Cardiorespiratory fitness, fatness and the acute blood pressure response to exercise in adolescence

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/SMS.13976

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Abstract

Objective. Exaggerated exercise blood pressure (BP) is associated with cardiovascular risk factors in adolescence. Cardiorespiratory fitness and adiposity (fatness) are independent contributors to cardiovascular risk, but their interrelated associations with exercise BP are unknown. This study aimed to determine the relationships between fitness, fatness and the acute BP response to exercise in a large birth cohort of adolescents. Methods. 2292 adolescents from the Avon Longitudinal Study of Parents and Children (aged 17.8±0.4 years, 38.5% male) completed a submaximal exercise step-test that allowed fitness (VO2 max) to be determined from workload and heart rate using a validated equation. Exercise BP was measured immediately on test cessation and fatness calculated as the ratio of total fat mass to total body mass measured by DXA. Results. Post-exercise systolic BP decreased stepwise with tertile of fitness (146 (18); 142 (17); 141 (16) mmHg) but increased with tertile of fatness (138 (15); 142 (16); 149 (18) mmHg). In separate models, fitness and fatness were associated with post-exercise systolic BP adjusted for sex, age,
height, smoking and socioeconomic status (standardized $\beta$: -1.80, 95%CI: -2.64, -0.95 mmHg/SD and 4.31, 95%CI: 3.49, 5.13 mmHg/SD). However, when fitness and fatness were included in the same model, only fatness remained associated with exercise BP (4.65, 95%CI: 3.69, 5.61 mmHg/SD). **Conclusion.** Both fitness and fatness are associated with the acute BP response to exercise in adolescence. The fitness-exercise BP association was not independent of fatness, implying the cardiovascular protective effects of cardiorespiratory fitness may only be realised with more-favourable body composition.

**Key words.** ALSPAC; Exercise; Blood pressure; Cardiorespiratory fitness; Body Composition; Adolescent

### Introduction

An exaggerated blood pressure (BP) response to exercise has been shown to be a risk factor for cardiovascular disease morbidity and mortality. Evidence of the prognostic importance of exaggerated exercise BP has mostly been drawn from studies involving middle-to-older age and clinical populations. However, several studies also indicate that associations between exercise BP and markers of cardiovascular disease (including raised left-ventricular (LV) mass, increased aortic stiffness and impaired vascular function) may be present even in adolescence. This highlights a need to understand the determinants of exercise BP in youth.

Poor cardiorespiratory fitness and raised adiposity (fatness) are important contributors to an adverse cardiovascular risk profile in adolescence and are related to future cardiometabolic disease outcomes. Cardiorespiratory fitness and fatness are also amongst several factors known to influence the acute BP response to exercise. Indeed, current evidence suggests that higher cardiorespiratory fitness is associated with improved exercise BP in adults. Moreover, our recent analysis from the Avon Longitudinal Study of Parents and Children (ALSPAC) showed that cardiorespiratory fitness also modifies the association between exercise BP and cardiac structure in 15-17 year old adolescents. Similarly, improved body composition (a decrease in body fatness) following exercise training has been shown to attenuate exercise BP in sedentary older people. Despite this, no study has directly assessed the individual and combined contributions of cardiorespiratory fitness and fatness to exercise BP in young people. Better understanding of the factors that contribute to elevated exercise BP in youth is of clinical importance since it may aid early detection of cardiovascular disease risk. Therefore, the aim of our study was to understand the
separate and joint associations between cardiorespiratory fitness, fatness and the acute BP response to exercise in a large group of adolescents.

Methodology

Participants. Data were drawn from the Avon Longitudinal Study of Parents and Children (ALSPAC), a large ongoing population-based birth cohort study in the United Kingdom. Information on the study cohort has been reported previously, and details of all data available is fully searchable via an online data dictionary (http://www.bristol.ac.uk/alspac/researchers/our-data/). The total sample size for analyses using any data collected after age seven is 15,454 pregnancies, that resulted in 15,589 foetuses, 14,901 who were alive at 1 year of age. The current study involved a complete-case cross-sectional analysis of data collected during the 17-year-old sweep of clinics, which were conducted over a two-year period (2008-2010) at the ALSPAC research clinic. Of the 5215 participants who took part in these clinics, a further 2923 individuals were excluded due to missing or incomplete exercise test data allowing valid estimation of cardiorespiratory fitness (VO\(_2\) max), missing post-exercise BP or dual-energy x-ray absorptiometry (DXA) body composition. A further 83 participants were excluded because systolic BP did not increase from pre-exercise to post-exercise. This left a total of 2209 individuals for this analysis (see supplementary figure 1 for participant flow). As this was a complete case analysis, a further 716 were excluded from regression analyses because of either missing height or socioeconomic status (SES). Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees.

