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COVID-19 Vaccine Hesitancy and Acceptance in the Global Context: A Systematic Review and Meta-Analysis

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ABSTRACT Large-scale vaccination is the only hope to end the COVID-19 pandemic. Previous studies show that many people are hesitant to get vaccinated and COVID-19 vaccine hesitancy varies between countries and minoritized groups. Our study aims to shed light on the latest trends in vaccine hesitancy and acceptance across countries and identify the predictors driving these trends in the global context. We used a meta-analysis of proportion to analyse the trends in vaccine hesitancy and acceptance and systematically reviewed their predictors in the global context. We found that, across all studies, the acceptance and hesitancy rates for taking the vaccine are 64% and 21% respectively. The acceptance rates among healthcare workers was found to be higher than the general adult population (70% vs 61%). Being a female, concerns about vaccine side effects, and perceiving the vaccine unsafe were the most reported predictors of hesitancy. Older age, higher educational level, flu vaccine history, and low perceived risks were found to predict COVID-19 vaccine acceptance. Many nations face huge challenges to get their significant proportion of populations immune to COVID-19. It is important to disseminate accurate information through trusted channels, and policymakers should address predictors of hesitancy when designing vaccination policies.

KEY WORDS COVID-19, vaccination, hesitancy, acceptance, predictors, vaccination policy

INTRODUCTION

Almost two years into the pandemic, the world's defensive measures against COVID-19 were upgraded from handwashing, social distancing, and masking to vaccination. As large-scale vaccination is suggestive to obtaining herd immunity, governments are racing to get their citizens vaccinated. Will this fast advancement in technology and government policies be enough to get 70% of the population – required for herd immunity – vaccinated so our communities are safe from this virus and its variants? Research indicates that a serious portion of many societies are found to be hesitant to receive doses of the vaccine. The hesitancy may slow the progression back to normalcy.

Developing a safe and effective vaccine within a short time period is a major step to stopping the coronavirus. While access to the vaccines to millions of people is an endeavour itself, the world faces an even bigger challenge: inadequate uptake of the vaccine. Since the first shot was administered in December 2020 to December 2021, about 8.21 billion doses of the COVID-19 vaccine were distributed globally, meaning about 55% of the world

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population received at least one dose. However, there are huge gaps between countries in the vaccination numbers. In low-income countries, only 6.2% of the population have received at least one dose of a COVID-19 vaccine [1].

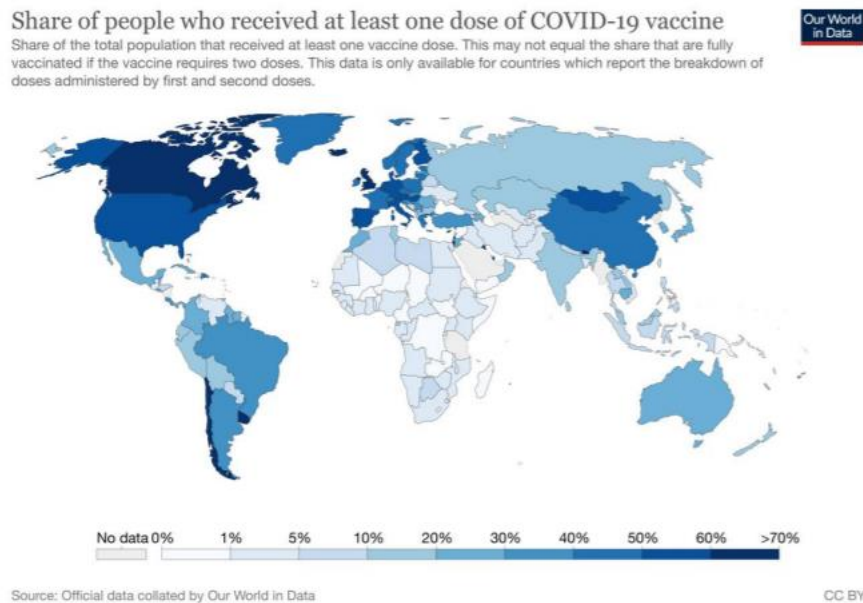


FIGURE 1. SHARE OF PEOPLE WHO RECEIVED AT LEAST ONE DOES OF COVID-19 VACCINE, JUNE 27, 2021

Even when vaccines are available, hesitancy towards receiving the vaccines raises another issue. The World Health Organization (WHO) defines vaccine hesitancy as “the behavior - refusal or delay in taking the vaccine despite their availability - that results from the decision-making process and reflects the factors influencing the process,” emphasizing its variability between and within countries [2]. Fast growing literature on this issue has evidence. For example, while survey results indicated that 35.2% of respondents were hesitant to get vaccinated for COVID-19 in France [3], in Australia only 4.8% were hesitant to be vaccinated [4] and in Japan the hesitancy rate was 12.8% [5]. The numbers vary for different populations within the countries as well. Among US-based studies, one study found that 54.1% nonelderly were hesitant in a Tennessee survey, other separate studies concluded that 75% of Ohio Amish, 68.9% of the underserved communities of North Carolina [6], and 10.8% across a nationally representative survey would not accept the shot [7]. Pointing at the ethnic differences, in Israel, 7.7% of Jewish men and 29.9% of Arab men responding to a survey that they would refuse to get vaccinated [8].

Surveys, polls, and systematic reviews show changing trends in COVID-19 vaccine hesitancy and acceptance rates. In a systematic review, Sallam et al. (2021) found in the US, the vaccine receptivity intent showed an upward trend from 56.9 % in April to 75.4% in June 2020 [9]. On the contrary, the same study found that despite the high level of intentions for the uptake of the vaccine in China, the acceptance rates continued to fall about 2.7% between three time points. A big drop in acceptance rates was reported in Italy from April to September 2020 with a rate of 23.6% (62.0% to 58.9%). Sampling different countries in their meta-analysis, Robinson et al. (2021) found 18 studies reported an increase in vaccination hesitancy from 12% to 20% among the Western countries [10]. Furthermore, there is evidence that the big declines in vaccine acceptance (20% drop from March to October 2020) displayed demographic, socioeconomic, and political view variability [11].

There are many factors that influence people’s intentions to receive the COVID-19 vaccine. Previously, separate studies focused on different populations from several countries including Australia, the U.K., France, Greece, Saudi Arabia, and the United States to investigate the factors that are associated with vaccine hesitancy. They found that factors of vaccine hesitancy included concerns about the safety, side effects and efficacy of the vaccine; demographic characteristics such as minority ethnic groups, females, and lower institutional educational backgrounds; being against vaccines in general; low perceived risk of disease; believing in conspiracy theories; and far left-wing political partisanship [4, 12–15]. In contrast, being older and male along with having a high educational level, higher income, high perceived risk of disease, past flu vaccination history, and democratic

ideology were found to be predictors of COVID-19 vaccine acceptance [7, 16–20].

