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Predicting COVID-19 and seasonal influenza vaccine uptake: The impact of fear and vasovagal symptoms

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Abstract

Vaccines are vital to protecting health. However, fear and experiencing vasovagal symptoms (e.g., dizziness) are deterrents to medical procedures. Thus, study aims were to test (1) if vaccine relevant fears predict vasovagal symptoms during or following seasonal influenza vaccination and (2) if vaccine relevant fears and vasovagal symptoms predict seasonal influenza and COVID-19 vaccine uptake. Using a prospective design, 1077 participants recruited online completed surveys during Oct 2019 assessing vaccine relevant fears, and May–June 2020 assessing 2019–2020 seasonal influenza vaccine uptake, ratings of vasovagal symptoms, and seasonal influenza and COVID-19 vaccination intention. A behavioral follow up assessing 2020–2021 seasonal influenza and COVID-19 vaccine uptake took place June–July 2021. Heightened vaccine relevant fears predicted reduced 2019–2020 seasonal influenza vaccine uptake and greater vasovagal symptoms among those who did receive a seasonal influenza vaccine. Serial mediation analyses identified significant indirect effects with greater vaccine relevant fears reducing 2020–2021 seasonal influenza vaccine uptake through intention and reducing COVID-19 vaccine uptake

through vasovagal symptoms and intention. Intervention research to reduce fear and prevent vasovagal symptoms to support vaccine uptake is warranted.

KEYWORDS

COVID-19, fear, intention, longitudinal design, seasonal influenza, vaccination, vasovagal symptoms

INTRODUCTION

Vaccines are effective at preventing, limiting spread, and reducing severity of infectious diseases, such as measles and seasonal influenza (Dubé et al., 2021; World Health Organization [WHO], 2019a). Thus, vaccines are broadly considered a public health success story. Vaccination protects not only the self but also other people with whom the individual interacts. Vaccine preventable diseases have decreased globally or have been eradicated from most regions of the world (WHO, 2019a). For example, global deaths due to measles decreased by 73% from 2000 to 2018 and polio is nearly eradicated worldwide (WHO, 2019a). However, due to declining vaccine uptake, some countries have seen a resurgence of vaccine preventable diseases, such as the multiple outbreaks of measles that were documented in the United States during 2014 (Zipprich et al., 2014) and France from 2017 to 2018 (Bernadou et al., 2018). This pattern of decreasing vaccine uptake contributed to the WHO identifying vaccine hesitancy, defined as the "delay in acceptance or refusal of vaccination despite availability," as one of 10 threats to global health (WHO, 2019b; see MacDonald & the SAGE Working Group on Vaccine Hesitancy, 2015). Vaccine hesitancy varies across time and by vaccines, and differences are present by sociodemographic characteristics, such as age, gender, and education (e.g., Schmid et al., 2017, for review; MacDonald & the SAGE Working Group on Vaccine Hesitancy, 2015). Most vaccines are administered during childhood and adolescence; however, some vaccines are recommended annually for both children and adults (e.g., seasonal influenza vaccine) or boosters are needed (e.g., every 10 years for tetanus; Centers for Disease Control and Prevention [CDC], 2016). Although seasonal influenza is often mild, for some, it can result in severe illness and death (Office of Disease Prevention and Health Promotion [ODPHP], n.d.). Seasonal influenza vaccine coverage in the United States falls below the recommended level of 70% (ODPHP, n.d.). As a result, increasing uptake of seasonal influenza vaccines is a high priority objective in the United States (ODPHP, n.d.) Similarly, COVID-19 vaccine uptake in the United States falls short of current goals. As of May 10, 2022, 66.3% of the population had been fully vaccinated against COVID-19 (Ritchie et al., 2022). Given the need to achieve sufficient vaccine coverage globally to achieve stable endemic levels of COVID-19, understanding factors that reduce vaccine uptake is vital.

Fear as a deterrent to vaccination

Fear contributes to vaccine hesitancy. Well-documented vaccine relevant fears include fear of needles, injections, side effects, and pain (Cull et al., 2021; Dubé et al., 2013;

Freeman et al., 2021). In addition to these more common fears, fear of fainting has been associated with vaccine hesitancy (Freeman et al., 2021). Up to 30% of adults endorse some fear of needles, and ~4% meet diagnostic criteria for blood–injection–injury phobia, which is characterized by an intense fear of blood, injections, and injury (Stinson et al., 2007; McLenon & Rogers, 2018). The literature documenting the relationship between heightened vaccine relevant fears and reduced vaccine intention or acceptance both prior to and during the COVID-19 pandemic is robust (Freeman et al., 2021; Gusmano & Michel, 2009; Hamilton et al., 2021; Landowska et al., 2017; McLenon & Rogers, 2018; Newman et al., 2013; Taddio et al., 2012). A demographically representative survey of 15,014 adults within the United Kingdom found that higher scores on the blood and injection subscales of the Medical Fears Survey-Short Form was associated with greater COVID-19 vaccine hesitancy (Freeman et al., 2021). Further, fear of injections specifically accounted for approximately 11% of adults with vaccine hesitancy. Beyond the COVID-19 pandemic, among adults, fear or dislike of needles have been reported as contributors to not getting vaccinated against seasonal influenza (from 6% for older adults to 71% in a survey of physicians), tetanus (20% of adults in general to 71% of physicians), and pneumococcal infection (from 2.6% among older adults to 69% of physicians; McLenon & Rogers, 2018). In addition to fear experienced in anticipation of a medical procedure, the potential to experience vasovagal symptoms prior to, during, or following injection-based vaccination is present.

Vasovagal symptoms and the vaccination process

During the vaccination process, vasovagal symptoms (e.g., dizziness and lightheadedness) and syncope (fainting or loss of consciousness) may occur for a subset of people. While syncope is rare, the experience of vasovagal symptoms is much more common and has been documented as being as high as 36.2% of cases among adolescents during routine vaccination (Kemper et al., 2017). The WHO (2019c) includes vasovagal symptoms (also referred to in the report as vasovagal reactions) and syncope within a broader category of "immunization stress-related responses" and highlights that research identifying people at risk for immunization stress-related responses and interventions to mitigate or attenuate these responses is needed. Although the physiological tipping point that triggers syncope is unknown, vasovagal symptoms and syncope are due to insufficient cerebral oxygenation following changes in blood pressure, heart rate, and/or constriction of blood vessels that serve the brain (cerebral vasoconstriction; Cipolla, 2009; Ritz et al., 2010). The experience of vasovagal symptoms and syncope are considered medically benign; however, the risk of injury due to falling is a concern and traumatic brain injury due to falls following vaccination has been documented (Braun et al., 1997). Fear has been identified as a predictor of vasovagal symptoms and syncope across a variety of medical procedures.