Assessment of cardiorespiratory fitness. Participants undertook a modified Tecumseh Step Test during the mornings of a clinic visit that consisted of stepping onto and off a step (20 cm high) with alternating feet at a rate of 24 steps/minute for 3 minutes. The tempo of steps was kept constant using a metronome. The test was terminated upon completion or on request of the participant. HR was recorded prior to, immediately following and after 3 minutes of recovery from the test. Using this test data, it was possible to calculate an estimate of cardiorespiratory fitness (VO\(_2\) max) using modifications of the equations developed by Astrand and Van Dobeln (equations 1 and 2).

\[
\text{(Male) } \text{VO}_2 \text{ max} = 1.29 \left( \frac{\text{Load [kg m min}^{-1}]\text{}}{\text{Exercise heart rate [bpm] } - 60} \right) e^{-0.0088}
\]

Equation 1.

Equation 2.
Load was calculated as the product of force and distance, where force was considered equivalent to individual body weight (kg) and distance the product of step rate (steps/min) and step height (m). Exercise HR was considered the HR recorded immediately on cessation of the exercise test. Separate equations were utilised for males and females. Pragmatic physiological limits for estimated VO$_2$ max were set according to the normal range for males and females <29 years of age, (26.5 - 60.5 ml.kg.min$^{-1}$ males, 23.7 - 54.5 ml.kg.min$^{-1}$ females outlined with the American College of Sports Medicine guidelines. When the equations produced VO$_2$ max values outside these limits, the result was deemed invalid and individuals were excluded from the analysis (as indicated in Supplementary figure 1).

Assessment of fatness. A DXA scanner (Lunar Prodigy, GE Medical Systems, Madison, WI, USA) was used to objectively assess body composition. Total fat mass, lean mass and bone mass (kg) were measured and summed to represent total mass. The primary measure of ‘fatness’ was fat proportion of total mass, calculated as fat mass divided by total mass and expressed as a percentage. Other measures of body composition or stature were also assessed, including lean proportion of total mass (calculated as the percentage of lean mass in total mass), central adiposity (trunk fat) as a proportion of total fat mass, height (measured using a Harpenden Stadiometer to the nearest 0.1cm) and weight (recorded to the nearest 0.1 kg using Tanita TBF 305 scales). Body mass index (BMI) was calculated as weight (kg)/ height squared (m$^2$).

Blood Pressure. BP was measured using a validated automatic monitor (Omron 705 IT, Omron Electronic Components Europe BV) with an appropriate size cuff. Pre-exercise BP was measured prior to the step test, while the participant was standing with both arms down at sides. The participant was asked to wear the BP cuff continuously throughout the exercise test. Post- and recovery-exercise BP were measured and recorded immediately upon completion of the test (within the first 30 seconds) and after three minutes of recovery respectively. Delta exercise BP was defined as post- minus pre-exercise BP. Using the same device as the exercise BP measures, a ‘clinic BP’ was measured in triplicate after a minimum of 5 minutes seated rest on the same day, but prior to, the exercise test. The average of the last two readings was recorded as the clinic BP.

