CORRESPONDENCE

Resurgence of SARS-CoV-2 Infection in a Highly Vaccinated Health System Workforce

TO THE EDITOR: In December 2020, the University of California San Diego Health (UCSDH) workforce experienced a dramatic increase in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections. Vaccination with mRNA vaccines began in mid-December 2020; by March, 76% of the workforce had been fully vaccinated, and by July, the percentage had risen to 87%. Infections had decreased dramatically by early February 2021.[1] Between March and June, fewer than 30 health care workers tested positive each month. However, coincident with the end of California's mask mandate on June 15 and the rapid dominance of the B.1.617.2 (delta) variant that first emerged in mid-April and accounted for over 95% of UCSDH isolates by the end of July (Fig. 1), infections increased rapidly, including cases among fully vaccinated persons. Institutional review board approval was obtained for use of administrative data on vaccinations and case-investigation data to examine mRNA SARS CoV-2 vaccine effectiveness.

UCSDH has a low threshold for SARS-CoV-2 testing, which is triggered by the presence of at least one symptom during daily screening or by an identified exposure, regardless of vaccination status. From March 1 to July 31, 2021, a total of 227 UCSDH health care workers tested positive for SARS-CoV-2 by reverse-transcriptase–quantitative polymerase-chain-reaction (RT-qPCR) assay of nasal swabs; 130 of the 227 workers (57.3%) were fully vaccinated. Symptoms were present in 109 of the 130 fully vaccinated workers (83.8%) and in 80 of the 90 unvaccinated workers (88.9%). (The remaining 7 workers were only partially vaccinated.) No deaths were reported in either group; one unvaccinated person was hospitalized for SARS-CoV-2–related symptoms.

Vaccine effectiveness was calculated for each month from March through July; the case definition was a positive PCR test and one or more symptoms among persons with no previous Covid-19 infection (see the Supplementary Appendix). Vaccine effectiveness exceeded 90% from March through June but fell to 65.5% (95% confidence interval [CI], 48.9 to 76.9) in July (Table 1). July case rates were analyzed according to the month in which workers with Covid-19 completed the vaccination series; in workers completing vaccination in January or February, the attack rate was 6.7 per 1000 persons (95% CI, 5.9 to 7.8), whereas the attack rate was 3.7 per 1000 persons (95% CI, 2.5 to 5.7) among those who completed vaccination during the

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period from March through May. Among unvaccinated persons, the July attack rate was 16.4 per 1000 persons (95% CI, 11.8 to 22.9).

The SARS CoV-2 mRNA vaccines, BNT162b2 (Pfizer–BioNTech) and mRNA-1273 (Moderna), have previously shown efficacy rates of 95% and 94.1%,[2] respectively, in their initial clinical trials, and for the BNT162b2 vaccine, sustained, albeit slightly decreased effectiveness (84%) 4 months after the second dose.[3] In England, where an extended dosing interval of up to 12 weeks was used, Lopez Bernal et al. reported a preserved vaccine effectiveness of 88% against symptomatic disease associated with the delta variant.[4] As observed by others in populations that received mRNA vaccines according to standard Emergency Use Authorization intervals,[5] our data suggest that vaccine effectiveness against any symptomatic disease is considerably lower against the delta variant and may wane over time since vaccination.

The dramatic change in vaccine effectiveness from June to July is likely to be due to both the emergence of the delta variant and waning immunity over time, compounded by the end of masking requirements in California and the resulting greater risk of exposure in the community. Our findings underline the importance of rapidly reinstating nonpharmaceutical interventions, such as indoor masking and intensive testing strategies, in addition to continued efforts to increase vaccinations, as strategies to prevent avoidable illness and deaths and to avoid mass disruptions to society during the spread of this formidable variant. Furthermore, if our findings on waning immunity are verified in other settings, booster doses may be indicated.

