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Major Article

Side effects of messenger RNA vaccines and prior history of COVID-19, a cross-sectional study

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Key Words:
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SARS-CoV-2
Moderna
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legislation
Predictors

Background: There are concerns regarding immunogenicity with coronavirus disease 2019 (COVID-19) mRNA vaccines among persons with prior history of COVID-19 (PHC). This study was to analyze the short-term side effects of mRNA vaccines among health care workers (HCWs) with and without PHC.

Methods: A cross-sectional study was performed using an independent online survey questionnaire that gathered responses from HCWs.

Results: Among 1,475 HCWs, 1268 (85.97%) completed the survey, 102/1268 (44/447 in Moderna group and 58/821 in Pfizer-BioNTech group) reported PHC during pre-vaccination period. Symptoms of flushing/P = .05, brain fogging/P= .005, vertigo/P= .041, numbness/P= .023, diarrhea/P= .047, hives/P= .028, itching/P= .028, swelling of lips/mouth/P= .001, shortness of breath/P= .022, and anxiety/P= .048 have greater occurrence among Pfizer-BioNtech group with PHC when compared to Pfizer-BioNtech group with no PHC. Symptoms of chills/P= .027, flushing/P= .045, tremor/P= .05, muscle spasm/P= .039, vomiting/P= .031, diarrhea/P= .015, and cough/P= .011 have higher occurrence among Moderna group with PHC when compared to Moderna group with no PHC.

Conclusions: Few short-term side effects among mRNA vaccine recipients with PHC may have necessitated transient time-off from work. The PHC can be considered as a predictor for severity of side effects. While the vaccination program continues in the United States, a future COVID legislation that mandates vaccination among employees along with paid time off provision may help with higher compliance and acceptance.

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Ethics approval and consent to participate: The approval for the parent study was obtained from the Institutional Review Board at Cape Fear Valley Health System, 1638 Owen Drive, Fayetteville, NC 28304. Informed consent was obtained from all survey participants involved in the study.

Availability of data and materials: Data is available upon request.

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BACKGROUND

Coronavirus disease 2019 (COVID-19) has become the third leading cause of death for persons aged 45 through 84 years and the second leading cause of death for those 85 years and older by October 2020.[1] COVID-19 related deaths as of September 15th, 2021, in the US were about 658,754.[2] The US is currently experiencing a full swing of third surge in COVID-19 infections posing a significant burden to health care system and severe economic consequences.[2,3] Several parts of US are already experiencing a third surge in COVID-19 infections posing a significant burden to health care system with lockdowns and severe economic consequences.[3] To alter these trends and flatten the curve, Food and Drug Administration in the US has authorized 2 mRNA vaccines (the Pfizer-BioNTech manufactured BNT162b2 vaccine, and the Moderna manufactured mRNA-1273 vaccine.[4,5] While the active ingredient of both mRNA vaccines encodethe viral spike (S) glycoprotein of SARS-CoV-2), each dose of the Moderna vaccine contains more vaccine (100 micrograms) than each dose of the Pfizer-BioNtech vaccine (30 micrograms).[6] In December 2020, the Advisory Committee on Immunization Practices issued recommendations for the use of a 2-dose regimen of BNT162b2 COVID-19 mRNA vaccine (which was shown to have 95% efficacy in protection against COVID-19) in persons aged 16 years or older,[5] and 2-dose regimen of mRNA-1273 vaccine (which was shown to have 94.1% efficacy in preventing COVID-19, including severe disease).[4] Data from the recent studies with detailed review of systems among mRNA COVID-19 vaccine recipients suggests that they would experience wide range of non-life threatening local and systemic post-vaccination symptoms but still has greater acceptance to these vaccines.[4,5,7-9]

Clinical trials have generally excluded patients with history of COVID-19, and it is unclear if this cohort will experience more post-vaccination side effects from mRNA vaccine.[4,5] However, Centers for Disease Control and Prevention (CDC) stated that the side effects in early post-vaccination period can be severe and higher in recipients with prior infection, but the details of symptomatology were not studied or revealed.[6] The objective of the present study was to analyze the safety and more detailed side effect profile of the mRNA vaccine using a self-reported online survey questionnaire among recipients with prior history of COVID-19. Therefore, we chose a random population of health care workers (HCW) in the United States and investigated the side effects of these vaccines using responses from the survey questionnaire (consisting of a more detailed review of organ systems in comparison to what the CDC is collecting through the Vaccine Adverse Event Reporting System).[10]