Blood biochemistry and socioeconomic status. Non-fasting blood was taken and biochemistry analysis including glucose, total cholesterol, triglycerides, glucose, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) performed following locally established procedures outlined previously. SES was determined based on the occupation of the mother’s partner (usually the father) and classified into eight classes (1, higher managerial and professional through to 8, never worked and long-term unemployed).
Statistical analysis. Data were analysed using Stata (version 16.0, Texas, 77845, USA, Stata Corp LLC). Normality of variables was assessed using the Shapiro-Wilk test and by visualization of distributions. The distribution of categorical variables was analyzed with frequencies and contingency table arrays. Cardiorespiratory fitness and fatness were standardized to age and sex for regression analyses and group comparisons. This was achieved via creation of cardiorespiratory fitness and fatness z scores by first dividing the study population into age (rounded to the nearest 1 year, ranging from 16-19 years) and sex (male and female) strata groups. Multivariable linear regression analyses were performed to determine the association between cardiorespiratory fitness or fatness and exercise systolic BP, followed by mutual adjustments to examine whether each variable (fitness and fatness) were still associated with exercise BP after adjustment for the other. Outcome variables included pre-, post-, recovery-, delta exercise systolic BP, with fitness or fatness (z scores) input as the primary independent variable in each model. Age (years), sex, height (cm), socioeconomic status (SES) and smoking status were included in regression models as covariates. Results were presented as β coefficients (95% confidence interval, CI) per 1 unit increment in standardized cardiorespiratory fitness or fatness. Assumptions for linear regression were assessed by inspection of residuals and variance inflation factors (VIF) >5 or a tolerance level <0.10 interpreted as indicating collinearity. Sex-pooled models were established for each BP outcome since there was no sex-cardiorespiratory fitness or -fatness interaction on any of the exercise BP outcomes. Statistical significance was defined as P <0.05. Data are presented as means (95% confidence intervals) or mean (standard deviation) unless otherwise indicated.

Results

Participant characteristics by cardiorespiratory fitness and fatness. Participant characteristics are outlined by cardiorespiratory fitness and fatness levels in table 1. The proportion of males, lean proportion of total mass and estimated VO\textsubscript{2} max was higher with greater cardiorespiratory fitness, whereas total cholesterol, LDL cholesterol level, clinic systolic and diastolic BP and HR, height, weight, BMI, total fat mass, total lean mass, fat proportion of total mass (fatness), delta exercise HR were lower. Total cholesterol, triglycerides, LDL cholesterol level, clinic systolic and diastolic BP, weight, BMI, total fat mass, total lean mass, fat proportion of total mass (fatness) and delta exercise HR were higher with greater fatness. The proportion of males was lowest in the middle fatness level. Clinic HR, height, lean proportion of total mass and estimated VO\textsubscript{2} max were lower with greater fatness level. Those with a higher level of cardiorespiratory fitness had higher paternal SES compared to those with lower cardiorespiratory fitness levels. Those with a higher level of fatness had lower paternal SES compared to those with lower fatness levels.
Exercise BP by cardiorespiratory fitness and fatness. Pre-exercise systolic and diastolic, post-exercise systolic and diastolic, recovery-exercise systolic and diastolic BPs were lower with higher level of cardiorespiratory fitness. Delta diastolic BP was similar in the moderate and high level of cardiorespiratory fitness but slightly lower in those with a low level of cardiorespiratory fitness. Pre-exercise systolic and diastolic, post-exercise systolic and diastolic, recovery-exercise systolic and delta exercise systolic BPs were higher in those with higher level of fatness. Recovery-exercise diastolic and delta diastolic BP was similar between low and moderate level of cardiorespiratory fitness groups, but slightly higher with a high level of fatness (see supplementary table 1 for data and statistical significance).

The association of cardiorespiratory fitness and fatness with exercise BP. Cardiorespiratory fitness was associated with pre-, post-, recovery-exercise systolic BP (model 1, table 2). After adjustment for sex, age, height, smoking status and socioeconomic status, cardiorespiratory fitness remained associated with pre-, post- and recovery-exercise systolic BP (model 2, table 2). When fatness was added into the model (model 3, table 2), the association between cardiorespiratory fitness and pre- and post-exercise systolic BP was attenuated, with only recovery-exercise systolic BP remaining associated with cardiorespiratory fitness. The association between cardiorespiratory fitness and delta-exercise systolic BP become stronger (model 3, table 2).

Fatness was associated with pre-, post-, recovery-, delta exercise systolic BP (model 4, table 2). These associations remained after adjustment for sex, age, height, smoking status and socioeconomic status (model 5, table 2). With the further addition of cardiorespiratory fitness to the model (model 6, table 2), fatness remained independently associated with pre-, post-, recovery-, delta exercise systolic BP.

Substituting fatness for leanness led to the results as presented in supplementary table 2. When lean proportion of total mass was added into the model 3 (supplementary table 2), the association between cardiorespiratory fitness and pre- and post-exercise systolic BP was attenuated, with only recovery-exercise, delta-exercise systolic BP remaining associated with cardiorespiratory fitness (model 3, supplementary table 2). All other associations between leanness and all exercise BPs were as per those of fatness. Substituting fatness for central adiposity led to the results as presented in Supplementary table x, which were broadly like those of fatness.

