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## Associations between psychiatric morbidity and COVID-19 vaccine hesitancy: An analysis of electronic health records and patient survey

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### ARTICLE INFO

#### Keywords:

Psychiatric illness  
COVID-19  
Vaccine hesitancy

### ABSTRACT

Psychiatric illness confers significant risk for severe COVID-19 morbidity and mortality; identifying psychiatric risk factors for vaccine hesitancy is critical to mitigating risk in this population. This study examined the prevalence of vaccine hesitancy among those with psychiatric illness and the associations between psychiatric morbidity and vaccine hesitancy. Data came from electronic health records and a patient survey obtained from 14,365 patients at a group medical practice between February and May 2021. Logistic regression was used to calculate odds for vaccine hesitancy adjusted for sociodemographic characteristics and physical comorbidity. Of 14,365 participants 1,761 (12.3%) participants reported vaccine hesitancy. Vaccine hesitancy was significantly more prevalent among participants with substance use (29.6%), attention deficit and hyperactivity (23.3%), posttraumatic stress (23.1%), bipolar (18.0%), generalized anxiety (16.5%), major depressive (16.1%), and other anxiety (15.5%) disorders, tobacco use (18.6%), and those previously infected with COVID-19 (19.8%) compared to participants without. After adjusting for sociodemographic characteristics and physical comorbidities, substance use disorders and tobacco use were significantly associated with increased odds for vaccine hesitancy and bipolar disorder was significantly inversely associated with vaccine hesitancy. Interventions to improve uptake in these populations may be warranted.

Three vaccines for COVID-19, the disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), have been approved and made widely available for adults in the United States (Centers for Disease Control 2021). These vaccines are 50–95% effective for reducing the risk of SARS-CoV-2 infection and 85–100% effective for reducing the risk for symptomatic COVID-19 disease and hospitalization (Lippi and Henry, 2021; Pilishvili et al., 2021; Mahase, 2020; Chagla, 2021). Despite demonstrated efficacy, safety, and availability, vaccine hesitancy, one's willingness to be vaccinated ranging from acceptance to uncertainty or refusal, despite adequate supply (Butler et al., 2015), is common in the United States and worldwide (Fisher et al., 2020; Sallam, 2021; Robertson et al., 2021). Understanding the factors associated with vaccine hesitancy and how to address it is therefore an important public health priority.

Psychiatric illness is one such factor. Psychiatric illness is associated

with increased risk for severe COVID-19 illness and mortality, independent of physical comorbidity (Wang et al., 2021; Taquet et al., 2021; Lee et al., 2020; Nemani et al., 2021; Baillargeon et al., 2021; Li et al., 2020). As of October 2021, the United States has joined other countries (De Picker et al., 2021) in recognizing this risk and prioritizing those with mental health conditions for COVID-19 vaccination and boosters. Despite this recognition, there is concern that patients with psychiatric conditions may be more susceptible to vaccine hesitancy. In a sample of non-institutionalized patients with mental health conditions in Denmark, 84.8% reported they were willing to be vaccinated for COVID-19 compared to 89.5% of the general population (Jefsen et al., 2021). Research on influenza vaccination in a population of Americans with severe mental illness identified a much larger gap, citing that only 24% of patients had been vaccinated, which was significantly lower than the prevalence of vaccination in the general population at that time

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<https://doi.org/10.1016/j.psychres.2021.114329>

Received 29 July 2021; Received in revised form 2 December 2021; Accepted 4 December 2021

Available online 7 December 2021

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(Lorenz et al., 2013). The reasons for COVID-19 vaccine hesitancy among those with psychiatric conditions are not well established. Similar to the general population, vaccine hesitancy may arise from negative perceptions or misinformation about vaccine safety and efficacy (Jefsen et al., 2021; Lorenz et al., 2013). However, this distrust may be amplified by experiences of stigma from healthcare providers or other poor treatment within the healthcare system (Blixen et al., 2016; Verhaeghe and Bracke, 2011). Moreover, those with psychiatric conditions may experience socioeconomic and structural barriers (Warren et al., 2020), and diminished self-efficacy, which can undermine follow through with vaccination.

While widespread uptake of the COVID-19 vaccine is critical for mitigating the spread of the virus, as of November 2021 only 59% (Centers for Disease Control, 2021) of American adults have been fully inoculated and between 17% (United States Census Bureau, 2021) and 42% (Fisher et al., 2020) report that they are uncertain about or resistant to being vaccinated. Addressing vaccine hesitancy presents a critical challenge to mitigating the spread of COVID-19, establishing broad population herd immunity, and ensuring a safe return to normalcy. Furthermore, identifying the extent of vaccine hesitancy among adults with psychiatric illness is a critical step towards developing strategies and interventions to improve vaccination uptake and reduce related morbidity and mortality in this vulnerable population (Lee et al., 2020; Nemani et al., 2021; Mazereel et al., 2021).

