Roberto Bertollini, M.D., M.P.H.*
Ministry of Public Health
Doha, Qatar
for the National Study Group for COVID-19 Epidemiology

*Members of the National Study Group for COVID-19 Epidemiology are listed in the Supplementary Appendix, available with the full text of this letter at NEJM.org.

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Viral Dynamics of SARS-CoV-2 Variants in Vaccinated and Unvaccinated Persons

TO THE EDITOR: Two opposing forces that are shaping the coronavirus disease 2019 (Covid-19) pandemic are the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of concern and the uptake of vaccines. Measurement of SARS-CoV-2 viral load over the course of acute infection can inform hypotheses about the mechanisms that underlie variation in transmissibility according to variant and vaccination status.[1]

Recent evidence suggests that infections with the delta variant feature higher peak viral loads than those in other lineages[2] and that vaccine recipients who are infected with SARS-CoV-2 may clear the infection more quickly than unvaccinated persons.[3] However, descriptions of SARS-CoV-2 viral dynamics have been principally based on cross-sectional studies in which testing was triggered by the onset of symptoms. Such study designs overlook viral dynamics during the early stages of infection and introduce bias in viral load measurements from different periods of the pandemic.[4] To overcome these limitations, we collected and analyzed a prospective, longitudinal set of 19,941 SARS-CoV-2 viral samples obtained from 173 participants as part of the occupational health program of the National Basketball Association between November 28, 2020, and August 11, 2021. (Details regarding the characteristics of the population are provided in Table S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org.)

Using a Bayesian hierarchical statistical model,[5] we compared SARS-CoV-2 viral dynamics among 36 participants who were infected with the B.1.1.7 (alpha) variant, 36 participants with the B.1.617.2 (delta) variant, and 41 participants with a variant that was not of current interest or concern, along with 37 vaccinated and 136 unvaccinated participants. We found no meaningful difference in the mean peak viral load (with a lower peak cycle threshold [Ct] indicating a higher viral load), proliferation duration, clearance duration, or duration of acute infection of either the alpha or the delta variant as compared with variants not of interest or concern, as evidenced by overlapping 95% credible intervals (Fig. 1A, 1B, and 1C, Table S2, and Fig. S1). We also found no meaningful difference in the mean peak viral load or proliferation duration between vaccinated and unvaccinated participants (Fig. 1D and 1E, Table S2, and Fig. S2).

A lower peak Ct was slightly more frequent in infections with the delta variant than in those with the alpha variant or variants not of interest or concern: 13.0% of the posterior delta trajectories had a Ct count of less than 15 (9.6 $\log_{10}$ RNA copies per milliliter), as compared with 6.9% for the alpha variant and 10.2% for variants not of interest or concern (Fig. 1F and Fig. S1G). It is unclear whether this finding reflects a biologic characteristic of the delta variant, the limited number of cases, the higher proportion of delta infections among vaccine recipients, or other factors. Breakthrough infections among vaccine recipients were characterized by a faster clearance time than that among unvaccinated participants, with a mean of 5.5 days (95% credible

