



# A study of acceptance and hesitation factors towards tetanus, diphtheria, and acellular pertussis (Tdap) and influenza vaccines during pregnancy

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## ABSTRACT

**Introduction:** Vaccination of pregnant women with tetanus, diphtheria, and acellular pertussis (Tdap) and influenza vaccines is desirable to reduce neonatal and maternal morbidity and mortality. However, vaccine coverage rates and acceptance are frequently below recommended rates.

**Objectives:** To ascertain Tdap and influenza vaccine coverage rates in our population and to study the reasons behind sub-optimal rates.

**Method:** A survey was submitted to pregnant or in their puerperium women at the University Hospital of São Paulo University. Data were obtained during two consecutive influenza seasons (2017–2018), and vaccination was verified through vaccination chart checking. Respondents were classified according to their status as “Received Tdap” and “Didn’t receive Tdap”, and as “Know” or “Doesn’t know” regarding their awareness of Tdap safety during pregnancy and protective effect on the newborn. Vaccine uptake and personal awareness of vaccination status were compared among these groups for Tdap and influenza vaccines.

**Results:** In a studied sample of 207 patients (representative of the whole), coverage rates for Tdap and influenza vaccines were respectively 85.5% and 95.2%. Additionally, 84.5% received both vaccines. There was no vaccine refusal for Tdap and only 0.5% for influenza. For either Tdap or influenza vaccines, the main reason for not vaccinating was a lack of knowledge/information. Factors associated with not vaccinating Tdap during pregnancy were lower number of prenatal visits, being unemployed or freelance worker, not being aware of vaccine safety or its benefits for the baby, not being oriented by the doctor to be vaccinated, not being aware of personal vaccination status, and not having been vaccinated for influenza.

**Conclusion:** While influenza vaccination coverage during pregnancy was ideal, Tdap rates were below recommended values. Significant factors associated with better coverage for Tdap during pregnancy included being employed and not being self-employed, (not yet reported in the Americas) and being aware of personal vaccination status.

## Introduction

Pertussis is a re-emergent disease. In 2014 there was a global peak in incidence, with an estimated 160.700 deaths, of which 53% were among children younger than one year [1,2]. Previous studies showed that vaccination during pregnancy with tetanus, diphtheria, and acellular

pertussis vaccine (Tdap) benefits both mother and child, substantially reducing pertussis morbidity and hospitalization rates in the first six months after birth [3–8]. Tdap may be safely administered to pregnant and breastfeeding women. [9–13] The vaccination coverage rate for Tdap in pregnant women in Brazil in 2018 was 62.4%, according to data from the Brazilian National Immunization Program (NIP).

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Influenza is a highly transmissible respiratory disease. Pregnant women and infants younger than six months are at a higher risk of complications, hospital admissions, and death [14–16]. Influenza viruses cause yearly epidemics, with an overall estimated incidence of 10% of the world population, leading to an estimated 5 million severe cases and 650,000 deaths each year, mainly when associated with pandemic strains, as in the 2009 H1N1 pandemic [17]. Influenza vaccination during pregnancy has been recommended for some time and is considered safe [15–21]. According to the NIP, the vaccination coverage rate for influenza in pregnant women in Brazil in 2018 was 80.8%.

The World Health Organization (WHO) target for influenza vaccination coverage is 75% for at-risk groups [22]. The WHO also encourages the improvement of vaccination programs for pregnant women, such as vaccination coverage for Tdap in Spain (84%) or in the United Kingdom (UK) (71%) [23]. Since April 2010, Brazilian NIP included a trivalent influenza vaccine to be given free of charge to all pregnant women, regardless of gestational age. In November 2014, Tdap was also included in the NIP for use after 28 weeks of gestation. Since 2017 it has been administered as early as 20 weeks of gestational age to increase vaccination coverage. Recommended coverage rates in Brazil are 90% for influenza and 100% for Tdap [24,25].

However, despite the evidence of reducing infant morbidity and mortality, vaccination rates in Brazil for influenza and pertussis during pregnancy fall very short of Brazilian and other countries' recommendations [3,5,8,26–28]. It is essential to analyze the factors associated with vaccination and vaccine hesitancy in this population to propose more effective interventions [29–39].

