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# Association of Exercise Heart Rate Response with Incidence of Hypertension in Men

**Vivek K. Prasad, MD**[1], **Gregory A. Hand, PhD**[1], **Xuemei Sui, MD, MPH, PhD**[1], **Deepika Shrestha, MS**[2], **Duck-chul Lee, PhD**[4], **Carl J. Lavie, MD**[3], **Jason R. Jaggers, PhD**[5], and **Steven N. Blair, PED**[1,2]

[1]Departments of Exercise Science, Arnold School of Public Health, University of South Carolina, Columbia, SC

[2]Department of Epidemiology and Biostatistics (S.N.B.), Arnold School of Public Health, University of South Carolina, Columbia, SC

[3]Department of Cardiovascular Diseases, Ochsner Clinical School-the University of Queensland School of Medicine, New Orleans, Louisiana and the Department of Preventive Medicine, Pennington Biomedical Research Center, Baton Rouge, Louisiana

[4]Department of Kinesiology, College of Human Science, Iowa state University Ames, Iowa

[5]Murray State University, Department of Applied Health Sciences, Murray, Kentucky

## Abstract

**Objective—**To examine the association between heart rate (HR) responses during rest, exercise and post exercise with incident hypertension (HTN) in men.

**Patients and methods—**A total of 10,418 healthy normotensive men, without an abnormal electrocardiogram or history of heart attack, stroke, cancer, or diabetes, performed a maximal exercise test and were followed for incidence of HTN. HR reserve was defined as the maximal HR minus resting HR. HR recovery was defined as HR 5 minutes post exercise test.

**Results—**During a mean follow-up of 6 years, there were 2831 cases of HTN. Compared with men who had lower HR Reserve, the risk of incident HTN was significantly lower for men with higher HR Reserve (Hazard Ratio (HazR): 0.84; 95% confidence interval (CI): 0.74–0.95 for the highest quartile versus lowest quartile of HR Reserve) when adjusted for age, baseline examination year, smoking, heavy drinking, body mass index, resting blood pressure, cholesterol, glucose and cardiorespiratory fitness. Compared with men who had higher HR Recovery, the risk of incident HTN was significantly lower for men with lower HR Recovery (HazR: 0.90; 95% CI:

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Correspondence to Xuemei Sui, MD, MPH, PhD, Public Health Research Center, 921 Assembly St, Room 226, Columbia, SC 29208. Fax No. 8037772504, Ph. No. 8037773881. msui@mailbox.sc.edu.

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0.80–0.99 for quartile 3 versus highest quartile) after adjusting for the above confounders. However, the overall linear trend for HR Recovery is not significant (P=0.26).

**Conclusion—**The risk of HTN decreased in men with higher HR Reserve. Therefore, HR Reserve may be considered as a useful exercise parameter for predicting the risk of HTN in men.

### Keywords

Cardiorespiratory fitness; chronic disease; epidemiology; high blood pressure

## Introduction

Hypertension (HTN) is the most prevalent risk factor for cardiovascular (CV) disease (CVD) among US adults, and affects nearly one-third of the population aged 18 and older.[1,2] The prevalence of HTN has increased by almost one-fourth over the past 15 years among adults in the US, increasing from 22.2% in 1995 to 27.8% in 2007.[3,4] Risk of stroke, coronary heart disease (CHD), congestive heart failure and renal failure is also increased in people with HTN.[5] The estimated direct cost of HTN for 2007 was $43.5 billion, a major burden on the US health care system.[6] The World Health Organization report on global health risk indicated that high blood pressure is the leading risk factor for cause of deaths worldwide.[7]

