COVID-19 Vaccination among Pregnant People in the U.S.: A Systematic Review

Smita RAWAL Pharm D, MS , Randall L. TACKETT PhD , Rebecca H. STONE Pharm D , Henry N. YOUNG PhD

PII: S2589-9333(22)00058-1
DOI: https://doi.org/10.1016/j.ajogmf.2022.100616
Reference: AJOGMF 100616

To appear in: *American Journal of Obstetrics & Gynecology MFM*

Received date: 6 January 2022
Revised date: 2 March 2022
Accepted date: 7 March 2022

Please cite this article as: Smita RAWAL Pharm D, MS , Randall L. TACKETT PhD , Rebecca H. STONE Pharm D , Henry N. YOUNG PhD , COVID-19 Vaccination among Pregnant People in the U.S.: A Systematic Review, *American Journal of Obstetrics & Gynecology MFM* (2022), doi: https://doi.org/10.1016/j.ajogmf.2022.100616

Title: COVID-19 Vaccination among Pregnant People in the U.S.: A Systematic Review

Smita RAWAL, Pharm D, MS,[a] Randall L. TACKETT, PhD,[a] Rebecca H. STONE, Pharm D,[a]

Henry N. YOUNG, PhD [a]

a. Department of Clinical and Administrative Pharmacy, University of Georgia, Athens, GA, 30602, USA.

Disclosure: The authors report no conflict of interest.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

PROSPERO Registration Number: CRD42021286726, Registration Date:11/01/2021

Presentation: The abstract has been submitted to the upcoming ISPOR 2022 meeting. The meeting will be held at the Gaylord National Resort and Convention Center, Washington, D.C., USA, from May 15-18.

Corresponding Author:

Smita Rawal
R.C. Wilson, Rm 231, 250 W. Green Street, Athens, Georgia 30602
Office: 706-542-7230
ORCID: 0000-0001-5209-2515
Email: sr54982@uga.edu

Word count

Abstract: 349

Main text: 3,055

Condensation: Evidence supports COVID-19 vaccine's safety and effectiveness among pregnant people in the U.S.; however, vaccine acceptance is low especially among minority populations.

Short Title: COVID-19 vaccination among pregnant people in the U.S.

AJOG at a Glance:

A. Why was this study conducted?

Pregnant people are at increased risk of COVID-19 related morbidity and mortality. There is limited data regarding the safety, effectiveness, and acceptance of COVID-19 vaccination among pregnant people in the U.S.

B. What are the key findings?

Peer-reviewed studies support COVID-19 vaccines' safety and effectiveness in pregnant people, their fetuses, or neonates; however, vaccine acceptance was low especially among minorities.

C. What does this study add to what is already known?

This is the first systematic review exploring the safety, effectiveness, and acceptance of COVID-19 vaccination among pregnant people in the U.S. The safety and effectiveness of COVID-19 vaccine among pregnant people are similar to the general population. However, pregnant people exhibited vaccine hesitancy due to fear of vaccine side effects and risks to the fetus and neonate.

Keywords: COVID-19 vaccine; mRNA vaccine; pregnancy; vaccine safety; immunogenicity; vaccine effectiveness; neonatal outcomes; pregnancy outcomes; vaccine acceptance; vaccine hesitancy

Abstract

Objectives

Pregnant people are at increased risk of COVID-19 related morbidity and mortality, and vaccination presents an important strategy to prevent negative outcomes. However, pregnant people were not included in vaccine trials, and there is limited data on COVID-19 vaccines during pregnancy. The objectives of this systematic review were to identify the safety, immunogenicity, effectiveness, and acceptance of COVID-19 vaccination among pregnant people in the U.S.

Data Sources

Four databases (PubMed, Web of Science, CINAHL, and Google Scholar) were used to identify eligible studies published from January 01, 2020, through February 06, 2022.

Study Eligibility Criteria

Inclusion criteria were peer-reviewed empirical research conducted in the U.S., published in English, and addressed one of the following topics: safety, immunogenicity, effectiveness, and acceptance of COVID-19 vaccination among pregnant people.

Study Appraisal and Synthesis Methods

A narrative synthesis approach was used to synthesize findings. Critical appraisal was done using the Joanna Briggs Institute (JBI) tool.

Results

Thirty-two studies were identified. The majority of studies (n = 25) reported the use of Pfizer and Moderna COVID-19 vaccines among pregnant people; only six reported the Janssen

vaccine. Of the 32 studies, 11 examined COVID-19 vaccine safety, 10 investigated immunogenicity and effectiveness, and 11 assessed vaccine acceptance among pregnant people. Injection site pain and fatigue were the most common adverse events. One case study reported immune thrombocytopenia (ITP). COVID-19 vaccination did not increase the risk of adverse pregnancy or neonatal outcomes in comparison to unvaccinated pregnant people. After COVID-19 vaccination, pregnant people elicited a robust immune response, and vaccinations conferred protective immunity to newborns through breast milk and the placental transfer. COVID-19 vaccine acceptance was low among pregnant people in the U.S. African American race, Hispanic ethnicity, younger age, low education, prior refusal of the influenza vaccine, and lack of provider counseling were associated with low vaccine acceptance.

Conclusions

Peer-reviewed studies support COVID-19 vaccine safety and protective effects on pregnant people and their newborns. Future studies that use rigorous methodologies and include diverse populations are needed to confirm current findings. In addition, targeted and tailored strategies are needed to improve vaccine acceptance especially among minorities.

1. Introduction

Pregnant people are at an increased risk of COVID-19 related morbidity and mortality. The heightened morbidities are noted in terms of an increased risk of preterm birth[1,2] and increased need for intensive care unit admission, invasive ventilation, and death.[3-5] Vaccination presents an important strategy to prevent negative outcomes in this population. The Center for Disease Control (CDC), American College of Obstetricians and Gynecologists (ACOG), and the Society for Maternal-Fetal Medicine (SMFM) recommend that pregnant people receive COVID-19 vaccines.[6-8]

Because pregnant people were not included in the COVID-19 vaccine trials, there is limited data on vaccination safety and pregnancy outcomes compared to the general population.[9,10] The lack of safety and efficacy data means that pregnant people are left with two options: get the vaccine, with limited safety and efficacy data, or skip the vaccine, thus leaving themselves and their fetuses vulnerable to adverse effects of COVID-19. Reviews of recent studies indicate that COVID-19 vaccination during pregnancy produces immune responses and does not cause major adverse effects and negative pregnancy or neonatal outcomes.[11,12] While there is exponential growth in research on COVID-19 vaccination during pregnancy, many of these reviews included vaccines that are not authorized in the United States (U.S.).[11,12] Furthermore, these reviews included studies conducted in international settings where vaccine availability, vaccine guidelines, and healthcare systems differ from the U.S. In addition, none of the reviews provided information about the acceptance and uptake of COVID-19 vaccines among pregnant people. Therefore, there is an urgent need for a clear understanding of the safety, efficacy, and acceptance of COVID-19 vaccination during pregnancy so that pregnant people may be supported in making the best decision for their individual situations.

2. Objectives

The objective of this systematic review was to identify and synthesize what is known about COVID-19 vaccination amongst pregnant people in the U.S., including safety, effectiveness, acceptance, hesitancy, and uptake of COVID-19 vaccinations.

3. Methods

The review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) under CRD42021286726 at https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=286726. The Population, Intervention, Comparison, and Outcome (PICO) framework was used to organize this review.[13] The population of interest was pregnant people in the U.S. The intervention included COVID-19 vaccinations. The outcomes were safety, immunogenicity, effectiveness, and acceptance of the COVID-19 vaccinations. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used to direct the methodology of this systematic review.[14]

3.1. Information Sources and Search Strategy

A literature search was conducted to include studies published from January 01, 2020, through February 06, 2022. Sources included the following databases: PubMed, Web of Science, CINAHL, and Google Scholar. The key terms included in the search were "pregnant OR pregnancy OR pregnant women" AND "COVID-19 vaccine OR COVID-19 vaccination." Search results from each database were exported to Endnote. The full details of the search strategy are available in a supplementary file table (**Table S1)**.

3.2. Study Selection and Data Extraction

Studies were included if they were peer-reviewed empirical studies conducted in the U.S. from January 01, 2020, through February 06, 2022, published in English, and addressed at least 1 of the following topics: (1) safety, immunogenicity, and effectiveness of COVID-19 vaccination in pregnant people, or (2) attitudes, beliefs, perceptions, acceptance, or hesitancy of pregnant people towards COVID-19 vaccination. The exclusion criteria were non-empirical and non-peer-reviewed research, published as an abstract only, literature reviews, commentaries, or editorials, animal model studies, studies not examining COVID-19 vaccination in pregnant people, publication language other than English, and studies conducted outside of the U.S. Research conducted outside the U.S. was excluded because of the difference in vaccine availability, health advisories, and health care system structures. The 2-year timeframe was used because the first case of COVID-19 was reported in the U.S. in January 2020, and vaccination began in December 2020.

