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## Understanding barriers and predictors of maternal immunization: Identifying gaps through an exploratory literature review

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## Abstract

Background: The Advisory Committee for Immunization Practices recommends that all pregnant women receive the seasonal influenza vaccine and the tetanus toxoid, diphtheria toxoid, and acellular pertussis (Tdap) vaccine during every pregnancy. However, vaccination coverage rates are suboptimal among pregnant women in the United States, leaving these women and their unborn children at risk of vaccine-preventable diseases and their complications.

**Objectives:** We sought to understand the current landscape of published literature regarding maternal immunization, including barriers to and predictors of vaccine acceptance, and identify gaps in the research in order to inform strategies for future programmatic improvement.

Methods: We conducted a literature search using MEDLINE (OVID), PsychlNFO, and CINAHL (Ebsco) databases. The search included published, English-language manuscripts that identified patient, provider, or system-level barriers to, predictors of, or interventions that improved uptake of maternal vaccines among pregnant women in the US. Studies were reviewed using an inductive thematic analysis approach.

**Results:** We included 75 studies in our review. Pregnant women identified 25 different barriers to accepting recommended maternal immunizations; barriers related to vaccine safety perceptions were the most common. Healthcare providers identified 24 different barriers to vaccinating their pregnant patients. The most commonly cited barriers among healthcare providers were financial concerns. Eighteen different predictors of vaccine acceptance were identified. Receipt of

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a healthcare provider's recommendation was the factor most frequently reported as a reason for vaccination among pregnant women.

**Conclusions:** We were able to identify gaps in the literature regarding maternal immunization and make recommendations for future research. Efforts to address the challenges of maternal immunization in the United States should include increasing the focus on Tdap, implementing more high-level assessments of safety perceptions and associated concerns, and determining most effective interventions.

#### Keywords

Influenza vaccine; Maternal immunization; Prenatal care; Tdap vaccine; Vaccination during pregnancy

## 1. Introduction

In the United States, elimination and reduction of vaccine- preventable diseases through immunization has directly increased life expectancy by reducing morbidity and mortality [1]. Despite the proven effectiveness of immunization, however, adult vaccinations remain underutilized, including those indicated for pregnant women [2–4]. Pregnant women are at high risk for influenza-related morbidity and mortality and adverse pregnancy outcomes, such as preterm birth and fetal demise [5–8]. Maternal immunization is particularly important when considering vaccine- preventable diseases, such as influenza and pertussis, for which there is no other option for protecting very young infants. Specifically, influenza vaccine is not licensed for use prior to six months of age, and adequate antipertussis antibodies are only achieved after 2–3 doses of the diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP) by six months of age [9].

The Advisory Committee on Immunization Practices (ACIP) makes recommendations for the use of vaccines among adults in the United States, including pregnant women. ACIP has recommended that all pregnant women receive the seasonal influenza vaccine since 2004 [10] and the tetanus toxoid, diphtheria toxoid, and acellular pertussis (Tdap) vaccine during every pregnancy (i.e., regardless of vaccination history) since 2012 [11]. The American College of Obstetricians and Gynecologists have endorsed these recommendations [12,13] and developed toolkits to facilitate maternal vaccination for providers and their patients [14,15]. In addition, the American College of Nurse Midwives also publicly supports maternal vaccine recommendations and has produced informational factsheets for pregnant women [16,17].

There is a robust body of literature available on the factors that influence maternal vaccination uptake in the United States, including a recent review synthesizing predictors of maternal vaccination [18]. However, this study does not address barriers and includes a considerably smaller pool of reviewed publications. Additional reviews largely focus on programmatic and policy issues surrounding clinical research on the use of vaccines among pregnant women, or clinical endpoints such as safety and effectiveness [19–21]. The current review synthesizes these, and other, considerations from the perspective of pregnant women and their healthcare providers. Our objective was to understand the current

landscape of published literature regarding barriers and predictors of immunization of US pregnant women, and identify gaps in the research through an exploratory literature review.

