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Presence of symptoms 6 weeks after COVID-19 among vaccinated and unvaccinated US healthcare personnel: a prospective cohort study

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ABSTRACT

Objectives Although COVID-19 vaccines offer protection against infection and severe disease, there is limited information on the effect of vaccination on prolonged symptoms following COVID-19. Our objective was to determine differences in prevalence of prolonged symptoms 6 weeks after onset of COVID-19 among healthcare personnel (HCP) by vaccination status, and to assess differences in timing of return to work.

Design Cohort analysis of HCP with COVID-19 enrolled in a multicentre vaccine effectiveness study. HCP with COVID-19 between December 2020 and August 2021 were followed up 6 weeks after illness onset.

Setting Health systems in 12 US states.

Participants HCP participating in a vaccine effectiveness study were eligible for inclusion if they had laboratory-confirmed symptomatic SARS-CoV-2 with mRNA vaccination (symptom onset ≥14 days after two doses) or no prior vaccination. Among 681 eligible participants, 419 (61%) completed a follow-up survey to assess symptoms reported 6 weeks after illness onset.

Exposures Two doses of a COVID-19 mRNA vaccine compared with no COVID-19 vaccine.

Main outcome measures Prevalence of symptoms 6 weeks after onset of COVID-19 illness and days to return to work.

Results Among 419 HCP with COVID-19, 298 (71%) reported one or more COVID-like symptoms 6 weeks after illness onset, with a lower prevalence among vaccinated participants compared with unvaccinated participants (60.6% vs 79.1%; adjusted risk ratio 0.70, 95% CI 0.58 to 0.84). Following their illness, vaccinated HCP returned to work a median 2.0 days (95% CI 1.0 to 3.0) sooner than unvaccinated HCP (adjusted HR 1.37, 95% CI 1.04 to 1.79).

Conclusions Receipt of two doses of a COVID-19 mRNA vaccine among HCP with COVID-19 illness was associated with decreased prevalence of COVID-like symptoms at 6 weeks and earlier return to work.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study reports a cohort of healthcare personnel with robust symptom inventories at 6 weeks and validated testing and vaccination data.
⇒ The cohort design is an observational study that could be open to residual confounding.
⇒ Our study period was conducted before booster doses.

INTRODUCTION

SARS-CoV-2 infection leads to a wide spectrum of illness from upper or lower respiratory tract infection to extrapulmonary manifestations including multiorgan complications.[1] Even with relatively mild initial illness, a proportion of individuals develop persistent or new symptoms that have been referred to as postacute sequelae of SARS-CoV-2 infection or 'long COVID'.[2 3] These sequelae reflect underlying pathology that is only partially elucidated.[3 4]

Prolonged symptoms occur in both hospitalised and non-hospitalised patients with COVID-19,[5] and commonly include fatigue, dyspnoea and neurocognitive deficits. Development of prolonged symptoms is more likely if acute illness is more severe.[6] Whether or not long-term sequelae occur, recovery of COVID-19 symptoms frequently takes several weeks and can limit return to usual activities.[6 7] For healthcare personnel (HCP), a return to health and work is important both personally and to maintain health system capacity.[8]

COVID-19 vaccination might limit the risk of a prolonged recovery from COVID-19 through several mechanisms: preventing COVID-19 infection, limiting the severity of acute illness through vaccine-mediated immunity and affecting the ongoing immune response even after acute infection. In a case series of 39 infections among healthcare workers vaccinated with two doses, symptoms

at 6 weeks were common.[9] Another study of self-reported vaccination status and symptoms among the general public found that COVID-19 symptoms 4 weeks after infection were less prevalent among the vaccinated.[10] An analysis of electronic medical record data suggested that vaccination might also prevent other postacute sequelae such as cardiovascular events, coagulation disorders, pulmonary disorders and other conditions associated with prolonged recovery.[11]

In this study, our primary objective was to compare the prevalence of symptoms 6 weeks after initial COVID-19 illness among HCP by vaccination status before their infection. We selected 6 weeks during study design in 2020 as the time period after which we anticipated most COVID-19 symptoms would have resolved, and we chose to analyse that time as an indicator of prolonged recovery from acute illness and a potential precursor of longer term symptoms.[6] We hypothesised that symptoms would be less common after 6 weeks among the vaccinated group because the initial illness among vaccine breakthrough cases is generally less severe, and severity of illness is one predictor of the likelihood of prolonged symptoms.[12 13] We conducted a secondary analysis to evaluate recovery from COVID-19 by assessing whether it took longer to return to work if unvaccinated.

