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"To Be Vaccinated or Not to Be Vaccinated": Factors Influencing COVID-19 Vaccine Hesitancy and Future Vaccination Willingness Amongst US Women of Reproductive Age

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Background & Objectives: Growing data on the impact of herd immunity and susceptibility of unvaccinated persons to chronic COVID sequelae requires deeper understanding of vaccine stigma and hesitancy to facilitate population needs. Reproductive-aged women (18–45 years) were at a "vaccine paradox" during COVID-19 – hesitant to receive the vaccine, yet at increased risk for COVID infection. In this study, we sought to: identify demographic predictors, reasons, geographic location of vaccine hesitancy, and COVID-specific attributes that predict future vaccination willingness. We hypothesized that high COVID risk perception and high COVID stress would be predictors of willingness.

Methods: Study Design: Cross-sectional survey of women across the United States. Main Outcomes and Measures: Vaccine hesitancy was defined as responding "No/Not Sure" to the question "Have you received any of the COVID-19 vaccines?" The COVID-Risk scale evaluate perceived COVID Risk, and the COVID-19 Perceived Stress Scale (PSS-10-C) evaluated COVID stress. Open ended questions inquired about participants' vaccine concerns.

Results: Of the 1,037 women who accessed the survey, 948 (91%) consented and completed. Predictors of vaccine hesitancy included younger aged parents (p=0.005), non-white race (p=0.003), and having high school or lower educational attainment (p<0.0001). Using smoking as a proxy measure of "health behavior", we found long-term smokers or quitters were more hesitant than those who never smoked (p=0.03). Geographic analyses showed the most vaccine hesitant women resided in Southeast and Midwest US. Hesitancy reasons included side effects (21%) and fertility/pregnancy concerns (4%). High COVID risk perception (p=0.0004) and high COVID stress (p=0.01) significantly predicted future willingness to get vaccinated.

Conclusions and Relevance: This research provides insights for managing the "vaccine paradox" in reproductive age women, and identifying factors that influence COVID-19 vaccine hesitancy and future vaccination willingness. Public health and policy advocates could target messaging around COVID risk and stress in Southeastern and Midwestern regions; as well as address women's concerns around fertility and other side effects.

Plain Language Summary:

What do we already know about this topic?: During the COVID-19 pandemic, the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) deemed women of reproductive age amongst "populations of high priority" for vaccination. However, these women were at a "vaccine paradox"- they were hesitant to receive the COVID vaccine, while concurrently at increased risk for severe COVID infections.

What did our group do?: We surveyed a geographically representative sample of women across the United States to understand who the unvaccinated were, where they were geographically located, why they were vaccine hesitant, and what COVID-specific attributes predicted current, and future willingness to get vaccinated.

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What we found: Age, parenting status, race, education, and geography were predictors of vaccine hesitancy. Women's vaccination decisions were also influenced by their household responsibilities, which increased during the pandemic. Future willingness to get vaccinated was higher if they had high COVID risk perception and high COVID stress.

Implications of our findings: This research provides insights for promoting access, acceptance, and uptake of recommended vaccines amongst women of reproductive age to manage future pandemics. Our findings are even more paramount as reports show, that even though the pandemic has stabilized, COVID vaccination rates for women are lagging, compared to men's.

Keywords: women's health, covid, vaccine hesitancy, covid stress, covid risk

Introduction

On March 11, 2020, the World Health Organization classified COVID-19 as a global pandemic.[1] At the time, there were 118,000 reported COVID cases across 114 countries. Thirteen months later, over 141 million cases of COVID-19 had been reported globally, with more than 3 million COVID-related deaths; 579,000 of those deaths recorded in the United States (US) alone.[1] Vaccinating a large percentage of the population against COVID has been a crucial part of the US strategy to curb the pandemic. On December 15th, 2020, the first American, a (Black) woman, received the Pfizer COVID vaccine.[2] As of May 2023, more than 670 million doses had been administered and 70% of the eligible US population had been fully vaccinated.[3,4] As the data continues to grow on the impact of herd immunity,[4–6] mutating COVID strains,[7–10] long COVID, and increased susceptibility of unvaccinated persons to chronic COVID sequelae,[11–14] it has become more and more imperative that public health officials understand the stigmas surrounding vaccination and the reasons for vaccine hesitancy to better manage the public's health in the event of another global pandemic.

