BLOOD PRESSURE MEASURES

In CARDIA Years 0–15, blood pressure measurements were obtained using a random-zero sphygmomanometer (Hawksley, Sussex, United Kingdom). At the Y_{20} examination, concerns about mercury contained in the apparatus required a switch to an automated oscillometric BP monitor (Omron HEM-907XL; Online Fitness, Santa Monica, CA). At the Year 20 examination, 906 persons were measured using both devices (random zero and Omron). Based on this calibration study, CARDIA used blood pressure values calibrated to the sphygmomanometric measures: CS=3.74 + 0.96*OS and CD=1.30 + 0.97*OD where CS is calibrated systolic blood pressure, CD is calibrated diastolic blood pressure, OS is observed Omron systolic blood pressure and OD is observed Omron diastolic blood pressure.[1,2] After calibration, there was only a small bias between the random zero sphygmomanometric measure and the model of the Omron oscillometer.

STATISTICAL ANALYSIS: MODEL CHECKS, LINEAR MIXED MODEL (LMM), AND SENSITIVITY ANALYSES

Although the physical activity average trajectories shown in Figure 1A are not completely linear, scatter plots for individual participants showed that fitted linear participant-specific regression lines were in good agreement with their repeated physical activity measures.

The physical activity slopes use all observations of the physical activity scores prior to hypertension onset in order to use as much of the data for each participant as possible and to stabilize the best linear unbiased predictions. Individuals were not excluded if they presented with hypertension during their baseline examination. The LMM in the first stage estimates an expected level at age 18 as well as an expected slope, even if only 1 observation is included, by using information from similar participants. For the linear mixed models (LMM), there was no minimum number of points for the creation of slopes; however, the LMM borrows information across participants to make up for this, and the number of participants with only 1 or 2 responses was 409/5,114. The inclusion of included fixed effects for a 4-level categorization of sex and race, age as continuous, and their interactions, as well as random effects for participant and age, with unstructured covariance along with observed outcomes makes the LMM assumption of missingness at random more plausible, though this assumption is not ultimately verifiable.

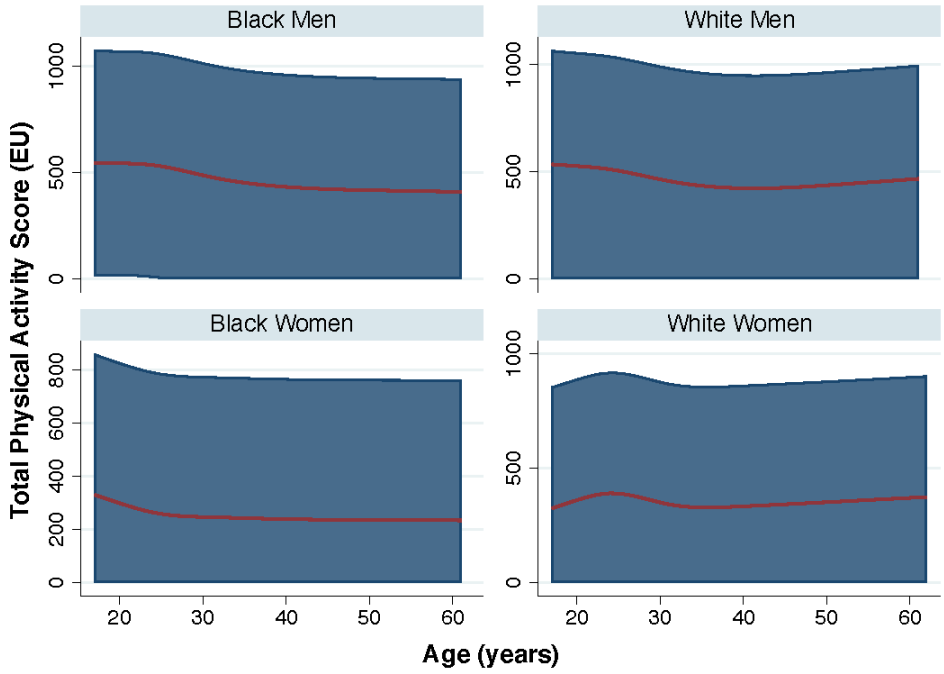
As a sensitivity analysis, the LMMs were fit using linear splines in age with knots at ages 30, 40, 50, and 60 years so that the fitted PA slopes were age-dependent. This did not substantially affect the result. Tests for effect modification occurred, specifically if physical activity level modified the effect of physical activity change and if there was any modification of the effects of level and change in physical activity by race/sex or BMI.