METHODS

Study design, data collection and population

As part of the Preventing Emerging Infections through Vaccine Effectiveness Testing Project (Project PREVENT), we enrolled HCP who were working on-site at participating academic medical centres and who had been tested for SARS-CoV-2 infection for symptoms that started between 28 December 2020 and 26 August 2021 (prior to emergence of the Omicron SARS-CoV-2 variant). Characteristics of the 15 participating sites are summarised in online supplemental table S1, and details of study protocols and forms for the parent study are available online.[14] PREVENT sites and other platforms contributed to vaccine effectiveness analyses that have been reported previously.[15 16] This report satisfies the Strengthening the Reporting of Observational Studies in Epidemiology criteria (online supplemental table S2).[17]

For this cohort substudy, we included HCP enrolled in PREVENT sites with symptomatic SARS-CoV-2 infection (COVID-19), defined as a positive SARS-CoV-2 nucleic acid amplification test or antigen test and consistent symptoms (as listed in online supplemental table S3) within 14 days before or after the positive test. Participants provided data by electronic surveys or interviews (online, by phone or in person). Each participant completed an enrolment survey 14–60 days after his/her positive test and was offered a follow-up survey from 6 weeks (42 days) after symptom onset (or at the time of enrolment if later than 42 days) to determine symptoms 6 weeks after the positive test. We excluded participants from the analysis who had partial vaccination, had received a non-mRNA COVID-19 vaccine, did not have available vaccination records, did not complete the baseline survey within 60 days or did not complete the follow-up survey by 10 weeks after symptom onset. Only preillness vaccinations were included in our analysis. During the period of analysis, no participants had received more than two vaccine doses.

Definitions and data collection

The 6-week follow-up survey included questions on the presence of a variety of symptoms that we categorised into three overlapping groups. We defined *COVID-like symptoms* to be fever, cough, shortness of breath, chills, fatigue, joint pains or muscle aches, headache, loss of taste or smell, sore throat, sinus congestion, diarrhoea, nausea or vomiting.[18 19] We defined *neurological symptoms* as dizziness, headache, muscle weakness, movement problems, confusion, memory difficulties, concentration problems or loss of taste or smell.[2 20 21] We defined *any 6-week symptoms* as the symptoms listed above or others included in the 6-week survey: trouble sleeping, exercise problems, chest pain or abdominal pain. For each symptom included in the 6-week survey, participants were asked to rate perceived severity as mild, moderate or severe. For participants who responded to the survey later than 6 weeks, we asked them to base responses on symptoms present at 6 weeks.

The study team verified vaccine status and testing results via confirmed records from occupational health clinics, vaccine cards, state registries or medical records as part of the overall study protocol. We considered participants to be unvaccinated if they had not received any COVID-19 vaccine doses and vaccinated if they had received a second dose of a COVID-19 mRNA vaccine ≥14 days prior to the positive test. We considered comorbidities to be present at the time of infection if reported on the survey or identified in medical records from the period of acute illness. We classified participants as having two or more comorbidities (since 2 was the median number of comorbidities in the sample) if they had at least two diagnoses from our predefined list including cardiopulmonary, immunological and mental health-related comorbidities (full list available in online supplemental table S4). Several of these conditions have been identified both as risk factors for severe COVID-19 outcomes and long-term symptoms following COVID-19 illness.[22 23]

As part of the follow-up survey, we asked participants to report the dates when they resumed work. We calculated time to return to work as the number of days from onset of symptoms until the first day at work after illness. None of the participating sites had return-to-work guidance that differed based on vaccination status.

Patient and public involvement

No patients or members of the public were involved in the conception, design or conduct of the study.

Statistical analysis

We defined our primary outcome as the prevalence of COVID-like symptoms at the time of the 6-week follow-up survey. We conducted additional analyses for neurological symptoms and for any 6-week symptoms, and we assessed whether symptoms at 6 weeks were also present within 14 days of the date of the positive test. For assessment of all symptom groups, we performed a sensitivity analysis restricted to symptoms rated by participants as 'moderate' or 'severe', and we also conducted a sensitivity analysis of only symptoms present at both the time of initial illness and also at the 6-week survey (excluding new symptoms developing during the follow-up period). To assess the role of time since vaccination, we conducted a subgroup analysis of those infected within 16 weeks versus those infected after 16 weeks, based on data that vaccine protection wanes after 16 weeks.[16 24] Because of our data validation steps, no data on symptom onset, exposures, outcomes or covariates included in models were missing.

