Gender/sex differences in Covid-19 vaccine acceptance among refugee, immigrant and migrant populations: An equity-focused systematic review and meta-analysis protocol

Yasaman Yazdani [1,2], Poojitha Pai [3], Shahab Sayfi [4], Shehzad Ali [1], Janet Martin[1,4], Kevin Pottie[1,2]

Department of Epidemiology and Biostatistics, Schulich School of Medicine & Dentistry, Western University, London, Ontario, Canada

Department of Family Medicine, Schulich School of Medicine & Dentistry, Western University, London, Ontario, Canada

Schulich School of Medicine & Dentistry, Western University, London, Ontario, Canada

Michael G. DeGroote Cochrane Canada and GRADE Centres, Department of Health Research Methods, Evidence and Impact, McMaster University, Hamilton, Ontario, Canada

Departments of Anesthesia & Perioperative Medicine and Epidemiology & Biostatistics, Western University, London, Ontario, Canada

Authors' Email addresses: Yasaman Yazdani: yyazdan3@uwo.ca

Poojitha Pai: Poojitha.Pai@lhsc.on.ca

Shahab Sayfi: ssayf086@uottawa.ca

Shehzad Ali: shehzad.ali@uwo.ca

Janet Martin: jmarti83@uwo.ca

Corresponding Author: Kevin Pottie, MD, MClSc, CCFP

Ian McWhinney Research Chair, Professor of Family Medicine, Epidemiology and Biostatistics, Western University, London, Ontario

Address: PHFM 2147, Department of Family Medicine, Western University, London, Ontario

E-mail: kpottie@uwo.ca

Abstract:

Background: The COVID-19 pandemic has posed significant global health challenges, with vaccination being a critical tool for reducing severe disease and hospitalizations. However, vaccine hesitancy, coupled with issues related to equitable vaccine access, has complicated efforts to achieve widespread vaccination coverage. Given the controversy over the existence of gender differences in Covid-19 vaccine acceptance, this study protocol outlines a comprehensive systematic review and meta-analysis aimed at understanding COVID-19 vaccine acceptance among Refugee, Immigrant, and Migrant (RIM) populations, with a specific focus on gender disparities.

Objectives: The primary objective of this study is to investigate whether COVID-19 vaccine acceptance rates differ by gender/sex among RIM populations. Secondary objectives include examining these differences within subgroups defined by ethnicity, migration status, and education level.

Methods: This systematic review and meta-analysis adhere to PRISMA and MOOSE guidelines for observational studies. A comprehensive search spanning from December

2020 to September 2023 will be conducted across multiple databases including MEDLINE, Embase, Scopus, APA PsycINFO, Cumulative Index of Nursing and Allied Health Literature (CINAHL) and relevant websites. Eligible studies will encompass observational research on COVID-19 vaccine acceptance, intention, or hesitancy within RIM populations. Studies must report data on both men and women or test gender/sex differences. Quality assessment will be conducted using the Newcastle-Ottawa Scale. Data synthesis will include quantitative analysis with random effect models and subgroup analysis, where available. Sensitivity analysis, publication bias exploration, and tests for interaction will be performed to ensure the robustness of findings.

Conclusion: This study protocol outlines a systematic approach to address crucial questions regarding COVID-19 vaccine acceptance within RIM populations, with a specific emphasis on gender disparities and their interplay with ethnicity, migration status, and education level. The findings from this review will contribute to a better understanding of vaccine hesitancy in these populations, aiding public health efforts in designing targeted interventions to enhance COVID-19 vaccine acceptance and coverage.

