Appendix 3 (as supplied by authors): A sensitivity analysis assessing the use of over the counter drugs in the study's population.

A theoretical limitation of the study may be the availability of ibuprofen as an over-the-counter drug. Dispensation at pharmacies that were not recorded in our databases could misclassify exposed women as unexposed, thus creating a bias toward the null hypothesis. Ibuprofen is available for purchase at the health services' clinics, at pharmacies affiliated with Clalit Health Services and at private pharmacies. Both clinic and affiliated pharmacies prescription and over the counter dispensations are recorded in our databases. In addition, there are only a few private, non-affiliated pharmacies in the southern district in which drug prices are higher, and therefore, the extent of misclassification is negligible

To assess the extent of potential misclassification, we interviewed 418 women who gave birth at Soroka Medical Center regarding their use and purchases throughout their current pregnancies of over-the-counter drugs, including acetaminophen, ibuprofen and dypiron. Women from all four maternity wards at Soroka Medical Center (the medical center in which the cohort of pregnancies was collected from) who agreed to participate were interviewed in their native language (Hebrew / Arabic) at random days of the week during a period of a month. Only 27 out of 445 women (6%) declined to be interviewed.

Of the 418 women interviewed, 106 (25.3%) used acetaminophen, 12 (2.8%) used dypiron and 6 (1.4%) used ibuprofen during pregnancy. Only four women reported purchasing drugs at pharmacies outside the clinic, and therefore, the estimated proportion of unrecorded dispensations within the unexposed group is 1.3% (4/298) (95% CI 0.21% to 2.39%).

Appendix to: Daniel S, Koren G, Lunenfeld E. Fetal exposure to nonsteroidal anti-inflammatory drugs and spontaneous abortions. *CMAJ* 2014. DOI:10.1503/cmaj.130605.

We conducted a sensitivity analysis by randomly assigning exposure to unexposed pregnancies, setting the mean gestational day of exposure to ibuprofen as the first day of exposure. Only when the proportion of the theoretically misclassified pregnancies was the higher limit of the confidence interval (2.4%) and the proportion of spontaneous abortions in the misclassified group was an extreme of 14% (40% higher than the proportion in the unexposed group) did the results become significant (proportion of spontaneous abortions of 9.5% and 10.0% in the exposed vs. the unexposed group, adjusted HR=1.12 95% CI 1.01 to 1.28).

Appendix to: Daniel S, Koren G, Lunenfeld E. Fetal exposure to nonsteroidal anti-inflammatory drugs and spontaneous abortions. *CMAJ* 2014. DOI:10.1503/cmaj.130605.