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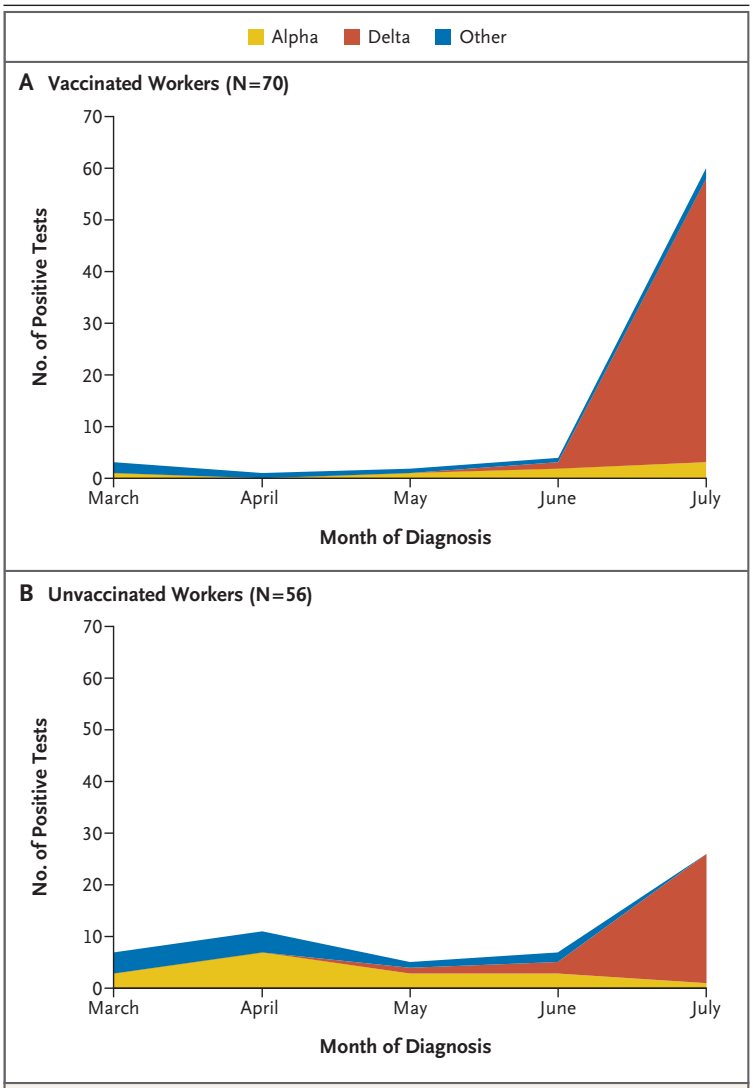

Figure 1. SARS-CoV-2 Variants among Symptomatic Health Workers.

Shown is the distribution of the B.1.1.7 (alpha), delta, and other SARS-CoV-2 variants according to vaccination status and month of diagnosis among health workers at University of California San Diego Health, March through July 2021. The number of workers indicates those who were symptomatic and had available variant data, and the number of positive tests indicates those that included data on variants.

Dr. Laurent serves as an author on behalf of the SEARCH Alliance. Collaborators in the SEARCH Alliance are listed in the Supplementary Appendix, available with the full text of this letter at NEJM.org.

Drs. Keehner and Horton and Drs. Abeles and Torriani contributed equally to this letter.

Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

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1. Keehner J, Abeles SR, Torriani FJ. More on SARS-CoV-2 infection after vaccination in health care workers. reply. N Engl J Med 2021;385(2):e8.

Table 1. Symptomatic SARS-CoV-2 Infection and mRNA Vaccine Effectiveness among UCSDH Health Workers, March through July 2021.*

	March	April	May	June	July
UCSDH workforce — no. of persons	18,964	18,992	19,000	19,035	19,016
Vaccination status — no. of persons					
Fully vaccinated†	14,470	15,510	16,157	16,426	16,492
mRNA-1273 (Moderna)	6,608	7,005	7,340	7,451	7,464
BNT162b2 (Pfizer–BioNTech)	7,862	8,505	8,817	8,975	9,028
Unvaccinated	3,230	2,509	2,187	2,059	1,895
Percentage of workers fully vaccinated	76.3	81.7	85.0	86.3	86.7
Symptomatic Covid-19					
Fully vaccinated workers	3	4	3	5	94
Unvaccinated workers	11	17	10	10	31
Percentage of cases in fully vaccinated workers	21.4	19.0	23.1	33.3	75.2
Attack rate per 1000 (95% CI)					
Fully vaccinated workers	0.21 (0.21–0.47)	0.26 (0.26–0.50)	0.19 (0.21–0.40)	0.30 (0.31–0.53)	5.7 (5.4–6.2)
Unvaccinated workers	3.4 (2.1–5.9)	6.8 (4.5–10.6)	4.6 (2.6–8.2)	4.9 (2.9–8.7)	16.4 (11.8–22.9)
Vaccine effectiveness — % (95% CI)	93.9 (78.2–97.9)	96.2 (88.7–98.3)	95.9 (85.3–98.9)	94.3 (83.7–98.0)	65.5 (48.9–76.9)

* UCSDH denotes University of California San Diego Health.
† Data are the total number of workers who had received two doses of an mRNA vaccine as of the last day of the month.

2. Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med 2021;384:403-16.
3. Thomas SJ, Moreira ED Jr, Kitchin N, et al. Six month safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. July 28, 2021 (https://www.medrxiv.org/content/10.1101/2021.07.28.21261159v1). preprint.
4. Lopez Bernal J, Andrews N, Gower C, et al. Effectiveness of Covid-19 vaccines against the B.1.617.2 (Delta) variant. N Engl J Med 2021;385:585-94.
5. Israel A, Merzon E, Schäffer AA, et al. Elapsed time since BNT162b2 vaccine and risk of SARS-CoV-2 infection in a large cohort. August 5, 2021 (https://www.medrxiv.org/content/10.1101/2021.08.03.21261496v1). preprint.