This study aims to better understand vaccination rates for influenza and Tdap during pregnancy in a population of Brazilian public hospital patients. We also aim to point out some reasons for suboptimal rates and vaccinal hesitation. Therefore, these analyses can assist strategic public health in improving vaccine coverage.

## Methods

This study is a cross-sectional, observational, and descriptive analysis of the pregnant or postpartum women population conducted at the University Hospital of São Paulo University (HU-USP). Our institution is a secondary-level public hospital located in São Paulo city, in southeastern Brazil, with a delivery frequency of approximately 2.800 births a year at the time of this study. It is one of the reference health services for a surrounding population of around 500.000 inhabitants.

Data was obtained by means of a questionnaire applied to all pregnant or postpartum women who were in the rooming-in or in the nursery on the days in which the researcher carried out the data collection. The inclusion criterion was to be pregnant or to have just given birth at the time of entry in the study. The vaccinal status of the interviewees was checked after they had answered the questionnaire, by checking their vaccination charts. Patients were excluded if they had no vaccination charts or other means of proving their vaccinal status or if they declined to participate. To include two influenza seasons, we obtained data from July 2017 to November 2017 and from March 2018 to November 2018. Written informed consent was obtained from all participants before enrolling. The HU-USP Ethics Committee approved this study under the registration number CEP-HU/USP: 1626/17.

Our questionnaire included demographic and social data such as age, marital status, parity, race, instruction rate, job, and labor market inclusion status. Patients were then asked about the number of prenatal medical visits in the present gestation, patients' knowledge of their vaccination status for influenza and pertussis, if the attending obstetrician had indicated these vaccines and the reasons for not vaccinating in case of non-compliance. Also, patients were asked about their general knowledge of pertussis severity during the first months of life and the utility of vaccinating during pregnancy.

The sample was divided into two groups: "Received Tdap" and

"Didn't receive Tdap", and the differences between these groups were analyzed. Participants were also classified as "Know" or "Don't Know" regarding awareness of the safety of Tdap during pregnancy, its protective effect on the newborn, reasons for taking it during pregnancy, and knowledge of their personal vaccination status for Tdap and Influenza. Vaccination rates were compared for each of these subgroups.

Participants were also classified as "Know" or "Doesn't know" regarding their awareness of Tdap safety during pregnancy, its protective effect on the newborn, and the reasons to receive it during pregnancy. Participants were furthermore assessed regarding their awareness of their personal vaccination status for Tdap and Influenza. Vaccination rates were compared for each of these subgroups.

All patients received their vaccines in public health facilities and no specific education about Tdap and influenza vaccines was given to them prior to the research.

## Statistical analysis

The sample was compared with the totality of deliveries in HU-USP during the same period in terms of maternal age and type of delivery to verify the sample's representativeness.

Patients in the pregnancy/puerperium were divided into two groups: "Received Tdap" and "Didn't receive Tdap", and further compared according to 15 nominal variables: age, marital status, race, situation in the labor market, income, type of delivery, mothers' parity (since this vaccine must be given at each pregnancy and seeing that a greater number of children at home can lead to a greater risk of acquiring the disease), maternal education, number of prenatal consultations, if there was a medical indication for the Tdap vaccine, if the patient correctly knew her vaccinal situation for Tdap and if she had the influenza vaccine in the same pregnancy, knowledge about the safety of the Tdap vaccine (of being safe for the pregnant woman and her fetus), knowledge about the Tdap vaccine to protect the RN, knowledge about the age at which the baby should receive the first dose of pertussis vaccine and knowledge about whooping cough. Each variable was described as frequency and compared between groups through Chi-square and Fisher exact test (2x2 and 2x3). Then we performed a logistic regression analysis, through Nagelkerke R<sup>2</sup>, using Tdap reception as the resulting variable and the variables with a statistically significant difference in the univariate analysis as dependent variables.

Likewise, for the "Know" or "Doesn't know" groups, each variable was described as frequency and compared between groups through Chi-square and Fisher exact test.

Data were analyzed using GraphPad InStat®, v. 3.00, and MedCalc®, v. 17.8.6. All analyses adopted a 5% significance level.

