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MAJOR ARTICLE

An Analysis of SARS-CoV-2 Vaccine Reactogenicity: Variation by Type, Dose, and History, Severity, and Recency of Prior SARS-CoV-2 Infection

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Background. There is limited information on the functional consequences of coronavirus disease 2019 (COVID-19) vaccine side effects. To support patient counseling and public health messaging, we describe the risk and correlates of COVID-19 vaccine side effects sufficient to prevent work or usual activities and/or lead to medical care ("severe" side effects).

Methods. The EPICC study is a longitudinal cohort study of Military Healthcare System beneficiaries including active duty service members, dependents, and retirees. We studied 2789 adults who were vaccinated between December 2020 and December 2021.

Results. Severe side effects were most common with the Ad26.COV2.S (Janssen/Johnson and Johnson) vaccine, followed by mRNA-1273 (Moderna) then BNT162b2 (Pfizer/BioNTech). Severe side effects were more common after the second than first dose (11% vs 4%; $P < .001$). First (but not second) dose side effects were more common in those with vs without prior severe acute respiratory syndrome coronavirus 2 infection (9% vs 2%; adjusted odds ratio [aOR], 5.84; 95% CI, 3.8–9.1), particularly if the prior illness was severe or critical (13% vs 2%; aOR, 10.57; 95% CI, 5.5–20.1) or resulted in inpatient care (17% vs 2%; aOR, 19.3; 95% CI, 5.1–72.5). Side effects were more common in women than men but not otherwise related to demographic factors.

Conclusions. Vaccine side effects sufficient to prevent usual activities were more common after the second than first dose and varied by vaccine type. First dose side effects were more likely in those with a history of COVID-19—particularly if that prior illness was severe or associated with inpatient care. These findings may assist clinicians and patients by providing a real-world evaluation of the likelihood of experiencing impactful postvaccine symptoms.

Keywords. COVID-19; reactogenicity; SARS-CoV-2; side effects; vaccination.

Effective severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines reduce the likelihood of severe outcomes associated with coronavirus disease 2019 (COVID-19) including death, hospitalization, and persistent sequelae [1]. Nonetheless, SARS-CoV-2 vaccines cause systemic side effects in many individuals, the most common of which are headache, fatigue, fever, and joint pain, among others [2, 3]. Vaccine reactogenicity has been defined by Herve et al. [4] as "a subset of reactions that occur soon after vaccination, and are a physical manifestation of the inflammatory response to vaccination." While side effects due to vaccine reactogenicity are typically mild, in some cases they are sufficiently bothersome to interfere with or prevent work or usual activities. The US Centers for Disease Control and Prevention has emphasized that understanding the risk and risk factors for vaccine reactogenicity is important, as "setting expectations with patients may alleviate some of the potential anxiety elicited by postvaccination reactogenicity" [3].

In the present study, we report on vaccine reactogenicity in a cohort of United States Military Health System (MHS) beneficiaries. We evaluated the prevalence and predictors of side effects including relationships with demographic factors, prior SARS-CoV-2 infection history, dose number, and vaccine type. Our focus on prior SARS-CoV-2 infection extends prior studies by using a null (SARS-CoV-2-negative) comparison group as well as examining how the severity and recency of prior COVID-19 illness correlate with the risk of postvaccine reactogenicity. These findings may assist individuals and clinicians by

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providing a real-world evaluation of the likelihood of experiencing patient-perceived severe postvaccine symptoms.

METHODS

Study Population, Recruitment, and Consent

The Epidemiology, Immunology and Clinical Characteristics of Emerging Infectious Diseases with Pandemic Potential (EPICC) study is a longitudinal cohort study of MHS beneficiaries including active duty service members, dependents, and retirees [5]. EPICC began enrollment by recruiting and interviewing participants at 10 military treatment facilities (MTFs) in March 2020 to study the epidemiology, risk factors, and outcomes of SARS-CoV-2 infection in patients seeking care or getting tested. In September 2020, EPICC was expanded to include a broader range of MHS beneficiaries in whom all study assessments were completed remotely via a secure online portal. This latter cohort, comprising the study population for the present analysis, were invited in one of three ways: via email or text invitation because they had a record of being tested, at the time of vaccination, or because they saw a flyer posted at one of the participating study sites.

