Methodological Insights into Vaccine Hesitancy Research in Respiratory Diseases in Adults At-Risk: Systematic Review

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OBJECTIVE

- To describe frameworks for influenza, COVID-19, or pneumococcal disease vaccine hesitancy (vaccine acceptance) among moderate and high-risk adults and the main hesitancy drivers.

Figure 1. PICOT question

P: Adults at-risk of respiratory disease (COVID-19, Influenza and Pneumococcal disease)

I/C: Risk factors associated vaccine hesitancy compared to acceptance of vaccine

O: Vaccine acceptance or hesitancy level

T: Cross-sectional, cohort or descriptive and analytical studies

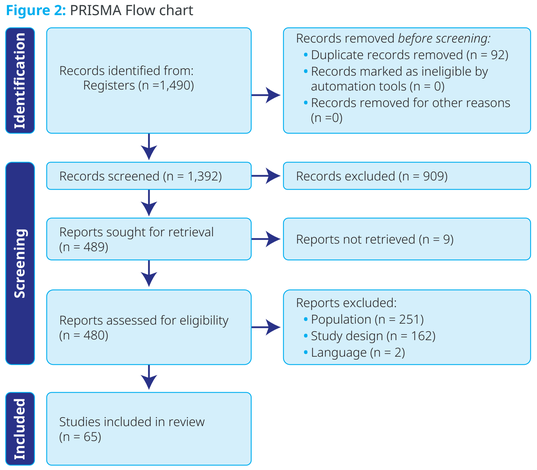
METHODS

- We conducted a systematic literature review following PRISMA guidelines using Medline and Embase from database inception to December 12, 2025.
- The search was based on the MeSH, Emtree and free-text terms for hesitancy/acceptance and on the risk factors for influenza, COVID-19, and pneumococcal disease, without publication date limitation. Language restriction was applied only to Chinese and Persian documents.
- Cross-sectional studies, cohort studies or descriptive and analytical studies that described vaccine hesitancy were included.
- Two independent researchers identified, selected and obtained full text documents for final decision for inclusion to the study. Ties were broken by mutual agreement between researchers. Data extraction was completed by multiple reviewers.
- Frameworks, number of items, sample size, and main drivers, among others were extracted and the outcomes were theme-coded as acceptance and hesitancy post hoc. Descriptive statistics were generated to summarize key findings.
- The AXIS tool was employed to assess the quality of studies.

RESULTS

- Among the 1,490 records reviewed, 65 studies met inclusion criteria (Figure 2).

Figure 2: PRISMA Flow chart

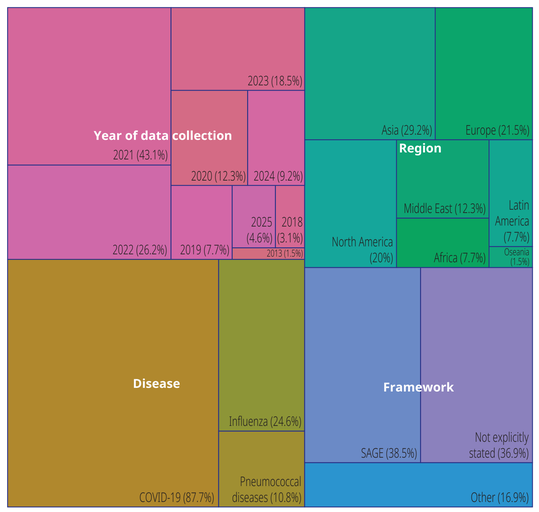


RESULTS (cont)

Characteristics of the studies

- A total of 27 studies originated from Europe and North America (41.5%), and a large share were conducted in Asia (29.2%), less than 20% were conducted in Africa or Latin America (Figure 3).
- Most studies focused on COVID-19 (87.7%), followed by Influenza (24.6%), and pneumococcal diseases (10.8%). Noticeably, 10 studies (15.4%) addressed two or three of these diseases (Figure 3).
- Over two-thirds of the studies collected data during the most critical phase of the COVID-19 pandemic (2020–2022)[1]. Only one study collected data in 2013 (1.5%), and less than 15% of studies collected data during 2024 and 2025 (Figure 3).
- The predominant measurement framework was the one proposed by the World Health Organization SAGE (Strategic Advisory Group of Experts on Immunization) framework[2] (three c's: Complacency, Convenience, Confidence) (38.5%). However, 36.9% of the studies did not explicitly stated any framework Other frameworks were less common (<5% each) like the Protection Motivation Theory, Health Belief Model, Theory of Planned Behavior, Necessity Concerns Framework, or the BASNEF model (Figure 3).

Figure 3. Treemap of key features of included studies



- Near to 90% of studies utilized cross-sectional designs, and the size sample was highly heterogeneous, from 46 to 38,184 subjects, and a median size of 558 participants. The majority relied on custom-made surveys (>70%), which were developed using expert panels, question banks from previous research, or their own investigator-developed questionnaires.
- In a lesser extent, validated instruments for overall diseases were also used, such as the Vaccine Hesitancy Scale (VHS)[3], the 5Cs scale[4], the Vaccination Attitudes Examination (VAX) Scale[5]. In addition, disease-specific validated scales were also common, for example the Oxford COVID-19 Vaccine Hesitancy Scale[6], the Willingness to be vaccinated for COVID-19 survey[7,8], and the COVID-19 vaccine hesitancy scale (CVHS)[9].
- In general, when vaccine hesitancy or acceptance was addressed directly, it was measured using between 1 to 7 items. When addressed using latent variable strategies in average 9 items were required (SD 5.5 items). Over one third of the studies reported the psychometric properties of their scales such as internal consistency (e.g. Cronbach's α, McDonald's Ω) or confirmatory factor analysis metrics (e.g. RMSEA, CFI, TLI).

