ORIGINAL RESEARCH



Cross-Sectional Survey of Factors Contributing to COVID-19 Testing Hesitancy Among US Adults at Risk of Severe Outcomes from COVID-19

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ABSTRACT

Introduction: The United States Centers for Disease Control and Prevention (CDC) advises testing individuals for COVID-19 after exposure or if they display symptoms. However, a deeper understanding of demographic factors associated with testing hesitancy is necessary.

Methods: A US nationwide cross-sectional survey of adults with risk factors for developing severe COVID-19 ("high-risk" individuals) was conducted from August 18–September 5, 2023.

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J. C. Cappelleri Biostatistics, Pfizer Inc, Groton, CT, USA Objectives included characterizing demographics and attitudes associated with COVID-19 testing. Inverse propensity weighting was used to weight the data to accurately reflect the high-risk adult US population as reflected in IQVIA medical claims data. We describe here the weighted results modeled to characterize demographic factors driving hesitancy.

Results: In the weighted sample of 5019 respondents at high risk for severe COVID-19, 58.2% were female, 37.8% were ≥65 years old, 77.1% were White, and 13.9% had a postgraduate degree. Overall, 67% were Non-testers (who indicated that they were unlikely or unsure of their likelihood of being tested within the

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Y. Cai · Z. Tian · Y. Liu Advanced Analytics, IQVIA, Wayne, PA, USA next 6 months); these respondents were significantly more likely than Testers (who indicated a higher probability of testing within 6 months) to be female (60.2 vs. 54.1%; odds ratio [OR] [95% confidence interval (CI)], 1.3 [1.1-1.4]), aged ≥ 65 years old (41.5 vs. 30.3%; OR [95% CI] compared with ages 18–34 years. 0.6 [0.5–0.7]), White (82.1 vs. 66.8%; OR [95% CI], 1.4 [1.1-1.8]), and to identify as politically conservative (40.9 vs. 18.1%; OR [95% CI], 2.6 [2.3–2.9]). In contrast, Testers were significantly more likely than Non-testers to have previous experience with COVID-19 testing, infection, or vaccination; greater knowledge regarding COVID-19 and testing; greater healthcare engagement; and concerns about COVID-19. Conclusions: Older, female, White, ruraldwelling, and politically conservative high-risk adults are the most likely individuals to experience COVID-19 testing hesitancy. Understanding these demographic factors will help guide strategies to improve US testing rates.

Keywords: COVID-19; Risk factors; SARS-CoV-2; Survey; Testing

Key Summary Points

Why carry out this study?

COVID-19 continues to be a major public health threat in the United States despite the availability of effective treatment for adults at high risk of progression to severe disease.

Testing for COVID-19 is the first step toward receiving treatment and is recommended for those experiencing symptoms or who have been exposed; however, evidence suggests that many individuals are hesitant to be tested for COVID-19.

In this study, a cross-sectional survey was used to identify the demographic, experiential, attitudinal, and healthcare engagement factors associated with COVID-19 testing hesitancy among US adults at high risk of progression to severe disease.

What was learned from the study?

Testing hesitancy was associated with female sex, White race, older age, rural communities, and conservative politics, whereas greater likelihood of testing was associated with past COVID-19 experience, greater knowledge of COVID-19–related topics, greater healthcare engagement, and greater concerns surrounding COVID-19.

Future strategies to improve testing rates among US adults at high risk of COVID-19 can be optimized by tailoring interventions to the patient signatures that are characterized by the greatest rates of testing hesitancy, which may transcend typical social determinants of health.

INTRODUCTION

In the United States, there have been more than 1 million deaths attributed to COVID-19 [1]. In May 2023, the World Health Organization declared that COVID-19 is no longer a public health emergency of international concern, citing declining mortality and morbidity rates and the considerable SARS-CoV-2 immunity levels in the population [2]. Despite the end of the public health emergency, however, COVID-19 remained a leading cause of US deaths in 2022 [3]; 300–500 Americans were dying each week from COVID-19, and many more were facing acute or chronic illness as a result of infection [4]. As of November 2023, COVID-19 was the cause of nearly 20,000 weekly hospitalizations and 2.5% of all weekly deaths reported in the United States [5]. Therefore, the US Centers for Disease Control and Prevention (CDC) continue to recommend SARS-CoV-2 testing for anyone who is experiencing COVID-19 symptoms or who has a known exposure to a SARS-CoV-2–positive individual [6].

The burden of poor COVID-19 outcomes is greatest among certain populations, including individuals aged \geq 65 years and those with certain comorbidities including obesity;

diabetes; chronic heart, kidney, lung, and liver disease; and an immunocompromised state [7–9] (termed "high-risk" individuals). These individuals remain particularly vulnerable to developing severe COVID-19 outcomes, including hospitalization and death, and surveillance and treatment remain critical to protect these vulnerable populations. Preventing these individuals from contracting SARS-CoV-2 is one important goal of testing, so that those who test positive can quarantine and avoid spreading the virus to those who may have risk factors for progression to severe disease [6, 10].