To date, research on vaccine hesitancy has focused primarily on sociodemographic characteristics, ideology, and personality traits (Fisher et al., 2020; Malik et al., 2020; Murphy et al., 2021; Freeman et al., 2021; Mannan and Farhana, 2020; Vrdelja et al., 2018). Studies have consistently found that greater social disadvantage, lower educational levels, younger age, and being female are associated with greater vaccine hesitancy (Fisher et al., 2020; Malik et al., 2020; Murphy et al., 2021; Freeman et al., 2021; Mercadante and Law, 2021; Khubchandani et al., 2021). Despite this exploration of risk factors, there is a significant gap in our understanding of the associations between psychiatric morbidity and vaccine hesitancy. Beyond the aforementioned work by Jefsen et al. in Denmark (Jefsen et al., 2021), extant research on psychiatric morbidity and COVID-19 vaccine hesitancy has been inconsistent and limited by reliance on self-report measures among a narrow set of conditions. Furthermore, this research has centered on European samples (Jefsen et al., 2021; Murphy et al., 2021; Bendau et al., 2021). One study reported that vaccine hesitancy was associated with specific anxieties about COVID-19 infection and health consequences, but not associated with generalized anxiety or depression as measured by the GAD-2 and PHQ-2 (Bendau et al., 2021). Yet another study identified a small but significant inverse association between self-reported mental health treatment and vaccine hesitancy among Irish participants, but not British participants (Murphy et al., 2021). While these studies contribute to our nascent understanding of the psychiatric correlates of vaccine hesitancy, they are limited in several ways. First, the validity of the PHQ-2 and GAD-2 is not well established (Gilbody et al., 1994; Plummer et al., 2016) and these brief screening tools may have limited sensitivity. Furthermore, none of the studies differentiated between specific psychiatric disorders or controlled for objective measures of physical comorbidity leaving the potential for residual confounding.

Critically, this approach may fail to identify heterogeneity in vaccine hesitancy across psychiatric conditions, which is plausible given the variability in symptoms, cognition, behavior, and experiences within the healthcare system. Indeed, some of the research on preventive behavior in response to infectious disease outbreaks and cardiac events has identified different patterns of behavior associated with different psychiatric symptoms and conditions. For example, several studies have reported that high levels of depressive symptoms are associated with reduced preventive behavior (e.g. social distancing, handwashing, and masking) in response to COVID-19 and SARS (Harper et al., 2020; Wang et al., 2020; Stickley et al., 2020). In a prospective study of patients following myocardial infarction, onset of major depression was

associated with diminished preventive health behavior, while the onset of generalized anxiety disorder was associated with increased uptake of preventive behavior (Benyamini et al., 2013). Similarly, in contrast to depression, the majority of studies report significant associations between anxiety symptoms and higher uptake of preventive measures in response to infectious disease outbreaks (Velikonja et al., 2021; Kwok et al., 2021; Leung et al., 2003; Kwok et al., 2020), though divergent findings have also been reported (Wang et al., 2020; Stickley et al., 2020). These inconsistencies may point to a threshold effect where increased worry and vigilance associated with moderate anxiety may be instrumental for promoting preventive behavior, but at high levels become maladaptive (Leung et al., 2003). Along these lines, one study reported that while moderate and high levels of anxiety were both associated with an increase in preventive behavior, the effect of moderate anxiety was much larger (Leung et al., 2003). Because the majority of these studies focus on symptoms, which may underlie a temporary response to an event or a pervasive condition, their generalizability to clinical levels of anxiety or depression is less clear.

While less-researched, Attention Deficit and Hyperactivity Disorder (ADHD) is associated with non-adherence to COVID-19 safety guidelines, potentially due to deficits in attention and executive function that mediate a higher propensity for risk taking behavior among those with ADHD (Pollak et al., 2019; Pollak et al., 2021). In another study, both alcohol and substance use disorders were significantly associated with COVID-19 disregard for social distancing and the belief that the severity of COVID-19 was exaggerated, though the effect sizes were larger among participants with substance use disorders compared to alcohol use disorders (Taylor et al., 2021). Finally, there is an association between bipolar disorder and poorer uptake of healthy behaviors (Kilbourne et al., 2007), though, to our knowledge, this has not been explored in relation to infectious disease prevention.

Given that psychiatric illness confers significant risk for severe COVID-19 illness and mortality and variability in the uptake of preventive measures across psychiatric conditions, there is a critical need to better understand the relationship between these conditions and vaccine hesitancy. To this end, this cross-sectional study examined the associations between psychiatric morbidities extracted from electronic health records (EHR) and vaccine hesitancy data collected in the second wave of a longitudinal survey of primary care patients at a large group medical practice in northeastern United States to address the following objectives:

First, we aimed to estimate the proportion of survey respondents who are hesitant/ resistant to being vaccinated.

Second, we aimed to identify the prevalence of vaccine hesitancy among respondents with diagnosed psychiatric and physical risk factors for COVID-19 disease.

Third, we aimed to examine the associations between psychiatric and physical risk-factors for COVID-19 disease and vaccine hesitancy.

