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Using adopted singletons to partition maternal genetic effects into pre- and post-natal effects on offspring phenotype

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ABSTRACT: Maternal genetic effects can be defined as the effect of a mother's genotype on the phenotype of her offspring, independent of the offspring's genotype. Maternal genetic effects can act via the intrauterine environment during pregnancy and/or via the post-natal environment. Here we develop a new model using structural equation modelling (SEM) to partition maternal genetic effects into pre- and post-natal effects. We assume that in biological families, offspring phenotypes are influenced prenatally by their mother's genotype and postnatally by their parents' genotypes, whereas adopted individuals' phenotypes are influenced prenatally by their biological mother's genotype and postnatally by their adoptive parents' genotypes. Critically, SEM allows us to model the potentially unobserved genotypes of biological and adoptive parents as latent variables, permitting us to leverage the thousands of adopted singletons in the UK Biobank. We examine the utility and power of our model using simulations and asymptotic power calculations. We apply our model to educational attainment and birthweight, in up to 4197 adopted singletons, 969 trios, 3545 mother-offspring pairs, 1635 father-offspring pairs and 291642 singletons from the UK Biobank. Our results show expected patterns of maternal effects on offspring birthweight, but unexpected large prenatal effects on offspring educational attainment. Sensitivity analyses suggest this result may be due to adopted individuals in UK Biobank being fostered by their relatives. We conclude that our model can be used to estimate prenatal and postnatal maternal effects on offspring phenotypes, which has exciting implications for the development of pleiotropy robust Mendelian randomization approaches.

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