METHODS

Design and sample selection

After obtaining institutional review board approval for this research, we conducted a cross-sectional study by circulating an independent online survey questionnaire through an internet-based survey platform called “Survey Monkey,” which gathered anonymous responses from HCWs from verified health care communities representing different unspecified regions of the country during the early phase of COVID-19 vaccination. No personal identifications were obtained. Survey Monkey web link was distributed to (1) coordinators of health care institutions and (2) verified communities of HCWs via social media. Informed consent was obtained at the beginning of the survey. Participants who voluntarily agreed and consented to proceed and who chose to receive 1 of the 2 mRNA-based COVID-19 vaccines were automatically allowed to move forward to answer subsequent questions about the side effects and other variables. Those who chose “None of them” were diverted to a disqualified page. The study obtained feedback in anonymous mode regarding the side effect and benefit profile (feelings of joy/relief/gratitude) during the post-vaccination period.

Inclusion criteria

This study included the health care providers and workers in health care settings (Phase 1a vaccine recipients who may be exposed to suspect or confirmed COVID-19 patients or infective materials) that have received 1 or 2 doses of the mRNA-based COVID-19 vaccine.

Exclusion criteria

1) Those who received 1 or 2 doses of the mRNA-based COVID-19 vaccine but belong to 1 of the following:
   a) Phase 1a “long-term care facility” residents,
   b) Phase 1b population (non-phase 1a persons aged ≥75 years), non-health care frontline essential workers),
   c) Phase 1c population (non-phase 1a persons aged 65-74 years, non-phase 1a persons aged 16-64 years with medical conditions that increase the risk for severe COVID-19), and
   d) Other general population

2) Those who did not receive mRNA-based COVID-19 vaccine

Duration of study

The “Survey Monkey” web link was left open and kept active to collect responses for approximately 6 weeks. The responses were collected between January 24, 2021 and March 10, 2021. We obtained responses from 1,475 HCWs (Fig 1) who reported receiving 1 or 2 doses of either BNT162b2 or mRNA-1273 vaccines. Out of 1,475 responses, 1,268 were complete responses. Only the complete responses were included in the final analysis of this study (Fig 1).

Statistical analysis

The study was conducted on HCWs and these respondents were stratified by the type of vaccine administered, the side effect reported and as well as having a PHC (yes/no). The percentage of response was calculated for each of the respective categories. The significance of association between the PHC and the related side effect for each type of vaccine was determined using Fisher's exact t test with an alpha threshold level of 0.05 was chosen for this study to identify the differences.

RESULTS

Among 1,268/1,475 HCW (85.96%) that completed the survey, 68/821 Pfizer-BioNtech vaccine recipients reported history of COVID-19 (with 58 HCWs suffered infection in the pre-vaccination period and 10 HCWs contracted infection between first and second doses of vaccine) and 46/447 Moderna vaccine recipients reported history of COVID-19 (with 44 HCWs suffered infection in the pre-vaccination period and 2 HCWs between first and second doses of vaccine) (Fig 1 and Fig 2). Although the majority of vaccine recipients with history of COVID-19 (80% Pfizer group and 70% Moderna group) received the second dose of the vaccine, the number of these vaccine recipients

