REVIEW ARTICLE

Obstetrics



Check for updates

The current state of pertussis vaccination in pregnancy around the world, with recommendations for improved care: Consensus statements from the Global Pertussis Initiative

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Abstract

Bordetella pertussis, which causes a respiratory disease known as pertussis ("whooping cough") remains an important global challenge, with the incidence in pertussis cases increasing in recent years. Newborns and infants are at increased risk for severe morbidity and mortality from this bacterium. Vaccination in pregnancy has become an important strategy to both passively transfer immunity as well as prevent infection in pregnant persons, who are a major source of newborn infection, thus attempting to decrease the impact of this serious disease. It is considered safe for the pregnant person, the developing fetus, and the infant, and during the first 3 months of life it has been shown to be highly effective in preventing pertussis. There are a variety of strategies, recommendations, and adherence rates associated with pertussis vaccination in pregnancy around the world. We summarize the 2021 Global Pertussis Initiative Annual Meeting that reviewed the current global status of pertussis vaccination in pregnancy and remaining medical and scientific questions, with a focus on vaccination challenges and strategies for obstetric and gynecologic healthcare providers.

KEYWORDS

Global Pertussis Initiative, pertussis, pregnancy, vaccination, protection, safety,

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Funding information

1 | INTRODUCTION

Bordetella pertussis, a gram-negative bacterium, is a highly contagious respiratory infection that causes pertussis, otherwise known as whooping cough. Whole-cell pertussis (wP) and acellular pertussis (aP) vaccines are available. Nevertheless, in recent decades, cases of pertussis have increased. The highest risk for severe morbidity and mortality remains in newborns and infants who are often too young to have completed their pertussis vaccination schedule.² Therefore, the number of countries that recommend pertussis vaccination in pregnancy has increased in recent years so as to address the susceptibility of newborns to pertussis prior to the completion of the infant's primary immunization series (three-dose schedule before the age of 1 year). Pertussis vaccination in pregnant persons has been shown to elicit specific immune responses, and the protection of the fetus occurs with B. pertussis antibodies transferring across the placenta. 4 Further protection of the newborn/infant occurs with antibody transfer via breast milk.4

While pregnancy is a dynamic state with many changes in the immune system, pregnant and nonpregnant people both have robust serologic responses to vaccination. Vaccination in pregnancy offers the benefit to the newborn of narrowing the period of vulnerability to infection between birth and the completion of the primary immunization against pertussis. Antibody levels in newborns and young infants appear to be highest after vaccination of the pregnant person in the early part of the third trimester due to active transfer of antibodies across the placenta. 6.7

There are many potential vaccination strategies to address pertussis in the population, but vaccination in pregnancy offers several advantages. First, there is robust evidence that vaccination in pregnancy allows for maternal antibodies to be placentally transferred, which protects the newborns/infants.⁸ Given that most pertussis deaths occur prior to completion of the infant's primary series of vaccinations, this is a critical intervention that saves lives. Second, there are numerous interactions/appointments with the medical care system during (and before) pregnancy, providing many opportunities to discuss pertussis and potentially administer the vaccine should the pregnant person so wish. Third, pertussis vaccination in pregnancy also provides protection for the pregnant person from pertussis infection. Finally, vaccination in pregnancy tends to provide greater coverage of the population compared with other booster strategies. 10 Pertussis vaccination in pregnancy is well tolerated by both the pregnant person and the newborn. 8,11 However,

pertussis vaccination uptake rates around the world remain suboptimal in pregnancy.¹²

Herein, we summarize Day 2 of a meeting of the Global Pertussis Initiative (GPI), which took place on November 30 and December 1, 2021, in which attendees discussed, reviewed, and analyzed available medical and scientific data regarding pertussis vaccination in pregnancy, as well as examined barriers that exist to global implementation, and the remaining challenges and scientific/medical questions. We focus on obstetric and gynecologic health care providers (Ob/Gyn) and the challenges faced, in addition to potential strategies for implementing worldwide pertussis vaccination in pregnancy. Day 1 discussions, recommendations, and outcomes are available.¹³

