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Reactogenicity Following Receipt of mRNA-Based COVID-19 Vaccines

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In December 2020, 2 mRNA-based COVID-19 vaccines (Pfizer-BioNTech and Moderna) were granted Emergency Use Authorization by the US Food and Drug Administration as 2-dose series and recommended for use by the Advisory Committee on Immunization Practices.[1-3] In late February 2021, the US Food and Drug Administration granted Emergency Use Authorization for a third COVID-19 vaccine, a single-dose adenovirus vector-based vaccine from Janssen (Johnson & Johnson).

Supplemental content

In clinical trials of the mRNA-based 2-dose vaccines, participants reported local and systemic reactions (reactogenicity).[4,5] Frequently reported reactions included injection site pain, fatigue, and headache; greater reactogenicity was reported following the second dose.[4,5] Continued monitoring of reactogenicity of COVID-19 vaccines outside of clinical trial settings may provide additional information for health care practitioners and the public about transient local and systemic reactions following COVID-19 vaccination.

V-safe Active Surveillance System

To facilitate rapid assessment of COVID-19 vaccines, in 2020, the Centers for Disease Control and Prevention (CDC) established v-safe, a new active surveillance system for collecting near–real-time data from COVID-19 vaccine recipients in the US. V-safe participants voluntarily self-enroll and receive periodic smartphone text messages to initiate web-based health surveys from the day of vaccination (day 0) through 12 months after the final dose of a COVID-19 vaccine.[6] From day 0 through day 7 after each vaccine dose, participants are asked questions about solicited local and systemic reactions (eg, injection site pain, fatigue, headache). These solicited reactions do not include allergic reactions or anaphylaxis; however, v-safe does allow participants to enter free-text information about their postvaccination experience and asks about adverse health events (eg, received medical care). Medically attended events are followed up on through active telephone outreach; future analyses will address these adverse vaccine experiences. This report describes information on solicited local and systemic reactogenicity reported to v-safe on days 0 to 7 after each dose of vaccine from December 14, 2020, through February 28, 2021. Responses were limited to individuals who were vaccinated by February 21, 2021, to allow a 7-day reporting period after the day of vaccination. Preliminary data from v-safe through January 13, 2021, have been previously reported.[7] This activity was reviewed by the CDC and was conducted consistent with applicable federal law and CDC policy (see Additional Information).

Table. Solicited Local and Systemic Reactions[a] to mRNA-Based COVID-19 Vaccines Reported 0 to 7 Days After Vaccination—Centers for Disease Control and Prevention V-safe Surveillance System, December 14, 2020, to February 28, 2021

	No. (%)					
	Dose 1			Dose 2		
Reaction	Both vaccines (N = 3 643 918)	Pfizer-BioNTech (n = 1 659 724)	Moderna (n = 1 984 194)	Both vaccines (N = 1 920 872)	Pfizer-BioNTech (n = 971 375)	Moderna (n = 949 497)
Any injection site reaction	2 550 710 (70.0)	1 085 242 (65.4)	1 465 468 (73.9)	1 443 899 (75.2)	666 635 (68.6)	777 264 (81.9)
Pain	2 472 373 (67.8)	1 055 604 (63.6)	1 416 769 (71.4)	1 389 629 (72.3)	645 917 (66.5)	743 712 (78.3)
Redness	204 097 (5.6)	56 780 (3.4)	147 317 (7.4)	240 265 (12.5)	57 956 (6.0)	182 309 (19.2)
Swelling	379 539 (10.4)	110 077 (6.6)	269 462 (13.6)	348 986 (18.2)	100 430 (10.3)	248 556 (26.2)
Itching	197 441 (5.4)	62 486 (3.8)	134 955 (6.8)	214 658 (11.2)	60 946 (6.3)	153 712 (16.2)
Any systemic reaction[a]	1 823 068 (50.0)	797 410 (48.0)	1 025 658 (51.7)	1 333 931 (69.4)	623 746 (64.2)	710 185 (74.8)
Fatigue	1 127 638 (30.9)	483 146 (29.1)	644 492 (32.5)	1 034 462 (53.9)	464 659 (47.8)	569 803 (60.0)
Headache	943 607 (25.9)	409 359 (24.7)	534 248 (26.9)	897 005 (46.7)	392 266 (40.4)	504 739 (53.2)
Myalgia	705 100 (19.4)	281 743 (17.0)	423 357 (21.3)	845 314 (44.0)	357 381 (36.8)	487 933 (51.4)
Chills	321 009 (8.8)	116 034 (7.0)	204 975 (10.3)	600 354 (31.3)	220 831 (22.7)	379 523 (40.0)
Fever	314 676 (8.6)	116 951 (7.0)	197 725 (10.0)	566 112 (29.5)	208 976 (21.5)	357 136 (37.6)
Joint pain	317 034 (8.7)	123 319 (7.4)	193 715 (9.8)	492 031 (25.6)	192 926 (19.9)	299 105 (31.5)
Nausea	275 423 (7.6)	114 087 (6.9)	161 336 (8.1)	319 248 (16.6)	127 454 (13.1)	191 794 (20.2)
Vomiting	25 425 (0.7)	9966 (0.6)	15 459 (0.8)	31 056 (1.6)	11 276 (1.2)	19 780 (2.1)
Diarrhea	189 878 (5.2)	83 016 (5.0)	106 862 (5.4)	133 877 (7.0)	60 641 (6.2)	73 236 (7.7)
Abdominal pain	111 044 (3.0)	47 096 (2.8)	63 948 (3.2)	117 494 (6.1)	48 129 (5.0)	69 365 (7.3)
Rash outside of injection site	42 409 (1.2)	17 765 (1.1)	24 644 (1.2)	32 686 (1.7)	13 132 (1.4)	19 554 (2.1)