SUPPLEMENTAL RESULTS

Physical Activity Trajectories

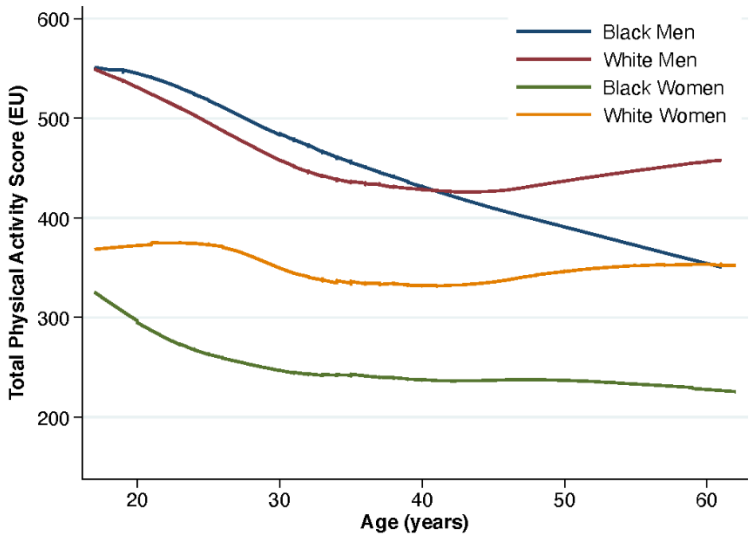
Appendix Figure 1 shows 95% prediction intervals for physical activity observations.

Appendix Figure 1. Average physical activity trajectories with 95% prediction intervals, by race and sex.



Appendix Figure 2 shows average physical activity trajectories when physical activity observations after hypertension onset do not contribute. The curve for White men and White women turns up at older ages. This may reflect the exclusion of individuals who had a negative physical activity slope and reflect the remaining sample of regular exercisers with reduced risk of hypertension.

Appendix Figure 2. Average physical activity trajectories, by race and sex.



Note: The figure represents the group average of total physical activity score by race and sex groups using lowess smoothing. Observations after hypertension onset do not contribute.

Correlations

Overall, the intraclass correlation coefficients (ICC) of physical activity is 0.59. The ICC among participants meeting twice the physical activity guideline (>600 EU) at age 18 is 0.17. The ICC among participants meeting twice the physical activity guideline (>600 EU) throughout follow-up is 0.18.

Loss to Follow-Up

Appendix Table 1 compares baseline characteristics of participants who were retained versus lost to follow-up at 30 years. Participants who were lost to follow-up were more likely to have lower education, higher systolic blood pressure, lower HDL cholesterol, higher triglycerides, higher diabetes, smoking status, and steeper reductions of physical activity. There were no significant differences in baseline total physical activity score, diastolic blood pressure, BMI, family history of hypertension, family history of CVD, or LDL cholesterol.

Appendix Table 2 demonstrates a fully-adjusted pooled logistic model for lost to follow-up or death. Finally, a sensitivity analysis of the fully-adjusted pooled logistic model for physical activity and incident hypertension was estimated, adding inverse probability of retention weights, and found similar results to the main findings (Appendix Table 3).

Appendix Table 1. Baseline Demographic and Health Characteristics of Participants in the Coronary Artery Risk Development in Young Adults (CARDIA) Study by Lost to Follow-Up vs Retained to Year 30

Baseline demographic characteristics	**Total** **N=5,114**	**Retained** **n=3,358**	**Lost to follow-up** **n=1,756**	***p*-value**
Age, years, median (IQR)	25.0 (22.0–28.0)	25.0 (22.0–28.0)	25.0 (21.0–28.0)	**<0.001**
Highest grade of school completed, median (IQR)	13.0 (12.0–16.0)	14.0 (12.0–16.0)	13.0 (12.0–15.0)	**<0.001**
Family history of hypertension, n (%)	2,670 (52.2)	1,749 (52.1)	921 (52.4)	0.8
Family history of cardiovascular disease, n (%)	1,022 (20.0)	655 (19.5)	367 (20.9)	0.24
BMI, median (IQR)	23.4 (21.2–26.4)	23.4 (21.2–26.2)	23.5 (21.1–26.8)	0.68
<25 kg/m^2, n (%)	3,328 (65.3)	2,206 (65.9)	1,122 (64.2)	**0.006**
25–30 kg/m^2, n (%)	1,170 (23.0)	783 (23.4)	387 (22.1)	**0.006**
>30 kg/m^2, n (%)	599 (11.8)	359 (10.7)	240 (13.7)	**0.006**
Smoking status, n (%)				
Never	2,856 (56.2)	2,009 (60.2)	847 (48.7)	**<0.001**
Former	676 (13.3)	458 (13.7)	218 (12.5)	**<0.001**
Current	1,546 (30.4)	359 (10.7)	240 (13.7)	**<0.001**
Total physical activity score at enrollment (EU), median (IQR)	360.0 (197.0–578.0)	366.0 (201.0–580.0)	351.0 (186.0–575.0)	0.13
Total physical activity score at age 18 (EU), median (IQR)	–3.7 (–5.4– –2.5)	–3.7 (–5.4– –2.5)	–3.8 (–5.4– –2.6)	0.82
Hypertension, n (%)	2,670 (52.2)	1,749 (52.1)	921 (52.4)	0.8
Systolic blood pressure, median (IQR)	110.0 (103.0–118.0)	109.0 (102.0–117.0)	110.5 (103.0–119.0)	**<0.001**
Diastolic blood pressure, median (IQR)	68.0 (62.0–75.0)	68.0 (63.0–74.0)	68.0 (62.0–75.0)	0.28
Diabetes, n (%)	32 (0.6)	8 (0.2)	24 (1.4)	**<0.001**
LDL cholesterol, median (IQR)	106.0 (87.0–127.0)	106.0 (87.0–127.0)	106.0 (86.0–127.0)	0.33
HDL cholesterol, median (IQR)	52.0 (44.0–61.0)	53.0 (45.0–62.0)	50.0 (43.0–59.0)	**<0.001**
Triglycerides, median (IQR)	62.0 (45.0–84.0)	61.0 (45.0–83.0)	65.0 (47.0–87.0)	**<0.001**