Although not statistically significant, pre-, post-, and recovery-exercise systolic BP was 3-8 mmHg higher in those with high fatness compared to those with low fatness at any level of cardiorespiratory fitness (Figure 1 a,b,c). Delta-exercise systolic BP was higher in those with high fatness compared to those with...
low fatness at low and moderate levels of cardiorespiratory fitness, but similar in those with a high level of
cardiorespiratory fitness (Figure 1 d).

Discussion

In this cohort of adolescents, cardiorespiratory fitness was negatively associated with exercise systolic BP,
whilst DXA measured fatness was found to be positively associated with exercise systolic BP. The
association between exercise systolic BP and cardiorespiratory fitness was not independent of fatness,
whereas fatness remained strongly associated with exercise BP after adjustment for cardiorespiratory
fitness. Moreover, for any level of cardiorespiratory fitness, exercise systolic BP was higher in those with
greater fatness. This suggests that fatness may be more closely related to exercise BP than cardiorespiratory
fitness in adolescence.

It is well known that low cardiorespiratory fitness increases risk of chronic disease and mortality across the
lifespan, satisfying criteria to be considered a fundamental cardiovascular disease risk factor. The
importance of attaining and improving cardiorespiratory fitness in youth is also clear. For example, results
of the large ‘Coronary Artery Risk Development in Young Adults (CARDIA)’ study indicated that each
additional minute of exercise completed during a treadmill exercise test (when aged 18-30 years) was
associated with a 15% risk reduction in all-cause mortality, independent of traditional cardiovascular risk
factors. Several other studies also show clear associations between adolescent cardiorespiratory fitness
and general cardiovascular health. Cardiorespiratory fitness is also known to influence the acute BP
response to exercise. Indeed, Cardiorespiratory fitness typically shares a negative linear association with
exercise BP, such that higher fitness appears to mitigate an abnormal rise in exercise systolic BP, therefore being associated with a more favourable exercise BP response and improved cardiovascular
health. Whilst we found such a linear relationship between cardiorespiratory fitness and exercise BP in our
general population sample of adolescents, one other analysis in young adults indicated that both low and
high fit individuals may exhibit elevated exercise BP, a relationship that is more ‘U-shaped’. We also
recently found cardiorespiratory fitness to modify the association between exercise BP and cardiac
structure in adolescence, such that those with both low and high cardiorespiratory fitness levels share a
similar exercise BP-cardiac structure relationship. Such a dependency on cardiorespiratory fitness would
imply that elevated exercise BP should not always be considered the result of pathological change, but also
physiologically induced adaptation. Indeed, those with high levels of cardiorespiratory fitness (such as
well-trained athletes) may have elevated exercise BP, but do not share the same underlying cardiovascular
dysfunction as low fit individuals. Thus, the differing aetiology of the cardiorespiratory fitness-exercise

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BP relationship implies there is unlikely to be a single or direct pathway between cardiorespiratory fitness and exercise BP.

In the current study the cardiorespiratory fitness-exercise BP association was not independent of fatness. On the one hand this could be interpreted to suggest that fatness is more strongly associated with exercise BP than is cardiorespiratory fitness. Some studies have indicated that exercise training that improves fitness also induces small-to-moderate reductions in exercise systolic BP.\textsuperscript{14} Whilst our study did not involve any exercise training intervention, exercise systolic BP was step-wise higher with each level of fatness. Moreover, for any level of cardiorespiratory fitness, exercise BP was higher in those with greater fatness. This finding is consistent with a study of apparently healthy young men and women, in which individuals with a higher waist circumference had elevated exercise systolic BP, irrespective of their cardiorespiratory fitness level.\textsuperscript{28} This could suggest that the benefits of greater cardiorespiratory fitness on exercise SBP may not be fully realised without improvements in adiposity.