## 1. Methods

### 1.1. Participants and survey administration

We conducted a cross-sectional study using data from the second wave of a longitudinal study of mental health and wellbeing during the COVID-19 pandemic. The study was conducted at a northeastern multi-specialty group medical practice serving 275,000 adult and pediatric patients annually. A survey was sent to all patients aged 18 and older via the online patient platform MyChart. Sixty-nine percent of our patient population uses MyChart. The survey was voluntary and informed consent was obtained from all participants. The first wave of data collection took place between October 2020 and January 2021. The second wave took place from February to May 2021 and was sent to 113,833 patients. Across the second wave, the survey was sent in consecutive weekly batches. When the survey was sent, patients received a notification that a new MyChart survey was available via

email. Patients were sent two reminders to complete the survey, which was available for two weeks before it was permanently closed. The survey was completed by 14,365 patients (12.3%). Survey respondents differed from the patient population in several ways which are displayed in eTable 2 of the online supplement. The analytic sample included more female respondents compared to the patient population. The analytic sample included fewer patients between the ages of 18–29, and who were Asian, Black, and Hispanic, or on Medicaid than the patient population. Across psychiatric and physical conditions, there were slightly more patients in the analytic sample with other anxiety disorders, and slightly fewer patients with attention deficit and hyperactivity disorder and alcohol and substance use disorders. The analytic sample also contained more patients with hypertension, cancer and respiratory disease, and who were overweight/obese than the patient population.

The survey included a battery of mental health assessments and several questions about the impact of COVID-19 and recent political events on wellbeing. The second wave of the study included items about vaccination. The surveys were linked to patient Electronic Health Record (EHR) data. The study was granted an exemption by the United Health Group Office of Human Research Affairs.

### 1.2. Measures

To assess vaccine hesitancy, participants were asked if they had received at least one dose of a COVID-19 vaccine. Participants who had not yet received the vaccine were then given a five-level Likert scale question about their intent to be vaccinated. Participants who reported that they were “unsure,” “don’t know,” “probably would not,” or “definitely would not” be vaccinated were classified as vaccine hesitant. Those who had received a vaccine and all others were classified as acceptant. Because vaccine hesitancy exists on a continuum ranging from uncertainty to outright resistance and due to the relatively small proportion of vaccine resistant respondents (2.9%), we constructed the vaccine hesitancy category by combining hesitancy and resistance. Psychiatric and physical morbidities were ascertained from the patients’ medical records and classified using the ICD-10 (eTable 1). We included major depressive disorder, generalized anxiety disorder, other anxiety disorders, posttraumatic stress disorder (PTSD), attention deficit and hyperactivity disorder (ADHD), alcohol use disorder (AUD), and substance use disorder (SUD). Physical comorbidities were based on known risk factors for COVID-19 (Bauer et al., 2021). We also included current nicotine dependence/tobacco use and clinical overweight/obesity from the EHR, and self-report of a previous COVID-19 infection.

We obtained participants’ age, race, and Hispanic ethnicity from the EHR. Age was categorized according to the Center for Disease Control’s guidelines based on risk for COVID-19 disease, hospitalization, and death (Risk for COVID-19 Infection 2021). We examined the distribution of age categories across vaccine hesitancy and aggregated age groups with similar response patterns. Final age categories included 18–29, 30–39, 40–64, and 65 and older. Socioeconomic status was indicated by the highest level of education that participants completed and household income in 2020. For education, response options included ‘Did not finish high school’, ‘High school/GED’, ‘College degree’, and ‘Masters/Doctorate’. ‘Less than high school’ was combined with ‘High school/GED’ due to the small number of respondents with less than a high school education. For household income, responses included \$25,000 increments up to \$150,000 or more. We collapsed income into four categories based on response patterns. Insurance type was indicated using the last recorded payer type.

### 1.3. Statistical analyses

Participant characteristics were described using frequencies and percentages. First, we cross-tabulated respondent characteristics across all levels of vaccine hesitancy (ranging from acceptant to resistant) and calculated chi-squared statistics. We then cross-tabulated participant

**Table 1**  
Sample characteristics, imputed,  $N = 14,365$ .

Variable	No.	%
<b>Gender</b>		
Female	8972	62.5
Male	5393	37.5
<b>Age</b>		
18–29	1765	12.3
30–39	2479	17.3
40–64	6355	44.2
65+	3766	26.2
<b>Race</b>		
White	12,890	89.7
Asian/Pacific Islander	592	4.1
Black or African American	342	2.4
Other race	541	(3.8)
<b>Hispanic ethnicity</b>		
Hispanic	784	5.5
Not Hispanic	13,581	94.5
<b>Income</b>		
<=\$25,000	1344	9.4
\$25,000–\$74,999	4786	33.3
\$75,000–\$149,999	5130	35.7
=>\$150,000	3106	21.6
<b>Last recorded payer</b>		
Medicaid	903	6.3
Medicare	3069	21.4
Other	728	5.1
Private	9665	67.3
<b>Education</b>		
High school/less than high school	4338	30.2
College	6138	42.7
Masters/doctorate	3889	27.1
<b>Psychiatric comorbidity</b>		
Major depressive disorder	1656	11.5
Bipolar disorder	189	1.3
Generalized anxiety disorder	785	5.5
Other anxiety disorders	2519	17.5
Attention deficit and hyperactivity disorder	365	2.5
Posttraumatic stress disorder	234	1.6
Substance use disorder	237	1.6
Alcohol use disorder	299	2.1
<b>Physical comorbidity</b>		
Cardiovascular disease	2008	14.0
Respiratory disease	2376	16.5
Hypertension	4350	30.3
Type I or Type II diabetes	1479	10.3
Chronic liver disease	706	4.9
Chronic kidney disease	840	5.8
Malignant cancer	1093	7.6
Immunodeficiency	592	4.1
Overweight/obesity	3989	27.8
Nicotine dependence/tobacco use	1096	7.6
<b>Self-reported COVID-19</b>		
Yes	1225	8.5
Unsure	1044	7.3
No	12,096	84.2
<b>Vaccine hesitant</b>	1761	12.3

