Letter to the editor regarding "The efficacy and safety of infliximab and calcineurin inhibitors in steroid-refractory UC patients: A meta-analysis"

Dear Editor,

We have read with great interest the meta-analysis by Zhao et al.^[1] evaluating the efficacy and safety of infliximab and calcineurin inhibitors (cyclosporine and tacrolimus) in steroid-refractory ulcerative colitis. We applaud their effort as the exact effectiveness of infliximab and calcineurin inhibitors is largely unknown. The article is well-written, however, some methodological issues should be addressed.

First, the authors claimed that the databases, including Medline, Web of Science, and so on, were searched in this study. Nevertheless, the gray literature, like ongoing and unpublished studies were not identified, which led to an non-comprehensive search strategy. Furthermore, only free-text terms by the keywords: "Infliximab," "Calcineurin inhibitors," and the like were used by the authors in the search strategy, which could reduce the search quality. As we are all aware, the combination of Medical Subject Headings (MeSH) and free-text terms would be more acceptable. In addition, we believe that a detailed search strategy should ideally have been included within the article or supplementary materials.

Second, the outcomes of the colectomy rates in non-randomized studies and other secondary outcomes showed a high heterogeneity ($I^2 > 50\%$), therefore, the authors should run a sensitivity analysis to detect the influence of a single study on the overall effects. In general, the pooled effect of a meta-analysis should not be performed until the sources of the heterogeneity were found, which was not mentioned in this review. And a high heterogeneity strongly impacts the reliability of the pooled results.

Third, the meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement and the Cochrane Handbook for Systematic Reviews of Interventions, the registration for which was not found in this article.

The registration of protocol details will help the peers and public to get a better understanding of the research information, promote cooperation with international colleagues, and publish high-quality reports for the researchers. Moreover, to minimize the risk of selective outcome reporting bias, we thought it may be better that the meta-analysis should be registered at the Cochrane Collaboration or the International Prospective Register of Systematic Reviews (PROSPERO), which is like most other similar studies^[2] published in this journal.

Obviously, the methodology of meta-analysis has a great influence on the pooled results. We thank Zhao *et al.*^[1] for their meaningful work in summarizing the evidence of infliximab and calcineurin inhibitors in treating steroid-refractory ulcerative colitis; however, this work would be more instructive with an appropriate search strategy, a sensitivity analysis, and a protocol registration.

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Conflicts of interest

There are no conflicts of interest.

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Letter to Editor

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