Considerable data has established the importance of heart rate (HR) characteristics and future CVD. Resting heart rate (RHR) has consistently been found to be a predictor of HTN, CHD, and other measures of CVD morbidity and mortality.[8–13] Some studies have shown that maximal HR is a strong predictor of CVD and all-cause mortality.[14,15] Very few studies, however, have examined the relationships between HR reserve and CVD mortality. We earlier reported that HR Reserve predicts CVD mortality in young men that is independent of cardiorespiratory fitness (CRF).[13,15] Other studies have shown that HR Recovery is also a predictor of CVD and all cause morbidity and mortality.[16,17] HR Reserve and HR Recovery are parameters influenced by CRF, and CRF also depends on various factors such as CV, lung, and muscle fitness. This distinction may be important since HTN is a CVD risk factor that is less related to pulmonary function and muscle fitness. Therefore, we hypothesize that HR Reserve and HR Recovery might be significant predictors of incident HTN. The purpose of this study was to analyze the association of HR Reserve and HR Recovery with incident HTN in a group of men who enrolled in the Aerobics Center Longitudinal Study (ACLS), a prospective epidemiological investigation.

## METHODS

### Study participants

Participants received a comprehensive health examination at the Cooper Clinic in Dallas, TX. The Cooper Institute institutional Review Board reviewed and approved the study annually and details of the study have been published previously.[18,19] Participants come to the Cooper Clinic for preventive medical examinations and counseling regarding exercise, diet, and other lifestyle factors associated with an increased risk of chronic disease. The present study consists of 10,418 men who completed at least two examinations including a



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maximal exercise test on a treadmill during 1974–2003. Study participants were predominantly non-Hispanic white (97%), well educated, and from the middle and upper socioeconomic strata. Although the sample came from middle and upper socioeconomic strata, they were similar to other well-characterized population-based cohorts in terms of blood pressure, cholesterol level, body weight, and CRF.[20] At baseline, all participants included in the analysis were free of known CVD, cancer, or diabetes; had a normal resting or exercise electrocardiogram (ECG); and achieved an 85% age-predicted maximal HR (220 - age) during the maximal exercise treadmill test. In addition, all participants had no known HTN at baseline. The current analysis only included men because the number of women with incident HTN in this population was too small for a meaningful statistical analysis. Figure 1 shows the flow diagram of the study population.

## Measurements

The baseline clinical examination was conducted after participants gave their informed written consent and followed an overnight fast of at least 12 h. The examination consisted of resting blood pressure, blood chemistry analyses, personal and family health history, anthropometry, and a maximal exercise test on a treadmill. Previous reports have described the clinical examination in detail.[18,21,22] Briefly, height and weight were measured on a standard balance beam scale and stadiometer. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Participants provided self-report of weekly alcohol consumption. Heavy drinking is defined as ≥14drinks/week. Serum samples were analyzed for lipids and glucose using standardized automated bioassays at the Cooper Clinic Laboratory, which participated in and met quality control criteria of the Centers for Disease Control and Prevention Lipid Standardization Program.

Resting blood pressure was measured in the seated position, and was recorded as the first and fifth Korotkoff sounds by auscultatory methods after at least 5 minutes of rest. A standard sphygmomanometer was used and two readings separated by 2 minutes were averaged. If the first two readings differed by >5 mm Hg, additional readings were obtained and averaged. The maximal exercise test was conducted following a modified Balke protocol.[23] Participants began walking at 88 m/min with no elevation. At the end of the first minute, grade was increased to 2% and thereafter increased 1% per minute until the 25th minute. After 25 min the grade remained constant while the speed increased each subsequent min by 5.4m/min. Participants were encouraged to give a maximal effort during the test. Heart rates were obtained from the exercise ECG. The highest value recorded from the ECG during exercise test was defined as the maximal HR. All men in the present analyses were able to complete the test to at least 85% of their age-predicted maximal HR (220 minus age in years). Each age group exceeded the age-predicted average maximal HR, which indicates that the exercise test can be considered a maximal performance. HR Recovery was the HR 5 minutes after the exercise test. Participants continued the test to the limits of volitional fatigue.[24] RHR was determined with the participants recumbent after 5-min rest before the test and was obtained from the resting ECG. CRF was estimated using maximal metabolic equivalents (METs) attained during the test (1 MET = resting metabolic rate (RMR), defined as an oxygen uptake of 3.5 $mL \cdot kg^{-1} \cdot min^{-1}$) assessment. Men who had

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exercise test treadmill time in the upper 80% of the average maximal treadmill time, were kept in high CRF group, rest were in low CRF group.