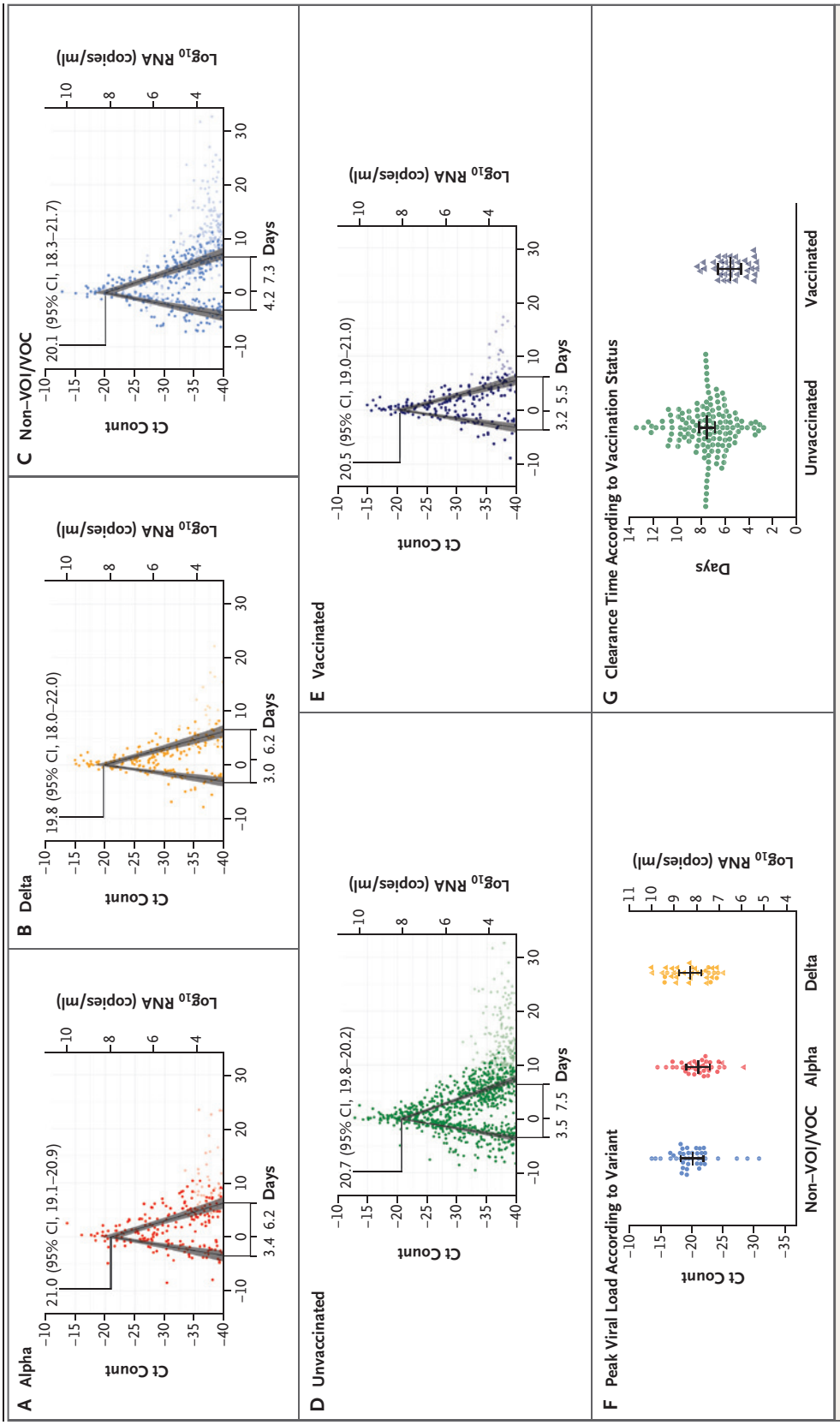

Figure 1. Cycle Threshold (Ct) Counts and Infection Clearance Time.

Shown are Ct counts for participants infected with the alpha variant (Panel A), delta variant (Panel B), and variants that were not of current interest or concern (non–VOI/VOCs) (Panel C). Also shown are Ct counts among unvaccinated participants (Panel D) and vaccinated participants (Panel E). Data points for Ct counts that were obtained after the conclusion of a participant's acute infection (as measured by the mean posterior infection clearance time) are partially transparent, since this period was not the focus of the study. The mean posterior viral trajectories are depicted as solid lines with 95% credible intervals indicated by the shaded regions. Also shown are individual-level posterior means for the peak viral load according to variant status (Panel F) and the mean clearance time according to vaccination status (Panel G). In Panels F and G, horizontal lines indicate means and I bars 95% credible intervals.

interval, 4.6 to 6.5) and 7.5 days (95% credible interval, 6.8 to 8.2), respectively. The shorter clearance time led to a shorter overall duration of infection among vaccine recipients (Fig. 1G).

Our ability to detect differences in SARS-CoV-2 viral dynamics was limited by the high degree of interpersonal variation among our study participants, as well as the small sample size, which also prevented us from subcategorizing the population further according to variant and vaccination status. The participants in this study were predominantly healthy young men and thus were not representative of the general population. Symptoms were not systematically tracked, nor did we test for the presence of infectious virus.

This study provides data on acute SARS-CoV-2 viral dynamics for some variants of concern among vaccinated and unvaccinated persons. Additional data regarding prospective, longitudinal testing among diverse cohorts are needed to better understand differences in SARS-CoV-2 viral trajectories and inform interventions to mitigate the effects of Covid-19.

Stephen M. Kissler, Ph.D.
Harvard T.H. Chan School of Public Health
Boston, MA
skissler@hsph.harvard.edu

Joseph R. Fauver, Ph.D.
Yale School of Public Health
New Haven, CT

Christina Mack, Ph.D.
Caroline G. Tai, Ph.D.
IQVIA
Durham, NC

Mallery I. Breban, Ph.D.
Anne E. Watkins, Ph.D.
Yale School of Public Health
New Haven, CT

Radhika M. Samant, Ph.D.
IQVIA
Durham, NC

Deverick J. Anderson, M.D., M.P.H.
Duke Center for Antimicrobial Stewardship and Infection Prevention
Durham, NC

Jessica Metti, Ph.D.
Gaurav Khullar, M.D.
Rachel Baits, Ph.D.
Matthew MacKay, Ph.D.
Daisy Salgado, Ph.D.
Tim Baker, Ph.D.
Joel T. Dudley, Ph.D.
Christopher E. Mason, Ph.D.
TEMPUS Labs
Chicago, IL

David D. Ho, M.D.
Columbia University Vagelos College of Physicians and Surgeons
New York, NY

Nathan D. Grubaugh, Ph.D.
Yale School of Public Health
New Haven, CT

Yonatan H. Grad, M.D., Ph.D.
Harvard T.H. Chan School of Public Health
Boston, MA

Drs. Kissler, Fauver, and Mack and Drs. Grubaugh and Grad contributed equally to this letter.

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Salt Substitute and Cardiovascular Events and Death

TO THE EDITOR: During the 5-year course of the Salt Substitute and Stroke Study (SSaSS) (Sept. 16 issue),[1] sodium intake was lowered by only 13%, whereas potassium intake was increased by 57%. The effect on blood pressure (–2.94/–0.37 mm Hg) can be ascribed to the potassium supplementation[2] rather than to the negligible sodium reduction.[3] A low potassium intake of 1.4 g daily