Initial screening of all abstracts and titles was conducted by SR and checked by another author (HNY) to determine whether to include or exclude a study based on the inclusion criteria. All full-text screening disagreements were reconciled through discussion between the authors (SR, RHS, RLT, and HNY) to achieve mutual consensus before moving to full-text review.

3.3. Assessment of Risk of Bias

Critical appraisals of included studies were conducted to evaluate the methodological quality of research; to what extent a study was designed, conducted, analyzed, interpreted, and reported to avoid systematic errors.[15] Appraisals focused on methodological domains through which bias may be introduced into the results.[15] All studies identified as meeting the inclusion criteria were

assessed for risk of bias by using the Joanna Briggs Institute (JBI) critical appraisal checklist for cohort studies, case-control, case report, case series, quasi-experimental (pre-post), and cross-sectional studies.[16] The checklist response options included: Yes (the criteria are clearly identifiable through the report description); Unclear (the criteria are not clearly identified in the report); and No (the criteria are not identifiable). Based on the number (%) of "Yes" responses, the risk of bias was ranked as "high" (less than or equal to 49%), "moderate" (50% to 69%), and "low" (greater than or equal to 70%).[16] Two independent reviewers (SR and HNY) conducted the appraisals, and both reviewers were blinded to each other's quality appraisal reviews. After independent review, the results were then collected by the first reviewer (SR), and discrepancies were discussed with a third reviewer (RLT). There were no exclusions made on the basis of a minimum threshold.

3.4. Data Synthesis

A standard data extraction form was used to collect the following information: study author(s) and year published, study title, study design, study setting, participants, COVID-19 vaccine type, outcomes, and conclusion(s). Data extraction and data synthesis were initially conducted by the first reviewer (SR) but discussed regularly with the review team (RHS, RLT, and HNY) to obtain agreement on all included studies and resolve any disagreements. A narrative synthesis approach was used to analyze studies included in this review.[17] The narrative synthesis approach synthesizes findings from multiple sources and primarily uses words and text to summarize and explain findings.[17] This approach is used when meta-analysis is not feasible due to high heterogeneity across studies.

4. Results

4.1. Study Selection

A total of 522 studies were obtained from PubMed, Web of Science, and CINAHL and imported into Endnote Software (Clarivate Analytics, Philadelphia, PA, U.S.). Removal of 93 duplicates yielded 429 studies. Of those, 363 studies were removed based on exclusion criteria during the title and abstract screening. The remaining 66 studies were screened for full-text review. Of these, 34 were excluded for not meeting the eligibility criteria. As a result, 32 studies were included in the review (**Figure 1**).

4.2. Study Characteristics

The characteristics of included studies are described in **Table 1.** All of the included studies used observational study designs; 15 were cohort, 10 were cross-sectional, 4 were case reports, 1 was pre-post, 1 was case-control, and 1 was case series. No randomized controlled trials were identified. Seven studies used COVID-19 vaccination registries and had sample sizes ranging from n = 2,002 to n =135,968; the remaining 25 had sample sizes less than n = 1,030. Twenty-one studies reported the use of Pfizer and Moderna COVID-19 vaccines among pregnant people; six reported the Janssen vaccine. Only one study reported the use of COVID-19 vaccine booster in pregnant people. Five studies compared vaccinated pregnant people with vaccinated non-pregnant people, and 5 studies compared vaccinated pregnant people with unvaccinated pregnant people.

4.3. Risk of Bias of Included Studies

Critical appraisals showed that 16 studies had a low risk of bias, 14 had moderate risk, and 2 exhibited high risk. One case-control study included in this review did not match participants,

and only seven studies controlled for confounders. Three studies were purely descriptive, and two studies did not explain which statistical test was used to compare differences in observations before and after an intervention. Cross-sectional studies assessing vaccine acceptance did not use valid and reliable instruments to measure acceptance. Additional details regarding the risk of bias are summarized in Supplementary Materials (**Table S2 – S7**).

4.4. Synthesis of Results

4.4.1. COVID-19 Vaccine Safety

Eleven of the 32 (34%) studies (**Figure 2**) discussed COVID-19 vaccination-related side effects in pregnant people,[18-23] pregnancy outcomes (gestational hypertension, pre-eclampsia, thromboembolism, placental injuries, miscarriage, and stillbirth),[19,24-28] and neonatal outcomes (preterm birth, congenital anomalies, small size for gestational age, neonatal ICU admission, and neonatal death).[19,27-29]

Included studies that evaluated pregnancy and neonatal outcomes following COVID-19 vaccination did not demonstrate harmful effects with respect to pregnancy,[19,24,25,26,27,28] fetal development,[19,27,28] or neonatal outcomes.[19,27-29] There were no statistical differences in pregnancy outcomes such as gestational hypertension ($p = 0.60$), pre-eclampsia ($p = 1.00$), and thromboembolism incidence ($p = 1.00$) between vaccinated and unvaccinated pregnant people.[28] There were no placental injuries[25] and no stillbirths.[27,28] The miscarriage rates after receiving COVID-19 vaccination ranged from 6.50% to 14.10%.[19,24,27] These rates of miscarriage risks after a COVID-19 vaccine were similar to the 11-16% expected rate of miscarriage in the general population.[30,31] With respect to newborns, there was no increased risk of adverse neonatal outcomes due to COVID-19 vaccination during pregnancy. No neonatal deaths were reported in the included studies.[19,27,28] Other neonatal outcomes including preterm birth (9.40%,

5.90%),[19,27,29] congenital anomalies (2.20%, 1.20%),[19,27] small size for gestational age (3.20%, 12.20%),[19,27,29] and neonatal ICU admission (0.70%, 15.30%) [27,28] following COVID-19 vaccination were similar to the expected rate of neonatal outcomes in the unvaccinated population.[32-36]

Side-effects reported in pregnant people were similar to the general population, and the most common side-effects included injection-site pain,[18-20] injection-site soreness,[20,21]fevers or chills,[18-21,23] fatigue,[18,20] and itching.[20] Immune thrombocytopenia (ITP) was reported in a case study.[22] Studies showed that the incidence of side-effects (injection-site pain, injection-site soreness, and fatigue) was higher in the second dose of vaccination compared with the first dose.[18,19,21]

4.4.2. COVID-19 Vaccine Immunogenicity and Effectiveness

Ten of the 32 (31%) studies (**Figure 2**) in pregnant people examined the immunogenicity or the ability of the COVID-19 vaccine to elicit an immune response.[21,28,37-44] These studies demonstrated that COVID-19 vaccination during pregnancy produced a robust immune response, and the antibody production was similar to those of non-pregnant people.[21,39] These antibodies were also found in umbilical cord blood,[21,37,40-44] which means COVID-19 vaccination during pregnancy may convey some immunity to neonates against COVID-19. In addition, the highest maternal and umbilical cord antibody levels were achieved through the completion of a full vaccination series and a booster dose.[44]

Regarding the strength of the vaccine, immunity produced by the COVID-19 vaccination was found to be significantly stronger than after natural infection with the virus ($p < 0.05$).[21] There was a rapid immunologic response following the first dose of the vaccine, and administration of the second dose further increased the antibody level among vaccinated

pregnant people.[21] Similar results were observed in an age-matched cohort study where pregnant people had lower antibody levels after the first dose, but by follow-up after the second dose, immune responses were achieved comparable to that of non-pregnant people.[45] With regard to the effectiveness, COVID-19 vaccination was effective in preventing COVID-19 infection among pregnant people. A study among pregnant people showed that only 0.40% (9/2136) and 0.20% (3/1822) experienced COVID-19 infection >14 days after the first Pfizer–BioNTech and Moderna vaccination, respectively.[19] Another study that compared vaccinated and unvaccinated pregnant people showed that vaccination significantly reduced the risk of future COVID-19 infection ($p < 0.05$).[28]

4.4.3. COVID-19 Vaccine Acceptance

Eleven of the 32 (34%) studies (**Figure 2**) examined pregnant people's acceptance or uptake of COVID-19 vaccination.[46-56] Overall, COVID-19 vaccine acceptance rates ranged between 3% and 65%. Studies conducted before the COVID-19 vaccine became available in the U.S. showed that 41%[54] and 47.80%[46] of pregnant people would be interested in receiving it. Vaccine hesitant pregnant people were concerned about side effects, sickness, allergy to the vaccine, and a perception that the vaccine is unnecessary.[46] A study reported 65% vaccine acceptance among pregnant people; this study had a sample consisting of people with higher education and greater income[55] in comparison to other studies.[46,47,50] The vaccine acceptance rate did not improve after the COVID-19 vaccine became available in the U.S. Studies conducted after the vaccine became available showed acceptance rates of 3%,[51] 16.30%,[48] 35.70%,[50]44.30%,[49] and 58.30%.[47]