Fear as a predictor of vasovagal symptoms

In addition to being a deterrent to medical procedures, such as routine blood draws, blood donation, and vaccination, blood and injection related fears also increase the risk for vasovagal symptoms and syncope leading up to, during, or following the procedure (France et al., 2012; Nir et al., 2003). In anticipation of the feared experience, as well as during the

exposure or procedure, sympathetic nervous system activation and "fight-or-flight" response occur. This causes an increase in heart rate and blood pressure. Thus far the response pattern is normal. However, for people who experience vasovagal symptoms, following this increase in heart rate and blood pressure, dysregulation of the autonomic nervous system occurs, blood pressure drops beyond what is normal resulting in insufficient cerebral oxygenation and vasovagal symptoms or syncope ensue (Ritz et al., 2010). It is worth noting this classic diphasic pattern is not universal (e.g., Sarlo et al., 2008), and other physiological factors such as hyperventilation may contribute to vasovagal symptoms and syncope (Ritz et al., 2010). This relationship between blood and injection fears and vasovagal symptoms is well documented among people who have blood–injection–injury phobia (Öst et al., 1991; Ritz et al., 2010) and in non-clinical populations where some fear is present. For example, fear of having blood drawn is the strongest predictor of vasovagal symptoms during and following blood donation, even after controlling for traditional risk factors such as estimated blood volume and blood pressure, as well as demographic characteristics such as age and sex (France et al., 2012; Labus et al., 2000). The medical procedure does differ between blood draws or blood donation, and vaccination. With blood draws and donation, a needle is inserted into a vein and blood is withdrawn; in contrast, with vaccination a needle is inserted into a muscular site of the body (e.g., deltoid) and the vaccine is injected using a syringe. Despite these procedural differences, fear of having blood drawn is relevant to vaccination given its strong association with vasovagal symptoms, and for the present study is conceptualized as a vaccine relevant fear along with fear of injections, pain, side effects, and fainting. Vasovagal symptoms likely have a negative impact on subsequent vaccine intention and uptake.

Fear, vasovagal symptoms, vaccine intention, and uptake

Heightened fear is negatively associated with seasonal influenza vaccine uptake; however, most research has relied on cross-sectional survey design (e.g., Hamilton et al., 2021; Landowska et al., 2017; Millner et al., 2010), and has focused on retrospective reports of vaccination behavior, or intention/anticipated likelihood of future vaccination behavior (Borthwick et al., 2021). It is rare that a longitudinal approach is taken to predict subsequent vaccine uptake behavior. Payaprom et al. (2011) found that self-efficacy and intention to get a seasonal influenza vaccine predicted vaccine uptake after a 2 month follow up period among individuals at higher risk for negative health outcomes due to seasonal influenza. Similarly, Fall et al. (2018) found that among college students, intention predicted 51% of the variability in seasonal influenza vaccine uptake at 1 year follow up. This is consistent with health behavior research broadly, with intention predicting approximately half of the variability in behavior (Sheeran & Webb, 2016). However, across these studies, fear was not assessed. In a recent review, Borthwick et al. (2021) highlight the need to move beyond cross-sectional research towards prospective, longitudinal research to understand psychological predictors of seasonal influenza vaccination behavior. When a person does present to receive a vaccine, their experience during the vaccination process may impact their likelihood of return for future vaccines. Within the medical setting broadly, negative patient experience is associated with reduced return to the medical care provider, less adherence, and lower use of preventive care (see Doyle et al., 2013 for review; Garman et al., 2004). Similarly, within blood donation, if a donor experiences vasovagal symptoms during or following blood donation, they are less likely to return to donate blood again

(France et al., 2005, 2013). Vasovagal symptoms may have a similarly negative effect within the vaccination context.

The first aim of the present study was to use a prospective, longitudinal cohort design to test if vaccine relevant fears (reflecting fear of injections, pain, side effects, having blood drawn, and fainting) predicted subsequent vasovagal symptoms associated with seasonal influenza vaccination among adults. It was hypothesized that heightened vaccine relevant fears would predict greater vasovagal symptoms during and following vaccination. The second aim of the study was to test the relationships among vaccine relevant fears, subsequent vasovagal symptoms, intention to vaccinate against seasonal influenza and COVID-19, and vaccine uptake 1 year later. It was hypothesized that heightened fear and greater vasovagal symptoms would be associated with reduced intention to vaccinate against seasonal influenza and COVID-19 and reduced vaccine uptake. Finally, it was hypothesized that the negative impact of vaccine relevant fears on vaccine uptake would be mediated by vasovagal symptoms and intention for (1) seasonal influenza vaccine uptake and (2) COVID-19 vaccine uptake.

METHOD

Study registrations, deidentified data, analytic output with syntax, and reporting checklist are available at https://osf.io/v4xc3/?view_only=d485d7d1159c426aa1992dcef2a9bf32. The hypothesis for the present study's first aim, testing if heightened vaccine relevant fears predicted greater vasovagal symptoms, was preregistered prior to participant recruitment. The second aim predicting vaccine uptake was registered prior to downloading the behavioral follow up data (blinded *ex post*). The current study was part of a larger experimental design testing the effect of anticipated regret messaging on seasonal influenza vaccine intention and uptake behavior. No intervention effects from the experimental design were present for the current study variables (see Supporting Information S1). The STROBE checklist was followed for reporting prospective cohort studies.

