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TITLE:

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

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KEYWORDS:

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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. $BMI \sim PRS_{BMI} + \text{meat-diet} + PRS_{BMI} \times \text{meat-diet}$). 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; $P < \text{Bonferroni-corrected threshold of } 0.002$). 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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