Seven of the 11 vaccine acceptance studies examined factors that were associated with vaccine acceptance. Pregnant people's receipt of the influenza vaccine in the previous year and

communication with a medical professional about vaccines were associated with increased likelihood of COVID-19 vaccine acceptance.[45,52,55] In contrast, pregnant people's prior refusal of the seasonal influenza vaccine,[47,54] lack of provider counseling,[50] younger age,[45,48] African American race,[47,48,50,53,54] Hispanic ethnicity,[47,48,50,54] and low education[50] were associated with refusal of vaccination. Frequently cited concerns included safety and effectiveness of COVID-19 vaccination, fears of birth defects, unknown long-term health effects on children, and risk of pregnancy loss.[47,53,56]

5. Comment

5.1. Principal Findings

This study reviewed the available literature on COVID-19 vaccination amongst pregnant people in the U.S. Peer-reviewed observational studies support the assertion that the COVID-19 vaccine is safe during pregnancy and provides protective effects for both pregnant people and their newborns. Most of the reported side-effects such as injection site pain, soreness, fever or chills, and fatigue were not severe and similar to those reported in the general population. Immune thrombocytopenia (ITP) was reported in one case study.[22] This very rare event has an incidence ranging from 1 case per 26,000 to 1 case per 127,000 doses,[57]and may be resolved by oral corticosteroids without subsequent complications.[22]

The protective effects of COVID-19 vaccines in pregnant people were similar to that of the general population. Pregnant people elicited a robust immune response after vaccination with immunogenicity equivalent to non-pregnant people.[21] The vaccines also conferred protective immunity to newborns through breast milk and placental transfer.[21,27,40] This demonstrates that COVID-19 vaccination in pregnancy likely has a dual benefit: both the mother and newborn

receive antibodies. Supported by studies that demonstrated the efficient maternofetal transplacental transfer of anti-COVID-19 antibodies,[58,59] Israel placed pregnant people on its vaccine priority list.[60] The U.S. has not formally prioritized COVID-19 vaccination for pregnant people, which may ultimately contribute to poorer maternal and fetal outcomes in the U.S. Even though COVID-19 vaccination is beneficial during both pregnancy and lactation, it may be most beneficial during pregnancy because higher levels of antibodies were found in early milk compared to later milk.[39]

Although randomized controlled clinical trials involving pregnant people are lacking, data from all observational studies indicate that pregnant people tolerate COVID-19 vaccines well. Major adverse events have not been reported for mother and fetus or neonate, and the scientific understanding of the vaccine's mechanism of action does not raise theoretical safety concerns.[19,24,26,48] Studies of COVID-19 vaccines authorized in the U.S. show that the vaccine virus does not cross the placenta.[37,59] Only protective antibodies produced in the vaccinated mother's body are transferred to the neonates through breastmilk or placental transfer.[21,42,40] COVID-19 vaccine safety and effectiveness are important factors in achieving population immunity; however, wider acceptance of vaccines is crucial for achieving sufficient immunization coverage.

Current research indicates a low acceptance of COVID-19 vaccination among pregnant people in the U.S. Specifically, Black and Latinx people have shown less trust in the vaccine and cited fear of side effects and risks to the fetus or neonate.[46,47,53,56] The lack of trust in the COVID-19 vaccine and vaccine refusal may stem from long-standing medical distrust among various communities due to historical misdeeds (e.g., Tuskegee syphilis study).[61] Contemporary healthcare encounters may also cultivate distrust of healthcare professionals and researchers. A

2020 Kaiser Family Foundation survey of 1,700 U.S. adults showed that 45% of Black patients reported at least 1 of 6 negative experiences with a health care professional, and 36% believed they would have received better care if they were of different race/ethnicity.[62]

Low acceptance of vaccines could be addressed by forming partnerships between healthcare and trusted community-based organizations (CBOs). Collaborations with trusted communities can work towards developing and delivering accurate, consistent, and transparent messaging to effectively promote vaccine acceptance and other positive health behaviors.[63-65] Virtual town hall meetings hosted by community leaders and local healthcare providers can engage communities in discussions regarding COVID-19 vaccines.[66] Targeted messages conveyed through multiple languages that focus on vaccine safety, efficacy, and vaccine's ability to confer protective immunity to neonates may alleviate fear and increase the likelihood of vaccination.[67] Healthcare providers (HCPs) discussing risk and benefit information with pregnant people during routine visits may be another strategy to alleviate fear and reduce vaccine hesitancy. Prior research has shown that vaccine communication comprising education and recommendations from HCPs bolstered Tdap and influenza vaccine acceptance among pregnant people.[68-70] Given what is known about COVID-19 vaccine safety and effectiveness, HCPs can use available data to educate and empower pregnant people to make informed decisions. In addition, HCPs who have received the COVID-19 vaccine when they were pregnant may be positioned to share their credible vaccination experiences. A national recommendation endorsing COVID-19 vaccine administration during pregnancy, with additional support and reinforcement by their HCP, may improve vaccine uptake by pregnant people.

5.2. Strengths and Limitations

To the best of our knowledge, this is the first systematic review exploring COVID-19 vaccination among pregnant people in the U.S. This comprehensive review included all peer-reviewed empirical studies published so far on this topic. However, certain limitations of the present study should be acknowledged. First, all studies included in this review were observational, non-randomized, and lacked long-term safety and effectiveness data. Thus, the evidence presented in this review may be limited due to prior study designs. Second, studies included in this review were not excluded based on critical appraisals of the research (i.e., risk of bias assessments). It was considered important to include all studies irrespective of the risk of bias to obtain a more comprehensive picture of relevant research pertaining to the aim of this review. However, it is acknowledged that the lack of a minimum threshold may hold some limitations for the findings. Lastly, the evidence presented in this review may be limited for the Janssen COVID-19 vaccine, since only six studies reported the use of the Janssen COVID-19 vaccine among pregnant people.

5.3. Conclusions and Implications

Peer-reviewed studies support COVID-19 vaccine safety and protective effects on pregnant people and their newborns. Future studies that use rigorous methodologies and include diverse populations (e.g., minorities and rural residents) are needed to confirm current findings and examine the effectiveness of COVID-19 vaccines and boosters on emerging SARS-CoV-2 variants during pregnancy. In addition, targeted and tailored strategies may help improve vaccine acceptance among pregnant people, especially vulnerable populations.

Author contributions

Smita Rawal: Conceptualization, Methodology, Investigation, Resources, Writing - original draft, Writing - review & editing.

Rebecca H. Stone: Conceptualization, Methodology, Resources, Writing - review & editing.

Randall L. Tackett: Conceptualization, Methodology, Resources, Writing - review & editing, Supervision, Project administration.

Henry N. Young: Conceptualization, Methodology, Resources, Writing - review & editing, Supervision, Project administration.

References

1. Woodworth KR, Olsen EOM, Neelam V, et al. Birth and infant outcomes following laboratory-confirmed SARS-CoV-2 infection in pregnancy—SET-NET, 16 jurisdictions, March 29–October 14, 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69(44):1635.
2. Khalil A, Von Dadelszen P, Draycott T, Ugwumadu A, O'Brien P, Magee L. Change in the incidence of stillbirth and preterm delivery during the COVID-19 pandemic. *JAMA.* 2020;324(7):705-706.
3. Zambrano LD, Ellington S, Strid P, et al. Update: characteristics of symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status—United States, January 22–October 3, 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69(44):1641.
4. Lokken EM, Huebner EM, Taylor GG, et al. Disease severity, pregnancy outcomes and maternal deaths among pregnant patients with SARS-CoV-2 infection in Washington State. *Am J Obstet Gynecol.* 2021.
5. Crovetto F, Crispi F, Llurba E, et al. Impact of SARS-CoV-2 Infection on Pregnancy Outcomes: A Population-Based Study. *Clin Infect Dis: an Official Publication of the Infectious Diseases Society of America.* 2021.
6. ACOG and SMFM Recommend COVID-19 Vaccination for Pregnant Individuals. . American College of Obstetricians and Gynecologists (ACOG). https://www.acog.org/news/news-releases/2021/07/acog-smfm-recommend-covid-19-vaccination-for-pregnant-individuals. Published 2021. Updated Jul 30, 2021. Accessed November 30, 2021.
7. COVID-19 vaccines while pregnant or breastfeeding. Centers for Disease Control and Prevention https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/pregnancy.html. Published 2021. Accessed November 30, 2021.
8. Rasmussen SA, Jamieson DJ. Pregnancy, postpartum care, and COVID-19 vaccination in 2021. *JAMA.* 2021;325(11):1099-1100.
9. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med.* 2020.
10. Pogue K, Jensen JL, Stancil CK, et al. Influences on attitudes regarding potential COVID-19 vaccination in the United States. *Vaccines.* 2020;8(4):582.
11. Fu W, Sivajohan B, McClymont E, et al. Systematic review of the safety, immunogenicity, and effectiveness of COVID-19 vaccines in pregnant and lactating individuals and their infants. *Int J Gynaecol Obstet.* 2021.
12. Falsaperla R, Leone G, Familiari M, Ruggieri M. COVID-19 vaccination in pregnant and lactating women: a systematic review. *Expert Rev Vaccines.* 2021:1-10.
13. Richardson WS, Wilson MC, Nishikawa J, Hayward RS. The well-built clinical question: a key to evidence-based decisions. *Acp j club.* 1995;123(3):A12-A13.
14. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev.* 2015;4(1):1-9.
15. Higgins JP, Savović J, Page MJ, Elbers RG, Sterne JA. Assessing risk of bias in a randomized trial. *Cochrane Database Syst Rev.* 2019:205-228.
16. Checklist for Systematic Reviews and Research syntheses, Critical Appraisal Tools. Joanna Briggs Institute, Adelaide, Australia. https://jbi.global/sites/default/files/2019-05/JBI_Critical_Appraisal-Checklist_for_Systematic_Reviews2017_0.pdf. Published 2017. Accessed December 1, 2021.
17. Popay J, Roberts H, Sowden A, et al. Guidance on the conduct of narrative synthesis in systematic reviews. *A product from the ESRC methods programme Version.* 2006;1:b92.

