	White Women	White Men
No. of participants	4,924	1,415	1,117	1,258	1,134
Testing center, %					
Birmingham	23	25	26	20	23
Chicago	22	22	21	22	24
Minnesota	27	21	26	31	32
Oakland	28	33	28	27	21
Age, years <sup>‡</sup>	24.8 (3.7)	24.4 (3.9)	24.2 (3.7)	25.4 (3.4)	25.4 (3.4)
Maximum Education by Year 20, %					
Associate's Degree or more	32	20	18	48	46
High school or less	68	80	82	52	54
Difficulty paying for basics, %					
Not very hard	65	61	59	68	73
Somewhat hard	35	39	41	32	27
Marital status, %					
Married or cohabitating	22	20	18	28	23
Other	78	80	82	72	77
Meeting Physical Activity Guidelines, %					
Yes	59	37	72	58	73
No	41	63	28	42	27
Alcohol use, %					
Yes	86	78	85	91	92
No	14	22	15	9.2	7.7
Smoking status, %					
Never smoked	57	60	54	53	58
former	13	8.4	9.1	20	16
current	30	31	37	27	26
Body mass index, kg/m <sup>2</sup> <sup>‡</sup>	24.5 (5.0)	25.8 (6.4)	24.5 (4.2)	23.0 (4.3)	24.3 (3.5)
Self-rated health, %					
Good	90	84	89	94	94
Fair	10.0	16	11	6.0	6.4

\* Data are from the baseline exam unless otherwise noted.

† Baseline data are not represented for 94 participants (1.9% of analytic sample) who did not complete the graded exercise test at the baseline exam but did complete the protocol at the Year 7 and/or Year 20 follow-up exams.

‡ Mean (standard deviation)