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.

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Letter to the Editor

Regdanvimab improves disease mortality and morbidity in patients with COVID-19: Too optimistic and too early to say?

Dear Editor,

We have read with great interest the recently published meta-analysis by Yang, M. et al.[1] in the *Journal of Infection* on the topic of regdanvimab use in COVID-19 patients. The authors included 7 studies in their meta-analysis and concluded that regdanvimab administration significantly reduced COVID-19 mortality and risk of disease progression according to a composite outcome. This publication is of particular interest and significance as it is currently the only meta-analysis published on the topic, however some of the authors' presented results and conclusions may potentially be misleading.

In the original meta-analysis (recreated on Fig. 1A) the authors included 4 studies in their mortality outcome analysis and concluded that regdanvimab use was associated with statistically significant lower mortality (OR = 0.14, 95% CI: 0.03 to 0.56, $P = 0.006$; I2 = 0%). In the meta-analysis, the study by Park, S. et al.[2] with a weight of 75.5% and an OR of 0.04 (95% CI: 0.00 to 0.64) contributed disproportionately more to the pooled result in comparison to other included studies. The Park, S. et al.[2] study was an observational retrospective study which explored outcomes of 377 regdanvimab treated patients and 520 standard of care controls in an overall primary cohort from which a propensity score matched cohort of 754 patients, 377 in each group, was created and analysed. In their meta-analysis, Yang, M. et al.[1] included the outcomes from the unmatched primary cohort, instead of the PS-matched cohort, which in our opinion was incorrect due to statistically significant differences between the two unmatched groups, as reported by Park, S. et al.[2], which favoured the treatment group. Patients in the control group: 1) were older (median age 65 [IQR, 57–75] vs. 61 [53–68] years, $P < 0.001$), 2) had a higher proportion of moderate COVID-19 pneumonia (54.1% vs. 45.9%, $P = 0.049$), 3) chronic lung disease (78.9% vs. 21.1%, $P = 0.007$) and 4) cardiovascular disease (73.9% vs. 26.1%, $P < 0.001$), which were all accounted for and no longer statistically significant in the PS-matched cohort. Thus, the decision to include the outcomes of the unmatched cohort seems inappropriate and presents a significant potential source of bias in the meta-analysis, especially when considering the significant weight of the Park, S. et al.[2] study. In order to eliminate the source of bias, we recreated the meta-analysis using the outcomes from the PS-matched cohort, Fig. 1B (OR = 0.49, 95% CI: 0.10 to 2.28, P = 0.38; I2 = 0%) and we also excluded the Park, S. et al.[2] study altogether due to the zero event rate, Fig. 1**C** (OR = 0.44, 95% CI: 0.08 to 2.53, P = 0.38; I2 = 0%) and we found no statistically significant impact of regdanvimab on COVID-19 mortality in either analysis. Moreover, we also recre-

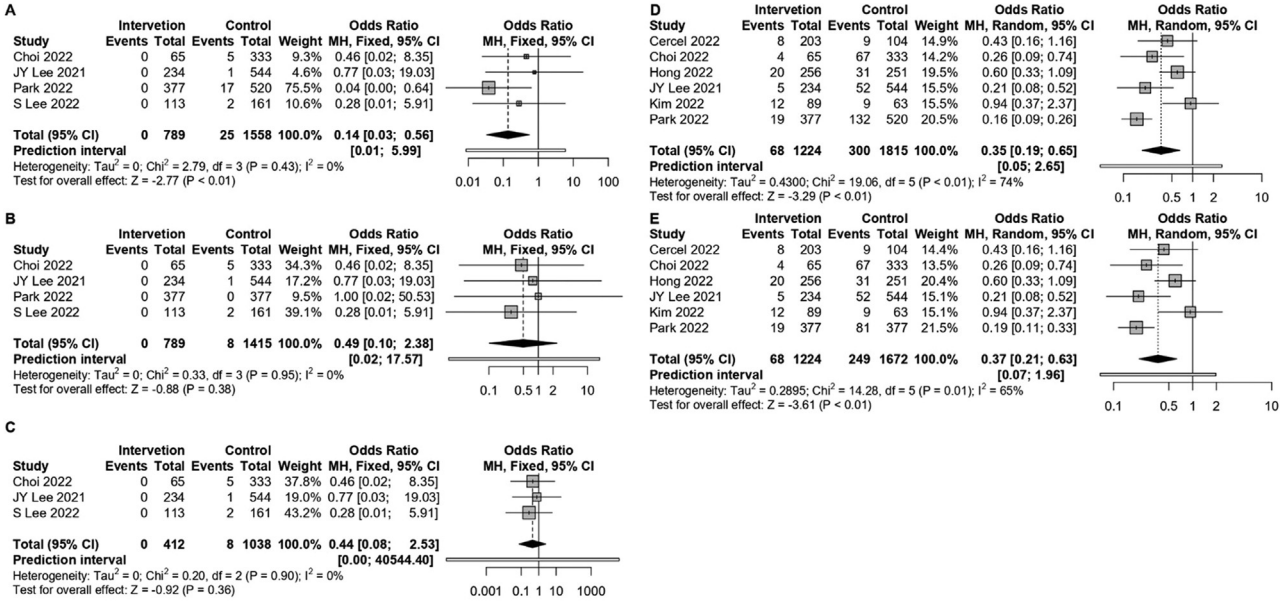

Fig. 1. Forest plots recreating the original meta-analysis results by Yang, M. et al.[1] regarding the mortality (Fig. 1A) and composite (Fig. 1D) outcomes. Reanalysis of the mortality (Fig. 1B) and composite (Fig. 1**E**) outcome meta-analysis using outcomes from the propensity score matched cohort from the Park, S. et al..[2] Mortality outcome meta-analysis (Fig. 1C) with the Park, S. et al.[2] study excluded due to a zero event rate.

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ated the composite outcome analysis, Fig. 1D and conducted an additional analysis with the PS-matched Park, S. et al.[2] cohort and found no significant difference between the results.

In conclusion, while it seems that regdanvimab may have a potential beneficial effect on COVID-19 patients based on the composite outcome, in our view, the conclusion made by Yang, M. et al.[1] that regdenvimab reduced patient mortality seems exaggerated. Finally, in all meta-analyses shown on Fig. 1, a considerable uncertainty of the results is perhaps best illustrated by the wide prediction intervals, which were present even in the original mortality outcome analysis by Yang, M. et al.[1], Fig. 1A. As the number of published studies remains small and with most current studies being retrospective in design, additional high quality, prospective, randomised trials exploring the potential beneficial effects of regdanvimab in COVID-19 patients are urgently needed.

Conflict of interest

No conflicts of interest to declare.

Authors' contributions

All authors participated equally in all parts of the manuscript.

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Data disclosure statement

All analysed data is presented in the manuscript.

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