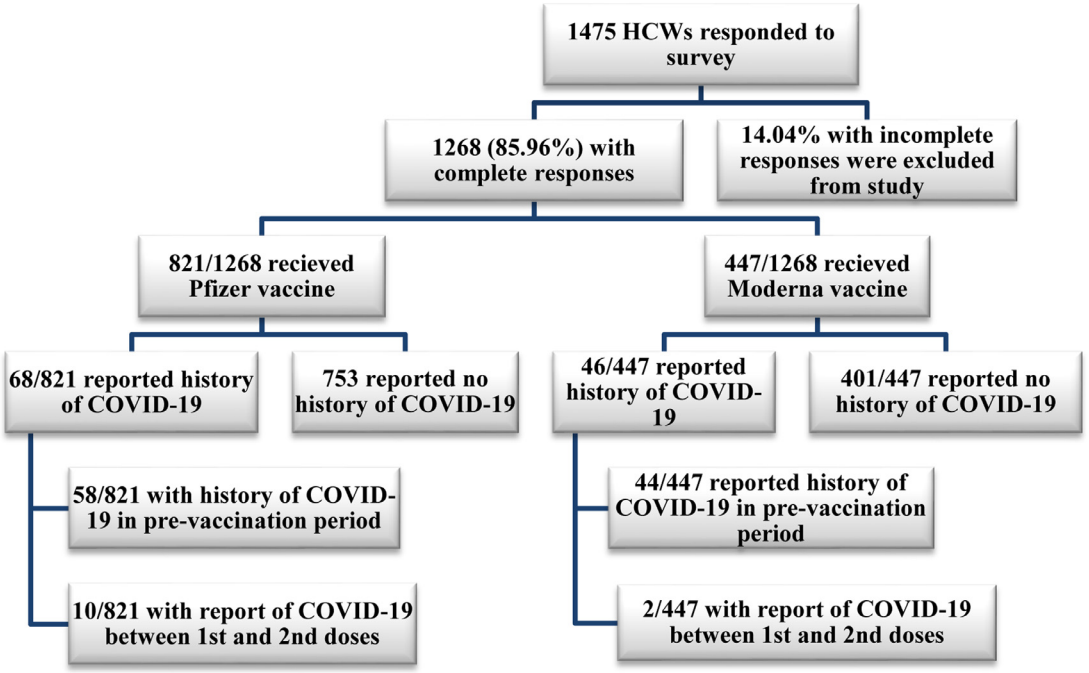

Fig 1. Classification of survey responses.

are significantly less (P= .0002 in Pfizer-BioNtech group and P= .0381 in Moderna group) when compared to the respective vaccine groups with no history of COVID-19. Table 1 and Figure 3 shows the list of self-reported side effects (based on organ systems) with both mRNA vaccines. The symptoms of flushing (P= .05), brain fogging (P= .005), vertigo (P= .041), numbness (P= .023), diarrhea (P= .047), hives (P= .028), itching (P= .028), swelling of lips/mouth (P= .001), shortness of breath (P= .022), and anxiety (P= .048) have greater occurrence among Pfizer-BioNtech group with PHC when compared to Pfizer-BioNtech group with no PHC. Among the Moderna vaccine recipients with history of COVID-19, symptoms such as chills (P= .027), flushing (P= .045), tremor (P= .05), muscle spasm (P= .039), vomiting (P= .031), diarrhea (P= .015), and cough (P= .011) have higher occurrence when compared to Moderna vaccine group with no PHC. Also, a significant number (22.41% vs 11.42%; P= .021) of Pfizer-BioNtech vaccine recipients with history of COVID-19 required to take time-off from work for transient period due to post-vaccination side effects compared with controls. In Moderna vaccine recipients, both receipts with and without COVID-19 history (27.27% vs 26.93%; P= 1) required to take off work for transient period.

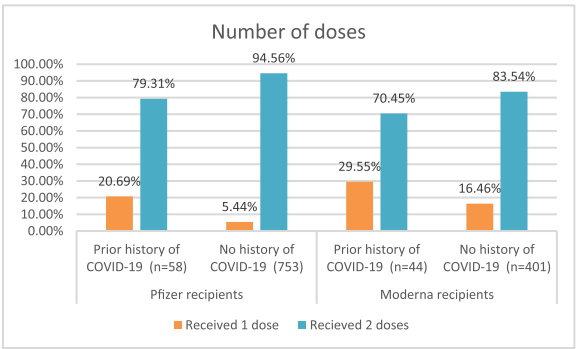

Fig 2. Number of doses.

DISCUSSION

In this cross-sectional survey study among HCWs, the post-vaccination side effects in those who received mRNA vaccine (Pfizer BioNtech or Moderna vaccine) were more severe and higher among Pfizer vaccine recipients, especially in those who contracted COVID-19 infection in the pre-vaccination period. Additionally, a greater number of Pfizer vaccine recipients who had prior COVID-19 were required to take time-off from work for a transient period which may have been related to post-vaccination side effects severity. Seeking medical care due to side effects was rare among vaccine recipients. Though majority reported no intention to skip the second dose of vaccine, fewer people with prior history of COVID-19 completed 2 doses when compared with those without history of prior COVID-19 infection.