The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) has deemed women of reproductive age amongst "populations of high priority" for vaccination,[15] noting that increased vaccine hesitancy could render these women in a "vaccine paradox"- hesitant to receive the COVID vaccine, while concurrently at increased risk for severe COVID infections.[16] A 2023 study evaluating sex differences in COVID-19 symptom severity and trajectories among US ambulatory adults[17] found that among females and males with COVID-19 infections, females reported more severe total and systemic symptoms during their illness period compared with males. Another study conducted at the height of the pandemic comparing COVID-related outcomes in pregnant and non-pregnant women of reproductive age (15–45 years)[18] found, that despite similar odds of intubation, pregnant women with COVID infections had higher odds of mortality (odds ratio (OR), 1.84; 95% CI, 1.26–2.69), pneumonia (OR, 1.86; 95% CI, 1.60–2.16) and ICU admissions (OR, 1.86; 95% CI, 1.41–2.45) than non-pregnant women. In evaluating vaccination willingness amongst this vulnerable population, Townsel et al[19] found that reproductive aged women who were pregnant or trying to conceive (TTC) had high rates of declining or delaying COVID-19 vaccinations compared to other women of reproductive age. Compared to other women of reproductive age, pregnant participants were six times more likely to delay COVID-19 vaccination and twice as likely to decline vaccination; and those who were TTC had nearly three times the odds of delaying and declining the vaccine.

Women in general tend to have lower vaccination intention than men, with men being 41% more likely to report intention to receive a vaccine (rather than being unwilling/undecided) compared to women.[20] In the context of COVID-19 however, it is crucial that we understand the strategies that promote access, acceptance, and uptake of recommended vaccines for reproductive aged women in order to minimize their risks of mortality and morbidities due to COVID-19 infections. We must to optimize the protection, health, and well-being of this vulnerable population.

In this study, we surveyed a geographically representative sample of women across the US at the height of the pandemic to understand *who* the unvaccinated are, *where* they were geographically located, *why* they were vaccine hesitant, and *what* COVID-specific attributes predicted their current vaccination status as well as future willingness to get vaccinated. We focused on women of reproductive age because of the increased risk of blood clots,[21,22] concerns related to pregnancy,[23] and fear of hormonally-driven vaccine side-effects[24,25] that may have dissuaded more women than men from getting vaccinated; particularly as more post-vaccination data emerges.

We hypothesized the following:
Who is vaccine hesitant and unvaccinated?:

- Age, Relationship status, parity status: Younger, single, nulliparous individuals will be more vaccine hesitant (vs older, married, has at least 1 child).
- Race/Ethnicity: Non-White race and Hispanic ethnicity will be more vaccine hesitant (vs White race, non-Hispanic ethnicity).
- Educational Attainment: High school educated or less will be more vaccine hesitant (vs those with greater than high school education).
- Using Smoking status as a proxy measure of "Health behavior": Smokers will be more vaccine hesitant (vs those who have never smoked).

Where should the geographic focus be?

- States in the Southern region will be more vaccine hesitant (vs Northern states).[26–28]
- What COVID-specific attributes predict current vaccination, and can be used to inform future vaccination?
- COVID Risk Perception: High COVID risk perception will predict (i)current vaccination and (ii)willingness to get vaccinated
- COVID Stress: High COVID stress will predict (i) current vaccination and (ii) willingness to get vaccinated.

Why are women vaccine hesitant?

- A variety of reasons provided with open-ended prompts.

Methods

Study Design & Participants

This was a cross-sectional study that recruited adult women between the ages of 18–45, using Dynata, a survey sampling company that maintains a web panel of survey takers across the United States.[29–31] Our recruitment plan involved the use of soft quotas (defined as an absolute minimum that researchers expect to be exceeded[32]) to ensure that the geographic, racial, and ethnic diversity of our study sample reflected US census data. We used REDCap (Research Electronic Data Capture, Vanderbilt University) for data collection, and because we focused on adult women of reproductive age, we excluded women over the age of 45 due to the increased likelihood of hormonal irregularities associated with the menopausal transition.[33–35] The inclusion criteria were: i) self-identifies as a woman ii) self-reported age between 18–45 years iii) resides in a US state/territory. Participants who did not fit any of the 3 inclusion criteria (male, <18 or >45 years old, does not live in a US state/territory) were excluded. Survey finishers received participation rewards per Dynata's incentive system.[29–31] The survey launched on May 4, 2021, and ended on May 7, 2021.

Sample Size Determination

Based on a vaccine hesitancy prevalence of 20% at study launch,[3,27,36,37] an alpha of 0.05 and 80% power, a sample size of 588 was needed. We over-estimated the calculation by 50% to ensure adequate geographic reach across the country.

Survey Instruments

Demographic Predictors of Vaccine Hesitancy

For demographic predictors of vaccine hesitancy, participants reported their age, race, ethnicity, educational attainment, marital status, number of living children (under 18), smoking status, and US State of residence.

Main Outcomes: Vaccine Hesitancy and Willingness

Vaccine hesitancy was defined as a "No/Not Sure" response to the question "Have you received any of the COVID-19 vaccines?"