Eligibility criteria for the present analysis required being age 18 or older, receiving at least 1 dose of a vaccine approved by the Food and Drug Administration (FDA) or under Emergency Use Authorization including BNT162b2 (Pfizer/BioNTech), mRNA-1273 (Moderna), and Ad26.COV2.S (Janssen/Johnson and Johnson), completing questions about vaccine side effects as described below, and being tested for SARS-CoV-2 at least once before vaccination. We excluded participants who reported that they had received a vaccine as part of a clinical trial due to uncertainty about whether they had received a vaccine or placebo.

Subject Consent

Participants provided informed consent when they were enrolled into EPICC including permission to access their electronic health records. The study was implemented according to the Declaration of Helsinki and Good Clinical Practice guidelines. The Uniformed Services University Institutional Review Board (IDCRP-085) and participating MTFs approved this study.

Data Collection

Data for the present analysis were collected online using REDCap at study enrollment, at 1-, 3-, 6-, 9-, and 12-month follow-up, and via electronic health records. Data relevant to the present analysis include demographic information, SARS-CoV-2 vaccination history, self-reported side effects from vaccination (first dose and second dose if applicable), SARS-CoV-2 testing history, and patient-reported history and severity of COVID symptoms.

Measuring Vaccine Receipt and Vaccine Reactogenicity

SARS-CoV-2 test history and vaccination history were ascertained via self-report in the enrollment and follow-up questionnaires and through electronic health records, with the electronic medical encounter data taking precedence. This analysis does not include side effects from third or booster doses due to small numbers at the time of analysis (January 2022). Vaccine reactogenicity was assessed using the question "Did you have any side effects after receiving your first dose?" and defined based on the patient-perceived impact on functional status: no symptoms, mild ("minor symptoms that did not affect my ability to do my usual activities or my job"), moderate ("affected my ability to do my usual activities or my job"), and severe ("prevented me from doing my usual activities, caused me to miss work, and/or caused me to seek medical care") [6]. An identical question was asked for the second dose when applicable.

Ascertaining Prior SARS-COV-2 Infection and Measuring the Severity of Prior COVID-19 Illness

Prevaccination SARS-CoV-2 infection was defined as having a positive SARS-CoV-2 test on the same day or before the date of the first vaccine dose. Participants were also asked about the date of onset and perceived severity of COVID-19 symptoms/illness "at their worst," categorized as follows: never had symptoms, mild ("noticeable but not impairing"), moderate ("impairing but not disabling; interferes with duties"), severe ("disabling; cannot perform duties"), and critical ("life-threatening"). Self-reported medical care for COVID-19 illness was categorized as none (includes those with no symptoms, who self-treated, or who did not seek care), outpatient evaluation (includes emergency department care that did not result in admission), and inpatient admission.

Analysis Methods

The primary aim was to characterize vaccine reactogenicity as a function of prevaccination SARS-CoV-2 infection (including recency and severity of COVID-19 symptoms/illness), vaccine type and dose, and demographic factors. Subjects with only negative test(s) before the date of the first vaccination dose comprised the comparison group. We excluded 10 individuals whose first positive test occurred within 2 weeks following the first vaccination dose due to the uncertainty of their infection status at the time of vaccination. We also excluded 7 subjects from the second dose analysis because they had their first positive test between vaccine doses. We only used side effect data if it had been collected at least 1 day after vaccination, which meant that for subjects who completed their baseline questionnaire on the day of vaccination we used the side effect report from a subsequent interview.

To look at recency and severity of COVID-19 symptoms, the positive group was subdivided by recency of first positive test

(within 89 days, or >89 days before vaccination) and severity of COVID-19 symptoms/illness and medical care as defined above. The cut-point of 89 days was the median time interval between the first positive test and vaccination.

