LETTERS

Response to: “Maternal infection can cause spontaneous abortion”

We thank Dr. Zipursky and colleagues¹ for their letter about our article on the risk of spontaneous abortion associated with the use of antibiotics during pregnancy.² We agree that whether the association observed in our study supports causality remains a critical question. It is likely to be determined by repetition of the findings in other studies on the same research questions.³

We disagree that our study findings are suggestive of confounding by indication. We recognized that infection was a potential risk factor for spontaneous abortions, and we proposed several strategies to control for this bias: multivariate analysis adjusting for the type of infections, as well as other risk factors for spontaneous abortions; limiting our study sample population to those who had infections that were treated during pregnancy and comparing the different treatment options (using first-line antibiotics as the reference category); and further limiting our study sample population to pregnant women with urinary tract and respiratory infections (comparing antibiotic options for the treatment of these two specific infections one at a time).

β-Lactamines are among the first-line treatments for noncomplicated urinary

tract infection and for the treatment of community-acquired pneumonia in the general population along with quinolones.^{4,5} Therefore, women receiving penicillins and cephalosporins are unlikely to be different from those receiving other antibiotics in these subgroup analyses. Thus, unlike Zipursky and colleagues stated, we have taken the type of infection into account in several ways and the results remain consistent, which was reassuring. Nevertheless, given all of that, we have acknowledged that residual confounding by severity of infection could not be completely ruled out.

Finally, Zipursky and colleagues used the absence of statistically significant association as equivalent to being safe, which is a major interpretation error. Contrary to what Zipursky and colleagues claimed, antibiotics given for respiratory tract infections were increasing the risk of spontaneous abortion, although this did not reach statistical significance (there was a lack of power from restricting the sample size). Indeed, the American Statistical Association 2016 statement warns against such interpretation of confidence intervals and *p* values.⁶

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Competing interests: Anick Bérard is a consultant for plaintiffs in litigations involving antidepressants and birth defects. No other competing interests were declared.