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## Women and children first: the importance of pertussis and influenza vaccination in pregnant women and how to increase vaccine uptake

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<b>Corresponding Author:</b>	Piyali Mukherjee BELGIUM
<b>Corresponding Author Secondary Information:</b>	
<b>Corresponding Author's Institution:</b>	
<b>Corresponding Author's Secondary Institution:</b>	
<b>First Author:</b>	Piyali Mukherjee
<b>First Author Secondary Information:</b>	
<b>Order of Authors:</b>	Piyali Mukherjee Attila Mihalyi Kate Ralph Richard H Beigi Andrea Genazzani Christine E Jones
<b>Order of Authors Secondary Information:</b>	
<b>Abstract:</b>	<p>Vaccination during pregnancy has been proven effective in protecting both pregnant women and their newborns from infectious diseases. An increasing number of countries have issued recommendations for the use of pertussis and influenza vaccines during pregnancy and are offering these vaccines free of charge. However, even in such countries, despite the demonstrated effectiveness and strong safety profile of maternal pertussis and influenza vaccination, vaccine uptake has remained suboptimal. This paper gives a succinct overview of the available evidence supporting maternal pertussis and influenza vaccination, summarizes the factors that can influence vaccine uptake during pregnancy and provides practical advice on how healthcare providers in an obstetrics setting can contribute to the successful implementation of maternal immunization programs.</p> <p>To help increase uptake, practitioners should recommend maternal pertussis and influenza vaccination to their patients during the first antenatal visit. They should give information about the effectiveness and safety of maternal immunization, and about the risk of infection and severity of the respective diseases in the absence of vaccination. Ideally, vaccines should be offered on-site during one of the routine antenatal visits, thereby maximizing convenience for the patient. Strategies to increase uptake will need to be tailored to the antenatal care model of the specific country but, regardless of the model, should aim to incorporate vaccination into standard antenatal care. To do so, healthcare professionals involved in the delivery of vaccines should be clearly identified and adequately trained, standing orders could be instituted (allowing midwives and obstetric nurses to administer vaccines), reminders about vaccination could be added to the patient's medical records and the patient's vaccination status</p>

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## Title page

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### **Women and children first: the importance of pertussis and influenza vaccination in pregnant women and how to increase vaccine uptake**

Piyali Mukherjee<sup>a</sup>, Attila Mihalyi<sup>a</sup>, Kate Ralph<sup>b</sup>, Richard H Beigi<sup>c</sup>, Andrea Genazzani<sup>d</sup>, Christine E Jones<sup>e</sup>

#### **Affiliations:**

<sup>a</sup> GSK, Wavre, Belgium

<sup>b</sup> Faculty of Medicine, University of Southampton, Southampton, UK

<sup>c</sup> Magee-Womens Hospital of UPMC, Pittsburgh, PA, USA

<sup>d</sup> Division of Obstetrics and Gynecology, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

<sup>e</sup> Faculty of Medicine, University of Southampton and NIHR Southampton Clinical Research Facility and NIHR Southampton Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust, Southampton, UK

#### **Corresponding author:**

Piyali Mukherjee, MBBS, MPH, GSK, Avenue Fleming 20, 1300 Wavre, Belgium;

email: piyali.x.mukherjee@gsk.com

**Abstract**

Vaccination during pregnancy has been proven effective in protecting both pregnant women and their newborns from infectious diseases. An increasing number of countries have issued recommendations for the use of pertussis and influenza vaccines during pregnancy and are offering these vaccines free of charge. However, even in such countries, despite the demonstrated effectiveness and strong safety profile of maternal pertussis and influenza vaccination, vaccine uptake has remained suboptimal. This paper gives a succinct overview of the available evidence supporting maternal pertussis and influenza vaccination, summarizes the factors that can influence vaccine uptake during pregnancy and provides practical advice on how healthcare providers in an obstetrics setting can contribute to the successful implementation of maternal immunization programs.

To help increase uptake, practitioners should recommend maternal pertussis and influenza vaccination to their patients during the first antenatal visit. They should give information about the effectiveness and safety of maternal immunization, and about the risk of infection and severity of the respective diseases in the absence of vaccination. Ideally, vaccines should be offered on-site during one of the routine antenatal visits, thereby maximizing convenience for the patient. Strategies to increase uptake will need to be tailored to the antenatal care model of the specific country but, regardless of the model, should aim to incorporate vaccination into standard antenatal care. To do so, healthcare professionals involved in the delivery of vaccines

should be clearly identified and adequately trained, standing orders could be instituted (allowing midwives and obstetric nurses to administer vaccines), reminders about vaccination could be added to the patient's medical records and the patient's vaccination status should be well documented. These measures could help establish maternal immunization as the norm in the general population and increase acceptance and uptake.