About the GPI

In 2001, the GPI was initiated to: (1) increase pertussis awareness in low-, middle-, and high-income countries; and (2) develop evidence-based vaccination recommendations/strategies to decrease the disease burden in persons of all ages. To accomplish these aims the GPI:

- Organizes meetings with a global and/or regional focus.
 - Specialized field experts work together at the meetings to discuss and, if deemed relevant, develop consensus pertussis vaccination recommendations/ strategies that will be within acceptable limits at all levels of resource availability and can be applied from local up to national levels.
- Developed a web-based pertussis community for anyone with an interest in pertussis, and where discussions and further documents are available.

2 | SAFETY AND VACCINE EFFECTIVENESS

Pertussis vaccination in pregnancy is both safe and effective for the individual to whom it is administered, but is also safe and provides protection of the fetus(es) and the infant(s), as confirmed by an abundance of evidence.^{8,11,14-22} The pediatric DTaP vaccine (diphtheria and tetanus toxoids and aP vaccine) contains higher

quantities of pertussis toxin and diphtheria toxoid than the acellular vaccine Tdap (tetanus, diphtheria, and pertussis vaccine). Tdap has been approved by the Food and Drug Administration for vaccination in pregnant persons to prevent pertussis in newborns. The incidence of severe pertussis in newborns/young infants sharply dropped following the widespread implementation of pertussis vaccination in pregnancy in various countries. 9,23-26 Several studies performed in different countries showed that pertussis vaccination in pregnancy was safe and highly effective to induce protection to the newborn/infant. 9,21,22,24-31 In the United States, England. and Australia, the pertussis vaccine in pregnancy is >90% effective in preventing hospitalization (n = 6252, 91% [95% confidence interval (CI), 65-97] to n=74, 94% [95% CI, 59-99]) and mortality (n = 243, 95% [95% CI, 79-100]) due to pertussis among infants <2-3 months of age.²² In Brazil, a case-control study (n=290; 42) cases and 248 controls included) found that this strategy had an unadjusted vaccine effectiveness of 82.6% (95% CI, 60.8-92.3) in the prevention of pertussis infection (laboratory-confirmed) in infants <2 months of age. 24 The World Health Organization agrees that pertussis vaccination in pregnancy is effective in reducing the risk of pertussis in both newborns and young infants who are unable to be vaccinated.

Prior to the 1990s, the first generation of initial pertussis vaccines (wP) consisted of heat-killed and detoxified bacteria. The wP vaccine had a relatively high risk for a localized skin reaction or even systemic side effects. The second generation of pertussis vaccine is the aP design, which is based on a purified bacterial component, and was introduced in the 1990s. 32 The aP vaccine has a reported lower incidence of adverse events (from local, to systemic, to serious) compared with the wP vaccines. 32 While both wP and aP vaccines can be used in the pediatric population, for individuals older than 7 years, only the acellular Tdap vaccine can be given. Therefore, the available information on pertussis vaccination in pregnancy refers to the use of the Tdap vaccine. This vaccine has been studied extensively in pregnancy without safety concerns. 11 Unfortunately, the acellular vaccine is associated with increased cost and decreased availability in some countries. This is a significant barrier to pertussis vaccine access for pregnant people.

During gestation there are multiple changes that occur to the maternal immune system, some of which help to support the pregnant person and the semiallogeneic fetus and assist in preventing them both from pertussis infection. Despite the immune system changes during gestation, the antibody response to the pertussis vaccine is robust in both pregnant and nonpregnant people. Cell-mediated responses to the aP vaccine is more pronounced in nonpregnant people compared with pregnant people who have an impaired cell-mediated vaccine response. However, pertussis vaccination causes an upregulation in both interferon type 1 responses and innate immunity genes in pregnant and nonpregnant people, thus suggesting that vaccine-induced immune responses due to pregnancy are not affected. Further information on the immunologic aspects can be found in Abu-Raya et al.'s 2022 paper. 13

3 | TIMING OF VACCINATION

The optimal timing of pertussis vaccination in pregnancy, although still under debate, scientifically should occur when the transplacental antibody transfer is highest, in addition to when there is maximal effectiveness for prevention of severe morbidity and mortality due to pertussis after the birth of the child. However, several studies addressing the impact regarding the timing of pertussis vaccination in pregnancy on clinical effectiveness have been inconclusive. The for this reason, immunogenicity studies assessing antibody response to the vaccine have been pivotal in guiding recommendations for the timing of pertussis vaccination in pregnancy.