We also asked questions related to participants': willingness to get vaccinated (if unvaccinated), ("Will you receive the COVID-19 vaccine if it is made available to you?") and open-ended reasons for refusing vaccination ("What are your reasons for not wanting/being unsure of the COVID vaccine?").

COVID-Related Predictors of Vaccine Hesitancy

Perceived COVID Risk

Using the *Perceived COVID Risk scale*,[38] participants were asked "How would you describe your risk of getting infected with COVID-19?" with responses ranging from "1-low risk" to "5-high risk".[38] We defined High Perceived COVID Risk as scores of 4 or 5. Scores <4 were grouped as Low Perceived COVID Risk.

COVID Stress

The COVID-19 Perceived Stress Scale (PSS-10-c)[39] evaluated participants' COVID-related stress. The PSS-10-c has 10 items, ranked on a 5-point Likert scale of "0-never" to "4-Always". Scores range from 0–40, with higher scores indicating greater stress. We defined Low COVID stress as scores <25 and High COVID stress as scores ≥25 as recommended.[39]

Survey questions were reviewed for relevance and context by the research team (MAO, Reproductive Epidemiologist, and SH, ObGyn). In its entirety, the survey was pre-tested with a sub-sample of women within the target population for face and content validity and deemed appropriate. Informed consent was obtained from all research participants. The study was approved by the University of Rochester Institutional Review Board (STUDY00005980) and complies with the Declaration of Helsinki.

Geographic Distribution

- We grouped states into 5 geographic regions using the following criteria, as shown in Table 1:[40]
- Northeast: Maine, Massachusetts, Rhode Island, Connecticut, New Hampshire, Vermont, New York, Pennsylvania, New Jersey, Delaware, Maryland, Washington DC.
- Southeast: West Virginia, Virginia, Kentucky, Tennessee, North Carolina, South Carolina, Georgia, Alabama, Mississippi, Arkansas, Louisiana, Florida
- Midwest: Ohio, Indiana, Michigan, Illinois, Missouri, Wisconsin, Minnesota, Iowa, Kansas, Nebraska, South Dakota, North Dakota.
- Southwest: Texas, Oklahoma, New Mexico, Arizona
- West: Colorado, Wyoming, Montana, Idaho, Washington, Oregon, Utah, Nevada, California, Alaska, Hawaii

Analyses

We used descriptive statistics (proportions, means, standard deviations, ranges, etc.) to describe participants by current vaccination status (Vaccine hesitancy = "No/Not Sure" response to the question "Have you received any of the COVID-19 vaccines?" Vaccinated = a "Yes" response). Chi-square and *t*-tests were used to compare survey responses in bivariate analyses and to empirically identify potentially important covariates. We used logistic regression models to estimate crude and adjusted effect sizes. All analyses used the standard two-sided $p<0.05$ cut-off to determine statistical significance. Analyses were completed using Stata software.

We used thematic coding to group participants' open-ended responses to the question "What are your reasons for not wanting/being unsure of the COVID vaccine?" SH reviewed and grouped participants' responses into relevant themes. MAO reviewed categorizations done by SH. Discrepancies were discussed and resolved by both authors.

Table 1 Basic Demographics of Study Participants

	Study Sample*	Census Data[40–43]
Age (n=899)		
Mean, SD	32.6 (± 7.1) Range 18–45	n/a
Children <18 (n=835)		
Mean, SD	1.1 (± 1.3) Range 1–11	n/a
Race (n=896)		
White (n,%)	680 (75.9%)	76.3%
Black/African American (n,%)	76 (8.5%)	13.4%
Asian n,%	86 (9.6%)	5.9%
American Indian/Alaska Native (n,%)	17 (1.9%)	1.3%
Native Hawaiian (n,%)	2 (0.2%)	0.2%
Other (n,%)	35 (3.9%)	2.8%
Ethnicity (n=883)		
Hispanic (n,%)	122 (13.8%)	18.5%
Non-Hispanic (n,%)	761 (86.2%)	60.1%
Educational attainment (n=897)		
High School or less (n,%)	310 (34.6%)	38%
Technical Training/Associates/Bachelor's	373 (41.6%)	50%
Master's Degree or Higher	214 (23.9%)	13%
Relationship status (n=896)		
Single/in a relationship but not married	435 (48.6%)	30.7%
Married	421 (47.0%)	46.3%
Divorced/Separated/Other	40 (4.5%)	23%
Regional Distribution (n=823)**		
Northeast (%)	13.0%	19.2%
Southeast (%)	19.9%	25.6%
Midwest (%)	14.8%	20.6%
Southwest (%)	19.3%	12.8%
West (%)	32.9%	20.8%

