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Continued effectiveness of COVID-19 vaccination among urban healthcare workers during delta variant predominance

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Abstract

Background: Data on COVID-19 vaccine effectiveness (VE) among healthcare workers (HCWs) during periods of delta variant predominance are limited.

Methods: We followed a population of urban Massachusetts HCWs (45% non-White) subject to epidemiologic surveillance. We accounted for covariates such as demographics and community background infection incidence, as well as information bias regarding COVID-19 diagnosis and vaccination status.

Results: During the study period (December 16, 2020 to September 30, 2021), 4615 HCWs contributed to a total of 1,152,486 person-days at risk (excluding 309 HCWs with prior infection) and had a COVID-19 incidence rate of 5.2/10,000 (114 infections out of 219,842 person-days) for unvaccinated person-days and 0.6/10,000 (49 infections out of 830,084 person-days) for fully vaccinated person-days, resulting in an adjusted VE of 82.3% (95% CI 75.1–87.4%). For the secondary analysis limited to the period of delta variant predominance in Massachusetts (i.e., July 1 to September 30, 2021), we observed an adjusted VE of 76.5% (95% CI 40.9–90.6%). Independently, we found no re-infection among those with prior COVID-19, contributing to 74,557 re-infection-free person-days, adding to the evidence base for the robustness of naturally acquired immunity.

Conclusions: We found a VE of 76.5% against the delta variant. Our work also provides further evidence of naturally acquired immunity.

Keywords: COVID, Immunity, Immunization, Real-world evidence, SARS-CoV-2, Vaccine

Background

Data on COVID-19 vaccine effectiveness (VE) among healthcare workers (HCWs) during periods of delta variant predominance are limited. Literature accounting for other potential determinants of infection rates (e.g., age, sex, race, and surrounding community rate [1]) is even more scarce. Therefore, we conducted this study to investigate the continued effectiveness of COVID-19 vaccination during the delta variant predominance in a diverse and urban healthcare setting, accounting for other transmission determinants.

Methods

A community-based healthcare system in Massachusetts runs a COVID-19 vaccination program for employees (described previously [2]), with the BNT162b2/Pfizer vaccine starting on December 16, mRNA-1273/Moderna on December 23, 2020, and Janssen vaccine/Ad26.COV2.S in February 2021. Vaccination was available to

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all workers regardless of their in-person/remote working status from December 29, 2020. In addition, the system announced a vaccine mandate on August 16, 2021, which requires employees to receive their final dose by October 18, 2021 barring an approved religious or medical exemption.

We followed all actively serving HCWs in the system from December 16, 2020 to September 30, 2021, excluding those with prior COVID-19 infection from the main analyses. The outcome was having a positive PCR assay during the study period documented by the healthcare system's Occupational Health department [3]. The established master database, comprised of workers' demographics, prior infection, de novo PCR positivity, vaccination (validated by the Massachusetts Immunization Information System and/or the healthcare system's medical records), and human resource administrative data, has been previously described [2, 3]. For each HCW, we calculated the person-days at risk and categorized them according to vaccination status. The categorization measure has been used in previous literature [2]. A HCW's follow-up person-days were censored at the end of the study period, his/her termination date, the date tested positive for COVID, or the date he/she received a booster/3rd vaccine dose (to account for the study period intersecting with the booster doses period), whichever came first. The present study is an extension of our previous VE study on the same population prior to delta variant predominance [2].

The Andersen–Gill extension of the Cox proportional hazards models were built to account for correlated data. We further adjusted for age, sex, race, and the Massachusetts statewide 7-day average of tested COVID cases [4] on the date the first dose was given to control for background rates. We estimated VE by calculating 100% × (1 − hazard ratio). The R software (version 3.6.3) was used for statistical analyses.

Results

A total of 4615 HCWs (average age of 45.0 ± 13.3 years and female predominance (76.0%)) contributed to 1,152,486 person-days at risk during the study period (Table 1). 45% of the study population was non-White (including 20% African American, 13.5% Hispanic, and 9.0% Asian). Of all HCWs, 4418 (95.7%) had received at least one dose by the end of the study. Among them, 58.3% got mRNA-1273/Moderna, 39.4% BNT162b2/Pfizer, 2.3% Janssen vaccine/Ad26.COV2.S, and one (0.02%) got mixed doses of Janssen vaccine/Ad26.COV2.S and mRNA-1273/Moderna. The results showed that throughout the study period, for fully vaccinated HCWs the VE is 82.3% (95% CI 75.1–87.4%) after multivariable adjustment (Table 1, Fig. 1).

We further conducted a secondary analysis limiting the study period from July 1, 2021 to September 30, 2021, corresponding to delta variant predominance in Massachusetts [5]. We observed an incidence rate of 5.8/10,000 (15 events out of 25,910 person-days) for unvaccinated person-days and 1.3/10,000 (39 events out of 308,267 person-days) for 14 days after fully vaccinated, resulting in an adjusted VE of 76.5% (95% CI 40.9–90.6%). The model coefficients derived from the main versus secondary analysis were compared to test whether the VEs were different. We used the equation proposed by Clogg et al. [6] and found the decline in VE from 82.3 to 76.5% was not statistically significant (P = 0.570).

When we examined HCWs (n = 423) with infections occurring before vaccination, no re-infection was observed, accumulating 74,557 re-infection-free person-days (starting 10 days after initial infection and censoring at the date of receiving their first vaccine dose). Further, after vaccination, previously infected HCWs did not contribute any breakthrough infection events among the vaccinated HCWs.

