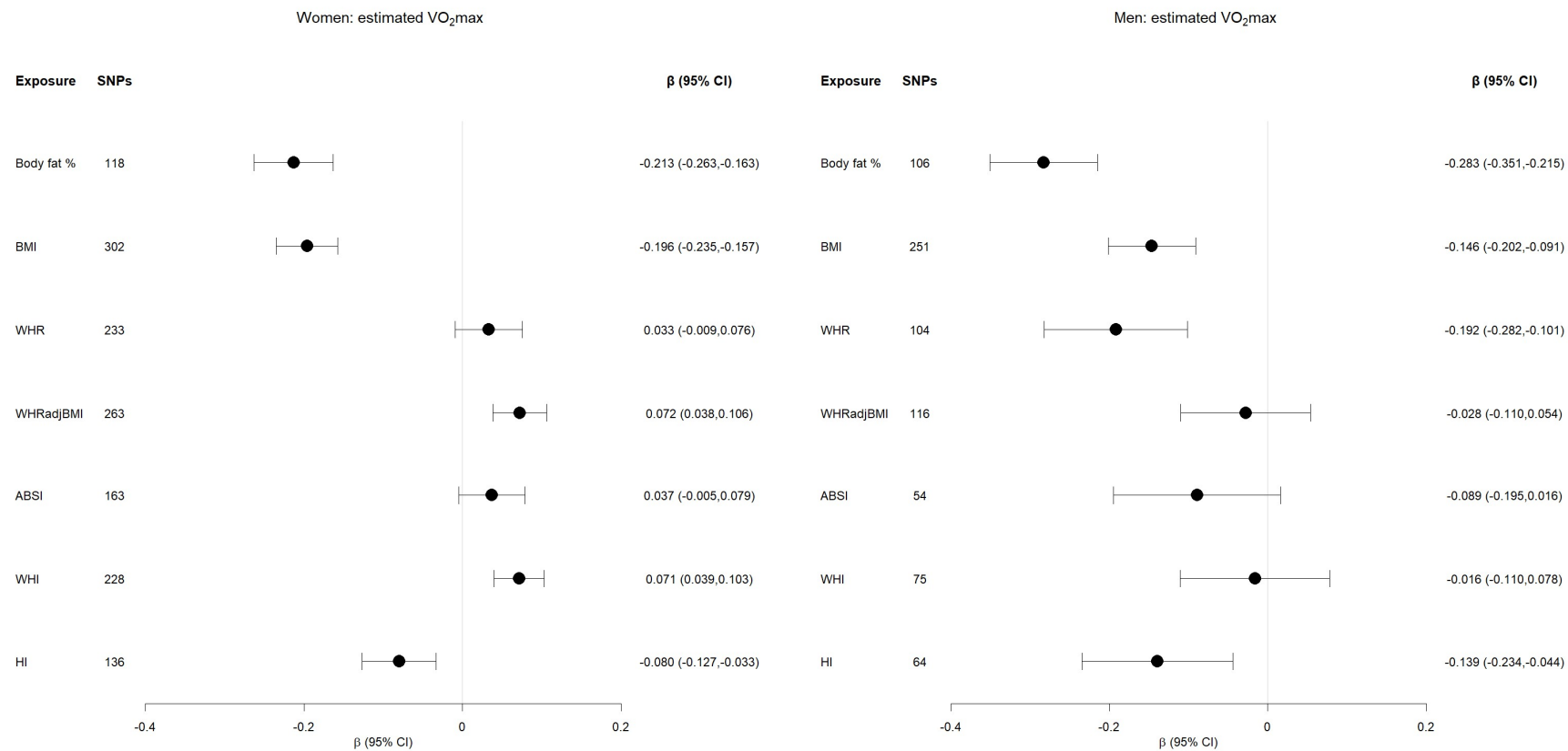


Supplementary figures

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Supplementary Figure 1. Causal effects of body composition on estimated VO_2max in women (left panel) and men (right panel).

Supplementary Figure 2. Causal effects of physical activity on estimated VO_2max .



