SYSTEMATIC REVIEW

Global intention of the general public to undergo COVID-19 vaccination: time trends and risk factors for vaccine refusal, a Systematic Review and Meta-analysis [version 1; peer review: 1 approved with reservations]

Ashwaghosha Parthasarathi ¹, Rahul Krishna Puvvada², S Basappa³, Mamidipudi Thirumala Krishna⁴, Mahesh P A ⁵

¹Allergy, Asthma and Chest Centre, Mysore, Karnataka, 570022, India

²Department of Physiology, Anatomy, and Microbiology, College of Science Health and Engineering, La Trobe University, Bundoora, Australia

³Department of Studies in Organic Chemistry, University of Mysore, Mysore, Karnataka, 570002, India

⁴Department of Allergy and Immunology, University Hospitals Birmingham NHS Foundation Trust; Institute of Immunology Immunotherapy and Institute of Clinical Sciences, University of Birmingham, Birmingham, UK

⁵Department of Pulmonology, JSS Medical College, Mysore, Karnataka, 570004, India

v1 First published: 19 Jan 2022, 7:17
<https://doi.org/10.12688/wellcomeopenres.17517.1>
 Latest published: 19 Jan 2022, 7:17
<https://doi.org/10.12688/wellcomeopenres.17517.1>

Abstract

Background: Knowledge of facilitators and barriers regarding the uptake of COVID-19 vaccination at a global population level is critical for combating the pandemic, saving lives, and protecting the economy. The aim of this work was to determine the proportion of people likely to accept or refuse to undergo COVID-19 vaccination. This study also investigated (a) time trends regarding the intention to undergo COVID-19 vaccination and (b) socio-demographic risk factors influencing vaccine refusal.

Methods: Databases (01 March 2020-01 March 2021) searched included PubMed, MEDLINE, and Scopus. The sample size was $n \geq 1000$ and selected studies were those that determined vaccine 'acceptance', 'refusal' and 'hesitancy'. A random-effects model was employed to obtain the overall odds ratio (OR) and 95% confidence interval (CI) for socio-demographic predictors for vaccine refusal.

Results: A total of 832 citations were screened and 35 studies from 21 countries ($n=130,179$) were analyzed. The pooled proportion of individuals reporting an intention to vaccinate was 0.70 (95% CI: 0.65 to 0.74; $I^2 = 99.68\%$). The proportion of people intending to vaccinate decreased (regression coefficient = -0.13; $p < 0.001$) during the study period and odds of refusal to vaccinate increased by 1.37-fold (95% CI: 1.33-1.41) during the second half. Risk factors identified for vaccine refusal included being female, rural residence, lower income, and

Open Peer Review

Approval Status ?

1

version 1

19 Jan 2022

[view](#)

1. Rema Ramakrishnan , University of Oxford, Oxford, UK

Any reports and responses or comments on the article can be found at the end of the article.

lower level of formal education.

Conclusions: A moderate proportion of people showed an intention to receive vaccination, although this declined during the study period. A global and national multi-pronged strategic and targeted approach is urgently needed to enhance vaccination uptake amongst females, those with a relatively lower educational and socioeconomic status, and those in rural areas.

Keywords

COVID-19, COVID-19 vaccine, vaccine refusal, vaccine hesitancy, risk factors

Corresponding author: Mahesh P A (maresh1971in@yahoo.com)

Author roles: **Parthasarathi A:** Conceptualization, Data Curation, Formal Analysis, Methodology, Writing – Original Draft Preparation, Writing – Review & Editing; **Puvvada RK:** Data Curation, Formal Analysis, Validation, Writing – Original Draft Preparation, Writing – Review & Editing; **Basappa S:** Methodology, Validation, Writing – Original Draft Preparation, Writing – Review & Editing; **Krishna MT:** Methodology, Supervision, Validation, Writing – Original Draft Preparation, Writing – Review & Editing; **P A M:** Conceptualization, Methodology, Project Administration, Supervision, Validation, Writing – Original Draft Preparation, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: This work was supported by Wellcome [IA/TSG/19/1/600026].

Copyright: © 2022 Parthasarathi A *et al.* This is an open access article distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Parthasarathi A, Puvvada RK, Basappa S *et al.* **Global intention of the general public to undergo COVID-19 vaccination: time trends and risk factors for vaccine refusal, a Systematic Review and Meta-analysis [version 1; peer review: 1 approved with reservations]** Wellcome Open Research 2022, 7:17 <https://doi.org/10.12688/wellcomeopenres.17517.1>

First published: 19 Jan 2022, 7:17 <https://doi.org/10.12688/wellcomeopenres.17517.1>

Introduction

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) causes coronavirus disease-19 (COVID-19); the World Health Organization (WHO) declared a pandemic status on 11 March 2020 and by 01 April 2021, an estimated 157 million people had been infected worldwide and the disease had claimed over 3.3m lives¹. A cumulative loss of nine trillion US dollars has been predicted by the end of 2022 due to the COVID-19 pandemic².

It has been suggested from a public health perspective that immunity in the population, or “herd” immunity, needs to be at least 67% to combat the pandemic³. This requires a successful global vaccination program. However, vaccine hesitancy or refusal is an important and recognized barrier to the attainment of herd immunity⁴. Previous experience suggests that multiple factors might influence vaccine uptake including age, gender, education and socio-economic status, rural/urban residence, co-morbidity, access to healthcare, health service framework, cultural, social, and religious determinants, adverse events, and other hitherto unknown reasons⁴. Therefore, vaccination uptake might be variable in different parts of the world, thereby leading to varying levels of herd immunity. Understanding facilitators and barriers to the vaccination program is critical to shaping concerted global and national strategies to enhance herd immunity, as a means to prevent transmission of infection in the community and save lives. Multiple studies have surveyed populations in different countries to investigate vaccine uptake, hesitancy, and/or refusal alongside exploring reasons underpinning these decisions and human behavior^{5–8}.

The primary objective of this systematic review and meta-analysis was to determine the proportion of people that are likely to accept or refuse to undergo COVID-19 vaccination. The secondary objective was to determine (a) time trends regarding the intention to undergo COVID-19 vaccination and (b) socio-demographic risk factors influencing vaccine refusal.

Methods

Eligibility criteria

The studies included in this study determined vaccine ‘acceptance’, ‘refusal’, and ‘hesitancy’. Only published studies with a minimum sample size of 1,000 involving the ‘general public’ were included. The rationale of this approach was to avoid sampling error⁹. To enhance generalizability and meaningful interpretation of the dataset in the context of the general population, studies restricted to specific subgroups such as healthcare workers, the elderly or vulnerable populations, or students, were excluded. All included studies measured ‘acceptance’ and ‘refusal’ of the COVID-19 vaccine. This systematic review was registered on PROSPERO (CRD42021251705).