Study design and participants

During October 2019, participants at least 18 years of age and residing within the United States were recruited through MTurk, for an online, prospective cohort study examining seasonal influenza vaccination behavior. With the onset of the COVID-19 pandemic, IRB approval was obtained to expand the study protocol to include COVID-19 vaccination behavior and collect a second year of data with participants re-consenting to participate. After excluding duplicate responses ($n = 190$), discontinuing ($n = 197$), having already received a flu shot ($n = 261$), or failing attention checks ($n = 174$), 2508 participants remained upon completion of the first survey. The second survey was available May–June 2020 with 1276 participants completing the second survey. Participants were excluded due to missing the random code to match to the first survey ($n = 176$), 19 failed the attention check, and 4 reported being uncertain if they had received a flu shot for the 2019–2020 flu season, resulting in an analytic sample of 1077 (yes for flu shot = 486, no = 591) for Aim 1 testing if vaccine relevant fears predicted subsequent vasovagal symptoms following seasonal influenza vaccination. The behavioral follow up survey assessing vaccine uptake was available at the end of the 2020–2021 flu season (June–July 2021),

with 725 participants completing the survey; 75 responses could not be matched to the Time 2 survey, and 7 participants failed the attention check. Among this sample of 643 participants, 301 had been vaccinated against seasonal influenza during the 2019–2020 flu season and were the final analytic sample for Aim 2 analyses testing if vaccine relevant fears and vasovagal symptoms following vaccination predicted subsequent vaccine uptake. Figures of the study timeline and flow diagram of participant attrition and exclusion are available in Supporting Information S2 and S3, respectively. Sensitivity analyses indicated that with a two-tailed test, power = .90, $\alpha = .05$, and $n = 1064$, a logistic regression predicting 2019–2020 seasonal influenza vaccine uptake could detect an odds ratio = .78. Using a two-tailed test, with power = .90, $\alpha = .05$, and $n = 482$, the linear regression analysis predicting vasovagal symptoms could detect a small effect size ($f^2 = .04$). Using the same criteria for power and alpha, but with $n = 301$, the logistic regression analyses predicting 2020–2021 seasonal influenza and COVID-19 vaccine uptake could detect an odds ratio = 1.61. Variation in sample sizes for power analyses compared with analytic sample sizes noted above are due to missing data for demographic characteristics. To allow for a more conservative estimate, the smaller sample size was used.

The consent forms and surveys were administered using Qualtrics software (Provo, UT). The study protocol and amendments were approved by the institutional review board at The Ohio State University.

Measures

Vaccine relevant fears were measured using a five-item Likert-type measure reflecting fear of: receiving an injection in the arm, pain associated with an injection in the arm, having blood drawn, feeling faint, and possible side effects associated with vaccination, from 0 = *not at all afraid or anxious* to 4 = *extremely afraid or anxious* ($\alpha = .84$). This measure integrated items from the Medical Fears Survey (e.g., fear of having blood drawn, receiving an injection; France et al., 2012; Kleinknecht et al., 1999), the Blood Donation Fears Inventory (fear of feeling faint; Kowalsky et al., 2014), and new items designed for this study to better reflect the vaccination context (e.g., fear of side effects).

The retrospective recall of the experience of vasovagal symptoms was assessed at the end of the 2019–2020 influenza season using an adapted version of the Blood Donation Reactions Inventory – Short Form, a four-item Likert-type measure that assesses the degree of faintness, dizziness, weakness, and lightheadedness experienced during or following blood donation from 0 = *not at all* to 5 = *to an extreme degree* ($\alpha = .91$; France et al., 2008). Concurrent validity has been supported with significant associations with other indicators of vasovagal symptoms (e.g., phlebotomist reclining the donation cot; France et al., 2008). The target behavior in the instructions was adapted from blood donation to "receiving the flu shot".

Intention to vaccinate against seasonal influenza was measured using a three-item Likert-type scale ($\alpha = .99$; Stevens et al., 2019). Questions were adapted to reflect the upcoming flu season (e.g., "How likely is it that you will get a flu shot for the next flu season (2020-2021)?") and a 7-point response scale was used (e.g., 1 = *not at all likely*, 7 = *very likely*). Validity has been supported with strong associations in the expected direction with past behavior and attitudes toward vaccination (Stevens et al., 2019). Intention to vaccinate against COVID-19 was measured using a single item, adapted from the seasonal influenza item to: "How likely is it that you will get the COVID-19 vaccine when it becomes available?" from 1 = *not at all likely* to 7 = *very likely*.

Seasonal influenza vaccine uptake was assessed at the end of each flu season by self-report. Similarly, COVID-19 vaccine uptake was assessed by self-report. Survey items, response options, factor loadings, and reliability coefficients are available in Supporting Information S4. Self-reported demographic information included: age, gender, race, education, and marital status.

Data analysis

Means for multi-item measures, descriptive statistics, difference tests (independent samples *t* tests and chi square tests of independence), Spearman's correlation coefficients, effect sizes (Cohen's *d* and Cramer's *V*), and internal consistency coefficients (Cronbach's α) were calculated. Strength of effect sizes was determined using Cohen's (1988) guidelines. Hierarchical logistic regression predicted 2019–2020 seasonal influenza vaccine uptake and hierarchical linear regression tested if vaccine relevant fears predicted vasovagal symptoms. A second set of hierarchical logistic regression analyses predicted 2020–2021 seasonal influenza and COVID-19 vaccine uptake. Finally, tests of serial mediation were calculated using logistic regression with 5000 bootstrap samples (Hayes, 2018). Exploratory analyses replicated the regression analyses at the item level for vaccine relevant fears. IBM SPSS Statistics version 27 (IBM Corp.) was used for all analyses except for the tests of serial mediation, which used the PROCESS 3.5 macro for SPSS (Hayes, 2018).

RESULTS

Seasonal influenza vaccine uptake for 2019–2020

Sample characteristics and tests for group differences

Sample descriptive statistics and tests for differences by 2019–2020 seasonal influenza vaccine uptake are detailed in Table 1. The sample was on average 44.0 years old (SD = 13.3), and the majority identified as White (83.7%), women (60.6%), married or living with a partner (57.1%), and most had completed at least some college course work (89.4%). Differences with a small effect or greater (≥.2) were present by seasonal influenza vaccine uptake. Compared with participants who did not obtain a seasonal influenza vaccine, participants who did were older, reported fewer vaccine relevant fears, greater intention to get a seasonal influenza vaccine for the upcoming flu season (2020–2021), and greater intention to get a COVID-19 vaccine when it became available.