### Ascertainment of HTN

The incidence of HTN was ascertained from clinical examination after their baseline examination, and HTN was defined as systolic blood pressure ≥140 or diastolic blood pressure ≥90, or physician diagnosed HTN.[25] The follow-up time for each participant was determined from the baseline examination to the first follow-up event of HTN or the last follow-up observation through 2006 in men who did not develop HTN. The mean number of follow-up visits by those who were diagnosed with HTN was approximately 6. Overall visits by the population were approximately 4.

## Statistical analyses

All analyses were performed using SAS statistical software, (version 9.2; SAS Institute, Cary, NC). HR Reserve and HR Recovery were analyzed categorically where categories were defined according to the quartiles of the observed distribution. Differences in baseline covariates were tested using chi-square tests for categorical variables and analysis of variance tests for continuous variables. Cox proportional hazards regression analysis was used to estimate hazard ratios (HazRs) and 95% confidence intervals (CIs) of incident HTN according to quartiles of HR Reserve and HR Recovery categories. Multivariable-adjusted models included controls for baseline measures: age (in years), examination year, BMI ($kg/m^2$), smoking habit (smokers or non-smokers), alcohol intake (≥14 drinks/day or not), resting systolic and diastolic blood pressure (mmHg), blood glucose, total cholesterol and maximal treadmill time. Inspection of empirical cumulative hazards plots grouped by exposure suggested that proportional hazards assumption was justified. All *P* values were 2-sided alternative hypotheses. *P* values <0.05 indicated statistically significant comparisons.

## Results

The baseline characteristics of the study sample by their HR Reserve and HR Recovery quartiles are presented in Tables 1 and 2 respectively. HR Reserve was calculated based on the difference between maximal HR during the exercise test and Resting HR. The quartiles of HR Reserve scores were, quartile 1 (<112 beats/min), quartile 2 (112–122 beats/min), quartile 3 (123–131 beats/min) and quartile 4 (≥132 beats/min). We identified quartiles of HR Recovery as quartile 1 (≤97 beats/min), quartile 2 (98–106 beats/min), quartile 3 (107–115 beats/min), and quartile 4 (≥116 beats/min). The mean (SD) values of HR Reserve in quartile 1, 2, 3, 4 were 103±8, 118±3, 127±2, 134±6 respectively and for HR Recovery, they were 90±7, 102±3, 111±3, 125±9 respectively. Participants with lower HR Reserve and higher HR Recovery tended to have higher BMI, lower CRF, and worse CV profiles than those with higher HR Reserve and lower HR Recovery. During the mean follow-up of 6 years, 2831 cases of HTN developed.

Table 3 shows that participants who had a greater HR Reserve were less likely to develop HTN. When adjusted for age and baseline examination year, BMI, smoking, heavy drinking, resting systolic and diastolic blood pressure, total cholesterol, and fasting glucose, there was

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a significantly inverse association between higher levels of HR Reserve and incident HTN (P for linear trend=0.002). Association of HR Reserve and HTN was similar in both younger and older men, with HazR of 0.77 and 0.78, respectively in quartile 4 (Data not shown). Table 4 shows a direct trend between HR Recovery and incidence of HTN. After adjusting for the above confounders, HR Recovery quartile 3 had a 10% lower risk of incident HTN, however, the linear trend is not significant across the quartiles (P for linear trend=0.26).

Mean maximal HR in the group that did not develop HTN was 181 (133–300) whereas, in the group that developed HTN it was 180 (138– 224). This shows that, max HR achieved by the group who did not develop HTN was higher than the group who developed HTN. We created 2 groups based on the year of the initial examination 1974–1988 and 1989–2003. Similar inverse associations were found between HR Reserve and incident HTN across the two groups. However, no significant associations were observed for HR Recovery.