## Results

The questionnaire was applied to a total of 258 pregnant or postpartum women in the University Hospital of São Paulo University (HU-USP). There was no refusal to participate in this study. In the same period, we identified 2225 births in our center. The study and general populations were similar regarding maternal age ( $p = 0.591$ ) and type of delivery ( $p = 0.966$ ).

Fig. 1 shows our study profile and outcomes.

In our sample, the age of most pregnant/postpartum women was between 19 and 34 years old (78.3%), only 10.1% were teenagers and 11.6% were over 35 years old. Vaginal delivery comprised 56.5% of the sample. Most participants had more than 9 years of schooling (87.9%) and had attended seven or more prenatal visits (87,6%). Of the participants, 51.2% were employed or self-employed and 75.8% had received a medical indication for the Tdap vaccine.

## Tdap vaccine

The main differences between the groups "Received Tdap" ( $n = 177$ )

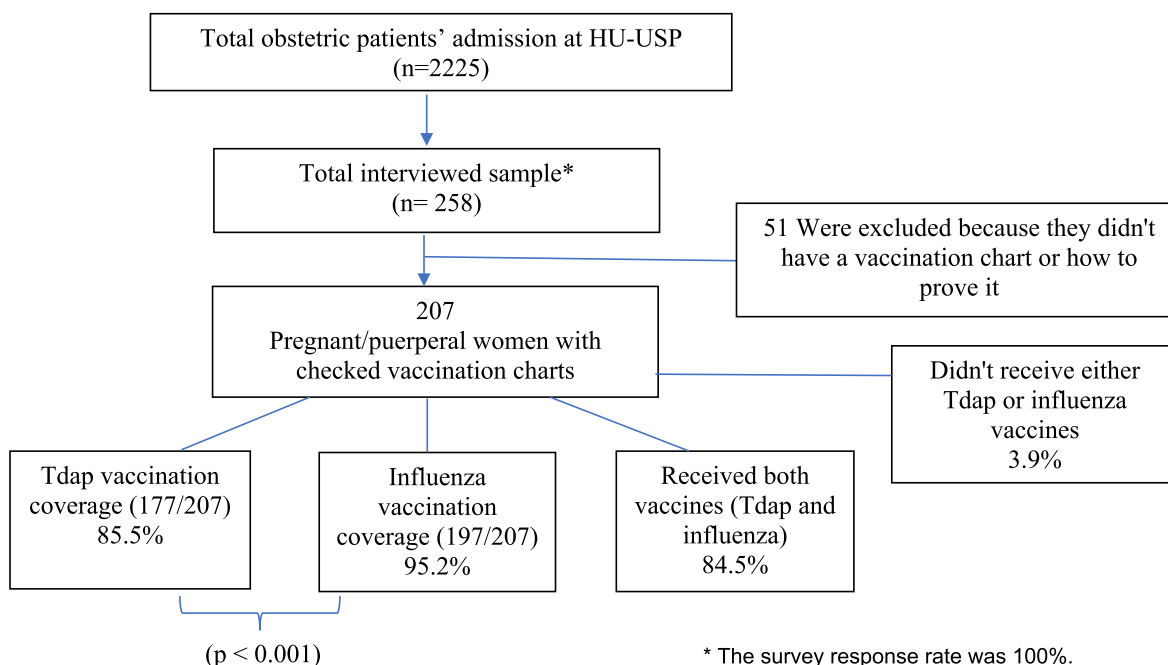


Fig. 1. Study profile and outcomes.

and “Didn’t receive Tdap” (n = 30) are shown in Table 1.

There was no statistically significant difference between these groups in terms of age (p = 0.882, 74% of patients being in the 20–34-year-old range), income (p = 0.918), maternal level of education (p = 0.405), way of delivery (vaginal or cesarean - p = 0.076) or parity (p = 0.201).

Regarding awareness of the potential severity of neonatal pertussis, pertussis itself, and the age at which infants should receive the first dose against this disease, there was no difference between groups (p = 0.353, p = 1.0, and p = 0.596, respectively).

Data were further analyzed by multivariable logistic regression, taking Tdap reception as the resulting variable. The independent variables statistically significant included: seven or more prenatal visits, Tdap having been recommended by a physician, correct awareness of individual vaccination status for Tdap, having received influenza vaccine, job/working status, awareness of Tdap safety, and awareness of its

Table 1  
Comparison between “Received Tdap” and “Didn’t receive Tdap” groups.