Thus far, the available data on mRNA-based COVID-19 vaccine short-term side effects have been reported by manufacturer-funded clinical trials and recent cross-sectional studies.[4,5,7-9] There was also greater acceptance for the second dose in spite of side effects.[7-9] A greater percentage of participants who received the Moderna vaccine, compared with the Pfizer-BioNTech vaccine, reported reactogenicity; this pattern was more pronounced after the second dose.[11] Our findings were consistent with these reports, however, we reported more detailed review of organ systems. The frequency of reported reactions was slightly higher in our cohort compared with those observed in clinical trials.[4,5,11] The uniqueness of our survey was to report and compare the side effects experienced in those with and without prior history to COVID-19 infection which was largely excluded in these clinical trials.[4,5] Our study demonstrated a significant association between a prior COVID-19 infection and incidence of self-reported side effects after a vaccination for COVID-19. Recent survey study reported that a prior history of COVID-19 was associated with the risk of experiencing a severe side effect requiring

Table 1
Comparison of short-term side effects

Reported symptom	Pfizer recipients			Moderna recipients		
	Prior history of COVID-19, n = 58	No history of COVID-19, n = 753	Fisher exact test (*P* value)	Prior history of COVID-19, n = 44	No history of COVID-19, n = 401	Fisher exact test (*P* value)
Gender (percentages are column percent's)						
Female	50 (86.2%)	651 (86.45%)	1	37 (84.09%)	363 (90.52%)	.187
Male	8 (13.79%)	102 (13.54%)	1	7 (15.91%)	37 (9.23%)	.18
Number of doses received (percentages are column percent's)						
Received 1 dose	12 (20.69%)	41 (5.44%)	.0002	13 (29.55%)	66 (16.46%)	<.00001
Received 2 doses	46 (79.31%)	712 (94.56%)	.0002	31 (70.45%)	335 (83.54%)	.038
Side effect reported (percentages are row percent's)						
Fever	14 (24.14%)	163 (21.65%)	.624	19 (43.18%)	139 (34.66%)	.319
Chills	25 (43.1%)	265 (35.19%)	.256	30 (68.18%)	202 (50.37%)	.027
Generalized weakness/fatigue	38 (65.52%)	440 (58.43%	.333	33 (75%)	261 (65.09%)	.24
Headache	27 (46.55%)	339 (45.02%)	.891	27 (61.36%)	236 (58.85%)	.872
Dizziness	5 (8.62%	62 (8.23%)	.807	7 (15.91%)	58 (14.46%)	.822
Sweating	2 (3.45%)	71 (9.43%)	.155	13 (29.55%)	70 (17.46%)	.065
Flushing	8 (13.79%)	48 (6.37%)	.05	8 (18.18%)	32 (7.98%)	.045
Rash	2 (3.45%)	18 (2.39%)	.648	4 (9.09%)	57 (14.21%)	.489
Sore arm/pain	52 (89.66%)	658 (87.38%)	.836	42 (95.45%)	375 (93.52%)	1
Itching	7 (12.07%)	36 (4.78%)	.028	9 (20.45%)	58 (14.46%)	.273
Swelling	6 (10.34%)	38 (5.05%)	.121	7 (15.91%)	60 (14.96%)	.826
Bleeding	0	3 (0.4%)	1	0	2 (0.5%)	1
Skin discoloration	2 (3.45%)	8 (1.06%)	.156	1 (2.27%)	14 (3.49%)	1
Seizures	0	1 (0.13%	1	0	1 (0.25%)	1