Another important goal of SARS-CoV-2 testing is to diagnose COVID-19 early so that affected individuals can be treated for the disease. In the United States, nonhospitalized adults and adolescents with mild to moderate COVID-19 who are at high risk of progression to severe disease are recommended to receive antiviral treatment in the following order of preference: nirmatrelvir/ritonavir, remdesivir, or molnupiravir (as an alternative for use in patients aged ≥ 18 years when preferred therapies are either unavailable, not feasible, or clinically inappropriate) [11]. Efficacy of treatment with nirmatrelvir/ritonavir in clinical trials has been demonstrated only with early commencement of antiviral therapy (i.e., within 5 days of symptom onset) [12], underscoring the need for timely testing and subsequent connection to care.

Despite CDC recommendations and the importance of testing for COVID-19, it is unclear to what extent individuals in the United States are getting tested when clinically indicated [13]. Many adults across countries including the United States experience testing hesitancy, defined as the reluctance or refusal to have oneself tested for COVID-19; this has been associated with various barriers including low health literacy or exposure to misinformation, lack of trust in the healthcare system, confusion regarding testing guidelines, limited testing site availability, fear of social stigma, fear of missed work and income due to a positive test, and perceiving the test as painful [10, 13-16]. In a previous survey of US adults, up to 30% of respondents indicated uncertainty or lack of willingness to be tested for COVID-19 [13]. However, there are limited data on the individual characteristics and beliefs that may be associated with testing hesitancy among high-risk adults in the United States.

Here, we conducted a nationwide survey designed to determine the demographic, experiential, and attitudinal factors associated with COVID-19 testing hesitancy among US adults at high risk for progression to severe COVID-19 during the Omicron era. Specifically, we asked whether testing hesitancy was associated with demographic factors such as age, gender, race/ ethnicity, educational attainment, income level, and political affiliation. We also asked whether testing hesitancy was associated with previous COVID-19 diagnosis, vaccination, treatment, or level of engagement with the healthcare system. The goal was to identify factors that may drive testing hesitancy to ensure that interventions aiming to improve testing rates are tailored to the populations with the greatest need.

METHODS

Study Design and Inclusion Criteria

This cross-sectional study was conducted through distribution of a survey regarding participants' demographic and clinical characteristics, as well as experience with and attitudes toward COVID-19 and COVID-19 testing. The approximately 15-min online survey was distributed between August 18, 2023, and September 5, 2023. For inclusion, participants had to be aged≥18 years and at high risk of developing severe complications from COVID-19 should they become infected; high risk categorization was based on criteria set forth by the CDC as of August 2023 [9].

Eligible participants were identified and recruited through clinical sites, physicians and other healthcare providers, referrals, advocacy group partnerships, and patient panels. An online screening tool was used to assess eligibility; patients deemed eligible were required to complete an informed consent form before they could receive a link to the survey. All participation was voluntary, and no monetary

compensation was provided for survey respondents. The protocol was reviewed and approved for exemption by the local Institutional Review Board, WCG Clinical, under Title 45 CFR Sect. 46.104(d)(2).

Survey Design and Piloting

Survey topics and questions were designed by referencing previous peer-reviewed publications regarding testing hesitancy and/or vaccine hesitancy [10, 13, 17, 18], US census demographic questions [19], and the US Census Household Pulse survey [20]; some survey questions were generated de novo through author collaboration. After the initial survey was prepared, it was rigorously tested by readers not involved in survey design to gauge appropriate length and readability. The survey then underwent a "soft launch," during which it was distributed to 50 participants, and their responses were reviewed before full distribution.

The appropriate sample size to target when distributing the survey was determined through power analysis using a one-sample chi-square test for proportions [21]. To ensure sufficient statistical power, we recruited a total of 5000 participants, and each high-risk cohort was represented by a minimum of 50 respondents. To maximize participation and achieve the target sample, multiple survey samples were sent, and reminder invites were sent to those who had not yet participated.

Survey Questions

The survey is included in its entirety in the Supplementary Material. Participants were asked to fill out demographic and clinical information such as age, sex/gender, race, ethnicity, highest level of educational attainment, and annual household income, as well as identifying any conditions placing them at high risk of developing severe complications from COVID-19 [9]. To assess testing hesitancy, participants were asked the question, "In the next 6 months, how likely are you to test for COVID-19?" The 6-month window of evaluation was selected to include the winter respiratory season (based on distribution

of the survey from August to September) but to be a limited enough horizon that the results could be interpreted meaningfully. When asked this question, participants could respond "definitely," "probably," "unsure," "probably not," or "definitely not." For the purposes of the analysis, those who replied "definitely" or "probably" were defined as "Testers," and those who replied "unsure," "probably not," or "definitely not" were defined as "Non-testers."

To understand more nuanced factors potentially associated with the likelihood of being a Tester or Non-tester, participants were asked a series of questions regarding their knowledge about COVID-19-related topics, for which they could indicate that they were "not at all knowledgeable" or "un-knowledgeable" (grouped for analysis as "not knowledgeable"); "somewhat knowledgeable"; or "knowledgeable" or "extremely knowledgeable" (grouped for analysis as "proficient"). They were also asked to provide their typical frequency of healthcare provider visits and any recent hospitalizations, their past experience with either COVID-19 diagnosis or vaccination, and their general attitudes and concerns regarding COVID-19. To assess attitudes, participants were asked to indicate their level of agreement with various statements (e.g., "If I have symptoms of COVID-19, it's important to me to test for COVID-19 right away") by responding "completely disagree," "disagree," "unsure," "agree," or "completely agree." Of note, those who responded "agree" or "completely agree" may also still be categorized as "Non-testers" based on responses to the query described above regarding their likelihood of testing for COVID-19 within the next 6 months. Each option was assigned a respective numeric value from 1 to 5 to calculate an average response value for Testers compared with Non-testers.