## 2. Methods

## 2.1 Inclusion criteria

We conducted a literature search using the following databases from the dates indicated through December 2017: MEDLINE (OVID) (1946), PsychlNFO (1967), and CINAHL (Ebsco) (1982). The search included published, English-language manuscripts that identified patient, provider, or system-level barriers to or predictors of uptake of maternal vaccines (i.e., seasonal influenza [influenza], novel 2009 pandemic influenza A [pH1N1], and/or tetanus toxoid, diphtheria toxoid, and acellular pertussis [Tdap]) among pregnant women in the US. The full search strategy, including catchment terms, is detailed in Appendix 1. Studies were excluded if they included only vaccine coverage, vaccine efficacy, non-modifiable factors (e.g., race/ethnicity), intentions to vaccinate, vaccination among postpartum women or other non-pregnant populations, or non-routine or contraindicated vaccines (e.g., pneumococcal vaccine). Studies conducted outside of the United States, cost-effectiveness studies, dissertations, case studies, modeling studies, methods papers, reviews, and articles with no abstract were also excluded. After abstracting all articles considered for inclusion, we reviewed manuscripts from a previous search that identified barriers, predictors, and facilitators of immunization uptake among all adults and included those that specifically identified pregnant women if they were not captured in our present search (Fig. 1).

#### 2.2 Data abstraction

Manuscripts were reviewed by one reviewer using an inductive thematic analysis approach [22]. Prior to abstraction, we created a review matrix with factor categories for six main themes (patientbarriers, provider-barriers, system-barriers, patient-predictors, provider-predictors, and systems-predictors) drawn from prior knowledge and subject matter expert (SME) consultation. We defined barriers as any patient-, provider-, or systems-level factor that resulted in decreased odds of a patient receiving a vaccine; any factor a patient reported as a reason for refusing or hindered their ability to receive a vaccine; any factor a provider reported hindered their ability to provide the vaccine to pregnant patients; or any factor beyond the control of a patient or provider-, or system-level factor that resulted in increased odds of a vaccine; any factor that resulted in increased odds of a patient, provider-, or system-level factor that resulted in increased odds of a vaccine; any factor that a patient reported as a reason for accepting an immunization; any factor that a provider reported as facilitating their ability to provide the vaccine to pregnant patient; or change made at the healthcare/clinic-level that resulted in measurable increases in maternal immunization uptake.

As the main objective was to understand the current landscape of published literature regarding maternal immunization and identify gaps in the research in order to inform strategies for future programmatic improvement, we did not evaluate the quality of individual studies or seek to quantify the magnitude of reported factors. Instead, for surveys,

interview, and focus group studies, we noted when a study participant identified a factor as a barrier or predictor. For observational, quasi-experimental, and experimental studies, all factors identified via descriptive statistics were included. In manuscripts that reported statistical analyses (e.g., using risk ratios), only statistically significant factors were included in the matrix, and if a manuscript reported bivariate and multivariable analyses, only significant results from the latter were included. During synthesis, we counted the number of times each factor was linked to vaccination acceptance or refusal overall and rank-ordered them from the most cited to least cited.

## 3. Results

Of 507 manuscripts identified in the search, 83 met eligibility criteria and 61 were included after full-text review [23–83]. Fourteen studies identified in the previous aforementioned search were also included [84–97], yielding 75 total publications (Fig. 1).

#### 3.1 Publication characteristics

Thirty-seven publications focused solely on seasonal influenza vaccine, seven focused solely on Tdap, and ten focused solely on novel 2009 pandemic influenza A (pH1N1) vaccine (Table I). The remaining 21 publications included a combination of these three vaccines; three of these also included vaccines not routinely recommended for pregnant women. Study designs implemented by authors were: prospective (n = 3) and retrospective (n = 6) cohort studies, focus groups or interviews (n = 4), randomized control trials (RCTs aka "experimental"; n = 8), non-randomized control trials (quasi-experimental, e.g. pilot studies; n=10), secondary data analyses (n = 11; nine used data from the Pregnancy Risk Assessment Monitoring System), and patient and/or provider surveys (n = 33). Fifty-eight studies focused solely on pregnant women, 11 on healthcare providers, and six included both populations.

