Ann Ig 2022 Jul-Aug; 34(4): 358-374 doi: 10.7416/ai.2022.2503. Epub 2022 Feb 24

Exploring Tdap and influenza vaccine uptake and its determinants in pregnancy: a cross-sectional study

E. Brillo[1,2], M. Ciampoletti[3], V. Tosto[1], E. Buonomo[2]

Key words: Vaccination, Maternal immunization, Pregnancy, Influenza, Pertussis, Vaccine recommendations

Parole chiave: Vaccinazione, Immunizzazione materna, Gravidanza, Influenza, Pertosse, Raccomandazioni vaccinali

Abstract

Background. *The literature claims that an increased risk of complications from pertussis and influenza exists for pregnant women and infants. Maternal tetanus, diphtheria, and acellular pertussis (Tdap) and influenza vaccines seem to decrease this risk so that several countries are committed to increase vaccination uptake, but not all of them know their own vaccination coverage and factors that motivate this population to vaccination.*

Study Design. *A cross-sectional survey was conducted.*

Methods. *We conducted this survey to estimate among pregnant women: 1) the vaccine coverage, 2) the availability of information, 3) the knowledge about maternal Tdap and influenza vaccination, 4) the factors that could have driven unvaccinated pregnant women to have themselves vaccinated. In addition, determinants of Tdap and influenza vaccine uptake and correct knowledge about vaccine-preventable diseases and vaccination in pregnancy were assessed using univariate and multivariate analyses.*

Results. *Of the 250 women included in the present study, only 58 (23.2%, 95% Confidence Interval (CI): 18-28.4%) and 21 (8.1%, 95% CI: 5-11.8%) reported that they had been vaccinated with Tdap and influenza vaccine, respectively, during their current pregnancy. The most common reasons cited for getting themselves vaccinated was having background knowledge of the health problems due to the diseases prevented by Tdap and influenza vaccines, awareness regarding these vaccines being recommended in pregnancy, knowledge of their effectiveness and/or side effects, and having been informed about vaccination by a healthcare professional.*

Conclusions*. Influenza and Tdap vaccine uptake among pregnant women in Italy is low, however, the present study showed that women are available to get vaccinated during pregnancy when adequately informed about the vaccines recommended.*

[1] *Centre for Research in Perinatal and Reproductive Medicine, University of Perugia, Perugia, Italy*
[2] *Department of Biomedicine and Prevention University of Rome Tor Vergata, Rome, Italy*
[3] *School of Midwifery, Department of Surgery and Biomedical Sciences, University of Perugia, Perugia, Italy*

Abbreviations: aOR: adjusted odds ratio; CI: confidence interval; HCPs: healthcare professionals; MMR: measles-mumps-rubella; OB/GYNs: obstetrician-gynecologists; OR: odds ratio; Tdap: tetanus-diphtheria-acellular pertussis; VIF: variance inflation factor; VPDs: vaccine-preventable diseases; WHO: World Health Organization

Annali di Igiene : Medicina Preventiva e di Comunità (Ann Ig)
ISSN 1120-9135 https://www.annali-igiene.it

Introduction

The reduction in vaccine-preventable diseases (VPDs) is one of the main public health objectives from the second half of the 1800s and especially today in the midst of COVID-19 Pandemic.

Some VPDs seem to cause serious harm in pregnant women, newborns and infants, in the absence of adequate immunization. Consequently, some live attenuated vaccines are recommended during the preconception period (i.e., measles-mumps-rubella, MMR, and varicella) (1) and some inactivated vaccines, as seasonal influenza vaccine and tetanus-diphtheria-acellular pertussis (Tdap) vaccine during pregnancy.

A dose of Tdap vaccine and one of influenza vaccine are recommended during every pregnancy, primarily to prevent pertussis, diphtheria, and influenza-related complications in pregnant women, fetuses, newborns and postpartum women (2, 3).

