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Can interventions mitigate genomic liability for obesity? Using causal inference based mediation analyses in genetically-sensitive studies

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ABSTRACT:

Polygenic scores are now commonly available in longitudinal cohort studies, leading to their integration into epidemiological research. In this work, our aim is to explore how polygenic scores can be used as exposures in causal inference based methods, specifically mediation analyses. We propose to apply the interventional disparity measure approach to estimate the extent to which the direct effect from an exposure to an outcome could be mitigated by a potential intervention on an intermediate mediator. In order to do this this, we use the interventional disparity measure approach, which allows us to compare the adjusted total causal effect of an exposure on an outcome, with the effect that would have occurred had we intervened on a intermediate mediator. As an example, we analyze data from two UK cohorts, the Avon Longitudinal Study of Parents and Children (ALSPAC) and the Millennium Cohort Study. In both, the exposure is genetic liability for obeisty (indicated by a polygenic risk score for BMI), the outcome is late childhood/early adolescent BMI, and the mediator and potential intervention target is physical activity, measured intermediately between exposure and outcome. Our results suggest that a potential intervention on child physical activity can mitigate some of the genetic liability for childhood obesity. Causal inference based methods can be beneficial as they ask researchers to state specific hypotheses and ground their research in the context of potential interventions, linking these investigations directly to clinical applications and wider public health.

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