Vaccine relevant fears and vasovagal symptoms

As highlighted in Table 2, younger age was associated with greater vaccine relevant fears and more vasovagal symptoms during and following seasonal influenza vaccination, with small effect sizes. Greater vaccine relevant fears were correlated with more vasovagal symptoms, with a medium effect size. The pattern of correlations was consistent at the item level for vaccine relevant fears, except for fear of side effects, which was not associated with age, but was negatively correlated with education such that greater education was associated with lower fear of side

TABLE 1 Descriptive statistics (mean [SD] or *n* [%]) and tests for group differences by 2019–2020 seasonal influenza vaccine uptake

Variable (unit)	Full sample ($n = 1077$)	Seasonal influenza vaccine uptake		Group differences	
		No ($n = 591$)	Yes ($n = 486$)	t or χ^2	d or V
Age (years)[a]	44.0 (13.3)	42.7 (12.4)	45.6 (14.2)	−3.57***	−.22
Gender[b]					
Women	650 (60.6%)	356 (54.8%)	294 (45.2%)	<.01	<.01
Men	422 (39.4%)	231 (54.7%)	191 (45.3%)		
Race				9.59*	.09
Asian	54 (5.0%)	25 (46.3%)	29 (53.7%)		
Black or African American	73 (6.8%)	49 (67.1%)	24 (32.9%)*		
White	901 (83.7%)	484 (53.7%)	417 (46.3%)		
Other[c]	49 (4.5%)	33 (67.3%)	16 (32.7%)		
Marital status				13.10**	.11
Married or living with partner	615 (57.1%)	317 (51.5%)	298 (48.5%)*		
Divorced or separated	134 (12.4%)	73 (54.5%)	61 (45.5%)		
Widowed	23 (2.1%)	9 (39.1%)	14 (60.9%)		
Never married	305 (28.3%)	192 (63.0%)	113 (37.0%)*		
Education				19.75***	.14
≤High school diploma or GED	114 (10.6%)	79 (69.3%)	35 (30.7%)*		
Some college or college graduate	730 (67.8%)	408 (55.9%)	322 (44.1%)		
Graduate coursework or degree	233 (21.6%)	104 (44.6%)	129 (55.4%)*		
Fear	.85 (.9)	.99 (.9)	.68 (.8)	5.62***	.34
Intention Flu[d]	4.42 (2.4)	2.71 (1.9)	6.51 (0.9)	−40.37***	−2.47
Intention COVID-19[e]	4.87 (2.3)	4.03 (2.3)	5.90 (1.7)	−14.88***	−.91

[a] $n = 8$ missing.
[b] $n = 5$ missing or other.
[c] Includes American Indian/Alaska Native, Native Hawaiian or Other Pacific Islander, more than one race, and other.
[d] Seasonal influenza vaccination intention for the 2020–2021 flu season.
[e] COVID-19 vaccination intention for when it becomes available.
*$p < .05$. **$p < .01$. ***$p < .001$.

effects (Supporting Information S5). Logistic regression tested the impact of vaccine relevant fears on seasonal influenza vaccine uptake during 2019–2020, controlling for demographic characteristics (see Table 3). The model was significant, $\chi^2(7) = 60.68$, $p < .001$, and tests of collinearity were acceptable (tolerance > .94, VIF < 1.06). Lower vaccine relevant fears had a small effect ($d = -.20$), older age had a trivial effect ($d < .01$), and more education had a small to

TABLE 2 Spearman correlation coefficients among demographic variables, fear, and vasovagal symptoms

Variable	Age	Education	Fear	Vasovagal symptoms
Age[a]	-	.03	−.17***	−.18***
Education		-	−.06*	−.05
Fear			-	.31***
Vasovagal symptoms[b]				-

[a]n = 483–1069. Range in sample size mainly due to vasovagal symptoms responses being limited to participants who were vaccinated against seasonal influenza during the 2019–2020 flu season.
[b]n = 483–486.
*p < .05. **p < .01. ***p < .001.

TABLE 3 Logistic regression predicting 2019–2020 seasonal influenza vaccine uptake, controlling for demographic characteristics

	Block 1					Block 2				
Variable	B	Wald	SE	OR	95% CI	B	Wald	SE	OR	95% CI
Age	.02**	9.75	.01	1.02	[1.01, 1.03]	.01*	5.77	.01	1.01	[1.00, 1.02]
Gender[a]	.02	.02	.13	1.02	[.79, 1.31]	−.06	.23	.13	.94	[.73, 1.22]
Race[b]	−.20	1.29	.18	.82	[.58, 1.16]	−.13	.52	.18	.88	[.62, 1.25]
Marital status[c]	−.25	3.72	.13	.78	[.61, 1.00]	−.24	3.51	.13	.78	[.61, 1.01]
Edu(1)[d]	.61**	7.59	.22	1.84	[1.19, 2.84]	.61**	7.31	.22	1.83	[1.18, 2.84]
Edu(2)[d]	1.04***	17.71	.25	2.84	[1.75, 4.61]	1.01***	16.34	.25	2.75	[1.68, 4.49]
Fear						−.35***	21.32	.08	.70	[.61, .82]
Nagelkerke R^2	.05					.07				

Note: n = 1064. 95% CI = 95% confidence interval for odds ratio. Edu = education.
[a]Reference category is women (coding: women = 0, men = 1).
[b]Reference category is White (coding: White = 0, Person of Color = 1).
[c]Reference category is married or living with partner (coding: married or living with partner = 0, divorced, separated, widowed, never married = 1).
[d]Reference category is high school diploma, GED, or less. Edu(1) = some college or college graduate. Edu(2) = graduate coursework or degree.
*p < .05. **p < .01. ***p < .001.

medium effect (d = .33 and .56) predicting greater odds of seasonal influenza vaccine uptake. Item-level analyses of vaccine relevant fears revealed that fear of injections and side effects were significant predictors of seasonal influenza vaccine uptake, and they remained significant when all five fear items were entered (Supporting Information S6.1–S6.6). Among those who were vaccinated against seasonal influenza, a hierarchical linear regression analysis tested if vaccine relevant fears predicted vasovagal symptoms, while controlling for demographic characteristics (Table 4). The final model was significant with a small effect, $F(6, 475) = 9.34$, $p < .001$,

TABLE 4 Hierarchical linear regression predicting vasovagal symptoms during or following 2019–2020 seasonal influenza vaccination, controlling for demographic characteristics

	Model 1				Model 2			
Variable	**B**	**β**	**SE**	**95% CI**	**B**	**β**	**SE**	**95% CI**
Age	−.01**	−.14	<.01	[−.01, −.00]	−.003	−.09	<.01	[−.01, .00]
Gender[a]	−.02	−.02	.04	[−.10, .06]	.003	.003	.04	[−.08, .08]
Race[b]	.07	.05	.06	[−.05, .19]	.04	.03	.06	[−.07, .16]
Marital status[c]	−.03	−.04	.04	[−.12, .05]	−.02	−.02	.04	[−.10, .06]
Education	−.07	−.08	.04	[−.14, .01]	−.06	−.07	.04	[−.13, .02]
Fear					.15***	.28	.02	[.10, .20]
R^2	.03				.11			
ΔR^2					.07			

Note: $n = 482$. 95% CI, 95% confidence interval for B.
[a]Coding is women = 0, men = 1.
[b]Coding is White = 0, Person of Color = 1.
[c]Coding is married or living with partner = 0, divorced, separated, widowed, never married = 1.
*$p < 0.05$. **$p < 0.01$. ***$p < 0.001$.