This evidence suggests the importance of understanding how hesitancy and acceptance rates vary by country and minoritized groups as well as the factors determining this variability. However, further research is required as many countries are not included in the literature. The first aim of this study is to shed light to differences in vaccine hesitancy and acceptance globally. In doing so, we intend to contribute to the literature by synthesizing information from more countries as more variation will help better understand the predictors of hesitancy. Secondly, we seek to identify the factors for the hesitancy and acceptance of the vaccine in the global context. The goal of this study is to synthesize research findings in this topic and provide evidence to the policymakers and global efforts to make the right policy decisions to improve public health.

MATERIALS AND METHODS

This study aims to answer two research questions: (1) What are the COVID-19 vaccine hesitancy and acceptance rates across countries? (2) What are the factors that determine the COVID-19 vaccine hesitancy and acceptance in the global context? The first question will be answered by a meta-analysis of proportion approach while we will employ a systematic review methodology to answer the second.

Study Selection

We searched for studies about COVID-19 vaccine hesitancy on the PubMed database in March 2021. The terms searched were “COVID-19, vaccine hesitancy, survey,” “COVID-19, vaccine hesitancy, race, survey,” and “COVID-19, vaccine hesitancy, culture, survey.” As the number of studies increased each day, we completed a total of three different searches at three different times, March 12, 2021, March 13, 2021, and March 31, 2021. Two researchers screened articles for inclusion in the study. In total 81 studies were screened for title review and 64 studies were screened for full-text review as illustrated in Figure 2. These 15 studies were excluded due to being the wrong study design or being in a language other than English. A total of 49 studies that met the selection criteria were included in this study.

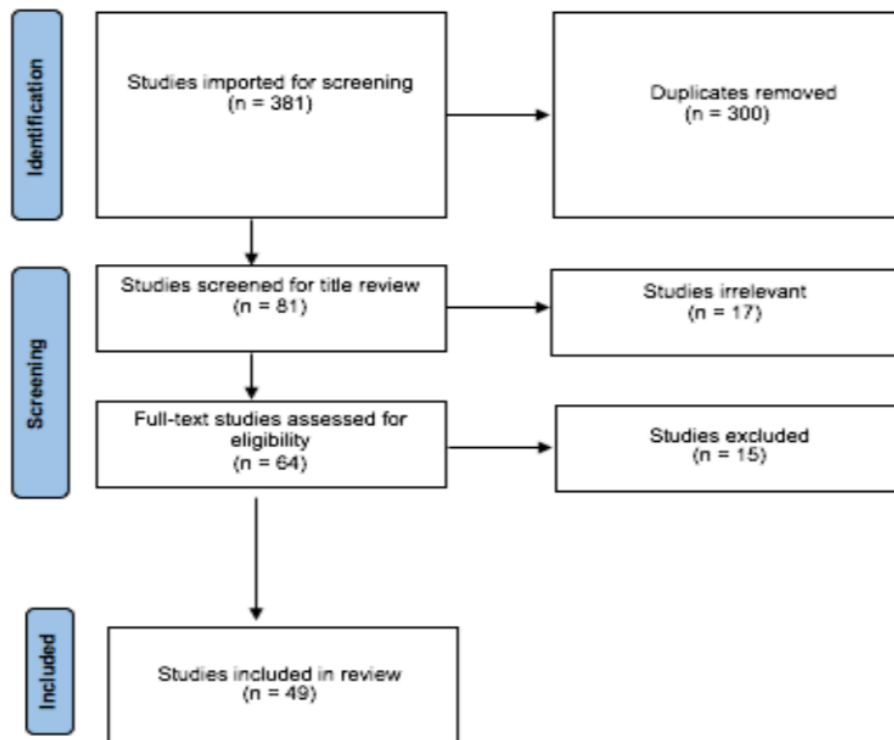


FIGURE 2. PRISMA STUDY SELECTION CHART

Our inclusion criteria consisted of four factors: (1) quantitative studies, (2) studies must have used a survey-based design (i.e., online questionnaires), (3) studies must have reported COVID-19 vaccine hesitancy and/or acceptance rate, (4) Data about COVID-19 vaccine hesitancy, beliefs and/or attitudes must be reported in English, (5) studies had to focus on an adult or health care worker (HCW) population and (6) be peer-reviewed

and published. We made no temporal or geographic restrictions. We excluded the studies that used (1) meta-analyses approach, (2) systematic review method, (3) qualitative method, and focused on (4) children, adolescents and (5) student populations.

Methodological Quality (Risk of Bias) Assessment

JBIC (Joanna Briggs Institute) critical appraisal tool for cross-sectional studies was used to assess the risk of bias in each study [21]. This checklist has 8 categories which constitutes 8 points. We used “Yes = 1”, “No = 0” and “Unclear = 0” as the values for the assessment of each category. We included the studies that scored 4 and above in our systematic review. Two researchers (author 1 and author 2) conducted the quality assessment together to ensure a strong interrater-reliability. All 49 studies that we assessed for risk of bias scored above 4 points. The quality assessment of the studies can be found in the Supplementary File 1.

Effect Size Data

The effect size of interest is a proportion statistic. Specifically, it is the proportion of vaccine hesitancy and acceptance reported in the sample. These two rates are treated in separate analyses. The effect size data used in this study is then a univariate statistic. This is different from most meta-analyses, which synthesize evidence for bivariate statistics. In most cases, the standard error was unreported for these proportion statistics. We therefore imputed the standard error (SE) in every case using the formula: $SE = \sqrt{p(1-p)/n}$. The SE is needed to use as inverse variance weights.

Data Coding

Two researchers extracted the data to be used in the analysis. Data was coded into excel using data validation settings to ensure data inputting accuracy. We coded information for the following between-study variables: study authors, country, year, survey population, study design (e.g. cross-sectional, longitudinal, etc.), sample size, information on mean demographic characteristics (percent female, educational level, income, and age), hesitancy rates, acceptance rates, quantitative results for predictors associated with hesitancy and predictors associated with acceptance, health behavior model used and reasons for hesitancy or acceptance. We met and coded a series of studies together so as a training exercise. Since most of our study-level used unambiguous definitions and required low-inference judgments, there were almost no coding disagreements as we worked together. We coded data separately and felt assured that our data would meet the high-quality standards that are necessary for conducting a systematic review and meta-analysis.