Data Analysis

To ensure generalizability of survey results to the population of US adults with COVID-19 risk factors, raw survey data were adjusted using inverse propensity weighting (IPW)[22]. This method was conducted by comparing demographic and

clinical characteristics of the survey population with the same characteristics among a selected target population of 116 million high-risk patients (defined using the International Classification of Diseases-10 diagnosis codes; see Supplementary Material) within IQVIA medical claims data, an office-based database capturing>75% of American Medical Association providers. Dating back to 2000, the IQVIA database sources over>1.5 billion medical claims per year, which represent transactions for services performed by physicians in office, ambulatory, or general healthcare sites that are billed using the 837p (CMS-1500) claim form. Key attributes include patient and provider demographics; diagnosis, procedure, and treatment information; and insurance and cost details. The IPW technique adjusted for survey sample selection bias by matching the survey sample distribution to the target population. The propensity score of each respondent being sampled was calculated using demographic variables of sex/gender, age, and 14 selected high-risk conditions (Table 1); these variables were selected because they were common features available in both survey and IQVIA claims data and were similarly defined in the two datasets.

To estimate propensity scores, we initially selected a sample of high-risk patients from the IOVIA database. The selection was conducted at a ratio of 20:1 with respect to the number of survey respondents. Subsequently, logistic regression and XGBoost models were employed to compute the propensity scores. The weights were then calculated as the reciprocals of the propensity scores and were standardized to match the number of survey respondents. XGBoost, a gradient boosting framework that utilizes decisiontree-based ensemble machine learning [23], was chosen for its potential to yield superior results compared with logistic regression when using propensity score weighting for specific datasets [24]. The XGBoost model was able to calculate weights that closely aligned with the characteristics of the target population and was therefore selected for generating final inverse probability weights.

Statistical comparisons were conducted using Python Statsmodels module (Python version 3.6.8, Statsmodels version 0.12.2) to calculate

odds ratios (ORs) and 95% CIs. Weighted univariate logistic regression was used to examine the association between the focal independent variables and COVID-19 testing hesitancy. Average attitudes were compared between Testers and Non-testers using Student's t tests, where P < 0.05 was considered significant.

RESULTS

Respondent Population

The survey was distributed to 35,000 individuals, of whom 9225 (26.4%) clicked on the distributed link to review the screening tool. Out of those 9225 individuals, 4104 either did not meet eligibility criteria, did not provide informed consent, or did not pass quality control; 13 began but did not complete the survey; and 5019 respondents (54.4%) completed all survey questions and comprised the full survey population. The population included a diverse sample of high-risk US adults representing several races. ethnicities, and levels of educational attainment; 66% were female, 52% were≥50 years old, 77% were White, 45% had at most a high school education or General Educational Development Test (GED), and 84% had a household income of < \$100,000 per year. The most commonly reported conditions placing respondents at high risk of developing severe COVID-19 complications were smoking (current or previous) and substance use disorders (n=2356). Other commonly reported conditions included mental health disorders (e.g., anxiety, post-traumatic stress disorder, bipolar disorder, depression, or schizophrenia; n = 1877), inactive lifestyles (including being overweight or obese; n = 1274), and type 1 or type 2 diabetes (n = 1162).

Inverse Propensity Weighting

Several important characteristics were dissimilar between the respondent population and the target population (Table 1; Supplemental Fig. 1). Specifically, survey respondents were more likely to be female, aged < 50 years, and have certain comorbidities, such as smoking/

Table 1 Survey population, target population, and weighted survey population distribution across demographic and clinical characteristics

Characteristic	Prevalence in survey population before IPW, %	Prevalence in target popula- tion, %	Prevalence in survey population after IPW, %
Demographic			
Female	65.6	56.4	58.2
Male	33.8	43.6	41.8
Aged 18–34 years	24.0	18.9	19.1
Aged 35–49 years	23.7	18.4	17.9
Aged 50–64 years	24.2	24.5	25.2
Aged ≥ 65 years	28.1	38.2	37.8
Risk factor			
Current or former smoking, and/or substance use disorder	46.9	14.0	15.5
Physical or mental disability	20.7	0.1	1.1
Pregnancy	2.7	2.1	2.1
Diabetes (type 1 or 2)	23.2	20.9	20.9
Cancer	5.5	14.1	11.9
Chronic pulmonary disease	17.2	39.5	37.5
Chronic cardiac, renal, or hepatic disease	18.1	46.4	42.9
Dementia or other neurologic disease, stroke history, or cerebrovascular disease	3.8	2.2	1.5
Immunocompromised	11.4	1.1	1.3
Mental health disorder	37.4	27.4	27.9
Hemoglobin blood disorder	1.8	0.1	0.2
Solid organ or blood stem cell transplant recipient	1.5	0.5	0.3
HIV or tuberculosis	1.7	0.5	0.3
Inactive lifestyle, overweight, or obese	25.4	13.3	13.1

IPW inverse propensity weighting

substance abuse (including being a current or former smoker) or a physical or mental disability. After IPW, the weighted survey distribution aligned well with the target population, where absolute standard mean differences were all < 0.1 (Table 1; Supplemental Fig. 1). Of the weighted population, 58.2% were female, 77.1% were White, 33.4% were politically conservative, 37.8% were ≥ 65 years old, 13.9% had a postgraduate degree, and 82.8% had a household income of < \$100,000 per year (Table 2).