18. Kachikis A, Englund JA, Singleton M, Covelli I, Drake AL, Eckert LO. Short-term Reactions Among Pregnant and Lactating Individuals in the First Wave of the COVID-19 Vaccine Rollout. *JAMA Netw Open.* 2021;4(8):e2121310.
19. Shimabukuro TT, Kim SY, Myers TR, et al. Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons. *N Engl J Med.* 2021;384(24):2273-2282.
20. Kadali RAK, Janagama R, Peruru SR, et al. Adverse effects of COVID-19 messenger RNA vaccines among pregnant women: a cross-sectional study on healthcare workers with detailed self-reported symptoms. *Am J Obstet Gynecol.* 2021.
21. Gray KJ, Bordt EA, Atyeo C, et al. Coronavirus disease 2019 vaccine response in pregnant and lactating women: a cohort study. *Am J Obstet Gynecol.* 2021.
22. Bennett C, Chambers LM, Son J, Goje O. Newly diagnosed immune thrombocytopenia in a pregnant patient after coronavirus disease 2019 vaccination. *J Obstet Gynaecol Res.* 2021.
23. Nakahara A, Biggio J, Elmayan A, Williams FB. Safety-related outcomes of novel mRNA COVID-19 vaccines in pregnancy. *American journal of perinatology.* 2022(AAM).
24. Zauche LH, Wallace B, Smoots AN, et al. Receipt of mRNA Covid-19 Vaccines and Risk of Spontaneous Abortion. *N Engl J Med.* 2021.
25. Shanes ED, Otero S, Mithal LB, Mupanomunda CA, Miller ES, Goldstein JA. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Vaccination in Pregnancy: Measures of Immunity and Placental Histopathology. *Obstet Gynecol.* 2021;138(2):281-283.
26. Kharbanda EO, Haapala J, DeSilva M, et al. Spontaneous Abortion Following COVID-19 Vaccination During Pregnancy. *JAMA.* 2021.
27. Trostle ME, Limaye MA, Avtushka V, Lighter JL, Penfield CA, Roman AS. COVID-19 vaccination in pregnancy: early experience from a single institution. *Am J Obstet Gynecol MFM.* 2021;3(6):100464.
28. Theiler RN, Wick M, Mehta R, Weaver AL, Virk A, Swift M. Pregnancy and birth outcomes after SARS-CoV-2 vaccination in pregnancy. *Am J Obstet Gynecol MFM.* 2021;3(6):100467-100467.
29. Lipkind HS, Vazquez-Benitez G, DeSilva M, et al. Receipt of COVID-19 Vaccine During Pregnancy and Preterm or Small-for-Gestational-Age at Birth—Eight Integrated Health Care Organizations, United States, December 15, 2020–July 22, 2021. *Morbidity and Mortality Weekly Report.* 2022;71(1):26.
30. Mukherjee S, Velez Edwards DR, Baird DD, Savitz DA, Hartmann KE. Risk of miscarriage among black women and white women in a US Prospective Cohort Study. *Am J Epidemiol.* 2013;177(11):1271-1278.
31. Magnus MC, Wilcox AJ, Morken N-H, Weinberg CR, Håberg SE. Role of maternal age and pregnancy history in risk of miscarriage: prospective register based study. *bmj.* 2019;364.
32. Ferré C, Callaghan W, Olson C, Sharma A, Barfield W. Effects of maternal age and age-specific preterm birth rates on overall preterm birth rates—United States, 2007 and 2014. *Morbidity and Mortality Weekly Report.* 2016;65(43):1181-1184.
33. Percentage of births born preterm by state. Centers for Disease Control and Prevention (CDC) National Center for Health Statistics. Web site. https://www.cdc.gov/nchs/pressroom/sosmap/preterm_births/preterm.htm. Published 2018. Accessed December 1, 2021.
34. Boghossian NS, Geraci M, Edwards EM, Horbar JD. Morbidity and mortality in small for gestational age infants at 22 to 29 weeks' gestation. *Pediatrics.* 2018;141(2).
35. Francis A, Hugh O, Gardosi J. Customized vs INTERGROWTH-21st standards for the assessment of birthweight and stillbirth risk at term. *Am J Obstet Gynecol.* 2018;218(2):S692-S699.
36. Update on overall prevalence of major birth defects--Atlanta, Georgia, 1978-2005. *MMWR Morb Mortal Wkly Rep.* 2008;57(1):1-5.

37. Mithal LB, Otero S, Shanes ED, Goldstein JA, Miller ES. Cord blood antibodies following maternal coronavirus disease 2019 vaccination during pregnancy. *Am J Obstet Gynecol.* 2021;225(2):192-194.
38. Gill L, Jones CW. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Antibodies in Neonatal Cord Blood After Vaccination in Pregnancy. *Obstet Gynecol.* 2021;137(5):894-896.
39. Collier AY, McMahan K, Yu J, et al. Immunogenicity of COVID-19 mRNA Vaccines in Pregnant and Lactating Women. *JAMA.* 2021;325(23):2370-2380.
40. Paul G, Chad R. Newborn antibodies to SARS-CoV-2 detected in cord blood after maternal vaccination–a case report. *BMC Pediatr.* 2021;21(1):1-2.
41. Prabhu M, Murphy EA, Sukhu AC, et al. Antibody Response to Coronavirus Disease 2019 (COVID-19) Messenger RNA Vaccination in Pregnant Women and Transplacental Passage Into Cord Blood. *Obstet Gynecol.* 2021:10.1097.
42. Trostle ME, Aguero-Rosenfeld ME, Roman AS, Lighter JL. High antibody levels in cord blood from pregnant women vaccinated against COVID-19. *American journal of obstetrics & gynecology MFM.* 2021.
43. Mangat C, Milosavljevic N. BNT162b2 Vaccination during Pregnancy Protects Both the Mother and Infant: Anti-SARS-CoV-2 S Antibodies Persistently Positive in an Infant at 6 Months of Age. *Case Reports in Pediatrics.* 2021;2021.
44. Yang YJ, Murphy EA, Singh S, et al. Association of Gestational Age at Coronavirus Disease 2019 (COVID-19) Vaccination, History of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection, and a Vaccine Booster Dose With Maternal and Umbilical Cord Antibody Levels at Delivery. *Obstetrics & Gynecology.* 2021:10.1097.
45. Atyeo C, DeRiso EA, Davis C, et al. COVID-19 mRNA vaccines drive differential antibody Fc-functional profiles in pregnant, lactating, and nonpregnant women. *Sci Transl Med.* 2021;13(617):eabi8631.
46. Ahlers-Schmidt CR, Hervey AM, Neil T, Kuhlmann S, Kuhlmann Z. Concerns of women regarding pregnancy and childbirth during the COVID-19 pandemic. *Patient Educ Couns.* 2020;103(12):2578-2582.
47. Levy AT, Singh S, Riley LE, Prabhu M. Acceptance of COVID-19 vaccination in pregnancy: a survey study. *Am J Obstet Gynecol MFM.* 2021;3(5):100399.
48. Razzaghi H, Meghani M, Pingali C, et al. COVID-19 Vaccination Coverage Among Pregnant Women During Pregnancy - Eight Integrated Health Care Organizations, United States, December 14, 2020-May 8, 2021. *MMWR Morb Mortal Wkly Rep.* 2021;70(24):895-899.
49. Sutton D, D'Alton M, Zhang Y, et al. COVID-19 vaccine acceptance among pregnant, breastfeeding, and nonpregnant reproductive-aged women. *Am J Obstet Gynecol MFM.* 2021;3(5):100403.
50. Huddleston HG, Jaswa EG, Lindquist KJ, et al. COVID-19 Vaccination Patterns and Attitudes Among American Pregnant Individuals. *Am J Obstet Gynecol MFM.* 2021.
51. Hirshberg JS, Huysman BC, Oakes MC, et al. Offering onsite COVID-19 vaccination to high-risk obstetrical patients: initial findings. *Am J Obstet Gynecol MFM.* 2021;3(6).
52. Desai P, Kaur G, Fanglong D, Rodriguez MH. COVID-19 Vaccine Acceptance In Pregnancy. *Neonatology Today.* 2021:11-15.
53. Townsel C, Moniz MH, Wagner AL, et al. COVID-19 vaccine hesitancy among reproductive-aged female tier 1A healthcare workers in a United States Medical Center. *J Perinatol.* 2021;41(10):2549-2551.
54. Battarbee AN, Stockwell MS, Varner M, et al. Attitudes toward COVID-19 illness and COVID-19 vaccination among pregnant women: a cross-sectional multicenter study during August–December 2020. *American journal of perinatology.* 2022;39(01):075-083.