Keywords: COVID-19, Immigrants, Refugees, Vaccine acceptance, gender differences, sex differences

1. Introduction:

The novel highly contagious Coronavirus disease has become a global health crisis during recent years (1). As there is no definite cure, and since treatment remains a challenge for severe disease, vaccines remain an important population intervention to

reduce severe disease and hospitalizations (2). Alongside obstacles to ensuring fair access to COVID-19 vaccines, vaccine hesitancy exacerbates the issues at hand, further complicating the efforts to attain broad vaccination coverage (3). Vaccine hesitancy, as characterized by the WHO Strategic Advisory Group of Experts on Immunization (SAGE) working group on vaccine hesitancy, refers to the delay or refusal of vaccination even when vaccines are readily available (4). Our scoping review on predictors of COVID-19 vaccine acceptance among Refugee, Immigrant, and Migrant (RIM) populations indicates that the majority of studies reported that females were more hesitant to get vaccinated (5. However, only 44% of studies examining the association between sex/gender and COVID-19 vaccine acceptance among RIM populations found significant results. This underscores the necessity for further analytical investigation through meta-analysis to determine whether COVID-19 vaccine acceptance rates differ by gender/sex among RIM populations.

Wang et al. suggest that women were less likely to accept Covid-19 than men within the general population (6). Another systematic review and meta-analysis reported no significant difference in pooled prevalence of vaccination intention between males and females in the general population (7). Also, In a meta-analysis conducted by Alimoradi et al. on COVID-19 vaccine acceptance among migrant and refugee populations, no significant difference between females and males regarding their acceptance of the COVID-19 vaccine was reported (8). However, no subgroup analysis was conducted in these studies. Additionally, there was inconsistency in the definition of target population and vaccine acceptance across existing studies. It is important to note that while the terms “vaccine acceptance” and “vaccine uptake” may appear to be similar in definition,

they are distinct concepts. While conducting systematic reviews in this field, acceptance does not always equate uptake, as there may be situations where vaccine uptake is high, but acceptance is low, especially in the unique context of COVID-19 and its mandates.

The hesitancy of women towards vaccines may hold greater significance. This is particularly crucial in attempts to boost vaccination rates, especially with regards to children's COVID-19 vaccination rates, given that mothers appear to have a lower inclination to vaccinate their children against COVID-19 compared to fathers (9,10) Exploring gender disparities in COVID-19 vaccine acceptance within the RIM population can provide valuable insights for customizing public health campaigns and interventions. This knowledge can help address the specific concerns or preferences of individuals who may be hesitant about vaccination. As education level, ethnicity and migration status are believed to be important influencers of COVID-19 vaccine acceptance (5,11, 12), understanding gender differences in these subgroups can help recognizing which groups within different categories may be more hesitant to allocate resources and interventions where they are needed most and tailoring vaccine information to specific demographic based on their unique concerns and preferences, using appropriate outreach strategies.

1.1. Objectives: This study protocol outlines the objectives of a comprehensive systematic review and meta-analysis designed to address following questions concerning COVID-19 vaccine acceptance within RIM populations:

Primary Objective:

To investigate whether COVID-19 vaccine acceptance rates differ by gender/sex among RIM populations.

Secondary Objectives:

To investigate whether COVID-19 vaccine acceptance rates differ by gender/sex, when considering subgroups based on ethnicity, migration status, and education level within RIM populations.

2. Methods

The systematic review and meta-analysis was registered in the PROSPERO network (registration number: CRD42023459524). If there are any modifications to the protocol, each amendment's date will be accompanied by an explanation of the alteration and the underlying reason for it.

2.1 Study Design This systematic review and meta-analysis will follow the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines.

2.2. Search Strategy We will conduct a comprehensive search of several databases, including MEDLINE, Embase, Scopus, APA PsycINFO, and Cumulative Index of Nursing and Allied Health Literature (CINAHL). The search will cover the period from December 2020, when the World Health Organization (WHO) issued its first emergency use validation for a COVID-19 vaccine, to September 2023. We will also search relevant

websites, including the WHO, The United Nations High Commissioner for Refugees (UNHCR), and the International Organization for Migration (IOM), for additional information. The complete Medline search strategy is provided in table 1.

