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### **Power, measurement error and pleiotropy robustness in twin design extensions to Mendelian randomization**

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Mendelian randomization (MR) has become an important tool for causal inference in health sciences, especially for psychiatric disorders and substance use problems. MR takes advantage of the random segregation of alleles to control for background confounding factors. This method works by using a genetic variant as an instrumental variable, but it depends on the assumption of exclusion restriction, i.e., that the variant affects the outcome exclusively via the exposure variable. Equivalently, the assumption states that there is no horizontal pleiotropy from the variant to the outcome. This assumption is unlikely to hold in nature, so several extensions to MR have been developed to increase its robustness against such pleiotropy, though not eliminating the problem entirely. The MR-DoC model (Minică et al 2018) explicitly models horizontal pleiotropy, therefore providing a direct assessment of the exclusion restriction assumption. This model was further extended to allow bidirectional causation in MR-DoC2 (Castro-de-Araujo et al. 2023). Here we compare the power of the Direction of Causation, MR-DoC, and MR-DoC2 models and test for presence of bias due to unmodelled measurement error at the phenotypes and lack of individual-specific environmental confounding.