Table 2 Demographics and clinical characteristics in the weighted survey population among all respondents, Testers, and Non-testers

Characteristic	Overall survey population $(N=5019)$, %	Testers (N = 1649), %	Non-testers $(N=3370)$, %
Gender			,
Female	58.2	54.1	60.2
Male	41.8	45.9	39.8
Age			
Aged 18–34 years	19.1	21.4	18.0
Aged 35–49 years	17.9	24.0	14.9
Aged 50–64 years	25.2	24.3	25.6
Aged ≥ 65 years	37.8	30.3	41.5
Race			
White	77.1	66.8	82.1
Black or African American	16.0	25.6	11.3
Asian	2.1	2.1	2.1
Other	1.6	1.7	1.6
Two or more races	1.4	1.3	1.4
American Indian or Alaska Native	1.0	1.3	0.8
Native Hawaiian or Pacific Islander	0.4	1.0	0.2
Prefer not to say	0.3	0.2	0.4
Ethnicity			
Non-Hispanic	89.8	86.4	91.5
Hispanic	10.2	13.6	8.5
Politics			
Very liberal	10.0	16.4	6.9
Liberal	10.9	15.1	8.8
Somewhat liberal	7.3	10.1	5.9
Moderate	31.1	34.5	29.4
Somewhat conservative	7.0	4.3	8.3
Conservative	12.8	6.0	16.1
Very conservative	13.6	7.8	16.5
Not political	6.4	5.1	7.0
Prefer not to say	1.0	0.7	1.2

Table 2 continued

Characteristic	Overall survey population $(N=5019)$, %	Testers (N = 1649), %	Non-testers (<i>N</i> = 3370), %
Education			,
No schooling	1.0	1.6	0.7
Some high school (no diploma or GED)	3.1	3.6	2.9
High school diploma or GED	36.1	32.6	37.9
Associate's degree	21.2	23.6	20.0
Bachelor's degree	20.9	20.4	21.2
Master's degree	9.1	11.0	8.2
Professional degree	3.2	4.3	2.6
Doctorate	1.6	1.4	1.7
Other	3.6	1.5	4.7
Prefer not to say	0.1	0.0	0.2
Household income			
< \$10,000	8.4	9.8	7.7
\$10,000-\$14,999	4.8	7.2	3.6
\$15,000-\$24,999	10.8	9.9	11.3
\$25,000-\$34,999	11.8	11.4	12.1
\$35,000-\$49,999	15.3	14.9	15.5
\$50,000-\$74,999	18.4	18.2	18.4
\$75,000-\$99,999	13.3	11.3	14.3
≥ \$100,000	14.8	16.4	14.0
Prefer not to say	2.4	0.9	3.1
Region			
Northeast	20.4	24.5	18.3
Midwest	19.2	14.9	21.3
South	43.5	42.7	43.9
West	16.9	17.9	16.4
Community			
Urban	26.4	34.0	22.6
Suburban	47.8	45.2	49.0
Rural	24.6	20.3	26.6
Other/unsure	1.3	0.5	1.7

GED General Educational Development Test

Respondent Demographics Associated with COVID-19 Testing Hesitancy

Overall, 3370 out of 5019 respondents in the weighted population (67.1%) indicated a low probability of being tested for COVID-19 within the next 6 months and were therefore classified as Non-testers (Supplemental Fig. 2). The likelihood of being a Non-tester was significantly associated with several demographic characteristics (Table 2; Fig. 1). Compared with Testers (those who indicated a high probability of being tested in the next 6 months), Nontesters had a significantly greater representation of respondents who were female (OR [95% CI], 1.3 [1.1–1.4]), aged \geq 65 years (OR [95% CI] compared with ages 18-34 years, 0.6 [0.5-0.7]), White (OR [95% CI] compared with all respondents who indicated a race other than White, 1.4 [1.1-1.8]), of non-Hispanic ethnicity (OR [95% CI] compared with all respondents who indicated Hispanic, Latino, or Spanish origin, 0.6 [0.5-0.7]), and politically conservative (OR [95% CI] compared with respondents who indicated liberal politics, 2.6 [2.3-2.9]). Regional trends were apparent as well, such that respondents in the Northeast region of the United States were significantly more likely to be Testers compared with respondents from the Midwest (OR [95% CI], 1.9 [1.6-2.3]), South (OR [95% CI], 1.4 [1.2–1.6]), or Western regions (OR [95% CI], 1.2 [1.0–1.5]). Non-testers were also underrepresented among respondents from urban areas compared with either suburban (OR [95% CI], 1.6 [1.4-1.9]) or rural communities (OR [95% CI], 2.0 [1.7-2.4]).

Respondents with a postgraduate degree (either Master's, professional, or doctoral degree) comprised a lower percentage of Nontesters versus Testers (12.5 vs. 16.7%; Table 2); this difference was significant when compared with respondents whose highest level of education was a high school diploma or GED, a Bachelor's degree, or other, but was not significant in comparison with those who reported no schooling/some high school or an Associate's degree (Fig. 1). There were no clear associations between likelihood of being a Non-tester

and household income (Table 2; Fig. 1): Non-testers versus Testers had a smaller percentage of respondents earning both the lowest and the highest incomes.