2.3. Condition This review focuses on the COVID-19 pandemic, specifically the vaccination within RIM populations.

2.4. Participants/Population Refugees, immigrants and other migrant populations would be our target population. The International Organization for Migration (IOM) defines a migrant as “A person who moves away from his or her place of usual residence”. However, our study focuses on international immigrants. The United Nations website also defines refugees and migrants as follows: “Refugees are persons who are outside their country of origin for reasons of feared persecution, conflict, generalized violence, or other circumstances that have seriously disturbed public order and, as a result, require international protection”. “An international migrant is someone who changes his or her country of usual residence, irrespective of the reason for migration or legal status”. We will not limit our study to immigrants and refugees residing in any particular country.

2.5. Exposure The primary exposure of interest in this review is gender/sex. We aim to evaluate the association of gender/sex with COVID-19 vaccine acceptance among RIM populations. Given that many studies in our previous scoping review lacked clear differentiation between gender and sex or did not specify which of these aspects they assessed and how, we will document the reported gender or sex based on the information provided in the articles and will treat it as a single data point. We will also

explore how this association varies within different ethnic subgroups, migration statuses, and levels of education.

2.6. Comparator(s)/Control As this review focuses on observational studies assessing vaccine acceptance, there will be no specific comparators or control groups.

2.7. Types of Study to be Included We will include observational studies, including cross-sectional studies, that have been peer-reviewed or are available as pre-print articles. Studies reporting intention/willingness to get vaccinated against COVID-19 for men and women separately or testing gender/sex differences in COVID-19 vaccine acceptability and similar concepts (vaccine hesitancy, vaccine intention) among RIM populations will be included, without any language restriction.Studies focusing on vaccine access and vaccine uptake will be excluded unless they have information about vaccine intention/acceptance. We will also include studies on the general population if they report separate subgroup analyses for RIM populations. Studies will be eligible if at least 50% of their participants are either refugees or first-generation migrants (foreign-born). We will include studies on the general population only if a separate sub-group analysis of RIM is reported. Review articles will be excluded. Nevertheless, the references of relevant reviews and included studies will be screened for eligible original research articles.

2.8. Context The context for this review is the COVID-19 pandemic, with a focus on RIM populations.

2.9. Main Outcome(s) We will compute the odds of men reporting COVID-19 vaccine acceptance in comparison to the odds of women reporting COVID-19 vaccine

acceptance/intention, using the frequencies presented in the papers or made available by the authors upon request. We will contrast the affirmative responses (including responses like 'definitely yes' and 'probably yes') with the other categories of responses that do not fall under the 'yes' category, which may also encompass answers such as 'do not know' or 'not sure.' In our subgroup analysis, we will investigate gender/sex disparities within various ethnic subgroups, migration statuses, and education levels . (This will depend on our ability to access the requisite data).

2.10. Data Extraction (Selection and Coding) Following the search, all identified publications will be collated and uploaded to COVIDENCE, a web-based platform for systematic review data management, to review and remove duplicates. Subsequently, two independent reviewers will screen titles and abstracts for relevance, and any conflicts will be resolved through discussion or consultation with a third senior reviewer. Full-text articles of selected studies will be reviewed by two independent reviewers to ensure they meet the inclusion criteria. The data extraction process will be systematically conducted using a predefined and piloted data extraction form. This form will be developed based on the specific variables and outcomes outlined in the review protocol. Prior to the formal extraction, a pilot test of the form will be conducted on a small subset of included studies to ensure clarity, consistency, and relevance. Adjustments to the form will be made as necessary based on the feedback and insights gained from the pilot.

We will extract the following information from each included study, by two independent reviewers:

Author's name

Study location

Sample size

Sampling method

Year(s) of data collection

Demographic characteristics of participants (ethnicity, immigration status, educational background)

Study type

Data required to calculate odds of vaccine acceptance among men and women

2.11. Risk of Bias (Quality) Assessment We will assess the quality of included non-randomized studies, including cross-sectional studies, using the Newcastle-Ottawa Quality Assessment Scale (NOS). The NOS evaluates study quality based on three categories: Selection, Comparability, and Outcome. Each category has specific criteria that are relevant to cross-sectional studies. Each criterion will be scored as 0 (does not meet the criteria or high risk of bias) or 1 (meets the criteria or low risk of bias). Total scores will typically range from 0 to 9 points, with the following interpretations:

High Quality: Total scores of 7-9 points

Moderate Quality: Total scores of 4-6 points

Low Quality: Total scores of 0-3 points

We will consider the quality assessment results alongside the research question to draw conclusions about the overall strength of the evidence provided by the included studies.