55. Sznajder KK, Kjerulff KH, Wang M, Hwang W, Ramirez SI, Gandhi CK. Covid-19 vaccine acceptance and associated factors among pregnant women in Pennsylvania 2020. *Preventive Medicine Reports.* 2022:101713.
56. Wang T, Krishnamurti T, Bernard M, Lopa S, Quinn B, Simhan H. Perceptions and knowledge of COVID-19 vaccine safety and efficacy among vaccinated and non-vaccinated obstetric healthcare workers. *Behavioral Medicine.* 2021:1-13.
57. Pai M, Chan B, Stall N, et al. Vaccine-induced immune thrombotic thrombocytopenia (VITT) following adenovirus vector COVID-19 vaccination. *Science Briefs of the Ontario COVID-19 Science Advisory Table.* 2021;2(17):1-7.
58. Rottenstreich A, Zarbiv G, Oiknine-Djian E, Zigron R, Wolf DG, Porat S. Efficient maternofetal transplacental transfer of anti- SARS-CoV-2 spike antibodies after antenatal SARS-CoV-2 BNT162b2 mRNA vaccination. *Clin Infect Dis.* 2021.
59. Beharier O, Mayo RP, Raz T, et al. Efficient maternal to neonatal transfer of antibodies against SARS-CoV-2 and BNT162b2 mRNA COVID-19 vaccine. *J Clin Investig.* 2021.
60. Vaccinating Women who are Planning a Pregnancy, Pregnant or Breastfeeding with the COVID-19 Vaccine – Clarification [press release]. Ministry of Health, January 28, 2021 2021.
61. Shavers VL, Lynch CF, Burmeister LF. Knowledge of the Tuskegee study and its impact on the willingness to participate in medical research studies. *Journal of the National Medical Association.* 2000;92(12):563.
62. Hamel L, Lopes L, Muñana C, Artiga S, Brodie M. The Undefeated Survey on Race and Health. Kaiser Family Foundation. San Francisco, CA: Kaiser Family Foundation Web site. https://www.kff.org/report-section/kff-the-undefeated-survey-on-race-and-health-main-findings/. Published 2020. Accessed February 06, 2022.
63. Quinn SC, Andrasik MP. Addressing vaccine hesitancy in BIPOC communities—toward trustworthiness, partnership, and reciprocity. *New England Journal of Medicine.* 2021;385(2):97-100.
64. Cowell AJ, Farrelly MC, Chou R, Vallone DM. Assessing the impact of the national 'truth'antismoking campaign on beliefs, attitudes, and intent to smoke by race/ethnicity. *Ethnicity & health.* 2009;14(1):75-91.
65. Carson SL, Gonzalez C, Lopez S, et al. Reflections on the importance of community-partnered research strategies for health equity in the era of COVID-19. *Journal of health care for the poor and underserved.* 2020;31(4):1515.
66. Wagner EF, Langwerden RJ, Morris SL, et al. Virtual town halls addressing vaccine hesitancy among racial and ethnic minorities: Preliminary findings. *Journal of the American Pharmacists Association.* 2022;62(1):317-325.
67. Feifer RA, Bethea L, White EM. Racial disparities in COVID-19 vaccine acceptance: Building trust to protect nursing home staff and residents. *Journal of the American Medical Directors Association.* 2021;22(9):1853-1855. e1851.
68. Strassberg ER, Power M, Schulkin J, et al. Patient attitudes toward influenza and tetanus, diphtheria and acellular pertussis vaccination in pregnancy. *Vaccine.* 2018;36(30):4548-4554.
69. Yuen CYS, Tarrant M. Determinants of uptake of influenza vaccination among pregnant women–a systematic review. *Vaccine.* 2014;32(36):4602-4613.
70. Myers KL. Predictors of maternal vaccination in the United States: An integrative review of the literature. *Vaccine.* 2016;34(34):3942-3949.

Table 1. Characteristics of Included Studies (n = 32)

COVID-19 Vaccine Safety							
Author(s), Year	**Study Title**	**Study Design**	**Study Setting**	**Participants (n)**	**COVID-19 Vaccine Types, % received**	**Outcomes**	**Conclusions**
Bennett et al., 2021	Newly diagnosed immune thrombocytopenia in a pregnant patient after coronavirus disease 2019 vaccination	Case report	Hospital in Ohio	Vaccinated pregnant woman at the first trimester of pregnancy (n = 1)	Moderna mRNA-1273 Patient had received first dose only.	**Vaccine side effects:** Immune thrombocytopenia (ITP) occurred 13 days after COVID-19 vaccination. ITP was resolved by oral corticosteroids and patient was discharged home on the fourth day of hospitalization with no complications.	COVID-19 vaccination benefits outweigh the risk of infection in pregnancy and that pregnant women should be included in clinical trials.

Kachikis et al., 2021	Short-term Reactions Among Pregnant and Lactating Individuals in the First Wave of the COVID-19 Vaccine Rollout	Cohort study	Online Registry in the US	Pregnant (n = 7,809), Lactating (n = 6,815) and neither pregnant nor lactating women but planning pregnancy (n = 2,901)	Pfizer-BioNTech BNT162b2: 61.9% Moderna mRNA-1273: 37.8% Janssen JNJ-78436735: 0.23% 85.9% of all participants received both doses.	**Vaccine side effects:** Women who received vaccine experienced pain at injection site (91.4%) and fatigue (31.3%). **Pregnancy outcomes:** 0.7 % of pregnant women reported miscarriages at the time of their second vaccine dose.	COVID-19 vaccines were well-tolerated among pregnant women.

Kadali et al., 2021	Adverse effects of COVID-19 messenger RNA vaccines among pregnant women: a cross-sectional study on healthcare workers with detailed self-reported symptoms	Cross-sectional survey	Online survey of US adults	Vaccinated pregnant healthcare workers (HCWs) (n = 38) and non-pregnant HCWs (n = 991)	Pfizer-BioNTech BNT162b2: 52.6% Moderna mRNA-1273 : 47.4% About 81.58% (31 of 38) of the pregnant HCWs received both doses of the mRNA vaccine.	**Vaccine side effects:** The vaccine side effects experienced by pregnant HCWs were minor and included sore arm (93%) and itching (5%). The side-effects appeared to be similar (with no significant statistical difference) when compared with non-pregnant HCWs.	COVID-19 vaccines side effects and safety were comparable among pregnant and non-pregnant HCWs.

Kharbanda et al., 2021	Spontaneous Abortion Following COVID-19 Vaccination During Pregnancy	Case-control surveillance of Vaccine Safety Datalink	8 health systems (5 Kaiser Permanente health systems; Denver Health; HealthPartners; and Marshfield Clinic in Washington, California, Colorado, Wisconsin	Pregnant women (n = 105,446)	Pfizer-BioNTech BNT162b2 : received 1 or more doses (7.80%) Moderna mRNA-1273 : received 1 or more doses (6.0%) Janssen JNJ-78436735 : 0.50%	**Pregnancy outcomes:** 13,160 miscarriages and 92,286 ongoing pregnancies were identified. Spontaneous abortions did not have an increased odds of exposure to a COVID-19 vaccination in the prior 28 days compared with ongoing pregnancies (aOR, 1.02; 95% CI, 0.96-1.08). Results were consistent for mRNA-1273 and BNT162b2 and by gestational age group.	Among women with miscarriages, the odds of COVID-19 vaccine exposure were not increased in the prior 28 days compared with women with ongoing pregnancies.

Lipkind et al., 2022	Receipt of COVID-19 Vaccine During Pregnancy and Preterm or Small-for-Gestational-Age at Birth — Eight Integrated Health Care Organizations, United States, December 15, 2020–July 22, 2021	Cohort study	8 health systems (5 Kaiser Permanente health systems; Denver Health; HealthPartners; and Marshfield Clinic in Washington, California, Colorado, Wisconsin	Unvaccinated pregnant women (n = 36,015) and vaccinated pregnant women (n = 10,064)	Pfizer-BioNTech BNT162b2 : received 1 or more doses (54.40 %) Moderna mRNA-1273 : received 1 or more doses (41.40%) Janssen JNJ-78436735 : 4.20%	**Pregnancy outcomes:** The prevalence of preterm birth and small-for-gestational-age (SGA) at birth were 6.6 and 8.2 per 100 live births, respectively. COVID-19 vaccination during pregnancy was not significantly associated with increased risk for preterm birth overall (aHR = 0.91; 95% CI = 0.82–1.01; p = 0.06) or SGA at birth (aHR = 0.95; 95% CI = 0.87–1.03; p = 0.24).	COVID-19 vaccination during pregnancy is not associated with negative neonatal outcomes, when compared with unvaccinated pregnant women.