We used multivariable Poisson regression with a sandwich variance estimator to model the relative risk of having symptoms at the 6-week follow-up for complete vaccination compared with no vaccination.[25] In the multivariable model, we included categorical variables of age, race and ethnicity, and comorbidities selected a priori. Comorbidities were represented in a dichotomous variable of two or more comorbidities at baseline to indicate whether chronic illness was present.[26] We included categorical variables for calendar month of illness and number of weeks from symptom onset and follow-up survey completion to account for temporal changes in the prevalence of symptoms. Using Poisson regression, we also calculated the adjusted risk difference as the difference in proportions of participants reporting symptoms in the follow-up survey by vaccination status.[27]

We compared median differences in time to return to work by vaccination status using the Wilcoxon rank-sum test. To compare the rate of return to work by vaccination status, we constructed Kaplan-Meier survival curves and used the log-rank test. We used a Cox proportional hazards model to calculate an adjusted HR (aHR) to compare time to return to work between vaccinated and unvaccinated participants, counting zero day if there were no days off work after symptom onset. We included the same covariates as we did in our multivariable Poisson regression, except for time to follow-up survey response. We assessed Schoenfeld residuals to ensure that the proportional hazards assumption was met.

We compared individual symptoms on the follow-up survey between vaccinated and unvaccinated cohorts using unadjusted prevalence, relative risk and risk difference (defined as the prevalence in vaccinated minus the prevalence in unvaccinated participants).[28]

RESULTS

Among 1012 HCP with laboratory-confirmed COVID-19, 331 were excluded because they were partially vaccinated,

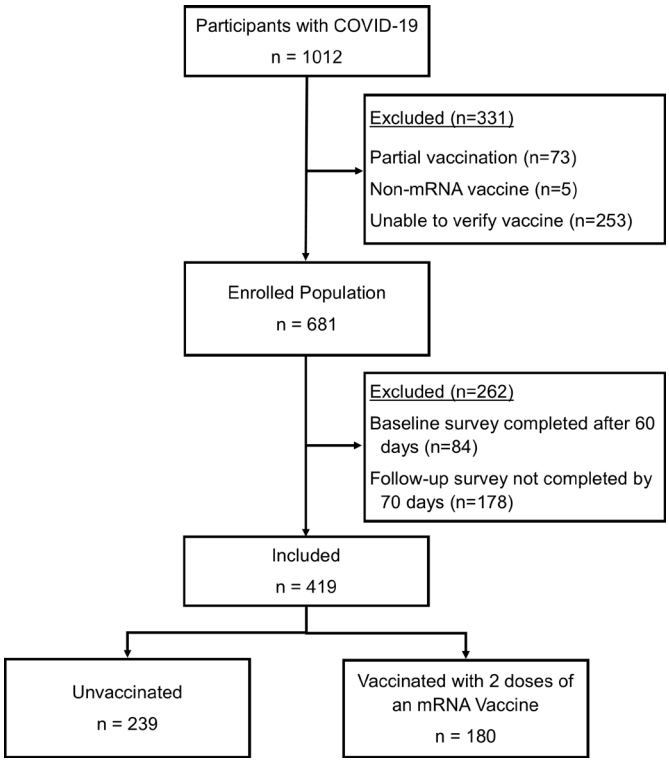

Figure 1 Enrolment of COVID-19 vaccinated and unvaccinated US healthcare personnel.

they received a non-mRNA vaccine or vaccination records were unavailable. Among the remaining 681 HCP, 597 (88%) completed the baseline survey by 60 days, and 419 (72%) also completed the follow-up survey between 42 and 70 days after symptom onset. Those who did not complete the follow-up survey had fewer comorbidities and were less likely to be white non-Hispanic (online supplemental table S5). We included 419 HCP: 180 (43.0%) who were vaccinated with two doses of an mRNA vaccine and 239 (57.0%) who were not vaccinated (figure 1). Among vaccinated participants there was a median of 24.1 weeks (IQR 15.3–28.1 weeks) between the second vaccine dose and the date of illness onset. Most vaccinated participants received the Pfizer-BioNTech vaccine (n=158, 87.8%); 22 (12.2%) received the Moderna vaccine. Vaccination status varied by race/ethnicity and education (table 1, online supplemental table S6). Ninety-five per cent (n=399) had symptoms prior to being tested. Among the 419 participants included in the analysis, 260 (62.1%) provided direct clinical care, and 296 (70.6%) worked in acute care hospitals. Only one participant (0.2%) required hospital admission for acute COVID-19, and no participants died.

