



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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Martina E McMenamin,
*Benjamin J Cowling
bcowling@hku.hk

WHO Collaborating Centre for Infectious Disease Epidemiology and Control, School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong Special Administrative Region, China

- 1 Tanriover MD, Doğanay HL, Akova MD, et al. Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in Turkey. *Lancet* 2021; **398**: 213–22.
- 2 Palacios R, Batista AP, Albuquerque CSN, et al. Efficacy and safety of a COVID-19 inactivated vaccine in healthcare professionals in Brazil: the PROFISCOV Study. *SSRN* 2021; published online April 11. <https://doi.org/10.2139/ssrn.3822780> (preprint).
- 3 Fadlyana E, Rusmil K, Tarigan R, et al. Phase III, observer-blind, randomized, placebo-controlled study of the efficacy, safety and immunogenicity of SARS-CoV-2 inactivated vaccine in healthy adults aged 18–59 years in Indonesia. *Vaccine* 2021; **39**: 6520–28.
- 4 Earle KA, Ambrosino DM, Fiore-Gartland A, et al. Evidence for antibody as a protective correlate for COVID-19 vaccines. *Vaccine* 2021; **39**: 4423–28.
- 5 Khoury DS, Cromer D, Reynaldi A, et al. Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. *Nat Med* 2021; **27**: 1205–11.

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.

Mine Durusu Tanriover,
Hamdi Levent Doğanay, Serhat Unal,
*Murat Akova
makova@hacettepe.edu.tr

Department of Internal Medicine (MDT) and Department of Infectious Diseases and Clinical Microbiology (SU, MA), Hacettepe University School of Medicine, Ankara 06230, Turkey; Hacettepe University Vaccine Institute, Ankara, Turkey (MDT, SU, MA); Department of Gastroenterology, Turkish Republic Ministry of Health, Istanbul Provincial Health Directorate, University of Health Sciences Istanbul Umraniye Training and Research Hospital, Istanbul, Turkey (HLD)

- 1 Tanriover MD, Doğanay HL, Akova M, et al. Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in Turkey. *Lancet* 2021; **398**: 213–22.
- 2 Palacios R, Batista AP, Albuquerque CSN, et al. Efficacy and safety of a COVID-19 inactivated vaccine in healthcare professionals in Brazil: the PROFISCOV Study. *SSRN* 2021; published online April 11. <https://doi.org/10.2139/ssrn.3822780> (preprint).
- 3 Fadlyana E, Rusmil K, Tarigan R, et al. Phase III, observer-blind, randomized, placebo-controlled study of the efficacy, safety and immunogenicity of SARS-CoV-2 inactivated vaccine in healthy adults aged 18–59 years in Indonesia. *Vaccine* 2021; **39**: 6520–28.
- 4 Jara A, Undurraga EA, González C, et al. Effectiveness of an inactivated SARS-CoV-2 vaccine in Chile. *N Engl J Med* 2021; **385**: 875–84.

Department of Error

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>



Published Online
November 8, 2021
[https://doi.org/10.1016/S0140-6736\(21\)02432-6](https://doi.org/10.1016/S0140-6736(21)02432-6)