Original Article

Symptom monitoring after coronavirus disease 2019 (COVID-19) vaccination in a large integrated healthcare system: Separating symptoms from severe acute respiratory coronavirus virus 2 (SARS-CoV-2) infection

Erica S. Shenoy MD, PhD^{1,2,3,a} , Paige G. Wickner MD, MPH^{3,4,a}, Lauren R. West MPH¹, Aleena Banerji MD⁵, Kimberly G. Blumenthal MD, MSc^{3,5,6}, Amanda J. Centi PhD⁷, Andrew Gottlieb NP⁸, Dean M. Hashimoto MD^{3,4,8}, Esther Kim ScD⁷, Marvel Kim MBA⁸, Hang Lee PhD^{3,9}, Lynn A. Simpson MPH, CCDM¹⁰ and Adam B. Landman MD^{3,7,11}

¹Infection Control Unit, Massachusetts General Hospital, Boston, Massachusetts, ²Division of Infectious Diseases, Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts, ³Harvard Medical School, Boston, Massachusetts, ⁴Department of Medicine, Brigham & Women's Hospital, Boston, Massachusetts, ⁵Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts, ⁶The Mongan Institute, Massachusetts General Hospital, Boston, Massachusetts, ⁷Enterprise Data and Digital Health, Mass General Brigham, Boston, Massachusetts, ⁸Occupational Health Services, Mass General Brigham, Boston, Massachusetts, ⁹Biostatistics Center, Massachusetts General Hospital, Boston, Massachusetts, ¹⁰Research Information Science and Computing, Massachusetts General Brigham, Boston, Massachusetts and ¹¹Department of Emergency Medicine, Brigham & Women's Hospital, Boston, Massachusetts

Abstract

Objective: To describe the incidence of systemic overlap and typical coronavirus disease 2019 (COVID-19) symptoms in healthcare personnel (HCP) following COVID-19 vaccination and association of reported symptoms with diagnosis of severe acute respiratory coronavirus virus 2 (SARS-CoV-2) infection in the context of public health recommendations regarding work exclusion.

Design: This prospective cohort study was conducted between December 16, 2020, and March 14, 2021, with HCP who had received at least 1 dose of either the Pfizer-BioNTech or Moderna COVID-19 vaccine.

Setting: Large healthcare system in New England.

Interventions: HCP were prompted to complete a symptom survey for 3 days after each vaccination. Reported symptoms generated automated guidance regarding symptom management, SARS-CoV-2 testing requirements, and work restrictions. Overlap symptoms (ie, fever, fatigue, myalgias, arthralgias, or headache) were categorized as either lower or higher severity. Typical COVID-19 symptoms included sore throat, cough, nasal congestion or rhinorrhea, shortness of breath, ageusia and anosmia.

Results: Among 64,187 HCP, a postvaccination electronic survey had response rates of 83% after dose 1 and 77% after dose 2. Report of ≥ 3 lower-severity overlap symptoms, ≥ 1 higher-severity overlap symptoms, or at least 1 typical COVID-19 symptom after dose 1 was associated with increased likelihood of testing positive. HCP with prior COVID-19 infection were significantly more likely to report severe overlap symptoms after dose 1.

Conclusions: Reported overlap symptoms were common; however, only report of ≥ 3 low-severity overlap symptoms, at least 1 higher-severity overlap symptom, or any typical COVID-19 symptom were associated with infection. Work-related restrictions for overlap symptoms should be reconsidered.

(Received 5 July 2021; accepted 4 October 2021)

Vaccination with currently available vaccines for coronavirus disease 2019 (COVID-19) was associated in clinical trials with substantial local and systemic side effects.^{1,2} Overlap symptoms including fever, headache, fatigue, myalgias, or arthralgias, which

may indicate vaccine reactogenicity or infection with severe acute respiratory coronavirus virus 2 (SARS-CoV-2), present distinct challenges for workforce preservation for healthcare facilities that routinely restrict healthcare personnel (HCP) from working with any symptom consistent with SARS-CoV-2 in accordance with public health guidance.^{3,4} Mass General Brigham (MGB), a large integrated healthcare system and the largest employer in Massachusetts (with >87,000 employees) began vaccination of healthcare personnel (HCP) on December 16, 2020. To support evaluation and management of postvaccination reactions and

Author for correspondence: Erica S. Shenoy, E-mail: eshenoy@mgh.harvard.edu

^aAuthors of equal contribution.

Cite this article: Shenoy ES, et al. (2021). Symptom monitoring after coronavirus disease 2019 (COVID-19) vaccination in a large integrated healthcare system: Separating symptoms from severe acute respiratory coronavirus virus 2 (SARS-CoV-2) infection. *Infection Control & Hospital Epidemiology*, <https://doi.org/10.1017/ice.2021.449>

symptoms, MGB developed a policy aligned with guidance from the Centers for Disease Control and Prevention (CDC)⁵ and the Massachusetts Department of Public Health (MDPH)⁶ to categorize and manage post-vaccination systemic overlap symptoms. To provide decision support for HCP postvaccination, HCP were actively surveyed in the 3 days after vaccination to categorize post-vaccination symptoms and to provide guidance to HCP regarding management and exclusion from work when required.