Notes: *Age-restricted sample; caution should be taken when comparing to broader US Census sample. Differences observed between the study sample and the larger Census data are likely due to the age-restricted nature of the study's inclusion criteria and objectives. ** Northeast: Maine, Massachusetts, Rhode Island, Connecticut, New Hampshire, Vermont, New York, Pennsylvania, New Jersey, Delaware, Maryland, Washington DC. Southeast: West Virginia, Virginia, Kentucky, Tennessee, North Carolina, South Carolina, Georgia, Alabama, Mississippi, Arkansas, Louisiana, Florida. Midwest: Ohio, Indiana, Michigan, Illinois, Missouri, Wisconsin, Minnesota, Iowa, Kansas, Nebraska, South Dakota, North Dakota. Southwest: Texas, Oklahoma, New Mexico, Arizona. West: Colorado, Wyoming, Montana, Idaho, Washington, Oregon, Utah, Nevada, California, Alaska, Hawaii.

Results

A sample size of 1,037 women met the inclusion criteria and consented to participate in the study. Over 90% (n=948) completed all survey questions. The overall rate of missing data was 5.4%; which is well below the statistical cutoff of 10%.[44] The remaining 89 respondents (9%) were deemed "incompletes" (ie suspended the survey midway, never made it to the final landing page) and excluded from the analyses. We show final sample sizes for all analyses in the Tables and Figures.

As shown in Table 1, our soft quotas resulted in a diversity of respondents across racial and ethnic groups; and adequate representation of every US state and region. Similar to Census data, Whites were the majority, and non-whites comprised about a quarter of the study sample. We had an over-representation of Asian Americans and American Indians/Alaska Natives which is not surprising, given that the West and Southwestern regions of the country were over-represented in the final study sample. Mean age of study participants was 32.6 years (± 7.1 SD). Women averaged 1.1 (± 1.3 SD) children. Study participants were highly educated compared to Census data, with about a quarter having

Table 2 Predictors of Vaccine Hesitancy Amongst US Women of Reproductive Age

	Odds of Vaccine Hesitancy (vs Vaccinated)	**p value**
Who is vaccine hesitant?		
Age (n=884)	0.97 (95% CI: 0.955, 0.99)	0.005
Marital Status (n=882)		
In a relationship not married (vs single) Married (vs single) Divorced/Separated/Widowed (vs single)	1.70 (95% CI: 1.14, 2.52) 0.70 (95% CI: 0.51, 0.96) 0.97 (95% CI: 0.49, 1.91)	<0.0001
Children <18 (n=822)		
≥1 child (vs no children)	1.53 (95% CI: 1.16, 2.02)	0.003
Race (n=881)		
Black (vs White) Other (vs White)	2.37 (95% CI: 1.41, 3.98) 1.01 (95% CI: 0.70, 1.46)	0.003
Ethnicity (n=868)		
Hispanic (vs non-Hispanic)	2.13 (95% CI: 1.42, 3.22)	0.0002
Educational Attainment (n=883)		
≤ High School (vs Technical/Associates/Bachelors) Masters/Advanced Degree (vs Technical/Associates/Bachelors)	2.28 (95% CI: 1.65, 3.14) 0.33 (95% CI: 0.23, 0.48)	p<0.0001
Smoking (n=882)		
Long term smoker: smoke now and before the pandemic (vs never smoked) Recent smoker: smoke now but not before the pandemic (vs never smoked) Quitter: does not smoke now, but smoked before the pandemic (vs never smoked)	1.48 (95% CI: 1.10, 2.00) 0.80 (95% CI: 0.48, 1.34) 1.22 (95% CI: 0.77, 1.94)	0.03
Where do they reside? (n=*812*)		
Northeast (vs West) Southeast (vs West) Midwest (vs West) Southwest (vs West)	0.76 (95% CI: 0.48, 1.19) 1.73 (95% CI: 1.16, 2.57) 1.34 (95% CI: 0.86, 20.7) 0.79 (95% CI: 0.53, 1.17)	p=0.0015

Notes: Vaccine Hesitant (n=468) Selected a "No/Not Sure" response to the question *"Have you received any of the COVID-19 vaccines?* Vaccinated (n=417) Selected a "Yes" response to the question *"Have you received any of the COVID-19 vaccines?*

a Master's degree or higher. Less than 5% of study participants had been divorced/separated, compared to 23% of the US population.