# Discussion

## Principle findings

In this large prospective study of men, we found that a higher HR Reserve was significantly associated with a lower risk of incident HTN. The inverse association between HR Reserve and incident HTN persisted even after adjusting for multiple confounders, including age and CRF. Compared with the lowest quartile of HR Reserve, the highest quartile of HR Reserve had approximately 16 % lower risk of developing HTN in the fully adjusted model. Men in the lower quartile of HR Recovery had approximately 10% lower risk of developing HTN in the fully adjusted model. However, the overall linear trend across quartiles of HR Recovery was not significant. The current study demonstrates that HR Reserve, but not HR Recovery is associated with higher incidence of HTN independent of other major predictors, including CRF.

## Comparison with previous reports

Previous studies have found that lower HR at peak exercise, high Resting HR, and high HR Recovery are independent risk factors for the development of CHD and CVD morbidity and mortality.[8–12,14–17] These studies used only one parameter, either Resting HR or maximal HR. Our study analyzed associations of HTN with HR Reserve which was calculated by using Resting HR and maximal HR. A 13 year longitudinal study concluded that HR Reserve, independent of CRF, was inversely associated with CVD mortality among men and can be an important exercise parameter to predict CVD mortality in younger men (20–39), whereas CRF and other established risk factors are better predictors of CVD and all-cause mortality in older men (30–59).[13] This prior study focused on a broad but important outcome, CVD mortality. Our study examined effect of HR Reserve and HR Recovery on incident HTN and found significant associations between HR Reserve and incident HTN in both younger and older men. The results suggest that HR Reserve might be a reliable indicator for predicting HTN in all age groups.

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### Mechanisms underlying the observed associations

Elevated Resting HR may be a result of increased sympathetic activity, reduced vagal activity or both, which explains the association of Resting HR and HTN to some extent.[26,27] Several underlying mechanisms have been suggested as being responsible for the association between elevated HR and HTN. A high Resting HR may intensify the pulsatile nature of the arterial blood flow which may favor injury to the endothelium and consequent initiation or exacerbation of the atherosclerosis.[28,29] Inability to increase HR properly during exercise is a phenomenon called chronotropic incompetence[30], which suggests that impaired baroreflex sensitivity modulates both the parasympathetic influence in early exercise and sympathetic effects in the later phase on HR response to exercise.[31] This phenomenon, however, does not apply to our data because the subjects who did not reach 85% of the expected maximum HR were excluded from the study. Although subjects who developed HTN later did not have chronotropic incompetence, most of them were nonetheless unable to increase their HR at peak exercise to the levels achieved by people who did not develop HTN, a finding that indicates an impairment in the ability to increase sympathetic activity to its maximum extent. It has been suggested that low HR Recovery is due to autonomic dysfunction. Defective auto regulation of the cerebral blood flow may lead to change in the balance of autonomic nervous system in the cerebral vasculature, which may be associated with elevated blood pressure.[32]

### Strength and limitations

Strengths of the current study includes the relatively large sample size, a mean follow-up of 6 years, objectively measured resting HR, maximum HR during the exercise test and HR Recovery 5 minutes following exercise test. The findings were adjusted for several potentially important confounders. In addition, this study includes an extensive baseline medical examination, which is important since undetected subclinical disease at baseline is a concern in prospective studies. The following limitations should be considered when interpreting our data. First, the majority of participants were well-educated white men, limiting the generalizability of the findings. Second, all of the participants were measured at the baseline visit, and HR Reserve and HR Recovery might have changed during the follow-up period. The lack of pharmacotherapy information in our database limits evaluation of the specific medications that may affect the results of the exercise treadmill test. Additionally, we defined HR Recovery based as the HR at 5 minutes post-exercise. There is evidence that heart rate at 1 or 2 min of recovery is sensitive to detection of the association of HR Recovery and CVD events.[10,33] HR Recovery at 1 or 2 minutes are not present in our data-base, so we used HR Recovery at 5 minutes. We were not able to determine the relative strengths of prediction at 1, 2, and 5 min HR Recovery values. A previous study shows that HR Recovery at 5 minutes was independent predictor of CVD and all-cause mortality.[34] Although there is little additional data on HR Recovery at 5 minutes for predicting major CVD events, our data demonstrates the potential usefulness of such an assessment, at least regarding the development of subsequent HTN.