Perceived Level of COVID-19 Knowledge Associated with COVID-19 Testing Hesitancy

Non-testers reported feeling less knowledgeable about COVID-19 compared with Testers (Fig. 2). Significant ORs for differences in percentages of Non-testers who reported themselves as "Not knowledgeable" versus "Proficient" were regarding the topics of conditions associated with high risk of developing severe COVID-19 (OR [95% CI], 1.3 [1.1–1.7]), where to find COVID-19 athome tests (OR [95% CI], 1.7 [1.3–2.1]), and where to find information about getting those tests (OR [95% CI], 1.4 [1.1–1.7]).

Past COVID-19 Experience and Associations with COVID-19 Testing Hesitancy

Compared with Non-testers, Testers were more likely to report previous experiences with COVID-19 testing, diagnosis, vaccination, death of someone they knew, or treatment (Fig. 3). Specifically, Testers included higher percentages of respondents who had been tested for COVID-19 within the past 12 months (OR [95% CII. 4.9 [4.2-5.6]); Fig. 3A), had been diagnosed with COVID-19 at least once (OR [95% CI], 1.2 [1.1–1.3]); Fig. 3B), had been vaccinated against COVID-19 (OR [95% CI], 2.8 [2.3–3.3]); Fig. 3C), had personally known anyone who died from COVID-19 (OR [95% CI], 1.6 [1.5–1.8]); Fig. 3D), or had received any type of treatment for COVID-19, including an inhaler, intravenous injection, or oral medication (OR [95% CI], 1.8 [1.5-2.0]); Fig. 3E).

Feelings and Attitudes About COVID-19 and Associations with COVID-19 Testing Hesitancy

A greater percentage of Testers versus Nontesters reported being "extremely worried" about becoming ill with COVID-19 (18.9 vs. 4.5%; Fig. 4A). Non-testers, by comparison were

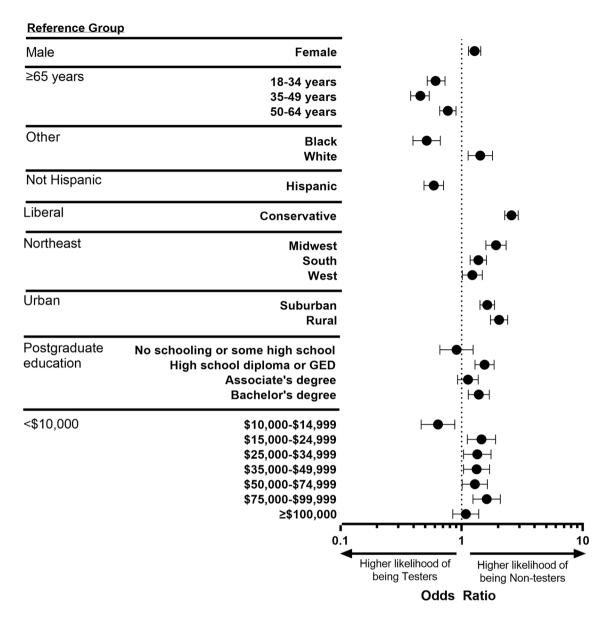


Fig. 1 Likelihood of testing hesitancy across demographic characteristics. *Filled circles* represent odds ratios, and *error bars* represent 95% CIs. Where the reference group is listed as "other" race, it encompasses all respondents who indicated any race other than White (where White is the test group) or Black (where Black is the test group). For the purposes of analysis, those who described their politics as "Very liberal," "Liberal," or "Somewhat liberal"

were grouped into a single "Liberal" category, and those who described their politics as "Very conservative," "Conservative," or "Somewhat conservative" were grouped into a single "Conservative" category. Likewise, those who indicated their highest level of education as "Master's Degree," "Professional Degree," or "Doctorate" were grouped into a single category of all postgraduate degrees. *GED* General Educational Development Test

more likely than Testers to report being "not at all" worried (31.1 vs. 13.1%; OR [95% CI] of "extremely" worried vs "not at all" worried, 9.9 [7.8–12.6]). ORs (95% CIs) of comparisons

between "extremely" worried versus "slightly," "somewhat," and "moderately" worried, respectively, were 6.2 (5.0–7.8), 3.2 (2.5–4.0), and 2.4 (1.9–3.0). Regarding several statements

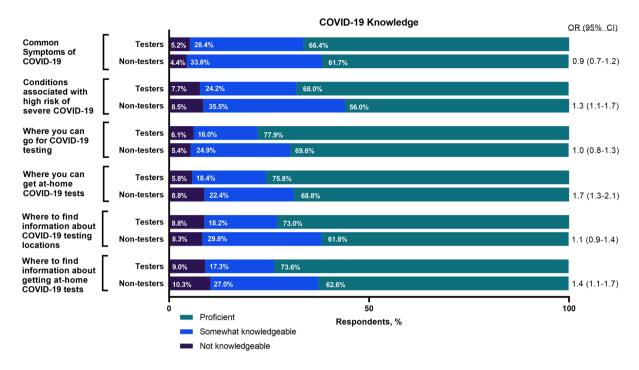


Fig. 2 Associations between COVID-19 testing hesitancy and self-reported knowledge of COVID-19—related topics among survey respondents. Potential responses were "not at all knowledgeable" or "un-knowledgeable" (combined for analysis as a single "Not knowledgeable" category); "somewhat knowledgeable;" or "knowledgeable" or "extremely knowledgeable" (combined for analysis as a single "Profi-

cient" category). ORs shown reflect comparisons between the likelihood of being a Non-tester within the "Not knowledgeable" versus the "Proficient" categories; for example, regarding Conditions associated with a high risk of severe COVID-19, those categorized as "Not knowledgeable" were 1.3 times more likely to be Non-testers compared with those categorized as "Proficient." OR = odds ratio