Beyond cardiorespiratory fitness, high fatness is an important cardiovascular disease risk factor. A large study of 6\textsuperscript{th} grade students in the United States indicated that fatness was associated with many cardiovascular disease risk markers (including BP, cholesterol, glucose and insulin) independently of fitness.\textsuperscript{29} Similarly, percent body fat has been shown to have a greater influence on overall CVD risk in adolescence than cardiorespiratory fitness measured as aerobic power.\textsuperscript{30} Obesity is a known correlate of metabolic induced vascular dysfunction (including raised arterial stiffness),\textsuperscript{31} that could give rise to a ‘pathological’ elevation in exercise BP when the exercise-induced demand for blood flow is not offset by normal vascular compliance. Indeed, steeper trajectories of central adiposity through adolescence and young adulthood are associated with greater large-artery (carotid) stiffness at mid-life, largely independent of other cardiovascular risk factors including cardiorespiratory fitness.\textsuperscript{32} We have also previously found associations between exercise systolic BP and aortic stiffness in the ALSPAC cohort.\textsuperscript{4} This cohort at the age of 17 is, however, generally healthy and largely free of any clinical cardiovascular disease. Whilst this allows determination of the associations between cardiorespiratory fitness, fatness and exercise BP not subject to reverse causality by disease, we cannot attribute causality in a cross-sectional study. Further studies are required to fully understand the mechanisms by which fatness contributes to elevations in exercise BP.

Limitations. The study sample is relatively homogenous with respect to ethnicity, being of predominately white European decent. Thus, our results may not be applicable to other population groups.

Cardiorespiratory fitness was estimated using an equation with parameters derived from a sub-maximal exercise test. In the absence of an objective cardiorespiratory fitness test (such as the gold-standard VO\textsubscript{2}}
max test), we are unable to fully understand the relationship between cardiorespiratory fitness and exercise BP.

Perspectives. Cardiorespiratory fitness is negatively associated with exercise BP, whilst DXA measured fatness is positively associated with exercise systolic BP. The association between exercise systolic BP and cardiorespiratory fitness was not independent of fatness, thus the cardiorespiratory fitness-exercise BP association is accounted for by fatness. This implies that the cardiovascular protective effects of cardiorespiratory fitness on exercise BP may only be fully realised with more favourable body composition. While further longitudinal studies are needed to describe the future cardiovascular disease risk associated with raised exercise BP in youth, interventions targeted at improving both cardiorespiratory fitness and fatness could have both an independent and additive effect on reducing exercise BP and preventing cardiovascular disease risk.

284 Acknowledgments

We are extremely grateful to all the families who took part in the study, the midwives for their help in recruiting them, and the whole ALSPAC team, which includes interviews, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists, and nurses.

Funding

The UK Medical Research Council and Wellcome Trust (217065/Z/19), together with the University of Bristol, provide core support for the ALSPAC study. A comprehensive list of grants funding the ALSPAC study is available on the ALSPAC website: http://www.bristol.ac.uk/alspac/external/documents/grant-acknowledgements.pdf. ADH received support from the Wellcome Trust (086676/7/08/Z) and the British Heart Foundation (PG/06/145 & CS/15/6/31468) in relation to the work presented in this analysis. MGS is supported by a National Heart Foundation of Australia Future Leader Research Fellowship (reference 102553). ADH and NC work in a unit that receives support from the UK Medical Research Council (Programme Code MC_UU_12019/1). LDH is supported by a Career Development Award from the UK

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Medical Research Council (MR/M020894/1) and works in a unit funded by the UK Medical Research Council (MC_UU_00011/6) and the University of Bristol. This publication is the work of the authors and the corresponding author will serve as guarantor for the contents of this paper.

Data Availability Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request. Moreover, the ALSPAC study investigators encourage and facilitate data sharing upon formal request.

Figure Legends

Figure 1. Exercise systolic BP by cardiorespiratory fitness and fatness level: a: pre-exercise systolic BP, b: post-exercise systolic BP, c: recovery-exercise systolic BP, d: delta-exercise systolic BP. Square: high fatness level, triangle: low fatness level. Differences in exercise BP between high and low fatness assessed by between group t-test at each fitness tertile. Values are presented as mean and error bars represent standard error.
References.


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Table 1. Participant characteristics by cardiorespiratory fitness and fatness level