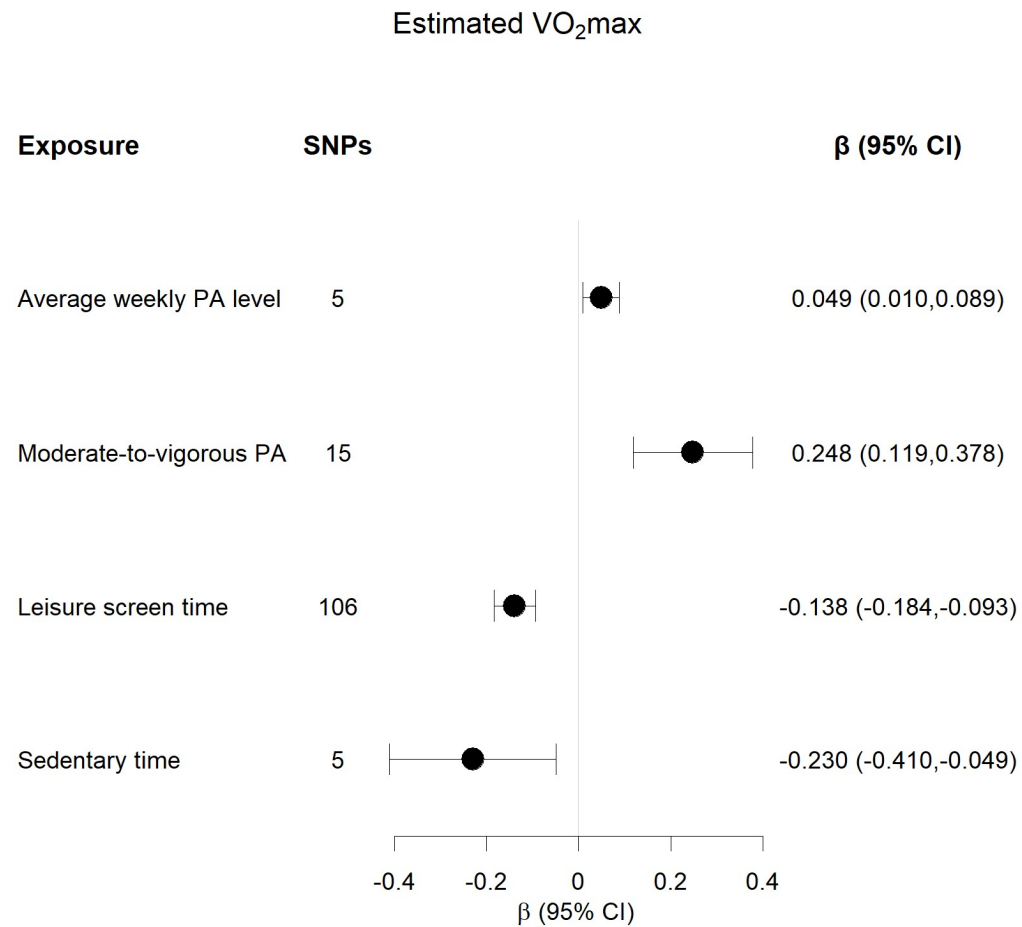
Supplementary Figure 1. Causal effects of body composition on estimated VO₂max in women (left panel) and men (right panel).

Estimates (β -coefficients and 95% confidence intervals [CIs]) are from the random-effects inverse variance weighted Mendelian randomization analysis, and expressed in log units per standard deviation increase in the relevant exposure. For each exposure, the number of single nucleotide polymorphisms (SNPs) included in the analysis is shown in parenthesis.

Body fat %, a body shape index (ABSI), waist-hip ratio (WHR), waist-hip index (WHI) and hip index (HI) were from the UK Biobank. Body mass index (BMI), waist-hip ratio (WHR) and WHR adjusted for BMI (WHRadjBMI) were from the GIANT (Genetic Investigation of ANthropometric Traits) Consortium, and included UK Biobank participants.

Estimated VO_2max , a proxy of cardiorespiratory fitness, was based on a submaximal cycle ramp test (in 70,783 UK Biobank participants) and estimated as the participants' maximum volume of oxygen consumption, per kilogram of body weight, per minute.

Sensitivity MR analyses are shown in Supplementary Tables 7-8.



Supplementary Figure 2. Causal effects of physical activity on estimated VO₂max.

Estimates (β -coefficients and 95% confidence intervals [CIs]) are from the random-effects inverse variance weighted Mendelian randomization analysis. For each exposure, the number of single nucleotide polymorphisms (SNPs) included in the analysis is shown in parenthesis.

Physical activity (PA) was either based on accelerometry data (measured average weekly PA level and machine-learning estimated sedentary time in $\approx 90,000$ UK Biobank participants) or self-reported (moderate-to-vigorous PA was binary [yes/no], whereas leisure screen time was a continuous trait of self-reported time spent watching TV, playing videogames, and sitting at the computer, etc in $>500,000$ individuals, including the UK Biobank).

Estimated $\text{VO}_{2\text{max}}$, a proxy of cardiorespiratory fitness, was based on a submaximal cycle ramp test (in 70,783 UK Biobank participants) and estimated as the participants' maximum volume of oxygen consumption, per kilogram of body weight, per minute.

Sensitivity MR analyses are shown in Supplementary Tables 3-4.