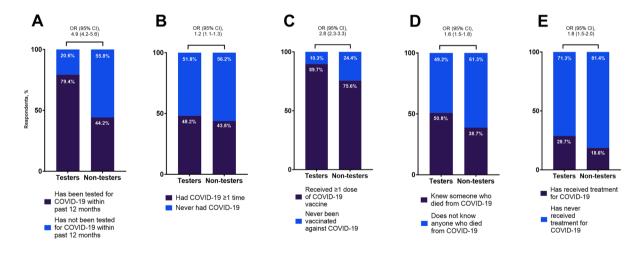
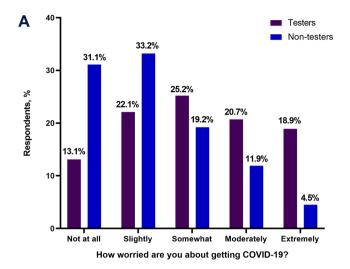


Fig. 3 Associations between COVID-19 testing hesitancy and previous experience with COVID-19 among survey respondents. Respondents were asked whether they A had been tested for SARS-CoV-2 in the past 12 months, B had ever been diagnosed with COVID-19 (for which in the analysis, responses of "not sure" were categorized

along with "never"), C had ever been vaccinated against COVID-19, D had ever known someone who died due to COVID-19 (for which in the analysis, responses of "unsure" were categorized along with "does not know anyone who died from COVID-19"), and E had ever received treatment for COVID-19. OR = odds ratio



BIf I have symptoms of COVID-19, it's important to me to test right away.

If I visited my doctor feeling sick, and my doctor recommended that I test for COVID-19. I would take the test.

I am concerned about public health, and I understand how public health impacts my life.

I have had bad experiences (pain, discomfort) with previous COVID tests.

I can afford to pay for a COVID-19 test.

My peer group (friends and family) regularly test for COVID-19.

I worry about how my peers (friends, family) might react if I tested positive.

I care or worry about potentially spreading COVID-19 to people who are at risk of severe COVID-19 infection if I had symptoms and didn't get tested.

I care or worry about potentially spreading COVID-19 to my friends and family if I had symptoms and didn't get tested.

I believe that I am at risk of severe complications from COVID-19 infection (hospitalization, ventilation, or death).

I believe that COVID-19 has the potential to be a severe disease and is a cause for concern.

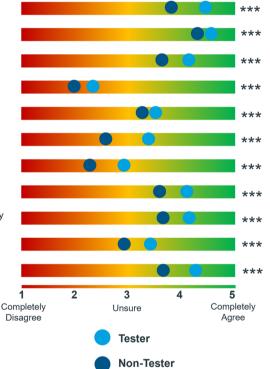


Fig. 4 Associations between COVID-19 testing hesitancy and attitudes regarding COVID-19 among survey respondents. Respondents were asked: A "How worried are you about getting COVID-19?" and B "How much do you agree or disagree with the following statements?" Poten-

tial responses of "completely disagree," "disagree," "unsure," "agree," or "completely agree" were assigned a respective numeric value from 1 to 5 to calculate an average response value for Testers compared with Non-testers, and these values were compared using t tests. ***Denotes P < 0.001

indicating general concern and appreciation for the potential severity of COVID-19, Testers were also more likely than Non-testers to indicate agreement on each particular statement (Fig. 4B). The greatest differences in average level of agreement were regarding the statements "If

I have symptoms of COVID-19, it's important for me to test right away" (P<0.001) and "My peer group (friends and family) regularly test for COVID-19" (P<0.001).

Healthcare System Engagement and Associations with COVID-19 Testing Hesitancy

Testers typically had a greater level of engagement with the healthcare system compared with Non-testers (Fig. 5). Specifically, Testers had more frequent visits to their routine healthcare provider, whereby those who reported healthcare provider visits once per month were significantly more likely to be Testers compared with those who visited their provider 4 times per year (OR [95% CI], 2.8 [2.3–3.4]), twice per year (OR [95% CI], 3.3 [2.7–4.0]), once per year (OR [95% CI], 4.4 [3.6–5.5]), or every 2 years or fewer (OR [95% CI], 5.9 [4.3–8.2]). Among those

who reported having had COVID-19 in the past, those who had spoken with their healthcare provider about their symptoms were significantly more likely to be Testers compared with those who had not (OR [95% CI], 1.4 [1.2–1.6]). Respondents were also more likely to be Testers if they had been hospitalized for COVID-19 within the past year compared with those who were either not hospitalized (OR [95% CI], 5.0 [3.7–6.7]) or were hospitalized for reasons other than COVID-19 (OR [95% CI], 3.2 [2.4–4.4]).

