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Reply to Dr Kawada late-gestation selective serotonin reuptake inhibitor exposure and perinatal mortality

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Title Page:

Reply: Late Gestation SSRI Exposure and Perinatal Mortality

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Reply: Late Gestation SSRI Exposure and Perinatal Mortality

To the Editor:

We appreciate the interest in our study investigating neonatal outcomes following late gestation exposure to selective serotonin reuptake inhibitors (SSRIs)[1] and the call for additional analyses to examine clinical manifestations of the infants, in particular, fatal outcomes. Given the rarity of fatal outcomes, such as stillbirth (3.69 per 1,000) and neonatal death (2.20 per 1,000) as reported by Stephansson *et al*.[2], our associated sample size was not sufficient to enable adequate statistical power to justify their investigation. We do, however, appreciate the significance of including data on infant mortality to more completely describe the effects of prenatal SSRI exposure on extreme clinical manifestations and the infant life-prognosis. In accordance with this we have included data on stillbirths and neonatal death below.

Our original analysis included the investigation of neonatal outcomes amongst live-born singletons. After including data on infants previously excluded from the study (i.e. fetal deaths), there was only 1 (0.61%; 6.1 per 1,000 births) stillbirth in the group of women who received a dispensing for a SSRI, 14 (0.89%; 8.9 per 1,000 births) stillbirths in the group of women who had a documented psychiatric illness but did not receive a dispensing for a SSRI and 198 (0.45%; 4.5 per 1,000 births) stillbirths in the group of women who did not have a psychiatric illness and did not receive a dispensing for a SSRI. With recognised limitations of sample size set aside, these differences were not statistically significant.

From the available data we can confirm that there were 2 (0.90%; 9.0 per 1,000 births) neonatal deaths in the group of women who received a dispensing for a SSRI, 5 (0.3%; 3.2 per 1,000 births) neonatal deaths in the group of women who had a documented psychiatric illness but did not received a dispensing for a SSRI and 96 (0.30%; 3.0 per 1,000 births) neonatal deaths in the group of women who did not have a psychiatric illness and did not receive a dispensing for a SSRI. Again, with recognised limitations of sample size set aside, these differences were not statistically significant. Furthermore, no data were available to us in relation to the cause of death.

Given the relatively small number of outcomes, we feel that these results should be interpreted with caution, making it difficult to draw accurate comparisons to previous studies, such as that published by Stephansson *et al*.[2] An important note is that our overall rates of fatal outcomes in our cohort are higher than that identified by Stephansson *et al*.[2] This could be a manifestation of our cohort being derived from a single specialist tertiary level teaching hospital that is likely to attract high-risk pregnancies[1], as opposed to the population based approach undertaken by Stephansson et al.[2] We also acknowledge the limitation of not having data available to assess severity of underlying maternal illness. Further studies with adequate sample size are required to clarify these findings and we look forward to this evolving literature.

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