In the United States, observational data have shown that vaccination of pregnant persons during the third trimester, that is between 27 and 36 weeks of gestational age, provided higher protection in infants >12 weeks of age (term delivery data) in regard to the prevention of pertussis (laboratory-confirmed) versus when vaccination was provided to pregnant persons outside of this gestational period.³¹ Another study in the United States reported no decrease in pertussis rates when the pertussis vaccine was given prior to 27 weeks of gestational age, but there were only a small number of pertussis cases in this study.³⁶ In Spain, vaccine effectiveness was found to be similar in those vaccinated between 26 and 31 weeks and at 32 weeks and above. 37 A recent study showed that vaccine administered between 16 and 32 weeks of pregnancy provided similar levels of antipertussis toxin and antipertactin IgG concentrations. 38 However, antifilamentous hemagglutinin IgG concentrations were shown to be increased with advanced gestational age at the time of vaccination in pregnancy that is between 28 and 32 gestational weeks.³⁸

Another factor in optimizing vaccine effectiveness is prematurity. An independent risk factor for severe morbidity and mortality related to pertussis infection is indeed preterm birth.³⁹ It is important to provide protection through vaccination in pregnancy for this higher-risk group. It could therefore be argued that earlier vaccination in pregnancy could lead to higher pertussis protection for preterm infants. A study in the United Kingdom found that expanding the window of timing for the pertussis vaccination to between 20 and 32 weeks from between 28 to 32 weeks led to half the number of preterm infants <60 days of age hospitalized with pertussis (n=20 cases [95% CI, 16.0–35.9] prepolicy expansion versus n=9 cases [95% CI, 6.0-22.7]) postpolicy introduction (P=0.06), although the overall number of hospitalized infants was low.⁴⁰ Definitive conclusions about widening the vaccination time frame have been challenging to achieve and remain to be elucidated.

Despite the lack of a clear surrogate immunologic marker for vaccine protection, immunogenicity studies have been, and remain, vital in the development of vaccine recommendations based on the current belief that higher concentrations of passively (placentally transferred) acquired *B. pertussis* antibodies by the fetus are associated with increased protection from pertussis morbidity and mortality after birth. ⁴¹ There has again been conflicting evidence regarding antibody concentrations with regards to the optimal time

point of vaccination during pregnancy. One study from Switzerland demonstrated higher neonatal IgG levels with vaccination between 13 and 25 weeks of gestation versus after 25 weeks of gestation, while another study from Argentina found no difference in IgG concentrations between vaccination in the second and third trimesters. A2,43 There are also conflicting results comparing B. pertussis antibody concentrations and antibody avidity after early third versus late third trimester vaccination. While multiple studies have demonstrated higher antibody concentrations with early third trimester vaccination, this has not been confirmed in all studies. A7,44-50 Studies are currently underway comparing the response to the Tdap vaccine before 24 weeks, between 24 and 28 weeks, and between 28 and 31 weeks, with initial results showing high placental pertussis antibody transfer to the fetus and that persisted well after birth.