<table>
<thead>
<tr>
<th></th>
<th>Cardiorespiratory fitness</th>
<th>Fatness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low (SD)</td>
<td>Moderate (SD)</td>
</tr>
<tr>
<td>Age, years</td>
<td>17.8 (0.4)</td>
<td>17.8 (0.4)</td>
</tr>
<tr>
<td>Male, percentage</td>
<td>180 (38.0)</td>
<td>186 (37.2)</td>
</tr>
<tr>
<td>Total cholesterol, mmol/l</td>
<td>3.9 (0.7)</td>
<td>3.8 (0.7)</td>
</tr>
<tr>
<td>^Triglycerides, mmol/l</td>
<td>0.9 (0.6-1.1)</td>
<td>0.8 (0.6-1.0)</td>
</tr>
<tr>
<td>^Glucose, mmol/l</td>
<td>5.0 (0.4)</td>
<td>5.0 (0.4)</td>
</tr>
<tr>
<td>^HDL, mmol/l</td>
<td>1.2 (0.3)</td>
<td>1.3 (0.3)</td>
</tr>
<tr>
<td>^LDL, mmol/l</td>
<td>2.3 (0.6)</td>
<td>2.2 (0.6)</td>
</tr>
<tr>
<td>Clinic SBP, mmHg</td>
<td>119 (11)</td>
<td>116 (11)</td>
</tr>
<tr>
<td>Clinic DBP, mmHg</td>
<td>66 (7)</td>
<td>65 (7)</td>
</tr>
<tr>
<td>Clinic HR, bpm</td>
<td>76 (10)</td>
<td>74 (9)</td>
</tr>
<tr>
<td>Height, cm</td>
<td>172.2 (9.6)</td>
<td>171.4 (9.1)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>76.8 (14.5)</td>
<td>66.3 (11.5)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>26.1 (4.8)</td>
<td>22.7 (3.4)</td>
</tr>
<tr>
<td>Total fat mass, kg</td>
<td>27.3 (11.0)</td>
<td>18.8 (8.6)</td>
</tr>
<tr>
<td>Total lean mass, kg</td>
<td>45.8 (9.7)</td>
<td>44.3 (9.5)</td>
</tr>
<tr>
<td>Fat proportion of total mass (fatness), %</td>
<td>35.3 (10.5)</td>
<td>28.2 (10.5)</td>
</tr>
<tr>
<td>Lean proportion of total mass, %</td>
<td>60.8 (10.3)</td>
<td>67.6 (10.3)</td>
</tr>
<tr>
<td>Estimated VO₂ max, ml/kg/min</td>
<td>39.6 (4.3)</td>
<td>47.1 (3.6)</td>
</tr>
<tr>
<td>Delta exercise HR, bpm</td>
<td>24 (14)</td>
<td>24 (12)</td>
</tr>
</tbody>
</table>

HDL, high-density lipoprotein; LDL, low-density lipoprotein. Data are presented as mean (SD) or n (%). Triglycerides was presented as median (interquartile range (IQR)). Fitness levels classified as low (first tertile), moderate (second tertile) and high (third tertile) level of age-sex standardised estimated VO₂ max. Fatness were classified as low (first tertile), moderate (second tertile) and high (third tertile) level of age-sex standardised fat proportion of total mass. ^ total n= 1521. Delta exercise HR: post-exercise HR less pre-exercise HR.
Table 2. Cardiorespiratory fitness, fatness and exercise systolic BP.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Cardiorespiratory fitness</th>
<th>Fatness</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Model 1 (β, 95% CI)</td>
<td>Model 2 (β, 95% CI)</td>
</tr>
<tr>
<td>Pre-exercise SBP</td>
<td>-1.79 (-2.44, -1.15) **</td>
<td>-1.84 (-2.45, -1.23) **</td>
</tr>
<tr>
<td>(n=1576)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-exercise SBP</td>
<td>-1.70 (-2.54, -0.87) **</td>
<td>-1.81 (-2.66, -0.97) **</td>
</tr>
<tr>
<td>(n=1597)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recovery-exercise SBP</td>
<td>-2.59 (-3.23, -1.95) **</td>
<td>-2.62 (-3.24, -2.00) **</td>
</tr>
<tr>
<td>(n=1556)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delta exercise SBP</td>
<td>-0.15 (-0.69, 0.72)</td>
<td>-0.04 (-0.74, -0.65)</td>
</tr>
<tr>
<td>(n=1576)</td>
<td></td>
<td></td>
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</table>

Fitness and fatness are age and sex standardized. Data are outcome (β, 95%CI) mmHg per one age-sex standardised unit of fitness or fatness increment of exercise systolic BP.  
**Model 1** - univariable; **Model 2** – model 1 plus adjustment for age (years), sex, height (cm), smoking status and socioeconomic status (SES);  **Model 3** - model 2 plus adjustment for one standardized unit of age-sex standardised fatness;  **Model 4** – univariable;  **Model 5** – model 4 plus adjustment for age (years), sex, height (cm), smoking status and SES;  **Model 6** - model 5 plus adjustment for one standardised unit of age-sex standardised fitness. **P<0.001, *P<0.05.**