Data extraction (selection and coding)

This review was conducted following the PRISMA guidelines (*Extended data*)¹⁰. PubMed, MEDLINE, and Scopus databases were searched for published articles in peer-reviewed journals from 01 March 2020 to 01 March 2021. Search terms related to COVID-19 vaccination intentions such as COVID-19,

coronavirus, or SARS-CoV-2 along with “vaccine acceptance, refusal or hesitancy” were used. Vaccine hesitancy was recorded as “unsure” in all the studies. A full list of search terms used is shown in Appendix-1 (*Extended data*)¹⁰.

Studies were managed using DistillerSR and Microsoft Excel v16. The study selection involved two rounds of screening:

1. Title/abstract screening: Two operators (AP and RKP) screened all articles independently. The title or abstract of included articles contained ‘vaccine intentions’ or a synonym. Any conflicts were resolved by a senior operator (PAM).
2. Full-text screening: AP and RKP independently performed the full-text review of included studies. Those with data on vaccine ‘acceptance’, ‘refusal’, or ‘hesitancy’ and the factors influencing vaccine uptake were included for the data synthesis. The third operator (PAM) was consulted when there were conflicts concerning decisions between operators AP and RKP.

Data synthesis. The data from all included studies were extracted and entered in a designed data collection form (Microsoft Excel) which included the following parameters:

- The surname of first author, year of publication, and sample size
- Prevalence of COVID-19 vaccine ‘acceptance’, ‘refusal’, and ‘hesitancy’
- Socioeconomic class, gender, level of education, age, area of housing (urban/rural)

Assessment of bias risk. The risk of bias for each publication was assessed using the following “quality assessment checklist for prevalence studies (adapted from Hoy *et al.*¹¹)” criteria:

- Study population (needed to be specified and defined).
- The study sample needed to be a close representation of the national population concerning relevant variables, e.g., age, gender.
- At least 50% participation rate.
- Direct data collection method as opposed to a proxy method.
- Uniform methodology of data collection.
- Clearly stated research question/s or study objective/s.
- Standardized process of participant recruitment including time period.

Synthesis of evidence

Analysis was performed in the ‘metaviz’, ‘meta’, ‘metafor’ and ‘ggplot2’ packages in Rstudio (R Development Core Team, 2008).

A forest plot was constructed to illustrate vaccine ‘acceptance’, ‘refusal’, or ‘hesitancy’ as raw proportions from individual

studies. A subgroup analysis of studies pooled based on continental classification including Asia, North America, Australia, and Europe was performed. The value of the proportions ranged from 0 to 1 (1=100% of the population). Raw proportions were also used to create a bubble plot, with each country identified by a specific color, the sample size denoted by the size of the bubble and the site allocation of the bubble representing the month of data collection for the study on the x-axis and the raw proportions on the y-axis.

In order to control for skewness between different studies, log transformation of raw proportions was conducted. This was followed by back-transformation¹²⁻¹⁴ to calculate pooled proportions for vaccine intentions and meta-regression for vaccine intentions between countries, continents, and Low- and Middle-Income Countries (LMIC) versus High-Income Countries (HIC) (the classification based on the World Bank's allocation of the world's economies¹⁵). A meta-regression analysis was also performed to evaluate the temporal variation, using two variables including transformed proportions of vaccine acceptance and the month of data collection.

Socio-demographic predictors such as gender, age group, formal education, urbanicity, and income were measured and analyzed across studies. We used [Review Manager](#) software

version 5.4 (Nordic Cochrane Center, Copenhagen, Denmark), to create forest plots to assess overall risk by pooling estimates for independent risk factors. The random-effects method was used to pool the odds ratios (ORs) and 95% confidence intervals (CIs).

Heterogeneity was assessed using I^2 statistic, which describes the percentage variation across studies that is due to heterogeneity rather than by chance¹⁶. Leave-one-out analysis was performed to examine the stability of the pooled estimates and to recognize any dominant samples within the analysis. To examine potential publication bias and small study bias, funnel plots for asymmetry and 'Rank test' were employed as the meta-analysis included >25 studies¹⁷. Trim and Fill analysis was employed to correct for asymmetry around the pooled estimates¹⁸. A sub-group analysis was conducted to investigate the results between different data collection methods, and whether they had an 'unsure' response option.

Results

Our search identified 832 citations between 01 March 2020 and 01 March 2021. After study screening and eligibility selection, 35 studies were included in the systematic review ([Figure 1](#)). The meta-analysis included large samples from

Figure 1. Study screening and selection flowchart. Study screening and selection mapped out as a PRISMA flow diagram depicting the flow of information through the different phases of the systematic review. It maps out the number of records identified, included, and excluded, and the reasons for exclusions.

21 countries with a total of 130,179 study subjects. The majority of the studies were from the USA (n=9) and the UK (n=9), China (n=4), and France (n=3). The studies included in the meta-analysis are listed in [Table 1](#). Of the 35 selected studies, the majority used convenience sampling (n=16), followed by quota sampling (n=12), and probability sampling (n=7) methods. The sample size of the studies included in the analysis ranged from 1,000 to 7,547 (median =1,369, interquartile range=1,581). There were 20 studies between 01 March 2020 and 30 June 2020, i.e., the first half of the study period, and 15 studies between 01 July 2020 and 31 January 2021, i.e., the second half of the study period.

Vaccine intentions

Across the 35 studies, the pooled proportion of individuals reporting an intention to vaccinate was 0.70 (95% CI: 0.65 to 0.74; $I^2 = 99.68\%$). The proportion of individuals not intending

to vaccinate was 0.16 (95% CI: 0.12 to 0.20; $I^2 = 99.56\%$). Those who were unsure about vaccination amounted to 0.22 (95% CI: 0.19 to 0.25; $I^2 = 98.87\%$) ([Figure 2](#)). The sum of these proportions does not equal 1 as not all studies included an “unsure” response option. See Appendix (*Extended data*)⁶ for further details.

There were no significant differences in the proportion of participants’ intention to vaccinate when considering two options (yes and no) versus three options (yes, unsure, and no) ($p=0.08$). Vaccine acceptance rates when only two options were given were 0.73 (95% CI: 0.66–0.78) while rates when three options were given, were 0.68 (95% CI: 0.62–0.74). The same was true for vaccine refusal rates.

Time trends for vaccine intentions

A significant association was detected between intention to undergo vaccination and time ([Figure 3 \(a\)](#)). Over the study

Table 1. Characteristics of the included studies.

