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item on anxiety or depression was not validated in Chinese populations. However, to our knowledge, the reliability of the Chinese EQ-5D has been validated in China, and it has shown acceptable construct validity and fair-to-moderate levels of test-retest reliability.³ Additionally, according to a large multinational study involving China, the EQ-5D-5L provided precise measurement at individual and group levels compared with the EQ-5D three-level, both in terms of descriptive system data and usefulness.⁴ Hence, we believe that descriptive system data from the EQ-5D-5L questionnaire could well reflect the health status of our cohort.

We acknowledged that the low proportion of patients admitted to the intensive care unit in our cohort limits the generalisability of the study findings. Similarly, the findings cannot be generalised to those who were excluded from the study.

We appreciate Yang and colleagues' interest in the association between cytokines and fatigue syndrome. As shown in the appendix of the Article,¹ no statistically significant association between cytokine change (at discharge until 6 months) and fatigue or muscle weakness was apparent. However, because of the small number of patients with cytokine tests, these findings should be interpreted as exploratory and need to be validated in a larger sample population.

Zhao and colleagues are concerned that all the somatic symptoms at follow-up could be attributed to depression or anxiety or both, rather than the so-called sequelae symptoms caused by COVID-19. We agree these sequelae symptoms might not be directly caused by COVID-19, a factor that is difficult to differentiate. The definition of sequelae symptoms in our study is consistent with the current concept of long COVID,⁵ whether directly caused by COVID-19 or partly attributed to depression or anxiety, so it is appropriate to call it COVID-19-related sequelae symptoms.

We appreciate Zhao and colleagues' suggestion to explore the post-traumatic stress disorder symptoms and stigma of patients recovered from COVID-19 in the future. In addition, Yang and colleagues pointed out that it is unclear whether patients with long COVID have an increased susceptibility to reinfection and whether COVID-19 vaccines could play a role in preventing long COVID. Answering these research questions will require the full breadth of scientific and high-quality clinical studies. The scientific and medical communities might wish to collaborate to explore the mechanism and pathogenesis of long COVID.

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CoronaVac efficacy data from Turkey

Mine Tanriover and colleagues¹ report that the efficacy of CoronaVac against laboratory-confirmed symptomatic COVID-19 in a trial in Turkey is 83.5% (95% CI 65.4–92.1). By contrast, the efficacy of CoronaVac against symptomatic COVID-19 has been estimated at 50.7% (36.0–62.0) in a Brazilian trial and at 65.3% (20.0–85.1) in an Indonesian trial.^{2,3} Noting that post-vaccination neutralising antibody titres are quite strongly associated with vaccine efficacy against symptomatic infection,^{4,5} the efficacy estimated from the Turkish dataset is much higher than we would expect given the modest post-vaccination neutralising antibody titres after the second dose of CoronaVac.

There was a high proportion of hospitalised COVID-19 cases in the placebo group, accounting for six (19%) of the 32 cases included in the interim analysis,¹ compared with 6% and 0% of cases in the Brazilian and Indonesian trials, respectively.^{2,3} It is possible that some milder cases were missed in this trial, and the efficacy could therefore be skewed towards a higher value given that CoronaVac, similar to other COVID-19 vaccines, has a higher efficacy against severe disease than mild disease. Moreover, the short median follow-up time of 15 days (IQR 8–20) at risk could reduce the generalisability of the findings.

Given the global shortage of vaccines, the approval and distribution of as many effective vaccines as possible will maximise the number of lives saved during the COVID-19 pandemic. However, reports of a high efficacy in clinical trials that are not borne out by real-world vaccine effectiveness data would damage confidence in vaccines.

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Authors' reply

We thank Martina McMenamin and Benjamin Cowling for raising important issues on vaccine trials in the context of our Article.¹ The work they refer to by Palacios and colleagues² has not been published in a peer reviewed journal; thus we cannot comment on the accuracy or the comparability of its methods. The Indonesian trial data have been published,³ and although the main method of this study was similar to ours, the case definition of COVID-19 and the methods used for active surveillance were different. Only 1620 volunteers were included, but over a longer period of follow-up (approximately 2.5 months) precluding a direct comparison of the primary outcome.³ Nevertheless, the efficacy of CoronaVac against severe disease in this study was 100% because there were no critical cases or deaths attributable to COVID-19, which is undoubtedly similar to our results.

Regarding post-vaccination neutralising antibody titres in the immunogenicity subset of our trial, the seroconversion rate was 89.7% in the vaccine group, of whom 92% had neutralising antibodies. This result might translate into 82.5% neutralising antibody positivity in these volunteers. The efficacy against symptomatic disease reported as 83.5% is compatible with this immunogenicity result. We performed active surveillance to detect COVID-19 in patients; however, because the primary outcome was symptomatic COVID-19, it is indeed possible that we missed asymptomatic patients. In fact, most of the COVID-19 vaccine trials target a similar outcome, focusing on efficacy to prevent symptomatic and severe disease rather than preventing infection. We were aware of the short follow-up period in our interim analysis and hence discussed this as a major limitation in the Article,¹ stating that the study would not allow for commenting on the long-term protection.

Real-world effectiveness data from pragmatic study designs will add value to phase 3 trials to see the performance of the vaccines in non-selected populations, as complementary rather than competing studies. For instance, Jara and colleagues⁴ reported the analysis of real-life data from Chile, including approximately 10.2 million people vaccinated with CoronaVac. The adjusted vaccine effectiveness among the fully immunised people was 65.9% (95% CI 65.2–66.6) for the prevention of COVID-19 and 87.5% (86.7–88.2) for the prevention of hospital admission.

During a pandemic where only 2.3% of people in low-income countries had received at least one dose of a COVID-19 vaccine as of October, 2021, every single effort to make safe COVID-19 vaccines available is valuable. We believe that our data are an important contribution to the scientific literature in a world where

we can no longer establish placebo-controlled randomised trials for COVID-19 vaccines for ethical reasons. The way forward to build confidence in vaccines is by reporting real-world data transparently.

We declare no competing interests.

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Sun J-M, Shen L, Shah MA, et al. Pembrolizumab plus chemotherapy versus chemotherapy alone for first-line treatment of advanced oesophageal cancer (KEYNOTE-590): a randomised, placebo-controlled, phase 3 study. *Lancet* 2021; **398**: 759–71—The appendix of this Article has been corrected as of Nov 18, 2021.

Jardine J, Walker K, Gurol-Urganci I, et al. Adverse pregnancy outcomes attributable to socioeconomic and ethnic inequalities in England: a national cohort study. *Lancet* 2021; **398**: 1905–12—In figure 3 of this Article, the lower bounds of two 95% CIs were incorrect. These corrections have been made to the online version as of Nov 8, 2021, and the printed version is correct.

For more on the percentage of people vaccinated against COVID-19 by country see <https://ourworldindata.org/covid-vaccinations>



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