Of the 948 completes, 885 (93%) answered the question "Have you received any of the COVID-19 vaccines?" Over half (53%) indicated a "No/Not Sure" response and were categorized as vaccine hesitant (n=468 (449 No's and 19 Not sure's)). The remaining 47% (n=417) selected a "Yes" response and were categorized as vaccinated (Table 2). Predictors of vaccine hesitancy are delineated in Table 2 and included younger age (p=0.005), never married but in a relationship (p<0.0001), and having no children (p=0.003). Non-white race (p=0.003), Hispanic ethnicity (p=0.0002), and having high school or lower educational attainment (p<0.0001) were also associated with vaccine hesitancy. Long-term smokers or quitters were more vaccine hesitant than those who never smoked (p=0.03). Geographic analyses showed the most vaccine hesitant women resided in the Southeastern and Midwestern US.

The reasons why women were hesitant about vaccination (Table 3) included: concern with the scientific process to vaccine production (short timeline to creation, limited data on efficacy, side effects and long-term impact), non-scientific

Table 3 Reasons for Vaccine Hesitancy (n=302) (Responses are Not Mutually Exclusive)

Reasons	N,%	Representative Examples of Qualitative Responses
Limited scientific information including efficacy and the fact that it's new	n=87 (29%)	"Question the effectiveness" "They brought out the vaccine to quickly, its not FDA approved"
Safety concerns, including sick from the vaccine or dying	n=63 (21%)	"There have been several deaths and blood clotting complications as well as people who later became infected". "I am paranoid about it actually working. What is the point of getting vaccinated if I still can catch it and have to wear a mask?"
Concern for side effects, including long term	n=63 (21%)	"I've heard side effects are harsh for women" "Waiting to see side effects and effectiveness"
Trust/Scared	n=49 (16%)	"I do not trust the vaccine" "There are too many problems that can arise from taking it. I am also really scared"
Fake/government conspiracy/chip/unclear ingredients/pharma/unnecessary	n=39 (13%)	"I do not support it because I think it's all a big scam and whoever has created the COVID virus is a sick individual and needs to be put in jail for killing a bunch of people" "I don't want to risk the vaccine messing with my DNA"
Do not want it/do not believe/do not get vaccines	n=32 (11%)	"I am just not sure I want it" "Personal beliefs"
Concern for pre-existing conditions, drug interaction, allergies	n=16 (5%)	"I have many medical issues I am worried about side effects of the vaccine with my other issues" "I have cancer, I'm afraid of getting COVID when I get the shot. And if I get COVID having cancer possibility of death is much higher. So it's a hard choice I'm very, very up in the air no idea if I should get it or not!"
Fertility, pregnancy concerns	n=11 (4%)	"I do not know the side effects and if it will prevent me from having kids" "It's too soon, we are trying to get pregnant" "Fertility concerns long term"
Busy/Life barriers	n=10 (3%)	"…I'm the primary caregiver for my kids since my husband [travels during the week] and if I have a bad reaction to the vaccine I'm worried about how I'd take care of my kids"
Other/unsure/do not know	n=37 (12%)	"Not sure, haven't decided" "not now" "I don't know"

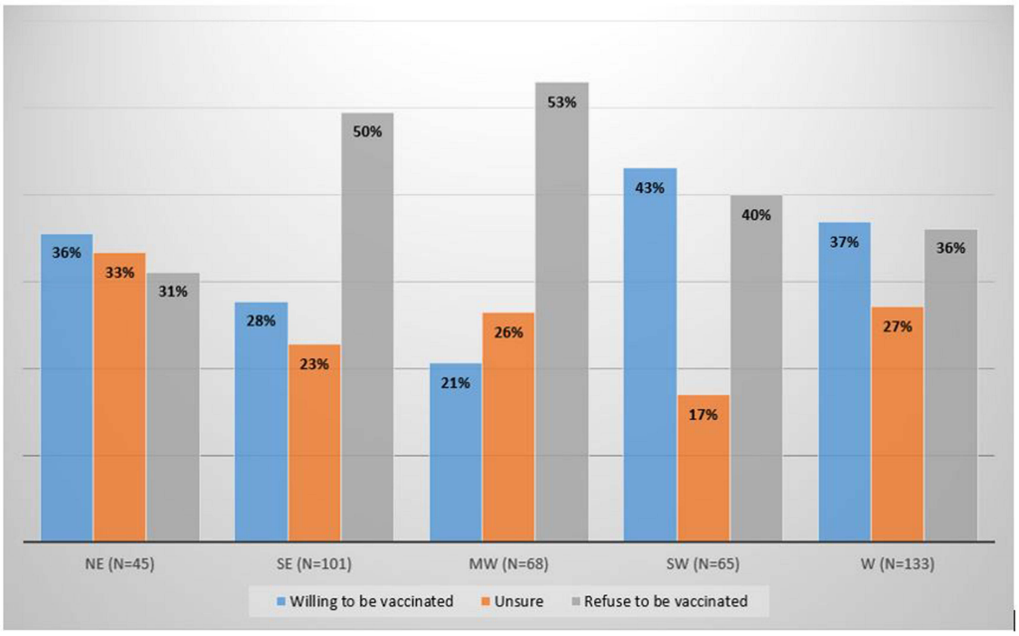
Notes: Vaccine Hesitant (n=468) Selected a "No/Not Sure" response to the question *"Have you received any of the COVID-19 vaccines?*

Table 4 What COVID-Specific Attributes Predict Current and Future Vaccination?