Finally, our study only included men who were able to achieve 85% of the age-predicted peak HR, so one could presume that those with more pronounced chronotropic insufficiency may have an even higher risk of HTN, as well as other CVD.

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### Conclusion and perspectives

HR Reserve was inversely associated with future development of HTN in a cohort of men who were normotensive and healthy at baseline. In terms of therapeutic or preventive implications, these observations might help explain known benefits of physical activity and exercise training, which may have beneficial effects on HR Reserve. We believe that clinicians should counsel their patients to be physically active to improve HR Reserve, which may lead to reductions in the subsequent risk of HTN. Future studies are also warranted to further examine the association between HR recovery and incident HTN.

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## Abbreviations

| | |
|---|---|
| **BMI** | body mass index |
| **CI** | confidence interval |
| **CRF** | cardiorespiratory fitness |
| **CVD** | cardiovascular disease |
| **ECG** | electrocardiogram |
| **HazR** | hazard ratio |
| **HTN** | hypertension |
| **HR** | heart rate |
| **RHR** | resting heart rate |

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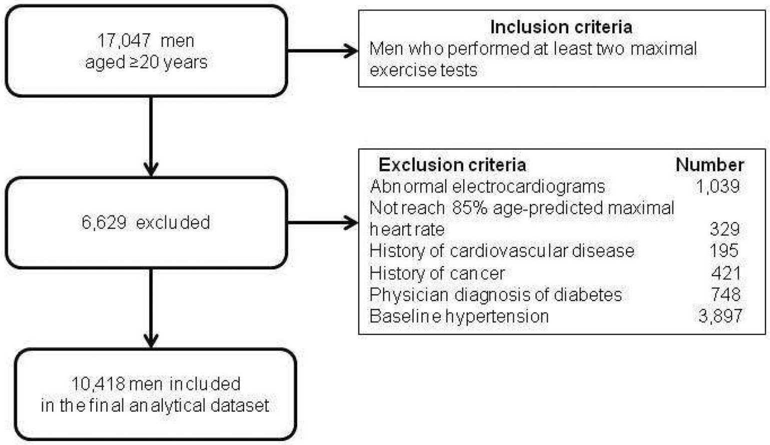


**Figure 1.**
Participant flow diagram

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**Table 1**

Baseline characteristics of study participants (N=10,418) by heart rate reserve quartiles, Aerobics Center Longitudinal Study (mean±SD)

| | **Quartile 1** | **Quartile 2** | **Quartile 3** | **Quartile 4** |
|---|---|---|---|---|
| **Age(years)** | **48.0±8.8** | **43.6±7.9** | **41.5±7.7** | **37.9±7.3** |
| Fasting glucose level (mg/dl) | 98.9±8.9 | 97.9±9.1 | 97±8.7 | 95.9±8.5 |
| Total Cholesterol level (mg/dl) | 210.9±38.3 | 207.6±37.4 | 203.7±37.8 | 196.1±35.5 |
| Resting Systolic Blood Pressure (mm Hg) | 118±10 | 117±9 | 116±9 | 115±9 |
| Resting diastolic blood Pressure (mm Hg) | 78±6 | 78±7 | 77±7 | 76±7 |
| Resting pulse (beats/min) | 65±10 | 61±9 | 57±8 | 52±8 |
| Maximum pulse (beats/min) | 168±11 | 178±9 | 183±8 | 191±9 |
| Body mass index (kg/m$^2$) | 26.6±3.1 | 25.7±2.7 | 25.2±2.6 | 24.7±2.5 |
| Maximal Treadmill Time (minutes) | 16±4 | 18.7±4 | 20.2±4 | 21.9±4 |
| Heart rate reserve (beats/min) | 103±8 | 118±3 | 127±2 | 134±6 |
| Current Smoker | 21.5 | 17.6 | 14.5 | 12.3 |
| Heavy drinkers | 17.4 | 16.1 | 16.8 | 14.9 |

