

Lancet Response

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Klaus Munkholm and colleagues raise several interesting issues; however, we disagree that our results¹ have a very low level of certainty. Our protocol was published a priori² and we went to extensive and exhaustive lengths to identify many completed trials, providing the most comprehensive summary of evidence to date using robust methods. More than half of the trials in our analysis were done for regulatory purposes and were held to high standards of study conduct. A 2018 network meta-analysis for depression³ also found high risk of bias according to the scale recommended by the *Cochrane Handbook for Systematic Reviews of Interventions*;⁴ in fact, none of those studies achieved a low risk of bias across all categories. Moreover, publication of all trial outcomes is rare in complex regulatory trials. Premature withdrawal leading to incomplete outcome data is unavoidable in placebo-controlled trials, as insufficient efficacy will be unacceptable to some patients. Thus, the bias assessment approach advocated by Munkholm and colleagues could be considered overly nihilistic, especially for trials in mental health. They are also correct that we did not use the Grading of Recommendations Assessment, Development, and Evaluation framework,⁵ which would have been inappropriate because our goal was to produce a transparent and robust review of the relevant evidence to inform health policy, rather than to develop clinical guidelines.

We agree with Qi Zhou and colleagues that trials published in China could have limitations. Indeed, assessing the limitations of Chinese studies is an area where we have contributed substantively to the methodological literature.⁶ There are many reporting issues that challenge our review of trials published in Chinese languages; for example, there is no direct substitute for the word randomised. This is why we did a supportive analysis, removing the Chinese trials to assess the degree to which their inclusion modified the results. Since the results did not change appreciably for the drugs assessed in Chinese and non-Chinese studies, we did not pursue methodological differences further. However, the inclusion of the Chinese trials provides head-to-head comparisons between active drugs that would be unavailable otherwise, and hence provides stability to the network of trials we included in the analysis.

AS reports personal fees from Medibio, outside the submitted work.

NF and IN declare no competing interests.

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