#### 3.2 Barriers

Forty-one publications documented barriers among pregnant women. From these, we identified 25 individual patient-level barriers to maternal immunization uptake (Table 2). Barriers related to patients' perceptions of the safety of vaccines for themselves or their unborn baby were documented the most frequently (n = 33). Among studies that reported proportions, 6.4–71.0% of pregnant women reported safety concerns for themselves (n = 21); at least 20% of pregnant women in all but five of these studies reported this concern. Among studies that reported the proportion of women who considered safety to their unborn baby as a barrier (n = 19), the range was 2.9% to 77.0%; this concern was documented among at least 20% of pregnant women in all but six of these studies. Other patient barriers documented in at least 25% of the patient-barrier publications were not receiving a provider recommendation for the vaccine, not usually receiving the influenza vaccine, and not perceiving themselves to be at risk for contracting the disease (Table 2).

Fourteen publications documented barriers among healthcare providers, from which we identified 24 individual factors (Table 3). Financial concerns (e.g., inadequate reimbursement), patient refusal, concerns about safety or side effects for pregnant patients,

and confusion regarding or being unaware of recommendations for pregnant women were the only barriers documented in 40% or more of provider-barrier publications. The only system-level barrier identified was inadequate vaccine supply and distribution, such as shortages during the 2009–2010 influenza H1N1 pandemic.

#### 3.3 Predictors

Thirty-eight publications documented predictors of maternal immunization uptake from the patient perspective, from which we identified 18 unique factors (Table 3). Receipt of a healthcare provider's recommendation - whether accompanied by an offer or not - was the factor most frequently reported as a reason for vaccination among pregnant women; over 60% of studies that documented predictors among pregnant women reported this factor. Of studies that identified this predictor, the majority (n = 22/26) reported percentages of women or ratios, and reflect that a large proportion of women consider this factor important in their decision-making (16.9–94.7%; ratios: 2.10–56.62). Furthermore, three of these studies reported the difference in vaccine uptake when a recommendation was accompanied by an offer versus when it was not. A greater percentage of women who received both a recommendation (33.5–47.5%). The following predictors were included in at least 20% of included patient-predictor publications: patient-perceived effectiveness of the vaccine, past receipt of the seasonal influenza vaccine, and patient-perceived risk of contracting the disease.

Only two studies specifically identified provider-oriented predictors, from which we identified three unique factors. Ten publications identified systems-level predictors that successfully improved vaccination among pregnant women; among these, there were 16 unique factors identified. Increasing provider and practice staff awareness through education and/or training was the most commonly reported method, followed by prompts/reminders for providers, standing order protocols, and increasing patient awareness through education. Five of these studies implemented several of these strategies at once and report successful uptake of maternal immunizations using a multicomponent intervention.

#### 3.4 Specific vaccines

Almost half (n = 18/37) of the publications that focused exclusively on seasonal influenza vaccine from the patient perspective identified safety concerns as a barrier to uptake (17 studies identified concerns for self [23,24,33,35,39,41,44,45,51,53,56,61,71,76,96]; 13 identified concerns for the fetus [23,24,33,35,36,51,53,61,67,69,76, 77,96]; and 7 identified misperceptions, such as the vaccine causes influenza [35,36,39,44,45,56,69]). Additionally, three studies demonstrated that healthcare providers were concerned about the safety of influenza vaccine for pregnant patients [30,79,83], and one study among providers indicated that patient-perceived safety was an issue in providing the vaccine [55]. Fourteen publications identified receiving a healthcare provider's recommendation as a predictor of accepting the seasonal influenza vaccine [23,35,36,39, 45,46,50,53,57,60,61,67,69,94]. Ten publications focused solely on the pH1N1 vaccine; of those, five publications identified safety concerns (for self and fetus) as barriers among patients [31,49,59,80,88]. Among the

eight publications that focused exclusively on Tdap, there were no barriers or predictors of vaccine acceptance or administration consistent between publications.

## 4. Discussion

This report summarizes key findings from the literature regarding barriers, predictors, and facilitators of uptake of maternal vaccinations among patients and healthcare providers. Similar to studies of infant, adolescent, and adult vaccination, a strong provider recommendation is an important factor in a pregnant woman being vaccinated. Among pregnant women, perceptions or concerns that the vaccine is not safe often influenced decisions to refuse vaccinations during pregnancy, especially the seasonal influenza vaccine. These concerns persist despite rigorous testing and proven safety of vaccines. Not receiving a recommendation from a healthcare provider was also a recurrent barrier. Financial concerns, concerns about safety or side effects for pregnant patients, and confusion regarding or being unaware of recommendations were the primary concerns cited by healthcare providers.