	Crude	Adjusted*
Perceived COVID risk and odds of being **currently vaccinated (n=884)**		
High COVID risk- perception (vs low COVID risk-perception)**	1.50 (95% 1.11, 2.02; p=0.008)	1.57 (95% CI: 1.51, 2.14; p<0.00001)
COVID stress and odds of being **currently vaccinated (n=835)**		
High COVID stress (vs low COVID stress)***	1.34 (95% CI: 0.87, 2.06; p=0.20)	n/a
Perceived COVID risk and willingness to get **vaccinated in the future (amongst those who are vaccine hesitant, n=455)**		
High COVID risk- perception (vs low COVID risk-perception)**	1.61 (95% CI: 1.03, 2.51; p=0.04)	1.65 (95% CI: 1.03, 2.62; p=0.0004)
COVID stress and willingness to get **vaccinated in the future (amongst those who are vaccine hesitant, n=427)**		
High COVID stress (vs low COVID stress)***	2.47 (95% CI: 1.31, 4.67; p=0.005)	2.40 (95% CI: 1.20, 4.60; p=0.01)
Does COVID risk** predict COVID Stress***? (n=837)		
High COVID risk- perception (vs low COVID risk-perception)	2.30 (95% CI: 1.47, 3.60; p<0.001)	2.30 (95% CI: 1.40; 3.60; p<0.001)

Notes: *Adjusted for age, race, ethnicity (most parsimonious model). **using Perceived COVID Risk Scale. High Perceived COVID Risk =scores ≥ 4; Low Perceived COVID Risk= scores <4.[38] ***using the COVID-19 Perceived Stress Scale (PSS-10-c). High COVID stress as scores ≥25; Low COVID stress= scores <25.[39]

motivations behind vaccine production (financial gains of the government and big pharma), and the unknown impact of the vaccine on women, particularly regarding fertility and pregnancy outcomes. Over a third of women demonstrated apathy, reporting no reason for their hesitancy.[45]



Northeast (NE): Maine, Massachusetts, Rhode Island, Connecticut, New Hampshire, Vermont, New York, Pennsylvania, New Jersey, Delaware, Maryland, Washington DC

Southeast (SE): West Virginia, Virginia, Kentucky, Tennessee, North Carolina, South Carolina, Georgia, Alabama, Mississippi, Arkansas, Louisiana, Florida

Midwest (MW): Ohio, Indiana, Michigan, Illinois, Missouri, Wisconsin, Minnesota, Iowa, Kansas, Nebraska, South Dakota, North Dakota

Southwest (SW): Texas, Oklahoma, New Mexico, Arizona

West (W): Colorado, Wyoming, Montana, Idaho, Washington, Oregon, Utah, Nevada, California, Alaska, Hawaii

Figure 1 Regional variations in willingness to get the COVID vaccine (amongst those who are vaccine hesitant) (n=412) p=0.0015.

In evaluating the question of w*hat* COVID-specific attributes predict current vaccination and can be used to inform future vaccination willingness, we found that whereas COVID risk predicted current vaccination, COVID risk and COVID stress predicted future willingness to get vaccinated. Women who deemed their COVID risk to be high were 65% more willing to be vaccinated in the future (p=0.0004). Those with high COVID stress were 140% more willing (p=0.01) (Table 4). Regional variations in willingness to get the COVID vaccine showed women in the Southeast and Midwest would be most challenging to convince (Figure 1).

