Accuracy of outcome definitions in Mendelian randomization of maternal health

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Dear Dr Papageorphiou,

We recently read the article by Dr Ardissino and colleagues entitled 'Genetically predicted body mass index and maternal outcomes of pregnancy: A two-sample Mendelian randomization study' [1], where 11 outcomes were investigated. To conduct Mendelian randomization (MR) analyses, this study extracted associations of selected genetic variants with those outcomes from publicly available GWAS (genome-wide association study) summary data from FinnGen (the sixth release, total N=147,061 women) – a national-wide network of Finish Biobank [2]. We noticed that "postpartum depression" included in Ardissino et al was inconsistent with the commonly used definition of postnatal depression occurring within a year of delivery [3,4]. FinnGen defined this outcome based on the International Classification of Diseases 10th Revision (ICD-10) codes (ICD-10 F32, F33 and F53.0) among women with at least one episode of delivery (ICD-10 O80-O84), without considering the time interval between delivery and diagnosis of depression. Therefore, cases of "postpartum depression" could be ascertained at any time after giving birth and, therefore, could be unrelated to pregnancy. As a consequence, findings for "postpartum depression" in Ardissino et al should be interpreted with caution due to the unspecific outcome definition.

The increasing availability of publicly available or accessible data from GWAS consortia (e.g. Early Growth Genetics) and large biobanks (e.g. UK Biobank and FinnGen), combined with the creation of automated pipelines (e.g. MR-Base [5] used by Ardissino et al), has supported an rapid increase in publications using two-sample MR. Though such a combination has great potential to promote open science and advance health research, including in maternal-child health, we cautioned that detailed understanding of procedures used to generate GWAS summary data underlying MR analyses is of major importance to obtain reliable evidence and interpretable findings.

Author contributions

QY conceived of the study idea and drafted the letter, with MCB making important critical revisions.

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Conflict of interest statement

None declared

Ethics approval

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