Pregnant women tend to exhibit high information-seeking behaviors [98]. Healthcare providers are critical and trusted sources of information for women during pregnancy, and the importance of a provider recommendation in a pregnant woman's decision to receive a vaccination has been extensively demonstrated [18,21,23,25,31,35,36,39,40,43,45– 47,50,52,53,57,60,61,67, 69,80,92,94]. However, several studies suggest that providers may not be effectively relaying maternal vaccine information to their pregnant patients, as evidenced by the high proportion of women who report not discussing maternal vaccination with their providers [44–46,99] or dissatisfaction with the information they are given [100]. Women have increasingly turned to supplemental sources of information during pregnancy, such as the Internet and social media [99–101], and many of the concerns identified among pregnant women may be the result of information-gathering outside of the healthcare setting. These resources may be important tools for information-seeking women during pregnancy, but it is important to note that there is little evidence to indicate the quality of the information accessed by pregnant women, and most women do not discuss the information they retrieve with their healthcare providers [98,102]. One included study specifically identified the influence of outside sources on pregnant women (e.g., the Internet) as a barrier for providers [55]. Therefore, it is critical to ensure that the information women find is clear and accurate, but more importantly, to increase awareness and encourage the use of provider organizations and public health sources.

This report identified gaps in the maternal immunization literature that future research should aim to address. Tdap vaccine was considered in less than one-quarter of included studies, and was the primary vaccine of interest in only eight of these. Although this is likely due to the newness of the recommendation [11], further research concerning barriers and predictors of this important maternal vaccine are warranted, especially as the recommendation becomes more universally adopted. In addition, although concern regarding vaccine safety has been well-defined (especially for influenza vaccine) as a barrier, safety perceptions among patients as a predictor of uptake is underrepresented. Only five publications included in this report demonstrated that patients who cited believing

the vaccine was safe were more likely to accept vaccinations. This factor could be better understood if, within the same study, efforts were made to distinguish safety perceptions across a spectrum, rather than the binary approach used in the majority of extant literature. For example, instead of only including perceived safety concerns among a list of factors to choose from as a reason for refusing the vaccine (i.e., yes it's a factor vs. no it's not a factor), future studies should consider including Likert scalestyle questions that ask respondents to rank how safe they perceive a vaccine to be, followed by how much perceived safety is a priority when making decisions regarding vaccination.

The interface between healthcare providers and patients is another area in which evidence is lacking. There is very limited information regarding the actual conversations that occur between healthcare providers and pregnant patients. In the absence of being able to prospectively observe these interactions, intervention efforts must rely on retrospective patient and provider reports, which are not corroborated and may be subject to memory error and recall bias. Efforts to better understand how healthcare providers can make the most effective recommendations to pregnant women should start with an in-depth evaluation of this critical encounter.

Another important nuance to explore more systematically is the impact of a strong provider recommendation on pregnant women's acceptance of vaccination despite negative perceptions regarding vaccine safety. Although both factors were considered individually in many of the included studies, there has been no identifiable effort to understand under what circumstances or what patient factors determine if a healthcare provider's recommendation does or does not outweigh perceived safety concerns. Sociodemographic and/or attitudinal differences may exist between women who accept vaccines because their healthcare provider recommended it in spite of their concerns about vaccine safety, and those women who reject the vaccine, regardless of whether a healthcare provider recommended it. Several studies have classified vaccine hesitance among parents of young children based on the type and strength of their concern [103–108]. It has been demonstrated that many vaccine-hesitant parents demonstrate nuanced attitudes towards immunization rather than dichotomous positive or negative attitudes, and that attitudes may differ depending on the vaccine type [106]. These nuances in attitudes are also likely present among pregnant women, so it is probable that many of the studies considered in our review failed to capture subtleties among patients regarding concerns over their own vaccination during pregnancy. In addition, there are several vaccines, such as Group B Streptococcus and Respiratory Syncytial Virus vaccines, that are under development. If recommended, understanding the spectrum of perceived safety of these newer vaccines will be critical to ensuring uptake. Capturing these data would not only prove highly beneficial for healthcare providers in communicating with pregnant patients regarding vaccinations, but is vital to informing effective future interventions.