DISCUSSION

Results presented here provide novel insights regarding individual factors associated with COVID-19 testing hesitancy among US adults at high risk of progression to severe disease during the Omicron era. Most respondents (67.2%) indicated a low or uncertain probability of being

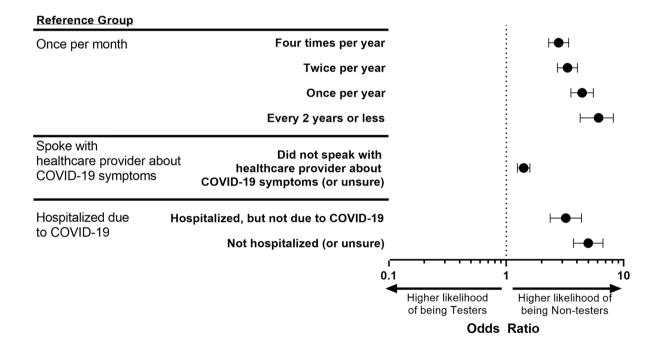


Fig. 5 Likelihood of testing hesitancy associated with different levels of healthcare system engagement. *Filled circles* represent odds ratios, and *error bars* represent 95% CIs. Respondents were asked: "About how often do you visit your provider that routinely provides you with healthcare (for example, your doctor/primary care physician, nurse

practitioner, physician assistant)?", "Did you speak with your doctor or other healthcare provider about your symptoms the last time you had COVID-19?" (only asked to those who indicated that they had COVID-19 in the past), and "Have you been hospitalized within the last 1 year?"

tested for COVID-19 within the next 6 months. Non-testers were more likely than Testers to be women, aged≥65 years, Non-Hispanic, White, from rural communities, and politically conservative. Compared with Testers, they were also less likely to report a high degree of knowledge regarding COVID-19–related topics, to have past experiences related to COVID-19, to report having concern about COVID-19 from a personal and public health perspective, and to have a high level of engagement with the healthcare system.

The high prevalence of COVID-19 testing hesitancy identified among survey respondents is particularly relevant in a landscape where effective treatments are available to reduce the likelihood of hospitalization and death among vulnerable individuals [11, 12]. Treatment can only be made available once SARS-CoV-2 positivity is determined. Even then, further barriers to treatment exist among individuals who test positive. In 2022, the CDC reported that out of all patients identified from a large nationwide database who were eligible to receive nirmatrelvir/ritonavir, only 28.4% had been prescribed the medication within 5 days of diagnosis [25]. This phenomenon of treatment underutilization has been corroborated by data from additional recent reports as well [26, 27]. Treatment for COVID-19 is also prescribed disparately across races and ethnicities, including among those who are high risk of progression to severe disease [28]. In our survey, 45.3% of respondents indicated a past COVID-19 diagnosis but only 21.9% of respondents indicated having received any type of treatment, despite all respondents having a high risk of progression to severe disease. As a caveat, however, it was not determined how many respondents may have been diagnosed before treatments were made available.

Many cultural and societal factors are likely to contribute to the differences in testing hesitancy across demographic groups, and the complex interactions between these factors may transcend typical social determinants of health. For instance, neither income level nor level of educational attainment was clearly associated with testing hesitancy in our survey, nor did we observe a greater likelihood of testing hesitancy among racial and ethnic minorities. We did,

however, observe a greater proportion of Nontesters among those dwelling in rural compared with urban or suburban communities, which supports the need to expand access to testing sites and points of purchase for home testing kits, as has been described previously [29, 30]. Given the importance of equitable testing access and the compounding issue that those with less access to pharmacies are often the individuals at greatest risk of severe COVID-19 [30], government-funded Test-to-Treat programs were developed in 2022 as a rapid means to provide testing, prescriptions, and medications to underserved populations [29]. Although this was productive, many rural communities remain without access [29, 31]. Recent efforts by the National Institutes of Health, the Administration for Strategic Preparedness and Response, and the CDC to deploy home-based Test-to-Treat programs hold significant promise to overcome geographical barriers [32, 33], but testing hesitancy may pose an upstream challenge for broader utilization of these initiatives.

We also observed a greater prevalence of Nontesters versus Testers among female respondents, indicating that testing hesitancy may be more prominent among women compared with men in the United States. This is likely related to various social factors, which may include a consistently identified preference among women for nonpharmaceutical methods of disease prevention and management (e.g., hand-washing) compared with pharmaceutical methods (e.g., vaccination) [16, 34–36].

Notably, our study identified a greater prevalence of Non-testers versus Testers among those who held politically conservative attitudes, as well as among those characterized by demographic characteristics associated with political conservatism in the United States (e.g., being non-Hispanic, White, aged≥50 years, and living in a rural community) [37]. This is consistent with previous studies showing that those who identify as politically conservative have increased rates of vaccine hesitancy, reduced compliance with public health guidelines regarding COVID-19, fewer concerns about the potential severity of COVID-19, and increased tolerance of societal risks [38–40]. Many of these factors were also independently associated with

testing hesitancy in the present study as well as others [10, 16]. These trends may be due in part to the spread of COVID-19 misinformation regarding the pandemic [16, 39], although they are likely to result from an interplay of many factors contributing to testing hesitancy.