Among the participants included in the analysis, baseline surveys were completed at a median of 3.1 weeks after first symptoms (IQR 2.3–4.4) and follow-up surveys were completed at a median of 6.0 weeks after first symptoms (IQR 6.0–6.3). Overall, 298 (71.1%) participants reported at least one COVID-like symptom present at 6 weeks, 236 (56.3%) reported at least one neurological symptom and 318 (75.9%) reported any symptom (figure 2). Among those who reported COVID-like symptoms at 6 weeks,

Table 1 Demographic characteristics and comorbidities of vaccinated and unvaccinated US healthcare personnel with COVID-19

	All participants (n=419) n (%)	Vaccinated (n=180) n (%)	Not vaccinated (n=239) n (%)	P value†
Age group (years)				0.019*
18–29	90 (21.5)	27 (15.0)	63 (26.4)	
30–39	167 (39.9)	73 (40.6)	94 (39.3)	
40–49	85 (20.3)	45 (25.0)	40 (16.7)	
50–64	77 (18.4)	35 (19.4)	42 (17.6)	
Sex				0.342
Male	64 (15.3)	32 (17.8)	32 (13.4)	
Female	352 (84.0)	146 (81.1)	206 (86.2)	
Non-binary	1 (0.2)	1 (0.6)	0	
Missing data	2 (0.5)	1 (0.6)	1 (0.4)	
Race and ethnic group				<0.001*
White, non-Hispanic	303 (72.3)	145 (80.6)	158 (66.1)	
Black, non-Hispanic	47 (11.2)	9 (5.0)	38 (15.9)	
Hispanic or Latino	41 (9.8)	13 (7.2)	28 (11.7)	
Other, non-Hispanic	28 (6.7)	13 (7.2)	15 (6.3)	
Education level				<0.001*
High school or less	25 (6.0)	6 (3.3)	19 (8.0)	
Undergraduate or technical degree	293 (69.9)	109 (60.6)	184 (77.0)	
Graduate or professional degree	101 (24.1)	65 (36.1)	36 (15.1)	
Job classification				<0.001*
Non-clinical	128 (30.5)	46 (25.6)	82 (34.3)	
Physician	20 (4.8)	18 (10.0)	2 (0.8)	
Advanced practice provider	12 (2.9)	10 (5.6)	2 (0.8)	
Nurse/nurse assistant	164 (39.1)	57 (31.7)	107 (44.8)	
Housekeeping	2 (0.5)	0	2 (0.8)	
Other clinical	48 (11.5)	27 (15.0)	21 (8.8)	
Other	45 (10.7)	22 (12.2)	23 (9.6)	
Health insurance				0.004*
Private	385 (91.9)	175 (97.2)	210 (87.9)	
Government	17 (4.1)	3 (1.7)	14 (5.9)	
None	3 (0.7)	0	3 (1.3)	
Unknown	14 (3.3)	2 (1.1)	12 (5.0)	
Presence of two or more comorbidities (see online supplemental table S6 for details)	216 (51.6)	98 (54.4)	118 (49.4)	0.325
Time from symptom onset to baseline (weeks), median (IQR)	3.1 (2.3–4.4)	3.0 (2.1–3.7)	3.4 (2.4–5.1)	<0.001*
Time from symptom onset to follow-up survey (weeks), median (IQR)	6.0 (6.0–6.3)	6.0 (6.0–6.3)	6.0 (6.0–6.6)	<0.001*

*P<0.05.
†Calculated using Fisher's exact test for categorical variables and Wilcoxon rank-sum test for numerical variables.