Furthermore, data describing pregnant women's reason(s) at the time of vaccine refusal or acceptance are lacking. Although the information available through this review is informative and establishes identifiable patterns regarding vaccination decision-making among pregnant women and their healthcare providers, there is little to no evidence that elucidates how attitudes translate into vaccine uptake and coverage. For example, although

women in their third trimester (compared to women in earlier stages of pregnancy) were more likely to report willingness to receive influenza and Tdap vaccines [55], only three studies explicitly indicated being in the first trimester of pregnancy as a reason for seasonal influenza vaccine refusal by pregnant women [23,33,41]. In addition, one recent study indicated that a statistically significant higher proportion of women in their third trimester (compared to those in their first or second) recalled discussing maternal vaccination with their healthcare provider [99]. Enrolling women in studies during their first trimester of pregnancy to further evaluate this association presents significant challenges, but efforts to document timing of acceptance or refusal in addition to the specific reason(s) are warranted.

#### 4.1 Limitations

Our review has limitations. First, this was an exploratory review and it is possible the literature search failed to capture all relevant publications. Second, the diversity of included study methodology precluded meta-analysis and we did not evaluate the quality of individual studies. It is important to note that even if a particular barrier or predictor is cited in a study, it may not be relevant if the study it was identified in is of poor quality. Furthermore, we did not document instances of failed interventions and were unable to determine why a factor may not have been reported. As it is not possible to know whether a particular factor was not reported due to study design decisions made by researchers, or if they were truly not considered barriers or predictors by participants, it may be challenging to interpret findings within a larger context. Despite these limitations, our report was strengthened by the comprehensive scope of barriers and predictors represented. We were able to identify critical gaps in the literature regarding maternal immunization and make recommendations for future research.

## 5. Conclusions

Our review suggests that negative perceptions among pregnant women regarding vaccine safety contribute to reduced uptake of maternal vaccinations, especially influenza. Meeting the challenges of maternal immunization in the United States will require addressing several important research gaps, including increasing the focus on Tdap, implementing more high-level assessments of safety perceptions and associated concerns, and assessing healthcare provider interactions. Among healthcare providers, financial concerns were the primary barriers. Addressing these will be more challenging, as alleviating burdens placed on providers (e.g. inadequate reimbursement for vaccine administration) will require fundamental systems and policy changes. However, this review should provide an informed evidence base for future policy decision-making.

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## Appendix 1

The search strategy was developed by subject matter experts (SMEs) and Centers for Disease Control and Prevention research librarians. Librarians developed an initial strategy based on the original search query submitted by SMEs, after which the strategy was refined by both parties. The below strategy is the final search used in this review.

## **Original Search Query:**

We are interested in the facilitators, barriers, and predictors of vaccination among pregnant women in the United States. Examples include: insurance status and insurance type, provider recommendation, complexity of payment, complexity of recommendations, ease of automation of the recommendations, record keeping, use of standing orders, use of electronic medical record adults, having an immunization champion, acceptability of the vaccine, etc.

## Search Strategy:

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Key to understanding OVID syntax:

/ = Subject Heading

Exp = explode

ADJ? = (adjacent to) within? number of words

mp. = title, abstract, keyword heading word, subject heading word

= truncation character

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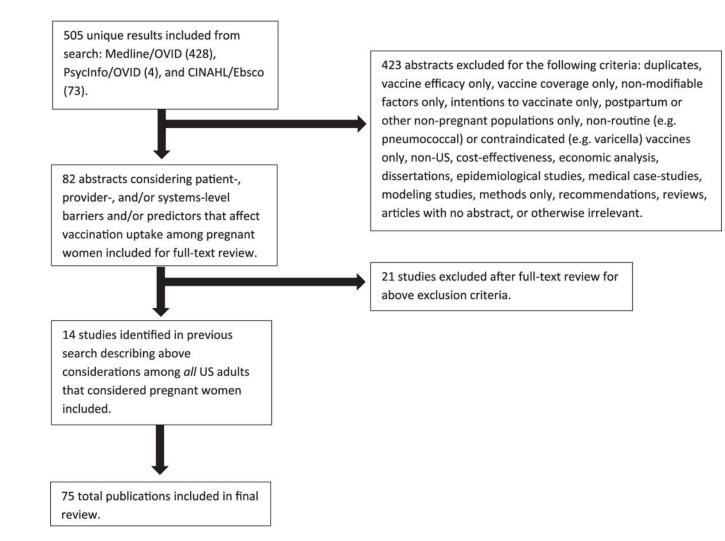
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Lutz et al.



