

Effectiveness of mRNA COVID-19 vaccines against SARS-CoV-2 infection in a cohort of healthcare personnel

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## Abstract

In a large cohort of US healthcare personnel (HCP) without prior COVID-19 infection, 94,382 doses of mRNA COVID-19 vaccine were administered to 49,220 individuals. The adjusted vaccine effectiveness following two doses of each of the two available brands of mRNA vaccine exceeded 96%.

Keywords: COVID-19, SARS-CoV-2, vaccine effectiveness, healthcare personnel, mRNA

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## INTRODUCTION

Healthcare personnel are among the highest risk workers for COVID-19 (1). In early December 2020, the Centers for Disease Control and Prevention (CDC) recommended that HCP be the first occupational group prioritized to receive newly authorized COVID-19 vaccines in the US (2). By mid-December, two mRNA vaccines had received emergency use authorization (EUA) by the Food and Drug Administration (FDA), both of which demonstrated approximately 95% efficacy against symptomatic COVID-19 in clinical trials (3, 4). We aim to provide an estimate of vaccine effectiveness (VE) in the subpopulation of HCP reached through employer vaccination programs, to enrich the rapidly growing body of evidence in this area (5-7).

## METHODS

### Study Design and Subjects

The Mayo Clinic consists of main campuses in Minnesota, Florida and Arizona, and a healthcare system spanning southern Minnesota and western Wisconsin, employing approximately 76,000 healthcare personnel (HCP). All actively employed HCP with a positive molecular assay for SARS-CoV-2 are contacted by Occupational Health Services (OHS) for systematic index case interview and contact tracing as described elsewhere (8). Test results, exposure investigation details, vaccination status and employee demographics are included in the OHS record. Diagnostic molecular assays are conducted for any new COVID-19 symptom. In addition, asymptomatic HCP are tested serially for long term care facility surveillance, for 2 weeks following COVID-19 exposure at work or in the community, and a variety of other reasons such as anticipated personal travel or medical procedures. Social distancing, universal masking, and eye protection in patient care areas were required at all sites. Public mask mandates were in place in the communities of operation throughout most of the study period. We conducted a retrospective review of all HCP newly diagnosed with COVID-19 from 1/1/2021 to 3/31/2021. During this timeframe, two-week COVID-19 incidence rates expressed in new cases per 10,000 population,

dropped from 48.2 to 30.9 in Minnesota and from 73.2 to 14.8 in Wisconsin, both states in which the organization has multiple sites spread across a large geographic area. Two-week incidence rates for Duval County, Florida and Maricopa County, Arizona, home to the southern Mayo Clinic sites, fell from 126.6 to 17.3 and from 188 to 6.6, respectively. Regional incidence rates were extracted from the Johns Hopkins Coronavirus Resource Center (9).

### Vaccination Program

The employee COVID-19 vaccination program launched in December 2020, in close collaboration with state and local public health, vaccinating HCP in a staged fashion, prioritized by occupational risk in a process described previously (10). Receipt of COVID-19 vaccine was voluntary. Both mRNA vaccines, Pfizer/BioNTech COVID-19 (BNT162b2) vaccine (Pfizer, Inc; Philadelphia, Pennsylvania) and Moderna vaccine (ModernaTX, Inc; Cambridge, Massachusetts), with FDA EUA were administered at each site based upon state-directed allocations. By January 11, 2021, all HCP eligible for vaccination under their respective state's public health guidelines had been offered vaccination.

### Data Collection

Employment status, personal demographics, vaccination dates, and SARS-CoV-2 molecular assay results were exported from OHS and Human Resources records. Symptom status at the time of diagnosis was extracted from the index case interviews. Vaccination status at the time of the positive test was arbitrarily defined as unvaccinated (no doses received through 14 days after first dose), partially vaccinated (>14 days from first dose and ≤14 days from second dose), or fully vaccinated (>14 days after second dose). Individuals with a positive molecular assay prior to 1/1/2021 or an inactive employment status were excluded. Because serology results are not routinely available to the employer, we were unable to identify employees with positive serology. Likewise, information on variant strains is not provided to the employer so no analysis of variant strains could be performed. Twenty individuals with missing or mismatched vaccine brands were excluded, along with 264 recipients of Janssen, AstraZeneca, or Sinopharm vaccine. Days 0

through 14 after the first dose were excluded from the final VE analysis. All records were deidentified prior to analysis.