Despite clear guidance from the CDC about benefits of treatment with nirmatrelvir/ritonavir for patients at high risk for progression to severe COVID-19 [11], recent reports suggest substantial underutilization of oral antivirals [25–27]. This treatment hesitancy may be emblematic of testing hesitancy. Greater recognition of testing hesitancy among high-risk patients and factors associated with it can allow care providers to address upstream barriers of suboptimal treatment of COVID-19. Considering the combinations of characteristics that were and were not associated with testing hesitancy in our survey, the effectiveness of any interventions designed to improve adherence with testing guidelines may be optimized by tailoring focus and communication styles to specific patient signatures, or groupings of demographics and other characteristics, rather than focusing on a single descriptor. By emphasizing a multifaceted, evidencebased approach tailored toward the appropriate audience, national and community efforts to increase COVID-19 testing can potentially be less costly and have greater overall efficiency.

Effective strategies to reduce testing hesitancy can be implemented at the level of healthcare providers, policy makers, and local community messaging. Healthcare providers can play a pivotal role in educating patients on the value of testing for COVID-19, especially during the influenza season given the potential for co-infection [41–43] and the importance of differentiating between the two infections to ensure appropriate clinical intervention. Based on the findings of our survey that testing hesitancy was associated with lower healthcare system engagement, it is imperative that providers optimize the limited time they may have with their patients to ensure adequate understanding of COVID-19 symptoms, testing options, and available treatments. Additionally, our findings suggest the need to develop targeted, culturally sensitive tactics to effectively address testing hesitancy across communities. These strategies may include tailored education aligned with conservative values, influential community messengers, messages emphasizing societal as well as personal benefits, rigorous misinformation mitigation, and ongoing data-driven assessments. Expanding the existing programs to deploy localized vaccination clinics, particularly in rural areas [29], should also be a priority.

Strengths of our study included a diverse survey population, as well as the IPW methodology used to improve generalizability of the survey population to the target population of US adults with risk factors for progression to severe COVID-19 based on a large, representative data set. Although the survey population was not a perfect representation of the target population (likely due to biased sampling selection, nonresponse bias, or sampling error), characteristics were well matched after IPW.

Our study also had some important limitations. First, all questions, potential responses, and statements included in the survey were selected by the authors rather than solicited through focus groups, which may have introduced investigator bias about which factors and considerations are the most important. In particular, cognitive bias may have been introduced based upon whether questions were framed positively or negatively regarding attitudes toward COVID-19 or COVID-19 testing (framing effect, whereby respondents may be influenced by how information is presented rather than by what they are being asked [44]). Second, knowledge was assessed only by selfreport; no objective measure was used to test understanding of each topic. Third, the survey population may have been impacted by survey responder bias, whereby certain demographics or other characteristics may have been associated with likelihood of accepting or declining the invitation to participate. Differences in survey response behavior across demographic groups have been identified previously, including a higher likelihood of online survey participation among women compared with men [45]. Because the survey was only available online, this also biased the sample to exclude anyone who did not have access to the internet or have the required technological skills. Some clear differences between the survey population and

the target population (from IQVIA claims data) were identified, such as much greater representation of certain comorbidities (e.g., current or former smoking and/or substance abuse) among respondents; these differences may have been the result of broadly worded questions regarding comorbidities as reflected in the CDC descriptions of high-risk conditions [9], compared with the comorbidity data from the IQVIA database, which are aggregated through medical claims rather than self-report. However, IPW was used to minimize any such differences as much as possible. Finally, respondents were grouped into categories of Testers and Non-testers based solely on their reported likelihood of testing within 6 months, regardless of the potential rationale for their response. This may have resulted in an overestimation of Non-testers, and it is not clear which respondents may have been willing or unwilling to test for COVID-19 under the CDC-recommended circumstances of either experiencing symptoms or having a known exposure to a SARS-CoV-2-positive individual. To address this limitation, a follow-up manuscript is planned that will describe the circumstances under which respondents would or would not choose to get tested for COVID-19.

CONCLUSIONS

Among US adults at high risk of progression to severe COVID-19, testing hesitancy was associated with being female, aged≥65 years, non-Hispanic, White, rural, and politically conservative. Higher rates of testing hesitancy were also associated with less knowledge, experience, and concern regarding COVID-19, as well as less engagement with the healthcare system. Understanding these factors can be used to promote adherence to testing guidelines by enabling healthcare providers and policy-makers to develop evidence-based communication strategies and access expansions that are tailored to the individuals with the greatest need.

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Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflicts of Interest. Annlouise R. Assaf, Gurinder Sidhu, Joseph C. Cappelleri, Florin Draica, Iqra Arham, Mehnaz Bader, Camille Jimenez, Michael Bois, and Stephen Watt are employees of Pfizer and may hold stock or stock options. Apurv Soni and Carly Herbert have no conflicts of interest to declare. Eliza Silvester, Jessica Meservey, Valerie Eng, Megan Nelson, Yong Cai, Aakansha Nangarlia, Zhiyi Tian, and Yanping Liu are employees of IQVIA, which received funding from Pfizer to perform analyses for the study.

Ethical Approval. The protocol was reviewed and approved for exemption by the local Institutional Review Board under Title 45 CFR Sect. 46.104(d)(2). All subjects provided informed consent to participate in the study.

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