## Comment

## Effect of alcohol during pregnancy: a public health issue

Alcohol is a known teratogen and associated with a range of adverse outcomes for pregnant women and children exposed in utero.<sup>1-3</sup> The most prominent of these is known as fetal alcohol spectrum disorder.<sup>4</sup> The Danish Health Authority, as well as the UK Chief Medical Officers, recommend women abstain from alcohol during pregnancy or when trying to conceive.<sup>5,6</sup>

However, it is estimated that almost half of women in both Demark and the UK, as well as a quarter of women in Europe, consume alcohol in pregnancy. Estimates suggest that Denmark ranks as the third worst country in the world for drinking during pregnancy, with the UK ranking fourth.<sup>7</sup> Continued monitoring and quantification of the risks associated with alcohol consumption in pregnancy is important for prevention and to ensure needs-based provision of services responding to alcohol-related harms.

Marcella Broccia and colleagues analyse 22 years of linked administrative and health data for all singleton babies born between 1996 and 2018 in Denmark to assess and quantify the association between maternal heavy alcohol use in the preconception period and during pregnancy, with prenatal, birth, and child health outcomes.<sup>8,9</sup> The first of their two papers focuses on obstetric and birth outcomes, while the second extends analysis to adverse child health outcomes up to age 18 years. These are ambitious, large-scale analyses that reveal complex associations.

Exposure to maternal heavy alcohol use is measured as maternal hospital treatment for alcohol attributable diagnoses, or prescriptions for alcohol dependence in the year before or during pregnancy, or alcohol attributable diagnoses in the fetus or newborn. In the first paper, after adjustment for important confounders, the authors report a link between maternal heavy alcohol use and increased risk of several adverse outcomes including: small for gestational age (OR 2·20 [95% CI 1·97–2·45]), preterm birth (OR 1·32 [1·19–1·46]), haemorrhage in late pregnancy (OR 1·25 [1·05–1·49]), and preterm prelabour rupture of membranes (OR 1·18 [1·00–1·39]).<sup>8</sup>

In the second paper using nationwide Danish data, Broccia and colleagues quantify increased risk of many previously identified associations—extending beyond fetal alcohol spectrum disorders—including with cerebral palsy and heart defects. They also report identification of previously unreported links with childhood infections, injury, child maltreatment, and harmful use of alcohol by the child.<sup>9</sup> They acknowledge that some of the latter diagnoses might not be directly caused by in utero exposure to alcohol, but rather might indicate post-natal exposure to continued parental harmful use of alcohol or other social vulnerability more prevalent in families with a history of harmful alcohol use.

An important limitation of both studies is the potential for misclassification bias. Accurate measurement of alcohol use is challenging and limited by recall and social desirability biases.<sup>10</sup> Studies comparing per capita alcohol consumption, estimated from survey self-reports, with those from alcohol sales data indicate that self-reported use underestimates consumption.<sup>11-13</sup>

Although this study uses hospital diagnoses, some of these are identified following maternal self-reporting of excessive alcohol consumption at the first antenatal appointment. Babies in the reference group might therefore also be exposed to maternal heavy alcohol use that has not come to the attention of services. Furthermore, given the high prevalence of alcohol use in pregnancy, many babies in the reference group will also have been exposed to some level of maternal alcohol use in pregnancy. Studies have shown a dose-response relationship between prenatal alcohol use and adverse outcomes.<sup>314</sup> Inclusion of babies exposed to maternal alcohol use compared with no alcohol exposure.

This methodology also raises the possibility that a percentage of babies in the group of interest were not exposed to heavy alcohol use during pregnancy. Women whose treatments in the year before pregnancy were successful would not have still been consuming alcohol heavily during pregnancy. Including babies born to these mothers is likely to underestimate an association between in utero exposure and adverse health outcomes. In acknowledgement of this limitation, the authors undertook a sensitivity analysis restricted to the subset of babies exposed to maternal heavy alcohol consumption during pregnancy only, which produced comparable results.



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Maternal BMI and tobacco consumption are potential confounding factors not accounted for in the second paper.<sup>9</sup> Although the lower average BMI of mothers of exposed babies is likely to underestimate the association of alcohol with several of the outcomes considered, unadjusted smoking rates are more likely to overestimate some associations—for example, increased risk of respiratory infections in childhood.

Survival bias is also an acknowledged limitation. The authors did not quantify pregnancy losses and previous research has shown an association between alcohol consumption and miscarriage.<sup>15</sup> Some pregnancies ending in miscarriage might do so due to undiagnosed fetal health problems. Similarly exposed infants had twice the infant mortality rate as those in the reference group and therefore some might not have survived long enough for emergent adverse outcomes to be diagnosed. Both possibilities risk underestimation of the strength of association between alcohol exposure and fetal or child health outcomes.

These large-scale Danish studies nonetheless add to the extensive international evidence base on the wide range of serious health risks to mothers and children from alcohol consumption during pregnancy. They contribute to knowledge on the diverse range of potential impacts and reinforce that fetal alcohol spectrum disorders are unlikely to exist in isolation.

The authors note the importance of preconception and prenatal support, especially for the most socially vulnerable populations. They call for a major shift in priorities toward prevention and preconception care. Additionally, given the high prevalence rates of alcohol use in pregnancy and the potential risk at any level of alcohol consumption,<sup>3,14</sup> policies acting at population level, such as regulation to reduce affordability and availability of alcohol will also be required to prevent alcohol-related harm at scale.<sup>16</sup> The authors have contributed a deeper analysis of the need for individual support coupled with system and structural changes. Both are required to reduce this earliest manifestation of alcohol harm. We declare no competing interests.

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