Brain fogging	9 (15.52%)	39 (5.18%)	.005	4 (9.09%)	40 (9.98%)	1
Fainting/Presyncope/Syncope	0	2 (0.27%)	1	0	3 (0.75%)	1
Extremity weakness	1 (1.72%)	5 (0.66%)	.360	0	3 (0.75%)	1
Facial paralysis	1 (1.72%)	1 (0.13%)	.138	0	0	1
Vertigo	4 (6.9%)	15 (1.99%)	.041	1 (2.27%)	14 (3.49%)	1
Numbness	5 (8.62%)	19 (2.52%)	.023	0	6 (1.5%)	1
Tingling	5 (8.62%)	35 (4.65%)	.198	1 (2.27%)	14 (3.49%)	1
Muscle atrophy	0	0	1	0	0	1
Tremor	0	0	1	2 (4.55%)	2 (0.5%)	.05
Incoordination	1 (1.72%)	3 (0.4%)	.257	0	4 (1%)	1
Myalgia	28 (48.28%)	336 (44.62%)	.587	30 (68.18%)	209 (52.12%)	.055
Joint pains	8 (13.79%)	124 (16.47%)	.714	14 (31.82%)	96 (23.94%)	.27
Muscle spasm	9 (15.52%)	68 (9.03%)	.106	9 (20.45%)	39 (9.73%)	.039
Nausea	14 (24.14%)	114 (15.14%)	.09	14 (31.82%)	105 (26.18%)	.473
Vomiting	2 (3.45%)	10 (1.33%)	.21	4 (9.09%)	9 (2.24%)	.031
Heartburn	0	9 (1.2%)	1	2 (4.55%)	12 (2.99%)	.639
Decreased appetite	5 (8.62%)	40 (5.31%)	.363	4 (9.09%)	56 (13.96%)	.488
Constipation	0	3 (0.4%	1	0	7 (1.75%)	1
Diarrhea	6 (10.34%)	32 (4.25%)	.047	8 (18.18%)	27 (6.73%)	.015
Abdominal pain	4 (6.9%)	21 (2.79%)	.096	3 (6.82%)	21 (5.24%)	.721
Hives	2 (3.45%)	2 (0.27%)	.028	1 (2.27%)	7 (1.75%)	.568
Swelling of lips/tongue/oral cavity)	3 (5.17%)	1 (0.13%)	.001	0	4 (1%)	1
Hay fever	0	0	1	0	3 (0.75%)	1
Asthma exacerbation	0	0	1	1 (2.27%)	2 (0.5%)	.269
Atopic eczema	0	2 (0.27%)	1	1 (2.27%)	3 (0.75%)	.342
Shortness of breath	4 (6.9%)	12 (1.59%)	.022	1 (2.27%)	11 (2.74%)	1
Cough	2 (3.45%)	5 (0.66%)	.084	5 (11.36%)	10 (2.49%)	.011
Wheezing	1 (1.72%)	0	.072	0	1 (0.25%)	1
Chest pain	0	9 (1.2%)	1	1 (2.27%)	8 (2%)	1
Palpitations	5 (8.62%)	29 (3.85%)	.088	4 (9.09%)	31 (7.73%)	.766
Blood pressure changes	1 (1.72%)	6 (0.8%)	.406	0	9 (2.24%)	1
Syncope	1 (1.72%)	0	.072	0	4 (1%)	1
Psychological stress	1 (1.72%)	5 (0.66%)	.36	0	3 (0.75%)	1
Anxiety	4 (6.9%)	16 (2.12%)	.048	1 (2.27%)	22 (5.49%)	.716
Low mood	0	3 (0.4%)	1	1 (2.27%)	5 (1.25%)	.467
Transient decrease in memory	2 (3.45%)	5 (0.66%)	.084	2 (4.55%)	5 (1.25%)	.146
Decrease in sleep	2 (3.45%)	41 (5.44%)	.762	5 (11.36%)	41 (10.22%)	.794
Increase in sleep	1 (1.72%)	18 (2.39%)	1	0	24 (5.99%)	.153
Manic/hyermanic episodes	1 (1.72%)	2 (0.27%)	.2	0	4 (1%)	1
Feelings of joy/relief/gratitude	2 (3.45%)	52 (6.91%)	.419	0	23 (5.74%)	.151
Overall effect from side effects						
Transiently unable to perform regular activities	8 (13.79%)	95 (12.62%)	.837	8 (18.18%)	106 (26.43%)	.278
Required to take off from work for transient period	13 (22.41%)	86 (11.42%)	.021	12 (27.27%)	108 (26.93%)	1
Required to seek help from outpatient provider	1 (1.72%)	18 (2.39%)	1	3 (6.82%)	13 (3.24%)	.203
Required to seek help from ED provider	0	5 (0.66%)	1	0	1 (0.25%)	1
Required to hospitalize/inpatient care	0	2 (0.27%)	1	0	0	1
No intention to skip 2nd dose	43 (93.48%)	581 (97.98%)	.628	34 (94.44%)	306 (97.45%)	1
Ethnicity						