DOI: 10.1056/NEJMc2112981

Myocarditis after Covid-19 mRNA Vaccination

TO THE EDITOR: The Centers for Disease Control and Prevention recently reported cases of myocarditis and pericarditis in the United States after coronavirus disease 2019 (Covid-19) messenger RNA (mRNA) vaccination.[1] In recently published reports, diagnosis of myocarditis was made with the use of noninvasive imaging and routine laboratory testing.[2-5] Here, we report two cases of histologically confirmed myocarditis after Covid-19 mRNA vaccination.

Patient 1, a 45-year-old woman without a viral prodrome, presented with dyspnea and dizziness 10 days after BNT162b2 vaccination (first dose). A nasopharyngeal viral panel was negative for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza A and B, enteroviruses, and adenovirus (Table S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org). A serum polymerase-chain-reaction (PCR) assay and serologic tests showed no evidence of active parvovirus, enterovirus, human immunodeficiency virus, or infection with SARS-CoV-2. At presentation, she had tachycardia; ST-segment depression detected on electrocardiography, which was most prominent in the lateral leads (Fig. S1); and a troponin I level of 6.14 ng

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Keehner J, Horton LE, Binkin NJ, et al. Resurgence of SARS-CoV-2 infection in a highly vaccinated health system workforce. N Engl J Med 2021;385:1330-2. DOI: 10.1056/NEJMc2112981

Supplemental Appendix

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Methods:

The study population was restricted to members of the UC San Diego Health's (UCSDH) and UC San Diego Health Sciences (UCSDHS) workforce who were 18 years of age and older. Workforce numbers varied slightly by study month, from 18,964 to 19,035 of whom approximately 58% worked in the Health System, which includes the hospitals and outpatient clinics, and the remainder were in Health Sciences which includes the faculty and staff in the Schools of Medicine, Pharmacy, and Public Health, the residency and fellowship programs, and biomedical research laboratory staff.

UCSDH made COVID-19 vaccination readily available to the clinical workforce initially at vaccination stations within the two hospitals and later to the rest of the workforce at its two superstations. Numbers of fully vaccinated persons were obtained from UCSDH's vaccine registry and were also collated from sources outside of UCSDH. These included the County of San Diego and California state COVID-19 vaccination registries and proof of vaccination uploaded by individuals as part of a July 15, 2021 vaccination mandate for all University of California personnel, students, or trainees. Numbers of unvaccinated individuals were obtained by subtracting the number of individuals who had received at least one dose of vaccine from the total workforce population.

Cases of SARS CoV-2 were identified through a variety of channels, including daily symptom screening for those working onsite using a smart phone application or a tablet available at the secured Health System's entrances, care seeking for symptoms, and testing of contacts to known cases. All cases underwent detailed investigation by a dedicated team, which was also responsible for contact tracing. PCR and sequencing of suspected cases were performed in two UCSDH laboratories. In addition to the cases investigated at UCSDH, the County of San Diego Public Health Services notified UCSDH of a small number of UCSDH workers who had undergone testing elsewhere. All cases were tracked in a REDCap database beginning October 25, 2020. Data collected on each case included the date of the start of symptoms, and the type of symptoms, known exposures, worksite location, and job type. If vaccinated, dates and type of vaccine were obtained from the medical record system and verified with the case and persons with no record of UCSDH vaccination were asked to provide these data.

For purposes of the analysis, only those cases with both a positive PCR and at least one symptom at the time of testing were included in the analysis. Symptoms queried included fever, chills, cough, shortness of breath, difficulty breathing, fatigue, myalgias, headache, loss of taste or smell, sore throat, congestion or runny nose, nausea, vomiting or diarrhea. The analyses excluded from both the case numbers and the population denominators those who (a) received the Janssen vaccine, (b) received only one dose of an mRNA vaccine, (c) had a positive PCR within 14 days of a second mRNA dose, or (d) had a positive PCR between October 25, 2020, and February 28, 2021.

We used the model described by Moline et al. (1) to calculate vaccine effectiveness, with a slight modification to the variance calculation that was necessary because of the structure of

our data. In this approach, Poisson regression with robust standard errors and offsets included for the proportions of vaccinated and unvaccinated individuals was used to calculate vaccine effectiveness and 95% confidence intervals (1). Confidence intervals for attack rates were calculated using the Wilson score interval with the finite population correction adjustment.

Reference

1. Moline HL, Whitaker M, Deng L, et al. Effectiveness of COVID-19 Vaccines in Preventing Hospitalization Among Adults Aged ≥65 Years — COVID-NET, 13 States, February–April 2021. MMWR Morb Mortal Wkly Rep. ePub: 6 August 2021. DOI: http://dx.doi.org/10.15585/mmwr.mm7032e3external icon