The World Health Organization (WHO) recommends influenza vaccination for pregnant women since 2005, but most European countries introduced seasonal influenza vaccination for this population only after the H1N1/2009 influenza pandemic, while Italy has done it in 2012 (4). The Tdap vaccine is recommended in Italy since 2017 (5). Subsequent measures identified the timing of Tdap vaccine administration between the 27th and 36th week of pregnancy and influenza vaccine at any week of pregnancy (6).

However, studies of vaccine coverage in Italy detected a maternal Tdap and/or influenza vaccine coverage rates of 0 to 9.7% (7-11). The current COVID-19 pandemic has also prompted many authorities to strongly recommend the influenza vaccine for groups at higher risk such as pregnant women (12-16), but we continue not to have national vaccination data for this population, although a national vaccination registry has been established since 2018 (17). For this reason, studies assessing vaccine coverage among this population are indispensable even when limited to one hospital, province or region of the Country, but only few studies of this kind can be found in the literature so far (7-11).

Therefore, we conducted a study to detect Tdap and influenza vaccine coverage among pregnant women in Italy, to describe factors that could have driven unvaccinated pregnant women to have themselves vaccinated, information received and knowledge possessed regarding Tdap and influenza and other information on this topic.

Aims of the study

The present study aimed primarily to estimate Tdap and influenza vaccine uptake rate among pregnant women in Perugia, Italy, during the influenza season 2019-2020. This study aimed also: a) to detect the number of women who underwent rubella and/or varicella tests before pregnancy; b) to detect the number of women who have been vaccinated with MMR and/or varicella vaccines before pregnancy and women who have been vaccinated with influenza vaccine in the last 5 years; c) to investigate information received and knowledge possessed regarding Tdap and influenza vaccines in this population; d) to detect factors that could have driven unvaccinated pregnant women to have themselves vaccinated; e) to identify determinants of pregnant women's Tdap and influenza vaccine uptake, and correct knowledge about VPDs and vaccination in pregnancy.

Materials and Methods

Study design

We conducted a cross-sectional single-center survey during the 2019-2020 influenza season.

Sample and sampling

The target population was represented by pregnant women, ages 18 years and older at the time of completing the questionnaire, attending for routine antenatal care the Department of Obstetrics and the Gynecology and Perinatal Center of the University Hospital of Perugia. The study excluded women who had contraindications to the Tdap or influenza vaccination, or refused to participate.

One data collector visited the clinic two or three days (MC), changing days each week. The data collector approached all pregnant women registering for an appointment in the clinic waiting room. Women were recruited in person by consecutive sampling from November 20th 2019 to March 5th 2020, the date in which lockdown was declared in Italy for COVID-19 Pandemic and all non-essential activities were suspended. Pregnant women were enrolled in the study after they gave the informed verbal consent. Participation was voluntary and no incentive was offered.

The estimated sample size was 237 using the Fleiss et al. formula (18) considering an expected prevalence of 9.7% (8) and an amplitude of the confidence interval at 95% (CI 95%) of .05.

Setting

The present study was conducted during the 2019-2020 influenza season in a II level of maternal and neonatal care Maternity Clinic in the Province of Perugia, Umbria, Italy. In all the Region Umbria there are only 2 places of birth of II level and 9 of I level (<1000 deliveries/year). The Department of Obstetrics and Gynecology where the study was carried out, has a birth rate of over 1800 births/year [1814 in 2018 and 1861 in 2019 (19)] that is about one third of the children born in the Umbria region (20).

In Italy, the National Immunization Prevention Plan 2012-2014 has recommended seasonal influenza vaccine for pregnant women since 2012 (4), and the National Immunization Prevention Plan 2017-2019 has also recommended Tdap vaccine for this group (5) (Tdap vaccine is recommended between the 27th and the 36th weeks of pregnancy and influenza vaccine at any week of pregnancy (6)). Both vaccines are recommended for all women during every pregnancy (i.e., regardless of vaccination history). The vaccine is offered free to every pregnant woman.