(*continued*)

Table 1 (*Continued*)

Reported symptom	Pfizer recipients			Moderna recipients		
	Prior history of COVID-19, n = 58	No history of COVID-19, n = 753	Fisher exact test (*P* value)	Prior history of COVID-19, n = 44	No history of COVID-19, n = 401	Fisher exact test (*P* value)
White	42 (72.41%)	609 (80.88%)	.125	36 (81.82%)	238 (84.29%)	.003
Hispanic/latino	6 (10.34%)	27 (3.59%)	.025	4 (9.09%)	13 (3.24%)	.076
African American	2 (3.45%)	18 (2.39%)	.648	0	9 (2.24%)	1
Asian	9 (15.52%)	84 (11.16%)	.29	4 (9.09%)	36 (8.98%)	1
Native American	0	4 (0.53%)	1	0	0	1
Pacific Islander	0	3 (0.4%)	1	0	1 (0.25%)	1

hospital care (1.56 [1.14-2.12]) however, none of our study participants with a prior history of COVID-19 reported to require hospitalization.[12] This finding can be explained by recent studies demonstrating that seropositive individuals developed rapid immune responses with higher antibody titers after the first vaccination dose compared with those without a previous COVID-19 infection.[13,14] Although the short-term side effects reported in Table 1 were attributed directly to the vaccine, some of the preexisting chronic medical problems such as (prior history of atopic or food or drug allergies, asthma, and or other illness reported in Table-2) may have contributed to some of these side effects, or they could be an unfortunate coincidence from new underlying medical problems that are not related to the vaccine. Chronic medical problems such as heart attacks, lung problems, blood disorders, cancer, stroke, and several other illnesses (reported in Table-2), have occurred before the pandemic and will continue to occur.

The excipients (the inactive ingredients which are used in the mRNA vaccine to stimulate a stronger immune response, prevent bacterial contamination, and stabilize the potency of the vaccine during transportation and storage) are the major contributors to specific IgE-mediated and immediate reactions associated with vaccines.[15]

Another key finding in our study is that a fewer people with prior history of COVID-19 completed 2 doses when compared with those without history of prior COVID-19 infection (79% vs 95% in Pfizer group, 70% vs 84% in Moderna group) even though majority reported no intention to skip the second dose of vaccine. This may be due to some recipients experiencing serious systemic side effects such as brain fogging, vertigo-like symptoms, numbness, hives, shortness of breath, allergic-type reactions (swelling of lips/tongue/oral cavity).

Our study reported that in HCWs with history of prior COVID-19 infection, a significant association was noted among those who required taking time-off from work transiently after receiving Pfizer vaccine (22.41% vs 11.42%). However, in comparison with Pfizer group, a greater percentage of HCWs who received Moderna vaccine had to take time-off which may be related to experiencing more reactogenicity but there was no difference between those with or without prior COVID-19 infection. HCWs with temporary, unpleasant debilitating side effects from COVID-19 vaccines may deserve to get appropriate time off especially those who contracted COVID-19 infection in pre-vaccination phase. Any new COVID relief legislation should allow employees to take paid time off for vaccine-related side effects. Hospital system and patients would benefit from highly vaccinated