**Key words**

Maternal immunization, Tdap, obstetricians, gynecologists, midwives

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### 1. INTRODUCTION

In the last two decades, tremendous progress has been made in reducing global child mortality, in part due to the successful implementation of infant vaccination programs to prevent infectious diseases.<sup>1-4</sup> As most pediatric vaccines are not administered until 6–12 weeks of age, and full protection is not normally achieved until completion of a multi-dose primary series several months later, newborns and young infants are particularly vulnerable to vaccine-preventable infectious diseases.<sup>5, 6</sup> Protection against these diseases during the first months of life relies on passive immunity by maternal antibodies transferred via the placenta, particularly during the third trimester.<sup>7-10</sup> However, maternal antibody levels are often suboptimal (if a mother has not been recently vaccinated against or exposed to the pathogen) and decline rapidly in infants during the first months of life, leaving a susceptibility gap of several months (**Figure 1**).<sup>8, 10, 11</sup> Maternal immunization is increasingly being used as a strategy to close this susceptibility gap: vaccination during pregnancy increases pathogen-specific antibody concentrations in the mother's serum and thereby aims to achieve protective levels of transplacentally transferred maternal antibodies in the newborn that persist until protection can be achieved from the infant vaccination series (**Figure 1**).<sup>6, 8-10</sup> Vaccine-induced antibodies in breast milk and a reduced risk of transmission from the mother to her infant after birth may further contribute to infant protection.<sup>12, 13</sup> Moreover, vaccinating pregnant women protects the women themselves during a period when they are more vulnerable to severe disease from some infections, due to pregnancy-related physiological and immunological changes.<sup>9, 10, 13</sup>

Tetanus vaccination of pregnant women in developing countries has been used successfully for decades to protect infants from neonatal tetanus.<sup>14-16</sup> Additionally, maternal pertussis and influenza vaccination programs have been introduced in many countries and have proven to be effective in preventing disease in young infants and/or pregnant women.<sup>17, 18</sup> Nevertheless, pertussis and influenza vaccine uptake during pregnancy remain suboptimal, even in countries where recommendations from governing bodies are in place and vaccines are reimbursed.<sup>19-24</sup>

Our paper i) provides an overview of the available evidence supporting maternal pertussis and influenza vaccination, ii) summarizes the factors that can influence vaccine uptake during pregnancy and iii) provides practical advice on how healthcare providers in an obstetrics setting can translate the available evidence into clinical practice and contribute to the successful implementation of maternal immunization programs.

A plain language summary is provided in **Figure 2**.

## **2. CLINICAL EVIDENCE SUPPORTING MATERNAL PERTUSSIS AND INFLUENZA VACCINATION**

### **2.1 Medical need for maternal pertussis and influenza vaccination**

#### ***Pertussis***

Pertussis (or whooping cough) is a highly contagious respiratory disease caused by the bacterium *Bordetella pertussis*. It has its greatest burden in infants, especially during the first months of life before protection through infant vaccination has been established.<sup>25-27</sup> Neonates and very young infants are at greatest risk of severe pertussis-related complications, including

hypoxia, seizures, encephalopathy, leukocytosis, pneumonia, pulmonary hypertension and death.<sup>28, 29</sup> Despite effective vaccination programs, *B. pertussis* continues to circulate within populations, and cyclical peaks of disease occur every 2–5 years.<sup>26, 30</sup> In response to a rise in the number of pertussis cases and associated infant deaths in some countries between 2008 and 2012, supplemental strategies to reduce infant mortality from pertussis infections were explored.<sup>26</sup> These include cocooning (vaccination of a newborn’s mother [postpartum], other household contacts and caregivers to reduce the newborn’s risk of exposure to *B. pertussis*), neonatal immunization and maternal immunization.<sup>26, 30</sup> While successes were observed with cocooning in some settings, immunization of all household contacts and caregivers can be logistically challenging and is estimated to be less cost-effective than maternal immunization. In addition, a susceptibility gap likely remains while immunity is being established in the mother/household contacts.<sup>26, 31, 32</sup> A birth dose of acellular pertussis vaccine (neonatal vaccination) was shown to be immunogenic and well tolerated in clinical trials, but protection cannot be expected in the first vulnerable weeks of life.<sup>26, 33-35</sup> Currently, maternal immunization is considered as the most effective and favorable option to supplement infant vaccination to combat pertussis disease in young infants.<sup>26, 30, 32</sup>

