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BRIEF REPORT

Effectiveness of Messenger RNA Coronavirus Disease 2019 (COVID-19) Vaccines Against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection in a Cohort of Healthcare Personnel

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In a large cohort of United States healthcare personnel without prior coronavirus disease 2019 (COVID-19) infection, 94 382 doses of messenger RNA (mRNA) COVID-19 vaccine were administered to 49 220 individuals. The adjusted vaccine effectiveness following 2 doses of each of the 2 available brands of mRNA vaccine exceeded 96%.

Keywords. COVID-19; SARS-CoV-2; vaccine effectiveness; healthcare personnel; mRNA.

Healthcare personnel (HCP) are among the highest-risk workers for coronavirus disease 2019 (COVID-19) [1]. In early December 2020, the Centers for Disease Control and Prevention recommended that HCP be the first occupational group prioritized to receive newly authorized COVID-19 vaccines in the United States (US) [2]. By mid-December, 2 messenger RNA (mRNA) vaccines had received emergency use authorization (EUA) by the US 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 HCP. All actively employed HCP with a positive molecular assay for severe acute respiratory syndrome coronavirus 2 (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 for 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 January 2021 to 31 March 2021. During this timeframe, 2-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, Moderna, Inc, Cambridge, Massachusetts) with FDA EUA were

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administered at each site based upon state-directed allocations. By 11 January 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 January 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 0–14 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 VE as 1 – 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), sex, 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, StataCorp, College Station, Texas). This study was approved by the Mayo Clinic Institutional Review Board (IRB number 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; 3421 Moderna), and another 4058 had received a single dose (2757 Pfizer/BioNTech; 1301 Moderna). For the recipients of 2 doses of Pfizer/BioNTech vaccine, the median time between doses was 21 days (interquartile range [IQR], 21–28 days); for Moderna vaccine, the median time between doses was 28 days (IQR, 28–30 days).

The median follow-up was 89 days (mean, 80 days [standard deviation, 16 days]; IQR, 78–89 days). During the study period, 1125 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. Nine hundred sixty-four 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, sex, region, job, and week of vaccination, VE for partial and complete vaccination with each of the 2 available brands of mRNA vaccine exceeded 78% and 96%, respectively (Table 1).

DISCUSSION

We found an extremely high estimate of VE in this large cohort of HCP at multiple US sites, with an adjusted VE >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 HCP in the United Kingdom [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 that 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 upward. Alternatively, it is also possible that vaccinated individuals may have relaxed other

Table 1. Severe Acute Respiratory Syndrome Coronavirus 2 Incidence Rate Ratios by Vaccination Status

Characteristic	Unvaccinated[a] (n = 23 931)	Partially Vaccinated[b] (n = 3210)	Fully Vaccinated[c] (n = 44 011)	*P* Value
Demographics				
Age, y, mean (SD)	40 (12)	46 (14)	44 (13)	<.001
Male sex	6635 (27.7)	841 (26.2)	13 700 (31.1)	<.001
Direct patient contact job[d]	9511 (41.3)	1381 (44.1)	29 781 (68.3)	<.001
Race/ethnicity[e]				<.001
American Indian/Alaska Native	75 (0.4)	7 (0.2)	137 (0.3)	
Asian	1183 (5.7)	219 (7.1)	3281 (7.7)	
Black	1343 (6.5)	196 (6.4)	1025 (2.4)	
Hispanic	936 (4.5)	144 (4.7)	1720 (4.0)	
Native Hawaiian/Pacific Islander	27 (0.1)	3 (0.1)	36 (0.1)	
White non-Hispanic	16 892 (81.2)	2449 (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)	
Vaccine received[f]				
Pfizer/BioNTech	1573 (78.1)	2038 (63.6)	40 887 (92.9)	<.001
Moderna	441 (21.9)	1166 (36.4)	3115 (7.1)	
New infection	997 (4.2)	98 (3.1)	30 (0.1)	<.001
Symptomatic infection[g]	876 (89.2)	66 (69.5)	22 (73.3)	<.001
IRR and VE				
Pfizer/BioNTech COVID-19 vaccine				
Crude IRR (95% CI)	…	0.237 (.195–.289)	0.036 (.025–.052)	<.001
Adjusted IRR[h] (95% CI)	…	0.219 (.180–.267)	0.032 (.022–.047)	<.001
VE (95% CI)	…	0.781 (.711–.820)	0.968 (.953–.978)	
Moderna COVID-19 vaccine				
Crude IRR (95% CI)	…	0.107 (.048–.237)	0.017 (.002–.123)	<.001
Adjusted IRR[h] (95% CI)	…	0.088 (.039–.194)	0.014 (.002–.099)	<.001
VE (95% CI)	…	0.912 (.806–.961)	0.986 (.901–.998)	