P-value for all variables is <0.001 except heavy drinkers which was 0.04

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## Table 2

Baseline characteristics of study participants (N=10,418) by heart rate recovery quartiles, Aerobics Center Longitudinal Study (mean±SD)

| | **Quartile 1** | **Quartile 2** | **Quartile 3** | **Quartile 4** |
|---|---|---|---|---|
| **Age(years)** | **44.0±9.3** | **42.6±8.7** | **42.6±8.4** | **41.3±8.2** |
| Fasting glucose level (mg/dl) | 96.8±8.9 | 97.4±9.0 | 97.5±9.2 | 97.7±8.9 |
| Total Cholesterol level (mg/dl) | 203.8±37.4 | 204±37.8 | 206.2±38.6 | 203.0±36.5 |
| Resting Systolic Blood Pressure (mm Hg) | 115±9 | 115±9 | 116±9 | 117±9 |
| Resting diastolic blood Pressure (mm Hg) | 76±6 | 77±7 | 77±6 | 78±6 |
| Resting pulse (beats/min) | 52±8 | 57±8 | 60±9 | 64±10 |
| Maximum pulse (beats/min) | 172±11 | 179±10 | 183±11 | 189±10 |
| Body mass index (kg/m$^2$) | 25.2±2.6 | 25.4±2.7 | 25.7±3.0 | 25.6±2.9 |
| Maximal Treadmill Time (minutes) | 20.3±4.9 | 19.5±5 | 18.9±4.4 | 18.7±4.0 |
| Heart rate recovery (beats/min) | 89.7±6.6 | 102±3 | 111±3 | 125±9 |
| Current Smoker | 16.9 | 16.5 | 16.4 | 14.9 |
| Heavy drinkers | 18.9 | 17.4 | 16.7 | 11.7 |

P-value for all variables is <0.001 except glucose which was 0.005

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## TABLE 3

Multivariable-adjusted hazard ratio and 95% confidence interval of incident hypertension by heart rate (HR) reserve quartiles, Aerobics center Longitudinal Study.

| Variables | Model 1 | Model 2 | Model 3 |
| --- | --- | --- | --- |
| HR Reserve Quartile 1 | 1 | 1 | 1 |
| HR Reserve Quartile 2 | **0.89 (0.80 – 0.99)** | 0.93 (0.86 – 1.10) | 0.96 (0.86 – 1.10) |
| HR Reserve Quartile 3 | **0.78 (0.70 – 0.88)** | **0.89 (0.80 – 0.99)** | 0.90 (0.80 – 1.01) |
| HR Reserve Quartile 4 | **0.67 (0.60 – 0.76)** | **0.82 (0.73 – 0.93)** | **0.84 (0.74 – 0.95)** |
| P for linear trend | <0.001 | <0.001 | 0.002 |

Model 1 adjusted for age and baseline exam year.

Model 2: adjusted for confounders in Model 1 and smoking, heavy alcohol drinking, body mass index, resting systolic and diastolic blood pressure, total cholesterol, and blood glucose.

Model 3: adjusted further for confounders in model 2 and cardiorespiratory fitness.

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## TABLE 4

Multivariable-adjusted hazard ratio and 95% confidence interval of incident hypertension by heart rate (HR) recovery quartiles, Aerobics center Longitudinal Study.

| **Variables** | **Model 1** | **Model 2** | **Model 3** |
|---|---|---|---|
| HR Recovery Quartile 1 | **0.8 (0.71 – 0.89)** | 0.91 (0.81 – 1.02) | 0.93 (0.83 – 1.04) |
| HR Recovery Quartile 2 | **0.81 (0.72 – 0.90)** | 0.90 (0.80 – 1.01) | 0.91 (0.82 – 1.02) |
| HR Recovery Quartile 3 | **0.88 (0.79 – 0.98)** | **0.89 (0.80 – 0.99)** | **0.90 (0.80 – 0.99)** |
| HR Recovery Quartile 4 | 1 | 1 | 1 |
| P for linear trend | <0.001 | 0.12 | 0.26 |

Model 1 adjusted for age and baseline exam year.

Model 2: adjusted for confounders in Model 1 and smoking, heavy alcohol drinking, body mass index, resting systolic and diastolic blood pressure, total cholesterol, and blood glucose.

Model 3: adjusted further for confounders in model 2 and cardiorespiratory fitness.