In Italy, influenza vaccine coverage in the general population in the last twenty years has never reached 20% and in particular in the 2019-2020 season was equal to 16.8%. The minimum objective for influenza vaccine coverage is to reach or exceed 75% uptake for individuals in each group at risk (optimal target is of at least 95%), as recommended by the WHO (21). Therefore at least 75 out of 100 pregnant women should receive influenza vaccination, but there are not national vaccine coverage data for this population. The only national coverage data available in Italy for influenza vaccination concerns people over 65 and this was 54.6% during the influenza season 2019-2020 (21).

Questionnaire

We developed an *ad hoc* survey specifically for use in this study, and thus had not been psychometrically validated. The questions to assess women's knowledge of influenza and its vaccination were partially based on those of the questionnaire used by Yudin et al. (22).

The survey, with its questions and answers, was reviewed by an advisory group of midwives and obstetrician-gynecologists (OB/GYNs) and to ensure appropriate wording and clarity. Before administration, the questionnaire was pilot-tested on a small sample of 25 pregnant women in the same setting and it was revised accordingly with minor revisions made to improve its questions and answers.

It consisted of 36 questions to collect information about: (a) knowledge about: (1) VPDs (pertussis and influenza), (2) vaccines, (3) VPDs and vaccination in pregnancy (two questions and 19 items to be answered true or false); (b) pregnant women's Tdap and influenza vaccine uptake (two questions); (c) factors that could have driven unvaccinated pregnant women to have themselves vaccinated (two questions and 16 items to be answered yes or no); (d) vaccination history (four questions and one of them with two items); (e) varicella and rubella tests before pregnancy (one question with two items); (f) information on vaccines received and desired, and self-assessment of one's knowledge on VPDs and vaccination in pregnancy (six questions); (g) socio-demographic data (six questions); (h) health and obstetrical data (11 questions and one of them with 18 items); (i) their children's vaccinations (two questions).

The following were the five items about VPDs: Whooping cough (pertussis) is a transmissible disease; Influenza is a transmissible disease; Influenza can be dangerous for some people' health; Influenza can lead to hospitalization; Whooping cough (pertussis) can be dangerous for some people' health. The following were the seven items about vaccines: Too many vaccines can overload or weaken an immune system; In general, a natural infection is better than immunization; Vaccines are effective in preventing infectious diseases; Getting whooping cough (pertussis) vaccination is dangerous; Getting influenza vaccination is dangerous; Getting whooping cough (pertussis) is more dangerous than vaccinating against it; Getting influenza is more dangerous than vaccinating against it. The following were the seven items about VPDs and vaccination in pregnancy: It is better to avoid vaccinations during pregnancy; Whooping cough (pertussis) vaccination is dangerous for pregnant women; Whooping cough (pertussis) vaccination is recommended for pregnant women; Influenza is dangerous for pregnant women; Influenza vaccination is dangerous in pregnancy; Influenza vaccination is recommended for pregnant women; Vaccinating pregnant women against whooping cough (pertussis) helps protect newborns in the first months of life.

The survey was anonymous and self-administered. A copy of a brochure, consisting of a single sheet of printed paper on both sides, was given to each woman after filling out the questionnaire. The brochure was designed *ad hoc* for the study and filled with evidence-based content to inform pregnant women about: (a) VPDs that can affect human health in pregnancy and infants in their first months of life, (b) vaccines recommended in pregnancy, (c) effectiveness and safety of recommended vaccines.

Statistical analyses

Statistical analyses were performed using IBM SPSS Version 25. Data were presented descriptively using absolute and relative frequencies for categorical variables.

Bivariate logistic regression was used to identify the main independent variables associated with the outcome variable and calculate their crude odds ratio. Variables with p-values < .2 were introduced into multivariate logistic regression models. Multicollinearity was examined using the tolerance test and the Variance Inflation Factor (VIF) to exclude variables with a VIF value > 2.0 from the multivariate regression analysis. Adjusted odds ratios (aORs) were calculated with their 95% confidence interval (95% CI). P-values < .05 were considered as statistically significant.