Author	Year of Publication	Month of the study conducted	Country	Sample size (N)	Intention results
Abedin ⁵	2021	January	Bangladesh	3646	<ul style="list-style-type: none"> o Yes: 74.5% o Unsure: 17% o No: 8.5%
Al-Qerem ¹⁹	2021	October	Jordan	1144	<ul style="list-style-type: none"> o Yes: 36.8% o Unsure: 26.4% o No: 36.8%
Alfageeh ²⁰	2021	December	Saudi Arabia	2137	<ul style="list-style-type: none"> o Yes: 48.4% o No: 52%
Allington ²¹	2020	June	UK	1663	<ul style="list-style-type: none"> o Yes: 69% o Unsure: 15% o No: 16%
Allington ²¹	2020	June	US	1198	<ul style="list-style-type: none"> o Yes: 59% o Unsure: 15% o No: 25%
Callaghan ²²	2021	May-June	United States	5009	<ul style="list-style-type: none"> o Yes: 69% o No: 31%
Chen ²³	2020	May-June	China	3195	<ul style="list-style-type: none"> o Yes: 83.8%) o No: 16.2%
Craig ²⁴	2021	November	US	1153	<ul style="list-style-type: none"> o Yes: 61.06% o Unsure: 22.38% o No: 16.57%
Daly ²⁵	2020	October	United States	7547	<ul style="list-style-type: none"> o Yes: 54% o Unsure: 14% o No: 32%
Edwards ²⁶	2021	August	Australia	3061	<ul style="list-style-type: none"> o Yes: 87% o No: 13%
Feleszko ⁶	2021	June	Poland	1066	<ul style="list-style-type: none"> o Yes: 37% o Unsure: 34% o No: 28%

Author	Year of Publication	Month of the study conducted	Country	Sample size (N)	Intention results
Freeman ²⁷	2020	May	UK	2501	<ul style="list-style-type: none"> Yes: 88% No: 12%
Gan ²⁸	2021	October-November	China	1009	<ul style="list-style-type: none"> Yes: 60.4% No: 7.13% Unsure: 32.5%
Graffigna ⁸	2020	May	Italy	1004	<ul style="list-style-type: none"> Yes: 59% Unsure: 26% No: 15%
Harapan ²⁹	2020	March-April	Indonesia	1359	<ul style="list-style-type: none"> Yes: 93.3% No: 6.7%
Khubchandani ³⁰	2021	June	US	1878	<ul style="list-style-type: none"> Yes: 67.8% No: 32.2%
Kourlaba ³¹	2021	April-May	Greece	1004	<ul style="list-style-type: none"> Yes: 57.7% No: 26% Unsure: 16.3%
Leigh ³²	2020	April-May	Canada	1996	<ul style="list-style-type: none"> Yes: 76% Unsure: 13% No: 11%
Lin ³³	2020	May	China	3541	<ul style="list-style-type: none"> Yes: 83.5% No: 16.4%
Loomba ³⁴	2021	September	UK	4000	<ul style="list-style-type: none"> Yes: 54.1% Unsure: 39.9% No: 6%
Loomba ³⁴	2021	September	US	4001	<ul style="list-style-type: none"> Yes: 44% Unsure: 41% No: 15%
Murphy ³⁵	2020	March-April	Ireland	1041	<ul style="list-style-type: none"> Yes: 65% Unsure: 26% No: 9%
Murphy ³⁵	2020	March	UK	2025	<ul style="list-style-type: none"> Yes: 69% Unsure: 25% No: 6%
Neumann-Böhme ⁷	2020	April	Netherlands	1012	<ul style="list-style-type: none"> Yes: 73% Unsure: 19% No: 8%
Neumann-Böhme ⁷	2020	April	Portugal	1064	<ul style="list-style-type: none"> Yes: 75% Unsure: 21% No: 5%
Neumann-Böhme ⁷	2020	April	Denmark	1000	<ul style="list-style-type: none"> Yes: 80% Unsure: 12% No: 8%
Neumann-Böhme ⁷	2020	April	France	1000	<ul style="list-style-type: none"> Yes: 62% Unsure: 28% No: 10%
Neumann-Böhme ⁷	2020	April	Germany	1002	<ul style="list-style-type: none"> Yes: 70% Unsure: 20% No: 10%
Neumann-Böhme ⁷	2020	April	UK	1009	<ul style="list-style-type: none"> Yes: 79% Unsure: 15% No: 6%

Author	Year of Publication	Month of the study conducted	Country	Sample size (N)	Intention results
Paul ³⁶	2020	September	UK	32,361	<ul style="list-style-type: none"> o Yes: 63.5% o Unsure: 22.5% o No: 14%
Reiter ³⁷	2020	May	US	2006	<ul style="list-style-type: none"> o Yes: 69% o No: 31%
Reno ³⁸	2021	January	Italy	1011	<ul style="list-style-type: none"> o Yes: 68.9% o Unsure: 31.1%
Romer ³⁹	2020	March	US	1050	<ul style="list-style-type: none"> o Yes: 86% o No: 15%
Roozenbeek ⁴⁰	2020	April-May	UK	1150	<ul style="list-style-type: none"> o Yes: 79% o No: 21%
Salali ⁴¹	2020	May	Turkey	3936	<ul style="list-style-type: none"> o Yes: 66% o Unsure: 31% o No: 3%
Salali ⁴¹	2020	May	UK	1088	<ul style="list-style-type: none"> o Yes: 83% o Unsure: 14% o No: 3%
Sallam ⁴²	2020	December	Jordan	2173	<ul style="list-style-type: none"> o Yes: 28.4% o No: 71.6%
Schwarzinger ⁴³	2021	June and July	France	1942	<ul style="list-style-type: none"> o No: 28.8% o Yes: 71.16%
Sherman ⁴⁴	2020	July	UK	1504	<ul style="list-style-type: none"> o Yes: 64% o Unsure: 27% o No: 9%
Taylor ⁴⁵	2020	May	Canada	1902	<ul style="list-style-type: none"> o Yes: 80% o No: 20%
Taylor ⁴⁵	2020	May	US	1772	<ul style="list-style-type: none"> o Yes: 75% o No: 25%
Wang ⁴⁶	2021	January	China	8742	<ul style="list-style-type: none"> o Yes: 67.1% o No: 9%
Ward ⁴⁷	2020	April	France	5018	<ul style="list-style-type: none"> o Yes: 76% o No: 24%
Wong ⁴⁸	2020	April	Malaysia	1159	<ul style="list-style-type: none"> o Yes: 94.3% o No: 5.7%
Yoda ⁴⁹	2021	September	Japan	1100	<ul style="list-style-type: none"> o Yes: 65.7% o No: 12.3% o Unsure: 22%

period, vaccine acceptance significantly ($p < 0.001$) decreased (regression coefficient [reg coeff]: -0.13). The odds of refusal to vaccinate increased by 1.37-fold (95% CI: 1.33–1.41) during the second half of the study period (Figure 3 (b)). See Appendix (Extended data)⁶ for further details.

