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Allergic symptoms after mRNA COVID-19 vaccination and risk of incomplete vaccination

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Clinical Implications

- Allergic symptoms after dose 1 of mRNA coronavirus disease 2019 (COVID-19) vaccine may contribute to incomplete vaccination. However, most patients with mild or nonimmediate symptoms can safely complete vaccination. Allergists must be prepared to counsel patients to prevent incomplete vaccination.

Allergic reactions have been reported after coronavirus disease 2019 (COVID-19) mRNA vaccination. Anaphylaxis to the first dose is a contraindication to subsequent mRNA vaccination; however, many mild or nonimmediate allergic symptoms are not.[1,2] We sought to determine whether self-reported allergic symptoms were associated with incomplete vaccination.

We prospectively studied Massachusetts General Brigham (MGB) employees who received their first dose of mRNA COVID-19 vaccine between December 16, 2020, and February 1, 2021, with follow-up through March 15, 2021 (eMethods). For the 3 days after vaccination, which was captured in the electronic health record, employees completed symptom surveys through e-mail, text, phone, or employee smartphone application links. Self-reported allergic symptoms included itching or rash (other than at the injection site), hives, swelling, and/or respiratory symptoms (available in this article's Online Repository at www.jaci-inpractice.org). The MGB allergists were available to assess any employees who self-reported a symptom more severe than itching and rash between doses.

We determined the frequency of self-reported allergic symptoms using the number of dose 1 survey respondents as the denominator. We compared frequencies using chi-squared tests, considering a 2-sided *P* value less than .05 statistically significant. The primary outcome was incomplete mRNA COVID-19 vaccination (ie, did not receive dose 2). We used a multivariable logistic regression model to assess the association of self-reported allergic symptoms and incomplete vaccination. We adjusted for age, sex, race, vaccine manufacturer, MGB site, and eligibility group. We also considered the exposure of severe allergic symptoms (respiratory symptoms plus 1 of the following: itching or rash other than injection site, hives, or swelling). This study was approved by the MGB Human Research Committee. Analyses were conducted in SAS version 9.4 (Cary, NC).

Of 61,057 employees who received their first dose of a COVID-19 mRNA vaccine, 22,683 (37%) received Pfizer-BioNtech and 38,374 (63%) received Moderna. Symptom surveys were completed by 50,167 employees (83%). Self-reported allergic symptoms were reported by 1,261 employees after dose 1 (2.5%; 95% confidence interval [95% CI] 2.4%-2.6%); 576 (46%) received an allergy/immunology consultation.

Overall, 50,269 (99%) received the second vaccine dose. Incomplete vaccination occurred in a total of 348 employees (0.7%): 43 (3%) who self-reported allergic symptoms after dose 1 versus 305 (0.6%) who did not. Incomplete vaccination was more common among women and differed by MGB site, but not by race or eligibility group (Table I).

Self-reported allergic symptoms after dose 1 were associated with an increased odds of incomplete vaccination (adjusted odds ratio [OR] 5.15; 95% CI 3.75-7.06; $P < .001$; Table II). Self-reported severe allergic symptoms were rare and associated with a markedly increased odds of incomplete vaccination (unadjusted OR 23.19; 95% CI 9.74-55.22; $P < .001$).

Of the 1,261 with self-reported allergic symptoms after dose 1, 1,218 received dose 2 and 860 (71%) completed the dose 2 symptom survey. Among the 860 survey respondents, there were 146 (17%) with recurrent allergic symptoms but none were severe.

In a prospective cohort of employees receiving mRNA COVID-19 vaccination, self-reported allergic symptoms (reported by 2.5% after dose 1) were associated with 5-fold increased odds of incomplete vaccination. The vast majority of individuals (97%) with self-reported allergic symptoms safely completed the vaccination series.

The currently 2 authorized mRNA COVID-19 vaccines which require a 2-dose vaccination series.[3,4] The implications of incomplete vaccination remain unclear, but decreased vaccine efficacy and/or durability is the primary public health concern.

Study limitations include the use of self-reported data, although the cohort included health care workers, and therefore, data reliability may be high. Hospital employees had direct access to MGB allergists and allergy protocols for dose 2 administration, a level of specialist access unlikely to be reproduced on a population level. As such, these findings likely represent a best-care scenario, biasing results toward the null. Allergic symptoms are likely to be a larger factor in other U.S. populations that are not health care employees and do not have easy access to specialist care.

An estimated 6.3 million adults in the United Stated may experience allergic symptoms after mRNA COVID vaccination, and this study warns that at least 200,000 are at risk of incomplete vaccination. Most patients with mild or nonimmediate symptoms can safely complete their vaccination.[5,6]

Recent estimates from the U.S. Centers for Disease Control and Prevention found that approximately 8% of adults in the United States have not completed the mRNA COVID-19 vaccination series.[7] Our data suggest that allergic symptoms may contribute to incomplete vaccination. Clinicians, particularly allergists, need to be aware of this risk and prepared to provide counseling to reduce the impact of incomplete vaccination.