$f^2 = .12$, and tests of collinearity were acceptable (tolerance > .92, VIF < 1.09). As hypothesized, heightened fear predicted greater vasovagal symptoms. Replication of the hierarchical linear regression by fear item found that each vaccine relevant fear significantly predicted vasovagal symptoms (Supporting Information S7.1–S7.5). Evaluating the items simultaneously revealed that fear of side effects was the strongest predictor of vasovagal symptoms (Supporting Information S7.6). Next, the impact of vaccine relevant fears and the experience of vasovagal symptoms on vaccine uptake during the following year was assessed.

Seasonal influenza and COVID-19 vaccine uptake for 2020–2021

Sample characteristics and tests for group differences

Descriptive statistics and tests for differences by 2020–2021 seasonal influenza and COVID-19 vaccine uptake are detailed in Table 5. Consistent with the larger sample, this subset of participants was on average 47.3 years old (SD = 14.2), and the majority identified as White (86.0%), women (59.1%), married or living with a partner (58.8%), and most had completed at least some college course work (92.6%). The majority of participants reported receiving seasonal influenza and COVID-19 vaccines. Among those who reported receiving a COVID-19 vaccine, most had been fully vaccinated. Among recipients of the Moderna or Pfizer-BioNTech vaccines, 7 participants indicated their second dose was coming up. No one reported discontinuing after the first dose. In line with the previous analyses, compared to participants who did not obtain a seasonal influenza vaccine, those who did reported lower vaccine relevant fears with a small effect, greater intention to get a seasonal influenza vaccine for the upcoming flu season (2020–2021) with a large effect, and greater intention to get a COVID-19 vaccine when it became available

TABLE 5 Descriptive statistics (mean [SD] or *n* [%]) and tests for group differences by 2020–2021 seasonal influenza and COVID-19 vaccine uptake

		Seasonal influenza vaccine uptake				COVID-19 vaccine uptake			
Variable (unit)	**Full sample**	**No ($n = 37$)**	**Yes ($n = 264$)**	***t* or χ^2**	***d* or *V***	**No ($n = 46$)**	**Yes ($n = 255$)**	***t* or χ^2**	***d* or *V***
Age (years)[a]	47.3 (14.2)	44.7 (14.8)	47.7 (14.1)	−1.22	−.22	44.4 (12.9)	47.9 (14.4)	−1.54	−.25
Gender				.57	.04			2.44	.09
Women	178 (59.1%)	24 (13.5%)	154 (86.5%)			32 (18.0%)	146 (82.0%)		
Men	123 (40.9%)	13 (10.6%)	110 (89.4%)			14 (11.4%)	109 (88.6%)		
Race				.05	.01			3.37	.11
Asian	18 (6.0%)	2 (11.1%)	16 (88.9%)			1 (5.6%)	17 (94.4%)		
Black or African American	15 (5.0%)	2 (13.3%)	13 (86.7%)			3 (20.0%)	12 (80.0%)		
White	259 (86.0%)	32 (12.4%)	227 (87.6%)			42 (16.2%)	217 (83.8%)		
Other[b]	9 (3.0%)	1 (11.1%)	8 (88.9%)			0 (0%)	9 (100%)		
Marital status				3.91	.11			1.97	.08
Married or living with partner	177 (58.8%)	18 (10.2%)	159 (89.8%)			24 (13.6%)	153 (86.4%)		
Divorced or separated	42 (14.0%)	7 (16.7%)	35 (83.3%)			9 (21.4%)	33 (78.6%)		
Widowed	9 (3.0%)	0 (0%)	9 (100%)			2 (22.2%)	7 (77.8%)		
Never married	73 (24.3%)	12 (16.4%)	61 (83.6%)			11 (15.1%)	62 (84.9%)		
Education				7.13*	.15			4.29	.12
≤ high school diploma or GED	22 (7.3%)	0 (0%)	22 (100%)			3 (13.6%)	19 (86.4%)		
Some college or college graduate	197 (65.4%)	31 (15.7%)	166 (84.3%)*			36 (18.3%)	161 (81.7%)		
Graduate coursework or degree	82 (27.2%)	6 (7.3%)	76 (92.7%)			7 (8.5%)	75 (91.5%)		
Fear	.67 (.8)	.94 (1.2)	.64 (.8)	2.04*	.36	.92 (.9)	.63 (.8)	2.16*	.35
Vasovagal symptoms	.11 (.4)	.17 (.4)	.10 (.3)	1.09	.19	.23 (.5)	.09 (.3)	2.49*	.40
Intention flu	6.56 (.9)	5.72 (1.7)	6.68 (.7)	−6.36***	−1.12	6.12 (1.3)	6.64 (.8)	−3.62***	−.58
Intention COVID-19	5.94 (1.7)	5.11 (2.0)	6.05 (1.6)	−3.28**	−.58	4.30 (2.2)	6.23 (1.4)	−7.92***	−1.27

[a] $n = 1$ missing.

[b] Includes American Indian/Alaska Native, Native Hawaiian or Other Pacific Islander, more than one race, and other.

*$p < .05$. **$p < .01$. ***$p < .001$.

with a medium effect. The same pattern was present by COVID-19 vaccine uptake, but with a significant difference with a small effect size also present for vasovagal symptoms. Participants who received a COVID-19 vaccine had reported fewer vasovagal symptoms following 2019–2020 seasonal influenza vaccination, compared to participants who had not received a COVID-19 vaccine.

Predicting 2020–2021 seasonal influenza vaccine uptake

Older age, lower vaccine relevant fears, and lower vasovagal symptoms were associated with greater seasonal influenza vaccination intention, with small effects (see Table 6). Intention alone was significantly associated with seasonal influenza vaccine uptake, also with a small effect. Item level analyses of vaccine relevant fears found that all fear items were associated with seasonal influenza vaccination intention and greater fear of side effects alone was associated with lower vaccine uptake (all small effects, Supporting Information S8). Next, vaccine relevant fears, vasovagal symptoms, and intention were tested as predictors 2020–2021 seasonal influenza vaccine uptake.