2.12. Strategy for Data Synthesis We will provide a narrative description and tabulated synthesis of the study findings. When multiple studies have reported data regarding vaccine acceptance by gender/sex, we will perform quantitative synthesis of the results in accordance with the Cochrane Handbook, utilizing R software version 4.3.3, provided that we obtain a sufficient number of eligible studies (a minimum of two). Random effect model will be used, given the marked heterogeneity in study designs and methods, to calculate the odds ratios, with 95% confidence interval, using the exact frequency statistics reported in the papers or provided by the authors upon request. We will assess heterogeneity using the I^2 statistic (values of 25%, 50%, and 75% correspond to low, moderate, and high levels of heterogeneity, respectively). Forest plots of odd ratios and pooled OR with 95% CIs will be generated.

We will conduct a sensitivity analysis by incorporating adjusted odds ratios (aORs) ,when available, to assess the potential impact of covariate adjustments on our findings. This analysis will involve comparing the aggregated results derived from aORs with those from unadjusted odds ratios (ORs) to determine whether the inclusion of covariate adjustments significantly alters the overall effect size estimate. Publication bias will be explored through visual inspection of funnel plots and using Egger's regression test.

In our subgroup analysis, we will investigate gender/sex differences within various ethnic subgroups, migration statuses, and education levels. This will be contingent upon

our access to the necessary data. For subgroup analyses, the test for interaction will be assessed, where $P<0.05$ will be considered indicative of significant subgroup effects.

3. Ethics

This Systematic review is exempt from the research ethics review as it is based on peer reviewed published works.

4. Funding

None

5. Competing interest

The authors declare no potential conflicts of interest.

6. Authors' contribution KP is the guarantor. YY, KP, JM and SA drafted the manuscript. All authors contributed to the development of the selection criteria, the risk of bias assessment strategy and data extraction criteria. YY, PP, SS and KP developed the search strategy. YY, JM and KP provided statistical expertise. KP provided expertise on refugee and migrant health field. All authors read, provided feedback and approved the final manuscript.

References:

1. Alsharif W, Qurashi A. Effectiveness of COVID-19 diagnosis and management tools: A review. Radiography. 2021;27(2):682-7.

2. Moghadas SM, Vilches TN, Zhang K, Wells CR, Shoukat A, Singer BH, et al. The impact of vaccination on COVID-19 outbreaks in the United States. Medrxiv: the Preprint Server for Health Sciences. 2021:2020.11. 27.20240051-2020.11. 27.

3. 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):6500-7.

4. Tankwanchi AS, Jaca A, Ndlambe AM, Zantsi ZP, Bowman B, Garrison MM, et al. Non-COVID-19 vaccine hesitancy among migrant populations worldwide: a scoping review of the literature, 2000-2020. Expert Review of Vaccines. 2022;21(9):1269-87.

5. Yasaman Y, Poojitha P, Shahab S, Arash M, Saber P, Denise S, et al. Predictors of COVID-19 Vaccine Acceptability Among Refugees and Other Migrant Populations: A Systematic Scoping Review. medRxiv. 2023:2023.09.15.23295608.

6.1.Wang Q, Yang L, Jin H, Lin L. Vaccination against COVID-19: A systematic review and meta-analysis of acceptability and its predictors. Prev Med. 2021 Sep;150:106694. doi: 10.1016/j.ypmed.2021.106694. Epub 2021 Jun 22. PMID: 34171345; PMCID: PMC8217737.

7. Terry E, Cartledge S, Damery S, Greenfield S. Factors associated with COVID-19 vaccine intentions during the COVID-19 pandemic; a systematic review and meta-analysis of cross-sectional studies. BMC Public Health. 2022 Sep 2;22(1):1667. doi: 10.1186/s12889-022-14029-4. PMID: 36056325; PMCID: PMC9437387.