Data Analysis

We conducted proportional meta-analyses using R software to analyze COVID-19 vaccine hesitancy and acceptance trends. Meta-analysis of proportion is used to compare and combine effect sizes across different studies. Meta-analysis of proportion in this study helps us pool COVID-19 vaccine hesitancy and acceptance rates based on the included study weights [54]. The statistical significance and the level of study heterogeneity were assessed based on Q statistic and I^2 statistic. A higher percentage of between-study heterogeneity suggested that a random effects approach would be suitable [54, 55, 56].

The two effect size metrics of interest in the current study are the proportion of individuals who expressed either hesitancy or acceptance of getting a COVID-19 vaccination. Note that many studies provided estimates for both hesitancy and acceptance separately. Two proportional meta-analyses were used to synthesize the evidence about COVID-19 vaccine acceptance and reluctance.

First, the evidence base is summarized by reporting a random-effects model. The random-effects model of meta-analysis is the most widely used model for integrating estimates from different studies into a single summary estimate [22]. Both the meta-analyses of COVID-19 vaccine hesitancy and acceptance had significant statistical heterogeneity. Specifically, we found that there was a significantly higher degree of heterogeneity in our overall effect size for COVID-19 vaccine acceptance with $Q(53) = 20946.9205$, $\tau^2 = 0.0479$, $p < .0001$, $I^2 = 99.81\%$, $p < .0001$. Our analysis of the overall effect size for COVID-19 vaccine hesitancy also showed a significantly higher degree of heterogeneity, with $Q(41) = 10659.3129$, $\tau^2 = 0.0288$, $p < .0001$, $I^2 = 99.83\%$, $p < .0001$. So, random-effects models were applied in our overall effect size analyses. Secondly, we also displayed forest plots. Forest plots are a visual device that focus on comparing different estimates of the same statistical parameter across different studies. In this study, the statistical parameters are acceptance and hesitancy proportion.

RESULTS

Characteristics of Studies

Our inquiry included 49 studies with a total sample size of 86,822. The studies included covered COVID-19 vaccine hesitancy and/or acceptance survey results in 23 countries. The most studied countries were France (n=5), UK (n=4), China (n=4), Turkey (n=4) and the United States with the US being the most studied country for vaccine hesitancy (n=17)]. The sample sizes ranged from 47 (Bhutan) to 12,035 (UK). The mean percentage of females in the samples ranged from 39% (Saudi Arabia) to 89% (China). All studies were conducted before COVID-19 vaccines became available and were published between March 2020 and March 2021. Table 1 shows descriptive statistics for all studies located for this systematic review.

TABLE 1. STUDY CHARACTERISTICS

Study ID	First author & Year	Country	Design	N
<i>Studies with effect sizes for adults</i>				
1	Dror 2020	Israeli	Cross-sectional	1112
2	Fisher 2020	US	Cross-sectional	991
4	Detoc 2020	France	Cross-sectional	3259
5	Pogue 2020	US	Cross-sectional	316
6	Ward 2020	France	Cross-sectional	5018
7	Salali 2020	Turkey	Cross-sectional	3936
7	Salali 2020	UK	Cross-sectional	1088
8	Kreps 2020	US	Cross-sectional	1971
9	Olagoke 2021	US	Cross-sectional	502
11	Al-Mohaithef 2020	Saudi Arabia	Cross-sectional	992
12	Freeman 2020	UK	Cross-sectional	5114
14	Lin 2020	China	Cross-sectional	3541
15	Borriello 2021	Australia	Cross-sectional	2136
17	Murphy 2021	UK	Cross-sectional	2025
17	Murphy 2021	Ireland	Cross-sectional	1041
18	Williams 2021	Scotland	Cross-sectional	3436
19	Yigit 2021	Turkey	Cross-sectional	428
20	Motta 2021	US	Cross-sectional	990
21	Mercadante 2020	US	Cross-sectional	525
22	Sallam 2021	Saudi Arabia	Cross-sectional	154
22	Sallam 2021	Jordan	Cross-sectional	2173

22	Sallam 2021	Kuwait	Cross-sectional	771
23	Ruiz 2021	US	Cross-sectional	804
24	Yoda 2021	Japan	Cross-sectional	1100
25	Alley 2021	Australia	Cross-sectional	575
27	Scott 2021	US	Cross-sectional	391
28	Kourlaba 2021	Greece	Cross-sectional	1004
29	Schwarzinger 2021	France	Cross-sectional	1942
30	Latkin 2021	US	Cross-sectional	1043
31	Alabdulla 2021	Qatar	Cross-sectional	7821
32	Kaplan 2021	US	Cross-sectional	1000
36	Wang 2021	China	Cross-sectional	791
37	Khubchandani 2021	US	Cross-sectional	1878
38	Papagiannis 2021	Greece	Cross-sectional	340
39	Edwards 2021	Australia	Longitudinal	3061
40	Al-Qerem 2021	Jordan	Cross-sectional	1144
41	Qattan 2021	Saudi Arabia	Cross-sectional	673
42	Salmon 2021	US	Longitudinal	2525
43	Gatwood 2021	US	Cross-sectional	1000
44	Robertson 2021	UK	Cross-sectional	12035
45	Latkin 2021	US	Longitudinal	592
46	Green 2021	Israel	Cross-sectional	606
46	Green 2021	Israel	Cross-sectional	351
47	Vallis 2021	Canada	Cross-sectional	2078
48	Yurttas 2021	Turkey	Cross-sectional	763

Studies with effect sizes of HCW

1	Dror 2020	Israeli	Cross-sectional	338
1	Dror 2020	Israeli	Cross-sectional	211
3	Wang 2020	China	Cross-sectional	806
10	Gagneux-Brunon 2021	France	Cross-sectional	431
10	Gagneux-Brunon 2021	France	Cross-sectional	371

13	Kwok 2021	China	Cross-sectional	1205
16	Unroe 2021	US	Cross-sectional	2372
26	Verger 2021	France	Cross-sectional	1209
26	Verger 2021	Belgium	Cross-sectional	414
26	Verger 2021	Canada	Cross-sectional	1055
33	Kuter 2021	US	Cross-sectional	12034
34	Di Gennaro 2021	Italy	Cross-sectional	1723
35	Doherty 2021	US	Cross-sectional	984
48	Yurttas 2021	Turkey	Cross-sectional	320
49	Chew 2021	China	Cross-sectional	303
49	Chew 2021	India	Cross-sectional	406
49	Chew 2021	Indonesia	Cross-sectional	430
49	Chew 2021	Singapore	Cross-sectional	61
49	Chew 2021	Vietnam	Cross-sectional	472
49	Chew 2021	Bhutan	Cross-sectional	47

Vaccine Acceptance and Hesitancy Rates

Figures 3 and 4 show forest plots for acceptance and hesitancy rates across studies. By focusing on the random-effects summary estimate of vaccine acceptance (Figure 3), we found across all studies, the acceptance rate for taking the COVID vaccine was approximately 64% (95% CI: [0.58, 0.70]). However, as the forest plot makes clear, there is a lot of variability around this 64%. The results are visibly sorted into two main groups. Some studies used samples from a general adult population, while others focused on medical professionals. As can be observed, the acceptance rate among medical professionals seems slightly higher than the acceptance rate among the general adult population. Subgroup summary effects for adults only or health care workers (HCWs) only are also shown. Among HCWs, the average acceptance rate is 70%, with a 95% CI of [0.59, 0.81]. As expected, this is much higher than the acceptance rate in the general adult population – which is 61% (95% CI: 0.54, 0.67). It is, however, not possible to conclude that the mean proportion of acceptance between adults and health care workers is statistically significant ($p < .0001$) since the confidence intervals overlap.