### Statistical Analysis

The number of at-risk days for each employee was defined as any day in the study period prior to a positive test or the end of the observation period for uninfected individuals. We used the incidence rate for unvaccinated employees as a reference. We calculated the crude and adjusted incidence rate ratio (IRR) and exact 95% confidence interval (CI) and defined vaccine effectiveness (VE) as  $1 - \text{IRR}$  (11), analyzing partially vaccinated and fully vaccinated individuals for each vaccine brand separately. We used a generalized linear regression model with robust standard errors in which we assumed the Poisson distribution for the response variable (COVID-19 infection) with a log link considering the natural log of exposure time to be the offset. We adjusted for age, race (white vs. others), gender, and job type (direct patient facing vs no direct patient contact). To account for variation in infection prevalence among various communities, we also adjusted the analysis for geographic location. All statistical analyses were performed using a standard software package (Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC.). This study was approved by the Mayo Clinic Institutional Review Board, IRB#20-003887

### RESULTS

By the end of the study period, 45,162 of 71,152 actively employed HCP without prior COVID-19 infection had received 2 doses of an mRNA COVID-19 vaccine (41,741 Pfizer/BioNTech; 3,421 Moderna), and another 4,058 had received a single dose (2,757 Pfizer/BioNTech; 1,301 Moderna). For the recipients of 2 doses of Pfizer/BioNTech vaccine, the median days between doses was 21 (IQR 21-28); for Moderna vaccine the median days between doses was 28 (IQR 28-30).

The median follow-up was 89 days (mean 80 days, SD 16, IQR 78-89). During the study period, 1,125 HCP tested positive for SARS-CoV-2 by molecular assay, corresponding to an average 2-week

incidence rate of 26.4 per 10,000 across all sites combined. 964 of the newly identified infections were symptomatic at the time of the index case interview, 143 were asymptomatic, and 18 could not be assessed.

The median age in the entire population was 41 years. Compared to unvaccinated individuals, fully vaccinated HCP were older, more likely to be white, Asian, or male, and more likely to have a job with direct patient contact (Table 1). Fully vaccinated individuals were more likely to have had Pfizer/BioNTech than Moderna vaccine compared to partially vaccinated HCP. Among individuals with a positive SARS-CoV-2 test during the study, unvaccinated individuals were more likely to report symptoms.

After adjusting for age, gender, region, job, and week of vaccination, VE for partial and complete vaccination with each of the two available brands of mRNA exceeded 78% and 96%, respectively (Table 1.)

## DISCUSSION

We found an extremely high estimate of vaccine effectiveness in this large cohort of HCP at multiple US sites, with an adjusted VE over 96% for both available brands of mRNA vaccine.

This study adds to the limited evidence that is currently available regarding the impact of the COVID-19 vaccine on asymptomatic SARS-CoV-2 infection. Our results are similar to a large, case-control study that found a 94% reduction in symptomatic infection and 90% reduction in asymptomatic infection 7 or more days after the second dose of the Pfizer/BioNTech vaccine (6). Our VE estimates are higher than those reported by a prospective cohort in UK HCP (7).

Our study is subject to several limitations. The most critical one is the lack of randomization and the likelihood of confounding. Since vaccination was voluntary, unmeasured personal and/or behavioral differences which exist between HCP who opted to take vaccine compared to those who did not may have introduced additional bias. Vaccinated HCP may be more compliant with precautions such as

masking and social distancing which would bias VE upwards. Alternatively, it is also possible that vaccinated individuals may have relaxed other precautions due to lower perceived infection risk, which could bias VE in the opposite direction. Additional confounders that could bias the estimate of VE upwards include the possibility that vaccinated HCP may be less likely to seek testing for minor symptoms, or to report unprotected exposures; and variation of infection intensity over time during the 3 month period of this study. This cohort consists of employed HCP with a median age of 41 years which is considerably younger than the median age of 51 to 53 years among subjects in the phase 3 vaccine trials which may in part explain differences in VE (3, 4). In addition, there were too few asymptomatic infections in this cohort to evaluate how symptom status moderated VE. Maximal immune response to vaccination is attained at different times for the different vaccine formulations, however the number of events (positive cases) was small and did not allow estimation of VE at various intervals.

