The objective of this study was to determine the independent associations between young adult level of physical activity and subsequent changes in physical activity through the transition to midlife and incidence of premature CVD events (coronary heart disease [CHD], heart failure, stroke). In addition, we examined if meeting the current adult aerobic physical activity guideline levels were protective of premature CVD events. We hypothesized that low physical activity levels at age 18 and declines in physical activity through the adult life course will be associated with incidence of premature CVD events.

**CVD Events:** Any fatal or non-fatal CVD events, including coronary heart disease (myocardial infarction, non-myocardial infarction acute coronary syndrome), heart failure, and stroke (stroke, transient ischemic attack), were determined through annual participant contacts, death certificates, telephone contact, and relevant medical records. Hospital records were sought for self-reported outcomes, and central adjudication was performed by trained physicians to ascertain CVD events.

**Statistical Analysis**

*Summarizing physical activity.* Physical activity trajectories were modeled among all CARDIA participants. We developed a linear mixed model (LMM) for repeated measures of physical activity in order to generate succinct summaries of exercise patterns over time. The physical activity slopes use all observations of the physical activity scores prior to CVD event onset in order to use as much of the data for each participant as possible and to stabilize the best linear unbiased predictions. The LMM included fixed effects for a four-level categorization of sex and race, age as continuous, and their interactions, as well as random effects for participant and age, with unstructured covariance. From the fixed and random effects estimates provided by this model, we calculated expected physical activity level at age 18 and annual change for each participant. For ease of interpretation, we changed the sign of both summaries, so as to capture the associations of lower level and faster decline in physical activity with increased CVD event risk.

*Modeling the association of lower physical activity with incident CVD events.* Unadjusted cumulative incidence of CVD events (coronary heart disease, congestive heart failure, and stroke) by sex and race/ethnicity were estimated using Kaplan-Meier methods. The data for each participant were then expanded to include a record for each age between study entry and either metabolic disease onset, assumed to occur at the first visit at which it was detected, or at censoring by the end of the study of loss to follow-up. Pooled logistic models were used to estimate the independent associations of the expected physical activity at age 18 and subsequent annual change with incidence of premature CVD events, adjusting for potential confounders including sex, race, family history of CVD, years of education, smoking status, alcohol use, and BMI (smoking status, alcohol use, and BMI were time varying, with the last observation carried forward), which have been adjusted for in prior analyses of physical activity and CVD risk.14 We tested if sex and race modified the effect of physical activity (level and change) on incident premature CVD events. Pooled logistic models estimated the associations of various physical activity guideline thresholds (>600 EU or 300-600 EU vs <300 EU) at age 18 and through follow-up with onset of CVD events. We used Stata 16.0 (Statacorp, College Station, TX) for all analyses.

