

Misclassification bias and unnecessary anxiety

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We read with concern the article by Gurol-Urganci and colleagues¹ purporting to show an increase in stillbirths and pre-eclampsia amongst women who had a positive test for SARS-CoV-2 at the time of a birth admission in England. This association may be explained entirely by the admission SARS-CoV-2 screening policy and hence associated misclassification bias, rather than by a causal impact of SARS-CoV-2. Evidence suggests that indirect impacts of the coronavirus pandemic on pregnant women, such as those caused by delayed presentation and mental health problems, are far greater than the direct impacts of COVID-19 itself.^{2,3} It is therefore imperative that extra care is taken to design and interpret epidemiological studies avoiding biases which lead to spurious findings that may cause unwarranted distress.

The authors have based their selection of the 'exposed cohort' on a positive SARS-CoV-2 test at the time of a birth admission. Defining the exposure in this way leads immediately to misclassification bias. Women who have an adverse pregnancy complication, such as antepartum stillbirth or pre-eclampsia, and who are therefore admitted, screened, and go on to have an induced birth, will have any coincidental asymptomatic infection identified. Women who do not have a pregnancy complication and are consequently not admitted will not be screened although they may have asymptomatic SARS-CoV-2 infection, and are therefore inappropriately excluded from the exposed cohort. By the time they are admitted to give birth, they are likely to have recovered from their infection and will be misclassified and placed in the unexposed cohort. The misclassification caused by the means of defining the exposed cohort will hence artificially elevate the apparent rate of death and complications in the exposed group, and artificially reduce them in the unexposed group. Given that around two thirds of COVID-19 infections in pregnant women are asymptomatic,⁴

65 this will be a substantial number of women and this design flaw may entirely explain the
66 findings.

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68 Studies such as this can only be undertaken on a population-basis, either in populations of
69 pregnant women where regular, asymptomatic screening programmes are in place in home
70 as well as hospital settings, or, in the absence of routine, regular population screening, by
71 comparison between population antepartum stillbirth and pre-eclampsia rates comparing
72 time periods when the virus is circulating and when it is not. Rigorous study designs must be
73 employed to avoid causing additional unnecessary anxieties to pregnant women and their
74 families.

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