Variable	“Received Tdap” n (%)	“Didn’t receive Tdap” n (%)	p
	177 (100%)	30 (100%)	
Working status: Employed	77 (43.5%)	7 (23.3%)	p = 0.01
Unemployed	85 (48.0%)	16 (53.4%)	
Freelance worker	15 (8.5%)	7 (23.3%)	
Seven or more prenatal visits	155 (87.6%)	19 (63.3%)	p < 0.001
Vaccine medical prescription: Yes	144 (81.4%)	13 (43.3%)	p < 0.001
No	22 (12.4%)	13 (43.3%)	
Do not recall	11 (6.2%)	4 (13.4%)	
Personal Tdap vaccine status:			
Aware	155 (87.6%)	7 (23.3%)	p < 0.001
Unaware	22 (12.4%)	23 (76.7%)	
Had influenza vaccine in the same pregnancy	175 (98.9%)	22 (73.3%)	p < 0.001
Know that Tdap is safe during pregnancy: Yes (116 mothers)	107 (60.5%)	9 (30%)	p = 0.001
Know that Tdap during pregnancy can protect the newborn? Yes (101 mothers)	93 (52.5%)	8 (26.7%)	p = 0.008

benefits for the newborn. The R-square, also known as the coefficient of determination, represents the proportion of variability in the response variable explained by the predictor variable, thus the Nagelkerke R<sup>2</sup> obtained was of 0.687, which means a 68.7% probability that taking Tdap during pregnancy could be explained by these seven variables.

When the sample was divided according to vaccine safety and benefits knowledge, we could observe a significantly higher vaccination coverage in the group that reported being aware - Table 2.

Regarding the reasons for not being vaccinated (n = 30), 14 participants erroneously believed they were vaccinated, having received only a diphtheria-tetanus vaccine. Other reasons were: not having received any vaccines during pregnancy (n = 4), not remembering (n = 6), not being informed (n = 3), having been vaccinated in a previous pregnancy, having lost the vaccine chart, and fear because of a previous miscarriage (n = 1 each).

Influenza vaccine and comparison between Tdap and influenza

In the studied population, 197 patients (95.2%) had received influenza vaccination. Of those, 98.5% were adequately aware of their

Table 2  
Coverage rates according to information regarding Tdap.

Question:	Yes - Know	No - Don't know	p
- Do you know that Tdap is safe? n = 207 (100%)	116 (56.0%)	91 (44%)	0.002
Received Tdap (n = 177)	70/91	76.9%	
Coverage rate (%)	107/116	92.2%	
- Do you know that Tdap can protect your baby? n = 207 (100%)	101 (48.8%)	106 (51.2%)	0.010
Received Tdap (n = 177)	93/101	84/106	
Coverage rate (%)	92.1%	79.2%	
- Do you know why you should receive Tdap during pregnancy? n = 207 (100%)	20 (9.7%)	187 (90.3%)	0.744
Received Tdap (n = 177)	18/20	159/187	
Coverage rate (%)	90.0%	85.0%	

vaccinal status. In the subgroup of 10 patients who had not been vaccinated, all (100%) were aware of their status. When answers about the individual status for each vaccine were compared between vaccinated and non-vaccinated groups, the difference was significant (Tdap vaccinated 87.6% vs. influenza vaccinated 98.5%,  $p = 0.001$ , and Tdap non-vaccinated 23.3% vs. influenza non-vaccinated 100%,  $p = 0.0001$ ).

The reasons for not taking the influenza vaccine were described as not having received any vaccines during pregnancy ( $n = 6$ ), fear of adverse effects ( $n = 1$ ), vaccination campaign starting after the last prenatal visit ( $n = 1$ ), medical contraindication ( $n = 1$ ), and egg allergy ( $n = 1$ ).

We observed that 76.7% of the patients who did not receive Tdap did so because of a lack of information or erroneous medical advice, but there was no vaccinal refusal in this sample. Most of these patients (60.9%) were erroneously assumed to be vaccinated. Similarly, the main reasons for influenza non-vaccination were lack of information or erroneous knowledge of their vaccinal status, except for one patient who did not want to take the vaccine for fear of adverse reactions (0.5%).