Discussion

Even before COVID vaccines were available, reports showed varying degrees of vaccine (dis)interest in subgroups of the US population.[45] However, the high transmissibility and mutative nature of the COVID-19 virus underscored the importance of achieving rapid, wide-spread vaccine uptake. As of July 6, 2021 (following our data collection) the virulent Delta variant was rapidly becoming the dominant COVID-19 strain globally.[7,9] By December 2021, the Omicron variant was causing case fatality rates to skyrocket into the millions, and by July 2022, 6 months later, a number of COVID-19 variants and subvariants had been identified; with vaccine development lagging behind.[5,46] US states with below-average vaccination rates had almost triple the number of new COVID cases.[27,28,46,47] The unvaccinated were the more severe COVID cases and comprised nearly all COVID deaths.[27] This study is one of a few that, to our knowledge, has focused on US women of reproductive age to understand what factors contributed to their vaccine hesitancy at such a time of urgency. Studying this subgroup was particularly relevant, given the gender gaps in COVID-19 vaccination attitudes-then, and now;[48,49] even in high-risk clinical populations.[50] The role of the government in vaccinating cannot be understated. In a multinational study evaluating trust in government, intention to vaccinate and COVID-19 vaccine hesitancy in the United States, United Kingdom, and Australia,[51] the authors found that in Australia, participants with high confidence in their current government had greater willingness to receive the vaccine, while in the United States, participants with high confidence in their current government were *less likely* to be willing to receive the COVID-19 vaccine. The researchers stated that this was unsurprising, as public health measures such as vaccines and masking have become politicized in the States. Although it is in the best interest of the US government to protect Americans by better understanding vaccine hesitancy among different populations and developing appropriate interventions to improve uptake, such public health efforts must be de-politicized. Policymakers and healthcare professionals can use comments from our study participants regarding the vaccine being "more harsh for women" and its impact on fertility, which are not fact-based "… it will prevent me from having kids" to debunk misinformation for women of reproductive age. Transparency and education about the vaccine development and approval process could also improve uptake and address comments such as "I don't want to risk the vaccine messing with my DNA" and "They brought out the vaccine to quickly, its not FDA approved".

Who is vaccine hesitant and why are they hesitant?: The 47% vaccination rate in our study sample was similar to the 45% US population-level vaccination rate at the time of the study;[3] meaning that over half of the surveyed women were vaccine hesitant and un vaccinated. As we hypothesized, vaccine hesitancy was associated with younger age,[12,13,49,50,52] non-white race and Hispanic ethnicity,[52,53] and lower educational attainment, consistent with several other reports.[38,48–50] Contrary to our hypothesis, women who were parents were more hesitant than nulliparous women, a finding that aligned with that of Simonson et al[48] from the COVID States Project, which surveyed over 20,000 individuals across the US in the Spring of 2021 found a similar pattern of their findings that vaccine hesitancy was more prevalent in women who were parents compared to nulliparous women was primarily driven by younger mothers. The authors report that these women were not only reluctant to receive the vaccine themselves but were also hesitant to have their young children vaccinated. Prior studies that have examined women's hesitancy to receive the influenza vaccine, TDaP and others recommended for women of reproductive age show that misinformation about vaccine safety and efficacy, perceived maternal-infant risk, and beliefs of increased susceptibility to other illnesses due to vaccination are the main drivers of the women's hesitancy.[49,50] Another plausible explanation relates to the shifting division of labor within the household[54,55] as the pandemic gave rise to new disruptions in the day-to-day life. Many mothers had to take on additional responsibilities during the pandemic, including household chores, management of household finances, management of child(ren)'s schedules, and direct supervision/involvement in child(ren)'s daily learning and recreational

activities. Therefore, volunteering to be vaccinated with a vaccine with unknown efficacy, falling ill anyway, and not being able to fulfill their "maternal" responsibilities may have seemed irresponsible. In the words of a participant, "[what] if I have a bad reaction to the vaccine? I'm worried about how I'd take care of my kids". Vaccine hesitancy is a mindful emotional/cognitive response to assessing risks and benefits of vaccination.[45,50] For women, the decision-making process for the COVID vaccine may have been more complex than a simple inoculation. For this participant in particular, the decision "To vaccinate or not to vaccinate" is weighed in the context of i) her role as primary caregiver (gender norm), ii) lack of child care resources due to structural/economic barriers, and iii) the possibility of a "bad reaction" to the vaccine (a healthcare consequence which the respondent has apprehension about, potentially due to reports of adverse reactions in women and/or the vaccine's impact on women).[21,25,49]

Public health officials must acknowledge the complexities inherent in women's health decision-making as "traditional" gender norms re-emerged during the pandemic, creating disparate gender roles for men and women with regard to care-giving and domestication.[54,55] Study participants' reasons for refusing the COVID vaccine ranged from mistrust of the scientific process, to reproductive concerns, time constraints, and normed "wife/ mother/ caretaker" barriers. Models like the Elaboration Likelihood Model (ELM),[45] which explore routes to persuasion, could be used by researchers, policy makers, and healthcare providers to better understand women's vaccine (and other healthcare) decision-making processes, for themselves and their families. With concerns over how the vaccine will affect fertility and pregnancy, understanding pregnant women's vaccine decision-making process is important. Pregnant women are at increased risk for severe illness, death, and possibly adverse pregnancy outcomes due to COVID infection.[56,57] Increasing vaccination in this demographic group will help to decrease deaths and hospitalizations amongst pregnant women. Ninety-nine percent of babies born to mothers who received two doses of an mRNA vaccine during pregnancy had COVID antibodies at birth.[58,59] Since the COVID vaccine is not currently approved for those under 12 years of age, maternal vaccination may be the only way for infants to receive protection from COVID. ELM has also been proposed to address vaccine apathy,[45] which was prevalent in our sample. Understanding the complexities in women's decision-making is important, as research already points to mothers being more hesitant than fathers to vaccinate their children.[60,61] By understanding the complexities and the reasons for vaccine hesitancy specific to this group, interventions can be implemented and target this demographics major concerns. For example, if misinformation is the biggest issue in terms of their hesitancy, educational campaigns can be conducted within obstetric or gynecology clinics to encourage and teach these women about the benefits of getting vaccinated.