We considered as correct knowledge about VPDs (pertussis and influenza), vaccines, or VPDs and vaccination in pregnancy when 5/5 items about VPDs, 7/7 about vaccines, and 7/7 about VPDs and vaccination in pregnancy, were respectively answered correctly (true /false answers).

Using logistic regression model, we tested the association between Tdap or influenza vaccine uptake and the socio-demographic, obstetric, maternal knowledge variables: highest level of education attained (non-graduate/graduate); nationality (non-Italian/Italian); current pathologies (no/yes); previous pregnancies (no; yes); planned current pregnancy (no; yes); prenatal exams (no; yes); pregnancy cared for by a private OB/GYN (no/yes); pregnancy cared for by a private midwife (no/yes); participation in childbirth education classes during current pregnancy (no/yes); information received about the vaccines recommended during pregnancy from one or more sources (OB/GYN, midwife, general practitioner, nurse, pharmacist, hospital, internet, social media, TV, friends/knowers or others) (no/yes); influenza vaccination in the last 5 years (no/yes); influenza infection in the last 5 years (no/yes); both rubella and varicella test before pregnancy (no/yes); measles-mumps-rubella (MMR) vaccination before pregnancy (no/yes); varicella vaccination before pregnancy (no/yes); correct knowledge about VPDs and vaccination in pregnancy (no/yes); correct knowledge about vaccines (no/yes); correct knowledge about VPDs (pertussis and influenza) (no/yes).

We also tested the association between correct knowledge about VPDs and vaccination in pregnancy and the socio-demographic, obstetric and maternal knowledge variables just described for Tdap or influenza vaccine uptake.

The manuscript was written using the STROBE checklist for cross sectional studies.

Results

Responses from 250 pregnant women were analyzed. Only 58 women (23.2%, 95% Confidence Interval (CI): 18-28.4%) and 21 women (8.1%, 95% CI: 5-11.8%) reported receiving Tdap and influenza vaccine respectively during their current pregnancy.

Nearly half of the women declared that they had not received any information regarding vaccines recommended during pregnancy (117/250; 46.8%). Only 71 women received information from one or more healthcare professionals (HCPs) and not from other sources, 20 from one or more other sources (web, television, friends, etc.), 41 from both the sources. Most of the informed women received information from OB/GYN, less women from midwives and general practitioners (Table 1).

The factors that could have driven unvaccinated pregnant women to get themselves vaccinated are displayed in Figure 1: having had knowledge of the health problems caused by diseases preventable by Tdap and influenza vaccines was the most commonly cited factor. A similar trend in responses was observed for both vaccines.

The 65.6% of the women evaluated their own knowledges about VPDs and vaccination in pregnancy as insufficient. The 93.6% declared the need for more information about VPDs and vaccination in pregnancy and the 87.6% of all women reported that they desired more information on this topic.

Factors associated with influenza vaccine uptake were having received influenza vaccination in the last 5 years (OR= 163.2; 95% CI: 20.99-1268.8), prenatal exams (OR= 2.91; 95% CI: 1.16-7.32), preconception rubella and varicella tests (OR= 3.93; 95% CI: 1.57-9.85), information about the vaccines recommended during pregnancy from one or more sources (OR= 20.53; 95% CI: 2.71-155.55), having correct knowledge about VPDs (OR= 7.35; 95% CI: 2.81-19.20), correct knowledge about vaccines (OR= 2.81; 95% CI: .99-7.92), and correct knowledge about VPDs and vaccination in pregnancy (OR= 9.89; 95% CI: 3.47-28.21).