Intercountry comparison

Sub-group analysis was conducted to compare differences between countries. Three countries with the largest number of studies, i.e., the USA, UK, and China were included. There were

nine studies from the USA showing similar results as the main analysis (reg coeff: -0.17, $p < 0.001$). The same pattern was seen in the nine samples from the UK (reg coeff: -0.21, $p = 0.006$) and four samples from China (reg coeff: -0.14, $p = 0.0237$).

An increase in vaccine refusal rates was detected across all countries. Whilst the odds of vaccine refusal in the USA increased by 1.12 (95%CI: 1.12–1.25) during the second half of the study period, studies from the UK and China showed a 1.66 (95%CI: 1.47–1.88) and 1.52 (95%CI: 1.39–1.66)-fold increase

Figure 2. Raw proportions for vaccine acceptance, refusal and hesitancy. The figure illustrates the raw proportions of vaccine intentions of participants. Vaccine acceptance and refusal were reported in all 35 studies, while hesitancy was reported in 19 studies. *Proportions are represented by boxes, with the size of the box representing its weight. Horizontal lines represent 95% CIs. The diamond represents combined pooled proportions.

in the odds of refusal to vaccination respectively (Figure 3 (b)). See Appendix (*Extended data*)⁶ for further details.

Continent-wise comparison

There were 12 studies from Asia, 11 from Europe, 21 from North America, and one from Australia. There were no significant differences in the intention to undergo vaccination between continents (reg coeff: 0.02, $p=0.62$). Intention to undergo vaccination was however highest in Australia at 0.87 (95% CI: 0.85–0.88) followed by Asia 0.70 (95% CI: 0.55–0.81), Europe 0.69 (95% CI: 0.644–0.744), while North America had the lowest at 0.68 (95% CI: 0.60–0.75). See Appendix (*Extended data*)⁶ for further details.

HICs versus LMICs

There were 35 studies involving 39 study sites from HICs whilst only 6 were from LMICs. There were no significant differences in intention to undergo vaccination between HICs and LMICs (reg coeff: 0.07, $p=0.84$). Vaccination acceptance proportions in HIC countries (0.69, 95% CI: 0.65–0.73) were similar to LMIC countries (0.71, 95% CI: 0.42–0.89). See Appendix-1 (*Extended data*)⁶ for further details.

Risk factors for vaccine refusal

Studies evaluated multiple risk factors associated with vaccine refusal including age, gender, education status, income status, and area of residence.

Gender. A total of 23 studies estimated the effect of gender as a risk for vaccine refusal. Whilst 12 studies found a significant

association, others showed no such association between gender and vaccine refusal. Pooled estimates of 23 studies showed that females (OR 1.34; 95%CI (1.23–1.45)) were more likely to refuse vaccination. Due to the presence of significant heterogeneity ($I^2=71\%$), a random effect model was opted for instead of a fixed-effect model (Figure 4 (a)).

Place of residence

A total of 11 studies evaluated the influence of the place of residence on vaccine refusal. Whilst seven studies observed no significant association between place of residence and vaccine refusal, four studies reported that rural residence was a risk factor for vaccine refusal. Of the four studies, one⁴⁶ significantly influenced the pooled estimates. It was observed that people residing in rural areas (OR 1.16; 95% CI (1.10–1.22)) had a higher risk of vaccine refusal. Due to the presence of very low heterogeneity ($I^2=27\%$), the fixed effect model was opted over the random effect model (Figure 4 (b)).

Level of education

A total of 18 studies evaluated whether the level of formal education (education by trained teachers in a systematic intentional way within an institution) influenced vaccine refusal. Six studies observed that people with lower formal education were more likely to refuse vaccination. The pooled estimates showed that a lower level of formal education (OR 1.18; 95% CI 1.05–1.33) enhanced odds for vaccine refusal when compared with people from a higher level of education. Due to significant heterogeneity ($I^2=76\%$), the random effect model was considered over the fixed effect model (Figure 5 (a)).

Figure 3. A: Temporal variation of vaccine acceptance in different countries. The bubble plot illustrates time trends of vaccine acceptance. Each country is identified by a specific color; the sample size denoted by the size of the bubble, and the site allocation of the bubble representing the month of data collection for the study in the x-axis and the raw proportions on the y-axis. **B:** Odds OF VACCINE refusal in the second half of the study period when compared to the first half. The figure illustrates the changes in odds of vaccine refusal rates in countries with multiple samples in the first and second halves of the study. *Proportions are represented using a circle marker. Horizontal lines represent 95% CIs.

Figure 4. A: Effect sizes and summary estimates of studies which have included gender as a risk for vaccine refusal. The forest plot illustrates the pooled estimate of the role of gender as a risk for vaccine refusal. The random effects model of analysis was used, as heterogeneity was high. Females were 34% more likely to refuse the vaccine compared to males. **B:** Effect sizes and summary estimates of studies which included the area of residence as a risk for vaccine refusal. The forest plot illustrates the pooled estimate of the role of the area of residence as a risk for vaccine refusal. The random effects model of analysis was used as heterogeneity was high. People living in rural areas were 17% more likely to refuse the vaccine compared to people residing in urban areas.

Income

A total of 12 studies evaluated the effect of income on vaccine refusal. Five studies observed that subjects with lower income had higher vaccine refusal rates, whilst other studies found no such association. Pooled estimates showed that people with lower income (OR 1.28; 95% CI 1.06–1.54) had a higher risk of vaccine refusal. The random-effect model was

chosen due to the presence of high heterogeneity ($I^2=85\%$) instead of the fixed-effect model (Figure 5 (b)).

Age

Seventeen studies evaluated whether age influenced vaccine refusal. Thirteen studies showed no significant association between age and vaccine refusal, whilst four studies showed

Figure 5. A: Effect sizes and summary estimates of studies which included level of education as a risk for vaccine refusal. The forest plot illustrates the pooled estimate of the role of formal education as a risk for vaccine refusal. The random effects model of analysis was used as heterogeneity was high. People with a lower level of education were 22% more likely to refuse the vaccine compared to those with a higher level of education. **B:** Effect sizes and summary estimates of studies which included income as a risk for vaccine refusal. The forest plot illustrates the pooled estimate of the role of income as a risk for vaccine refusal. The random effects model of analysis was used as heterogeneity was high. People with a lower income were 32% more likely to refuse the vaccine compared with higher income.

that age had an effect. The pooled estimates revealed that age did not significantly (OR 0.88; 95% CI (0.72–1.07)) influence vaccine refusal. There was significant heterogeneity ($I^2=89\%$) in these studies, therefore, a random effect model was chosen (Appendix: Figure s4, *Extended data*⁶).

Tests for publication bias

A minimal publication bias was detected. There was little evidence for differences in findings between studies using probability versus non-probability-based sampling method, with the exception of vaccine hesitancy subset, whose responses were lower in probability-based samples selection. A detailed report on publication bias is shown in Appendix (*Extended data*)⁶.