### ***Influenza***

Data from influenza pandemics and epidemics have shown that pregnant women are at increased risk of severe influenza-related complications, hospitalization and death.<sup>17, 36</sup> Influenza infection during pregnancy may also lead to fetal growth restriction, preterm delivery, stillbirth and neonatal death.<sup>17, 36</sup> Moreover, infants younger than 6 months (who are not eligible to receive influenza vaccination) have a high risk of developing severe influenza



disease.<sup>17, 36</sup> As a result, maternal influenza vaccination is offered in many countries to reduce these risks to mother and infant.<sup>10, 17</sup>

## **2.2 Effectiveness and safety of maternal pertussis and influenza vaccination**

### ***Pertussis***

(Systematic) reviews including up to nearly 200,000 women immunized with acellular pertussis-containing vaccines during pregnancy showed no significant differences between pertussis-vaccinated and unvaccinated women in terms of pregnancy- and neonate-related safety outcomes, except for a small increased relative risk (but low absolute risk) of chorioamnionitis (i.e., an infection of the amniotic cavity).<sup>18, 37-41</sup> However, no increased risk for clinical sequelae related to chorioamnionitis (such as preterm birth or neonatal sepsis) were found.<sup>18, 39, 41</sup> Hence, the clinical significance of this finding is questionable. A possible association between maternal Tdap vaccination and chorioamnionitis is being further evaluated.<sup>42</sup> Vaccine effectiveness estimates were 69%–93% for laboratory-confirmed pertussis, 91%–94% for pertussis-related hospitalizations and 95% for pertussis-related deaths in infants younger than 2 or 3 months.<sup>18, 43-49</sup> These data underscore the great benefit and strong safety profile of maternal pertussis vaccination.

### ***Influenza***

Inactivated influenza vaccines have been administered to millions of pregnant women to date, and no increased risk of maternal complications or adverse fetal outcomes associated with influenza vaccination have been found.<sup>17</sup> Maternal influenza vaccination was proven to protect pregnant women from laboratory-confirmed influenza,<sup>17, 50</sup> reduce the risk of adverse

pregnancy outcomes (e.g., pre-eclampsia, stillbirth),<sup>17, 51</sup> and protect infants from laboratory-confirmed influenza and influenza-related hospitalization.<sup>17, 52, 53</sup>

### 3. CURRENT RECOMMENDATIONS

#### *Pertussis*

Prompted by a rise in the reported number of pertussis cases leading to several infant deaths, the United States (US) and the United Kingdom (UK) were the first countries to recommend the administration of pertussis-containing vaccines during pregnancy (from 2011 and 2012, respectively).<sup>54-57</sup> Both countries currently recommend vaccination of all pregnant women in each pregnancy with the tetanus-reduced-antigen-content-diphtheria-acellular pertussis vaccine (Tdap, in the US) or Tdap-inactivated poliovirus vaccine (Tdap-IPV, in the UK).<sup>55, 58</sup>

Currently (as of June 2020), more than 40 countries worldwide (including at least 15 countries in Europe) have official Tdap maternal immunization recommendations in place, issued by national recommending bodies or professional organizations (**Table 1, Figure 3**). The World Health Organization (WHO) recommends vaccination of pregnant women with one dose of Tdap (in the second or third trimester and preferably at least 15 days before the end of pregnancy to ensure sufficient time for antibody transfer) in countries or settings with high or increasing pertussis-related infant morbidity or mortality.<sup>30</sup>

## ***Influenza***

Influenza vaccination in pregnant women was first recommended in the US in the 1960s, after a higher risk of complications was noted in this population during the 1957 flu pandemic.<sup>14, 15</sup> Recommendations changed over time in terms of target group and window of vaccination, but since 2004, the Advisory Committee on Immunization Practices recommends immunization with inactivated influenza vaccines for all pregnant women who are or will be pregnant during the influenza season at any gestation.<sup>59</sup> In 2012, the WHO issued a recommendation for countries to include pregnant women in their seasonal influenza vaccination programs and give them the highest priority.<sup>60</sup> Recommendations for maternal influenza vaccination are now in place in many countries across the Americas, Europe and Asia.<sup>10</sup> As of June 2020, at least 90 countries have influenza vaccination programs specifically aimed at pregnant women.<sup>61</sup>