All analyses were performed using Stata, version 17 (StataCorp, College Station, TX, USA). Summary statistics of study participants by prevaccination SARS-CoV-2 history are presented as means and proportions and compared using analysis of variance and chi-square tests as appropriate. Multinomial logistic regression was used to calculate adjusted odds ratios (aORs) and 95% confidence intervals. The dependent/outcome variable was vaccine side effects (none, mild, moderate = affected work or usual activities, severe = prevented work or usual activities), with "none" as the reference category. We adjusted a priori for age (years), race (White, Black, Asian, other/unknown/prefer not to answer), ethnicity (Hispanic ethnicity, not Hispanic ethnicity, unknown/prefer not to answer), sex (male, female, missing), active duty status (yes, no), and first dose type. The predictor variable for the main model was SARS-CoV-2 test history (negative, positive). Three additional models stratified the positive group by recency of infection, COVID-19 severity, and COVID-19 medical care as defined above. Separate models were fit for the first dose side effects and the second dose side effects.

RESULTS

The study population consists of 2789 adult vaccinated MHS beneficiaries (Table 1) who met all eligibility criteria as described above. Participants received their first vaccine dose between December 14, 2020, and November 22, 2021, and 2574 participants received a second dose between January 3, 2021, and December 13, 2021. The mean age of the participants (range) was 35 (18–79) years, with the majority being active duty (88%), male (62%), and White (70%). Most participants (n = 2221, 79%) were negative for SARS-CoV-2 on all prevaccination tests.

Table 2 (crude) and Table 3 (adjusted) show the crude prevalence and adjusted odds of self-reported side effects associated with the first dose (left side) and second dose (right side) by prevaccination SARS-CoV-2 history. Notably, 4% of the study population (2% of those who tested negative and 9% of those who tested positive) reported first dose side effects sufficient to prevent work or usual activities. For the second dose, 11% reported these side effects overall, a rate that was similar for those who tested negative (11%) and those who tested positive (10%) before vaccination. The adjusted odds ratios of mild, moderate, or severe vaccine side effects, relative to no side effects, in those with a prevaccination history of SARS-CoV-2 infection vs those without were $aOR_{mild} = 1.25$ (95% CI, 1.0–1.6), $aOR_{moderate} = 3.00$ (95% CI, 2.2–4.0), and $aOR_{severe} = 5.84$ (95% CI, 3.8–9.1) (Table 3). When stratified by recency of infection (≤88 vs >88 days prior), the odds ratios were numerically higher in those with more recent infection, although the test for interaction was only significant for the moderate category (Table 3, left). Self-reported severity of prior COVID-19 as measured by symptom severity and by inpatient medical care was generally associated with more severe vaccine side effects (Table 3, left). Side effects for the second vaccine dose generally did not differ between those with and without prior infection, although there was an association between self-reported severity of prior SARS-CoV-2 symptoms and severe vaccine side effects (Table 3, right).

Supplementary Table 1 shows the crude prevalence of first dose side effects by demographic factors and vaccine type without consideration of SARS-CoV-2 infection history. Of the factors considered, women reported more severe side effects than men ($P < .002$), and side effects were least frequent in those receiving BNT162b2 (Pfizer/BioNTech), followed by

Table 1. Description of Study Population (n = 2789)

			Prevaccination SARS-CoV-2 Test Status[a]			
		No.	Total (n = 2761), %	Negative (n = 2287), %	Positive (n = 593), %	*P* Value[b]
Age	Mean (SD), y	2789	35 (10)	35 (10)	36 (10)	.32
Race	White	1965	70	71	67	.011
	Black	286	10	10	12	
	Asian	191	7	7	5	
	Unknown[c]	347	12	12	15	
			100	100	100	
Hispanic/ Latino	No	1942	70	70	67	.21
	Yes	421	15	15	17	
	Unknown[d]	426	15	15	15	
			100	100	100	
Sex	Male	1719	62	62	58	.18
	Female	887	32	31	35	
	Missing	183	7	6	7	
% active duty		2456	88	90	81	<.001
Vaccine (1st dose)	mRNA-1273/ Moderna	919	33	36	23	<.001
	BNT162b2/ Pfizer/ BioNTech	1650	59	57	68	
	Ad26.COV2.S/ Janssen/ Johnson and Johnson	202	7	7	9	
	Missing	18	<1	<1	<1	
			100	100	100	

Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a]Prevaccination SARS-CoV-2 test status defined as follows: negative: all tests up to the same day as the first dose are negative; positive: 1 or more positive tests up to the same day as the first dose.