Discussion

This is the first study to conduct a systematic review and meta-analysis of studies that investigated public intention to undergo COVID-19 vaccination, report time trends, and evaluate effect sizes of risk factors influencing these decisions. This study included a relatively large cumulative sample size of 130,179 participants from 35 nationally representative studies across 21 countries and 4 continents. Pooled data showed that a moderate proportion of the global population showed an intention to undergo COVID-19 vaccination. However, across all countries, there was a consistent but variable decline in the proportion of participants willing to undergo vaccination during the study period. Pooled data showed that female gender, rural residence, lower income, and lower formal education were associated with a higher risk of vaccine refusal.

A negative attitude towards vaccination is a recognized human behavior and has been previously reported in the context of diphtheria, tetanus, and pertussis (DTaP) boosters, pneumococcus,

and annual seasonal influenza vaccines amongst adults and childhood vaccines such as measles, mumps, rubella, and DTaP⁵⁰.

Several factors might potentially explain COVID-19 vaccine refusal or hesitancy amongst the general population. First, the unprecedented nature of the global crisis, its potential impact on the socio-economic situation and mental wellbeing^{51,52}, alongside the fast-tracked research and development, and licensing of vaccines has not allowed sufficient time for strategic dissemination and education amongst the general population and healthcare professionals (HCPs) worldwide⁵³. Second, disproportionately publicized adverse events such as anaphylaxis⁵⁴ and thrombotic thrombocytopenia⁵⁵ in social media and other channels, without meaningful contextualization for the general public, the latter particularly in females <30 years of age reported during the post-licensing phase, might have potentially contributed to uncertainty and anxiety amongst the general population and healthcare professionals, and influenced behavior and perceptions. For example, the UK vaccination program was temporarily paused amongst patients with unrelated allergies such as to food, *Hymenoptera* venom, and drugs, for a few weeks, until revised recommendations were published by the Medicines and Healthcare Products Regulatory Agency⁵⁶. Other unsubstantiated reports regarding vaccines potentially affecting menstrual periods and fertility may also have influenced women against COVID-19 vaccination^{57,58}. Third, mixed messages delivered via mass media might also have influenced public perceptions, behavior, and beliefs.

Pooled estimates of studies that evaluated income as a risk factor revealed that those with lower incomes were

significantly more likely to refuse the vaccination. This is in contrast to previous experience concerning childhood immunization, which showed that educated and wealthier parents had greater concerns about vaccine safety^{59–61}. It is worth pointing out that only about one-third of the total studies investigated income as one of the predictors.

There are some limitations to this systematic review and meta-analysis. First, LMICs were not adequately represented, making data more biased towards HICs and China. To put this into context, there were no studies from India, which represents nearly 20% of the global population. Given the fundamental differences with respect to ethnicity, religion, social and economic, and other relevant demographic factors, these findings cannot be extrapolated to all LMICs. There is an urgent need to generate data from LMICs in Asia, Africa, and South America to develop robust global strategies for a successful vaccination program. Second, there was no standardized definition for ‘nationally representative’ samples across different countries, making study sampling methods heterogeneous. Third, there were differences in study methodology between countries. Fourth, sample sizes were variable and wide-ranging (1,000–32,361), although we included studies with a minimum response rate of 50%. Fifth, this systematic review did not delineate vaccine intentions for both doses that are required to achieve maximum protection. It is plausible that a small proportion might potentially drop out of the vaccination program following the first dose.

In conclusion, this study showed a moderate global acceptance rate for COVID-19 vaccination, although there was a decline in the intention to undergo vaccination during the study period. Data showed that female gender, lower-income and educational status, and rural area of residence contributed to vaccine hesitancy and refusal. There is an urgent need for further studies, particularly in LMICs to understand facilitators and barriers for vaccine uptake to devise feasible and fit-for-purpose intervention strategies to convert ‘hesitant’ subjects to ‘vaccine acceptors’, to achieve much-needed herd immunity to combat the COVID-19 pandemic.

Data availability

Underlying

Open Science Framework: COVID vaccination SR, <https://doi.org/10.17605/OSF.IO/PX73Q62>

This project contains the following underlying data:

- COVID_SR_All_studies.xlsx: All study characteristics

Extended data

Open Science Framework: COVID vaccination SR, <https://doi.org/10.17605/OSF.IO/PX73Q62>

This project contains the following extended data:

- COVID_SR_Appendix_Wellcome.docx : Supplementary data (study search terms, additional results, supplementary figures)
- COVID_SR_PRISMA checklist and flowchart.docx: PRISMA Checklist and Flowchart

Analysis code

Analysis code available from GitHub at https://github.com/Ashwa17/COVID_VACCINE_SR

Archived analysis code as at time of publication: <https://zenodo.org/badge/latestdoi/10.5281/zenodo.439583986>

License: [Apache-2.0](#)

Reporting guidelines

Open Science Framework: PRISMA checklist for “Global intention of the general public to undergo COVID-19 vaccination: time trends and risk factors for vaccine refusal, a Systematic Review and Meta-analysis”, <https://doi.org/10.17605/OSF.IO/PX73Q62>

Data are available under the terms of the [Creative Commons Attribution 4.0 International license](#) (CC-BY 4.0).

References

1. Worldmeter. [Reference Source](#)
2. International Monetary Fund Blog: **The great lockdown: worst economic downturn since the great depression.** [Reference Source](#)
3. Randolph HE, Barreiro LB: **Herd Immunity: Understanding COVID-19.** *Immunity.* 2020; **52**(5): 737–741. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
4. Dubé E, Laberge C, Guay M, *et al.*: **Vaccine hesitancy: an overview.** *Hum Vaccin Immunother.* 2013; **9**(8): 1763–1773. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
5. Abedin M, Islam MA, Rahman FN, *et al.*: **Willingness to vaccinate against COVID-19 among Bangladeshi adults: Understanding the strategies to optimize vaccination coverage.** *PLoS One.* 2021; **16**(4): e0250495. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
6. Feleszko W, Lewulis P, Czarnecki A, *et al.*: **Flattening the Curve of COVID-19 Vaccine Rejection-An International Overview.** *Vaccines (Basel).* 2021; **9**(1): 44. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
7. Neumann-Böhme S, Varghese NE, Sabat I, *et al.*: **Once we have it, will we use it? A European survey on willingness to be vaccinated against COVID-19.** *Eur J Health Econ.* 2020; **21**(7): 977–982. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
8. Graffigna G, Palamenghi L, Boccia S, *et al.*: **Relationship between Citizens' Health Engagement and Intention to Take the COVID-19 Vaccine in Italy: A Mediation Analysis.** *Vaccines (Basel).* 2020; **8**(4): 576. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)