We describe postvaccination survey compliance, reported systemic overlap symptoms as well as typical COVID-19 symptoms, and results of SARS-CoV-2 testing. We assessed differences in outcomes across HCP demographic characteristics as well as prior known infection with SARS-CoV-2. We additionally report on approaches to implementing this strategy in employees with limited computer skills as well as those with limited English proficiency and access to ensure equity in implementation.

Methods

Study setting and design

The Mass General Brigham (MGB) system is a large, integrated healthcare network operating in Massachusetts and New Hampshire with >87,000 HCP. Vaccination of HCP began across the MGB system on December 16, 2020, initially with Pfizer-BioNTech vaccine and the following week with the Moderna COVID-19 vaccine. The Employee COVID-19 Vaccination Program operated 13 clinics across the enterprise and was completed on March 14, 2021. All 13 clinics followed the same MGB procedures and policies for HCP vaccination. After this time, HCP requesting vaccination were directed to patient vaccination clinics, and they were not included in this analysis. The Johnson & Johnson/Janssen COVID-19 vaccine was introduced in limited supply on March 4, 2021; the results for HCP vaccinated with this product were excluded from the analysis. The activities studied here were considered routine infection control and occupational health procedures and not human subjects research by the Massachusetts General Brigham Institutional Review Board.

COVID-19 employee vaccination policy

The Centers for Disease Control and Prevention (CDC) and the Massachusetts Department of Public Health (MDPH) recommendations for HCP restrictions from work after vaccination base testing and exclusion from work on the type and severity of symptoms experienced after vaccination.^{5,6} The MGB employee vaccination policy described postvaccination symptoms and requirements for employees experiencing those symptoms with respect to testing for SARS-CoV-2 and return to work restrictions. “Overlap” symptoms included fever, fatigue, myalgias, arthralgias, or headache. “Typical” COVID-19 symptoms included sore throat, cough, nasal congestion or rhinorrhea, shortness of breath, and anosmia or ageusia. Over the course of the study period, modifications to the policy were made, some of which affected the categorization of severity of overlap symptoms as well as requirements for SARS-CoV-2 testing. Relevant to the current study, between December 16, 2020, and December 31, 2021, employees experiencing mild overlap symptoms for any period after vaccination were referred for testing but could continue to work on site. After January 1, 2021, employees experiencing mild overlap symptoms after vaccination were only referred for testing if the symptom duration exceeded 24 hours in total. After January 21, 2021, the mild overlap symptom category was expanded to describe mild-

to-moderate overlap symptoms, separating those from severe post-vaccination overlap symptoms. Also, the temperature cutoff between mild-to-moderate versus severe fever was increased from $\geq 37.7^{\circ}\text{C}$ (100°F) to $\geq 38.3^{\circ}\text{C}$ (101°F) to align with MDPH guidance. To compare responses across the entire period, overlap symptoms were grouped into “lower severity,” which included mild and mild-to-moderate symptoms, and “higher severity,” which included severe symptoms, across the study period to reflect the relative categorization of overlap symptoms. Typical COVID-19 symptoms were consistent throughout the study period.

Data collection

Survey instrument

Study data were collected and managed using REDCap (Research Electronic Data Capture) tools hosted at MGB.^{7,8} The survey utilized REDCap standard features as well as the Shazam External Module to customize code to display return-to-work guidance on the survey completion screen based on the symptoms entered by the employee. The REDCap application programming interface (API) was used to import daily information about the previous day’s employee vaccination records from the MGB electronic data warehouse. The REDCap Alerts & Notifications module with conditional logic was used to automatically e-mail HCP 3 daily surveys after their vaccination date(s) and to provide their return-to-work guidance after survey completion. For HCP without access to e-mail, they could access the website Mass General Brigham Vaccine Check (<https://redcap.partners.org/redcap/surveys/?s=L8R3KFWJ88>) to enter vaccination survey data. The survey continued through March 18, 2021, after which HCP were instructed to refer to a handout describing postvaccination symptoms and reactions management and return-to-work policy (Supplementary Material A online).

Compliance was defined as response of at least 1 survey within 3 days of a vaccine administration and required completion of all components of the survey.

Employee handout

At the time of vaccination, in addition to providing information on the Centers for Disease Control and Prevention V-Safe program,⁹ employees were provided a postvaccination employee “tip sheet.” The tip sheet was created to describe possible postvaccination reactions and symptoms and requirements with respect to testing and on-site work restrictions, and support implementation of the policy (Supplementary Material B online). The tip sheet was translated into 6 languages.

Use of navigators

Beginning December 30, 2020, a phone-based navigator program was initiated to increase the participation of HCP with limited or no computer access, who required assistance with completing the survey in another language, or who had not completed their day 1 survey and worked among a subset of departments where access to the survey was considered at risk. Details on the implementation of the navigator program are provided (Supplementary Material C online).