The hesitancy rates in Figure 3 reveal similar patterns – the difference between adults and HCWs is not statistically significant although the summary effect for HCWs is lower (16% vs 23%). Pooling across all studies, the average hesitancy rate is 21% (95% CI: 0.16, 0.26).

Predictors of Vaccine Hesitancy

A total of 49 studies were included in the systematic review and were analyzed qualitatively to identify the predictors of vaccine hesitancy. The most reported predictors of COVID-19 vaccine reluctance fall into three main categories; (1) *demographic characteristics* such as being female (n=10), Black people (n=10), and young age (n=7), (2) *vaccine characteristics* including side effects (n=17), vaccine efficacy (n=6), and origin of vaccine (n=3), (3) *perceptions and beliefs* including beliefs (n=13) and perceived risks (n=10).

Demographic Characteristics

Of the 49 studies, 19 reported demographics-related (sex, age, ethnicity) predictors which are associated with vaccine hesitancy. 10 of 19 studies saw sex as a differentiating factor, as females were more likely to be hesitant

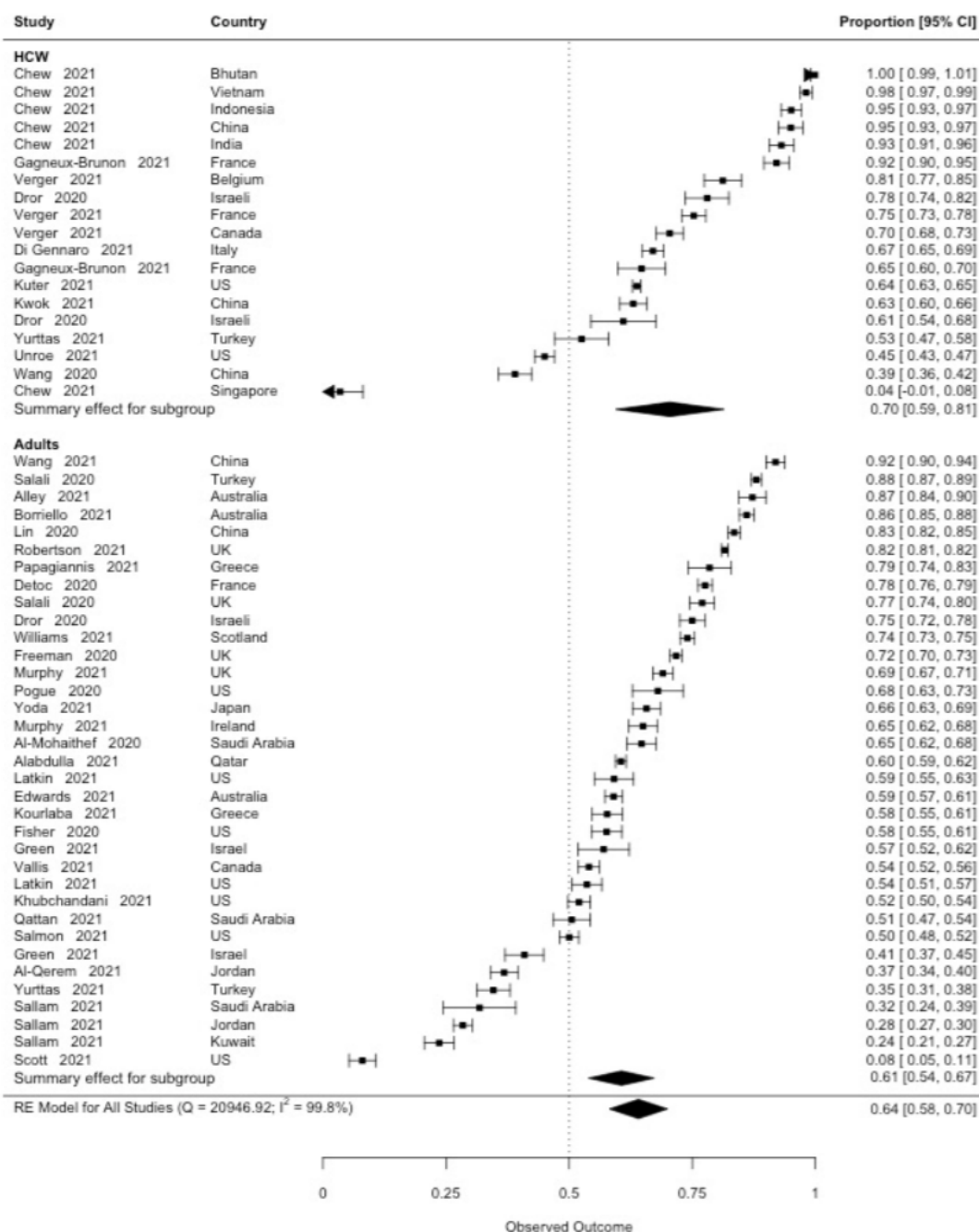


FIGURE 3. FOREST PLOT OF ACCEPTANCE RATES FOUND ACROSS STUDIES

compared to males. Among the nine studies that used a nationally representative sample of the US population, four found significant sex-based differences; females had higher odds of reporting they would not get vaccinated if a vaccine were available compared to males [7, 15, 23, 24]. One study investigated vaccine hesitancy in the under-resourced communities of North Carolina and found that females were 1.90 times more likely to report negative COVID-19 vaccination intentions [6]. These results are consistent with the findings of the European studies (n=3). Results of one UK study showed that 21% of female respondents were hesitant compared to 14.7% males due to concerns of vaccine side effects and distrust in the safety of vaccines [12]. Two French studies reported strong associations between hesitancy and being female [13, 25], the latter noted that women were more likely to refuse the vaccine compared to men and were against vaccines generally [13]. Consistent with these results, Alley et al. (2021) found Australian women were 1.89 times more likely to report being unsure

