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FIRST TRIMESTER EXPOSURE TO PAROXETINE AND PREVALENCE OF CARDIAC DEFECTS: META-ANALYSIS OF THE LITERATURE: UNFORTUNATELY INCOMPLETE

To the editor:

It was with great interest that we read the recent publication ''Paroxetine Exposure during Pregnancy and Cardiac Malformations'' (Wurst et al., 2010) and the accompanying two opposing commentaries (Berard, 2010; Scialli, 2010). We were thinking that this ''updated meta-analysis'' would settle the ongoing debate for the last 5 years regarding paroxetine and cardiac malformations. This has become especially important, following the precedent-setting jury trial held in September 2009, when the parents of a boy born with a cardiovascular defect following exposure in utero were awarded $2.5 million to be paid by GSK, although the decision was opinion-based rather than evidence-based (Tanne, 2009).

Unfortunately, Wurst's study did not settle anything, because not all of the relevant publications were included in the analysis. The authors and Dr. Scialli in his accompanying commentary both noted that if our study (Einarson et al., 2008) had been included, it would have decreased the estimate of the prevalence odds ratio in the meta-analysis. In addition, other negative studies that have been published in the last year and a half would have lowered the odds ratio even further (Pedersen et al., 2009; Wichman et al., 2009). On the other hand, two recent studies published earlier this year also reported a small increased risk for cardiovascular defects associated with paroxetine exposure during pregnancy (Bakker et al., 2010; Reis et al., 2010). Would the addition of these four new studies have changed the final result?

Of particular interest to us is why our paper was not included in the meta-analysis. The rationale the authors gave for exclusion is unconvincing, as it has the largest sample size of any of the cohort studies (N = 1174), our Methods section was very detailed, and there was nothing further that we could have added that would have changed the results. The authors' argument that TIS centers differ in collection of data is incorrect, as data are collected for these types of studies using a standardized questionnaire in each TIS around the world. We stated in both the Methods and Discussion that women in the comparison group had similar maternal characteristics, such as SES, and were matched for alcohol and smoking. Critically, the authors commented that we had published data from five TIS centers with no paroxetine exposures, when it is clearly evident in our table that this was not so. Most importantly, we have published numerous studies in the peer review literature, using this TIS collaboration, and the validity of this method has never been questioned.

Unfortunately, this study combined with the opposing commentaries will only increase the worry and anxiety surrounding the use of antidepressants in pregnancy. If a physician is trying to practice evidence-based medicine and finds this publication while conducting a literature search, what will he or she say to a woman who has just found out she is pregnant at 6 weeks gestation and has been taking paroxetine for the last year and wants to know if she has harmed her baby?

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