Where should the geographic focus be?: Our findings showed vaccine hesitancy was greatest in the Southeastern and Midwestern regions of the US, with at least half of these respondents indicating they would refuse COVID vaccination if given the opportunity (Figure 1). These findings are critical, given that rates of new COVID cases were almost 3 times higher in states with low vaccination rates.[49] States with lower vaccination rates reported an incidence rate of 6 new COVID cases per 100,000 compared to 2.2/100,000 new cases in states with higher vaccination rates.[49] In the Southeastern state of Arkansas, which, at the time of the study, had a vaccination rate of 35%, the incidence of new COVID cases was almost 3 times the expected rate.[49] Programs aiming to decrease vaccine hesitancy should focus on these geographic regions of the country, which tend to be more rural, with worse healthcare access compared to the rest of the US. Additionally, educational efforts and resources emphasizing the importance of vaccines could be provided to local and state health departments in these areas. These resources could be provided to healthcare facilities that cater to women of reproductive age in order to increase their understanding on the importance of vaccinations for their health and dispel any fears/misinformation about adverse effects.

What COVID-specific attributes predict vaccination, and can be used to inform future vaccination?: We found COVID risk and COVID stress predicted current and future willingness to get vaccinated; as we hypothesized. Women perceiving their risk of COVID infection to be high were 57% more likely to be currently vaccinated, and 65% more willing to be vaccinated in the future (p=0.0004) compared to those who perceived their risk to be low. Those with high COVID stress were 140% more willing to get vaccinated in the future (p=0.01) compared to those with lower COVID stress. These findings suggest that emphasizing COVID infection risk, particularly with the increasing prevalence of various COVID strains, may be an effective means to convince the hesitant. Public health messages should emphasize risk of COVID death *and* the long-term, physiological impact of COVID, which may include cardiovascular disease, neurological perturbations, pulmonary dysfunction, renal involvement, and reproductive

dysfunctions[14,62–64] Emphasizing the reduced stress that herd immunity yields, could also be an effective strategy, as many women experiencing COVID stress were willing to be vaccinated. It is important to keep in mind the differences in vaccine hesitancy between subgroups in the population and cater interventions to them for greater impact.

Strengths and Limitations

Our novel sampling strategy using Dynata gave us a large and diverse sample to test salient hypotheses that fulfilled the study's aims of understanding who, where, why, and what drives vaccine hesitancy. We had a representative distribution of racial, ethnic, and geographic heterogeneity of respondents. Despite these strengths, our study had some limitations, mainly due to lack of longitudinal assessments. Although the pandemic has stabilized, long-COVID survivors and many others are still dealing with its ramifications. A study like ours could benefit from more than a cross-sectional assessment of exposures and outcomes. Future studies should monitor how vaccine hesitancy evolves over time geographically, by parenting status, and by shifting norms. Additionally, future studies could go beyond demographic predictors and include other important factors like knowledge about vaccines, previous media intervention experiences, previous healthcare professional interactions, current health status, and government mistrust; all of which were recognized as predictors of vaccine hesitancy even before the emergence of COVID-19, and are reflected in the reasons for vaccine hesitancy listed in Table 3.

Conclusion

The WHO named vaccine hesitancy as one of the top ten threats to global health in 2019.[65] This study provides insights for identifying COVID-19 vaccine hesitancy and future vaccination willingness amongst US women of reproductive age. Our findings are paramount as reports show COVID vaccination rates among women are lagging compared to men. Our findings can be used to create targeted messaging around COVID risk and stress in Southeastern and Midwestern regions; as well as debunk misinformation about infertility and other vaccine side effects. Public health efforts should be disentangled from political agendas to decrease mistrust.

Data Sharing Statement

Data and materials available upon request from the corresponding author.

Ethical/Consent Statement

The study was approved by the University of Rochester Institutional Review Board (STUDY00005980) with a waiver of documentation of consent; common for online surveys that collect no personal identifying information. The study complies with the Declaration of Helsinki.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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