## **4. FACTORS AFFECTING VACCINE UPTAKE DURING PREGNANCY**

### **4.1 Pertussis and influenza vaccine uptake during pregnancy**

Despite the strong safety profile and demonstrated effectiveness of maternal pertussis and influenza vaccination in protecting newborns and/or pregnant women, vaccine uptake has remained suboptimal, even in countries with recommendations for their use.<sup>19</sup> Pertussis vaccine uptake during pregnancy is often higher than that of influenza (possibly because mothers prioritize their newborns' health over their own and perceive pertussis vaccination as protecting the newborn and influenza vaccination as protecting the mother<sup>62</sup>) but remains below desired levels.<sup>20-24</sup> Based on results from an internet panel survey, vaccination coverage

in the US in the 2017–18 influenza season was 54% for Tdap during pregnancy (among women with live births) and 49% for influenza before or during pregnancy (among women pregnant during the peak influenza period).<sup>21</sup> The estimated vaccine uptake in pregnancy in the UK (2018–19) and Belgium (2016) was around 70% for pertussis and 45% for influenza.<sup>22–24</sup> Vaccination coverage varies widely between countries, even among those with recommendations in place. For instance, among 11 European countries with readily available coverage data, influenza vaccine uptake during pregnancy varied from <1% to 86.5% in 2014–15, with a median of 8.7%.<sup>20</sup>

#### **4.2 Factors affecting vaccine uptake**

Several factors have been identified that either positively or negatively affect vaccine uptake in pregnant women. These have been discussed in detail in recent reviews<sup>17, 63–67</sup> and are summarized in **Figure 4**. A key factor in vaccine acceptance and uptake by pregnant women is a recommendation by a trusted healthcare provider.<sup>64, 65</sup> This was reported in multiple studies and surveys addressing barriers and facilitators for vaccine uptake in pregnant women.<sup>17, 64, 65</sup> A meta-analysis showed that pregnant women who had received a recommendation from a healthcare provider had 12-times and 10-times greater odds of accepting seasonal influenza and pertussis vaccination, respectively.<sup>68</sup> Other important barriers identified by pregnant women may vary between vaccines and include concerns about their own safety and (most importantly) that of their fetus and newborn, lack of knowledge about the risk of infection and severity of the diseases, doubts about vaccine effectiveness (mostly noted for influenza) and general vaccine hesitancy.<sup>17, 64, 65</sup> In addition, access to a healthcare facility offering the vaccine, cost/insurance coverage (in settings in which the vaccines are not offered free of charge) and

demographic and psychosocial factors influence a woman's decision to get vaccinated (**Figure 4**).<sup>17, 64, 65</sup>

Barriers identified by healthcare workers partly overlap with those reported by pregnant women and include concerns about vaccine safety and effectiveness, and lack of knowledge about disease risk and severity. Healthcare workers also highlight additional barriers related to knowledge and education (e.g., inadequate training on how to administer vaccines and educate pregnant women, confusion or unawareness about guidelines and recommendations), related to implementation (e.g., vaccination not being part of their routine practice, logistical and financial concerns around obtaining, ordering, storing and administering vaccines, difficulties in accessing patients' vaccination records, increased workload and staff shortage, questions about liability), and related to uptake (e.g., unwillingness of pregnant women to be vaccinated).<sup>17, 64, 65</sup>

## **5. HOW TO IMPROVE VACCINE UPTAKE DURING PREGNANCY**

Below, we highlight actions that healthcare providers in an obstetrics setting can take to improve vaccine uptake among pregnant women (**Figure 5**). We focused on interventions for which evidence is available from randomized, controlled trials or prospective or retrospective observational studies.<sup>69-71</sup> Most available evidence originates from studies in the US and may not always fully apply to other parts of the world. Strategies to increase uptake need to be tailored to the maternal healthcare infrastructure of the specific country.<sup>72</sup> For instance, official recommendations may or may not be in place, vaccines may or may not be available free of

charge, and the principal care of pregnant women may be provided by the obstetrician, the midwife or the general practitioner.

### **5.1 Recommend and educate**

One of the strongest motivators for women to get vaccinated during pregnancy is a recommendation from a trusted healthcare provider.<sup>64, 65, 73-79</sup> We therefore advise that, during the first antenatal visit, **practitioners recommend vaccination** to their patients and **give information and resources** about antenatal pertussis and influenza vaccination, in particular about the official recommendations, the benefits for the newborn baby, the reassuring safety profile in mother and child and the risks of infection and severity of the respective diseases in the absence of vaccination.