Table 1 Rate of infection during the study period (Dec 16, 2020–Sep 30, 2021) across the four vaccination categories (excluding 309 people infected before Dec 15, 2020)

Status	Person-days	No. of infections	Rate per 10,000 person-days	Unadjusted vaccine effectiveness % (95% CI)	Adjusted vaccine effectiveness % (95% CI)*
Unvaccinated	219,842	114	5.19	Reference	Reference
First dose (< 14 days)	51,329	17	3.31	44.8 (0.13–69.5)	38.8 (— 10.8–66.2)
First dose (14+ days)†	51,231	7	1.37	78.9 (51.6–90.8)	75.5 (43.9–89.3)
Fully vaccinated‡	830,084	49	0.59	87.5 (83.0–90.8)	82.3 (75.1–87.4)

Vaccine effectiveness (95% CI) derived from the Andersen–Gill extension of the Cox proportional hazards models

* Adjust for age, sex, race, and the Massachusetts statewide 7-day average of new tested COVID-19 cases at the date for the first vaccine dose. Those with the race of "American Indian or Alaska Native", "Hawaiian or Pacific Islander", or "Two or More" were pooled into one level "other race"

† Not eligible for those receiving J&J/Janssen

‡ Equal or more than 14 days after single dose of Janssen vaccine/Ad26.COV2.S or having received the second shot of BNT162b2/Pfizer or mRNA-1273/Moderna

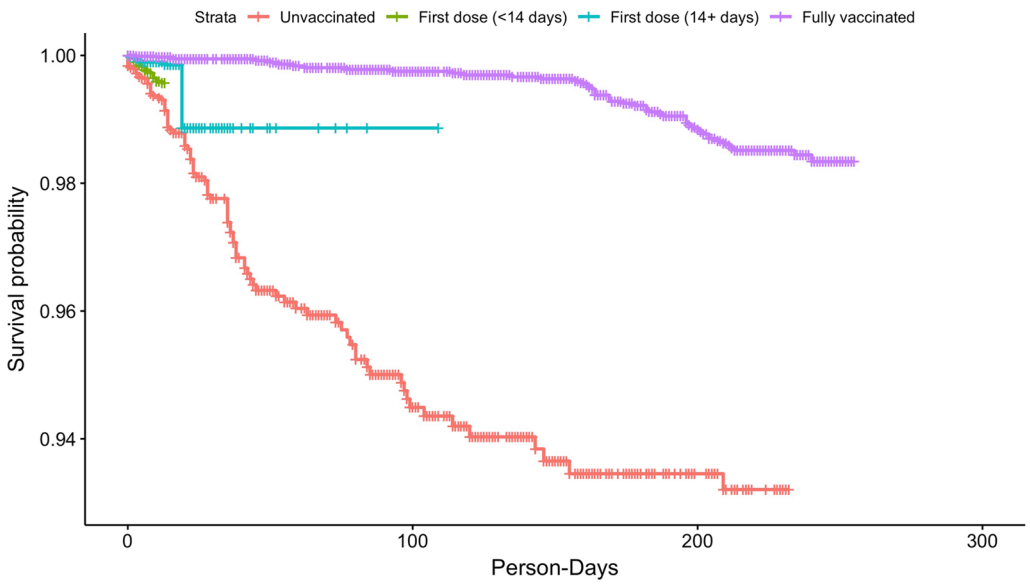

Fig. 1 The Kaplan–Meier curve for the survival (i.e. infection-free) person-days across the four categories based on vaccination status

Discussion and conclusions

To our knowledge, this study is one of the first in healthcare settings regarding continued VE during delta variant predominance. Our work also provides further evidence of naturally acquired immunity as we did not observe any reinfections or breakthrough infections among those having contracted COVID-19 prior to vaccination during nearly 75,000 person-days of exposure. We found similar VE against the delta variant, 76%, compared to another study's findings, 66% [7]. Strengths included accounting for covariates and information bias such as demographics and background incidence, a multiethnic study population, consistent COVID-19 screening criteria, and well-validated vaccination records. Nonetheless, we did not examine individual manufacturers' VE due to a limited power. In addition, we did not account for remote/in-person working status due to a lack of information. Finally, our observations were limited by the study period and events may occur after the end of the follow-up (i.e., September 30, 2021).

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Author contributions
FYL, AS, EI, and SNK formulated the study question and research design. FYL performed the statistical analyses. EI and SNK consulted on the analyses. FYL, AS, and SNK drafted the manuscript. FYL, AS, EI, JB, NN, LAB-M, and SNK worked on data methods, data acquisition and data verification. All authors contributed to the interpretation of data and critical revision of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets generated and/or analysed during the current study are stored on an internal server of Cambridge Health Alliance, which is not publicly available, but the de-identified datasets are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The data we used were de-identified. The need for a consent was waived by the Cambridge Health Alliance Institutional Review Board (Protocol number 4/29/202-003). Additionally, the study was exempted by the Cambridge Health Alliance Institutional Review Board (Protocol number 4/29/202-003). We confirm that all methods were carried out in accordance with the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
S.N.K. has received COVID-19-related consulting fees from Open Health and has owned shares of Regeneron, Moderna and Astra-Zeneca. All other authors declare no competing interests.

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