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Using Mendelian randomization to assess maternal effects on offspring outcomes.

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The influence of factors acting during the intrauterine period on health outcomes of offspring is of considerable research and public health interest. There are, however, considerable methodological challenges in establishing robust causal links, since exposures often act many decades before outcomes of interest, emerge may act before it is evident that women are pregnant and would enter pregnancy birth cohorts, and may also be strongly related to other factors, generating considerable degrees of potential confounding. Mendelian randomization approaches to this problem utilize genetic variants of known functional effect that, if carried by the mother, would influence the intrauterine environment. These genetic variants are stable over time and can be assessed after pregnancy is complete or even after outcomes in the offspring have been observed. The variants would also not generally be related to potential confounding factors. A series of examples of the application this methodology will be presented and its potentials and limitations discussed.