There is no question that pertussis vaccination in pregnancy provides significant protection to the newborn and infant (when compared with children born to unvaccinated individuals). However, the optimal timing of vaccination remains an area of great debate, and timing is likely to be linked to additional factors related to the pregnant person and the developing fetus(es). The current knowledge supports that vaccination during either the second or early third trimester of pregnancy should be the primary goal. ^{51,52} Of note, a meta-analysis published in 2021 reported that the timing of pertussis vaccination in pregnant persons, and the ensuing infant immune response to both primary and booster immunization post birth, were not affected. ⁵³

4 | B. PERTUSSIS-SPECIFIC ANTIBODIES IN BREAST MILK

Antibodies against *B. pertussis* antigens have been detected in breast milk (including the colostrum) following vaccination in pregnancy. However, it is currently unclear whether these breast milk antibodies provide an additional clinical benefit on top of the transplacental transfer of pertussis antibodies. If so, it is probably limited given the high protection provided by antipertussis toxin serum IgG antibodies. More information is needed to understand how the antibodies in breast milk may provide further protection against pertussis in newborns/infants. Data from the United States have shown antibody survival in the newborn's/infant's gut after receiving breast milk.⁵⁴ This could lead to intestinal transfer of pertussis-specific antibodies (from the parent's breast milk) into neonatal circulation.⁵⁴

5 | GLOBAL RECOMMENDATIONS FOR PERTUSSIS VACCINATION DURING PREGNANCY

Many countries and professional organizations across the world have composed guidelines that recommend pertussis vaccination for pregnant persons. Despite this, vaccine coverage remains highly variable, even in high-income countries. Barriers to vaccine acceptance remain, and further education is needed, including clear communication of the recommendations, to improve vaccine uptake.

The GPI group included participants from many countries around the world that either recommend pertussis vaccination in pregnancy, through a national statement, or from a professional medical society. There is a variety of strategies used for vaccine administration in these countries. Vaccine coverage in these countries ranges from 25% to 83% (Table 1). A representative from the Bill & Melinda Gates Foundation also addressed vaccination in low-income countries through Gavi (formerly known as the Global Alliance for Vaccines and Immunization) with the group. While pertussis vaccination in pregnancy is a target, the current focus in these countries is on lowering the cost of the vaccine as cost continues to be a limiting factor for uptake in low-income countries. Once a lower-cost vaccine is approved, individual low-income countries will address further uptake depending on their health system and population.

The GPI identified several themes among their countries for barriers to both establishment of a national recommendation as well as vaccine uptake. Without adequate data available regarding the local burden of pertussis in infants, it can be difficult to advocate for national recommendations for the pertussis vaccine. For example, in India, there has been insufficient data available to convince policymakers. There is a lack of active surveillance for pertussis as well as a lack of adequate diagnostic facilities, which leads to underreporting of cases. Thus, the burden of pertussis remains largely unknown in India. While there are national professional societies that recommend pertussis vaccination in India (Indian Academy of Pediatrics and The Federation of Obstetric and Gynecological Societies of India), many obstetricians still need better local data to promote vaccination.

Underreporting is also a challenge. In the Philippines, few hospitals diagnose infants with pertussis using a polymerase chain reaction test, and this underestimates the burden of pertussis. In other countries, such as South Africa, a lack of data about relevant subpopulations leads to lower vaccine uptake rates. There is minimal information about the immune response and impact in the HIV-infected population. This is relevant because infants who are exposed to HIV may have a higher burden of pertussis, and other vaccines have demonstrated a less robust immune response with less placental transfer of antibodies in those living with HIV. 55,56

Lack of data can also impact the provider and patient perception of risk. Many health care providers who care for pregnant persons do not see the impact of pertussis on infants firsthand. This makes improved dissemination of data and information essential. While there is an increasing burden of pertussis in the pediatric population of Malaysia, obstetricians there also do not see this as much in their own patients. Spain is focused on health care provider education to achieve higher vaccination rates. Practitioner training must occur to make sure they are aware of the risks of pertussis and the efficacy and safety of the vaccine.