Measurements

Employee characteristics and SARS-CoV-2 test results

Basic demographic data on employees (ie, age, sex, race, primary language, ethnicity, job title, job group description, employee job group, facility) were obtained from internal human resources databases and were linked to vaccination date and time and brand of

vaccine. Employee role groups, including administrative, clinical, other, research, and support services, were created by mapping 36 job titles and group descriptions to these 5 role groups. Employee SARS-CoV-2 testing results obtained within the MGB system and infection statuses maintained in the electronic health record (EHR) by MGB Occupational Health Services (OHS) were identified. The infection status was utilized because some SARS-CoV-2 testing was performed outside the MGB system and was entered manually into the EHR prompting the appropriate infection status when positive for SARS-CoV-2. Employee test results, infection statuses, and REDCap survey responses were linked.

Testing for SARS-CoV-2 and determination of SARS-CoV-2 infection in the postvaccination period

During the study period, employees could obtain testing through standard MGB pathways: when symptomatic, asymptomatic with exposures, when asymptomatic all other reasons, and when referred by their responses to the survey. The various MGB testing sites used a variety of nucleic acid amplification tests (NAATs) approved by the FDA (Supplementary Material D online). Antigen testing was reserved for public health-directed testing at 2 MGB sites including 1 rehabilitation center and a community health center; however, only NAAT results were included in this analysis. When tested outside the MGB system, OHS entered external results in a protocolized manner that allowed these results to be identified through the EHR extract. Compliance with testing requirements and restrictions from work were the responsibility of the employee. If, however, the employee reported any high-severity symptom or any typical COVID-19 symptom, he or she was instructed to remain away from work and to obtain testing. Test orders were simplified through a mobile application (COVID Pass, Mass General Brigham Information Systems, Boston, MA).¹⁰

Each positive SARS-CoV-2 assay was followed up by MGB OHS as part of contact tracing and employee counseling. For employees with prior infection with SARS-CoV-2, MGB criteria to determine whether the positive test represented active infection or a persistent positive from remote infection was applied independently by 2 authors (A.G. and E.S.S.) with concordance and no requirement for adjudication.

Outcomes

Outcomes assessed included survey compliance, reported lower- and higher-severity overlap symptoms and typical COVID-19 symptoms, and SARS-CoV-2 testing that occurred within 7 days after vaccination. Although the survey was used in the 3 days after vaccination, 7 days after each vaccination was chosen to allow for time to schedule and obtain testing based on symptoms occurring on day 3 after vaccination.

Evaluation and management of allergic symptoms after vaccination, which were included in the prospective surveillance strategy, have been reported previously, and they are not included in this analysis.^{11,12}

Statistical analysis

Categorical outcomes of demographic characteristics, reported symptoms, and testing outcomes among HCP were summarized by counts and proportions (%). Age distributions were compared using the Wilcoxon rank-sum test. We compared frequencies using the Pearson χ^2 test. All tests were 2-sided, and $P < .05$ was considered statistically significant. Multivariable logistic regression was applied to assess the association of demographic

Table 1. Selected Characteristics of Mass General Brigham Healthcare Personnel Receiving COVID-19 Vaccination, By Survey Compliance

Characteristic	Nonresponder (N = 8,095), No. (%) ^a	Responder (N = 56,092), No. (%) ^a	P Value ^b
Age, median y (IQR)	40 (29–55)	40 (30–54)	.63
Sex			<.001
Female	5,359 (66.2)	40,531 (72.3)	
Male	2,736 (33.8)	15,561 (27.7)	
Race			<.001
White	4,246 (52.5)	37,090 (66.1)	
Asian	643 (7.9)	5,097 (9.1)	
Black	910 (11.2)	2,979 (5.3)	
Other	612 (7.6)	2,510 (4.5)	
≥2	76 (0.9)	590 (1.1)	
Unknown	1,608 (19.9)	7,826 (14.0)	
Primary language			<.001
English	6,327 (78.2)	48,893 (87.2)	
Non-English	414 (5.1)	933 (1.7)	
Unknown	1,354 (16.7)	6,266 (11.2)	
Ethnicity			<.001
Non-Hispanic	4,824 (59.6)	38,155 (68.0)	
Hispanic	693 (8.6)	2,860 (5.1)	
Unknown	2,578 (31.8)	15,077 (26.9)	
Employee role group			<.001
Administrative	807 (10.0)	10,378 (18.5)	
Clinical	4,240 (52.4)	34,846 (62.1)	
Other	1,595 (19.7)	2,730 (4.9)	
Research	374 (4.6)	4,160 (7.4)	
Support services	1,079 (13.3)	3,978 (7.1)	

^aUnless otherwise stated. ^bWilcoxon rank-sum test; Pearson χ^2 test.

characteristics, vaccine manufacturer, and test results with reported symptom severity and type. Analyses were conducted in R version 4.0.5 software.^{13–15} The Pfizer-BioNTech vaccine was used as the referent vaccine in these analyses because it was the first vaccine introduced to the MGB employee population.

