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**Project Title**

Pleiotropy verification in Mendelian randomization: methodological assessment and application to the estimation of the causal effect of adiposity on blood pressure

**Project Summary**

Mendelian randomization (MR) is a method that estimates the causal effect of an exposure (to a non-genetic risk factor) on an outcome using a genetic variant as an instrument. The validity of MR is based among others on the hypothesis of non-pleiotropy, i.e. that the instrument does not affect the outcome in other ways outside of the exposure of interest. However, the risk of pleiotropy is difficult to verify in MR using a single instrument, i.e. a SNP (single-nucleotide polymorphism) or a GRS (genetic risk score). Using data from the Canadian Longitudinal Study on Aging, our study will compare the performance of the Glymour's method (2012) and the causal mediation analysis in detecting the possible pleiotropy of the FTO gene (Fat mass and obesity-associated) and a GRS including FTO as a single instrument in an MR analysis to estimate the causal effect of adiposity on blood pressure.

**Keywords**

Mendelian randomization, Pleiotropy, Simple instrument, Genetic risk score, FTO gene