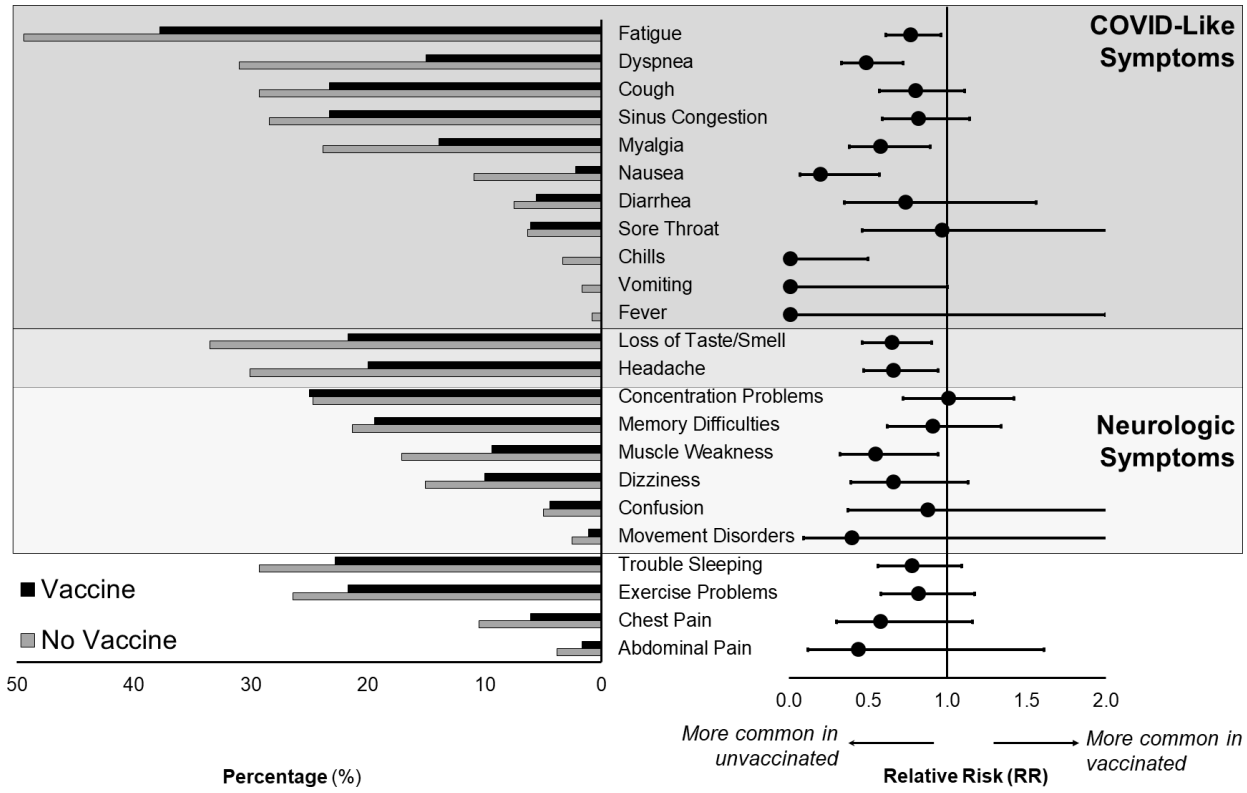

Figure 2 Prevalence of new or persistent symptoms 6 weeks after COVID-19 symptom onset among US healthcare personnel. Each bar in the left pane shows the percentage of participants reporting symptoms at the 6-week follow-up, stratified by vaccination status. For each symptom, the relative risk (RR, unadjusted) and 95% CI are shown on the forest plot to the right. For RR <1.0, the symptom is less prevalent among the vaccinated. Note that several symptoms are part of both COVID-19 symptoms and neurological symptoms. *COVID-like symptoms* included fever, cough, dyspnoea, chills, fatigue, myalgia, headache, new loss of taste or smell, sore throat, nasal congestion, diarrhoea and nausea or vomiting. *Neurological symptoms* included dizziness, headache, muscle weakness, movement disorders, confusion, memory difficulties, concentration problems or loss of taste or smell. *Any symptoms* included trouble sleeping, exercise problems, chest pain or abdominal pain, in addition to COVID-19 symptoms and neurological symptoms, defined above.

245 (95.7%) reported symptoms that were also reported during the initial illness. Within 2 weeks of symptom onset, 323 (77.1%) participants had returned to work; by 6 weeks, only seven (1.7%) still had not returned.

Vaccinated participants had a lower prevalence of COVID-like symptoms at 6 weeks compared with those who were not vaccinated (60.6% vs 79.1%), with an unadjusted relative risk of 0.77 (95% CI 0.67 to 0.88) and an adjusted relative risk of 0.70 (95% CI 0.58 to 0.84). This risk ratio (RR) corresponded to an adjusted risk difference after 6 weeks of 24.1 percentage points (95% CI 11.6 to 36.6). Other classifications of symptoms were also less likely after vaccination—for neurological symptoms the adjusted risk ratio (aRR) was 0.71 (95% CI 0.55 to 0.93) with a 17.9 percentage point reduction (95% CI 5.1 to 30.7); for any 6-week symptoms the aRR was 0.76 (95% CI 0.65 to 0.90) with a 20.1 percentage point reduction (95% CI 8.0 to 32.1) if vaccinated (figure 3, online supplemental table S7).