characteristics with the binary indicator of vaccine hesitancy and calculated crude odds ratios. Multivariable logistic regression was used to estimate the log-odds of vaccine hesitancy, adjusting for gender, age, race, education, income, and payer type. We ran two models: in the first model we included participant sociodemographic characteristics and psychiatric diagnoses (Online Supplement). In the final model, we also include physical comorbidities: cardiovascular disease, respiratory disease, hypertension, diabetes, liver disease, kidney disease, immunodeficiency, nicotine dependence/tobacco use, and overweight/obesity (Figs. 1–3). All covariates were retained in the models regardless of statistical significance. Log-odds were exponentiated and interpreted as odds ratios with 95% confidence intervals. We conducted multiple imputation by chained equations with the mice package in R (van Buuren and Groothuis-Oudshoorn, 2011; Hailu, 2021) to obtain missing values for income (37.6%), education (32.8%), and race (16.4%). The

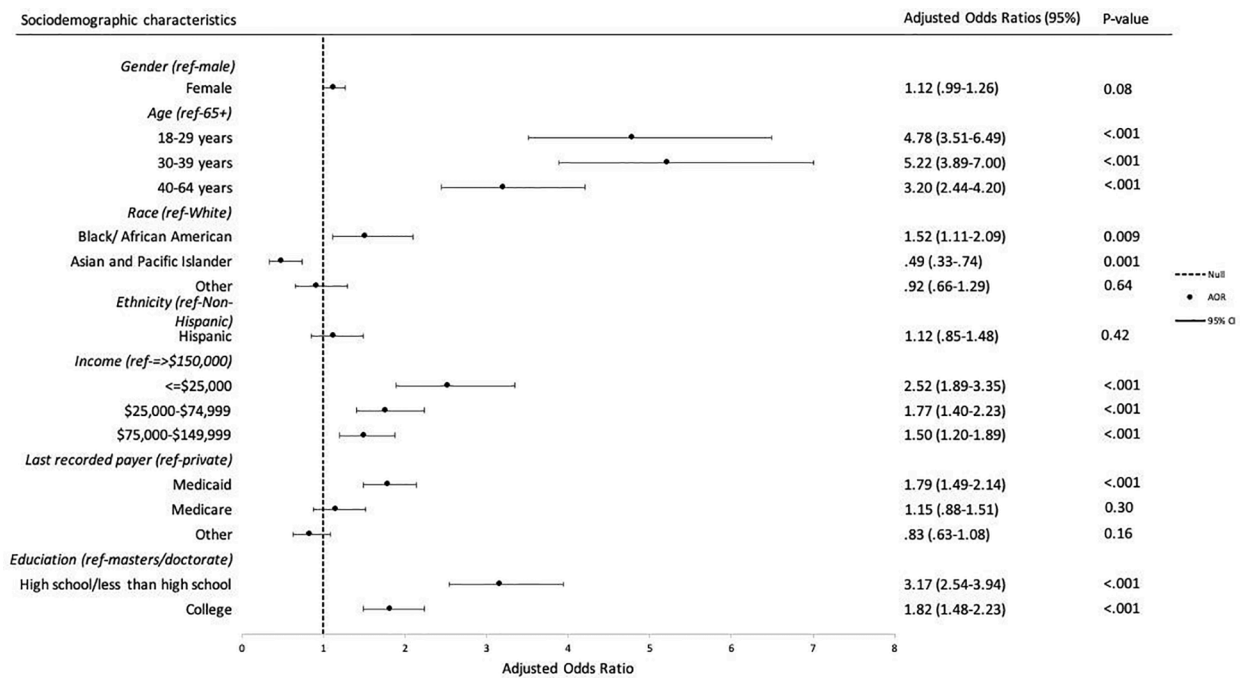


Fig. 1. Adjusted associations between sociodemographic characteristics and vaccine hesitancy.

imputation strategy is described in the online supplement. We ran 45 imputations and pooled results using Rubin’s rules to obtain estimates and standard errors (White et al., 2011). All statistical analyses were conducted in R 3.6.1 (Team, 2020).

## 2. Results

We received 14,365 responses (12.3% response rate) to Wave 2 of the survey. Participants were 62.5% female and 89.7% White (Table 1). Thirty-three percent reported household income between \$25,000 and \$74,999, 35.7% reported income between \$75,000 and \$149,999, and 69.8% had completed college or higher. Most participants used private insurance for their last encounter (67.3%). Other anxiety disorders were the most common psychiatric diagnosis (17.5%) followed by major depressive disorder (11.5%). Hypertension was the most common physical comorbidity (30.3%).