[b]*T* test (age), chi-square test (proportions).

[c]Other, unknown, prefer not to answer.

[d]Unknown, prefer not to answer.

Table 2. Vaccine Reactogenicity by COVID-19 History, Recency, and Severity

	Vaccine Side Effects (First Dose)					Vaccine Side Effects (Second Dose)				
	No.	None, %	Mild, %	Moderate, %	Severe, %	No.	None, %	Mild, %	Moderate, %	Severe, %
COVID-19 history										
Negative	2221	46	41	10	2	2056	31	32	26	11
Positive	568	34	37	20	9	501	35	34	22	10
COVID-19 recency										
Negative	2221	46	41	10	2	2056	31	32	26	11
Positive >88 d	283	39	35	17	9	241	37	33	21	9
Positive ≤88 d	285	29	38	24	8	260	32	34	23	10
COVID-19 severity										
Negative	2221	46	41	10	2	2056	31	32	26	11
Positive no COVID-19 Sx	58	50	26	14	10	47	45	30	13	13
Positive mild/moderate COVID-19 Sx	295	37	42	15	6	263	34	40	20	6
Positive severe/critical COVID-19 Sx	144	29	28	30	13	130	26	27	31	16
Positive unknown COVID-19 Sx	71	23	39	30	8	61	46	25	20	10
COVID-19 medical care										
Negative	2221	46	41	10	2	2056	31	32	26	11
Positive no COVID-19 medical care	257	37	37	20	5	230	29	40	23	9
Positive outpatient COVID-19 care	153	30	41	18	11	139	38	30	23	9
Positive inpatient COVID-19 care	23	30	17	35	17	22	23	27	36	14
Positive unknown COVID-19 care	135	35	33	21	10	110	45	27	17	11
Total	2789	44	40	12	4	2557	32	32	25	11

Abbreviation: COVID-19, coronavirus disease 2019.

Moderate vaccine side effects: affected work or usual activities; severe vaccine side effects: prevented work or usual activities or sought medical care.

Table 3. Adjusted Vaccine Reactogenicity by COVID-19 History, Recency, and Severity

	Vaccine Symptoms (First Dose)			Vaccine Symptoms (Second Dose)		
	Mild vs None (aOR)	Moderate vs None (aOR)	Severe vs None (aOR)	Mild vs None (aOR)	Moderate vs None (aOR)	Severe vs None (aOR)
Prevaccination SARS-CoV-2 test history						
Negative (reference)	Ref	Ref	Ref	Ref	Ref	Ref
Positive	**1.25 [1.0–1.6]**	**3.00 [2.2–4.0]**	**5.84 [3.8–9.1]**	1.02 [0.8–1.3]	0.92 [0.7–1.2]	1.04 [0.7–1.5]
COVID-19 recency						
Negative (reference)	Ref	Ref	Ref	Ref	Ref	Ref
Positive before vaccine (>88 d)	1.05 [0.8–1.4]	**2.02 [1.4–3.0]**	**5.00 [2.9–8.6]**	0.93 [0.7–1.3]	0.81 [0.6–1.2]	0.90 [0.5–1.5]
Positive before vaccine (≤88 d)	**1.51 [1.1–2.0]**	**4.30 [3.0–6.2][a]**	**6.89 [4.0–11.9]**	1.12 [0.8–1.6]	1.03 [0.7–1.5]	1.19 [0.7–1.9]
COVID-19 severity						
Negative (reference)	Ref	Ref	Ref	Ref	Ref	Ref
Positive no symptoms	0.58 [0.3–1.1]	1.12 [0.5–2.6]	**3.58 [1.3–9.5]**	0.78 [0.4–1.6]	0.44 [0.2–1.2]	1.08 [0.4–2.9]
Positive mild/moderate symptoms	**1.35 [1.0–1.8][a]**	**2.11 [1.4–3.1]**	**4.16 [2.3–7.5]**	1.18 [0.9–1.6]	0.84 [0.6–1.2]	0.66 [0.4–1.2]
Positive severe/critical symptoms	1.13 [0.7–1.8]	**5.53 [3.5–8.8][b]**	**10.57 [5.5–20.1]**	1.16 [0.7–1.9]	**1.79 [1.1–3.0][b]**	**2.58 [1.4–4.7]**
COVID-19 medical care						
Negative (reference)	Ref	Ref	Ref	Ref	Ref	Ref
Positive no treatment	1.20 [0.9–1.6]	**2.88 [2.0–4.2]**	**3.46 [1.8–6.6]**	**1.50 [1.1–2.1]**	1.43 [0.8–2.5]	1.50 [0.9–2.6]
Positive outpatient	**1.54 [1.0–2.3]**	**3.03 [1.8–5.1]**	**8.81 [4.6–16.8][c]**	0.74 [0.5–1.1][c]	0.73 [0.4–1.4]	0.74 [0.4–1.4]
Positive inpatient	0.67 [0.2–2.3]	**7.09 [2.4–20.7]**	**19.3 [5.1–72.5][c]**	1.49 [0.4–5.3]	3.33 [0.7–16.0]	3.35 [0.7–16.1]