**One-to-one education sessions, pamphlets and posters** have all been shown to improve vaccination rates (**Figure 5**).<sup>80-82</sup> A randomized controlled trial in Hong Kong during the 2013–14 and 2014–15 influenza seasons showed higher influenza vaccination rates in women who had received a 10-minute one-to-one education compared to women who had received standard care.<sup>82</sup> A randomized trial in Connecticut (US) during the 2011–12 influenza season found higher influenza vaccination rates in pregnant women who had received an education pamphlet with or without a benefit statement compared to women who had received neither.<sup>80</sup>

Additionally, a randomized trial conducted between 2013 and 2016 in Colorado (US) showed a significant impact of a vaccine information website with or without interactive social media components on the uptake of influenza but not Tdap vaccine,<sup>83</sup> indicating that strategies to improve vaccine uptake likely need to be **tailored to the specific vaccine**.

## 5.2 Incorporate vaccination as standard antenatal care

Because the obstetrician and/or midwife are in many countries the only (or principal) healthcare provider a woman sees during her pregnancy, we advise that—in such countries—pertussis and influenza vaccines should be administered by the obstetrician or, if authorized by local law, by the midwife or obstetric nurse **during one of the routine antenatal visits**. This avoids an additional visit to a general practitioner, saves time and effort and maximizes convenience for the pregnant woman. **Offering the vaccine(s) on-site** has been shown to increase uptake (**Figure 5**).<sup>21, 84</sup> Even in countries where the principal healthcare provider is the general practitioner, a recommendation by the obstetrician and midwife to vaccinate as part of standard care would be important.

To incorporate vaccination as a standard part of antenatal care and thereby making women (and the general population) see it as a normal component of pregnancy care, it is important to create a **culture of immunization** among all staff.<sup>72, 85</sup> Staff should be **trained and educated** in terms of vaccine and disease knowledge, recommendations about maternal vaccination and the technical aspects of stocking and administering vaccines, such that they feel confident about implementing an immunization program, a task that has not historically been theirs. A retrospective study in Texas (US) saw improved antenatal Tdap vaccination rates after a physician training program was set up (**Figure 5**).<sup>86</sup> The American College of Obstetricians and Gynecologists suggests **assigning an immunization “champion” (or team)** serving as a resource center for other staff members and taking the responsibility of ordering, receiving and storing vaccines.<sup>85</sup>

In countries where midwives provide a substantial portion of antenatal care, midwives are a highly accessed and trusted source of vaccine information.<sup>87, 88</sup> Surveys in Australia and the UK indicate that while the majority of midwives support antenatal immunizations, a large fraction do not feel adequately trained but would be willing to discuss and administer vaccines with appropriate training (provided this is authorized pursuant to local laws).<sup>89-91</sup> Considering the important roles midwives play in prenatal follow-up of patients in many countries, it is advisable to **institute standing orders** for the indicated vaccinations, **authorizing midwives to administer vaccines** according to a protocol approved by a physician but without needing an individual physician order or prescription.<sup>85</sup> A prospective study in South Australia in 2014–16 showed an increased pertussis vaccine uptake after implementation of a midwife-delivered vaccination program for pregnant women (**Figure 5**).<sup>73</sup> Similarly, a study in three hospitals in Melbourne (Australia) in 2015–17 saw a positive impact on maternal Tdap uptake after implementation of standing orders (**Figure 5**).<sup>92</sup>

**Implementing an alert on medical records** to remind the provider to discuss and offer antenatal vaccination to their pregnant patients can also be effective in improving uptake. A retrospective study in a hospital in Texas (US) noted a higher Tdap vaccine uptake in pregnant women after changing recommendations from postpartum to antepartum vaccination and implementing best-practice alerts in their electronic charting system that were repeated at each visit until documentation of vaccination or delivery (**Figure 5**).<sup>93</sup> Likewise, a hospital in Wisconsin (US) saw significant increases in influenza vaccine uptake in pregnant women after implementation of a best-practice alert.<sup>94</sup> Linking vaccination to one of the routine visits, for



instance at the same time as the 20-week fetal anomaly scan visit or testing for gestational diabetes can create a natural prompt.<sup>72, 85</sup>

In addition, **documenting a woman's vaccination status in all records** (secondary and primary care) and assessing the status is key to successful implementation of immunization programs. Being able to easily track whether a woman has or has not received the recommended antenatal immunizations allows reintroducing the discussion and offering the vaccine(s) at the next visit.<sup>85</sup> It also makes overall assessments of immunization rates and possible impact of interventions possible.