Overall, 12.3% (1761) of participants reported vaccine hesitancy. In unadjusted bivariate associations (Table 2), vaccine hesitancy was associated with being female and younger age. African American participants were the most likely to report vaccine hesitancy (23.9%). Hispanic respondents were also more likely to report vaccine hesitancy (21.8%). Vaccine hesitancy was more prevalent across all psychiatric comorbidities except for AUD, ranging from 15.5% for other anxiety disorders to 29.6% for SUD. The prevalence of vaccine hesitancy was significantly lower across most physical comorbidities. However, nicotine dependence/tobacco use and previous COVID-19 infection were significantly associated with greater vaccine hesitancy in unadjusted models. Overall, 2.9% of respondents reported vaccine resistance and there was slight variation in the distribution of vaccine resistance compared to hesitancy (eTable3). Slightly greater proportions of respondents reporting <\$25,000 annual income, high school education or less, last payer Medicaid, and with depression, bipolar disorder and generalized anxiety reported vaccine resistance compared to reference groups.

In the final model including sociodemographic characteristics and psychiatric and physical comorbidities, being younger was associated with greater vaccine hesitancy across each age category, where those aged 18–29 had nearly five-fold odds for vaccine hesitancy (95% CI 3.58

– 6.50,  $p < .001$ ) compared to those 65 and older. Black/African Americans had 1.52 times the odds for vaccine hesitancy compared to Whites (95% CI 1.11–2.09,  $p < .001$ ). Lower income and education, and Medicaid payer type were associated with increased odds for vaccine hesitancy (Fig. 1).

After adjustment for sociodemographic characteristics and physical comorbidities, SUD conferred 68% higher odds for vaccine hesitancy (OR=1.68, 95% 1.21–2.33,  $p = .002$ ) (Fig. 2). Bipolar disorder was associated with 35% lower odds for vaccine hesitancy (OR=.65, 95% CI 0.43–0.98,  $p = .04$ ). Those who were unsure as to whether they had been previously infected with COVID-19 had 86% increased odds for vaccine hesitancy (95% CI 1.56–2.21,  $p < .001$ ) and those who reported previous COVID-19 had 54% increased odds for vaccine hesitancy (95% CI 1.31–2.82,  $p < .001$ ) (Fig. 3). Nicotine dependence/tobacco use was associated with vaccine hesitancy (OR 1.44,  $p < .001$ ). Immunodeficiency was associated with 31% lower odds for hesitancy ( $p = .03$ ) (Fig. 3).

## 3. Discussion

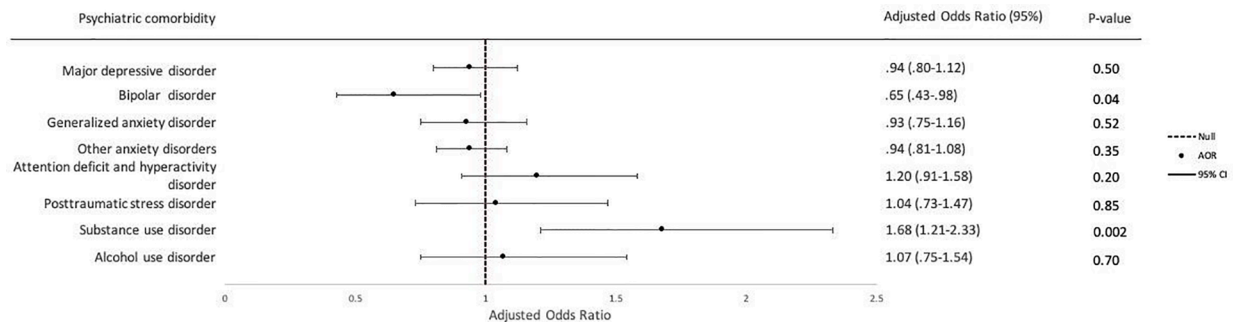
The present study examined the associations between psychiatric morbidity and vaccine hesitancy. Overall, 12.3% of patients reported vaccine hesitancy or resistance to receiving a COVID-19 vaccine. In this sample, vaccine hesitancy was more prevalent across all psychiatric morbidities except for alcohol use disorders (AUD), and less prevalent among several physical comorbidities. Substance use disorders (SUD), nicotine dependence/tobacco use (ND/TU) and previous COVID-19 infection conferred significant odds for vaccine hesitancy when accounting for potentially confounding sociodemographic factors. Contrary to previous research identifying an association between anxiety and increased preventive behavior, we found that vaccine hesitancy was similar across those with anxiety disorders and other conditions. This may be because we used diagnoses which are more sensitive to identifying clinically meaningful levels of anxiety and related impairment rather than natural variation in anxiety levels among otherwise healthy adults.

Our finding that 12.3% of our sample is vaccine hesitant is low relative to nationwide estimates between 32% and 43% reported as of Spring 2020. However, more recent data from the Census Bureau

**Table 2**

Vaccine hesitancy by participant characteristics and unadjusted odds for vaccine hesitancy, imputed, n = 14,365.