9. American Association for Public Opinion Research: **Margin of Sampling Error/ Credibility Interval**. 2020.
[Reference Source](#)
10. Moher D, Liberati A, Tetzlaff J, et al.: **Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement**. *PLoS Med*. 2009; 6(7): e1000097.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
11. Hoy D, Brooks P, Woolf A, et al.: **Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement**. *J Clin Epidemiol*. 2012; 65(9): 934–939.
[PubMed Abstract](#) | [Publisher Full Text](#)
12. Feng C, Wang H, Lu N, et al.: **Log-transformation and its implications for data analysis**. *Shanghai Arch Psychiatry*. 2014; 26(2): 105–109.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
13. Nyaga VN, Arbyn M, Aerts M: **Metaprop: a Stata command to perform meta-analysis of binomial data**. *Arch Public Health*. 2014; 72(1): 39.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
14. Borenstein M, Cooper H, Hedges L, et al.: **Effect sizes for continuous data**. *Handb Res Synth Meta-Anal*. 2009; 2: 221–235.
[Reference Source](#)
15. World Bank: **New World Bank country classifications by income level: 2020–2021**. 2020.
[Reference Source](#)
16. Higgins JPT, Thompson SG: **Quantifying heterogeneity in a meta-analysis**. *Stat Med*. 2002; 21(11): 1539–1558.
[PubMed Abstract](#) | [Publisher Full Text](#)
17. Wang N: **How to Conduct a Meta-Analysis of Proportions in R: A Comprehensive Tutorial**. 2018.
[Publisher Full Text](#)
18. Duval S, Tweedie R: **Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis**. *Biometrics*. 2000; 56(2): 455–463.
[PubMed Abstract](#) | [Publisher Full Text](#)
19. Al-Qerem WA, Jarab AS: **COVID-19 Vaccination Acceptance and Its Associated Factors Among a Middle Eastern Population**. *Front Public Health*. 2021; 9: 632914.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
20. Alfageeh EI, Alshareef N, Angawi K, et al.: **Acceptability of a COVID-19 Vaccine among the Saudi Population**. *Vaccines (Basel)*. 2021; 9(3): 226.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
21. Allington D, McAndrew S, Moxham-Hall V, et al.: **Coronavirus conspiracy suspicions, general vaccine attitudes, trust and coronavirus information source as predictors of vaccine hesitancy among UK residents during the COVID-19 pandemic**. *Psychol Med*. 2021; 1–12.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
22. Callaghan T, Moghtaderi A, Lueck JA, et al.: **Correlates and disparities of intention to vaccinate against COVID-19**. *Soc Sci Med*. 2021; 272: 113638.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
23. Chen M, Li Y, Chen J, et al.: **An online survey of the attitude and willingness of Chinese adults to receive COVID-19 vaccination**. *Hum Vaccin Immunother*. 2021; 17(7): 2279–2288.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
24. Craig BM: **United States COVID-19 Vaccination Preferences (CVP): 2020 Hindsight**. *Patient*. 2021; 14(3): 309–318.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
25. Daly M, Robinson E: **Willingness to Vaccinate Against COVID-19 in the U.S.: Representative Longitudinal Evidence From April to October 2020**. *Am J Prev Med*. 2021; 60(6): 766–773.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
26. Edwards B, Biddle N, Gray M, et al.: **COVID-19 vaccine hesitancy and resistance: Correlates in a nationally representative longitudinal survey of the Australian population**. *PLoS One*. 2021; 16(3): e0248892.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
27. Freeman D, Loe BS, Chadwick A, et al.: **COVID-19 vaccine hesitancy in the UK: the Oxford coronavirus explanations, attitudes, and narratives survey (Oceans) II**. *Psychol Med*. 2020; 1–15.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
28. Gan L, Chen Y, Hu P, et al.: **Willingness to Receive SARS-CoV-2 Vaccination and Associated Factors among Chinese Adults: A Cross Sectional Survey**. *Int J Environ Res Public Health*. 2021; 18(4): 1993.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
29. Harapan H, Wagner AL, Yufika A, et al.: **Acceptance of a COVID-19 Vaccine in Southeast Asia: A Cross-Sectional Study in Indonesia**. *Front Public Health*. 2020; 8: 381.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
30. Khubchandani J, Sharma S, Price JH, et al.: **COVID-19 Vaccination Hesitancy in the United States: A Rapid National Assessment**. *J Community Health*. 2021; 46(2): 270–277.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
31. Kourlaba G, Kourkouni E, Maistrelli S, et al.: **Willingness of Greek general population to get a COVID-19 vaccine**. *Glob Health Res Policy*. 2021; 6(1): 3.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
32. Parsons Leigh J, Fiest K, Brundin-Mather R, et al.: **A national cross-sectional survey of public perceptions of the COVID-19 pandemic: Self-reported beliefs, knowledge, and behaviors**. *PLoS One*. 2020; 15(10): e0241259.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
33. Lin Y, Hu Z, Zhao Q, et al.: **Understanding COVID-19 vaccine demand and hesitancy: A nationwide online survey in China**. *PLoS Negl Trop Dis*. 2020; 14(12): e0008961.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
34. Loomba S, de Figueiredo A, Piatek SJ, et al.: **Measuring the impact of COVID-19 vaccine misinformation on vaccination intent in the UK and USA**. *Nat Hum Behav*. 2021; 5(3): 337–348.
[PubMed Abstract](#) | [Publisher Full Text](#)
35. Murphy J, Vallières F, Bental RP, et al.: **Psychological characteristics associated with COVID-19 vaccine hesitancy and resistance in Ireland and the United Kingdom**. *Nat Commun*. 2021; 12(1): 29.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
36. Paul E, Steptoe A, Fancourt D: **Attitudes towards vaccines and intention to vaccinate against COVID-19: Implications for public health communications**. *Lancet Reg Health Eur*. 2021; 1: 100012.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
37. Reiter PL, Pennell ML, Katz ML: **Acceptability of a COVID-19 vaccine among adults in the United States: How many people would get vaccinated?** *Vaccine*. 2020; 38(42): 6500–6507.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
38. Reno C, Maietti E, Fantini MP, et al.: **Enhancing COVID-19 Vaccines Acceptance: Results from a Survey on Vaccine Hesitancy in Northern Italy**. *Vaccines (Basel)*. 2021; 9(4): 378.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
39. Romer D, Jamieson KH: **Conspiracy theories as barriers to controlling the spread of COVID-19 in the U.S.** *Soc Sci Med*. 2020; 263: 113356.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
40. Roozenbeek J, Schneider CR, Dryhurst S, et al.: **Susceptibility to misinformation about COVID-19 around the world**. *R Soc Open Sci*. 2020; 7(10): 201199.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
41. Salali GD, Uysal MS: **COVID-19 vaccine hesitancy is associated with beliefs on the origin of the novel coronavirus in the UK and Turkey**. *Psychol Med*. 2020; 1–3.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
42. Sallam M, Dababseh D, Eid H, et al.: **High Rates of COVID-19 Vaccine Hesitancy and Its Association with Conspiracy Beliefs: A Study in Jordan and Kuwait among Other Arab Countries**. *Vaccines (Basel)*. 2021; 9(1): 42.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
43. Schwarzingen M, Watson V, Arwidson P, et al.: **COVID-19 vaccine hesitancy in a representative working-age population in France: a survey experiment based on vaccine characteristics**. *Lancet Public Health*. 2021; 6(4): e210–e221.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
44. Sherman SM, Smith LE, Sim J, et al.: **COVID-19 vaccination intention in the UK: results from the COVID-19 vaccination acceptability study (CoVaccs), a nationally representative cross-sectional survey**. *Hum Vaccines Immunother*. 2021; 17(6): 1612–1621.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
45. Taylor S, Landry CA, Paluszek MM, et al.: **A Proactive Approach for Managing COVID-19: The Importance of Understanding the Motivational Roots of Vaccination Hesitancy for SARS-CoV2**. *Front Psychol*. 2020; 11: 575950.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
46. Wang C, Han B, Zhao T, et al.: **Vaccination willingness, vaccine hesitancy, and estimated coverage at the first round of COVID-19 vaccination in China: A national cross-sectional study**. *Vaccine*. 2021; 39(21): 2833–2842.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
47. Ward JK, Alleaume C, Peretti-Watel P, et al.: **The French public's attitudes to a future COVID-19 vaccine: The politicization of a public health issue**. *Soc Sci Med*. 2020; 265: 113414.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
48. Wong LP, Alias H, Wong PF, et al.: **The use of the health belief model to assess predictors of intent to receive the COVID-19 vaccine and willingness to pay**. *Hum Vaccines Immunother*. 2020; 16(9): 2204–2214.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
49. Yoda T, Katsuyama H: **Willingness to Receive COVID-19 Vaccination in Japan**. *Vaccines (Basel)*. 2021; 9(1): 48.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
50. CDC: **Immunization**. FastStats, 2020.
[Reference Source](#)
51. Serafini G, Parmigiani B, Amerio A, et al.: **The psychological impact of COVID-19 on the mental health in the general population**. *QJM*. 2020; 113(8): 531–537.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
52. Jaspal R, Breakwell GM: **Socio-economic inequalities in social network, loneliness and mental health during the COVID-19 pandemic**. *Int J Soc Psychiatry*. 2020; 20764020976694.
[PubMed Abstract](#) | [Publisher Full Text](#)
53. McAteer J, Yildirim I, Chahroudi A: **The VACCINES Act: Deciphering Vaccine Hesitancy in the Time of COVID-19**. *Clin Infect Dis*. 2020; 71(15): 703–705.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
54. Shimabukuro T, Nair N: **Allergic Reactions Including Anaphylaxis After**

- Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine.** *JAMA*. 2021; 325(8): 780–781.
[PubMed Abstract](#) | [Publisher Full Text](#)
55. Wise J: **Covid-19: European countries suspend use of Oxford-AstraZeneca vaccine after reports of blood clots.** *BMJ*. 2021; 372: n699.
[PubMed Abstract](#) | [Publisher Full Text](#)
 56. Mahase E: **Covid-19: Oxford researchers halt vaccine trial while adverse reaction is investigated.** *BMJ*. 2020; 370: m3525.
[PubMed Abstract](#) | [Publisher Full Text](#)
 57. Stock: **Some people are reporting abnormal periods after a COVID-19 vaccine. U. of I. professor is looking for answers.**
[Reference Source](#)
 58. Dangerfeild: **Why women are bearing the brunt of COVID-19 vaccine side effects.**
[Reference Source](#)
 59. Cata-Preta B de O, Wehrmeister FC, Santos TM, *et al.*: **Patterns in Wealth-related Inequalities in 86 Low- and Middle-Income Countries: Global Evidence on the Emergence of Vaccine Hesitancy.** *Am J Prev Med*. 2021; 60(1 Suppl 1): S24–S33.
[PubMed Abstract](#) | [Publisher Full Text](#)
 60. Kempe A, Saville AW, Albertin C, *et al.*: **Parental Hesitancy About Routine Childhood and Influenza Vaccinations: A National Survey.** *Pediatrics*. 2020; 146(1): e20193852.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 61. Silveira MF, Buffarini R, Bertoldi AD, *et al.*: **The emergence of vaccine hesitancy among upper-class Brazilians: Results from four birth cohorts, 1982-2015.** *Vaccine*. 2020; 38(3): 482–488.
[PubMed Abstract](#) | [Publisher Full Text](#)
 62. Parthasarathi A: **COVID vaccination SR.** 2022.
<http://www.doi.org/10.17605/OSF.IO/PX73Q>

Open Peer Review

Current Peer Review Status: ?

Version 1

Reviewer Report 24 March 2022

<https://doi.org/10.21956/wellcomeopenres.19369.r49155>

© 2022 Ramakrishnan R. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Rema Ramakrishnan

National Perinatal Epidemiology Unit, Nuffield Department of Population Health, University of Oxford, Oxford, UK

The authors conducted a systematic review and meta-analysis to examine the proportion of people who are likely to accept/refuse COVID vaccine and express hesitancy towards vaccine uptake. They also examine temporal trends and risk factors for vaccine refusal. This is an important topic. The writing is good. However, the methods' section needs some more work and concerns need to be addressed for the results to accurately reflect the study objectives. Specific comments are provided below.

Specific comments:

Title:

- The title should include the primary objective.

Abstract:

- The methods section includes information on only the model used to estimate the odds ratio of socio-demographic predictors for vaccine refusal. It is important to state the effect estimates for all the objectives (especially for the primary objective). That is, random-effects models were used to compute pooled prevalence/proportion, pooled odds ratio...

Introduction:

- Reference #2 is a blog and it specifically indicates that the views expressed are those of the author(s) and do not necessarily represent the views of the IMF and its Executive Board. Please provide another citation.
- The objective could be revised to something along the lines: to determine the proportion of people who are likely to accept and hesitant about COVID vaccines. One can argue that acceptance and refusal are two sides of the same coin. However, hesitancy is important (the results for which the authors have presented but not included in the study objective). If both acceptance and refusal are to be included as study objectives then please provide

justification for this.

- Please consider revising the objective about time trends. It seems inappropriate to compute time trends in intention to undergo vaccination because at each time point the studies are from different countries and therefore wouldn't be appropriate to conduct temporal trend analysis. It would perhaps be more appropriate if the trends were computed by country. Even then this would not be generalizable unless the data were from a nationally-represented sample. If one were to revise this objective then comments related to temporal trends in subsequent sections should be revised too.

Methods:

- Please use the term, 'reviewer', instead of 'operator'.