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| Table 1. Baseline demographic and health characteristics of participants in the Coronary Artery Risk Development in Young Adults (CARDIA) study | | | | | | |
|  | Total | White women | Black women | White men | Black men |  |
| N | 5,114 | 1,307 | 1,480 | 1,170 | 1,157 |  |
| **Baseline demographic characteristics** | Median (IQR) / n (%) | Median (IQR) / n (%) | Median (IQR) / n (%) | Median (IQR) / n (%) | Median (IQR) / n (%) | p-value |
| Age (years) | 25.0 (22.0-28.0) | 26.0 (23.0-28.0) | 24.0 (21.0-28.0) | 26.0 (23.0-28.0) | 24.0 (21.0-28.0) | <0.001 |
| Highest grade of school completed | 13.0 (12.0-16.0) | 15.0 (12.0-16.0) | 13.0 (12.0-14.0) | 15.0 (12.0-16.0) | 12.0 (12.0-14.0) | <0.001 |
| Family history of cardiovascular disease | 1,022 (20.0%) | 250 (19.1%) | 310 (20.9%) | 227 (19.4%) | 235 (20.3%) | 0.62 |
| Body mass index (BMI) | 23.4 (21.2-26.4) | 22.0 (20.3-24.6) | 24.2 (21.2-28.9) | 23.7 (21.9-26.0) | 23.7 (21.7-26.4) | <0.001 |
| <25 kg/m2 | 3,328 (65.3%) | 1,012 (77.7%) | 823 (55.8%) | 761 (65.2%) | 732 (63.5%) |  |
| 25-30 kg/m2 | 1,170 (23.0%) | 195 (15.0%) | 337 (22.8%) | 334 (28.6%) | 304 (26.4%) |  |
| >30 kg/m2 | 599 (11.8%) | 95 (7.3%) | 315 (21.4%) | 72 (6.2%) | 117 (10.1%) |  |
| Smoking status |  |  |  |  |  | <0.001 |
| Never | 2,856 (56.2%) | 685 (52.7%) | 885 (60.1%) | 670 (57.8%) | 616 (53.8%) |  |
| Former | 676 (13.3%) | 261 (20.1%) | 127 ( 8.6%) | 182 (15.7%) | 106 ( 9.3%) |  |
| Current | 1,546 (30.4%) | 355 (27.3%) | 461 (31.3%) | 307 (26.5%) | 423 (36.9%) |  |
| Alcohol (mL of alcohol consumed per day) | 5.4 (0.9-15.5) | 4.8 (0.9-12.1) | 1.8 (0.0-6.9) | 11.1 (3.7-23.2) | 10.2 (2.0-25.2) | <0.001 |
| Total physical activity score at enrollment (EU) | 360.0 (197.0-578.0) | 351.0 (207.0-543.0) | 228.0 (103.0-396.0) | 462.0 (288.0-672.0) | 472.0 (271.0-723.0) | <0.001 |
| Total physical activity score at age 18 (EU) | 373.7 (251.9-536.0) | 340.0 (243.0-472.2) | 238.5 (163.8-337.4) | 480.7 (352.3-613.9) | 516.0 (384.3-673.9) | <0.001 |
| Annual reduction in total physical activity score (EU) | 2.3 (0.6-4.5) | 1.3 (-0.3-3.1) | 1.3 (0.2-2.8) | 2.5 (1.1-4.2) | 5.1 (3.7-7.3) | <0.001 |
| Expected total physical activity at age 18 |  |  |  |  |  |  |
| <300 EU | 1,915 (37.5%) | 545 (41.7%) | 989 (67.0%) | 231 (19.8%) | 150 (13.0%) | <0.001 |
| 300-600 EU | 2,274 (44.6%) | 633 (48.5%) | 432 (29.2%) | 635 (54.4%) | 574 (49.8%) |  |
| >600 EU | 913 (17.9%) | 128 (9.8%) | 56 (3.8%) | 301 (25.8%) | 428 (37.2%) |  |
| Always meeting total physical activity level from young adulthood to middle age |  |  |  |  |  |  |
| <300 EU | 2,128 (41.7%) | 589 (45.1%) | 1,067 (72.2%) | 263 (22.5%) | 209 (18.1%) | <0.001 |
| 300-600 EU | 2,202 (43.2%) | 612 (46.9%) | 362 (24.5%) | 646 (55.4%) | 582 (50.5%) |  |
| >600 EU | 772 (15.1%) | 105 (8.0%) | 48 (3.2%) | 258 (22.1%) | 361 (31.3%) |  |
| IQR = Interquartile range; EU = Exercise units | | | | | | |
| A total physical activity score of 300 exercise units (EU) approximates the Health and Human Services recommendations of approximately 150 minutes of moderate-intensity activity per week. | | | | | | |

Figure 1. Average physical activity trajectories, by race and sex



Note: A total physical activity score of 300 exercise units (EU) approximates the Health and Human Services recommendations of approximately 150 minutes of moderate-intensity activity per week.