Prolonged symptoms 6 weeks after symptom onset that were associated with being unvaccinated included dyspnoea, myalgia, muscle weakness, fatigue, chills, loss of taste or smell, headache and nausea; prevalence of other individual symptoms reported at 6 weeks was similar between vaccinated and unvaccinated participants (figure 2). Sensitivity analysis restricted to persistent symptoms (excluding symptoms developing between illness and follow-up) revealed similar findings (online supplemental figure S1). Subgroup analysis, stratified on time since vaccination, showed that the affect was somewhat attenuated for COVID-like symptoms and any symptoms for those vaccinated more than 16 weeks prior to infection (online supplemental table S8).

Median time from symptom onset to return to work (among those who had returned to work before follow-up) was 13 days (IQR 11–16 days). Vaccinated participants returned to work a median of 2.0 days (95% CI 1.0 to 3.0) sooner than the unvaccinated and were less likely to return to work more than 10 days after illness onset (78.9% vs 87.5%; RR 0.90, 95% CI 0.82 to 0.99). Adjusting for covariates, vaccinated participants returned to work sooner than unvaccinated participants (aHR 1.37, 95% CI 1.04 to 1.79; online supplemental table S9). Vaccinated participants were also less likely to have COVID-like symptoms on return to work, although without statistical significance (49.4% vs 66.2%; RR 0.83, 95% CI 0.67 to

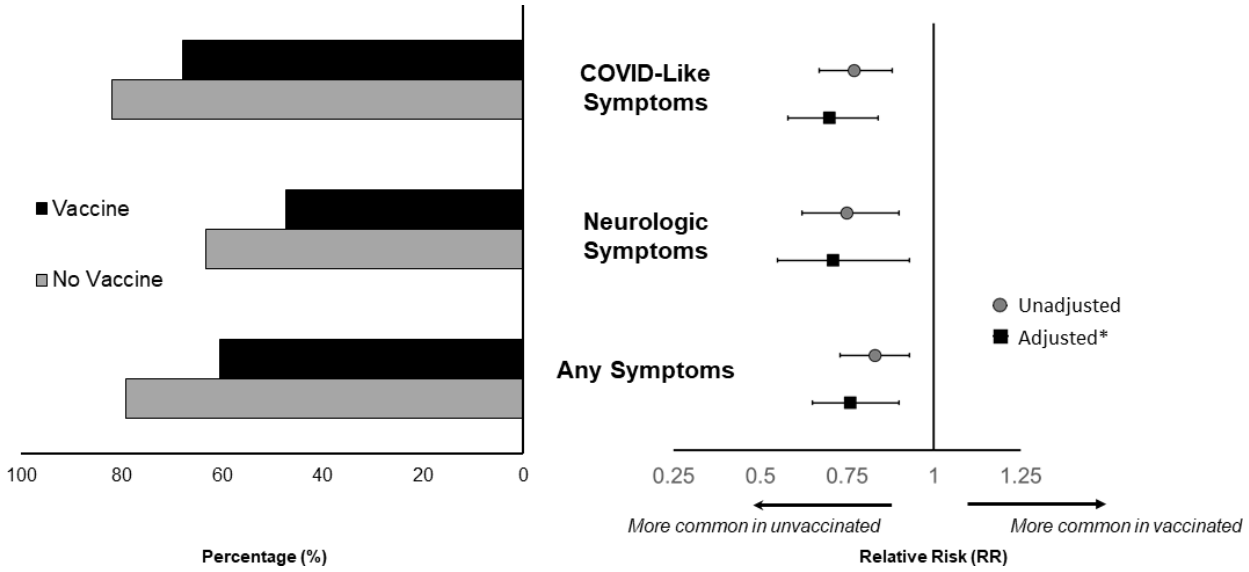

Figure 3 New or persistent symptoms at 6 weeks after COVID-19 symptom onset in vaccinated versus unvaccinated US healthcare personnel. Each bar in the left pane shows the percentage of participants reporting symptoms at the 6-week follow-up, stratified by vaccination status. This forest plot in the right pane shows the estimated risk of new or persistent symptoms present at the 6-week survey. The relative risk (RR) shows the ratio between the probability of having symptoms in the vaccinated versus the unvaccinated (values <1.0 indicate that the prevalence of symptoms is lower in the vaccinated than the unvaccinated group). Grey circles show the unadjusted estimates and black squares show the estimates adjusted for age, race, ethnicity, comorbidities, calendar month of diagnosis and weeks since symptoms started. Error bars indicate 95% CIs around the point estimate. *COVID-like symptoms* included fever, cough, dyspnoea, chills, fatigue, myalgia, headache, new loss of taste or smell, sore throat, nasal congestion, diarrhoea and nausea or vomiting. *Neurological symptoms* included dizziness, headache, muscle weakness, movement disorders, confusion, memory difficulties, concentration problems or loss of taste or smell. *Any symptoms* included trouble sleeping, exercise problems, chest pain or abdominal pain, in addition to COVID-19 symptoms and neurological symptoms, defined above. *Adjusted for age, race, ethnicity, comorbidities, calendar month of diagnosis and weeks since symptoms started.