## **6. CONCLUSIONS**

Maternal immunization is an effective method of protecting pregnant women and their infants from vaccine-preventable diseases. Despite significant evidence supporting the effectiveness and safety of pertussis and influenza vaccines in pregnant women, uptake is suboptimal. Recommendation from a trusted healthcare provider and on-site availability of the vaccines are key factors in encouraging women to be immunized and increasing uptake. Educating pregnant women (through one-to-one discussions, pamphlets and posters) on the risk of infection, severity of pertussis and influenza disease in young infants and the effectiveness and safety of maternal immunization are means to further increase uptake. Healthcare professionals involved in delivery of vaccines should be clearly identified and adequately trained as part of their role. Optimal strategies will depend on the antenatal care model applicable in a country, but regardless of the model, vaccination should be integrated into routine antenatal care and,

where possible, tied to one of the routine antenatal visits. These measures could help establish maternal immunization as the norm in the general population and increase acceptance and uptake.

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### **Conflict of interest statement**

A Mihalyi and P Mukherjee are employees of the GSK group of companies (GSK) and declare financial (including shares) and non-financial relationships and activities. C Jones reports personal fees from MSD and Pfizer outside the submitted work; C Jones is also an investigator for clinical trials carried out on behalf of her institution, sponsored by various vaccine manufacturers (including GSK and Novavax) but receives no personal funding for these activities. R Beigi, A Genazzani and K Ralph declare no financial or non-financial relationships and activities, and no conflicts of interest.

### **Author contributions**

P Mukherjee: conception of the paper, structure and scope; preparation of the initial outline; suggestion of references; critical review and input on drafts; approval of final version. A

Mihalyi: conception of the paper; contribution to structure and scope; suggestion of references; critical review and input on drafts; approval of final version. K Ralph: contribution to structure and scope; provided conceptual framework of factors influencing vaccine-related decision-making among pregnant women; suggestion of references; critical review and input on drafts; approval of final version. RH Beigi: contribution to structure and scope; critical review and input on drafts; approval of final version. A Genazzani: contribution to structure and scope; critical review and input on drafts; approval of final version. CE Jones: contribution to structure and scope; critical review and input on drafts; approval of final version.

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## Figure captions

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### **Figure 1. Protecting young infants through maternal immunization**

Maternal antibody levels in infants from mothers that have not been recently exposed to or vaccinated against a specific pathogen (dotted blue line) are often suboptimal and decline rapidly after birth, leaving a susceptibility gap of several months (green line) until the infant is protected through its primary vaccination series. Vaccination during pregnancy aims to increase pathogen-specific antibody concentrations in the mother's serum and achieve protective levels of transplacentally transferred maternal antibodies in the newborn (full blue line) that persist until the infant is protected through its primary vaccination series.

### **Figure 2. Plain language summary**

### **Figure 3. Countries with recommendations for maternal immunization with pertussis-containing vaccines**

See references in Table 1.

### **Figure 4. Factors affecting uptake of vaccines during pregnancy, identified by pregnant women and healthcare providers**

### **Figure 5. Interventions to increase vaccine uptake during pregnancy**

Tdap, tetanus-reduced-antigen-content-diphtheria-acellular pertussis vaccine; US, United States; CT, Connecticut; TX, Texas.

## Tables

**Table 1. Recommendations for pertussis vaccination during pregnancy in different countries and by international organizations**

Country/Organization	Recommendation	Reference
Argentina	Tdap from 20 weeks' gestation	95
Australia	Tdap ideally at 20–32 weeks' gestation	96
Bahamas	Tdap in each pregnancy	97
Belgium	Tdap ideally at 24–32 weeks' gestation	98
Bermuda	Tdap in second or third trimester	99
Brazil	Tdap ideally at 27–36 weeks' gestation <sup>a</sup>	100
Canada	Tdap ideally at 27–32 weeks' gestation <sup>b</sup>	101
Chile	Acellular pertussis vaccine at 27–36 weeks' gestation	102
Colombia	Tdap from 26 weeks' gestation	103
Costa Rica	Tdap in third trimester	104
Czech Republic	Tdap ideally at 28–36 weeks' gestation	105
Denmark	Tdap ideally at 32 weeks' gestation <sup>c</sup>	106
El Salvador	Tdap from 20 weeks' gestation	107
French Territories (Mayotte)	Tdap-IPV ideally at 18–39 weeks' gestation <sup>d</sup>	108
Germany	Tdap at the beginning of the third trimester <sup>e</sup>	109
Greece	Tdap at 27–36 weeks' gestation	110