Notes: Boldface indicates statistical significance (p<0.05). A total physical activity score of 300 exercise units (EU) approximates the HHS recommendations of approximately 150 minutes of moderate-intensity activity per week.

EU, exercise units; LDL, low density lipoprotein; HDL, high density lipoprotein.

Appendix Table 2. Fully Adjusted Pooled Logistic Model for Lost to Follow-Up or Died

Variable	OR (95% CI)	*p*-value
Total physical activity score at age 18 years (EU)	1.03 (1.00, 1.06)	0.059
Annual reduction in total physical activity score (EU)	1.01 (1.00, 1.03)	**0.032**
Age, years		
18–30	ref	
30–40	0.71 (0.62, 0.80)	**<0.001**
40–50	0.84 (0.74, 0.96)	**0.012**
50–60	0.89 (0.76, 1.04)	0.14
Race/ethnicity and sex		
White women	ref	
Black women	1.20 (1.04, 1.39)	**0.015**
White men	1.23 (1.05, 1.42)	**0.008**
Black men	1.57 (1.34, 1.84)	**<0.001**
Highest grade of school completed	0.95 (0.92, 0.98)	**0.002**
Family history of hypertension	0.97 (0.88, 1.07)	0.59
Family history of cardiovascular disease	1.02 (0.91, 1.15)	0.71
BMI		
<25 kg/m^2	ref	
25–30 kg/m^2	0.98 (0.87, 1.11)	0.79
>30 kg/m^2	1.15 (1.02, 1.29)	**0.027**
Smoking status		
Never	ref	
Former	1.02 (0.88, 1.17)	0.81
Current	1.37 (1.22, 1.54)	**<0.001**
Alcohol (mL of alcohol consumed per day)	1.00 (1.00, 1.00)	0.22

Note: Boldface indicates statistical significance ($p<0.05$).

EU, exercise units.

Appendix Table 3. Fully-Adjusted Pooled Logistic Model for Associations Between Lower Physical Activity Score or Physical Activity Reductions and Onset of Hypertension in the CARDIA Study, Inverse Probability of Retention (IPR)-Weighted Estimates

Fully adjusted model[a]	OR (95% CI)	*p*-value
Expected total physical activity score at age 18 years[b]	1.03 (1.01, 1.06)	**0.006**
Expected annual reduction in total physical activity score[c]	1.01 (1.00, 1.02)	**0.021**

Note: Boldface indicates statistical significance ($p<0.05$).

[a]Covariates: age, race, sex, education, family history of hypertension, family history of cardiovascular disease, smoking status, alcohol, BMI.

[b]In 100s of exercise units from high to low.

[c]In exercise units.

CARDIA, Coronary Artery Risk Development in Young Adults Study.

Appendix Table 4. Interactions of Age 18 Years Physical Activity Level and Annual Reduction of Physical Activity With Onset of Hypertension in the CARDIA Study

Variable	OR (95% CI)	*p*-value
Unadjusted		
Expected total physical activity score at age 18 years[a]	1.02 (1.00, 1.04)	0.06
Expected annual reduction in total physical activity score[b]	1.05 (1.04, 1.06)	**<0.001**
Interaction of lower age 18 years level and faster reduction	1.01 (1.00, 1.01)	**0.004**
Fully adjusted[c]		
Expected total physical activity score at age 18 years[a]	1.01 (0.98, 1.04)	0.56
Expected annual reduction in total physical activity score[b]	1.04 (1.02, 1.07)	**<0.001**
Interaction of lower age 18 years level and faster reduction	1.01 (1.00, 1.01)	**0.002**

Note: Boldface indicates statistical significance ($p<0.05$).
[a]In 100s of exercise units from high to low.
[b]In exercise units.
[c]Covariates: age, race, sex, education, family history of hypertension, family history of cardiovascular disease, smoking status, alcohol, and BMI.