The upper section of Table 7 presents the binary logistic regression predicting seasonal influenza vaccine uptake with vaccine relevant fears, vasovagal symptoms, and seasonal influenza vaccination intention. The final model was significant, $\chi^2(3) = 26.25$, $p < .001$, and tests of collinearity were acceptable (tolerance $> .82$, VIF < 1.22). With all three predictors in the model, intention alone predicted greater odds of subsequent seasonal influenza vaccine uptake, with a small effect. This pattern was replicated with the vaccine relevant fears item-level analyses (Supporting Information S9). The analysis was re-run with demographic characteristics included as covariates, and the results remained consistent (Supporting Information S10). Next, hypothesized indirect effects of fear and vasovagal symptoms on vaccine uptake were examined.

To test if vaccine relevant fears had an indirect effect on vaccine uptake through vasovagal symptoms and vaccine intention, serial mediation analysis was employed. The results supported model fit predicting seasonal influenza vaccine uptake, $\chi^2(3) = 26.25$, $p < 0.001$, Nagelkerke $R^2 = 0.16$, and significant direct effects were present for greater fear predicting higher vasovagal symptom scores, higher symptom scores predicting lower intention, and lower intention predicting not getting vaccinated (see top model in Figure 1). A significant indirect effect was present for greater vaccine relevant fears reducing seasonal influenza vaccine uptake through intention. A trend for an indirect effect was present for fear reducing vaccine uptake through vasovagal symptoms and intention ($a_1d_{21}b_2 = -.05$, $SE = .03$, 90% CI $= -.12, -.01$). Exploratory analyses revealed a similar pattern when testing vaccine relevant fears at the item level (Supporting Information S11). The model was re-run with demographic covariates included, and the results remained consistent (Supporting Information S12).

Predicting COVID-19 vaccine uptake

A similar pattern of significant correlations was present for COVID-19 vaccine intention and uptake, with several notable relationships present (see Table 6). Greater vasovagal symptoms were correlated with lower intention to vaccinate against COVID-19 with a small effect, and lower vaccine relevant fears and greater intention to vaccinate against COVID-19 were

TABLE 6 Spearman correlation coefficients among demographic variables, vaccine relevant fears, vasovagal symptoms, seasonal influenza and COVID-19 vaccination intention and uptake

Variable	Age	Education	Fear	Vasovagal symptoms	Intention flu	Intention COVID-19	Uptake flu	Uptake COVID-19
Age[a]	-	−.02	−.26***	−.21***	.19**	.16**	.07	.08
Education		-	.03	−.02	.01	.12*	.04	.09
Fear			-	.37***	−.27***	−.11	−.08	−.15*
Vasovagal symptoms				-	−.25***	−.17**	−.09	−.11
Intention flu					-	.39***	.27***	.22***
Intention COVID-19						-	.19**	.36***
Uptake flu							-	.24***
Uptake COVID-19								-

[a]$n = 1$ missing.
*$p < .05$. **$p < .01$. ***$p < .001$.

TABLE 7 Logistic regression predicting 2020–2021 seasonal influenza and COVID-19 vaccine uptake

	Block 1					Block 2					Block 3				
Variable	**B**	**Wald**	**SE**	**OR**	**95% CI**	**B**	**Wald**	**SE**	**OR**	**95% CI**	**B**	**Wald**	**SE**	**OR**	**95% CI**
Seasonal influenza vaccine uptake															
Fear	−.36*	3.98	.18	.70	[.49, .99]	−.34	2.90	.20	.71	[.48, 1.05]	−.20	.83	.22	.82	[.53, 1.26]
Vasovagal symptoms						−.12	.07	.46	.89	[.36, 2.18]	.25	.26	.50	1.29	[.49, 3.41]
Intention											.76***	20.25	.17	2.14	[1.54, 2.98]
Nagelkerke R^2	.02					.02					.16				
COVID-19 vaccine uptake															
Fear	−.35*	4.45	.17	.70	[.51, .98]	−.24	1.65	.19	.79	[.54, 1.14]	−.33	2.39	.21	.72	[.48, 1.09]
Vasovagal symptoms						−.60	2.31	.39	.55	[.26, 1.19]	.09	.04	.48	1.10	[.43, 2.80]
Intention											.56***	36.35	.09	1.75	[1.46, 2.10]
Nagelkerke R^2	.02					.04					.24				

Note: $n = 301$. 95% CI, 95% confidence interval for odds ratio.
*$p < .05$. **$p < .01$. ***$p < .001$.

associated with vaccine uptake 1 year later, with small and medium effects, respectively. Next, vaccine relevant fears, vasovagal symptoms, and intention to get a COVID-19 vaccine were tested as predictors of COVID-19 vaccine uptake.

The lower section of Table 7 details the binary logistic regression predicting COVID-19 vaccine uptake with vaccine relevant fears, vasovagal symptoms, and COVID-19 vaccination intention. The final model was significant, $\chi^2(3) = 45.52$, $p < 0.001$, and tests of collinearity were acceptable (tolerance > .80, VIF < 1.25). Consistent with seasonal influenza, with all three predictors in the model, intention alone was a significant predictor of greater odds of subsequent COVID-19 vaccine uptake with a small effect ($d = .31$). Again, this pattern was replicated with the vaccine relevant fears item-level analyses, except for fear of side effects, which remained a significant predictor after adding intention to the model (Supporting Information S13). The analysis was re-run with demographic characteristics included as covariates, and the results remained consistent (Supporting Information S10). Next, hypothesized indirect effects of fear and vasovagal symptoms on vaccine uptake were examined.

To test if vaccine relevant fears had an indirect effect on vaccine uptake through vasovagal symptoms and vaccine intention, serial mediation analysis was used. The results supported model fit predicting COVID-19 vaccine uptake, $\chi^2(3) = 45.52$, $p < .001$, Nagelkerke $R^2 = .24$, with significant direct effects present for greater fear predicting higher vasovagal symptom scores, higher symptom scores predicting lower intention, and lower intention predicting reduced vaccine uptake (see bottom model in Figure 1). A significant indirect effect was present for greater fear reducing COVID-19 vaccine uptake through vasovagal symptoms and intention. This pattern was replicated with the vaccine relevant fears item-level analyses (Supporting Information S14). The model was re-run with demographic covariates included, and the results remained consistent (Supporting Information S12).

DISCUSSION

The present study provides prospective evidence that vaccine relevant fears predict vasovagal symptoms associated with seasonal influenza vaccination among adults. Exploratory analyses indicated that fear of injections and side effects may be particularly relevant. Further, vaccine relevant fears have a negative effect on seasonal influenza and COVID-19 vaccine uptake.