Honduras	Tdap during pregnancy in whooping cough outbreak situations	111
Hong Kong	Tdap (or Tdap-IPV) in second or third trimester (ideally before 35 weeks)	112
Iceland	Tdap or Tdap-IPV in in second or third trimester	113, 114
India	Tdap in third trimester (ideally at 27–36 weeks)	115
Ireland	Tdap ideally at 16–36 weeks' gestation	116
Israel	Tdap at 27–36 weeks' gestation	117
Italy	Tdap at 27–36 (ideally 28) weeks' gestation	118
Mexico	Tdap at 20–32 weeks' gestation	119
Netherlands	Tdap from 22 weeks' gestation	120
New Zealand	Tdap from 16 weeks' gestation	121
Panama	Tdap in third trimester	122
Paraguay	Tdap from 20 weeks' gestation	123
Peru	Tdap at 27–36 weeks' gestation	124
Philippines	Tdap at 28–36 weeks' gestation	125
Poland	Tdap at 27–36 weeks' gestation	126
Portugal	Tdap at 20–36 weeks' gestation	114
Qatar	Tdap at 27–36 weeks' gestation	127
San Marino	Tdap at 21–36 weeks' gestation	128
Saudi Arabia	Tdap in third trimester	129
Singapore	Tdap ideally at 16–32 weeks' gestation	130

Slovenia	Tdap from 24 weeks' gestation	114
South Korea	Tdap at 27–36 weeks' gestation	131
Spain	Tdap from 27 weeks' gestation	132
Switzerland	Tdap ideally at 13–26 weeks' gestation <sup>f</sup>	133
Taiwan	Tdap at 28–36 weeks' gestation	134
Thailand	Tdap in third trimester	135
UK	Tdap-IPV ideally at 16–32 weeks' gestation (up to 38 weeks)	136, 137
Uruguay	Tdap in each pregnancy	138
USA	Tdap at 27–36 weeks' gestation	55
<hr/>		
EBCOG	Tdap ideally at 27–36 weeks' gestation <sup>g</sup>	139
FIGO	Tdap ideally at 27–36 weeks' gestation	140
PAHO	Tdap in second or third trimester <sup>h</sup>	141
WHO	Tdap in second or third trimester <sup>h</sup>	30

Note, this list may not be complete and may change over time.

EBCOG, European Board and College of Obstetrics and Gynecology; FIGO, International Federation of Gynecology and Obstetrics; PAHO, Pan American Health Organization; Tdap, tetanus-reduced-antigen-content-diphtheria-acellular pertussis vaccine; Tdap-IPV, tetanus-reduced-antigen-content-diphtheria-acellular pertussis-inactivated poliovirus vaccine; UK, United Kingdom; USA, United States of America; WHO, World Health Organization.

<sup>a</sup>In areas that are hard to reach, vaccines can be administered from 20 weeks' gestation.

Women should ideally be vaccinated at least 20 days before planned delivery.



<sup>b</sup>Vaccination between 13 and 26 weeks of gestation may be considered in women with an increased risk of preterm delivery. Women should ideally be vaccinated at least 4 weeks before planned delivery.

<sup>c</sup>Temporary program starting on 1 November 2019 and concluding on 31 January 2020.

Vaccines can be offered after 32 weeks' gestation, until 1 week before planned delivery.

Women with a high risk of preterm delivery should be vaccinated in the second trimester (but not before 16 weeks' gestation).