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; IRR, incidence rate ratio; SD, standard deviation; VE, vaccine effectiveness.

[a]Received no vaccine, or received first dose within 14 days of the end of the observation period.

[b]More than 14 days from first dose and ≤14 days from second dose.

[c]More than 14 days from second dose.

[d]Job involves direct patient contact (eg, physician, nurse practitioner, nurse, technician).

[e]Race and ethnicity are stored as a single combined variable in the Occupational Health Services record.

[f]Includes initial doses received within 14 days of the end of the observation period classified as unvaccinated.

[g]Reported experiencing any COVID-19 symptom; ascertained by interview following a positive test.

[h]Adjusted for age, sex, job type, and geographic location.

precautions due to lower perceived infection risk, which could bias VE in the opposite direction. Additional confounders that could bias the estimate of VE upward 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 51–53 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.

Notes

Potential conflicts of interest. E. F. B. reports honoraria from UpToDate, outside the submitted work. A. V. is inventor for the Mayo Clinic Travel App interaction with Smart Medical Kit and Medical Kit for Pilgrims. M. D. S. and M. H. M. received research funding from Pfizer via Duke University for a national vaccine adverse event registry. All other authors report no potential conflicts of interest.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Nguyen LH, Drew DA, Graham MS, et al; Coronavirus Pandemic Epidemiology Consortium. Risk of COVID-19 among front-line health-care workers and the general community: a prospective cohort study. Lancet Public Health **2020**; 5:e475–83.
2. Dooling K. The Advisory Committee on Immunization Practices' interim recommendation for allocating initial supplies of COVID-19 vaccine—United States, 2020. MMWR Morb Mortal Wkly Rep **2020**; 69:1857–59.
3. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med **2020**; 383:2603–15.
4. 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.
5. Amit S, Regev-Yochay G, Afek A, Kreiss Y, Leshem E. Early rate reductions of SARS-CoV-2 infection and COVID-19 in BNT162b2 vaccine recipients. Lancet **2021**; 397:875–7.
6. Dagan N, Barda N, Kepten E, et al. BNT162b2 mRNA Covid-19 vaccine in a nationwide mass vaccination setting. N Engl J Med **2021**; 384:1412–23.
7. Hall VJ, Foulkes S, Saei A, et al. COVID-19 vaccine coverage in health-care workers in England and effectiveness of BNT162b2 mRNA vaccine against infection (SIREN): a prospective, multicentre, cohort study [manuscript published online ahead of print 23 April 2021]. Lancet **2021**. doi:10.1016/S0140-6736(21)00790-X.
8. Breeher L, Boon A, Hainy C, Murad MH, Wittich C, Swift M. A framework for sustainable contact tracing and exposure investigation for large health systems. Mayo Clin Proc **2020**; 95:1432–44.
9. Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. Lancet Infect Dis **2020**; 20:533–4.
10. Swift MD, Sampathkumar P, Breeher LE, Ting HH, Virk A. Mayo Clinic's multidisciplinary approach to Covid-19 vaccine allocation and distribution. NEJM Catal **2021**; 1–9.
11. Chu H, Halloran ME. Bayesian estimation of vaccine efficacy. Clin Trials **2004**; 1:306–14.