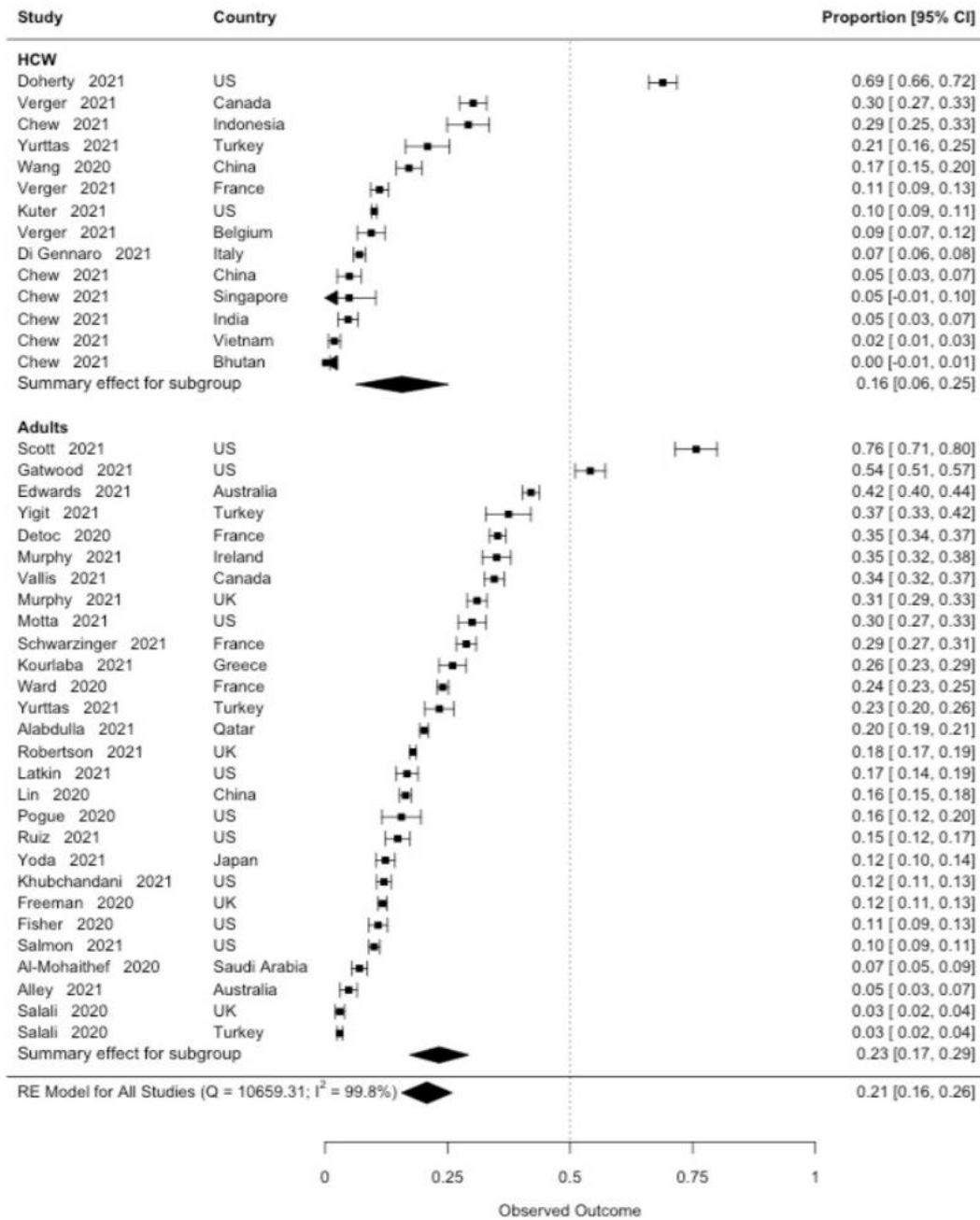


FIGURE 4. FOREST PLOT OF HESITANCY RATES FOUND ACROSS STUDIES

to get vaccinated compared to men [4]. Al-Qerem and Jarab (2021) also stated that Jordanian females have 3-fold higher relative likelihood of refusing to receive the vaccine and 1.5-fold higher relative likelihood of being unsure [26]. Finally, Turkish women were found to be less likely to be receptive to either domestic or foreign vaccines than men [27].

Age is found to be another predictor of COVID-19 vaccine hesitancy as seven of 18 studies showed that younger adults are more hesitant to get the vaccine [5, 12–14, 24, 25, 28]. Gatwood et al. (2021) reported that US adults less than 55 years have a greater likelihood of being reluctant [14]. Similarly, in the UK and Ireland, Murphy et al. (2021) found that adults between the ages of 35-44 years were 3.33 times more likely to have no intention of getting vaccinated [28]. Robertson et al. (2021) also demonstrated evidence in a UK survey that the likelihood of rejecting vaccination is 1.48 times higher for adults between the 16-24-year-old category [12]. Finally, in Japan,

Yoda and Katsuyama (2021) found that the 20-29-year-old age group expressed uncertain intentions towards the vaccine [5]. In contrast, Dror et al. (2020) and Al-Qerem and Jarab (2021) did not find significant associations between age and hesitancy [29].

The results show that vaccine hesitancy in western countries is higher among Black people. The results of 10 of 49 studies indicated that Black people are more likely to be reluctant to get vaccinated [6, 7, 14–16, 23, 24, 30–32]. Fisher et al. (2021) found that Black people are 6-fold more likely to refuse to be vaccinated compared to white people [7]. One study reported that Black and Latinx people refuse to take the vaccine due to time constraints in accessing the vaccine [15]. Two other studies point to distrust in vaccines [12], and mistrust in the government [6] as the reasons for Black peoples's hesitancy towards a COVID-19 vaccine. The results are consistent for general the population and medical professionals. In a study conducted in two Philadelphia hospitals, Black hospital employees expressed negative intentions to get COVID-19 inoculations [16]. Doherty et al. (2021) also noted that vaccine hesitancy showed a lower decline over time among Black people compared to white people in a U.S. sample [6].

Vaccine Characteristics

Vaccine safety is found to be the top concern reported by hesitant individuals including the HCWs. Seventeen of forty-nine studies reported potential side effects or future unknown effects as the main reason for vaccine reluctance [5, 6, 11, 12, 26, 29, 33–43]. In the U.S., Doherty et al. (2021) found a strong association between safety concerns and vaccine hesitancy [6], and in Israel, Dror et al. (2020) showed that 70% of both the general adult and HCW populations reported safety concerns as their reason for being unwilling to receive the vaccine [29]. Three studies concluded that HCWs and the general population reported side effects as a reason for hesitancy in Turkey and in Greece [34–36]. Five studies conducted in other Western and Asian countries stated fear of adverse effects and worries about contracting COVID-19 from the vaccine as common concerns (US: [38, 39] Australia: [40]; China, Indonesia, Bhutan, Singapore, Vietnam, India: [33]; China: [42]. It is important to note that HCWs in the Asian-based studies also reflected similar concerns [33, 42].