Eligibility criteria

- In systematic reviews/meta-analysis, it is important to state what type of studies were included – cross-sectional, cohort studies, case-control, etc.
- The rationale for including only studies with a minimum sample size of 1,000 is insufficient. The reference cited includes information on the margin of error that is mainly applicable to probability-based surveys. In the results, it is given that only seven studies used probability sampling.
Please cite an appropriate reference (peer reviewed paper or textbook) to justify this sample size.

Data extraction (selection and coding)

- One of the terms included in the paper was vaccine intention (32 times in the main text including the title). It is, however, unclear why this term was not included in the search strategy. Some papers may have been excluded because of this.
- The search date is a year old. There are many more studies published after March 2021. Please consider revising the results to include studies after this period so that the evidence is current.

Data synthesis:

- It is important to know if there were an overlap between studies/multiple publications from the same cohort and what was done if this happened.
- For risk factors, presumably, odds ratios or some other effect estimate were abstracted and not the raw numbers/proportions. If yes, then please state this. If no, then please provide appropriate information.

Synthesis of evidence:

- The title for this section should be data analysis. Data synthesis was described in the previous section.
- The need for log transformation of proportions is unclear. One does not log-transform categorical/dichotomous variables. Testing for skewness is applicable for continuous variables and not for categorical/dichotomous variables (unless perhaps one estimates

probabilities for a categorical variable).

- Please provide what estimate was computed from the meta-regression analysis of vaccine intentions between countries, continents, and LMIC/HIC. Similarly, provide estimate derived from the meta-regression for temporal variation.
- It is given that sub-group analysis was conducted to investigate the results between different data collection methods, and whether they had an 'unsure' response option. Please specify the subgroups.
- Could you please specify if an analysis was conducted to examine heterogeneity? This is important because from Figure 1 it is evident that was significant heterogeneity not explained by country.
- It is specified that a random effects model was used to pool the odds ratios for the risk factors. Please specify the model used to pool proportions for vaccine intentions. If random effects model was used a sentence common to all analysis can be included.

Results:

- Please use either 832 'articles' or 832 'published studies' or something along these lines instead of 832 citations.
- There is a discrepancy between the number of studies in Table 1 and the description provided in the flowchart and first paragraph of results. It is given that the meta-analysis included large samples from 21 studies with a total of 130,179 study subjects. There are 45 studies in Table 1. The information that there are 9 studies from the UK, 9 from the US (please use either US or United States in the table), 4 from China and 3 from France is correct based on the table. However, the rest of the information in this paragraph are related to 35 studies. Please resolve this confusion/discrepancy.

Vaccine intentions:

- 2nd paragraph: Please provide justification for these results in the methods section. That is, why is it necessary to compare two response options vs three response options?

Time trends for vaccine intentions

- From Figure 2 it seems that vaccine acceptance decline over time in a linear fashion. However, it is not specified that statistical tests were carried out for trends. Therefore, one cannot say that a significant association was detected between intention to receive vaccines. Please provide results of trend test. Furthermore, please provide justification for splitting time into two intervals. It seems to be an arbitrary cutoff (perhaps not with justification). It would be preferable to demonstrate trends using the data itself. One could use something similar to Joinpoint regression which not only allows to examine trends over time but also demonstrate if this trend is linear or if nonlinear at what point in time this change occurs and if this change is significant or not. Other methods could also be used to examine temporal trends more effectively such as adopting an empirical Bayes meta-analysis method outlined in the paper, <https://onlinelibrary.wiley.com/doi/10.1002/bimj.200900307>¹ or interrupted time series to detect change before and after a policy change.

- Another comment is: how studies for which data were not collected in a single month such as Callaghan *et al.* (data collected in May-June) was considered in the temporal trend analysis.

Inter-country comparison:

- It is unclear what these regression coefficients are. It should be proportioned if the authors compared the prevalence of vaccine acceptance between the countries (predictor is country and outcome is prevalence) and the estimates odds ratios/risk ratios. The same comment is applicable for results by continent, country, and HICs vs LMICs.

Risk factors for vaccine refusal:

- Instead of stating in each paragraph that, due to the presence of significant heterogeneity ($I^2 = 71\%$), a random effect model was opted for instead of a fixed-effect model, please state in the methods section that for risk factors a random effects model was used due to significant heterogeneity except for place of residence.
- In the methods, please provide the definition of low education and whether age was considered a continuous variable or did the odds ratio compare certain age groups?

Publication bias:

- The interpretation about no publication bias seems inaccurate for figure S2 because there are no studies at the bottom of the pyramid. The sentence about little evidence for differences in findings between studies using probability versus non-probability-based sampling method seems out of place. The results in the Appendix (section 2.8) for comparison between probability and non-probability-based sampling methods do not pertain to publication bias but to sampling method subgroup analysis.
- Please comment on the risk of bias and consider sensitivity analysis levels of ROB to assess if the estimates differ. The information provided in the figure about the risk of bias is ignored in the text.

Figure 2:

- Please provide a column for weights provided the random effects model after the vaccine acceptance column and columns with numerator/denominator after the studies column. As mentioned above, it is preferable to report either vaccine acceptance or refusal and hesitancy. If both, please provide justification in the introduction section.

Figure 3:

- The authors have reported an increase in vaccine refusal rates during the 2nd half; however, from Figure 2 it seems to be decreasing linear trend. It is confusing because 3A is about vaccine acceptance trends but for comparison between periods it is refusal and so one is not sure these are from the same studies or not. It is preferable to keep either acceptance or refusal.

Figure 4:

- Presentation of log of odds ratio when odds ratios are presented is not necessary. There is no need to present standard error. Please revise Figure 4B to make it clearer and similar in

appearance to Figure 4A.

Appendix:

Sampling methods subgroup analysis:

- It is given that there was a significant association between study design and vaccine hesitancy. However, all studies were cross-sectional studies. Did the authors mean: sampling method instead of study design?

Figure S2:

- It seems that there are two copies of this figure. Please delete one.

Figure S4:

- As for Figure 4, it is not necessary to include both log of odds ratio and odds ratio and the SE. Please provide information in the methods section the definition of younger and older age.

Discussion:

- A limitation is that sources of heterogeneity could not be assessed in detail. Another limitation is that asking a single question about acceptance/refusal and hesitancy provides limited information on a person's intention to vaccinate.

References

1. Baker R, Jackson D: Inference for meta-analysis with a suspected temporal trend. *Biom J.* 2010; **52** (4): 538-51 [PubMed Abstract](#) | [Publisher Full Text](#)

Are the rationale for, and objectives of, the Systematic Review clearly stated?

Yes

Are sufficient details of the methods and analysis provided to allow replication by others?

Partly

Is the statistical analysis and its interpretation appropriate?

Partly

Are the conclusions drawn adequately supported by the results presented in the review?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Systematic review; meta-analysis; perinatal, reproductive and life-course epidemiology.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.