#### Fig. 1.

The literature search yielded 505 unique results, of which 423 were excluded during abstract review. We reviewed 82 full-text articles and included 61; we identified 14 additional articles appropriate for inclusion from a prior literature search. The total number of publications abstracted and included in the present review is 75.

Table 1

Included publication characteristics.

Characteristic	Publication citation(s)
Vaccine of interest	
Seasonal influenza only	[23,24,26,30,32,33,35,36,39,41,44-46,50,51,53,54,56,57,60,61,63,67,69-71,73,75-77,79,81,83,93-96]
T dap only	[29,64,65,72,89,91,97]
pH1N1 only	[31, 42, 47, 49, 59, 80, 82, 85, 88, 90]
Seasonal influenza and pH1N1	[25, 34, 37, 38, 43, 48, 52, 62, 74, 84, 86, 87]
Seasonal influenza and Tdap	[27,28,40,55,58,92]
Seasonal influenza, Tdap, other $^{*}$	[68,78]
Seasonal influenza, pH1N1, Tdap, other $^*$	[66]
Study design	
Prospective cohort	[56,57,96]
Retrospective cohort	[54,75,84,85,89,93]
Focus groups/interviews	[31,61,67,69]
Randomized control trials	[40,50,51,53,65,70,71,81]
Non-randomized control trials	[58,63,68,72,73,76,77,90,91,95]
Secondary data analysis	[23-25,27,33,34,37,38,41,60,64]
Surveys	[26,28-30,32,35,36,39,42-49,52,55,59,62,66,74,78-80,82,83,86-88,92,94,97]
Study population	
Pregnant women only	[23-25,27,28,31,33-41,43-47,49-57,59-61,63-65,67-72,75,77,80-82,84-93,96,97]
Healthcare providers (HCP) only	[26,29,30,32,48,58,62,66,74,79,83]
Pregnant women and HCPs	[42,73,76,78,94,95]

	Control trial (RCT <sup>*</sup> or Quasi <sup>†</sup> )	Observational cohort	Secondary data analysis	Surveys	Interviews/ Focus groups
Patient-Identified Barriers					
Vaccine and/or disease-related factors (n= 103)					
Concerns about safety and/or side effects to self	[51,53,71,76]	[57,96]	[23- 25,33,34,38,41]	[35, 39, 43, 49, 52, 55, 59, 80, 86 - 88, 92]	[31,61,67,69]
Concerns about safety/harm to fetus	[51,53,76,77]	[96]	[23–25,33,34]	[35, 36, 44, 45, 49, 52, 55, 59, 80, 87, 88]	[31,61,67,69]
Perceiving self not at risk for the disease or unlikely to get sick	[51,53,65,71]	[96]		[49, 59, 80, 82, 87]	[69]
Belief that disease is not severe or serious, even if one were to become ill	[51]	[56]		[35, 36, 39, 49, 80, 86]	[31,69]
Misconceptions that vaccine causes disease, illness, death, or other negative outcomes	[51]	[56]		[35, 36, 39, 44, 45, 80, 86]	[69]
Concerns about vaccine effectiveness; do not think the vaccine works or will protect against disease	[51]			[35,36,38,45,86]	[67]
Belief that healthy people do not need vaccinations; the vaccine is not important		[96]		[36,43,44]	[61,69]
Concerned about ingredients (e.g. mercury)	[71]			[49,52,86]	
Adverse reactions to previous vaccination	[71,76]				
Structural and logistical barriers $(n = 28)$					
Cannot find provider to administer the vaccine; the vaccine was not available or offered	[76]		[23,38]	[52,59,62,87]	
Insurance coverage (e.g. inadequate insurance, Medicaid)	[76]		[25,64]	[28,36,44]	
Time, access, transportation, or inconvenience	[76]			[28, 36, 43, 52, 55]	
Out-of-pocket cost				[28, 36, 55, 59, 80]	
No insurance			[27]	[39,44,45]	
General attitudes towards health and vaccines $(n = 30)$					
Do not normally receive the influenza vaccine			[23 - 25, 33, 38, 41]	[49, 59, 82, 88]	[69]
Fear of needles, injections, or "shots"	[51,71]	[96]	[23]	[28,36,55]	
Fear, disbelief, or opposition to vaccines/vaccination	[51,65]			[28, 36, 49, 94]	[31]
Just do not want the vaccine; intentionally delayed; too much trouble	[63]			[62, 88]	
Inadequate or intermediate prenatal care			[27]		
In first trimester			[23,33,41]		