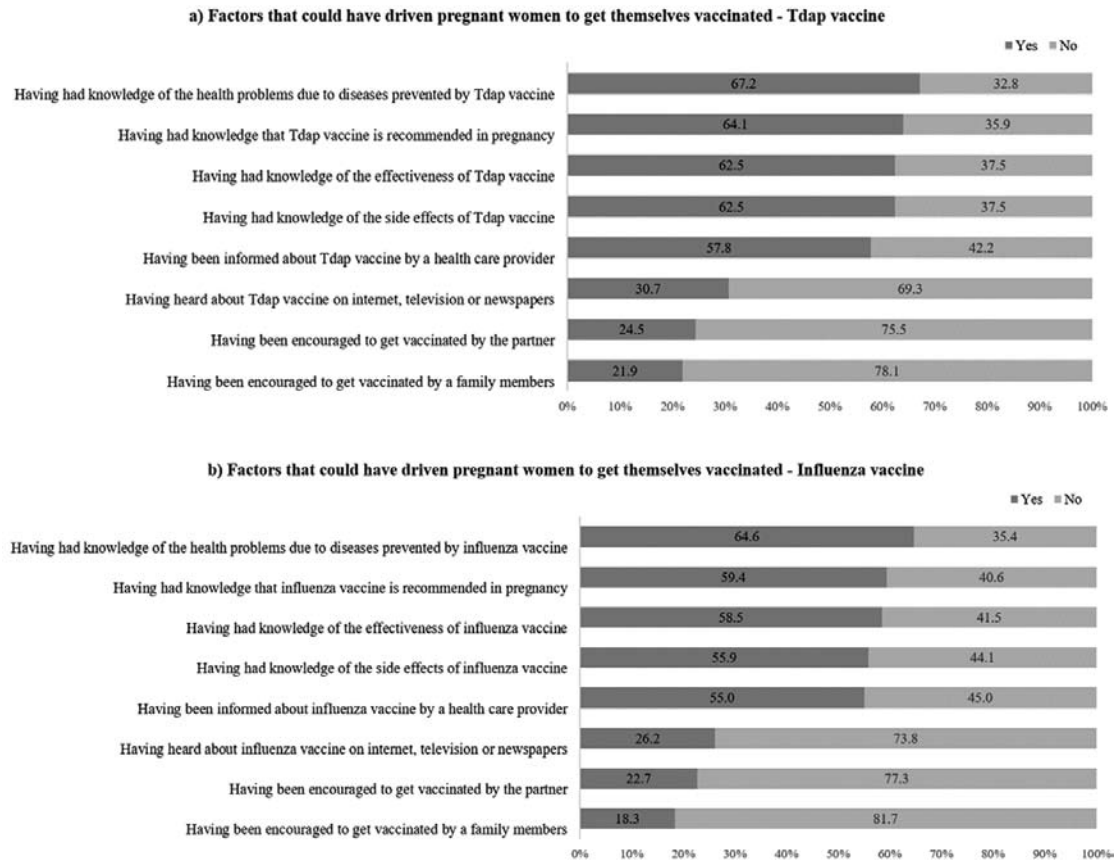

Figure 1 - Factors that could have driven pregnant women to get themselves vaccinated

Factors associated with Tdap vaccine uptake were having received influenza vaccination in the last 5 years (OR= 5.08; 95% CI: 2.55-10.11), prenatal exams (OR= 2.52; 95% CI: 1.39-4.59), both rubella and varicella test (OR= 3.17; 95% CI: 1.65-6.11), MMR vaccination before pregnancy (OR= 2.63; 95% CI: 1.21-5.73), varicella vaccination before pregnancy (OR= 3.25; 95% CI: 1.19-8.87), information about the vaccines recommended during pregnancy from one or more sources (OR= 26.80; 95% CI: 8.02-88.71), having planned current pregnancy (OR= 1.97; 95% CI: 1.01-3.84), having participated in childbirth education classes during current pregnancy (OR= 2.52; 95% CI:1.38-4.59), correct knowledge about VPDs (OR= 3.40; 95% CI: 1.81-6.39), correct knowledge about vaccines (OR= 2.13; 95% CI: 1.14-3.98), correct knowledge about VPDs and vaccination in pregnancy (OR= 7.09; 95% CI: 3.73-13.48).