Results

Employee characteristics and survey response

In total, 64,187 employees received 1 or more doses of vaccine during the study period. Survey compliance was 83% (53,270 of 64,187) for dose 1 and 77% (48,550 of 62,846) for dose 2. There were 8,095 nonrespondents.

Respondents and nonrespondents did not differ by age. Compared to respondents, nonrespondents were more often male, non-White, non-English speaking, Hispanic or unknown ethnicity, and within other or support services roles as opposed to administrative, clinical, or research roles (Table 1).

Use of navigator

From December 30, 2020, through March 19, 2021, 2,193 employees were contacted by the navigator team via phone to complete the

Table 2. Reported Overlap Symptoms, by Severity, and Typical COVID-19 Symptoms, within 3 days of Dose 1 and Dose 2

Characteristic	Dose 1 (N = 53,270), No. (%)	Dose 2 (N = 48,550), No. (%)
Overlap symptoms		
Fever		
None	49,324 (92.6)	31,883 (65.7)
Lower severity	3,392 (6.4)	13,231 (27.3)
Higher severity	554 (1.0)	3,436 (7.1)
Fatigue		
None	35,146 (66.0)	17,288 (35.6)
Lower severity	16,790 (31.5)	26,435 (54.4)
Higher severity	1,334 (2.5)	4,827 (9.9)
Myalgias		
None	44,035 (82.7)	25,942 (53.4)
Lower severity	8,470 (15.9)	19,165 (39.5)
Higher severity	765 (1.4)	3,443 (7.1)
Arthralgias		
None	46,218 (86.8)	29,944 (61.7)
Lower severity	6,543 (12.3)	15,798 (32.5)
Higher severity	509 (1.0)	2,808 (5.8)
Headache		
None	39,504 (74.2)	23,270 (47.9)
Lower severity	12,919 (24.3)	22,236 (45.8)
Higher severity	847 (1.6)	3,044 (6.3)
Typical COVID-19 symptoms		
Sore throat	1,110 (2.1)	1,300 (2.7)
New cough	411 (0.8)	506 (1.0)
New nasal congestion or rhinorrhea	2,034 (3.8)	2,447 (5.0)
Shortness of breath	244 (0.5)	466 (1.0)
New loss of taste or smell	80 (0.2)	130 (0.3)

survey. In total, 1,795 employees completed 2,456 surveys. Overall, 893 surveys were completed prior to outreach from navigators. The navigators made an additional 3,620 calls with no response. Additionally, between January 19, 2021, and March 19, 2021, 183 employees consented to receiving the survey by text during manual scheduling of their first vaccination dose and 169 provided valid mobile numbers for outreach. In total, 547 surveys were completed via a texted link, and 135 respondents (80%) completed at least 1 of the 6 surveys.

Reported symptoms: Lower- and higher-severity overlap symptoms and typical COVID-19 symptoms

The frequency and percentage of reported symptoms, by dose, is reported in Table 2. Among respondents, reported overlap symptoms of any severity were more common after dose 2 than after dose 1. The proportion of respondents with higher severity overlap symptoms increased several fold after dose 2 across all overlap symptoms. Self-reported typical COVID-19 symptoms of sore throat, cough, nasal congestion or rhinorrhea, shortness of breath, and anosmia or ageusia, which would not be expected to be

associated with vaccine administration, were similar after dose 1 and dose 2 (Table 2).

History of infection with SARS-CoV-2 prior to vaccination (adjusted odds ratio [aOR], 5.61; 95% confidence interval [CI], 5.01–6.27) was associated with self-reported higher-severity overlap symptoms after dose 1; however, history of infection was not associated with an increase in higher-severity overlap symptoms after dose 2 (aOR, 0.83; 95% CI, 0.74–0.93). Severity of reported symptoms after both dose 1 and dose 2 decreased with age. Non-white race and Hispanic ethnicity were both associated with report of higher-severity symptoms (Table 3).

Testing and testing outcomes

Among 3,208 respondents after dose 1 tested for SARS-CoV-2 within 7 days of dose 1, 162 (5.0%) were positive; this corresponded to 162 (0.3%) of all 53,270 respondents after dose 1. Of 7,039 respondents tested for SARS-CoV-2 within 7 days of dose 2, 23 (.33%) were positive. These results corresponded to 23 (0.05%) of 48,550 of all respondents being positive after dose 2. Of the 10,917 nonrespondents after dose 1, 33 (11.0%) new infections of 300 tested were identified, and of the 14,296 nonrespondents after dose 2, and 7 (1.1%) new infections of 620 tested were identified. These results corresponded to 33 (0.3%) of 10,917 of all nonrespondents being positive after dose 1 and 7 (0.05%) of 14,296 of all nonrespondents being positive after dose 2 (data not shown).

Testing after self-reported symptoms

After dose 1, the percent positivity was 4.6% for those reporting either lower- or higher-severity overlap symptoms. Percent positivity for HCP reporting typical COVID-19 symptoms ranged from 6.6% to 51.5%, depending on specific symptom.