Variable	Vaccine acceptant N = 12,604		Vaccine hesitant No. N = 1761		Unadjusted OR	95% CI	p-value
Gender	N	%	N	%			
Female	7714	86.0	1258	14.0	1.59	1.42 - 1.77	<0.001
Male	4890	90.7	503	9.3	Reference		
<b>Age</b>							
18–29	1335	75.6	430	24.4	7.50	6.18 - 9.11	<0.001
30–39	2027	81.8	452	18.2	5.20	4.29 - 6.28	<0.001
40–64	5631	88.6	724	11.4	3.00	2.51 - 3.58	<0.001
65+	3611	95.9	155	4.1	Reference		
<b>Race</b>							
Black/African American	260	76.1	82	23.9	2.29	1.72 - 3.05	<0.001
Asian and Pacific Islander	557	94.2	34	5.8	0.45	.31 - 0.66	<0.001
Other	449	82.9	93	17.1	1.51	1.17 - 1.95	.002
White	11,339	88.0	1552	12.0	Reference		
<b>Hispanic ethnicity</b>							
Hispanic	614	78.3	171	21.8	2.10	1.70 - 2.58	<0.001
Non-Hispanic	11,990	88.3	1590	11.7	Reference		
<b>Income</b>							
≤\$25,000	996	74.1	349	25.9	5.40	4.30 - 6.77	<0.001
\$25,000-\$74,999	4082	85.3	704	14.7	2.66	2.17 - 3.25	<0.001
\$75,000-\$149,999	4611	89.9	519	10.1	1.73	1.40 - 2.15	<0.001
≥\$150,000	2917	93.9	189	6.1	Reference		
<b>Last recorded payer</b>							
Medicaid	582	64.1	326	35.9	3.99	3.44 - 4.62	<0.001
Medicare	2900	94.4	173	5.6	0.43	.36 - 0.50	<0.001
Other	647	90.1	71	9.9	0.78	.61 - 1.01	.06
Private	8476	87.7	1191	12.3	Reference		
<b>Educational attainment</b>							
High school/less than high school	3445	79.4	894	20.6	4.83	3.98 - 5.87	<0.001
Bachelors	5469	89.1	669	10.9	2.28	1.87 - 2.78	<0.001
Masters/doctorate	3690	94.9	198	5.1	Reference		
<b>Psychiatric comorbidity</b>							
Major depressive disorder	1389	83.9	267	16.1	1.44	1.25 - 1.66	<0.001
Bipolar disorder	155	82.0	34	18.0	1.58	1.09 - 2.30	.02
Generalized anxiety disorder	655	83.5	130	16.5	1.45	1.20 - 1.77	<0.001
Other anxiety disorder	2128	84.5	391	15.5	1.41	1.24 - 1.59	<0.001
Attention deficit and hyperactivity disorder	280	76.7	85	23.3	2.23	1.74 - 2.86	<0.001
Posttraumatic stress disorder	180	76.9	54	23.1	2.18	1.60 - 2.97	<0.001
Substance use disorder	166	70.4	70	29.6	3.08	2.32 - 4.09	<0.001
Alcohol use disorder	255	85.0	45	15.0	1.28	.92 - 1.76	.14
<b>Physical comorbidity</b>							
Cardiovascular disease	1850	92.1	158	7.9	0.57	.48 - 0.68	<0.001
Respiratory disease	2058	86.6	318	13.4	1.13	.99 - 1.29	.07
Hypertension	4009	92.2	341	7.8	0.52	.45 - 0.58	<0.001
Type I or II diabetes	1344	90.9	135	9.1	0.70	.58 - 0.84	<0.001
Chronic liver disease	634	89.8	72	10.2	0.81	.63 - 1.03	.09
Chronic kidney disease	786	93.7	53	6.3	0.47	.35 - 0.62	<0.001
Immunodeficiency	547	92.4	45	7.6	0.58	.42 - 0.79	<0.001
Malignant cancer	1026	93.9	67	6.1	0.45	.35 - 0.57	<0.001
Overweight/obesity	3494	87.6	495	12.4	1.02	0.91 - 1.14	.73
Nicotine dependence/tobacco use	892	81.4	204	8.6	1.72	1.46 - 2.02	<0.001
<b>Self-reported COVID-19</b>							
Yes	983	80.3	242	19.8	2.03	1.75 - 2.37	<0.001
Unsure	831	79.6	213	20.4	2.12	1.80 - 2.49	<0.001
No	10,790	89.2	1306	10.8	Reference		



**Fig. 2.** Adjusted associations between psychiatric comorbidities and vaccine hesitancy.

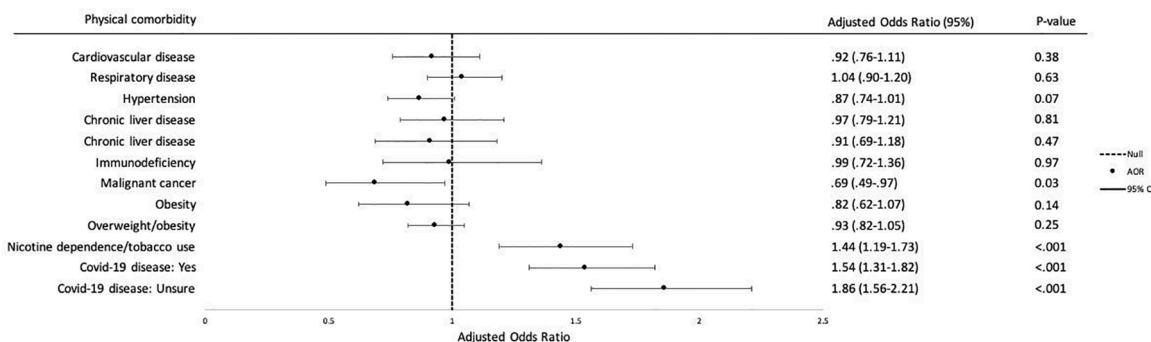


Fig. 3. Adjusted associations between physical comorbidities and vaccine hesitancy.

suggests a decline in vaccine hesitancy by March 2021 when 84% of Americans reported they had already been vaccinated or definitely/probably would be vaccinated (United States Census Bureau, 2021). This may also reflect relatively higher levels of vaccine acceptance in northeastern states relative to other parts of the United States, as well as the high proportion of college educated participants in our sample.

