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Cabaillet and colleagues' misrepresentation of the harms and benefits from selective serotonin–serotonin reuptake inhibitors (SSRI) in their pharmaco-epidemiological study of antidepressants use during pregnancy in France deserves comment.¹

First, Cabaillet and colleagues' introductory statement "(SSRI) ...appear to be safe in pregnant women"¹ ignores the robust evidence that has been accumulating since the 2005 warning letter from the FDA about paroxetine's risk for congenital malformations. SSRIs cause preterm birth, neonatal respiratory distress, neonatal persistent pulmonary hypertension newborn and severe cardiac malformations.^{2,3} The odds ratio for maternal use of SSRIs during the first trimester of pregnancy and the presence of congenital heart defects is 1.57 (95%CI 1.25–1.97) for paroxetine, 1.36 (95% CI 1.08–1.72) for fluoxetine, and 1.29 (95% CI 1.14–1.45) for sertraline.⁴ Further, observational studies reported developmental disorders that are in line with results from experimental studies and MRI studies of human infants: SSRIs exposure has an association with changes in brain structure, white matter microstructure, brain connectivity, and cerebral metabolism, particularly in brain regions critical to emotional processing.⁵

This denial of SSRIs harms is scientifically wrong and ethically unacceptable. It precludes being able to provide adequate information for shared decision making. The mothers will live with their child's life-long sequelae forever, not academics or opinion leaders.

Second, Cabaillet et al misrepresent the references that they cite in their statement that "(SSRIs) are recommended by the National Agency for Health and Medicines (ANSM) and the 2018 International Cochrane Review International Publications."¹

1. The link for the recommendation (ref. 19 in Cabaillet et al) does not work and the summary of product characteristics for fluoxetine warns "Overall, the data suggest that the risk of cardiovascular malformation in children after maternal exposure to fluoxetine is approximately 2/100 ... Fluoxetine should not be used during pregnancy unless the clinical condition of the patient requires treatment with fluoxetine and justifies the potential risk to the fetus."⁶
2. potential risk to the fetus."⁶

The Cochrane Review (ref. 20 in Cabaillet et al) is about postnatal depression, not depression in pregnancy. It concluded: "Due to the limitations of the current evidence base ..., it is not possible to draw any clear conclusions about the effectiveness of antidepressants for the prevention of postnatal depression."

The United States Birth Defects Prevention Study confirmed the association between SSRIs and birth defects and that the observational evidence for the benefits of psychotropics during pregnancy is weak.⁷ Downplaying the harms of antidepressants and unduly recommending their use does not serve the interests of patients.

COMPETING INTEREST

Alain Braillon, JL, and SB are among industry independent experts on Jeanne Lenzer's list (<https://jeannelenzer.com/list-independent-experts>). SB chairs Healthwatch, a charity promoting science and integrity in health care (<https://www.healthwatch-uk.org/>) and her interests are declared at <https://www.whopaysthisdctor.org/doctor/58/active>. JL received payments for writing a brief in an action for side effects of a drug for Michael F. Smith, Lawyer and a second brief on the role of promotion in generating prescriptions for Goodmans LLP in 2017–2020. He is a member of the Foundation Board of Health Action International. He receives royalties from the University of Toronto Press and James Lorimer & Co. Ltd. for books he has written.

CONTRIBUTORS

Alain Braillon drafted the initial manuscript. Susan Bewley, Aubrey Blumsohn, Florian Naudet, Jean-Louis Montastruc, and Joel R Lexchin reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

KEYWORDS

developmental disorders, drug safety, serotonin reuptake inhibitors, teratogenicity

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