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TITLE:
Interaction between polygenic risks of obesity related traits and lifestyle in the UK Biobank

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KEYWORDS:
Polygenic risk score, BMI, obesity, lifestyle, interaction.

ABSTRACT:
Obesity-related health conditions have well-documented lifestyle and genetic components. There is growing interest in translational applications of polygenic risk scores (PRS) for risk prediction of obesity-related conditions, however it remains unclear whether PRS can be used for prioritizing behavioural change interventions. We constructed PRS of six common obesity risk factors (body mass index [BMI], high-density lipoprotein cholesterol [HDL], low-density lipoprotein cholesterol [LDL], triglycerides [TG], systolic blood pressure [SBP], diastolic blood pressure [DBP]) in 382,376 unrelated Europeans in the UK Biobank. We tested interactions between these PRS and four lifestyle traits (meat-based diet, physical activity, sedentary time, sleep duration) using linear regression models (e.g. BMI ~ PRS_{BMI} + meat-diet + PRS_{BMI} × meat-diet). We found nine interactions (PRS_{BMI} with diet and physical activity, PRS_{HDL} with physical activity and sedentary time, PRS_{LDL} with sedentary activity, PRS_{TG} with diet and sedentary activity, PRS_{SBP} with diet, and PRS_{DBP} with diet; P < Bonferroni-corrected threshold of 0.002). In general, the effects of lifestyle on BMI were larger
among participants at higher genetic risk of BMI and the effects on blood pressures were in the opposite direction; the effects on lipids varied. For example, BMI unit change per z-score increase in meat-based diet was higher among participants in the top quartile of PRS_{BMI} (beta [95% confidence interval] = 0.748 [0.710, 0.786]) than among those in the bottom quartile (beta [95% confidence interval] = 0.644 [0.609, 0.680]). Our findings suggest that behavioural change interventions may have different effects on obesity risk reduction depending on an individual’s genetic risk.

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