[a] Systemic reactions do not include allergic reactions or anaphylaxis.

Self-reported Local and Systemic Reactions Among V-safe Participants

By February 21, 2021, more than 46 million persons received at least 1 dose of an mRNA-based COVID-19 vaccine.[8] A total of 3 643 918 persons were enrolled in v-safe and completed at least 1 health survey within 7 days following their first vaccine dose; 1 920 872 v-safe participants reported receiving a second vaccine dose and completed at least 1 daily health survey within 7 days following the second dose. Solicited local and systemic reactions during days 0 to 7 after each dose were assessed.

Most v-safe participants reported an injection site reaction (dose 1: 70.0%; dose 2: 75.2%) or a systemic reaction (dose 1: 50.0%; dose 2: 69.4%) during days 0 to 7 after vaccination (**Table**). The most frequently reported solicited local and systemic reactions after the first dose of COVID-19 vaccine were injection site pain (67.8%), fatigue (30.9%), headache (25.9%), and myalgia (19.4%). Reactogenicity was substantially greater after the second dose for both vaccines, particularly for systemic reactions, including fatigue (53.9%), headache (46.7%), myalgia (44.0%), chills (31.3%), fever (29.5%), and joint pain (25.6%).

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 (Table). When stratified by age (<65 vs ≥65 years), differences in reactogenicity by vaccine remained consistent with overall findings (data not shown). Local and systemic reactions were less commonly reported by v-safe participants 65 years and older compared with those younger than 65 years, but greater reactogenicity after the second dose was observed for both age groups (eFigure in the Supplement). For both doses of both vaccines, the percentage of v-safe participants who reported local and systemic reactions was highest on day 1 after vaccination and declined markedly through day 7.

The frequency of reported reactions was generally consistent with results observed in clinical trials.[4,5] Data from millions of v-safe participants indicate that injection site pain is common after both the first and second doses of either mRNA-based vaccine. Systemic reactions, including fatigue, headache, myalgia, chills, fever, and joint pain, occurred in participants after the first dose, although they were more frequently reported after the second dose among both Pfizer-BioNTech and Moderna vaccine recipients. Persons 65 years and older reported less reactogenicity than younger persons. Limitations of v-safe include voluntary participation via an opt-in smartphone-based system that includes less than 10% of vaccinated persons.

Although local and systemic reactions are expected and often transient, they may have the most immediate influence on patients' perceptions of the vaccination experience. Setting expectations with patients may alleviate some of the potential anxiety elicited by postvaccination reactogenicity. Clinicians should counsel vaccine recipients that these solicited local and systemic reactions are most commonly reported during the first day following their second dose; a short period before symptom resolution can be expected.[9]

ARTICLE INFORMATION

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Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the US Centers for Disease Control and Prevention (CDC). Mention of a product or company name is for identification purposes only and does not constitute endorsement by the CDC.

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Additional Information: See eg, 45 CFR part 46.102(l)(2); 21 CFR part 56; 42 USC §241(d); 5 USC §552a; 44 USC §3501 et seq.

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