Figure 2. Any CHD incidence, by race and sex



Figure 3. Any heart failure incidence, by race and sex



Figure 4. Any stroke incidence, by race and sex



Figure 5. Any CVD incidence, by race and sex



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| Table 2. Associations between physical activity trajectories and incidence of premature cardiovascular disease (CVD) events in the CARDIA study | | | | | | | | |
|  | Lower physical activity score  (per 100 Exercise Units) at age 18 | | |  | Annual reduction in total physical activity score (per 1 Exercise Unit) | | |
|  | OR | 95% CI | p |  | OR | 95% CI | p |
| **Any coronary heart disease (CHD) - fatal or nonfatal** (myocardial infarction, non-myocardial infarction acute coronary syndrome) | | | | | | | | |
| Model 1 (adjusted for age)a | 1.06 | 0.94, 1.20 | 0.330 |  | **1.07** | **1.01, 1.13** | **0.021** |
| Model 2 (fully adjusted)b | 1.15 | 0.99, 1.34 | 0.070 |  | 1.06 | 0.99, 1.13 | 0.090 |
| **Any heart failure - fatal or nonfatal** (congestive heart failure) | | | | | | | | |
| Model 1 (adjusted for age)a | **1.55** | **1.23, 1.95** | **<0.001** |  | **1.30** | **1.16, 1.44** | **<0.001** |
| Model 2 (fully adjusted)b | **1.43** | **1.15, 1.79** | **0.001** |  | **1.16** | **1.05, 1.28** | **0.004** |
| **Any Stroke - fatal or nonfatal** (stroke, transient ischemic attack) | | | | | | | | |
| Model 1 (adjusted for age)a | **1.49** | **1.24, 1.80** | **<0.001** |  | **1.26** | **1.15, 1.38** | **<0.001** |
| Model 2 (fully adjusted)b | **1.34** | **1.12, 1.62** | **0.002** |  | **1.17** | **1.07, 1.28** | **<0.001** |
| **Any CVD - fatal or nonfatal** (myocardial infarction, coronary revascularization, non-NI acute coronary syndrome, congestive heart failure, stroke, transient ischemic attack, carotid artery disease, peripheral artery disease, abdominal aortic aneurysm) | | | | | | | | |
| Model 1 (adjusted for age)a | **1.22** | **1.11, 1.34** | **<0.001** |  | **1.14** | **1.09, 1.20** | **<0.001** |
| Model 2 (fully adjusted)b | **1.22** | **1.10, 1.35** | **<0.001** |  | **1.09** | **1.04, 1.14** | **<0.001** |
| Note: Boldface indicates statistical significance (p<0.05). | | | | | | | | |
| a Model 1 includes: physical activity level at age 18, annual reduction in physical activity, age | | | | | | | | |
| b Model 2 includes: physical activity level at age 18, annual reduction in physical activity, age, race, sex, education, family history of CVD, smoking status, alcohol, and body mass index | | | | | | | | |

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| Table 3. Associations between meeting the Department of Health and Human Services physical activity guidelines at age 18 and through the follow-up period and onset of cardiovascular disease events in the CARDIA study | | | | | | | | | | | | | | | |
|  | Any CHD | | |  | Any heart failure | | |  | Any Stroke | | |  | Any CVD | | |
|  | OR | 95% CI | p |  | OR | 95% CI | p |  | OR | 95% CI | p |  | OR | 95% CI | p |
| Expected total physical activity at age 18a |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| <300 EU | reference | | |  | reference | | |  | reference | | |  | reference | | |
| 300-600 EU | **0.38** | **0.24, 0.62** | **<0.001** |  | 0.70 | 0.36, 1.34 | 0.280 |  | 0.73 | 0.41, 1.29 | 0.280 |  | **0.63** | **0.44, 0.89** | **0.009** |
| >600 EU | **0.55** | **0.32, 0.96** | **0.034** |  | **0.35** | **0.13, 0.92** | **0.033** |  | 0.57 | 0.23, 1.41 | 0.230 |  | **0.60** | **0.38, 0.94** | **0.028** |
| Always meeting total physical activity level from young adulthood to middle agea |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| <300 EU | reference | | |  | reference | | |  | reference | | |  | reference | | |
| 300-600 EU | **0.48** | **0.30, 0.76** | **0.002** |  | **0.45** | **0.23, 0.87** | **0.017** |  | 0.69 | 0.38, 1.26 | 0.230 |  | **0.58** | **0.42, 0.82** | **0.002** |
| >600 EU | 0.78 | 0.41, 1.50 | 0.450 |  | 0.42 | 0.13, 1.39 | 0.150 |  | 0.15 | 0.02, 1.15 | 0.070 |  | **0.54** | **0.30, 0.96** | **0.037** |
| A total physical activity score of 300 exercise units (EU) approximates the Health and Human Services recommendations of approximately 150 minutes of moderate-intensity activity per week. | | | | | | | | | | | | | | | |
| a Covariates: age, race, sex, education, family history of cardiovascular disease, smoking status, alcohol, and body mass index. | | | | | | | | | | | | | | | |