Biobank-scale survey of gene-diet interactions informs precision nutrition polygenic scores

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Genome-guided dietary advice is a goal of precision nutrition. However, the contribution of gene-diet interactions (G×Ds) to disease risk remains unclear, hindering the identification of diet-outcome pairs more likely amenable to genetic-based recommendations. We thus implemented a two-step approach: first, we comprehensively assessed the contributions of genome-wide G×Ds to cardiometabolic outcomes across a broad array of dietary exposures in UK Biobank participants (N = 141,144 to 325,989). Second, we selected the 20 significant diet-outcome pairs from the 713 pairs tested ($p < 7.0\times10^{-5}$) and derived G×D polygenic scores. In an independent sample, all scores were nominally associated with their corresponding outcomes, with 12 of 20 polygenic scores Bonferroni significant ($p < 0.0025$). Further analyses revealed G×D polygenic scores were associated with clinical outcomes such as incident gout, suggesting translational potential. For instance, each additional alcoholic drink per day was associated with increased odds of gout (OR=23.9% 95% CI 1.11-1.38) in individuals in the highest quintile of the corresponding G×D polygenic score, whereas no significant change was observed in the lowest quintile (OR=4.8% 95% CI 0.91-1.18). Altogether, these results showcase the promise of G×D scores to inform precision nutrition.