



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.

- 2 Chakrabarti SS, Kaur U, Singh A, et al. Of cross-immunity, herd immunity and country-specific plans: experiences from COVID-19 in India. *Aging Dis* 2020; **11**: 1339–44.
- 3 Sette A, Crotty S. Pre-existing immunity to SARS-CoV-2: the knowns and unknowns. *Nat Rev Immunol* 2020; **20**: 457–58.
- 4 Chua H, Feng S, Lewnard JA, et al. The use of test-negative controls to monitor vaccine effectiveness: a systematic review of methodology. *Epidemiology* 2020; **31**: 43–64.

Authors' reply

We thank Sasanka Chakrabarti and colleagues for their interest in our Article¹ and would like to clarify some issues. Their concern is that younger vaccinated participants were probably health-care workers with a higher exposure risk than the controls in our study, making estimation of vaccine effectiveness difficult. However, we did clarify in the appendix of our Article that we accounted for this potential higher risk of exposure by adjusting for the confounding factors of age, sex, and exposure.

The possibility of previous asymptomatic or mildly symptomatic infections remains similar in both the groups and is not confined to controls. Serology for nucleocapsid antibodies could have been useful for diagnosing asymptomatic infections but vaccine effectiveness studies have generally focused on symptomatic infections. Estimates of vaccine effectiveness that consider asymptomatic infections can be quite imprecise. Furthermore, considering the large sample size, collecting samples and performing serological testing would have been prohibitively time consuming and would have defeated the purpose of generating estimates of vaccine effectiveness in a timely manner during the SARS-CoV-2 delta (B.1.617.2) variant surge in India.

Regarding the number of participants tested for cellular responses, the chosen sample size for T-cell assays was one of the largest to date to show that the T-cell responses were conserved between the ancestral virus and the delta variant of SARS-CoV-2, as

has been confirmed by recent reports as well.² Studying a larger sample size would have been challenging because of sample availability, resources, and the time required. Most vaccine effectiveness studies have tested around 10% of the vaccinated population for cellular responses.³

Studying the T-cell responses against endogenous coronaviruses in unvaccinated individuals was beyond our study objectives, and we would welcome such a study. Nonetheless, published literature indicates that the magnitude of T-cell responses in unexposed individuals is considerably lower than in COVID-19 convalescent and vaccinated individuals.⁴ It is possible, although speculative, that the cross-reactivity of T cells against endogenous coronaviruses might provide some protection against SARS-CoV-2 and its variants.

The test-negative case-control design is a WHO-recommended and well established design for assessing real-world vaccine effectiveness—eg, for influenza, rotavirus, and SARS-CoV-2 vaccines.⁵ This design balances risk profile, health-care seeking behaviour, and access to care among vaccinated and non-vaccinated people. We considered the severity of COVID-19 as a secondary outcome and not as a confounder, and therefore it was not included in the multivariable model.

We declare no competing interests.

Ramachandran Thiruvengadam, Amit Awasthi, Shinjini Bhatnagar, *Pramod Kumar Garg, on behalf of DBT Consortium for COVID-19 Research
pgarg@thsti.res.in

Translational Health Science and Technology Institute, Faridabad 121001, India

- 1 Thiruvengadam R, Awasthi A, Medigeshi G, et al. Effectiveness of ChAdOx1 nCoV-19 vaccine against SARS-CoV-2 infection during the delta (B.1.617.2) variant surge in India: a test-negative, case-control study and a mechanistic study of post-vaccination immune responses. *Lancet Infect Dis* 2022; published online Nov 25. [https://doi.org/10.1016/S1473-3099\(21\)00680-0](https://doi.org/10.1016/S1473-3099(21)00680-0).
- 2 Jordan SC, Shin B-H, Gadsden TM, et al. T cell immune responses to SARS-CoV-2 and variants of concern (alpha and delta) in infected and vaccinated individuals. *Cell Mol Immunol* 2021; **18**: 2554–56.

- 3 Ramasamy MN, Minassian AM, Ewer KJ, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. *Lancet* 2021; **396**: 1979–93.
- 4 Grifoni A, Weiskopf D, Ramirez SI, et al. Targets of T cell responses to SARS-CoV-2 coronavirus in humans with COVID-19 disease and unexposed individuals. *Cell* 2020; **181**: 1489–501.
- 5 WHO. Evaluation of COVID-19 vaccine effectiveness. Geneva: World Health Organization, 2021. https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-vaccine_effectiveness-measurement-2021.1 (accessed June 11, 2021).

Evaluating the risk compensation of HIV/AIDS prevention measures

Yang Zheng and colleagues¹ assessed the global disease burden and trends of five sexually transmitted infections (STIs) over the past three decades. An interesting finding was that, contrary to the overall stable trend of the incidence rate, the incidence of syphilis increased in adolescents after 2010, especially in high-income countries.¹ Zheng and colleagues suggested that this increase might be due to condom fatigue, complacency about HIV, and optimism about HIV treatments caused by the success of HIV/AIDS prevention and control measures among high-risk populations.¹ The increasing use of medical protection against HIV might lead to more risky sexual practices and increase the transmission of other STIs, also known as risk compensation.

In 2019, Chow and colleagues² described the changes in STI epidemics among men who have sex with men (MSM) under the present context of HIV control. In the USA and European countries, notified syphilis cases among MSM showed the most dramatic increase among several STIs during the 2010s when pre-exposure prophylaxis (PrEP) was introduced and promoted.² Coincidentally, Zheng and colleagues' study showed a similar trend on a