After dose 2, the percent positivity was 0.5% for self-reported lower-severity symptoms and 0.2% for self-reported higher-severity symptoms. Percent positivity was between 0.0% and 1.4% among those reporting typical COVID-19 symptoms, depending on the specific symptom (Table 4).

Association of symptom type, number of symptoms, and other factors with infection after vaccination

Self-reporting of 1 typical or ≥ 2 typical COVID-19 symptoms was associated with increased likelihood of testing positive: for 1 typical symptom, aOR, 6.85 (95% CI, 4.59–10.1) after dose 1 and aOR, 6.72 (95% CI, 2.41–17.4) after dose 2, and for ≥ 2 typical COVID-19 symptoms, aOR, 19.0 (95% CI, 11.7–30.2) after dose 1 and aOR, 7.72 (95% CI, 1.15–30.8) after dose 2. Sex and ethnicity were not associated with diagnosis of infection (Table 5). Black and unknown race and research role groups were less likely to be associated with infection after dose 1 but not after dose 2.

Discussion

In this prospective cohort of HCP vaccinated with mRNA vaccines, postvaccination symptom survey compliance was high; however, despite efforts to address potential technological and language barriers, response rates varied by sex, race, primary language, ethnicity, and employee role group. The incidence of overlap systemic symptoms including fever, fatigue, myalgias, arthralgias, and headache was similar to those reported in clinical trials for both vaccines, and systemic symptoms were more prominent after dose 2 than after dose 1.^{16,17} Reported higher-severity overlap symptoms and typical COVID-19 symptoms were predictive of

Table 3. Factors Associated With Reported Higher Severity Symptoms After Dose 1 and Dose 2

Characteristic	Dose 1			Dose 2		
	OR	95% CI	P Value	OR	95% CI	P Value
History of COVID-19 prior to vaccine	5.61	5.01, 6.27	<.001	0.83	0.74, 0.93	.002
Vaccine manufacturer						
Pfizer	Ref			Ref		
Moderna	1.53	1.41, 1.67	<.001	2.82	2.68, 2.97	<.001
Age, y						
16–24	Ref			Ref		
25–39	0.86	0.76, 0.97	.015	0.92	0.85, 1.00	.037
40–64	0.60	0.53, 0.68	<.001	0.65	0.60, 0.70	<.001
≥65	0.32	0.24, 0.41	<.001	0.43	0.37, 0.49	<.001
Sex						
Female	Ref			Ref		
Male	0.52	0.47, 0.58	<.001	0.61	0.58, 0.65	<.001
Race						
White	Ref			Ref		
Asian	1.18	1.02, 1.35	.021	1.27	1.17, 1.37	<.001
Black	1.28	1.09, 1.51	.003	0.98	0.88, 1.10	.8
Other	1.26	1.03, 1.55	.024	1.20	1.05, 1.37	.007
≥2	0.91	0.61, 1.32	.60	1.05	0.83, 1.30	.7
Unknown	1.30	1.13, 1.49	<.001	1.02	0.94, 1.11	.6
Ethnicity						
Non-Hispanic	Ref			Ref		
Hispanic	1.42	1.17, 1.70	<.001	1.17	1.03, 1.33	.014
Unknown	0.78	0.69, 0.87	<.001	0.92	0.86, 0.98	.007

Note. OR, odds ratio; CI, confidence interval; Ref, referent. There were 53,270 survey responses after vaccine dose 1, and 48,550 survey responses after vaccine dose 2.

Table 4. Reported Overlap and Typical COVID-19 Symptoms, by Testing Outcomes and Vaccine Dose

Characteristic	Overlap Symptoms		Typical COVID-19 Symptoms				
	Lower Severity	Higher Severity	New Cough	Sore Throat	New Nasal Congestion	Shortness of Breath	New Loss of Taste or Smell
Dose 1							
Total	23,398	2,793	411	1,110	2,034	244	80
Dose 1: Tested	1,615 (6.9)	856 (30.6)	159 (38.7)	391 (35.2)	617 (30.3)	70 (28.7)	33 (41.2)
Dose 1: New positive	75 (4.6)	39 (4.6)	23 (14.5)	26 (6.6)	50 (8.1)	5 (7.1)	17 (51.5)
Dose 2							
Total	27,341	9,533	506	1,300	2,447	466	130
Dose 2: Tested	2,822 (10.3)	3,727 (39.1)	217 (42.9)	536 (41.2)	870 (35.6)	175 (37.6)	58 (44.6)
Dose 2: New positive	13 (0.5)	6 (0.2)	3 (1.4)	2 (0.4)	7 (0.8)	0 (0.0)	0 (0.0)

Note: Only respondents reporting symptoms are included in this analysis; individuals may contribute to testing outcomes multiple times if they report >1 symptom.

infection with SARS-CoV-2; however, lower-severity overlap symptoms were only associated with infection after dose 1 when ≥3 symptoms were present. Prior infection with SARS-CoV-2 was associated with report of increased higher severity systemic symptoms after dose 1. Among HCP, new infections were rare, and identified in 0.30% and 0.05% after dose 1 and dose 2, respectively.