On the other hand, six studies showed that low vaccine efficacy is associated with hesitancy [5, 24–26, 29, 44]. One study demonstrated that the decrease in the probability of efficacy of the vaccine (50% compared to 70%, or 90%) was associated with higher probability of refusing vaccination [44]. The results of a survey experiment conducted in France indicated that the respondents were more hesitant towards a hypothetical vaccine with 50% efficacy compared to one with 90% [25]. The results of a conjoint experiment also indicated that a 20% to 40% increase in the efficacy of a hypothetical vaccine and longer protection duration were associated with an increase in the probability of receiving the COVID-19 vaccine [24].

Vaccine origin is another important feature that led to hesitancy in five of 49 studies. Four studies indicated that respondents are more likely to be reluctant towards the vaccines manufactured in China [24, 25, 38] or in Russia [38], and in one study, 80.4% Turkish respondents reported distrust in a foreign vaccine [35].

Perceptions and Beliefs

Beliefs and perceived risks were found to play an important role for hesitancy for both the general population and the HCWs. Beliefs refer to one's accepting something to be true, and perceptions refer to an individual's interpretation and understanding of something through their senses. While perceptions are a common construct found to be a predictor for hesitancy in 10 of the 49 studies, beliefs were identified as influencing hesitancy in 13 studies. Across five studies, respondents were not reassured by the fast development of the vaccine and perceived it to be dangerous [13, 26, 36–38]. One study emphasized that respondents with perceived risk of contracting infection from the vaccine are more likely to refuse being vaccinated [42]. Four studies reported that perceiving COVID-19 as harmless [13, 18, 25, 29] increased the odds of being against vaccination and one study found that hesitant individuals were at greater probability of believing that vaccines don't work due to the mild nature of the disease [6].

In four Middle Eastern and European studies, the authors found that believing in conspiracy theories or believing that the coronavirus was developed by humans in laboratories are influencing factors for unwillingness to receive the vaccine [9, 17, 26, 28]. Other studies demonstrated that hesitancy manifested in higher levels of COVID-19 related anxiety or low confidence in vaccines [35, 37]. Higher levels of religiosity [28, 32], being against vaccines in general [7, 13, 32], higher levels of scepticism [31], lack of trust in government, health authorities or scientists [6, 7, 18, 28, 31, 45], receiving little or conflicting information about vaccines [41], relying on social media [20,

41] were all associated with vaccine hesitancy across the different countries. Ideologies also mattered for Covid-19 vaccination hesitancy. Five studies indicated that respondents supporting far left-wing, conservative, Republican, or moderate parties were more likely to reject getting Covid-19 vaccination [13–15, 28, 31].

TABLE 2. PREDICTORS OF VACCINE HESITANCY AND ACCEPTANCE ACROSS COUNTRIES

Country ID	Country	Predictors of Vaccine Hesitancy	Predictors of Vaccine Acceptance
1	Australia	<ul style="list-style-type: none"> • Being a female • Side effects 	<ul style="list-style-type: none"> • Older age • Higher educated
2	Belgium	<ul style="list-style-type: none"> • Beliefs 	
3	Bhutan	<ul style="list-style-type: none"> • Side effects 	<ul style="list-style-type: none"> • High perceived risk of getting the disease
4	Canada	<ul style="list-style-type: none"> • Side effects • Beliefs 	
5	China	<ul style="list-style-type: none"> • Side effects 	<ul style="list-style-type: none"> • Being a male • Older age • High perceived risk of getting the disease • Vaccine history
6	France	<ul style="list-style-type: none"> • Being a female • Vaccine efficacy • Side effects • Origin of vaccine • Beliefs 	<ul style="list-style-type: none"> • Being a male • High perceived risk of getting the disease • Vaccine history
7	Greece	<ul style="list-style-type: none"> • Side effects • Beliefs 	<ul style="list-style-type: none"> • Being a male • Older age • Vaccine history
8	India	<ul style="list-style-type: none"> • Side effects 	<ul style="list-style-type: none"> • High perceived risk of getting the disease
9	Indonesia	<ul style="list-style-type: none"> • Side effects 	<ul style="list-style-type: none"> • High perceived risk of getting the disease
10	Ireland	<ul style="list-style-type: none"> • Beliefs 	
11	Israeli	<ul style="list-style-type: none"> • Side effects 	<ul style="list-style-type: none"> • Higher educated • Vaccine history
12	Italy	<ul style="list-style-type: none"> • Beliefs 	<ul style="list-style-type: none"> • Being a male • Older age
13	Japan	<ul style="list-style-type: none"> • Young age 	<ul style="list-style-type: none"> • Being a male • Older age

14	Jordan	<ul style="list-style-type: none"> • Being a female • Beliefs 	
15	Kuwait	<ul style="list-style-type: none"> • Beliefs 	
16	Qatar		<ul style="list-style-type: none"> • Older age • Vaccine history
17	Saudi Arabia	<ul style="list-style-type: none"> • Side effects • Beliefs 	<ul style="list-style-type: none"> • Being a male • High perceived risk of getting the disease
18	Scotland		<ul style="list-style-type: none"> • Higher educated
19	Singapore	<ul style="list-style-type: none"> • Side effects 	<ul style="list-style-type: none"> • High perceived risk of getting the disease
20	Turkey	<ul style="list-style-type: none"> • Being a female • Side effects • Origin of vaccine • Beliefs 	<ul style="list-style-type: none"> • Being a male • Higher educated
21	UK	<ul style="list-style-type: none"> • Being a female • Young age • Being Black • Beliefs 	<ul style="list-style-type: none"> • High perceived risk of getting the disease
22	US	<ul style="list-style-type: none"> • Being a female • Being Black • Young age • Side effects • Vaccine efficacy • Origin of vaccine • Beliefs 	<ul style="list-style-type: none"> • Being a male • Older age • Higher educated • High perceived risk of getting the disease • Vaccine History
23	Vietnam	<ul style="list-style-type: none"> • Side effects 	<ul style="list-style-type: none"> • High perceived risk of getting the disease

Predictors of Vaccine Acceptance

Across 49 studies, vaccine acceptance is found to be mostly associated with certain (1) demographic characteristics including male (n= 9), higher education level (n=6), higher income levels (n=18), (2) perceived risks and severity of disease (n=12), and (3) vaccine history (n=12).

Demographic Characteristics

In terms of demographic characteristics that influence the reception of the COVID-19 vaccine, nine studies (across most countries studied) found that being male is associated with vaccine acceptance [5, 16, 20, 35, 36, 41, 42, 46, 47]. While in France Gagneux-Brunon et al. (2021) and, in Japan, Yoda et al. (2021) reported that male HCWs were more likely to get COVID-19 vaccination, in Saudi Arabia and the US, the likelihood was double for men compared to women [16, 46].