Abbreviations: aOR, adjusted odds ratio; COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Adjusted odds ratios and 95% CIs were calculated using multinomial logistic regression, adjusting for ethnicity, race, age, active duty status, vaccine type, and sex. Unknown severity/treatment groups not presented. The dependent variable is vaccine side effects, with "none" being the reference category; bolded ORs indicate statistical significance.

[a]Statistical difference between the aOR for ≤88 days and <88 days.

[b]Statistical difference between the aOR for severe/critical symptoms and no symptoms.

[c]Statistical difference between the aOR for outpatient/inpatient treatment and for no treatment;

moderate vaccine side effects: affected work or usual activities; severe vaccine side effects: prevented work or usual activities or sought medical care.

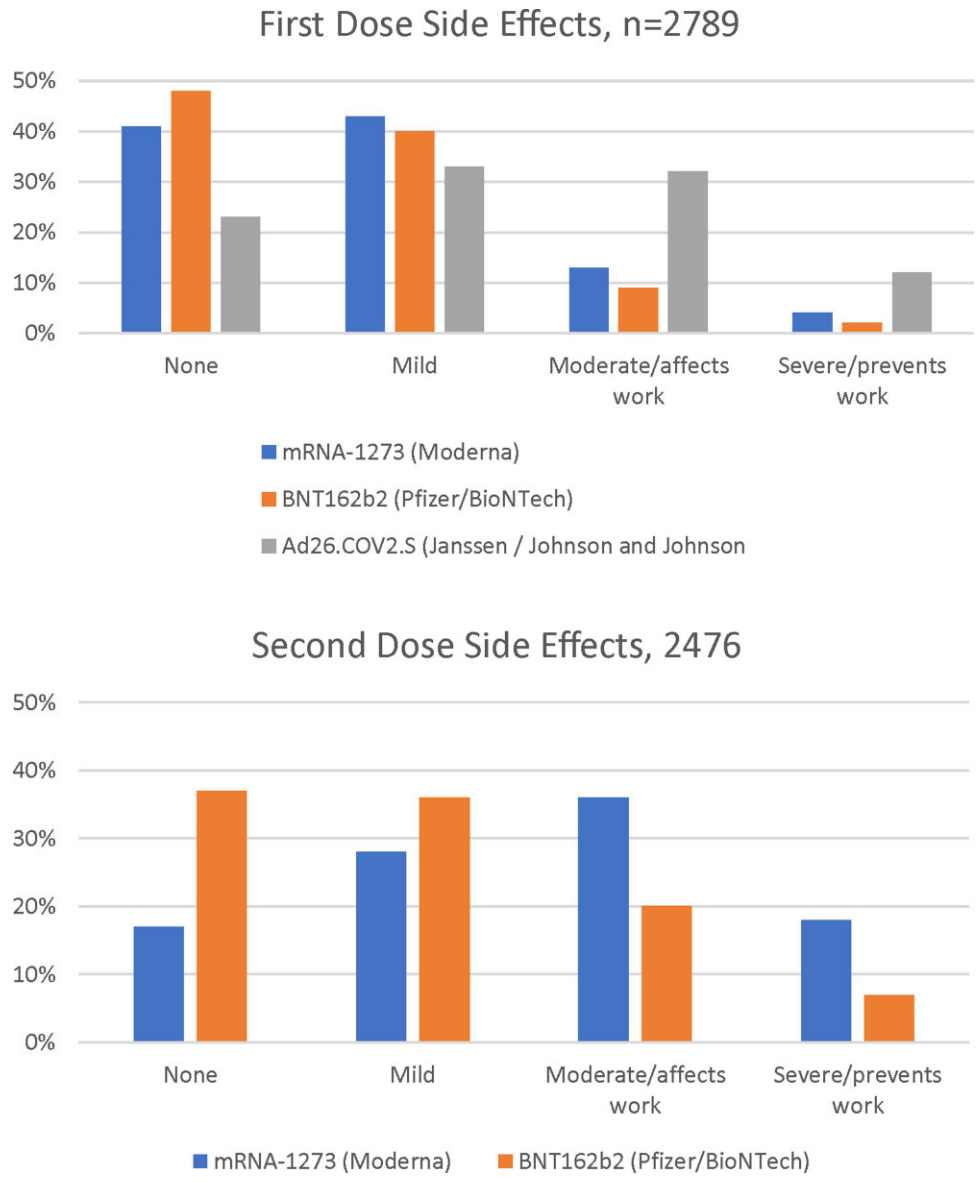

Figure 1. Self-reported vaccine side effects by type and dose.

mRNA-1273 (Moderna) and Ad26.COV2.S (Janssen/Johnson and Johnson; $P < .001$) (Figure 1). In a model adjusting for demographic factors and vaccine type without SARS-CoV-2 infection history (data not shown), predictors of increased first dose vaccine side effects included female sex (aORs ranging from 1.6 to 1.9 for levels of side effects compared with male sex; all $P < .01$), mRNA-1273 (Moderna) vaccine (aORs ranging from 1.4 to 2.0 compared with BNT162b2 [Pfizer/BioNTech]; all $P < .01$), and Ad26.COV2.S (Janssen/Johnson and Johnson; aORs ranging from 2.2 to 15.0; all $P < .01$; compared with BNT162b2 [Pfizer/BioNTech]). There were no other consistent differences in first dose vaccine side effects for the other demographic factors considered (age, race, ethnicity, and active duty status).

DISCUSSION