Among those respondents who were tested within 7 days of vaccination, only those reporting multiple lower severity systemic overlap symptoms, at least 1 higher-severity overlap symptom, or typical COVID-19 symptoms were associated with test positivity after dose 1, and only typical COVID-19 symptoms were associated with test positivity after dose 2. This finding suggests that public health authorities and healthcare facilities can consider less

Table 5. Reported Symptom Type, Number, and Other Factors Associated with Diagnosis of COVID-19 Infection within 7 days of vaccination

Characteristic	Dose 1			Dose 2		
	OR	95% CI	P Value	OR	95% CI	P Value
No. of typical COVID-19 symptoms						
None	Ref			Ref		
1	6.85	4.59–10.1	<.001	6.72	2.41–17.4	<.001
2 or more	19.0	11.7–30.2	<.001	7.72	1.15–30.8	.010
Overlap symptoms						
None	Ref			Ref		
Lower severity symptoms (1 or 2)	0.93	0.61–1.43	.80	0.59	0.12–2.70	.50
Lower severity symptoms (≥ 3)	1.84	1.14–2.93	.011	1.42	0.44–5.41	.60
Any higher severity symptom	2.88	1.77–4.65	<.001	0.90	0.22–3.88	.90
Age, y						
16–24	Ref			Ref		
25–39	0.60	0.38–1.00	.041	1.11	0.28–7.50	.90
40–64	0.48	0.30–0.81	.005	0.78	0.19–5.38	.80
≥ 65	0.21	0.05–0.61	.011	1.56	0.18–13.9	.70
Sex						
Female	Ref			Ref		
Male	0.88	0.58–1.31	.50	0.67	0.21–1.77	.50
Race						
White	Ref			ref		
Asian	0.56	0.27–1.02	.082	0.92	0.14–3.32	>.90
Black	0.35	0.11–0.85	.042	0.78	0.04–3.92	.80
Other	1.59	0.76–3.13	.20	1.00	0.11–6.04	>.90
≥ 2	0.49	0.03–2.26	.50	3.17	0.17–17.3	.30
Unknown	0.49	0.24–0.92	.033	0.21	0.01–1.25	.20
Ethnicity						
Non-Hispanic	Ref			Ref		
Hispanic	0.92	0.43–1.85	.80	2.36	0.36–10.4	.30
Unknown	1.01	0.63–1.55	>.90	1.74	0.58–4.53	.30
Employee role group						
Administrative	Ref			Ref		
Clinical	1.06	0.72–1.61	.80	1.02	0.36–3.66	>.90
Other	0.35	0.08–0.98	.082	2.19	0.30–11.5	.40
Research	0.39	0.14–0.91	.044	0.61	0.03–4.44	.70
Support services	0.87	0.38–1.80	.70	2.44	0.46–11.7	.30

Note. OR, odds ratio; CI, confidence interval; Ref, referent. There were 53,270 survey responses after vaccine dose 1, and 48,550 survey responses after vaccine dose 2.

restrictive policies related to postvaccination overlap symptoms and possibly only exclude HCP from work after dose 2 for typical COVID-19 symptoms. If booster doses are necessary, and overlap symptoms are similar or more pronounced than current dose 2 symptoms, a less restrictive policy may be necessary to ensure adequate staffing.

Given the effectiveness of the mRNA vaccines at preventing both symptomatic and asymptomatic infection,^{3,4,18–25} the utility of postvaccination testing for SARS-CoV-2 systemic symptoms within 7 days of receipt of vaccine is questionable, especially in the setting of declining community prevalence. The 7-day weighted average of percent positive molecular assays in

Massachusetts during the study period ranged from 1.8% to 8.7%.²⁶ In settings with lower community prevalence, the likelihood of overlap symptoms representing infection would be expected to be even lower. As we look ahead to potential booster strategies, especially in the setting of overall reduced community prevalence, policies related to HCP exclusion from work for non-typical COVID-19 symptoms are likely to be overly conservative and should be reconsidered. Others have reported on more severe postvaccination symptoms in individuals with prior history of infection,^{27–29} a pattern confirmed in the current study.

The study had several limitations. The voluntary nature of the survey and self-reporting of symptoms may have introduced bias

in the results. Some HCP may have been reluctant to report symptoms or severity of symptoms if doing so would prompt either recommendation for testing or exclusion from work, or both. Although testing was performed at no cost to employees and was accessible¹⁰ and time off for testing was supported by flexible human resources policies, HCP may have minimized or underreported symptoms. HCP completing the web-based survey, once submitted, were unable to modify their answers and thus if they inadvertently entered incorrect responses, these could not be corrected. Testing for SARS-CoV-2, when indicated based on survey responses, was not completed for a substantial portion of those reporting symptoms that required testing, and in some cases, exclusion from work pending the test result. The study population consisted of HCP from a single healthcare system; thus, these findings may not be generalizable to other workforces.

