Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Rethinking the efficacy of awake prone positioning in COVID-19-related acute hypoxaemic respiratory failure

Jie Li and colleagues[1] examined the efficacy of awake prone positioning on patients with COVID-19-related acute hypoxaemic respiratory failure. However, we have serious concerns about the assessment of the risk of bias, the data analysis, and the rating of certainty of evidence in the two cluster randomised controlled trials (RCTs) and eight individual RCTs that were included in the study.

First, the tool the authors used to assess the risk of bias in cluster RCTs is not optimal. In contrast to individual RCTs, in which individual participants are randomly assigned to a group, cluster RCTs are designed to evaluate interventions delivered at the group level.[2] This design increases the possibility of some types of bias, such as identification or recruitment bias and loss of clusters.[2] Therefore, the Cochrane collaboration recommends a specific tool, the risk-of-bias 2.0 for cluster-randomised trials tool for assessing the risk of bias in cluster RCTs.[3] Li and colleagues,[1] however, used the conventional tool intended for individual RCTs. We reappraised the cluster RCTs that were included using the recommended tool, and found that more sources of bias were classified as high compared with the findings of Li and colleagues,[1] especially sources related to the cluster design (appendix). Therefore, the overall risk of bias in these cluster RCTs should be graded as high.

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Second, Li and colleagues[1] did not take into account the design effect of clustering.[4] After adjusting for design effect, we found that the results on the need for escalating respiratory support (relative risk 1·03, 95% CI 0·78 to 1·36), admission to an intensive care unit (relative risk 0·80, 95% CI 0·52 to 1·22), and hospital length of stay (mean difference +0·55 days, 95% CI −0·52 to +1·62) differed from those calculated by Li and colleagues (appendix).

Finally, we found that Li and colleagues[1] did not appropriately consider the risk of bias when evaluating the certainty of the evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. Absent or unclear blinding has been shown to have a substantial effect on the results of RCTs, exaggerating the intervention effects by up to 13%.[5] According to the Cochrane criteria, the overall risk of bias in all the RCTs included in the study should be categorised as high because of the absence of blinding.[3] Therefore, the certainty of the evidence on all outcomes should be downgraded by one GRADE level from those reported by Li and colleagues[1] because of the serious risk of bias (appendix). The low certainty of evidence indicates that new research is likely to change the estimate. Therefore, caution is needed when interpreting the efficacy of awake prone positioning and when using awake prone positioning in clinical practice.

We declare no competing interests.

*Qinyuan Li, Qi Zhou, Kehu Yang, *Zhengxiu Luo, Yaolong Chen*
luozhengxiu816@hospital.cqmu.edu.cn

Department of Respiratory Medicine Children's Hospital of Chongqing Medical University, National Clinical Research Centre for Child Health and Disorders, Ministry of Education Key Laboratory of Child Development and Disorders, Chongqing Key Laboratory of Paediatrics, Chongqing 400014, China (QL, ZL); Evidence-Based Medicine Centre, School of Basic Medical Sciences, Lanzhou University, Lanzhou, China (QZ, KY, YC); Lanzhou University GRADE Centre, Lanzhou, China (QZ, KY, YC); Lanzhou University, Affiliate of the Cochrane China Network, Lanzhou, China (QZ, KY, YC)

See **Online** for appendix

1 Li J, Luo J, Pavlov I, et al. Awake prone positioning for non-intubated patients with COVID-19-related acute hypoxaemic respiratory failure: a systematic review and meta-analysis. *Lancet Respir Med* 2022; **10:** 573–583.
2 Dron L, Taljaard M, Cheung YB, et al. The role and challenges of cluster randomised trials for global health. *Lancet Glob Health* 2021; **9:** e701–10.
3 Higgins JPT, Thomas J, Chandler J, et al. Cochrane handbook for systematic reviews of interventions version 6·3, 2022. 2022. https://training.cochrane.org/handbook/current (accessed April 3, 2022).
4 Donner A, Piaggio G, Villar J. Statistical methods for the meta-analysis of cluster randomization trials. *Stat Methods Med Res* 2001; **10**: 325–38.
5 Savović J, Jones HE, Altman DG, et al. Influence of reported study design characteristics on intervention effect estimates from randomized, controlled trials. *Ann Intern Med* 2012; **157:** 429–38.