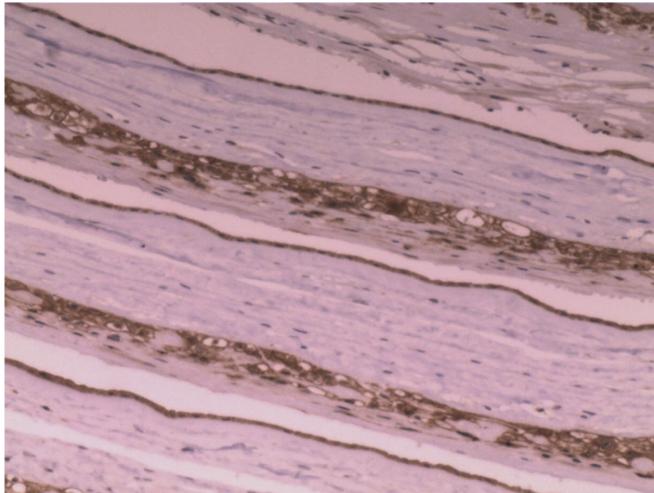


**FIGURE**  
Layers of purinergic P2X3 “stretch” receptors



Layers of purinergic P2X3 “stretch” receptors (thick *brown* layers) in the chorion rolled up on a plastic rod, fixed in formalin, and stained with anti-P2X3 (x200). The amnion contains an adjacent layer of aquaporins (AQP-1) that may contribute to the onset of labor through similar process of purinergic mechanosensory transduction.

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require further pharmacologic support to control any postpartum hemorrhage. ■

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## Postsurgical barrier strategies to avoid the recurrence of intrauterine adhesion formation after hysteroscopic adhesiolysis: a comment



**TO THE EDITORS:** In this network meta-analysis (NMA), Vitale et al<sup>1</sup> compared antiadhesive strategies for women undergoing hysteroscopic adhesiolysis followed by mechanical prevention of intrauterine adhesions. The authors used the surface under the cumulative ranking (SUCRA) method to rank the interventions. Based on the SUCRA scores, the study concluded a copper intrauterine device together with an intrauterine balloon (46.4%), hyaluronic acid gel (79.8%), hyaluronic acid gel plus intrauterine device (49.9%), and dried amnion graft (53.8%) ranked the highest for preventing adhesions recurrence, improving fecundity, postsurgical adhesion severity, and menstrual pattern improvement, respectively.<sup>1</sup> However, when considering the limitation of SUCRA, this conclusion might be inappropriate.

It could be very misleading to conclude the effectiveness or harmfulness of treatments by only relying on the SUCRA score but ignoring the certainty of the evidence, as the SUCRA approach only focuses on point estimates of effect.

This approach ignores the possibility that chance can explain the differences between SUCRA scores (precision of estimates), the magnitude of the absolute difference between rankings, and, most importantly, the certainty of the evidence.<sup>2</sup> For example, in 1 NMA of pain treatments for non—low back musculoskeletal injuries, Busse et al<sup>3</sup> reported both the SUCRA and certainty of the evidence. Fentanyl ranked the highest effect for pain relief (<2 hours after treatment) but proved to be low or very low certainty evidence. This means that it is very unsure that the high effect seen for fentanyl is true.

Unfortunately, the authors did not consider the certainty of the evidence for network estimates. Considering the wide confidence intervals for the network estimates in adhesions recurrence (the primary outcome), the certainty of evidence might be low. If the authors used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) contextualized framework to rank the treatments,<sup>4</sup>

which avoids the limitations of SUCRA, they might get different but more reliable rankings.

In conclusion, when ranking the effectiveness and/or harm of treatments in an NMA, we suggest that the authors should not only rely on the SUCRA scores of treatments but also consider the certainty of evidence to avoid making misleading conclusions. ■

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# Postsurgical antiadhesive barriers to reduce the risk of recurrence after hysteroscopic adhesiolysis: a reply



We would like to thank He et al<sup>1</sup> for their interest in our network meta-analysis evaluating the efficacy of postsurgical antiadhesive barriers to reduce the risk of recurrence after hysteroscopic adhesiolysis.<sup>2</sup>

The authors expressed their concern regarding the lack of the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) criteria to assess the certainty of the evidence of the evaluated outcomes, especially for the primary outcome (intrauterine adhesions recurrence). He et al<sup>1</sup> concluded that the lack of the GRADE criteria could deliver misleading conclusions.

It is indeed true, and we agree with He et al<sup>1</sup> that the use of the GRADE criteria would have been an added value to validate the reported evidence.<sup>1</sup> However, it should be acknowledged that our approach for study selection adopted extremely strict criteria, which resulted in including only high-quality, with low risk of bias, articles in the quantitative synthesis and network meta-analysis. In addition, to confirm the considerability of the evaluated evidence for both direct and indirect comparisons, the Separating Indirect from Direct Evidence—splitting method was used. This approach enhances the possibility that the considerability of results is related to the effects of the interventions rather than randomness.<sup>3</sup> At the same time, there was no inconsistency reported for both direct and indirect comparisons among the study outcomes, which also increases the validity of the main findings.

Considering all the aforementioned elements, although agreeing with He et al<sup>1</sup> regarding the importance of implementing GRADE criteria, we believe that the conclusions of our network meta-analysis must be considered appropriate. As we stated in our article and its conclusions, because of the lack of a superior approach among the analyzed barrier strategies, it is necessary to carry out further research to validate and confirm these findings. We hope with our article to encourage the research community to perform the needed additional studies to provide clinicians with valuable information on this fascinating topic. ■

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