Vaccine. Author manuscript; available in PMC 2023 August 16.

Lutz et al.

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Table 2

Social and psychological barriers (n = 17)       [51,63,65]         No provider recommendation       [51,63,65]         Provider recommendation       [51,63,65]         Provider recommended against the vaccine       [51,63,65]         Social norms or influence       [65]         Do not believe "media hype"       [65]         Knowledge and awareness (n = 12)       [65]         Insufficient knowledge (e.g., general; regarding risks, benefits, availability; where to       [65]         Did not know a vaccine was needed; unaware of recommendations       [65]         Other (n = 1)       "Other"       [65]         'Other"       Provider-Identified Barriers       [65]         Other (n = 1)       "Other"       [65]         'Other"       Provider-Identified Barriers       [65]         Other (n = 1)       "Other"       [65]         'Other"       Provider-Identified Barriers       [65]         'Other" <th></th> <th>analysis</th> <th></th> <th>Focus groups</th>		analysis		Focus groups
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<ul> <li>= 1)</li> <li>-Identified Barriers</li> <li><i>I and structural barriers (n = 36)</i></li> <li><i>I concern (e.g. inadequate reimbursement, payment, and/or complexity of</i></li> <li><i>agh time (e.g. for patient education, administer vaccines)</i></li> <li><i>I s about liability</i></li> <li><i>s about liability</i><td></td><td></td><td>[86]</td><td>[61]</td></li></ul>			[86]	[61]
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uinister vaccines) ry			[29,62,65,66,74,78,79,83]	
È			[55,66,79,83]	
Ď			[48,66,79,83]	
È			[42,48,66,83]	
Ď			[29,78]	
ory			[29,66,83]	
ory			[26,62,78]	
			[55,79,83]	
			[32]	
No practice policy, or lack of information regarding policy			[48]	
Patient-oriented barriers $(n = 13)$				
Patient does not think they need it; patient refused [58]			[29, 42, 48, 66, 79, 83]	
Inadequate insurance coverage; cost to patient			[48,55]	
Other patient concerns (e.g. religious, fear of needles)			[55,78]	
Influence on patient from outside sources (e.g. Internet)			[55]	

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Barrier	Control trial (RCT <sup>*</sup> or Quasi <sup>†</sup> )	Observational cohort	Secondary data analysis	Surveys Interviews/ Focus groups
Patient concerned about safety				[55]
Knowledge and awareness $(n=11)$				
Confusion regarding or unaware of recommendations, indications, contraindications, and/or precautions; ambiguous guidelines				[29,30,66,78,79,83]
Uncomfortable educating patients or administering vaccines				[29,66,78]
Lack of knowledge or training				[30,55]
Vaccine and/or disease-related factors $(n=10)$				
Concerns about side effects and/or safety (to pregnant patient and/or fetus)				$\left[29,30,48,66,78,79,83 ight]$
Concerns about efficacy				[79.83]
Concerned about ingredients				[48]
General attitudes towards health and vaccines $(n = 6)$				
Not appropriate (e.g. not seeing enough indicated patients; not a primary care provider; belief that patient should receive it from their PCP or OB/GYN, or "not my responsibility")				29,48,62,78]
Vaccination not seen as necessary or important				[62]
No physician support (among nurses or pharmacists)				[48]

 $\dot{f}$ Quasi = quasi-experimental study (e.g. before-and-after trial, pilot study).