1.03). Participants who reported COVID-like symptoms on return to work were more likely than those without to report COVID-like symptoms at 6 weeks (84.7% vs 50.9%; RR 1.36, 95% CI 1.11 to 1.67). The time to return to work by vaccination status is shown in figure 4.

DISCUSSION

In this study of HCP with COVID-19 between December 2020 and August 2021, we observed that 71% of participants with a confirmed diagnosis of COVID-19 reported at least one COVID-like symptom was present 6 weeks after symptom onset, and 76% reported any symptoms were present. This high proportion of symptoms at 6 weeks suggests that HCP might experience a substantial disease burden; during this period the most frequently reported symptoms were fatigue, dyspnoea, loss of taste/smell and headache. We observed that COVID-19 infection after full vaccination (breakthrough infection) was associated with a 24 percentage point absolute risk reduction of symptoms at 6 weeks compared with COVID-19 in unvaccinated HCP.

We found that several specific symptoms 6 weeks after illness onset were most strongly associated with having no prior vaccination, including nausea, dyspnoea, muscle weakness, myalgia, loss of taste or smell and headache. Other symptoms had point estimates in the direction of vaccine effectiveness, even if the magnitude of effect did not reach statistical significance. These findings are important because neurological and other symptoms are frequently reported several months after COVID-19.[29] The differential association with vaccination of these symptoms might provide insight into their pathophysiology. Lower frequency of these symptoms following vaccination could be associated with decreased severity of initial illness, as vaccination is known to decrease severity of disease, and prior studies have found that prolonged symptoms might be more common among those with severe COVID-19 illness.[13 23] Because an effect of vaccines in preventing prolonged symptoms is likely to be mediated by the immune response, further research is needed to understand the mechanisms of prolonged symptoms that might be amenable to other prevention strategies.

COVID-19 mRNA vaccines have been shown to be both safe and effective,[13 16 30] but the effect on duration of symptoms following infection is less clear. The UK-based COVID Symptom Study using self-reported data from a mobile app-based data collection instrument with unvalidated vaccination status and COVID-19 diagnosis found that any of 32 symptoms lasting ≥28 days were less prevalent among those who were vaccinated with two doses (adjusted OR 0.51, 95% CI 0.32 to 0.82).[10] This effect size is similar to findings in our study. Recent preliminary

