

by age, as vaccination status is associated with age, and younger age is associated with reduced susceptibility to acquiring SARS-CoV-2 infection.<sup>5</sup>

In these times, when evidence-based confidence in vaccines is crucial to reduce the impact of the COVID-19 pandemic on mortality and morbidity, data on effects of vaccination should be adequately and unambiguously reported by the scientific community in order to avoid misinterpretation of the data by the public and the media.

We declare no competing interests.

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- 1 Singanayagam A, Hakki S, Dunning J, et al. Community transmission and viral load kinetics of the SARS-CoV-2 delta (B.1.617.2) variant in vaccinated and unvaccinated individuals in the UK: a prospective, longitudinal, cohort study. *Lancet Infect Dis* 2021; published online Oct 29. [https://doi.org/10.1016/S1473-3099\(21\)00648-4](https://doi.org/10.1016/S1473-3099(21)00648-4).
- 2 Roberts M. Covid: double vaccinated can still spread virus at home. Oct 29, 2021. <https://www.bbc.com/news/health-59077036> (accessed Oct 30, 2021).
- 3 @RTLnieuws. Oct 28, 2021. <https://twitter.com/RTLnieuws/status/1453806095693225984> (accessed Oct 30, 2021).
- 4 de Gier B, Andeweg S, Backer JA, et al. Vaccine effectiveness against SARS-CoV-2 transmission to household contacts during dominance of delta variant (B.1.617.2), August–September 2021, the Netherlands. *Euro Surveill* 2021; **26**: 2100977.
- 5 Viner RM, Mytton OT, Bonell C, et al. Susceptibility to SARS-CoV-2 infection among children and adolescents compared with adults: a systematic review and meta-analysis. *JAMA Pediatr* 2021; **175**: 143–56.

The important analysis by Anika Singanayagam and colleagues<sup>1</sup> demonstrated that individuals fully vaccinated against SARS-CoV-2 with breakthrough infections have similar peak viral loads to unvaccinated people and might infect other fully vaccinated individuals within the same household. Of particular concern, vaccines that permit transmission do not confer sterilising

immunity, thus potentially resulting in accumulation of large viral loads and increased risk of immune escape.<sup>2</sup> By mainly targeting the SARS-CoV-2 spike protein, vaccines can favour propagation of variants with immune-escape mutations.<sup>3</sup> Single point mutations in the receptor-binding domain of the viral spike protein are sufficient to facilitate the immune escape and transmission of resistant viruses.<sup>2</sup> By further examining the unpublished whole-genome sequencing data of vaccinated and unvaccinated participants in the study by Singanayagam and colleagues,<sup>1</sup> invaluable information could be gleaned about whether the current first-generation COVID-19 vaccines potentially exerted selective pressure for resistant SARS-CoV-2 variants.

Tracing the whole-genome sequencing data of all unvaccinated participants chronologically from the pre-alpha-variant (B.1.1.7) phase (September–November, 2020), to the alpha-variant phase (December, 2020, to March, 2021), and to the delta-variant (B.1.617.2) period (May 25–Sept 15, 2021) would likely reveal a trend of increasing number of mutations that converge towards the resultant whole-genome sequence aligned with delta lineage-defining mutations presented in figure 2 of the Article.<sup>1</sup> To determine if vaccines possibly contributed to this genetic drift, the whole-genome sequencing data from patients who tested PCR positive (vaccinated and unvaccinated) can be compared with data from their respective contacts over time from the pre-alpha to the delta phases.

Identical whole-genome sequences between PCR-positive participants and their respective contacts demonstrates direct viral transmission without mutation. Clearly distinct whole-genome sequences between both groups indicate cross-infection of contacts by a different viral lineage. Slight variations in whole-genome sequences between both groups

show mutation has occurred, in which case the vaccination status of the contact should be examined. If mutation occurred predominantly among vaccinated contacts but not within unvaccinated contacts, it suggests vaccine-induced mutation has developed. Because the sample size in the research by Singanayagam and colleagues<sup>1</sup> is relatively small, it will be worrisome if a fair number of vaccinated contacts of PCR-positive participants are identified with mutations, especially with the amino acid mutations summarised in the appendix.

The earliest detection of the delta variant was in India on Oct 14, 2020,<sup>4</sup> before India's vaccination commencement on Jan 16, 2021.<sup>5</sup> However, with fastidious propagation of these variants over time by non-sterilising vaccines targeting the spike protein, it is still reasonably plausible that selective pressure could have contributed to the current dominance of the delta variant.

It would be much appreciated if Singanayagam and colleagues would consider analysing their unpublished whole-genome sequencing data as suggested above. If theoretical risk of evolutionary escape from the existing COVID-19 vaccines<sup>2</sup> translates into real-life evidence, which could be verified via whole-genome sequencing data from this study,<sup>1</sup> then it will be prudent to expedite resources towards second-generation COVID-19 vaccines that exert sterilising immunity, in addition to non-pharmacological interventions.

I declare no competing interests.

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- 1 Singanayagam A, Hakki S, Dunning J, et al. Community transmission and viral load kinetics of the SARS-CoV-2 delta (B.1.617.2) variant in vaccinated and unvaccinated individuals in the UK: a prospective, longitudinal, cohort study. *Lancet Infect Dis* 2021; published online Oct 29. [https://doi.org/10.1016/S1473-3099\(21\)00648-4](https://doi.org/10.1016/S1473-3099(21)00648-4).

See Online for appendix