\* RCT = randomized controlled trial.

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Predictor	Control Trial (RCT <sup>†</sup> or Quasi <sup>**</sup> )	Observational cohort	Secondary data analysis	Surveys	Interviews/focus groups
Patient-Identified Predictors					
Social and psychological predictors $(n = 50)$					
Provider recommendation and/or offer	[40, 50, 53]	[57]	[23, 25, 34, 37, 38, 60]	[35,36,39,43,45– 47,52,59,80,92,94]	[31,61,67,69]
Altruism, responsibility, duty				[39,44,45,80]	[62,69]
Patient perceived benefits (e.g., it's a good idea, not wanting disease, not wanting to miss work)		[56]		[39,92,97]	[61,67,69]
Positive social norms or pressure	[50]			[49.52,97]	[69]
Patient-provider contact (e.g., having a regular physician, good communication with physician, adequate prenatal care)	[50]		[64]	[45,46]	
Patient regret of refusing vaccine then contracting the disease, or belief that a person who isn't immunized will likely get the disease				[43,56]	
Vaccine and/or disease-related factors $(n = 29)$					
Patient perceived effectiveness; belief that vaccine will prevent disease	[50]	[56]		[43,46,52,53,80,86,97]	[69]
Patient perceived susceptibility to, or risk of, disease	[50,70]	[56]		[43, 80, 92, 94, 97]	[69]
Patient perceived safety of vaccine (e.g. does not believe vaccines cause illness)				[46,47,80,86]	[69]
Patient perceived severity of disease or infection		[56]		[59, 80, 88]	[69]
General attitudes towards health and vaccines $(n=18)$					
Habit (i.e., past receipt of influenza or other vaccines)	[70]	[54, 84, 89]		[39,47,49,80,86,94]	
Patient trust in ACIP, doctors, medicine, and/or the government		[56]		[47,52]	[31]
Structural and logistical predictors $(n = 9)$					
Isurance coverage (private vs. public/none)			[38]	[36, 45, 46, 49]	
Insurance coverage (any vs. none)				[43,45]	
Accessibility (e.g., offered at work, easy to get)					[69]
Knowledge and awareness $(n = 4)$					
Patient knowledge of disease and/or recommendations				[86,97]	
Media coverage				[52]	
Believe provider is knowledgeable		[85]			

Predictor	Control Trial (RCT <sup>†</sup> or Quasi <sup>**</sup> )	Observational cohort	Secondary data analysis	Surveys	Interviews/focus groups
Provider-Identified Predictors					
Provider received vaccines themselves				[48]	
Provider perceived benefits to practice; provider buy-in				[48,74]	
Provider compliance with CDC guidelines				[48]	
Systems-Level Predictors					
Tools, technology, etc. (times identified $= 24$ )					
Prompts or reminders for providers	[63,72,77,90,95]	[93]			
Standing order protocols	[68, 73, 90, 91]	[75]			
Multicomponent interventions/system-wide changes	[68, 73, 90, 91, 95]				
Patient reminder-recalls	[68, 81, 90]				
Provider assessment and feedback	[68,73]				
Electronic medical record linkage, immunization information systems, and/or standardized documentation	[90.91]				
Incentives (e.g. recognize clinic with highest patient immunization rates)	[73]				
Increasing knowledge and awareness $(n = 20)$					
Provider education/increase awareness	[68, 73, 76, 90, 91, 95]	[75]			
Patient education/increase awareness	[40,70,73,76,90]				
Provider and/or staff training	[73,90,91]				
Greater nurse and/or staff involvement	[91]	[75]			
Immunization champion/manager	[68,73]				
"Culturally appropriate" interventions	[06]				
Improving access and/or availability $(n = 4)$					
Offer vaccines ''on-site'' (e.g. vaccination carts or workplace vaccination campaigns)	[73]	[75]			
Reduce out-of-pocket costs or provide vaccines at no cost	[68,73]				

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vote: Bolded citations indicate that the predictor was a singular component, part of a multicomponent interventio

 $\dot{\tau}_{RCT}$  = randomized controlled trial.

\*\* Quasi = quasi-experimental study (e.g. before-and-after trial, pilot study).

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