In summary, in this large prospective cohort of HCP receiving COVID-19 vaccination, compliance with postvaccination surveys was high and self-reported symptoms were common, especially after dose 2. More research is needed to better understand the reasons for more prominent reported symptoms among individuals with prior history of COVID-19. Return-to-work policies that exclude or require SARS-CoV-2 testing of HCP who report post-vaccination overlap symptoms, especially in the setting of prior infection or after dose 2, should be re-examined. Specifically, public health guidance and facility policies should recognize the low risk of infection in HCP reporting limited mild-to-moderate-severity overlap symptoms including fever. The risk is likely to be even lower in the setting of additional doses beyond the primary vaccination series. Such guidance and policies would serve to both preserve workforce capacity at a time when healthcare facilities are challenged by chronic understaffing with superimposed pandemic demands^{30,31} and would reduce the unnecessary burden of testing and work disruption to HCP.

Supplementary material. To view supplementary material for this article, please visit <https://doi.org/10.1017/ice.2021.449>

Acknowledgments. The authors thank David C. Hooper, MD, for his thoughtful review and comment on the manuscript; the staff of the Mass General Brigham OHS for support of the MGB Employee COVID-19 vaccination program; the MGB Digital Care Transformation (DCT) group for assistance with patient outreach including Samuel Aronson, MD, Ivonne L. Bennett-King, BSc, Jo Charles, MPH, Karen Choe, BS, Eugene Clark, Christian Figueroa, BS, Polovna Laine, MM, Marian McPartlin, Mike Oates, Nina Pappacostas, BS, Noheli Romero, BA, Tabitha V. Rutkowski, BA, and Michela Tucci, BA, Dimitar Dimitrov, MSSE, and Eduardo Morales, PhD, for their assistance with REDCap programming that automated data workflows and returned custom workplace guidance; Michael C. Pandolfi for guidance on data extracts to support the project; and Thomas D. Sequist, MD, and Rosemary R. Sheehan, MBA, for their support of the employee vaccination program. The content is solely the responsibility of the authors and does not necessarily represent the official views of Harvard Catalyst, Harvard University and its affiliated academic healthcare centers, or the National Institutes of Health.

Financial support. This work was supported by the Roger I. and Ruth B. MacFarlane Foundation (to E.S.S.). This study was conducted with support from Harvard Catalyst, The Harvard Clinical and Translational Science Center (National Center for Advancing Translational Sciences, National Institutes of Health award no. 1TR002541) and financial contributions from Harvard University and its affiliated academic healthcare centers (to H.L.).

Conflicts of interest. Dr Paige Wickner began dual employment at CVS Health and Brigham and Women's Hospital in May 2021. Dr Adam Landman was previously a consultant for the Abbott Medical Device Cybersecurity Council.

References

1. Oliver SE, Gargano JW, Marin M, *et al.* The Advisory Committee on Immunization Practices' interim recommendation for use of Moderna COVID-19 vaccine—United States, December 2020. *Morb Mortal Wkly Rep* 2021;69:1653–1656.
2. Oliver SE, Gargano JW, Marin M, *et al.* The Advisory Committee on Immunization Practices' interim recommendation for use of Pfizer-BioNTech COVID-19 vaccine—United States, December 2020. *Morb Mortal Wkly Rep* 2020;69:1922–1924.
3. Polack FP, Thomas SJ, Kitchin N, *et al.* Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. *N Engl J Med* 2020;383:2603–2615.
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;384:403–416.
5. Postvaccine considerations for healthcare personnel. Centers for Disease Control and Prevention website. https://www.cdc.gov/coronavirus/2019-ncov/community/workplaces-businesses/?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fhcp%2Fpost-vaccine-considerations-healthcare-personnel.html. Published 2020. Accessed December 16, 2020.
6. Considerations for healthcare personnel after COVID-19 vaccination. Massachusetts Department of Public Health website. <https://www.mass.gov/doc/considerations-for-health-care-personnel-after-covid-19-vaccination/download>. Published 2020. Accessed December 16, 2020.
7. Harris PA, Taylor R, Minor BL, *et al.* The REDCap consortium: building an international community of software platform partners. *J Biomed Informat* 2019;95:103208.
8. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Informat* 2009;42:377–381.
9. V-safe after vaccination health checker. Centers for Disease Control and Prevention website. <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/vsafe.html>. Accessed April 19, 2021.
10. Zhang H, Dimitrov D, Simpson L, *et al.* A web-based, mobile-responsive application to screen healthcare workers for COVID-19 symptoms: rapid design, deployment, and usage. *JMIR Form Res* 2020;4:e19533.
11. Blumenthal KG, Robinson LB, Camargo CA Jr, *et al.* Acute allergic reactions to mRNA COVID-19 vaccines. *JAMA* 2021;325:1562–1565.
12. Blumenthal KG, Freeman EE, Saff RR, *et al.* Delayed large local reactions to mRNA-1273 vaccine against SARS-CoV-2. *N Engl J Med* 2021;384:1273–1277.
13. Dowle MS. data.table: extension of data.frame. R package version 1.14.0., 2021. <https://CRAN.R-project.org/package=data.table>.
14. Sjoberg DC, M Hannum, M Whiting, K Zabor, EC. gtsummary: presentation-ready data summary and analytic result tables, R package version 1.3.7. 2021. <https://CRAN.R-project.org/package=gtsummary>. Accessed April 19, 2021.
15. R Core Team. R: a language and environment for statistical computing. <https://www.R-project.org/>. Accessed April 19, 2021.
16. Local reactions, systemic reactions, adverse events, and serious adverse events: Pfizer-BioNTech COVID-19 vaccine. Centers for Disease Control and Prevention website. <https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/reactogenicity.html>. Accessed April 19, 2021.
17. Local reactions, systemic reactions, adverse events, and serious adverse events: Moderna COVID-19 vaccine. Centers for Disease Control and Prevention website. <https://www.cdc.gov/vaccines/covid-19/info-by-product/moderna/reactogenicity.html>. Accessed April 19, 2021.
18. Hall VJ, Foulkes S, Saei A, *et al.* Effectiveness of BNT162b2 mRNA vaccine against infection and COVID-19 vaccine coverage in healthcare workers in England, multicentre prospective cohort study (the SIREN Study). *Lancet* 2021 8;397:1725–1735.
19. Pawlowski C, Lenehan P, Puranik A, *et al.* FDA-authorized mRNA COVID-19 vaccines are effective per real-world evidence synthesized across a multi-state health system. *Med (N Y)* 2021;2:979–992.
20. Thompson MG, Burgess JL, Naleway AL, *et al.* Interim estimates of vaccine effectiveness of BNT162b2 and mRNA-1273 COVID-19 vaccines in preventing SARS-CoV-2 infection among healthcare personnel, first