Table 2
Chronic medical conditions reported

Chronic medical condition reported	Pfizer-BioNtech vaccine group		Moderna vaccine group	
	History of COVID-19 in pre-vaccination period (n_1 = 58)	No history of COVID-19 in pre-vaccination period (n_2 = 753)	History of COVID-19 in pre-vaccination period (n_1 = 44)	No history of COVID-19 in pre-vaccination period (n_2 = 401)
Hypertension	13.79% (8)	13.28% (100)	13.63% (6)	12.96% (52)
Heart disease	0	1.59% (12)	0	2.24% (9)
Stroke	0	0.66% (5)	0	0.5% (2)
Epilepsy/seizure disorder	0	0.53% (4)	0	0.5% (2)
Chronic lung disease/ asthma/ chronic obstructive pulmonary disease	10.34% (6)	10.89% (82)	15.9% (7)	8.97% (36)
Atopic/ food/drug allergies	0	0.79% (6)	6.8% (3)	0.74% (3)
Liver disease	0	0.66% (5)	0	0.74% (3)
Diabetes mellitus	5.17% (3)	2.92% (22)	2.27% (1)	3.74% (15)
Thyroid condition	13.79% (8)	11.16% (84)	4.54% (2)	16.21% (65)
Blood disorders	0	0.80% (6)	4.54% (2)	2.49% (10)
Chronic kidney disease	0	0.40% (3)	0	0
Cancer/tumor	0	1.99% (15)	2.27% (1)	1.74% (7)
Tuberculosis/human immunodeficiency virus infection/immunocompromised condition	0	0	0	0.25% (1)
Gastrointestinal problems	10.34% (6)	7.70% (58)	11.36% (5)	9.22% (37)
Osteoarthritis	3.45% (2)	4.12% (31)	9.09% (4)	6.48% (26)
Rheumatoid arthritis	0	1.46% (11)	0	2% (8)
Fibromyalgia	1.72% (1)	0.40% (3)	2.27% (1)	0.74% (3)
Mental Illness	1.72% (1)	4.91% (37)	2.27% (1)	4.73% (19)
Chronic alcohol intake	1.72% (1)	1.06% (8)	2.27% (1)	1.74% (7)
Chronic smoking (or quit within last 5 y)	0	1.99% (15)	2.27% (1)	1.74% (7)
Substance abuse	0	0.13% (1)	0	0.25% (1)
None	53.45% (31)	54.71% (412)	54.54% (24)	46.63% (187)

