Continued Effectiveness of COVID-19 Vaccination among Urban Healthcare Workers during Delta Variant Predominance

Running title: Continued COVID-19 VE 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 and Discussion: 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.

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 is even more scarce.

Objective

To investigate the continued effectiveness of COVID-19 vaccination during the Delta

variant predominance in a diverse and urban healthcare setting.

Methods and Findings

A community-based healthcare system in Massachusetts runs a COVID-19

vaccination program for employees (described previously (1)), with the Pfizer vaccine

starting on December 16, Moderna on December 23, 2020, and J&J/Janssen in

February 2021. Vaccination was available to 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 (2). 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 (1, 2). For each HCW, we

calculated the person-days at risk and categorized them according to vaccination

status. 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 3rd vaccine dose , whichever came first.

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 (3) on the date the first

dose was given to control for background rates. We estimated VE by calculating

$100\% \times (1 - \text{hazard ratio})$. The R software (version 3.6.3) was used for statistical

analyses.

A total of 4,615 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. Forty-five percent of the study population was non-White (including 20% African American, 13.5% Hispanic, and 9.0% Asian). Of all HCWs, 4,418 (95.7%) had received at least one dose by the end of the study. Among them, 58.3% got Moderna, 39.4% Pfizer, 2.3% J&J/Janssen, and one (0.02%) got mixed doses of J&J/Janssen and 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, Figure).

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 (4). 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%).

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.

Discussion

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. We found similar VE against the delta variant, 76%, compared to another study's findings, 66% (5). 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.

References

1. Iliaki E, Lan FY, Christophi CA, et al. COVID-19 vaccine efficacy in a diverse urban healthcare worker population. medRxiv. Preprint posted online 6 September 2021. doi:10.1101/2021.09.02.21263038

2. Lan FY, Filler R, Mathew S, et al. COVID-19 symptoms predictive of healthcare workers' SARS-CoV-2 PCR results. PLoS One. 2020;15(6):e0235460. doi:10.1371/journal.pone.0235460

3. Massachusetts Department of Public Health. Archive of COVID-19 cases in Massachusetts. Accessed at https://www.mass.gov/info-details/archive-of-covid-19-cases-in-massachusetts on 2 November 2021.

4. Brown CM, Vostok J, Johnson H, et al. Outbreak of SARS-CoV-2 infections, including COVID-19 vaccine breakthrough infections, associated with large public gatherings - Barnstable County, Massachusetts, July 2021. MMWR Morb Mortal Wkly Rep. 2021;70(31):1059-1062. doi:10.15585/mmwr.mm7031e2

5. Fowlkes A, Gaglani M, Groover K, et al. Effectiveness of COVID-19 vaccines in preventing SARS-CoV-2 infection among frontline workers before and during B.1.617.2 (Delta) variant predominance - Eight U.S. locations, December 2020-August 2021.

Table. 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	219842	114	5.19	Reference	Reference
First dose (<14 days)	51329	17	3.31	44.8 (0.13–69.5)	38.8 (-10.8–66.2)
First dose (14+ days)[†]	51231	7	1.37	78.9 (51.6–90.8)	75.5 (43.9–89.3)
Fully vaccinated[‡]	830084	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 model

[*] 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 J&J/Janssen or having received the second shot of Pfizer or Moderna

Figure. The Kaplan-Meier curve for the survival (i.e. infection-free) person-days across the

four categories based on vaccination status