TABLE 1 Status of Tdap vaccination in countries around the globe.

globe.	
Country	Status of Tdap vaccination
Argentina	National recommendation since 2012; 2013 Tdap booster in single pregnancy included in the National Calendar (mandatory and free of charge)
	In 2016 there was a recommendation widening to Tdap booster during each pregnancy
	Vaccines are given by Ob/Gyn or a specific center
	70% coverage
Australia	Health department recommendation
	Vaccinators include general practitioners and midwives
	83% coverage
Belgium	Recommended since 2013
	General practitioner vaccinates
	70% coverage
<mark>Brazi</mark> l	Recommended since 2014
	Vaccination given in health centers
6 1	65% coverage
Canada	National recommendation since 2018 but not all provinces have endorsed it
	Given by general practitioners, Ob/Gyn, or midwives
	45% coverage
Costa Rica	Recommended since 2012
	Vaccines given by midwives, general nurses, or general practitioners
	81% coverage
United	Recommended since 2012
Kingdom	General practitioners and midwives give the vaccine
	68% coverage
Germany ⁷⁸	Recommended from 2020
	Given by Ob/Gyn or general practitioner
	40% coverage
India	Recommended by professional society in 2013
	Coverage rates are unknown but under evaluation
Malaysia	Recommended by professional societies
	Given by Ob/Gyn, specialists, and general practitioners
	Mostly provided in the private sector as the government only recommends tetanus
Pakistan	National recommendation
	Given by Ob/Gyn
	65% coverage
Philippines	Recommended
	Given by Ob/Gyn
	Only high rates of uptake with private consultation
	High rates of loss to follow up with the Ob/Gyn

TABLE 1 (Continued)

Country	Status of Tdap vaccination
Qatar	Recommended in 2019
	Given by general practitioner
	Unknown uptake rates
South Africa	Differences between public and private sector
	Guidelines are being updated; as of June 2023, pertussis vaccination in pregnancy is now available in some provinces. In addition, it is expected that pertussis vaccination in pregnancy will be available in the public sector in 2024
	Unclear coverage rates
Spain ^{12,27}	Recommended since 2013 (January 2015 for the Valencian community; all regions by the end of 2016)
	Given by general practitioner
	Coverage rates are not reported
Switzerland	Recommended since 2013
	Usually given by Ob/Gyn
	Uptake ~50% (varies by region of country)
Thailan d	Recommended by national professional societies (e.g. The Royal Thai College of Obstetricians and Gynecologists)
	Unclear coverage in the public sector
	70% covered in private sector
United States	Recommended since 2012
	Vaccines given by Ob/Gyn, midwives, general practitioner, health department
	Coverage 50%-70%.

Abbreviations: Ob/Gyn, obstetric and gynecologic health care providers; Tdap, tetanus, diphtheria, and pertussis vaccine.

Historically, in Brazil, vaccination efforts have been reactive and introduced after outbreaks. Both health care providers and the population seem to lose interest in vaccination when there is not an outbreak in the reported media. This leads to a drop in vaccination rates. Uptake is driven by perception of risk, both from health care providers and pregnant persons (and their support network). Provider recommendations for the vaccine drop when there is a decreased perception of risk. In Switzerland and Germany, immunization during pregnancy is not yet considered part of normal prenatal care. It is still considered potentially dangerous by pregnant persons and some health care providers as well. Unless there is personal experience or knowledge of the evidence, pertussis often is not viewed as a threat and, therefore, is not a priority for many gynecologists to discuss with pregnant people.

Despite the scientific and medical evidence regarding the benefits of pertussis vaccination in pregnancy, product labeling information continues to use cautionary language in some countries. This labeling can contribute to health care provider concerns about the safety of vaccination in pregnancy. The Canadian Vaccine Product Monograph Working Group updated the Tdap vaccine product

label to ensure that the product label is evidence-based and well-structured and uses clear and understandable language. 57,58 The group involved stakeholders, including public health, communication experts, legal scholars, social scientists, health care providers, and vaccine regulatory and industry representatives. 57 A large survey of health care providers (n=449) later showed that over double reported that they would recommend the Tdap vaccination in pregnancy based on the revised rather than the existing product label (63% vs 27%; note that health care providers only had to answer one of the questions regarding product information to be included in the analysis). 58 The providers noted improved readability and clear evidence. 58 Dissemination of similar product label updates to other countries may be helpful in improving Tdap vaccination rates in pregnancy.