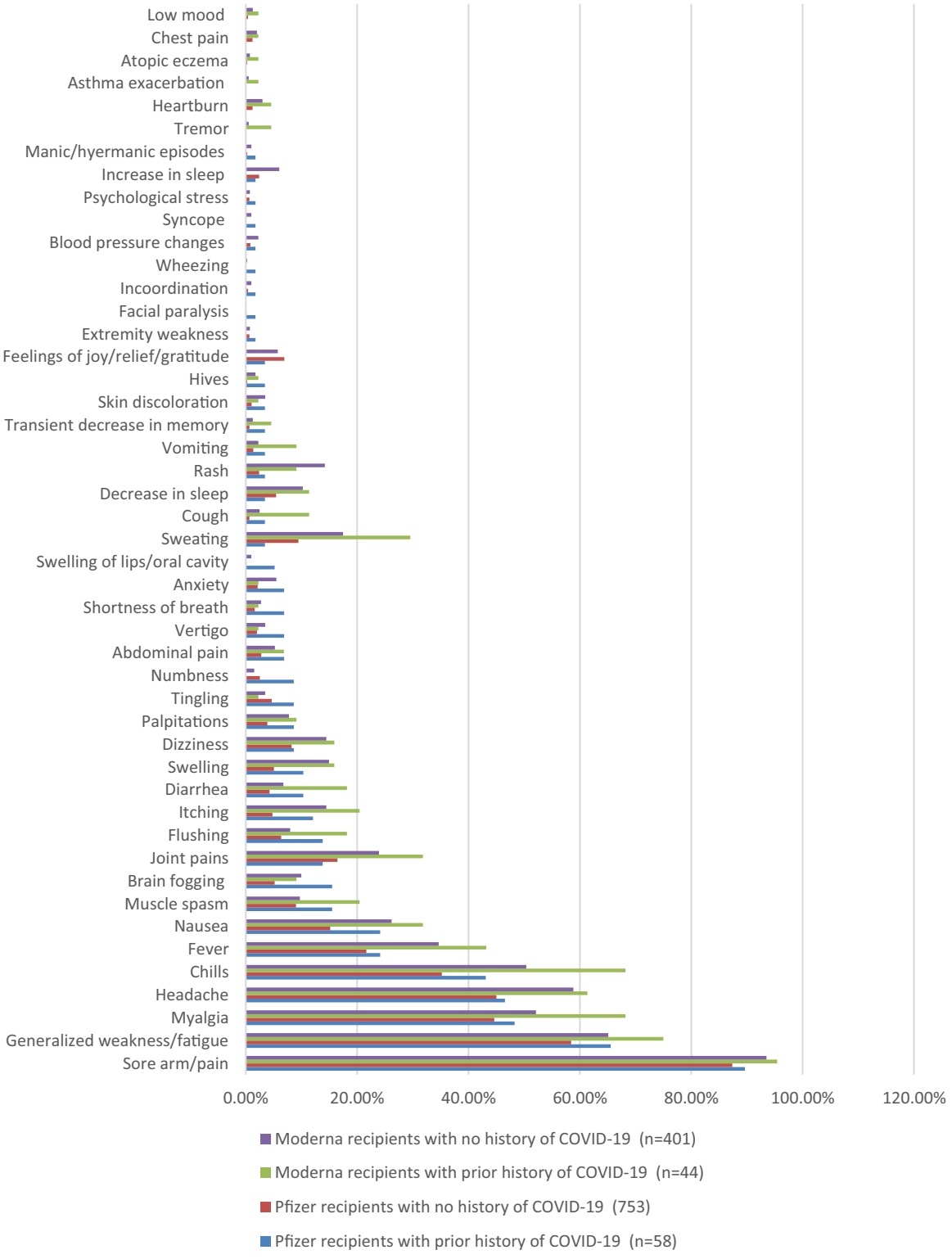

Fig 3. Dosing distribution.

workforce as this means fewer worker shortages and fewer outbreaks among staff if vaccination program is planned in a staggered fashion. As we have seen in our cross sectional study, although there is no intention to skip the second dose- a statistically significant proportion did not receive the second dose (about 80% HCWs with prior history of COVID-19 as opposed to about 95% HCWs without the history in Pfizer-BioNtech group received the vaccine and similarly 70% HCWs with prior history of COVID-19 as opposed to about 84%HCWs without the history in Moderna group received the vaccine) likely due to fear of side effects or unable to take time-off leading to

increased vaccine hesitancy undermining herd immunity. Given the high percentage of protection with these available mRNA vaccines against COVID-19, it is important that state and federal policy makers issue regulations to mandate the vaccination to employees and to provide paid time-off for the employees experiencing these side effects. Such regulations may help with more compliance and acceptance towards the second dose of the vaccine.

The main strengths of our study included a large study population which reflected real-life compared with the populations studied in the clinical trials, the availability of much detailed organ system-based symptomatology experienced, adequate details about the participants and the safety profiles of the vaccines. There are several limitations to our study. The potential recall bias through the study population is HCWs who would more than likely remember the symptoms they experienced. The sample of the study is a convenient sample and so the conclusions were attributed to the given sample but did not infer to the total population. Most of the symptoms reported are within the early post-vaccination phase of the vaccine, so the latent effects could not be identified. Although, we did not gather information on history of allergies, only about 18% of vaccine recipients experienced mild-moderate allergic reactions. Of note, the investigators believed that the sensitivity of symptoms perceived by HCWs might be more accurate and reliable with their higher level of education and their day-to-day experience in the health care field when compared to general population. Our questionnaire with the extended number of questions has covered a wide range of organ systems (with a long list of symptomatology) than any other study or the original vaccine trial. Also, we tried to avoid the response fatigue from survey respondents from general population but the results discussed above can be extended to general population.

CONCLUSIONS

Although local and systemic reactions are expected and often transient, they may have the most immediate influence on patients' perceptions of the vaccination experience. Monitoring of these COVID-19 vaccine-related short-term side effects outside of clinical trial settings may provide additional information for health care providers and the public about local and systemic reactions. Our independent survey among HCW focused on a detailed review of organ systems and was not limited to those mentioned in the Vaccine Adverse Event Reporting System managed by CDC.[10] The PHC can be considered as a predictor for severity of short-term side effects from messenger RNA vaccines. Setting expectations with patients may alleviate some of the potential anxiety elicited by post-vaccination side effects. While the vaccination program continues in the United States, a future COVID related legislation (facilitating for mandatory vaccination among employees along with providing paid time off for vaccine-related side effects) may help promote employees with higher compliance and acceptance with the vaccination especially in those to recover from unpleasant nonthreatening vaccine-related side effects.

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