We characterized self-reported side effects associated with SARS-CoV-2 vaccination in a large MHS cohort consisting mostly of active duty service members but also including adult dependents and retirees. We noted that vaccine reactogenicity sufficient to preclude work or usual activities was reported by 4% of vaccinees (first dose) and 11% of vaccinees (second dose). These aggregate reactogenicity estimates are roughly similar to the frequency of the Grade III and Grade IV event frequencies reported in phase III clinical trials and some observational studies—though they were not defined exactly the same way across such studies [7–10]. Our finding that side effects were stronger for the second vs first dose is consistent with

findings from postlicensure surveillance systems like V-SAFE and OpenSAFELY [2, 3, 11].

Our analysis identified several additional factors associated with reactogenicity. Functionally significant side effects were more pronounced for the mRNA-1273 (Moderna) and Ad26.COV2.S (Janssen/Johnson and Johnson) vaccine products compared with the BNT162b2 (Pfizer/BioNTech) vaccine. This relatively increased reactogenicity with the mRNA-1273 vaccine postauthorization has been noted in other observational studies [3, 12]. In contrast to what was reported in the phase 3 clinical trial [13] and in 1 prior observational study [9], we found a much higher likelihood of side effects for the Ad26.COV2.S (Janssen/Johnson and Johnson) vaccine compared with the other vaccine products. While statistically significant, this finding needs to be interpreted with caution given the small size of the subgroup that was administered this vaccine as well as the hypothetical possibility that there are unmeasured systematic differences between participants choosing this product over 1 of the mRNA products. Side effects were more frequent in women than men but did not differ by any of the other demographic factors considered in the adjusted models. This association with female sex and COVID-19 vaccine reactogenicity has been noted in other COVID-19 studies [2] and has been described in other infectious disease vaccines (eg, influenza) in which there is a known correlation between female sex, vaccine reactions, immunity, and clinical protection [14].