Consistent with the literature, lower levels of educational attainment and income and Medicaid payer type were all associated with hesitancy. Hesitancy was also more prevalent among females, African Americans/Blacks, and Hispanics. In previous research, Blacks have reported significantly greater vaccine hesitancy relative to Whites (Fisher et al., 2020; Malik et al., 2020), which has been attributed to medical mistrust stemming from systemic racism (Woko et al., 2020; Jamison et al., 2019). Similarly, in this sample, there was a 12% difference in vaccine hesitancy between African American/Blacks and Whites. However, this disparity is substantially smaller than disparities of 24–28% reported in Spring 2020 (Fisher et al., 2020; Malik et al., 2020), and may reflect increased vaccine acceptance among Blacks through the Winter of 2021 (State Health Access Data Assistance Center, 2021), and the high proportion of our sample with college education. Additionally, the proportion reporting vaccine resistance was particularly low in our sample (2.9%), though there were deviations. Younger respondents and those with lower socioeconomic status (e.g. income, education, and last payer Medicaid) were all slightly more likely to report resistance compared to those in other categories, consistent with the literature (Fisher et al., 2020; Murphy et al., 2021). Vaccine resistance was also slightly more prevalent among those with depression, generalized anxiety and bipolar disorder compared to other conditions. Although much of the work to date takes a similar approach to addressing vaccine uncertainty and resistance, future work should identify potential mediators and moderators of resistance as this population may require more tailored interventions.

Given the heightened prevalence of vaccine hesitancy and vulnerability to the negative sequelae of COVID-19 among those with psychiatric illness, addressing vaccine hesitancy is an important, yet overlooked priority for national and state policymakers (Mazereel et al., 2021). While older adults and those with physical risk factors for COVID-19 have been prioritized for vaccine distribution since the vaccines became available (Centers for Disease Control and Prevention, 2021), provisions for people with mental health conditions in the United States were not made until October of 2021. We identified a higher prevalence of vaccine hesitancy among patients with mental health conditions, with the exception of alcohol use disorders. However, in regression models controlling for sociodemographic characteristics, the relationship between vaccine hesitancy a most psychiatric conditions were completely attenuated with the exception of substance use disorders and tobacco use. This suggests that the higher prevalence observed across most conditions may be related to the distribution of socio-demographic characteristics in this population as opposed to intrinsic differences in vaccine hesitancy among those with psychiatric

conditions. Nonetheless, information regarding the heightened prevalence of vaccine hesitancy among those with psychiatric disorders can help inform interventions in clinical settings, regardless of the specific mechanisms for vaccine hesitancy.

Patients with SUD and TU/ND are more likely to report vaccine hesitancy independent of other socioeconomic factors. This is concerning given SUDs are associated with 9-fold risk for COVID-19 disease and tobacco use is associated with 8-fold risk (Wang et al., 2021). These findings align with research identifying poorer engagement in preventive healthcare among those with SUD and tobacco use (Boyle et al., 2000; Lasser et al., 2011). Possible explanations for poorer compliance with preventive care include socioeconomic deprivation, challenges prioritizing healthcare over substance use, and stigmatization from medical providers (Melamed et al., 2020; Motavalli et al., 2021; Van Boekel et al., 2013).

Strategies for improving vaccine uptake in other populations may provide guidance for improving acceptance among those with psychiatric illness. Simple interventions such as text message reminders to patients eligible for the COVID-19 vaccine can improve uptake by 84% (Dai et al., 2021). This can help by removing barriers to finding appointments and scheduling, which has been shown to be effective among individuals with substance use disorders but may also be relevant to other populations (Motavalli et al., 2021). Direct outreach by doctors' offices may also be effective. One study reported that information from doctors was among the most important factors for making health decisions among individuals with history of SUDs (Mellis et al., 2021). Another study reported that among patients with mental illness, those who received vaccine education from their physician had four-fold odds for obtaining an influenza vaccine (Lorenz et al., 2013). In addition, outreach by mental health professionals may be particularly beneficial as they can tailor vaccine education to their patients' needs (Warren et al., 2020) and can address psychological and structural barriers to vaccination. In addition, development of shared decision-making tools among providers may educate patients about the benefits of receiving the vaccine (Kuehne et al., 2020; Durand et al., 2021). Vaccination clinics embedded in substance use treatment and mental health services may also remove barriers to uptake; embedding a vaccine clinic in a mental healthcare facility improved Td/Tdap vaccination rates by nearly 34% among patients with mental illness (Miles et al., 2020). However, many individuals with psychiatric illness or SUD do not receive appropriate medical or mental health care and it is important to reach those outside of organized care settings. Possible strategies to reach these vulnerable populations include implementing educational campaigns and vaccine clinics at clean injection sites, detox centers, shelters, and community centers.