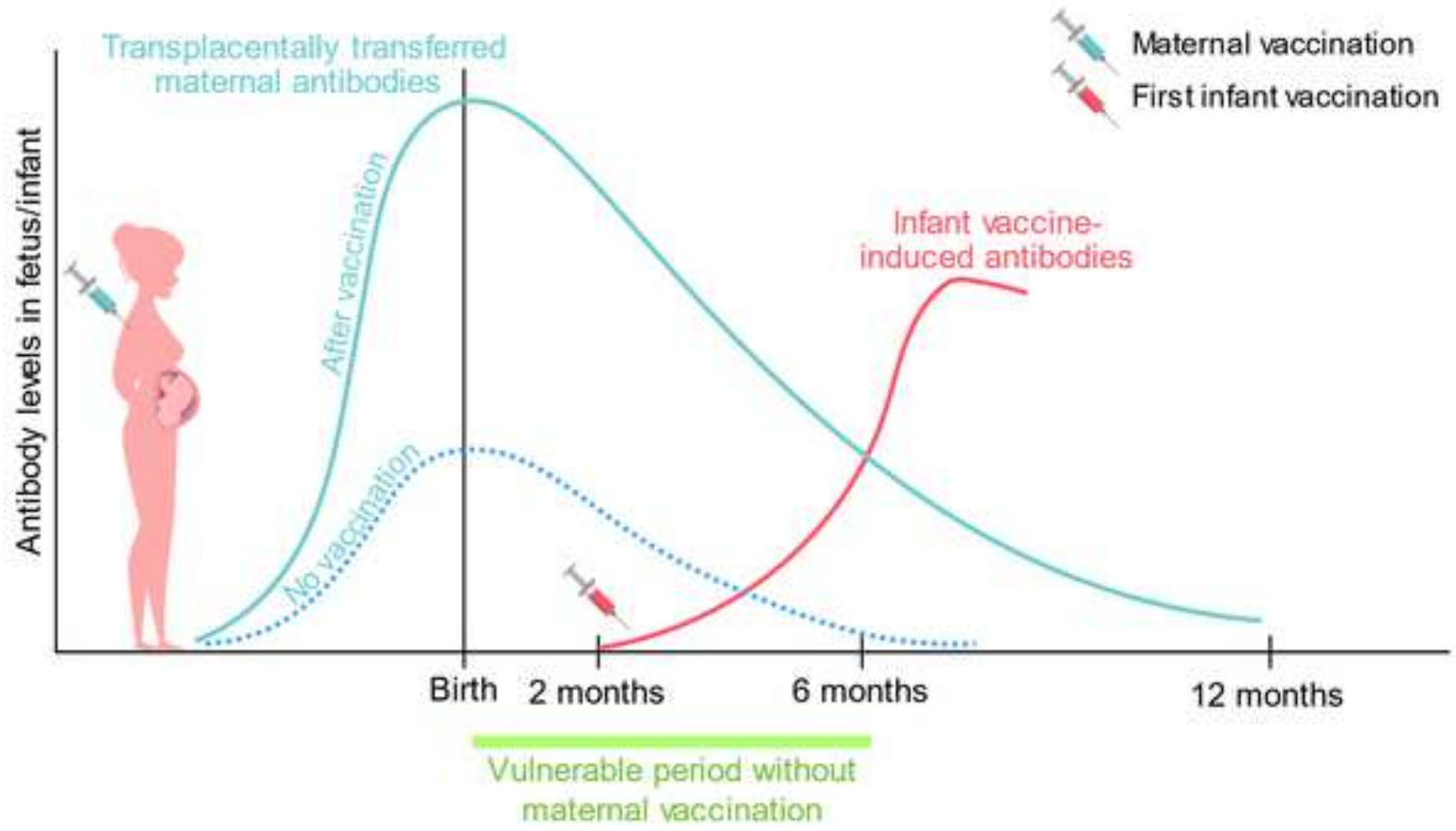
<sup>d</sup>Program in place for the duration of the ongoing pertussis epidemic.

<sup>e</sup>Women with a high risk of preterm delivery should be vaccinated in the second trimester.

<sup>f</sup>Vaccination allowed throughout the second or third trimester.

<sup>g</sup>Tdap can be given any time during pregnancy.

<sup>h</sup>Vaccination preferably at least 15 days before delivery.



# Plain language summary

## What is the context?

- Diseases such as whooping cough and flu can be very serious for young babies before they are protected by childhood vaccinations. Flu can also be harmful to pregnant women.
- Vaccinating mothers during pregnancy can help protect them and their babies from these diseases.
- Although many countries recommend vaccination against whooping cough and flu during pregnancy, vaccine uptake remains suboptimal in pregnant women..

## What is new?

- This paper summarizes the factors that can influence vaccine uptake during pregnancy and advises how healthcare practitioners such as obstetricians, midwives and nurses can encourage vaccination in pregnant women.
- To improve vaccine uptake, healthcare providers in an obstetric setting should:
  - recommend vaccination to their pregnant patients at their first antenatal visit
  - educate about the effectiveness and safety of vaccines
  - explain the potential consequences of not vaccinating
- In addition, obstetric facilities should consider:
  - offering the vaccines on-site
  - administering the vaccines during a routine antenatal visit

## What is the impact?

- These approaches should help raise awareness of the benefits of maternal immunization, encourage its standardization in antenatal care and improve vaccine uptake in pregnant women.