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TABLE I. Characteristics of employees with incomplete mRNA COVID vaccination

Characteristics	Incomplete vaccination (n = 348)	Any self-reported allergic symptoms after dose 1* (n = 43)	No self-reported allergic symptoms after dose 1 (n = 305)	*P* value
Age, mean (SD)	41 (14)	43 (13)	41 (14)	.21
Sex, n (%)				.08
Male	77 (22)	5 (12)	72 (24)	
Female	271 (78)	38 (88)	233 (76)	
Race, n (%)				.31
White	228 (66)	31 (72)	197 (65)	
Black	31 (9)	3 (7)	28 (9)	
Asian	19 (5)	4 (9)	15 (5)	
Other/unknown	70 (20)	5 (12)	65 (21)	
Vaccine manufacturer				.17
Moderna	244 (70)	34 (79)	210 (69)	
Pfizer-BioNTech	104 (30)	9 (21)	95 (31)	
MGB site†				.004
1	126 (36)	8 (19)	118 (39)	
2	107 (31)	13 (30)	94 (31)	
3	26 (7)	8 (19)	18 (6)	
4	89 (26)	14 (33)	75 (25)	
Eligibility group‡				.71
A	9 (28)	11 (26)	88 (29)	
B	67 (19)	8 (19)	59 (19)	
C	51 (15)	9 (21)	42 (14)	
D	58 (17)	7 (16)	51 (17)	
E	42 (12)	3 (7)	39 (13)	

*Self-reported allergic symptoms included itching or rash (other than injection site) in 27 (8%), hives in 13 (4%), swelling in 12 (3%), respiratory in 13 (4%) and potentially severe (respiratory plus at least 1 other symptom) in 6 (2%).

†MGB vaccination sites included academic medical centers, community hospitals, and local vaccine clinics. Sites 1 and 2 are academic medical centers and sites 3 and 4 include community hospitals and local sites.

‡Eligibility groups were designed by location of employee work, beginning with wave A ambulatory location for COVID-19 evaluation/testing/care, emergency departments, inpatient and observation units, laboratories working with COVID-19, occupational health clinics, patient homes (home health), and urgent care centers. Wave B included primary care, periprocedural areas, and radiation oncology. Wave C included all other outpatient clinical care areas, laboratories, and outpatient radiology. Wave D included all other hospital-based employees, including hospital workers who worked both remotely and in the hospital. Wave E included all other eligible employees. Missing eligbility for 31 (9%) overall, 5 (12%) with self-reported allergic symptoms and 26 (9%) without self-reported allergic symptoms.

TABLE II. Incomplete vaccination among employees by self-reported allergic symptoms after dose one of mRNA COVID-19 vaccination

Incomplete vaccination	No self-reported allergic symptoms (OR, 95% CI)	Any self-reported allergic symptoms after dose 1 (OR, 95% CI)	*P* value
Number of events	305	43	
Unadjusted	1.00 (reference)	5.68 (4.11-7.85)	<.001
Adjusted*	1.00 (reference)	5.15 (3.75-7.06)	<.001

Incomplete vaccination	No self-reported allergic symptoms (OR, 95% CI)	Severe self-reported allergic symptoms after dose one (OR, 95% CI)	*P* value
Number of events	305	6	
Unadjusted	1.00 (reference)	23.2 (9.7-55.2)	<.001

*Multivariable model adjusted for age, sex, race, vaccine manufacturer, MGB site, wave of vaccine eligibility.

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eMethods

Massachusetts General Brigham (MGB) began employee coronavirus disease 19 (COVID-19) vaccination on December 16, 2020. Vaccination occurred across 17 vaccine clinics in phases with the earliest vaccinations (wave A) in employees whose primary location of work included ambulatory location for COVID-19 evaluation/testing/care, emergency departments, inpatient and observation units, laboratories working with COVID-19, occupational health clinics, patient homes (home health), and urgent care centers. Wave B included primary care, periprocedural areas, and radiation oncology. Wave C included all other outpatient clinical care areas, laboratories, and outpatient radiology. Wave D included all other hospital-based employees, including those who performed some remote work and also worked in the hospital to perform remote work. Wave E included all other eligible employees. The only allergy-related exclusion criterion for initial vaccination was a history of a severe allergic reaction (eg, anaphylaxis) to a component of the vaccine (eg, polyethylene glycol or polysorbate 80). After vaccination in the MGB vaccine clinics, employees were observed for 15 or 30 minutes according to guidelines set by the U.S. Centers for Disease Control and Prevention.

Any potential allergic reactions associated with vaccination observed in the vaccine clinics were documented in the employee's electronic health record (EHR). For allergic reactions, pages to a dedicated MGB allergy/immunology pager, implemented December 17, 2020, to support employee vaccination, were encouraged. The MGB allergists maintained a shared pager log and all potentially allergic reactions were specialist-documented in the employee's EHR. Filing of (1) a Vaccine Adverse Event Reporting System report and (2) a safety report was encouraged for all possible anaphylactic reaction events. Each MGB-affiliated hospital sent MGB allergists COVID-19 vaccine-related safety reports biweekly during employee vaccination.

Daily for 3 days after vaccination, employees were contacted regarding postvaccination symptoms through a multipronged approach including e-mail, text message, phone, and employee smartphone application links; symptom checks were completed through a Web-based Research Electronic Data Capture (REDCap) survey or telephone. Survey completion was defined as full completion of at least 1 of the 3 postvaccine symptom surveys. Employees with possible allergic events identified from the pager, safety reports, or self-reports (more severe than itching and rash alone) were referred to MGB allergists for evaluation and dose 2 guidance with specified protocols.

eAppendix: employee symptom survey—allergy question

Version 1. December 17 through December 31, 2020

Have you had any of the following allergic symptoms over the past day? (Check all that apply.)

- ○ Rash or itching (other than at injection site)
- ○ Hives
- ○ Swollen lips, tongue, eyes, or face
- ○ Wheezing, chest tightness, or shortness of breath
- ○ None of the above

Version 2. January 1, 2021, through March 15, 2021

Over the past day, have you had any of the following allergic symptoms? (Check all that apply.)

- ○ Rash or itching (other than where you got your shot)
- ○ Hives (itchy, raised bumps that can look like mosquito bites)
- ○ Swollen lips, tongue, eyes, or face
- ○ Wheezing, chest tightness, or shortness of breath that has continued since your shot
- ○ None of the above