Details from included studies

- The included studies collected data from 161,911 participants, who were mainly working-age adults with a weighted mean age of 42.3 years (SD 14.4), and a weighted average of 46.5% were male (SD 19.7%).

RESULTS (cont)

- On a different note, the most common comorbidities identified across the studies were related to disorders of the circulatory system (11 studies, 16.9%) and HIV (7 studies). Notably, in only 4 studies, respiratory diseases were reported as the most predominant comorbidity (Table 1).

Table 1. Demographic and clinical characteristics by population and study level

Population level		
Variable	**n= 161,911 (participants)**	**Not reported, n (%)**
Age, mean (SD) years	42.3 (14.4)	16,904 (10.4%)
Male, mean proportion (SD)	46.5% (19.7%)	223 (0.1%)
Study level		
Variable	**n=65 (studies)**	**Studies where the variable was not reported, n(%)**
Comorbidities, n (%)	58 (89.2%)	
Most predominant comorbidities in the population		
Diseases of the circulatory system	11 (16.9%)	
HIV	7 (10.8%)	
Diabetes	5 (7.7%)	
Malignant neoplasms	4 (6.2%)	
Diseases of the Musculoskeletal System and Connective Tissue	4 (6.2%)	7 (10.8%)
Respiratory disease	4 (6.2%)	
Depression	2 (3.1%)	
Kidney disease	2 (3.1%)	
Gastritis	1 (1.5%)	
Sarcoidosis	1 (1.5%)	
Dyslipidemia	1 (1.5%)	
Opioid addiction	1 (1.5%)	
Labor/occupational status related information, n (%)	29 (44.6%)	36 (55.4%)
Income or socioeconomic status information, n (%)	21 (32.3%)	44 (67.7%)
Educational attainment information, n (%)	47 (72.3%)	18 (27.7%)
Prior vaccination experience, n (%)	45 (69.2%)	20 (30.8%)

- Frequently analyzed drivers included medical history, confidence, previous knowledge about vaccination, age and gender, income or socioeconomic status, perceptions about safety, educational attainment and occupational status (Table 1).
- Fewer than 30% of studies incorporated validated scales to supplement the assessment of hesitancy drivers. For instance, some studies utilized the COVID-19-anxiety questionnaire[10], the Fear of COVID-19 scale[11], the Perception of SARS-CoV-2 Vaccines Acceptance[12], the Drivers of COVID-19 Vaccination Acceptance Scale[13], the Asthma Control Test[14], the depression severity measure PHQ-9[15], the cognitive screening tool 6-CIT[16]; while other more broad scales such as the Group-Based Medical Mistrust Scale[17], the medication adherence scale[18], the Spatial Perception of Risk (PRITASC) survey[19], and the The Assessment of Quality of Life (AQoL) instrument[20], to mention a few.

Hesitancy definition

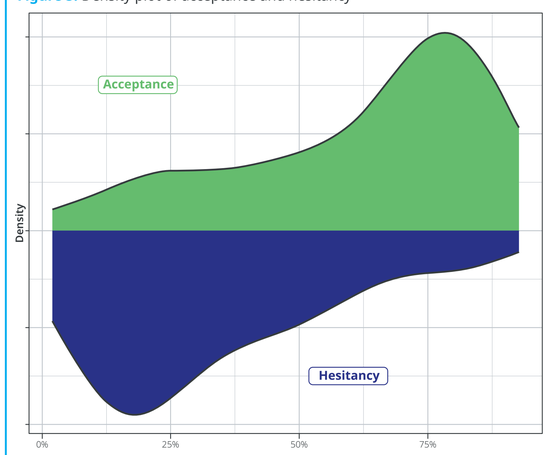
- The definitions of hesitancy and acceptance exposed considerable heterogeneity, with instances where multiple definitions were concurrently applied. Some studies addressed as the number of previous vaccinations, or having recently received a vaccination (32.3%), others as the intention to vaccinate or to keep up to date with vaccination (26.2%), and the willingness to vaccinate (20%).
- To a lesser degree, certain studies have employed definitions associated to the 3C's framework such as fear, confidence and perceptions about vaccine safety (9.2%) and as an interest in getting vaccinated, usually linked to the availability of vaccines (9.2%). In addition, in an important share of studies hesitancy or acceptance were measured as a latent variable or were not directly defined (27.7%).

RESULTS (cont)

Hesitancy levels

- From 38 studies who defined a specific metric for hesitancy, the acceptance proportion was on average 66.1% (SD 24.4%), and a median of 72.5% (MAD 18.7%). On the other hand, vaccination hesitancy was around 33.3% (SD 22.9%) and a median of 25.5% (MAD 22.7%). Considering that the hesitation or acceptance definition was not homogeneous across studies, and their measurement was not always conducted or reported; and in some cases, were reported only for subgroups (e.g. respiratory disease, hospitalized cases, healthy population) the aforementioned results should be read as a descriptive measure and not as an inferential one.

Figure 5. Density plot of acceptance and hesitancy



CONCLUSION

- The SAGE framework was the most applied, however there is not a unique hesitancy definition, nor a unique scale that allows us to measure this variable across studies. The study indicates that this variable has been measured in several strategies, which has led to different authors into using custom-made questionnaires or surveys.
- Most research investigated hesitancy/acceptance in COVID-19 vaccination. Hesitancy or acceptance was usually defined by prior vaccinations, recent vaccination, intention to vaccinate, or willingness to stay current with vaccines.
- The highly heterogeneous main drivers range from demographical and clinical characteristics to specific traits related to vaccination knowledge and beliefs. Nonetheless, SAGE framework adaptability to emerging economies must be assessed.

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