Nakahara et al., 2022	Safety-related outcomes of novel mRNA COVID-19 vaccines in pregnancy	Cohort study	Ochsner health system in Louisiana and Mississippi	Unvaccinated women (n = 166) and vaccinated pregnant women (n = 83)	mRNA vaccine (Type not stated)	Pregnant individuals were more likely to report fever (4.80% vs 0.60%, p = 0.04) and gastrointestinal symptoms (4.80% vs 0%, p = 0.01). Frequency of complaint following vaccine administration was not different between pregnant and non-pregnant persons (18.10% vs 16.90%, P = 0.20).	Side effects following the COVID-19 vaccination administration were similar between pregnant and non-pregnant individuals.

Shanes et al., 2021	Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Vaccination in Pregnancy	Cohort study	Hospital in Chicago	Unvaccinated pregnant (n = 116) and vaccinated pregnant women (n = 84)	mRNA vaccine (Type not stated)	**Pregnancy outcomes:** Placental examination in women with vaccination showed no increased incidence of placental injuries compared with the control group.	There was no observed adverse pregnancy outcomes and placental injuries in vaccinated pregnant women.
Shimabukuro et al., 2021	Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons	Cohort study	COVID-19 vaccine pregnancy registry in the US	Vaccinated pregnant women (n = 35,691)	Pfizer-BioNTech BNT162b2: 53.9% Moderna mRNA-1273: 46.10%	**Vaccine side effects:** Injection-site pain reported. **Pregnancy outcomes:** No neonatal deaths were reported.12.60% had a spontaneous abortion, 9.40% a preterm birth, and 3.20% a baby small for gestational age (SGA).	Preliminary findings did not show any major safety issues among pregnant, mRNA vaccine recipients.

Theiler et al., 2021	Pregnancy and birth outcomes after SARS-CoV-2 vaccination in pregnancy	Cohort study	Mayo Clinic Health System in Minnesota and Wisconsin	Unvaccinated pregnant women (n = 1,862) and vaccinated pregnant women (n = 140)	Pfizer-BioNTech BNT162b2: 90.70% Moderna mRNA-1273: 8.57% Janssen JNJ-78436735: 0.71%. 73.60% of pregnant women completed both doses of vaccination before delivery.	**Pregnancy outcomes:** Thromboembolic events, gestational hypertension and preeclampsia risk was similar between vaccinated and unvaccinated pregnant women. **Neonatal outcomes:** Preterm birth, neonatal birthweight in pregnant vaccinated people were similar when compared with unvaccinated pregnant women.	Compared to unvaccinated pregnant women, vaccinated pregnant women were less likely to experience COVID-19 infection. And vaccination during pregnancy was not associated with increased pregnancy or delivery complications.

Trostle et al., 2021	COVID-19 vaccination in pregnancy: early experience from a single institution	Cohort study	Academic medical center in New York	Vaccinated pregnant women (n = 424)	mRNA vaccine: 100% Of those, 82.10% had received both doses and 17.90% had received only 1 dose.	**Pregnancy outcomes:** 9 women had spontaneous abortions, 3 terminated their pregnancies, and 327 had ongoing pregnancies. There were no stillbirths. **Neonatal outcomes:** The rate of preterm birth was 5.90%. 15.30% of neonates required admission to the neonatal intensive care unit (NICU). 12.20% were small for gestational age (SGA) per the WHO standards.	The rate of spontaneous abortion in this study was within the expected rate of 10%, and preterm birth rate of 5.9% was below the national average of 9.50%, and 12.20% rate of SGA neonates was near the expected value.

Zauche et al., 2021	Receipt of mRNA Covid-19 Vaccines and Risk of Spontaneous Abortion	Cohort study	COVID-19 vaccine pregnancy registry in the US	Vaccinated pregnant women (n = 2,456)	Pfizer-BioNTech BNT162b2 : 52.70% Moderna mRNA-1273: 47.30%	**Pregnancy outcomes:** The cumulative risk of spontaneous abortion from 6 to less than 20 weeks of gestation was 14.10% (95% CI,12.10 to 16.10) in the primary analysis and 12.80% (95% CI, 10.80 to 14.80) in an analysis using direct maternal age–standardization to the reference population.	The risk of spontaneous abortion after mRNA COVID-19 vaccination is consistent with the expected risk of spontaneous abortion. The mRNA COVID-19 vaccination is safe in pregnancy.

COVID-19 Vaccine Immunogenicity and Effectiveness							
Author(s), Year	**Study Title**	**Study Design**	**Study Setting**	**Participants (n)**	**COVID-19 Vaccine Type, % received**	**Outcomes**	**Conclusions**
Atyeo et al., 2021	COVID-19 mRNA vaccines drive differential antibody Fc-functional profiles in pregnant, lactating, and non-pregnant women	Cohort study	Tertiary care centers in the US	Vaccinated, pregnant (n = 84), lactating (n = 31), and non-pregnant (n = 16) age-matched controls	Both doses of Pfizer-BioNTech BNT162b2 or Moderna mRNA-1273	Vaccine-specific antibody levels were lower compared to non-pregnant women after the first vaccine dose, which normalized after the second dose.	There is a need to complete both doses of COVID-19 vaccine in pregnant population to ensure full immunity is attained.

Collier et al., 2021	Immunogenicity of COVID-19 mRNA Vaccines in Pregnant and Lactating Women	Cohort study	Hospital in Massachusetts	Pregnant (n = 30), lactating (n = 16), and neither pregnant nor lactating women (n = 57) who were vaccinated or had had confirmed COVID-19 infection in the past	Both doses of Pfizer-BioNTech BNT162b2 or Moderna mRNA-1273	Pregnant, lactating, and non-pregnant women who were vaccinated developed antibody responses and T-cell responses against COVID-19 infection.	Pregnant and non-pregnant women who were vaccinated developed antibody responses and T-cell responses against SARS-CoV-2 variants.

Gill and Jones, 2021	Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Antibodies in Neonatal Cord Blood After Vaccination in Pregnancy	Case study	Hospital in Minnesota	Pregnant woman vaccinated in the third trimester of pregnancy (n = 1)	Both doses of Pfizer-BioNTech BNT162b2 mRNA vaccine	Uncomplicated spontaneous vaginal delivery of a female neonate occurred at term. The patient's blood and neonatal cord blood were evaluated for SARS-CoV-2–specific antibodies. Both the patient and the neonate were positive for antibodies. There was transplacental transfer of neutralizing SARS-CoV-2 antibodies.	This is the first case report documenting transplacental transfer of neutralizing SARS-CoV-2 antibodies after vaccination in the third trimester of pregnancy.

Gray et al., 2021	Coronavirus disease 2019 vaccine response in pregnant and lactating women: a cohort study	Cohort study	Academic medical centers in Massachusetts	Vaccinated pregnant (n = 84), lactating (n = 31), and non-pregnant women (n = 16)	Pfizer-BioNTech BNT162b2: 49% Moderna mRNA-1273: 51%	Vaccine created robust humoral immunity in pregnant and lactating women, with immunogenicity similar to that of non-pregnant women (pregnant, median, 5.59; IQR, 4.68-5.89; lactating, median, 5.74; IQR, 5.06-6.22; non-pregnant, median, 5.62; IQR, 4.77-5.98, p = 0.24). Also, vaccine-generated antibodies were present in all umbilical cord blood and breastmilk samples.	COVID-19 mRNA vaccines generated immunity in pregnant and lactating women, with immunogenicity similar to that observed in non-pregnant women. Immune transfer to neonates occurred via placental transfer and breastmilk.

Mangat et al., 2021	BNT162b2 Vaccination during Pregnancy Protects Both the Mother and Infant: Anti-SARS-CoV-2 S Antibodies Persistently Positive in an Infant at 6 Months of Age	Case study	Mayo clinic health system	Pregnant woman vaccinated with 2 doses of COVID-19 vaccine at 22 and 26 weeks of gestation (n = 1)	Both doses of Pfizer-BioNTech BNT162b2 mRNA vaccine	At 33 weeks of gestation, a preterm neonate was delivered via emergency cesarean section. To evaluate for SARS-CoV-2–specific antibodies, a serological test was done on the newborn at 6 weeks, 3 months, and 6 months. Positive anti-SARS-CoV-2 S antibodies were detected in the infant at 6 weeks, 3 months, and 6 months of age.	There was transplacental transfer of neutralizing SARS-CoV-2 antibodies after vaccination during pregnancy and the immune persisted at the infant's 6 months of age.