We also found that older age is an important factor for vaccination receptivity across 11 studies. [5, 15–17, 30, 36, 41–43, 48, 49]. Three studies reported the elderly >70 are more likely to accept vaccination compared to people at younger age brackets [5, 49]. In Australia, Edwards et al. (2021) [48] reported positive intentions towards vaccination among individuals >55 and other studies report similar findings with individuals 65 and over [16, 17]. In the Unroe et al. (2020) [30] study, HCWs older than 60 years old were found to be more inclined to get the vaccine.

Finally, in six studies, individuals holding a university degree or a higher level of education were reported to have greater odds of being unopposed to the vaccine [4, 8, 16, 35, 38, 50].

Perceived Risks

We found individuals willing to accept the vaccine have similar perceptions and beliefs among HCWs and general adult populations across countries. High perceived risk of acquiring COVID-19 infection was associated with vaccine acceptance in seven of the 49 studies [3, 7, 19, 33, 46, 47, 51]. Saudi Arabian, Asian, and French HCWs who perceived a high risk of getting coronavirus had greater chances to accept the COVID-19 vaccine [33, 46, 47]. In a Middle Eastern survey, Qattan et al. (2021) reported that HCWs with high perception of getting COVID-19 had a 1.8 times greater likelihood of accepting the vaccine [46] while Gagneux-Brunon et al. (2021) reported similar evidence for French HCWs [47], and Chew et al. (2021) showed similar findings for HCWs in Asia including India, Indonesia, Bhutan, Vietnam, Singapore, and China [33].

Two studies, Salali and Uysal (2020) and Yigit et al. (2021) showed that among Turkish or British samples, higher levels of fear and anxiety scores are associated with vaccine acceptance [51]. Kwok et al. (2021) noted that work stress associated with unfavorable attitudes towards infection control policies acts as a mediator for the intentions for obtaining the COVID-19 vaccine among Chinese HCWs [52]. Four studies reported that people who perceived COVID-19 as a severe disease or its monumental impact on society have higher odds of receptivity [18, 20, 25, 53]. Three studies also reported that respondents who believe that vaccination will help to avoid getting COVID-19 are more likely to report willingness [11, 18, 49]. Moreover, two of the studies that examined the predictors of COVID-19 vaccine acceptance using a Health Belief Model, reported that under the perceived benefit construct, being unconcerned about the new vaccine's side effects as well as its efficacy increased the intentions to get vaccinated significantly [11, 49].

Vaccine History

Finally, a very important predictor for vaccine uptake is found to be an individual's vaccine history. 12 of 49 studies showed that positive attitudes towards influenza vaccines is a predictor of COVID-19 vaccine acceptance. Nine studies concluded that individuals who had flu vaccinations in the past are found to be more likely to vaccinate [7, 17, 18, 20, 29, 42, 43, 47, 53]. This is also the main predictor of vaccine uptake among French HCWs [47]. Furthermore, one U.S. study stated being up-to-date with vaccines is an indicator of receptivity [16].

DISCUSSION

In this study, COVID-19 vaccine hesitancy and acceptance trends across countries and their predictors were investigated. Across all studies, the COVID-19 vaccine hesitancy and acceptance rates were found to be 21% and 64% respectively. The results indicate a huge variability in the vaccine acceptance and hesitancy rates across countries and minoritized populations. Concerns about vaccine side effects and perception of the fast development of the vaccine to be unsafe by certain demographics, such as being female, young age, and race, were found to be the main drivers for vaccine refusal. On the other hand, being male, older age, having a high level of education, perceived risk of COVID-19, and receiving the flu vaccine in the past predicted the willingness to uptake the COVID-19 vaccine.

The results of this study indicate the current vaccine acceptance rate is found to be less than needed for reaching herd immunity. Scientists state that at least 70%-80% of the population needs to get vaccinated to halt the spread of COVID-19. Existing evidence for skepticism of vaccination across countries and minoritized groups, show that nations face huge challenges to get an adequate percentage of populations immune to COVID-19. This impedes the efforts to stop the pandemic and improve public and global health. Policymakers should consider the context and hesitancy of different minoritized demographics when designing vaccination policies.

The findings on the predictors of hesitancy and acceptance reveal evidence for causes of health disparities. People with certain demographic characteristics differ in their intentions to get vaccinated. Females [6, 7, 13, 15, 23, 24],

people with low schooling levels [7, 12, 13, 23, 38], and young people [5, 12–14, 24, 25, 28] are more hesitant to get the vaccine. Consistent with the results of previous studies, Black people reported less willingness to get vaccinated compared to Latinx or white people [6, 7, 14–16, 23, 24, 30–32]. Their hesitancy stems from both lacking resources, and the valid distrust in vaccines, government, or healthcare authorities which have historically abused marginalized communities in the U.S. and Puerto Rico, such as the unethical Tuskegee experiment and sterilization of Boricua women. The hesitancy is especially alarming because it is well known that culturally oppressed populations are disproportionately vulnerable to the COVID-19 pandemic, as they lack access to basic healthcare. Ultimately, these populations have higher rates of pre-existing conditions that make them more susceptible to COVID-19.

Ethics and evidence matter. Firstly, there is a tremendous need for transparency of information from trusted authorities. This study shows people have different perceptions and beliefs of the COVID-19 disease and the vaccination based on the channels of information they have. Stopping the virus might begin with changing the perceptions and the behaviors of the community. Within the Health Belief Model framework, a person's perception of the risks for getting the virus, the severity of the disease, the effectiveness of getting vaccinated, and the stimulus from others to get vaccinated determines the effectiveness of the COVID-19 vaccine. Therefore, it is crucial to organize the spread of accurate information to these communities. Granted, health care systems need to build trust with their communities first. This effort relies on the partnership of the community, educational organizations, health institutions, political leaders, the media, among other stakeholders.

Public advocacy of the vaccine is also key to improving our collective health. It lays the groundwork for the spread of accurate information which should be instated at the community level in order to boost vaccination at the local level. Additionally, community activism will create the opportunity for communicating the needs of communities to political leaders. As this study demonstrates, some people's vaccination intentions are influenced by political ideologies. It is vital for the political leaders to keep the entire society's interests in mind when giving vaccination messages to the public. Vaccine policies and interventions should be centered on addressing the needs of all, beginning with most vulnerable populations.