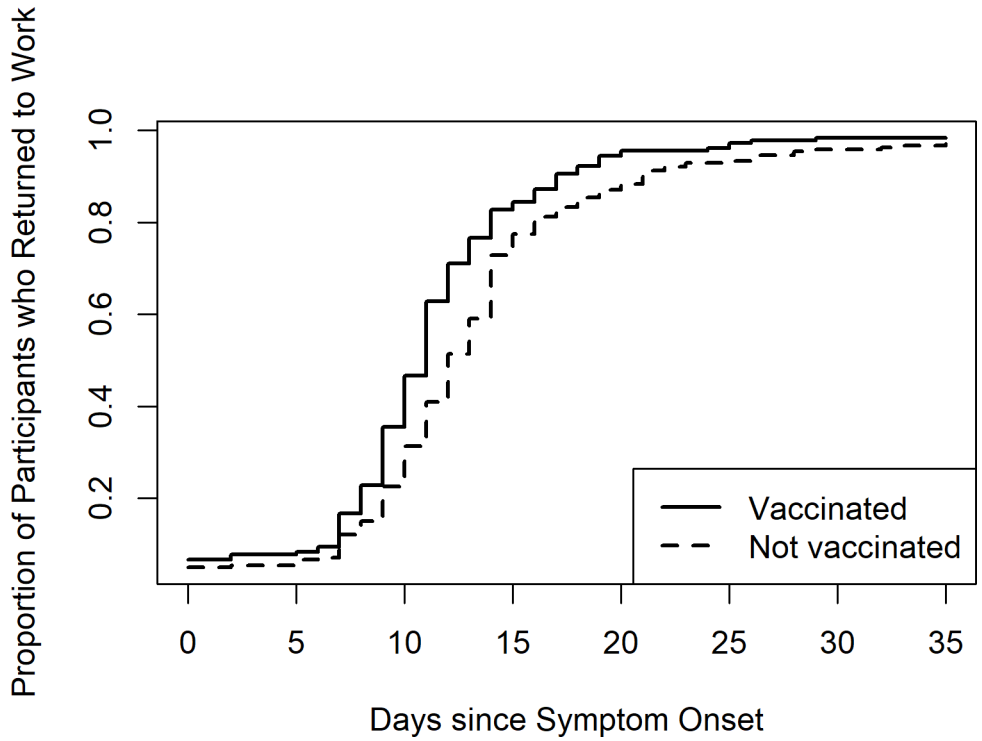

Figure 4 Kaplan-Meier plot of proportion of US healthcare personnel returning to work after onset of COVID-19 symptoms, stratified on COVID-19 vaccination. The Kaplan-Meier plot shows the actual time to return to work, stratified by vaccination status (log-rank test, p<0.001). A Cox proportional hazards model was constructed, adjusting for age, race, ethnicity, comorbidities and calendar month of diagnosis. The adjusted HR (aHR) for the adjusted model is 1.37 (95% CI 1.04 to 1.79). Note that aHR >1.0 indicates that participants *resume work* more quickly.

reports have also noted a lower prevalence of reported symptoms if infection occurred after vaccination, as well as a lower risk of medical encounters after illness.[11 31–33] Strengths of the current analysis include the validation of testing and vaccination status, a separate baseline and follow-up survey, assessment of symptoms at defined time points and follow-up of a broad cohort of HCP.

Reduced likelihood of prolonged symptoms after COVID-19 indicates a benefit of vaccination that is in addition to prevention of initial illness, and it is consistent with other recent analyses on this topic. Vaccination is therefore likely to prevent prolonged symptoms both by preventing infection in the first place[15 16] and by hastening recovery from infections that occur after vaccination. As a result of both effects, vaccine effectiveness against developing COVID-19 with prolonged symptoms is likely to be higher than effectiveness against COVID-19 alone.[34] Vaccine effectiveness against symptomatic infection has been previously assessed using the same study platform as this analysis.[16]

Vaccinated participants also returned to work 2 days sooner than non-vaccinated participants. It appears that vaccinated HCP were able to return to work sooner after infection due to fewer ongoing symptoms. Any effect, magnified over 22 million HCP in the USA, is in addition to the benefit of vaccines in preventing infections, which can affect health system capacity and the ability to respond to public health emergencies.[35] Similar effects might be expected among vaccinated employees in other critical industries.

Our study has several limitations. First, our follow-up was limited to 6 weeks after symptom onset. Although many persistent symptoms are likely to develop by this time, the prevalence of symptoms is likely to decay over time, and we did not assess longer term effects.[6] We also designed our data collection prior to widespread recognition of the prevalence of persistent COVID-19 symptoms. We were also not able to determine whether symptoms were directly caused by SARS-CoV-2 infection because our analysis only compared symptoms by vaccination status among patients with COVID-19. However, a study of 4182 patients with COVID-19 with longitudinal self-reported symptom inventories indicated that symptoms reported 6 weeks after illness onset are usually specific to COVID-19.[6] Second, we relied on self-reported symptoms (rather than diagnoses) in participants who knew their vaccination status. Many reported symptoms are subjective, leaving open the possibility that vaccinated participants had more confidence that their symptoms would resolve quickly. To consider whether symptom severity might have affected response rates, we conducted a sensitivity analysis that yielded similar findings after excluding symptoms that were rated as mild by participants. Third, our study period preceded recommendations for booster doses and the introduction of the Omicron variant and precluded analysis of booster doses—bivalent mRNA booster doses have

since been recommended in the USA.[36 37] It is possible that booster doses might provide additional protection against symptoms after initial COVID-19. Our analysis was also limited to infections before introduction of the Omicron variant, which might lead to a different spectrum of illness because of relative tropism to the upper respiratory tract.[38–40] Finally, there could be differences between those vaccinated and unvaccinated that predispose some participants to having persistent symptoms or returning to work more quickly. We attempted to account for the most influential of these factors in our regression models, and sensitivity analyses yielded similar findings to our primary analysis, but residual confounding could still have influenced our results.

In conclusion, a primary series of COVID-19 vaccination was associated with a decreased adjusted prevalence of new or persistent symptoms at 6 weeks and sooner return to work in a cohort of HCP. Future work is warranted to assess underlying biological mechanisms and the association between vaccination on longer term symptoms, daily function, quality of life and the effect in other populations.

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