8.Alimoradi Z, Sallam M, Jafari E, Potenza MN, Pakpour AH. Prevalence of COVID-19 vaccine acceptance among migrant and refugee groups: A systematic review and meta-analysis. Vaccine X. 2023 Aug;14:100308. doi: 10.1016/j.jvacx.2023.100308. Epub 2023 May 6. PMID: 37223070; PMCID: PMC10163798.

9. Guerin RJ, Naeim A, Baxter-King R, Okun AH, Holliday D, Vavreck L. Parental intentions to vaccinate children against COVID-19: Findings from a US National Survey. Vaccine. 2023;41(1):101-108.

10. Goldman RD, Yan TD, Seiler M, et al. Caregiver willingness to vaccinate their children against COVID-19: Cross sectional survey. Vacc*ine.* 2020;38(48):7668-7673.

11. Mondal P, Sinharoy A, Su L. Sociodemographic predictors of COVID-19 vaccine acceptance: a nationwide US-based survey study. Public Health. 2021 Sep 1;198:252-9.

12. Rego RT, Ngugi AK, Sophie Delius AJ, Luchters S, Kolars JC, Irfan FB, Weinheimer-Haus E, Abubakar A, Shah R, Zhu J, Boulton ML. COVID-19 vaccine hesitancy among non-refugees and refugees in Kenya. PLOS Global Public Health. 2022 Aug 24;2(8):e0000917.

Table 1. Search strategy for Medline, without any search limit (Dec 2020- Sep 2023)

Search terms	Search Results
(immigrant*.tw,kf. or "Emigrants and Immigrants"/) OR ("Transients and Migrants"/ or migrant*.tw,kf.) OR emigrant*.tw,kf. OR (Refugees/ or refugee*. tw,kf.) OR “asylum seeker*”. tw,kf. OR (diaspora. tw,kf. or Human Migration/) OR newcomer*. tw,kf. OR foreigner*. tw,kf. OR foreign-born*. tw,kf. OR foreign worker*. tw,kf) OR ("undocumented	

immigrant*" OR undocumented immigrants/) OR international student* .tw,kf. AND (covid-19.tw,kf. or COVID-19/) OR covid.tw,kf. OR (Severe Acute Respiratory Syndrome.tw,kf. or severe acute respiratory syndrome/) OR (Coronavirus.tw,kf. or Coronavirus/ or Coronavirus infection/) OR (Sars-cov-2.tw,kf. or SARS-CoV-2/) AND (Immunization/ or immunization.tw,kf.) OR (vaccine.tw,kf. or Vaccines/) OR (vaccination.tw,kf. or Vaccination/) OR (Vaccine hesitancy.tw,kf. or Vaccination Hesitancy/) OR Vaccination hesitancy.tw,kf. OR (Vaccine refusal.tw,kf. or Vaccination Refusal/) OR Vaccination refusal.tw,kf. OR (anti-vaccine*.tw,kf. OR Anti-Vaccination Movement/) OR anti-vax*.tw,kf. OR hesitancy.tw,kf. OR hesitation.tw,kf. OR (trust.tw,kf. or Trust/) OR acceptance.tw,kf. OR refusal.tw,kf. OR willingness.tw,kf. OR (Attitude/ or attitude.tw,kf.) OR choice.tw,kf. OR denial.tw,kf. OR (phobia.tw,kf. or Phobic Disorders/) OR avoidance.tw,kf. OR decision.tw,kf. OR uptake.tw,kf. OR doubt.tw,kf. OR resistance.tw,kf. OR reluctance.tw,kf. OR exemption.tw,kf. OR controversy.tw,kf. OR dilemma.tw,kf. OR (intention.tw,kf. or Intention/) OR skeptic.tw,kf. OR delay.tw,kf. OR distrust.tw,kf. OR mistrust.tw,kf.	968

292