Those with a history of prior SARS-CoV-2 infection had stronger reactogenicity to the first dose (but not second) compared with those without prior infection. These data also suggest that the severity of prior infection (measured by patient-perceived severity and inpatient care) was associated with higher reactogenicity to the first vaccine dose and less consistently with the second dose. This association (between prior COVID-19 and vaccine side effects) has been noted in several other observational studies, including those that studied the Pfizer/BioNTech-BNT162b2 vaccine product [2]. Our findings confirm this association, and we extend prior studies with use of an important SARS-CoV-2-negative population null model, showing a "dose-response" association (with the severity of prior COVID-19 illness associated with an increased risk of first dose vaccine reactogenicity) and a finding of patient-reported infection severity predicting postvaccine reactogenicity.

Those with more recent SARS-CoV-2 infection (eg, within 89 days) had numerically higher but not statistically significant vaccine reactogenicity in most instances. This cut-point was chosen as it was the median time between illness and vaccination. It is possible that a larger study may have been able to elucidate this time effect with more granularity.

The possible biological reasons for the association of prior SARS-CoV-2 infection and greater vaccine reactogenicity are speculative. Examining the reverse sequence from what was observed here (eg, that prior SARS-CoV2 infection predicts vaccine reactogenicity), vaccine-induced inflammation before infection may be relevant. Antibody-dependent enhancement has not been shown to occur in those vaccinated and then exposed to SARS-CoV-2 in preclinical models or in clinical trials, so this is unlikely to be a mechanism [15]. Indeed, those who are vaccinated for SARS-CoV-2 and experience breakthrough infections report fewer SARS-CoV-2 symptoms compared with those who are unvaccinated [16]. Moreover, vaccine reactogenicity is thought to be predominantly driven by innate immune responses rather than adaptive immunity [4]. Interestingly, prior studies of influenza vaccines have noted that prevaccine subject B-cell profiles may predict short-term cytokine responses after vaccination [4]. We note that some [12, 17] but not all [18, 19] studies have noted that vaccine side effects correlate with measured vaccine immunogenicity. Mechanistic studies to further elucidate how inflammatory responses differ in those with and without significant COVID-19 vaccine reactogenicity and prior COVID-19 illness would be valuable.

The strengths of the study include the large sample size and our SARS-CoV-2-negative comparison group. Data were collected via self-report and electronic health records related to SARS-CoV-2 vaccination and testing. Another strength of the study is the use of patient-reported outcomes (such as patient-perceived vaccine or COVID-19 severity), which are difficult to ascertain though medical documentation. Our analysis is focused on functional consequences of vaccine side effects in the aggregate (eg, inability to work or perform usual activities) rather than a specific side effect.

There were several weaknesses to this study. Our study population was majority active duty service members, and therefore predominantly young men, which may limit the generalizability of these results. Selection bias may have occurred if those who enrolled were more likely to have or report vaccine side effects than those who did not enroll, although this presumably would not differ by prior history of COVID-19, and the criteria for enrollment were not specifically focused on vaccines. Our study population consisted of military health care beneficiaries and differed in some ways from the broader military community, and we therefore adjusted for demographic factors.

One additional limitation of this and similar studies is that prevaccination infections were unrecognized if they were subclinical, did not lead to testing, or resulted in a false-negative test. Further, it is possible that some subjects had false-positive tests or reported their test history incorrectly. These types of errors, if present to a large degree, would most likely attenuate our results. Unlike clinical trials, there was no medical adjudication or placebo to ascertain whether such events were directly related to the vaccine. Unfortunately, potential attribution of postvaccine symptoms and their severity to the vaccine itself

is a well-known limitation in the vaccine reactogenicity literature, which is difficult to mitigate [4]. Finally, while self-reported patient outcomes are a strength of this study, there is the possibility of recall bias in the recollection of COVID-19 severity and vaccine side effects.

In summary, we note that sex, vaccine product, and prior COVID-19 infection severity all predict the degree of first dose side effects sufficient to preclude work or usual activities. These findings are important for transparent patient counseling and may contribute to evidence-based discussions of optimal timing of vaccination. Future studies will be important to examine how reactogenicity of the primary dose series predicts third and later boosting dose symptoms in those with and without a history of COVID-19.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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