Cost is a barrier to pertussis vaccination in some countries. In Malaysia, pertussis vaccination is only available in the private market. If national guidelines existed in Malaysia, then the vaccine would be provided free of charge by the Ministry of Health. Cost-effectiveness data could be helpful in advocating for governmental coverage. In Thailand, the vaccine is not reimbursed or available in many locations, so only those with access to certain hospitals can receive the vaccine. The cost of vaccines in Thailand is more of an issue than lack of data. The cost of Tdap is also prohibitive to many people in India.

South Africa is working on operationalizing vaccination in pregnancy, including distribution of vaccines to antenatal clinics in both urban and rural areas, as well as improving pregnant patient attendance in clinic. In some other African countries, there are infrequent antenatal visits, so this leads to fewer opportunities for vaccination, but there is marked variation between countries.

In Canada, lack of convenience is a barrier to vaccination in pregnancy. ⁵⁹ Primary physicians have better uptake rates than obstetric providers. ⁵⁹ There are several potential proposed plans for improving uptake including provider compensation, improving convenience for receiving the vaccine, and using pharmacies for distribution. Belgium does not currently administer vaccines through obstetricians or midwives, but this could be a valuable method to improve uptake as these providers are most aware of the importance of vaccination in pregnancy.

Several countries have celebrated successes regarding uptake, particularly with media campaigns promoting pertussis vaccination in pregnancy. Costa Rica is exploring education through social media, including information on the safety of Tdap in pregnancy, as well as outreach to health care providers on how to deliver an effective message to pregnant persons and their support network about vaccination.

Australia had the benefit of active national surveillance and adequate diagnostic testing to demonstrate that infants were dying from pertussis, and these supportive data go back several decades. ^{60,61} There is a general public trust in vaccines, although this became somewhat fractured during the coronavirus disease 2019

(COVID-19) pandemic.⁶² Providing data to authorities has been critical to promote the importance of vaccination in pregnancy.

The United Kingdom encounters health inequities and disparities in pertussis vaccination in pregnancy and reported an increase in pertussis cases as well as infant deaths in 2012, but they experienced an increase in vaccine uptake through effective media coverage of pertussis-related infant deaths. 63-66 The messaging was implemented in the pertussis vaccination program for pregnant people (introduced in 2012), with the program additionally focusing on the safety and efficacy of the vaccine. In the United Kingdom, recommendations from trusted health care providers and public health agencies play an important role in vaccine uptake. Agencies and health care providers, such as the National Health Service and the Joint Committee on Vaccination and Immunization, are working on incorporating all prenatal care providers in the vaccination messaging, including midwives.

Other barriers occurring in both developing and developed countries include a shift in focus to the COVID-19 pandemic and additional vaccination priorities such as typhoid and tetanus. ⁶⁸⁻⁷⁰ The Ministry of Health in South Africa was given a proposed recommendation statement for pertussis vaccination in pregnancy in 2019, but no initial motion to adopt these recommendations, due to the COVID-19 pandemic, was developed. Funding, even from private sources, may be adversely affected by the absence of a formal national recommendation. Furthermore, transitions in central and provincial governments also occur, which make it difficult to coordinate communication and advocacy for pertussis vaccination. However, in some provinces, as of June 2023, pertussis vaccination in pregnancy is available. In addition, it is expected that pertussis vaccination in pregnancy will be available in the public sector in 2024.

In the United States, obstetricians are largely responsible for administering the pertussis vaccine in pregnancy. Unfortunately, they also have competing clinical priorities and are not always focused on vaccination. In addition, vaccine provision does not generally add to the payment of the health care provider. Consistency in messaging from providers is key as many pregnant persons, and their support network, highly value their provider's recommendations. The US representatives at the GPI group suggested partnering with pharmacies for Tdap vaccination in pregnancy. This has been one mode of disseminating other vaccines such as COVID-19 and influenza. In fact, the lessons from COVID-19 vaccination dissemination can also likely provide insights into pertussis vaccine barriers during pregnancy.

A summary of the data and opinions of the GPI are shown in Table 2.