Vaccination is the single most promising tool to bring about widespread immunity and end the COVID-19 pandemic. Widespread uptake is crucial to achieving herd immunity. In a pandemic-weary society, the ability to discontinue nonpharmacologic control measures such as masking and social distancing may provide strong incentive for people to accept vaccination. Unknowns regarding the impact of vaccination on asymptomatic infection could result in prolonged precautionary measures which could dampen public willingness to receive the vaccine. Our findings provide evidence that mRNA COVID-19 vaccines are highly effective in working adults outside the controlled conditions of clinical trials.

### **Potential Conflicts of Interest**

E.B. reports honoraria from UpToDate, outside the submitted work. A.V. is inventor for Mayo Clinic Travel App interaction with Smart Medical Kit and Medical Kit for Pilgrims. All other authors report no potential conflicts of interest.

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Table 1. SARS-CoV-2 Incidence Rate Ratios by Vaccination Status

	Unvaccinate <sup>d</sup> <sup>a</sup>	Partially Vaccinated <sup>b</sup>	Fully Vaccinated <sup>c</sup>	p-value
	N=23,931	N=3,210	N=44,011	
<b>Demographics</b>				
Age (SD)	40 (12)	46 (14)	44 (13)	<0.001
Male Gender	6,635 (27.7%)	841 (26.2%)	13,700 (31.1%)	<0.001
Direct Patient Contact Job <sup>e</sup>	9,511 (41.3%)	1,381 (44.1%)	29,781 (68.3%)	<0.001
Race/Ethnicity <sup>f</sup>				<0.001
American Indian or Alaska Native	75 (0.4%)	7 (0.2%)	137 (0.3%)	
Asian	1,183 (5.7%)	219 (7.1%)	3,281 (7.7%)	
Black	1,343 (6.5%)	196 (6.4%)	1,025 (2.4%)	
Hispanic	936 (4.5%)	144 (4.7%)	1,720 (4.0%)	
Native Hawaiian or Pacific Islander	27 (0.1%)	3 (0.1%)	36 (0.1%)	
White Non-Hispanic	16,892 (81.2%)	2,449 (79.9%)	35,864 (84.1%)	
Multiracial	323 (1.6%)	41 (1.3%)	481 (1.1%)	
Unknown	33 (0.2%)	7 (0.2%)	122 (0.3%)	
<b>Vaccine Received<sup>g</sup></b>				
Pfizer/BioNTech	1,573 (78.1%)	2,038 (63.6%)	40,887 (92.9%)	<0.001
Moderna	441 (21.9%)	1,166 (36.4%)	3,115 (7.1%)	
<b>New Infection</b>				
	997 (4.2%)	98 (3.1%)	30 (0.1%)	<0.001
<b>Symptomatic Infection<sup>d</sup></b>				
	876 (89.2%)	66 (69.5%)	22 (73.3%)	<0.001
<b>Incidence rate ratio and vaccine effectiveness</b>				
<b>Pfizer/BioNTech COVID Vaccine</b>				
Crude IRR (95% CI)	-	0.237 (0.195, 0.289)	0.036 (0.025, 0.052)	<0.001
Adjusted <sup>h</sup> IRR (95% CI)	-	0.219 (0.180, 0.267)	0.032 (0.022, 0.047)	<0.001
VE (95% CI)	-	0.781 (0.711, 0.820)	0.968 (0.953, 0.978)	

Moderna COVID Vaccine				
Crude IRR (95% CI)	-	0.107 (0.048, 0.237)	0.017 (0.002, 0.123)	<0.001
Adjusted <sup>h</sup> IRR (95% CI)	-	0.088 (0.039, 0.194)	0.014 (0.002, 0.099)	<0.001
VE (95% CI)	-	0.912 (0.806, 0.961)	0.986 (0.901, 0.998)	

Footnotes:

<sup>a</sup>Received no vaccine, or received first dose within 14 days of end of observation period.

<sup>b</sup>More than 14 days from first dose and <=14 days from second dose

<sup>c</sup>More than 14 days from second dose

<sup>d</sup>Reported experiencing any COVID-19 symptom. Ascertained by interview following a positive test.

<sup>e</sup>Job involves direct patient contact (e.g. physician, nurse practitioner, nurse, technician)

<sup>f</sup>Race and ethnicity are stored as a single combined variable in the OHS record

<sup>g</sup>Includes initial doses received within 14 days of the end of the observation period classified as Unvaccinated

<sup>h</sup>Adjusted for age, gender, job type, and geographic location

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