CARDIA, Coronary Artery Risk Development in Young Adults Study.

EFFECT MODIFICATION AND TEST FOR INTERACTIONS

Appendix Table 4 examines effect modification between physical activity level at age 18 years and the change in physical activity for hypertension onset. Although there is evidence of effect modification between baseline physical activity level and change in physical activity (statistically significant *p* for interaction), the overall effect is weak and does not change the overall interpretation of the main findings.

In order to help interpret this effect modification, we categorize the physical activity level at age 18 years (<300 EU, 300–600 EU, >600 EU) and physical activity change (gain, loss <2.5 EU/year, loss >2.5 EU/year) which creates nine groups (Appendix Table 5). We show these results in Appendix Table 6. Among participants with high levels of physical activity at age 18 (>600 EU), dramatic subsequent decreases (loss >2.5 EU/year) in physical activity compared to gains were associated with hypertension onset (AOR=4.11, 95% CI=2.58, 6.52). Among participants with low levels of physical activity at age 18 years (<300 EU), subsequent increases in physical activity compared to rapid decreases (loss >2.5 EU/year) were not significantly protective of hypertension onset (AOR=1.08, 95% CI=0.89, 1.31).

Appendix Table 5. Numbers of CARDIA Participants With Categorized Total Expected Physical Activity Score

Expected total physical activity at age 18 years, annual reduction	Total N=5,114	White women n=1,307	Black women n=1,480	White men n=1,170	Black men n=1,157
>600 EU at age 18 years, gain	75	26	2	29	18
>600 EU at age 18 years, loss <2.5 EU/year	60	13	6	29	12
>600 EU at age 18 years, loss >2.5 EU/year	775	82	48	256	389
300–600 at age 18 years, gain	333	160	60	87	26
300–600 at age 18 years, loss <2.5 EU/year	724	245	140	286	53
300–600 at age 18 years, loss >2.5 EU/year	1,360	262	233	309	556
<300 at age 18 years, gain	497	187	246	55	9
<300 at age 18 years, loss <2.5 EU/year	995	251	614	92	38
<300 at age 18 years, loss >2.5 EU/year	294	81	131	26	56

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

CARDIA, Coronary Artery Risk Development in Young Adults Study.

Appendix Table 6. Age 18 Years Physical Activity Level Categories, Annual Reduction of Physical Activity Categories, and Associations With Onset of Hypertension in the CARDIA Study

Variable	OR (95% CI)	*p*-value
Model treating physical activity as additive, fully adjusted[a]		
Expected total physical activity score at age 18 years		
>600 EU	ref	
300–600 EU	1.19 (1.05, 1.34)	**0.006**
<300 EU	1.05 (0.91, 1.22)	0.49
Expected annual reduction in total physical activity score		
Gain	ref	
Reduction 0–2.5 EU/year	2.41 (2.13, 2.73)	**<0.001**
Reduction >2.5 EU/year	1.81 (1.60, 2.03)	**<0.001**
Age 18 years level below median, annual reduction above median	1.31 (1.13, 1.52)	**<0.001**
Model allowing physical activity categories to interact, fully adjusted[a]		
>600 EU at age 18 years, gain	ref	
>600 EU at age 18 years, loss <2.5 EU/year	1.56 (0.82, 2.95)	0.17
>600 EU at age 18 years, loss >2.5 EU/year	4.11 (2.58, 6.52)	**<0.001**
300–600 at age 18 years, gain	1.78 (1.10, 2.88)	**0.02**
300–600 at age 18 years, loss <2.5 EU/year	5.94 (3.73, 9.47)	**<0.001**
300–600 at age 18 years, loss >2.5 EU/year	4.38 (2.77, 6.92)	**<0.001**
<300 at age 18 years, gain	2.75 (1.71, 4.42)	**<0.001**
<300 at age 18 years, loss <2.5 EU/year	5.27 (3.31, 8.38)	**<0.001**
<300 at age 18 years, loss >2.5 EU/year	2.54 (1.57, 4.09)	**<0.001**

Note: A total physical activity score of 300 exercise units (EU) approximates the HHS recommendations of approximately 150 minutes of moderate-intensity activity per week. Boldface indicates statistical significance ($p<0.05$).

[a]Covariates: age, race, sex, education, family history of hypertension, family history of cardiovascular disease, smoking status, alcohol, and BMI.

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