## Discussion

To our knowledge, this is Brazil's first study to simultaneously analyze acceptance and hesitation factors towards Tdap and influenza vaccines in pregnant or postpartum women. In our sample, coverage rates for Tdap and influenza vaccines were respectively 85.5% and 95.2%. Additionally, 84.5% received both vaccines. We observed Tdap vaccine coverage below Brazilian NIP's 100% recommended values. Fortunately, we identified adequate vaccination coverage in pregnant/ puerperal women for influenza (95.2%).

We aimed to study the factors influencing maternal vaccination uptake. We found that being employed and not being self-employed was a significant factor associated with better coverage for Tdap. This data is a novelty in the Americas that should be better understood; it could be even more significant in countries where the vaccine is not freely distributed by public health care. Remarkably, while women's working status was statistically significant, their actual income was not. Also, other significant factors associated with improved Tdap vaccination were: having had seven or more prenatal consultations, having had the medical indication of this vaccine, knowing her Tdap vaccination status correctly, having had the influenza vaccine in the same pregnancy, knowing about the safety of the Tdap vaccine (it is safe for the pregnant woman and her fetus) and about the protection on the newborn. Overall, misinformation and lack of information are the most critical factors in low adherence to vaccination.

An American study simultaneous to ours – conducted by Murthy et al., from March to April 2018 – concluded that strategies to improve pregnant women's uptake of Tdap and influenza vaccines include improving their knowledge and awareness about vaccine recommendations and efficiency. They also had higher vaccination coverage among those women who reported having received a prescription to vaccinate or referral to vaccination clinics from the healthcare professional (influenza = 63.4%; Tdap = 77.8%), like our study. They have found a racial difference in their population, which in our study was impossible to ascertain because of our country's peculiar demographics and miscegenation [40].

In our study, we found that a medical recommendation for vaccination is a fundamental factor in improving Tdap coverage rates in pregnancy and has been reported in many other studies as one of the most relevant factors related to improving vaccine coverage rates [26,34,41–45]. The power of a trusted healthcare provider recommendation to positively affect vaccine uptake was demonstrated in a European study that interviewed 27,524 subjects from diverse social and demographic strata. The authors found that nearly 80% of respondents would ask a doctor to be informed about vaccines. In addition, nearly two-thirds of those vaccinated in the previous five years had done so because a doctor had recommended it. About 65% declared trust in their

doctors on vaccine information [45].

In our population, the influenza vaccine received during pregnancy was an additional factor significantly related to higher Tdap vaccine coverage. Wales et al. also demonstrated that women who received the influenza vaccine were more likely to receive Tdap.[46]. Therefore, strategies to ensure readily available Tdap and influenza vaccines and trained health care providers to recommend these vaccines are essential to improve maternal immunization.

Our study has some limitations. The most important is having been performed in a restricted period and in a single center. We found higher vaccine coverage rates than Brazilian official data. Nevertheless, our sample characteristics were like those of the total population of women who gave birth at the HU-USP during the study period. Therefore, the reasons for acceptance and hesitation toward Tdap and influenza vaccines must be stable, and our main findings were consistent with those previously described in other populations. Finally, our study was conducted before the Covid-19 pandemic, so it is necessary to review these coverages and reasons nowadays, as they might have possibly changed. These pre- and post-pandemic assessments are relevant on the world stage.

## Conclusion

In this study, the vaccine coverage rates of the pregnant women studied were adequate for Influenza (95.2%) and below the recommended for Tdap (85.5%). There was no vaccine refusal in our sample for Tdap and only one patient for influenza (0.5%). The main factors associated with an increase in the vaccination coverage rate for the Tdap vaccine were being employed and not being self-employed (a fact not previously observed in the Americas); having had seven or more prenatal appointments; having received a medical prescription; being aware of personal vaccination status for the Tdap vaccine; having received the vaccine for Influenza during pregnancy; knowing that the Tdap vaccine is safe during pregnancy and knowing that the Tdap vaccine protects the newborn from pertussis.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data availability

Data will be made available on request.

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