Mithal et al., 2021	Cord blood antibodies following maternal coronavirus disease 2019 vaccination during pregnancy	Case series	Hospital in Chicago	Vaccinated pregnant women (n = 27)	Pfizer-BioNTech BNT162b2: 64% Moderna mRNA-1273: 18% Unknown: 14%	Maternal plasma and cord blood testing showed that 96.29% had a positive SARS-CoV-2 IgG test at the time of delivery. Of 28 neonates, 25 had positive IgG tests . The observed mean IgG transfer ratio demonstrated that infant antibody levels are about equal to the maternal levels.	Pregnant women who received a COVID-19 mRNA vaccine during the third trimester had transplacental transfer of IgG to the infant.

Paul and Chad, 2021	Newborn antibodies to SARS-CoV-2 detected in cord blood after maternal vaccination – a case report	Case study	Hospital in Florida	Vaccinated pregnant woman (n = 1)	Single dose of Moderna mRNA-1273	COVID-19 naïve mother who had received a single dose of mRNA vaccine 3 weeks prior to delivery delivered an infant with SARS-CoV-2 IgG antibodies detectable in cord blood.	SARS-CoV-2 IgG antibodies are detectable in a newborn's cord blood sample after only a single dose of the Moderna vaccine. Thus, there is potential for protection and infection risk reduction from SARS-CoV-2 with maternal vaccination.

Prabhu et al., 2021	Antibody Response to Coronavirus Disease 2019 (COVID-19) Messenger RNA Vaccination in Pregnant Women and Transplacental Passage Into Cord Blood	Cross-sectional study	Academic medical center in New York	Vaccinated pregnant women (n = 122)	Pfizer-BioNTech BNT162b2: 69.67% Moderna mRNA-1273: 30.32% 55 received one and 67 had received both doses of the COVID-19 vaccine	Cord blood testing of vaccinated pregnant women showed antibody production. Maternal antibody production started on the 5th day and transfer of immunity to the neonate at 16th day after the first vaccination dose. Maternal IgG levels increment was statistically significant .The association of maternal IgG levels with cord blood IgG levels was also statistically significant.	Pregnant women who received a COVID-19 mRNA vaccine elicited immune response and there was transplacental transfer of IgG to the neonate.

Trostle et al., 2021	High antibody levels in cord blood from pregnant women vaccinated against COVID-19	Cohort study	Academic medical center in New York	Vaccinated pregnant women (n = 36)	Pfizer-BioNTech BNT162b2: 72% Moderna mRNA-1273: 28%	Cord blood testing after delivery showed transplacental antibody transfer, with cord blood specimens having high levels of anti-S antibodies.	COVID-19 vaccination during pregnancy confers higher levels of antibody transfer in the neonates suggesting immune protection against SARS-CoV-2.

Yang et al., 2021	Association of Gestational Age at COVID-19 Vaccination, History of SARS-CoV-2 Infection, and a Vaccine Booster Dose With Maternal and Umbilical Cord Antibody Levels at Delivery	Cohort study	Medical center in New York	Vaccinated pregnant women (n = 1,359)	Pfizer-BioNTech BNT162b2: 75.42% Booster:1.80% Moderna mRNA-1273: 22.15% Janssen JNJ-78436735: 2.43% Booster: 0.70%	The highest maternal and umbilical cord blood IgG antibody levels occurred with early 3rd -trimester vaccination. However, neonates born to fully vaccinated women, early in Ist trimester had similar or higher cord IgG levels than neonates born to women who got vaccinated in the 3rd trimester but were not fully vaccinated before delivery.	A complete COVID-19 vaccination course and a third trimester booster dose were associated with the highest maternal and umbilical cord antibody levels.

COVID-19 Vaccine Acceptance							
Author(s), Year	**Study Title**	**Study Design**	**Study Setting**	**Participants (n)**	**COVID-19 Vaccine Type, % received**	**Outcomes**	**Conclusions**
Ahlers-Schmidt et al., 2020	Concerns of women regarding pregnancy and childbirth during the COVID-19 pandemic	Cohort study	Sedgwick county prenatal programs in Kansas	Pregnant (n = 46) and postpartum women (n = 68) enrolled in prenatal programs	Not stated	**Vaccine acceptance:** If a COVID-19 vaccine became available, 47.80 % (n = 54) were interested in receiving it ; 23% were not and 29.20 % were unsure. Concerns were side effects/ sickness (55.90 %), cost (5.10 %), and perception it is unnecessary (3.40 %).	More than half of the participants would not or were unsure of receiving the COVID-19 vaccination.

Battarbee et al., 2022	Attitudes Toward COVID-19 Illness and COVID-19 Vaccination among Pregnant Women: A Cross-Sectional Multicenter Study during August-December 2020	Cross-sectional survey study	Salt Lake City, UT, Birmingham, AL, and New York, NY	Pregnant women (n = 915)	Not stated	**Vaccine acceptance:** 41% of pregnant women were willing to get a COVID-19 vaccine. Major concern was vaccine safety (82%). Receipt of influenza vaccine in the past year was associated with higher odds of vaccine acceptance (aOR 2.10, 95% CI 1.50-3.00). Black and Hispanic women had lower odds of accepting a vaccine compared with White women (aOR 0.40, 95% CI 0.20-0.60 for both).	More than half of the pregnant participants were unwilling to get vaccinated. Minorities and those without prior influenza vaccination were less likely to accept the COVID-19 vaccine.

Desai et al., 2021	COVID-19 vaccine acceptance in pregnancy	Cross-sectional survey study	Perinatal center at the Pomona Valley Hospital in California	Pregnant women (n = 124)	Not stated	**Vaccine uptake**: Pregnant women who had received the annual influenza vaccine were significantly more likely to get the COVID-19 vaccine (50% vs. 9.70%, p <0.05). Additionally, those who had previously discussed the COVID-19 vaccine with a physician were significantly more likely to receive the vaccine (45.80% vs. 26%, p = 0.04).	Pregnant women who discussed the COVID-19 vaccine with a healthcare provider were statistically more willing to receive the vaccine.

Hirshberg et al., 2021	Offering onsite COVID-19 vaccination to high-risk obstetric patients: Initial Findings	Pre-post study	Obstetric clinic at a single academic medical center in Missouri and Illinois	High-risk obstetric patients (n = 93)	Pfizer-BioNTech BNT162b2 vaccine	**Vaccine uptake**: Of 32 eligible patients counseled prior to onsite vaccine availability, 1 (3%) received vaccination offsite. Of 55 eligible patients counseled after onsite vaccine availability, 2 (3%) received onsite vaccination, and 4 (7%) proceeded with vaccination offsite. Onsite vaccination availability did not significantly increase vaccination rates (3% v 11% p = 0.22).	Vaccine hesitancy, not availability, is a critical driver of low vaccination rates in high-risk obstetric patients.

Huddleston et al., 2021	COVID-19 Vaccination Patterns and Attitudes Among American Pregnant Individuals	Cross-sectional survey study	Online survey of US pregnant women	Pregnant women at <10 weeks' gestation (n = 2,506)	Not stated	**Vaccine acceptance:** Among the unvaccinated , only 35.70% reported vaccine acceptance. Predictors of lower odds of vaccination were Black race and being counseled not to vaccinate by a provider .	There was substantial vaccine hesitancy among unvaccinated respondents.

Levy at el., 2021	Acceptance of COVID-19 vaccination in pregnancy: a survey study	Cross-sectional survey study	Single ultrasound unit in New York	Pregnant women (n = 653)	Not stated	**Vaccine acceptance:** 58.30% of pregnant women reported vaccine acceptance. Among those who declined vaccination, common concerns were risk to the fetus or neonate (45.80%), and vaccine side effects (17.70%). African American race, Hispanic ethnicity, low education, and declining the influenza vaccine were associated with nonacceptance of COVID-19 vaccination in pregnancy.	The COVID-19 vaccine acceptance rate of 58.4% was consistent with the acceptance of other recommended vaccines in pregnancy (DTaP, influenza) and is associated with patient characteristics and previous vaccine history.

Razzaghi et al., 2021	COVID-19 Vaccination Coverage Among Pregnant Women During Pregnancy —Eight Integrated Health Care Organizations, United States, December 14, 2020–May 8, 2021	Cohort study	8 health systems (5 Kaiser Permanente health systems; Denver Health; HealthPartners; and Marshfield Clinic in Washington, California, Colorado, Wisconsin	Total population in the registry (N = 135,968) Pregnant women who received ≥1 dose of COVID-19 vaccination during pregnancy (n = 22,197)	Pfizer-BioNTech BNT162b2: 8.7% Moderna mRNA-1273: 7.0% Janssen JNJ-78436735: 0.6%	**Vaccine uptake:** 16.3% of pregnant women identified in CDC's Vaccine Safety Datalink had received ≥1 dose of a COVID-19 vaccine during pregnancy. Vaccination was lowest among Hispanic (11.90%), Black (6%) and women aged 18–24 years (5.50%). Concerns were limited safety data in pregnancy and possibility of harm to the fetus.	COVID-19 vaccination coverage is low among pregnant women.