- responders, and other essential and frontline workers—eight US locations, December 2020–March 2021. *Morbidity and Mortality Weekly Report* 2021;70:495.
21. Moderna COVID-19 vaccine. Vaccines and Related Biological Products Advisory Committee December 17, 2020, meeting briefing document addendum- sponsor. Food and Drug Administration website. <https://www.fda.gov/media/144453/>. Published 2020. Accessed October 13, 2021.
 22. Moderna COVID-19 vaccine. Vaccines and Related Biological Products Advisory Committee December 17, 2020, meeting briefing document- sponsor, 2020. Food and Drug Administration website. <https://www.fda.gov/media/144452/>. Published 2020. Accessed October 13, 2021.
 23. Pfizer-BioNTech COVID-19 vaccine. Vaccines and Related Biological Products Advisory Committee briefing document – sponsor. Food and Drug Administration website. <https://www.fda.gov/media/144246/>. Published 2020. Accessed October 13, 2021.
 24. Janssen COVID-19 vaccine. Vaccines and Related Biological Products Advisory Committee February 26, 2021, meeting briefing document – sponsor. Food and Drug Administration website. <https://www.fda.gov/media/146219/>. Published 2021. Accessed October 13, 2021.
 25. Janssen COVID-19 vaccine. Vaccines and Related Biological Products Advisory Committee, February 26, 2021, meeting briefing document addendum – sponsor. 2021. Food and Drug Administration website. <https://www.fda.gov/media/146218/>. Published 2021. Accessed October 13, 2021.
 26. COVID-19 dashboard. Massachusetts Department of Public Health Bureau of Infectious Diseases and Laboratory Sciences and the Registry of Vital Records and Statistics, Office of Integrated Surveillance and Informatics Services. State of Massachusetts website. <https://www.mass.gov/info-details/covid-19-response-reporting#covid-19-interactive-data-dashboard->. Published 2021. Accessed October 13, 2021.
 27. Menni C, Klaser K, May A, *et al*. Vaccine side-effects and SARS-CoV-2 infection after vaccination in users of the COVID Symptom Study app in the UK: a prospective observational study. *Lancet Infect Dis* 2021;21: 939–949.
 28. Krammer F, Srivastava K, Alshammary H, *et al*. Antibody responses in seropositive persons after a single dose of SARS-CoV-2 mRNA vaccine. *N Engl J Med* 2021;384:1372–1374.
 29. d'Arminio Monforte A, Tavelli A, Perrone PM, *et al*. Association between previous infection with SARS CoV-2 and the risk of self-reported symptoms after mRNA BNT162b2 vaccination: data from 3,078 healthcare workers. *EClinicalMedicine* 2021;36:100914.
 30. Lasater KB, Aiken LH, Sloane DM, *et al*. Chronic hospital nurse understaffing meets COVID-19: an observational study. *BMJ Qual Saf* 2021;30:639–647.
 31. Kadri SS, Sun J, Lawandi A, *et al*. Association between caseload surge and COVID-19 survival in 558 US hospitals, March to August 2020. *Ann Intern Med* 2021;174:1240–1251.