Comment on “Evaluation of Potential Drug–Drug Interactions in Adults in the Intensive Care Unit: A Systematic Review and Meta-analysis”

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Dear Editor,

We read with interest the systematic review and meta-analysis by Fitzmaurice et al. published in the May 2019 issue of *Drug Safety* [1]. The clinical significance of drug–drug interactions is a significantly important yet understudied domain and the authors have made a notable contribution in this area. However, we also believe that there are two important limitations that should be further discussed.

Measuring and dealing with inconsistency and heterogeneity is one of the critical aspects for a well-conducted meta-analysis. Although the authors reported that their study had high heterogeneity, it is not clear how the authors handled this issue. The type of intensive care unit and the various drug–drug interactions were mentioned as sources of heterogeneity; however, the rationale behind this inference is not clear. We would expect to see further work carried out in this area, such as a sensitivity analysis or meta-regression, which would help us to better understand the possible source(s) of heterogeneity [2].

Another critical point that seems to be missing is the quality assessment of the included studies. It is a general

principle that the quality of a meta-analysis directly depends on the included studies. Several quality assessment scales for different types of studies, which can enable researchers to spot the possible biases in the included studies, are available for this purpose. For this particular study, the ‘Agency for Healthcare Research and Quality Methodology Checklist’ or the ‘Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies’ published by the National Heart, Lung and Blood Institute might have been applicable since the authors included cross-sectional studies [3, 4].

We appreciate the authors’ efforts on this study and hope that the points we mentioned above will provide a foundation for further discussion.

Compliance with Ethical Standards

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Conflicts of Interest Nusret Uysal, Elif Keskin-Arslan, Hilal Erol, Selin Acar and Yusuf Cem Kaplan have no conflicts of interest that are directly relevant to the content of this study.

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