Vaccine relevant fears and vasovagal symptoms

As hypothesized, vaccine relevant fears predicted vasovagal symptoms during or following seasonal influenza vaccination within an adult sample. This is consistent with blood–injection–injury phobia and blood donation research, where heightened fear predicts greater vasovagal symptoms when confronted with the target fear or when undergoing the blood donation procedure (France et al., 2012; Öst et al., 1991). The present study found slightly stronger effects of fear on vasovagal symptoms (medium effect $r = .31$) compared to previous research with blood donors (small effect $r = .28$; France et al., 2012) and vaccination research with children and adolescents (small effect $d = .35$; Kemper et al., 2017).

Identifying potential screening items that predict who is at greater risk for vasovagal symptoms, or the broadly conceptualized immunization stress-related responses, is a target area for research globally (WHO, 2019c). The present study provides support that screening for fear is a

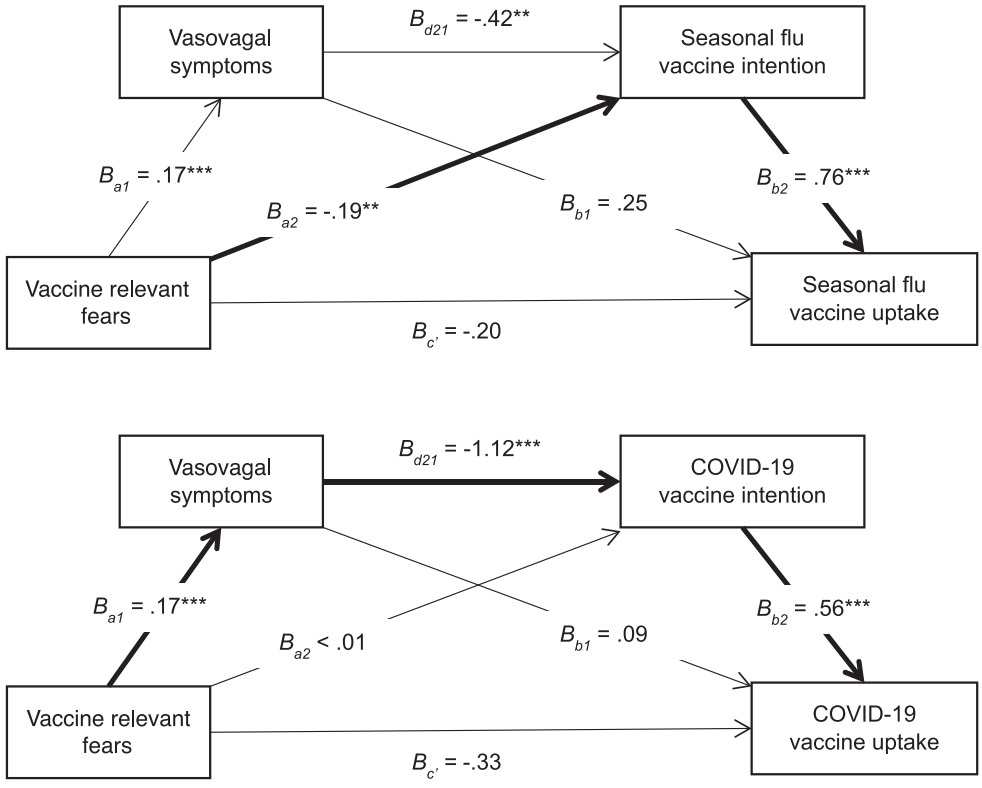

FIGURE 1 Serial mediation of experience of vasovagal symptoms and vaccine intention between vaccine relevant fears and (a) seasonal influenza vaccine uptake (top figure) and (b) COVID-19 vaccine uptake (bottom figure) with unstandardized coefficients (B). Vaccine uptake is coded as 0 = no, 1 = yes. Significant indirect effects are depicted by heavier weight paths (top figure: $a_2b_2 = -.14$, SE = .07, 95% CI = −.29, −.04; bottom figure: $a_1d_{21}b_2 = -.10$, SE = .05, 95% CI = −.22, −.02). *$p < .05$. **$p < .01$. ***$p < .001$

strong place to start for identifying potential items. Item-level analyses revealed that although each vaccine relevant fear used within the present study predicted vasovagal symptoms, fear of injections and fear of side effects were particularly relevant. Due to the exploratory nature of the item-level analyses, research to replicate and extend these findings is advised. Importantly, assessing fear prior to medical procedures does not increase risk for vasovagal symptoms or syncope. (France et al., 2012; Gilchrist et al., 2021). Once a person endorsing elevated fear has been identified, tailored strategies to mitigate or attenuate fear can be implemented. Distraction is a commonly recommended intervention to reduce not only fear, but also pain associated with needle-related procedures (Birnie et al., 2018). WHO (2019c) clinical guidelines recommend that for people with high levels of fear, counseling, behavioral interventions, or pharmacological intervention (e.g., anxiolytics) should be considered prior to receiving a vaccine. While the recommendation to pursue counseling or exposure therapy is valuable, it may not be accessible for everyone due to time and cost. Thus, the development and evaluation of brief tailored interventions, including virtual interventions, which could be administered on site, are warranted. Recommended provider level interventions to reduce fear include training to build rapport and system level interventions include minimizing wait time and providing privacy when possible (WHO, 2019c).

Given the experience of vasovagal symptoms during or following vaccination documented within the present study, interventions targeting these symptoms warrant consideration.

Applied muscle tension (repeated isometric tensing of the muscles in legs, buttocks, and abdomen) heightens cerebral oxygenation by increasing the return rate of blood to the heart and providing a transient elevation in blood pressure (Groothuis et al., 2007; Kowalsky et al., 2011; Öst et al., 1991). This intervention successfully reduces the severity of vasovagal symptoms and risk of syncope among patients with blood–injection–injury phobia and orthostatic hypotension (characterized by an exaggerated decrease in blood pressure upon standing up from seated or lying down positions, resulting in vasovagal symptoms and syncope), as well as among non-clinical populations such as blood donors (Krediet et al., 2007; Ritz et al., 2010; Thijsen & Masser, 2019). Clinical practice guidelines for vaccination recommend the use of applied muscle tension (Taddio et al., 2015; WHO, 2019c). However, the cited research pertaining to applied muscle tension within the practice guidelines is very limited, drawing from non-vaccine settings, such as blood donation (Taddio et al., 2015), or implementing exercise, such as the use of resistance bands and squats, prior to and following vaccination, but not during the procedure (Lee et al., 2018, cited within WHO, 2019c). Thus, a notable opportunity is present for research evaluating applied muscle tension for use during vaccination.