Sutton et al., 2021	COVID-19 vaccine acceptance among pregnant, breastfeeding, and non-pregnant reproductive-aged women	Cross-sectional online survey study	Healthcare institution in New York	Pregnant (n = 216), non-pregnant (n = 656), and breastfeeding women (n = 122) (including patients, providers, and staff) at a healthcare institution	Not stated	**Vaccine acceptance:** Pregnant women had the lowest rate of vaccine acceptance (44.30%; $p < 0.05$) compared to other groups. Non-pregnant women were most likely to accept vaccination (n = 457, 76.20%; $p < 0.05$) with breastfeeding women the second most likely (55.20%). Working in healthcare was not associated with vaccine acceptance.	Pregnant respondents were more likely to decline vaccination than non-pregnant and breastfeeding women.

Sznajder et al., 2022	Covid-19 vaccine acceptance and associated factors among pregnant women in Pennsylvania 2020	Cross-sectional online survey study	Academic medical center in Pennsylvania	Pregnant women (n = 196)	Not stated	**Vaccine acceptance:** 65% of pregnant respondents were willing to receive the COVID-19 vaccine. Being employed full-time (aOR 2.22; 95% CI 1.02, 4.81), being overloaded (stressed) (aOR 2.18; 95% CI 1.02, 4.68), and having had an influenza vaccine in the past year (aOR 4.82; 95% CI 2.17) were significantly associated with COVID-19 vaccine acceptance.	Factors associated with COVID-19 vaccine acceptance included having had an influenza vaccine in the previous year, being employed full time, and a general feeling of being overloaded.

Townsel et al., 2021	COVID-19 vaccine hesitancy among reproductive-aged female tier 1A healthcare workers in a United States Medical Center	Cross-sectional online survey study	Academic medical center in Michigan	Pregnant (n = 245),Trying to conceive (TTC) (n = 891), and breastfeeding women (n = 177) employee at a medical center	Not stated	**Vaccine acceptance:** Pregnant participants were six times more likely to delay COVID-19 vaccination and twice as likely to decline ($p < 0.05$), compared to other women of reproductive age. The highest rates of concern were observed for safety and effectiveness of the vaccine.	Pregnant women had significantly higher rates of declining or delaying COVID-19 vaccination compared to other women of reproductive age.

Wang et al., 2022	Perceptions and knowledge of COVID-19 vaccine safety and efficacy among vaccinated and nonvaccinated obstetric healthcare workers	Cross-sectional online survey study	Tertiary care institution in Pennsylvania	Vaccinated pregnant HCWs (n = 65), Non-Vaccinated pregnant HCWs (n = 18) Pregnant	At least one dose of Pfizer-BioNTech BNT162b2 or Moderna mRNA-1273: 78.30%	**Vaccine acceptance:** Vaccine receipt was 16.90%. Pregnancy status influenced 44.4% (8 out of 18) of non-vaccinated HCWs to not receive the COVID-19 vaccine, but conversely influenced 1.50% (1 out of 65) of vaccinated HCWs to receive the vaccine.	Pregnancy status, especially the uncertainty of COVID-19 vaccination safety in pregnancy, was a major reason for vaccine refusal among non-vaccinated HCWs .

Figure legend

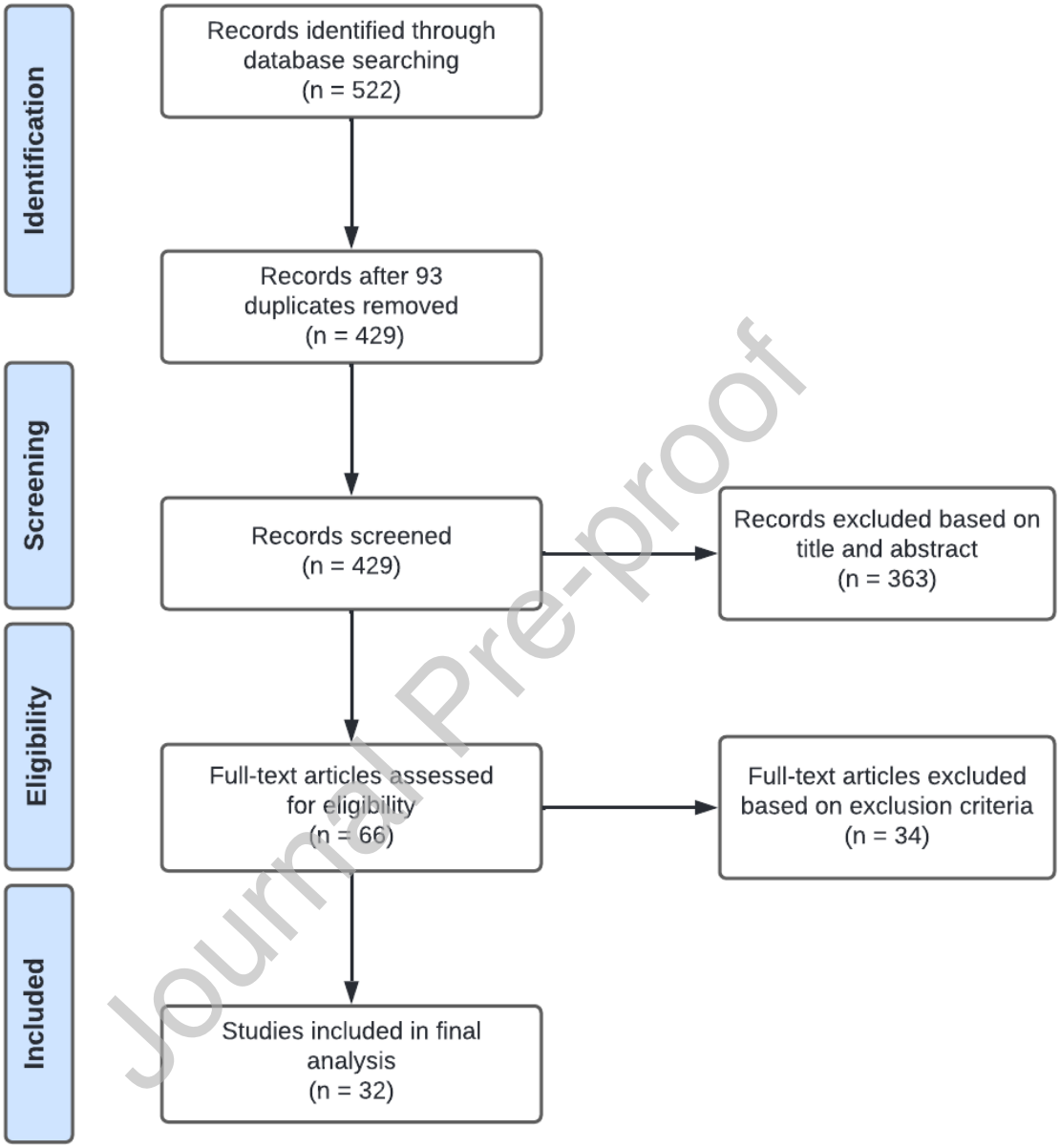

Figure 1. PRISMA flow diagram of the included studies. Caption: The PRISMA flow diagram for the systematic review detailing the database searches, the number of abstracts screened, full texts retrieved, and the final studies included in the analysis.

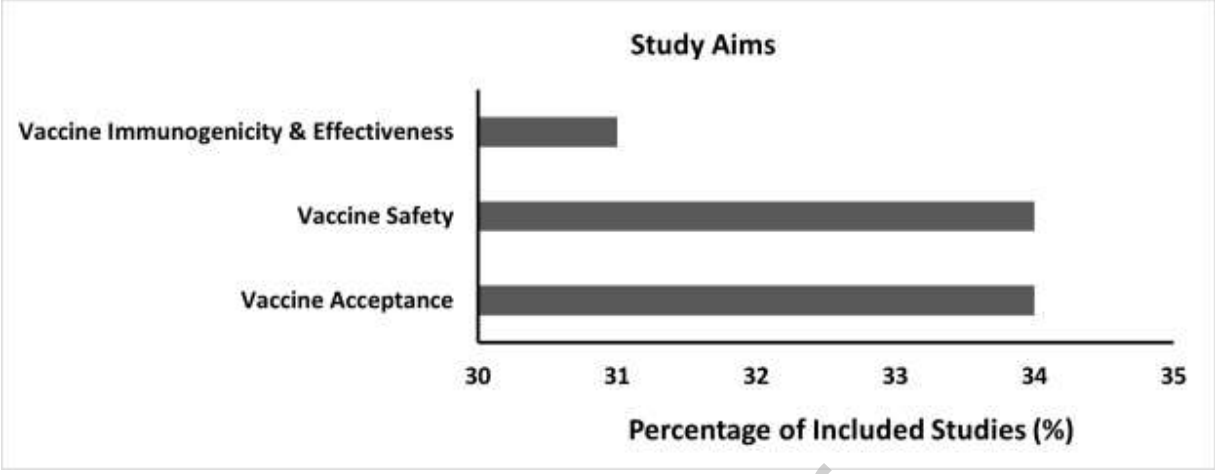

Figure 2. Study Aims and Percentage of Included Studies