These findings also suggest that vaccine hesitancy is greater among those with previous COVID-19 infection and those who are unsure if they were previously infected. Although some research reports low rates of reinfection among previously infected individuals (Abu-Raddad et al., 2020; Alabdulla et al., 2021), the neutralizing antibodies produced

through natural infection may not be as effective for preventing COVID-19 disease as those in the vaccines and deteriorate more rapidly over time, particularly in immunocompromised individuals and older adults (Boyton and Altmann, 2021; Vitale et al., 2021; Hansen et al., 2021). Furthermore, the effectiveness of natural immunity to new variants is poorly understood and there are concerns about the emergence of variants such as the Delta variant (Boyton and Altmann, 2021; Vitale et al., 2021; Hansen et al., 2021). While the CDC currently recommends COVID-19 vaccines for those with previous infections (Centers for Disease Control and Prevention, 2021), more work is needed to understand the risk of reinfection and educate the public about the benefits of vaccination among naturally infected individuals.

### 3.1. Limitations

This study has several important limitations. First, this is a cross-sectional study and we are unable to establish temporality. Second, our study sample consisted of majority White, higher socioeconomic status primary care patients in New England and these findings may not be generalizable to other populations. Future work is needed to examine the psychiatric and physical health correlates of vaccine hesitancy in other populations globally. Third, the patient survey was only sent to MyChart users and participation was voluntary leaving the potential for selection bias. MyChart users who are willing to participate in a healthcare survey may be more engaged in their care and therefore more likely to accept vaccination, contributing to the overall low levels of vaccine hesitancy reported. Additionally, there were slightly smaller proportions of younger respondents, non-white respondents and respondents with last payer listed as Medicaid in the analytic sample leaving the potential for non-response bias as these populations are more likely to report vaccine hesitancy, thus underestimating the prevalence of hesitancy. Further, if those who did not respond to the survey are systematically more likely to report vaccine hesitancy than responders, our odds ratios may be biased towards the null hypothesis. Fourth, although behavioral health and primary care providers regularly report psychiatric diagnoses in the EHR, a minority of providers do not enter this data to limit including potentially stigmatizing information in patients' records. This could result in misclassification and information bias towards the null-hypothesis, which suggests that the associations between psychiatric diagnoses and vaccine hesitancy may be stronger than those observed. Despite these limitations, this study has several notable strengths. To our knowledge, this is the first study to examine the psychiatric and physical correlates of COVID-19 vaccine hesitancy in the United States. Additionally, this study captured vaccine uptake and hesitancy between February and May of 2021, providing more recent information on vaccination behavior and intent. This study uses a large sample size and controls for a robust set of covariates. Additionally, we use objective measures of psychiatric and physical comorbidities obtained from the EHR rather than self-reported diagnosis.

### 3.2. Conclusions

Although there have been great strides in vaccine development and uptake, vaccine hesitancy remains a significant problem worldwide. This is particularly important as social distancing and masking requirements are lifted and vaccination becomes the predominant means for avoiding infection. In addition to the personal impact of COVID-19, failure to address vaccine hesitancy will likely enhance development of new variants and place undue burden on the healthcare system and economy for years to come. Our findings suggest that individuals with substance and tobacco use disorders are significantly more likely to report vaccine hesitancy relative to those without. Future research should examine the association between psychiatric illness and vaccine hesitancy in other populations. Interventions should be tested to better inform patients about the benefits and risks for vaccinations. In addition to tailoring vaccination outreach for individuals with psychiatric

illnesses, more work is needed to understand reasons for vaccine hesitancy in this population.

### Conflicts of interest

Alexander Dang, John Buresh, and Scott Shimotsu are employees of OptumLabs, part of UnitedHealth Group. Alexander Dang, John Buresh, and Scott Shimotsu own stock in the company. The other authors have no conflicts of interest to disclose.

### Funding /Support

The Practice Research Network is funded by OptumLabs, part of UnitedHealth Group.

### CRedit authorship contribution statement

**Mara Eyllon:** Conceptualization, Methodology, Writing – original draft, Supervision, Project administration. **Alexander P. Dang:** Formal analysis, Software, Methodology, Data curation, Writing – review & editing. **J. Ben Barnes:** Conceptualization, Writing – review & editing. **John Buresh:** Formal analysis, Software, Methodology, Data curation, Writing – review & editing. **Gabrielle D. Peloquin:** Writing – review & editing, Visualization. **Annika C. Hogan:** Writing – review & editing, Visualization. **Scott T. Shimotsu:** Conceptualization, Methodology, Writing – review & editing. **Susan R. Sama:** Conceptualization, Methodology, Writing – review & editing. **Samuel S. Nordberg:** Conceptualization, Writing – review & editing, Funding acquisition.

### Acknowledgements

We would like to acknowledge Lawrence Garber, MD, Artur Cosquete, and Meagan Fair of Reliant Medical Group for implementing and disseminating the MyChart survey to patients and for setting up the data transfer between Reliant Medical Group and UnitedHealth Group.

### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2021.114329.

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