Our study revealed some gaps in the literature. For one, there are not enough studies to provide evidence for the causes of hesitancy for many groups across the globe, which prevents the creation of evidence-based policies. Additionally, evidence is scarce for how vaccination policies are implemented across countries including whether they are government-mandated or voluntary. It is critical to know who has access to available vaccines and what types and to what degrees investments are allocated for vaccination objectives. Additionally, what are the vaccine brands available to whom and what are the variances across vaccine intents and behaviors ultimately affect public health.

There are some limitations to this study. First, only PubMed database was used to search for literature. Other databases may have had other published articles that could enhance this review. In addition, we used only the studies that are written in English, which may limit our understanding of the COVID-19 vaccine hesitancy and acceptance globally. Secondly, results of this study show evidence for several countries, and some samples were not representative of the populations of the respective countries. For this reason, the results of this current systematic review cannot be generalized to all countries or all people within their respective countries. Thirdly, the studies included the use of different study designs, survey questions, or data analysis methods. Therefore, the predictors that were found are only associations and causality cannot be claimed. Finally, the studies in this project conducted surveys before the COVID-19 vaccines were developed. The trends in acceptance might have changed after the vaccination programs were put in place. Future research may examine the latest trends across countries and compare before and after trends in order to understand which policies work best. To have solid evidence on the causes of COVID -19 vaccine hesitancy and acceptance, future research may analyze the predictors of hesitancy quantitatively.

CONCLUSION

The results of this study show that large proportions of the population in many countries are still hesitant to get vaccinated even though vaccination is an important tool for our communities to be safe from COVID-19. Large variability in COVID-19 vaccine hesitancy across countries and minoritized groups were found. The predictors of hesitancy and acceptance show similar trends across some subpopulations. These results point to the importance of disseminating accurate information through trusted channels, as well as through political support. Findings from the current systematic review can be used by policymakers as general evidence when proposing

policies that target vaccination behaviors of specific populations.

SUPPLEMENTARY FILE 1

JBI Quality (Risk of Bias) Assessment									
Study	Were the criteria for inclusion in the sample clearly defined?	Were the study subjects and the setting described in detail?	Was the exposure measured in a valid and reliable way?	Were objective, standard criteria used for measurement of the condition?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the outcomes measured in a valid and reliable way?	Was appropriate statistical analysis used?	Score
Detoc et al. (2020)	Y	Y	U	Y	U	U	Y	Y	5
Alley et al. (2021)	Y	Y	Y	Y	Y	Y	Y	Y	8
Yoda et al. (2021)	Y	Y	Y	Y	Y	N	Y	Y	7
Doherty et al. (2021)	Y	Y	Y	Y	U	U	Y	Y	6
Fisher et al. (2020)	Y	Y	Y	Y	Y	Y	Y	Y	8
Green et al. (2021)	Y	Y	Y	Y	Y	Y	Y	Y	8
Sallam et al. (2021)	Y	Y	N	N	U	U	Y	Y	4
Lin et al. (2020)	Y	Y	U	U	Y	N	Y	Y	5
Robertson et al. (2021)	Y	Y	Y	Y	Y	Y	Y	Y	8
Ward et al. (2020)	Y	Y	U	Y	Y	U	Y	Y	6
Gatwood et al. (2021)	Y	Y	Y	Y	Y	Y	Y	Y	8
Latkin et al. (2021) - <i>MASK USAGE</i>	Y	Y	U	Y	Y	Y	Y	Y	7
Kuter et al. (2021)	Y	Y	Y	Y	Y	U	Y	Y	7
Kourlaba et al. (2021)	Y	Y	Y	Y	Y	Y	Y	Y	8
Salmon et al. (2021)	Y	Y	Y	Y	Y	U	Y	Y	7
Al-Mohaithef et al. (2020)	Y	Y	Y	Y	U	U	Y	Y	6
Ruiz et al. (2021)	Y	Y	U	Y	Y	U	Y	Y	6
Khubchandani et al. (2021)	Y	Y	Y	Y	Y	U	Y	Y	7
Kreps et al. (2020)	Y	Y	Y	Y	Y	Y	Y	Y	8
Schwarzinger et al. (2021)	Y	Y	Y	Y	Y	Y	Y	Y	8
Al-Qerem et al. (2021)	Y	Y	Y	Y	U	U	Y	Y	6
Yigit et al. (2021)	Y	Y	Y	Y	N	N	Y	Y	6
Murphy et al. (2021)	Y	Y	Y	Y	U	U	Y	Y	6
Dror et al. (2020)	Y	Y	Y	Y	Y	Y	Y	Y	8
Unroe et al. (2021)	Y	Y	U	U	Y	U	Y	Y	5
Latkin et al. (2021) - <i>COVID-19 VACCINE INTENTIONS</i>	Y	Y	Y	Y	Y	U	Y	Y	7
Olagoke et al. (2021)	Y	Y	Y	Y	Y	Y	Y	Y	8
Chew et al. (2021)	Y	Y	Y	U	U	U	Y	Y	5
Freeman et al. (2020)	Y	Y	Y	Y	Y	Y	Y	Y	8

Yurttas et al. (2021)	Y	Y	Y	Y	Y	N	Y	Y	6
Papagiannis et al. (2021)	Y	Y	U	Y	N	N	Y	Y	5
Vallis et al. (2021)	Y	Y	Y	Y	Y	N	Y	Y	7
Motta et al. (2021)	Y	Y	Y	Y	Y	Y	Y	Y	8
Scott et al. (2021)	Y	Y	Y	Y	U	U	Y	Y	6
Borriello et al. (2021)	Y	Y	Y	Y	Y	N	Y	Y	7
di Gennaro et al. (2021)	Y	Y	Y	Y	U	U	Y	Y	6
Wang et al. (2021)	Y	Y	U	U	Y	U	Y	Y	5
Alabdulla et al. (2021)	Y	Y	U	Y	Y	Y	Y	Y	7
Kaplan et al. (2021)	Y	Y	Y	Y	U	U	Y	Y	6
Verger et al. (2021)	Y	Y	Y	Y	Y	Y	Y	Y	8
Qattan et al. (2021)	Y	Y	Y	Y	Y	U	Y	Y	7
Gagneux-Brunon et al. (2021)	Y	Y	U	U	Y	N	Y	Y	5
Edwards et al. (2021)	Y	Y	Y	Y	Y	Y	Y	Y	8
Mercadante et al. (2020)	Y	Y	Y	Y	Y	N	Y	Y	7
Williams et al. (2021)	Y	Y	Y	Y	Y	N	Y	Y	7
Salali et al. (2020)	Y	Y	N	N	U	U	Y	Y	4
Kwok et al. (2021)	Y	Y	Y	Y	Y	Y	Y	Y	8
Pogue et al. (2020)	Y	Y	Y	Y	Y	U	Y	Y	7
Wang et al. (2020)	Y	Y	U	U	U	N	Y	Y	4

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