6 | IMPACT OF COVID-19 ON PERTUSSIS

There appears to have been a significant decrease in the burden of *B. pertussis* infections during the COVID-19 pandemic. 71-74 Indeed,



TABLE 2 Barriers (a) and strategies (b) regarding vaccination in pregnancy.

(a) Barriers to pertussis vaccination in pregnancy

Underreporting and lack of data on location pertussis rates and associated morbidity and mortality

Lack of national recommendations for pertussis vaccination in pregnancy

Obstetric providers with limited experience with *Bordetella* pertussis infections

Cautionary vaccine product labeling

Acellular pertussis vaccine is of more immunologic benefit but not available in all countries

Cost of the pertussis vaccine

Lack of convenience or access to the pertussis vaccine

Shift to focus on COVID-19 pandemic and other vaccine priorities

(b) Strategies for pertussis vaccination in pregnancy

Media campaigns promoting the benefits and safety of pertussis vaccination in pregnancy

Health care provider education including guidance on communication with pregnant people and their support network

Improving provider compensation for vaccine administration

Redesigned vaccine product labels

Increased access to the vaccine

Acellular pertussis vaccine to be approved in further countries and provided to pregnant persons

Increased surveillance and reporting of pertussis rates to authorities

Partnering with pharmacies for vaccine dissemination

Abbreviation: COVID-19, coronavirus disease 2019.

in the United Kingdom, there was a reduction in pertussis incidence among all age groups, including young infants during 2020 and 2021.⁷⁰ In Switzerland, hospitalization due to pertussis in children suddenly ceased shortly after the beginning of the pandemic (pertussis vaccination in pregnancy was recommended and implemented in 2013).²⁶ There were only 15 cases of pertussis reported in 2021 in Ontario, Canada, which is glaringly lower than the average of 402 cases per year over the prior 5 years.⁷⁵ COVID-19 mitigation measures (such as social distancing, lockdowns, and mask wearing) may have assisted in lowering the cases of pertussis at the population level.

At the same time, Canadian data, from 2020 to 2021, showed that there was a drop in the concentration of pertussis antibodies in persons of childbearing age. This has occurred both in the context of COVID-19 mitigation measures as well as a recent decrease in vaccination. A decline in preexisting immunity is also likely, at least in part, to blame. Enhanced surveillance of pertussis will be of utmost importance with the relaxation of COVID-19 mitigation measures, especially given that there was a global reduction in vaccination coverage against pertussis during the COVID-19 pandemic. Furthermore, the recommendations for pertussis vaccination in

TABLE 3 Global pertussis initiative statement on vaccination against pertussis in pregnancy.

Safety and vaccine effectiveness

Vaccination against pertussis in pregnancy is safe for pregnant persons and newborns and highly effective in preventing pertussis in early-term and preterm infants

Timing of vaccination

Vaccination against pertussis in the third trimester of pregnancy is highly effective in the prevention of pertussis in both term and preterm infants

A growing body of evidence supports that vaccination late in the second or early in the third trimester is associated with higher newborn *Bordetella pertussis* antibody concentrations compared with vaccination in the late third trimester

More data are required to confirm this observation and whether these differences in antibody concentration correlate with differences in vaccine effectiveness

There is currently no evidence to suggest that timing of vaccination in pregnancy affects postprimary and postbooster vaccination antibody concentrations in infants, although more formal studies designed to answer this question are needed

Vaccination against pertussis during the second trimester and beyond is still important to ensure protection of infants against pertussis

B. pertussis antibodies in breast milk

Vaccination in pregnancy induces *B. pertussis* antibodies in breast milk until 12 weeks post partum

The added benefit of breastfeeding in infants of vaccinated people to clinical protection is unclear.

Effect of COVID-19 on pertussis

COVID-19 mitigation strategies have resulted in a significant decrease in *B. pertussis* circulation, which could affect population immunity against *B. pertussis*

Continued enhanced surveillance during COVID-19 and emphasis on continued vaccination is needed

Abbreviation: COVID-19, coronavirus disease 2019.

