

## Prior uterine evacuation and risk for preterm birth



**TO THE EDITORS:** We read with interest the meta-analysis by Saccone et al<sup>1</sup> regarding the risk of preterm birth in women with a history of uterine evacuation. While the authors used rigorous methodology to conduct their meta-analysis, the outcomes are only as good as the original data from which they are derived. Since most of the original studies did not include a number of known confounders for preterm birth, including prior preterm birth, multiple gestations, and short interpregnancy interval to name a few, it is important to highlight the potential for bias and false assumptions based on the meta-analysis.

The vast majority of the reported odds ratios (OR) in this article were <2, most with a confidence interval (CI) approaching 1.0. Because of the large sample sizes, small differences in the outcomes can provide significant *P* values and narrow CI, which may yield *statistically* significant results but do not reflect meaningful clinical differences.<sup>2</sup> Additionally, we were surprised by the significantly higher OR provided by the Zhou et al<sup>3</sup> article in Figures 4, A; 5, A; 6, A; 10; and 12 (OR, 19.51; CI, 17.61–21.61) and were unable to verify those results in the original article.

The authors suggest that perhaps women should be encouraged to use medical methods for uterine evacuation or to consider surgical methods with cervical preparation. We believe it is premature to make these recommendations because: (1) the overall association is weak; and (2) none of the studies included controlled for the variety of surgical techniques that may be used to evacuate a uterus, such as cervical preparation. Until we have more detailed information about the impact of various procedures and cervical preparation by gestational age, it is difficult to fully inform patients on the potential risk for preterm birth as a result of uterine evacuation.

We would encourage the authors to reconsider their recommendations in light of the weak association between surgical uterine evacuation and subsequent preterm birth given that this is based on observational studies and the inherent limitations of this approach. Given the already hostile environment and stigma surrounding abortion care, we need to ensure that we avoid placing premature blame on surgical evacuation as a risk factor for preterm birth. ■

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## REFERENCES

1. Saccone G, Perriera L, Berghella V. Prior uterine evacuation of pregnancy as independent risk factor for preterm birth: a systematic review and metaanalysis. *Am J Obstet Gynecol* 2016;214:572-91.
2. Grimes DA, Schulz KF. False alarms and pseudo-epidemics: the limitations of observational epidemiology. *Obstet Gynecol* 2012;120:920-7.
3. Zhou W, Sorensen HT, Olsen J. Induced abortion and subsequent pregnancy duration. *Obstet Gynecol* 1999;94:948-53.

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## REPLY



We thank Macafee et al for their interest in our study.<sup>1</sup> They emphasize important issues, with which we in general agree. In our manuscript we highlighted the limitations of the meta-analysis, including that about half of the original studies did not adjust for confounders, and because of the stigma associated with abortion, previous procedures may have been underreported in the case and control groups. Lack of adjustment for confounders is indeed an important limitation. Approximately 18 of the 36 included studies (references 24–27, 29–35, 37–39, 44–47) did adjust for some confounders, and most found an association with surgical termination and preterm birth, even after they adjusted for confounders. We also call for future research and for well-designed randomized trials. This call for more research in the effect of uterine evacuation on future pregnancies is probably our strongest recommendation. We acknowledge that medical and surgical abortion are incredibly safe procedures and seek to know the true impact that abortion may have on future pregnancies in prospective trials. We think that patient preference for the type of abortion experience should help guide the decision-making and that women should be given the choice between a surgical and a medical approach.

Our meta-analysis, based on the available literature, included more than 1,000,000 women; it suggests that previous surgical uterine evacuation is an independent risk factor for spontaneous preterm delivery and that women with history of surgical abortion have about twice the odds of preterm birth in the subsequent pregnancy compared with women without such a history. We are hopeful that our study will inspire prospective research to determine which method of termination results in the lowest risk of preterm birth in future pregnancies.

We agree that the odds ratios (ORs) provided by Zhou et al are much greater (OR 19.51, 95% confidence interval, 17.61–21.61) than the other studies.<sup>1,2</sup> The percentage of women are reported in Table 3 of the original study

(774/1775 vs 2377/62,350); however, the weight of the study on the pooled meta-analysis data is less than 4%. Moreover, the OR is much lower after confounders were adjusted (OR 1.89; 95% CI, 1.70–2.11; Figure 7 of the meta-analysis<sup>1,2</sup>).

Finally, we would like to emphasize that increasing the use of highly effective contraceptive methods in women who desire them should be an important solution to the persistent problem of health disparities of unplanned and teen pregnancies in the United States and would lead to improvements in women's and children's health, including a decrease in the incidence of preterm birth. Individual-level access barriers such as providers' misconceptions and gaps in technical training as well as patients' lack of awareness can be addressed directly by professional medical organizations, health care training programs, and others.<sup>3</sup> ■

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#### REFERENCES

1. Saccone G, Perriera L, Berghella V. Prior uterine evacuation of pregnancy as independent risk factor for preterm birth: a systematic review and metaanalysis. *Am J Obstet Gynecol* 2016;214:572-91.
2. Zhou W, Sorensen HT, Olsen J. Induced abortion and subsequent pregnancy duration. *Obstet Gynecol* 1999;94:948-53.
3. Parks C, Peipert JF. Eliminating health disparities in unintended pregnancy with long-acting reversible contraception (LARC). *Am J Obstet Gynecol* 2016;214:681-8.

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## The risk of infant and fetal death by each additional week of expectant management in intrahepatic cholestasis of pregnancy by gestational age: various objections



**TO THE EDITORS:** The recent publication by Puljic et al<sup>1</sup> on the management of intrahepatic cholestasis of pregnancy (ICP), while stimulating, has various major issues that invalidate the results and conclusions.

The risk measure that the authors introduce has an inbuilt bias: mortality during *1 week* for the intervention group is compared to mortality during *2 weeks* for the expectant management group. The latter will naturally tend to be higher. While it is true that infants can no longer suffer fetal death, (too) early delivery could still result in higher infant mortality. Yet, although mortality during the first full year postnatal was available in the data, it was not involved in the calculations. As a result of this bias, inducing labor in women with uncomplicated pregnancies would be recommended from week  $\geq 38$  according to the authors' calculations (Table 3, notice that the bottom row seems incorrect, because risk of expectant management does not exceed stillbirth risk). This would be an interesting proposal, but cannot be made based on these calculations.

The results are also driven by seemingly odd absolute numbers. At 36 weeks, precisely when the authors recommend intervention, mortality of infants born to ICP mothers is an order of magnitude lower than for infants born to healthy mothers (Table 2). If true this would be a very interesting insight, but perhaps it is better taken as an indication of potential data limitations. Regardless of correction for potential confounders, such numbers need some explanation.

The evidence on the correlation between bile acid levels and adverse fetal outcomes such as stillbirth<sup>2-4</sup> is too substantive to be dismissed as "hypothesis" (pg. 667.e1). The authors further insist on significant delay when obtaining bile acid levels, necessitating decision making without laboratory results. Yet the laboratory at my institution assures me that bile acid can be measured within the hour using standard equipment. In any event, because level-dependence of risk directly affects the calculations and conclusions, this issue should have been addressed head-on rather than sidestepped with: "However, numerous retrospective studies and case