Association between age and vaccine relevant fears

In line with previous research, an association between increasing age and decreasing fear of vaccines was present. This pattern has been consistently documented within the literature (e.g., McLenon & Rogers, 2018, for review). It is likely that with more positive experiences with injections and blood draws as we age, decreases in fear are the result of exposure and learning. It is also possible that younger adults are reporting more fear in part due to greater susceptibility to misinformation. An experiment examining susceptibility to COVID-19 misinformation found a relationship by age such that younger adults held stronger misinformation beliefs compared to older adults (Vijaykumar et al., 2021). Thus, the potential impact of misinformation on vaccine relevant fears within younger age groups should be evaluated.

Understanding seasonal influenza and COVID-19 vaccine uptake

The effect of vaccine relevant fears prior to vaccination and experience of vasovagal symptoms during and following vaccination on future vaccine uptake was also examined in the present study. Evidence of serial mediation of the relationship between fear and vaccine uptake was partially found. Vaccine relevant fears had an indirect effect on seasonal influenza vaccine uptake through intention to vaccinate. In contrast, vaccine relevant fears had a negative indirect effect on COVID-19 vaccine uptake through the experience of vasovagal symptoms and the corresponding decrease in intention to vaccinate against COVID-19. This pattern of fear having an indirect effect on vaccine uptake is consistent with blood donor research. The experience of vasovagal symptoms during or following blood donation predicted lower donor return, with a small effect size present (France et al., 2005). More complex modeling with a separate sample of blood donors found that fear of having blood drawn and the experience of vasovagal symptoms each had indirect effects on blood donor return through intention to donate again (France et al., 2013).

Within the present study, seasonal influenza vaccine uptake during the 2019–2020 influenza season was similar to the United States population with 45.1% vaccine coverage versus 48.4%,

respectively (CDC, 2021). As expected, greater vaccine relevant fears predicted lower seasonal influenza vaccine uptake. The 2020–2021 influenza season analyses focused on the subset of participants who had previously received a seasonal influenza vaccine during the previous year. Not surprisingly, vaccine uptake was greater within this sample of previous vaccine adopters than the general population for both COVID-19 (84.7% vs. 55.8% as of July 8, 2021; Ritchie et al., 2022) and seasonal influenza (87.7% vs. 50.2%; CDC, 2021) vaccines. Importantly, among previously vaccine accepting people (those who obtained a seasonal influenza vaccine during the 2019–2020 flu season), not everyone obtained a seasonal influenza vaccine the following year or a COVID-19 vaccine when it became available. This is consistent with research examining vaccine hesitancy. The presence of vaccine hesitancy among vaccine adopters has been documented with HPV vaccine uptake, such that vaccine relevant fears and mistrust remained present after vaccination (Walker et al., 2020). The present study extends earlier research by showing the negative impact of experiential factors (i.e., vasovagal symptoms) on future vaccine uptake. Given that certain vaccines are recommended annually (e.g., seasonal influenza), or require a multi-dose sequence to produce a sufficient immune response (e.g., COVID-19, HPV), strategies to improve the vaccination experience to support return behavior are worth investigating.

An adverse experience with one vaccine, in this case a seasonal influenza vaccine, can negatively impact uptake of a different vaccine, in this case the COVID-19 vaccine. It is possible that because the vaccines that protect against COVID-19 are new, uptake of COVID-19 vaccines was more readily influenced by past vaccine experience (i.e., the experience of vasovagal symptoms associated with seasonal influenza vaccination). In contrast, although the seasonal influenza vaccines are updated annually to better match the anticipated predominant strains of circulating influenza virus, it is not considered a new vaccine. Future research should examine if this effect is consistent across familiar versus new vaccines and if factors such as trust may buffer against the impact of vasovagal symptoms on vaccine uptake. Additionally, research could assess the degree to which vasovagal symptoms have an impact across different vaccines or across medical procedures.

Strengths and limitations

The use of a longitudinal cohort design is important because strong predictors of intention or past behavior are not always strong predictors of future behavior. This discrepancy between intention and behavior is known as the intention-behavior gap (Sheeran & Webb, 2016). The longitudinal prospective design of the present study to document vaccine uptake behavior is a key strength and informs causal paths of relevant psychological and experiential contributors to vaccine uptake. Although much of the literature assesses vasovagal symptoms immediately following a procedure (e.g., Kemper et al., 2017) and the accuracy of recall of symptoms in the present study may be reduced due to the delayed assessment, the present study shows that longer term recall of vasovagal symptoms also matters. Future research should assess potential individual differences in trajectory of vasovagal symptom recall from immediately post-procedure to a more distal follow up. The present study assessed recall of vasovagal symptoms during and following vaccination; however, these symptoms can occur prior to the procedure. Symptoms experienced prior to vaccination were not assessed in the present study and is a limitation. Several limitations are present that pertain to generalizability. First, this was a convenience sample and thus is not demographically representative of the United States. Second, out of necessity to

test the impact of vasovagal symptoms on vaccine uptake, the 2020–2021 seasonal influenza and COVID-19 vaccine uptake was assessed using people who had previously adopted at least one dose of the seasonal influenza vaccine.

In sum, vaccine relevant fears predict vasovagal symptoms during or following seasonal influenza vaccination. Further, pre-existing vaccine relevant fears can reduce subsequent seasonal influenza vaccine uptake among previously seasonal influenza vaccine accepting adults within the United States. Similarly, vaccine relevant fears and the experience of vasovagal symptoms can reduce COVID-19 vaccine uptake among the same, previously vaccine accepting adults. Understanding vaccine hesitancy and supporting vaccine uptake is relevant to both the COVID-19 pandemic and public health more generally. Thus, future research should evaluate behavioral and psychological interventions to attenuate fear, reduce risk and severity of vasovagal symptoms, and improve the vaccine experience to support vaccine uptake.

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CONFLICT OF INTEREST

I have no known conflicts of interest to disclose.

ETHICS STATEMENT

Ethics approval for the study protocol and amendments was provided by the institutional review board at The Ohio State University.

PERMISSIONS TO REPRODUCE MATERIAL

No copyrighted material was used; thus, permissions are not applicable.

DATA AVAILABILITY STATEMENT

The study Aim 1 was pre-registered (prior to data collection) on Open Science Framework, Aim 2 was registered blinded *ex post* (prior to accessing the data). The registrations, deidentified data, materials, output with syntax, and STROBE reporting checklist are available at https://osf.io/v4xc3/?view_only=8924d04342d64f9a8788b0b9512ee00b.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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