Source: Table adapted, with permission, from Abu-Raya et al. 13

pregnancy should continue and health care providers should assist in ensuring the messages regarding the benefits of vaccination, for example to protect their newborn(s)/infant(s) against severe pertussis disease, are known to the pregnant person, and must also be stressed at the population level.⁷⁷

7 | CONCLUSIONS

Based on the GPI meeting, held on November 30 and December 1, 2021, the outcomes of the discussions were supplemented with a literature review, with Day 2 of the meeting focusing on the Ob/Gyn community and pertussis vaccination in pregnancy. Subsequently, several consensus statements were developed by the GPI writing committee regarding pertussis vaccination in pregnancy (Table 3).

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TABLE 4 Further exploration for pertussis vaccination in pregnancy.

More definitive recommendations from governing bodies about the importance of vaccination in pregnancy to protect newborns from pertussis and other infectious diseases

Additional data to demonstrate burden of pertussis

Cost-effectiveness data on the value of Tdap vaccination in pregnancy

Further assessment of factors that impact Tdap vaccination uptake

Health care provider education about pertussis and the need for Tdap vaccination in pregnancy

Potential implications of multiple coadministered vaccines in pregnancy regarding effectiveness, safety, timing, and acceptance

An improved understanding of the additional value of breastfeeding among those who received pertussis vaccination in pregnancy

Identification of an immunologic surrogate marker for protection from pertussis

Further data on the epidemiology of pertussis infection in specific regions and countries worldwide

Abbreviation: Tdap, tetanus diphtheria and pertussis vaccine.

The GPI group concluded that there are several potential areas that require further exploration to address Tdap vaccination rates in pregnancy (Table 4).

AUTHOR CONTRIBUTIONS

Conceptualization, all authors; writing—original draft, Courtney Olson-Chen; writing—review and editing, all authors; approval and agreement to be accountable for all aspects of the work, all authors.

FUNDING INFORMATION

Sanofi supports the GPI. The GPI was formed in 2001 to examine the ongoing pertussis challenges, and potential solutions, across the globe and recommend appropriate pertussis control strategies. Sanofi continues to support this valuable initiative to provide a forum, and community, for scientific-, clinical-, and policy-based experts to have open discussions and share their findings with the wider community. The opinions and views expressed in this article are solely those of the authors and do not reflect the position of Sanofi. As such, the views and opinions may include the usage of products inconsistent with the product(s) current labeling or licensed indication. We thank Shelley Maria Lindley, PhD, House of Artemis Ltd, for her editorial assistance, which was funded by Sanofi. Funding for open access of this article was provided by Sanofi.

CONFLICT OF INTEREST STATEMENT

The authors are scientific experts and, as such, received honoraria for their participation in this live meeting from Sanofi. In addition, S.G. served as the Chair for Pfizer, GSK, and Sanofi on vaccines trials regarding pregnant people. She also contributed to UpToDate. U.H. was a member of the Collaboration of European Experts on

Pertussis Awareness Generation (CEEPAG; this group terminated its activities in 2021) and has received honoraria for participation in previously associated live meetings from Sanofi, USA, and Sanofi, France, respectively, as well as receiving honoraria for educational activities from Pfizer, MSD, and InfectoPharm. K.F, and A.J.C. have also previously received honoraria from Sanofi. T.T.Q. has received grants from Merck and Sanofi and personal fees from GSK Biologicals and Sanofi, and honoraria from Sanofi. C.H.W von K. has received honoraria for attending meetings sponsored by Sanofi, GSK Biologicals SA, MSD, and Novartis Vaccines. K.A.T. was a coinvestigator on grants from GlaxoSmithKline to her institution; she declined the honorarium for participation in this live meeting. R.M. has received honoraria for educational activities from MSD and Sanofi. The authors declare no other conflicts of interest.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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How to cite this article: Olson-Chen C, Swamy GK, Gonik B, et al. The current state of pertussis vaccination in pregnancy around the world, with recommendations for improved care: Consensus statements from the Global Pertussis Initiative. *Int J Gynecol Obstet*. 2024;165:860-869. doi:10.1002/ijgo.15311