Two-dose vs single-dose methotrexate for treatment of ectopic pregnancy

TO THE EDITORS: Dr Alur-Gupta et al published a systematic review and metaanalysis concerning 2-dose vs single-dose methotrexate for treatment of ectopic pregnancy. However, their statistical analyses are confounded by several potential biases.

First, their systematic review should have been registered with an International Prospective Register of Systematic Reviews (PROSPERO, https://www.crd.york.ac.uk/) or other international databases of prospective registration to avoid duplication and reduce the opportunity for reporting bias by enabling comparison of the completed systematic review with what was planned in the protocol.

Second, the primary outcomes, treatment success, were 87.2% and 78.9% for 2-dose and 1-dose groups, respectively; however, their metaanalysis used of the odds ratio to estimate pooled treatment effects. It seems that they have not followed the Cochrane Handbook, which stated that odds ratios are more difficult to interpret than risk ratio and can overestimate and magnify risk when events are not rare.

Third, publication bias was assessed via funnel plots in their study. That is incorrect. The use of funnel plots to analyze publication bias went to the 1980s and 1990s. However, over time, researchers realized that there could be numerous causes for asymmetry of funnel plots. Asymmetry in a funnel plot does not tell whether there is publication bias. Therefore, the term publication bias has been replaced largely with the term small study effects in the analysis of funnel plots.

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