Factors associated with analysis of determinants of pregnant women's correct knowledge about VPDs and vaccination in pregnancy were having highest level of education attained (OR= 1.78; 95% CI: 1.02-3.12), Italian nationality (OR= 4.97; 95% CI: 1.47-16.79), having participated in childbirth education classes during current

Table 1 - Demographic, general health, obstetric, vaccination history data and sources of information about vaccines recommended during pregnancy

Data	n/N; %	Data	n/N; %
Age range		**Level of education**	
20–24 years	10/250; 4%	No school education	1/250; 0.4%
25–34 years	136/250; 54.4%	Primary School Degree	0/250; 0
35–45 years	104/250; 41.6%	Secondary School Degree	18/250; 7.2%
Relationship status		High School Degree	100/250; 40%
Single	1/250; 0.4%	University Degree/Three years	49/250; 19.6%
Engaged	3/250; 1.2%	University Degree/Five years	76/250; 30.4%
Cohabiting	101/250; 41.6%	Master/PHD	6/250; 2.4%
Married	145/250; 58%	**MMR vaccine in infancy/childhood or adulthood**	
Migrant status		Done	192/250; 76.8%
Native-born Italians	214/250; 85.6%	Not done	24/250; 9.6%
Migrants	36/250; 14.4%	I do not remember	34/250; 13.6%
Employment status		**Varicella vaccine in infancy/childhood or adulthood**	
Unemployed	38/250; 15.2%	Done	100/250; 40%
Student	5/250; 0.02%	Not done	102/250; 40.8%
Housewife	24/250; 9.6%	I do not remember	48/250; 19.2%
Employed	183/250; 73.2%	**Both rubella and varicella test**[b]	
Health status at the study enrollment		Done	53/250; 21.2%
Healthy	209/250; 83.6%	Not done	197/250; 78.8%
One ore more diseases[a]	41/250; 16.4%	**Rubella test with or without varicella test**[b]	
Number of previous pregnancy		Done	77/250; 30.8%
0	118/250; 47.2%	Not done	173/250; 69.2%
1	80/250; 32.0%	**Varicella test with or without rubella test**[b]	
2	31/250; 12.4%	Done	53/250; 21.2%
3 or more	21/250; 8.4%	Not done	197/250; 78.8%
Number of children		**Both MMR and varicella vaccine**[b]	
0	17/132; 12.9%	Done	15/250; 6%
1	89/132; 67.4%	Not done	235/250; 94%
2	23/132; 17.4%	**MMR vaccine with or without varicella vaccine**[b]	
3 or more	3/132; 2.3%	Done	32/250; 12.8%
Planned current pregnancy		Not done	218/250; 87.2%
Planned	162/250; 64.8%	**Varicella vaccine with or without MMR vaccine**[b]	
Unplanned	88/250; 35.2%	Done	17/250; 6.8%
Prenatal exams		Not done	233/250; 93.2%
Done	95/250; 38%	**Influenza vaccination in the last 5 years**	
Not done	155/250; 62%	Done	45/250; 18%
HCP for pregnancy		Not done	205/250; 82%
Private Midwife	4 /250; 1.6%	**Influenza infection in the last 5 years**	
Private OB/GYN	192/250; 76.8%	Yes	212/250; 84.8%
Family health clinic	28/250; 11.2%	No	38/250; 15.2%
Hospital	25/250; 10%		
Nobody	1/250; 0.4%		

Sources from which women obtained information about vaccines in pregnancy		Sources from which women would like to receive information about vaccines in pregnancy	
Midwife	51/250; 20.4%	Midwife	165/250; 66%
OB/GYN	79/250; 31.6%	OB/GYN	210/250; 84%
General practitioner	46/250; 18.4%	General practitioner	180/250; 72%
Nurse	2/250; 0.8%	Nurse	55/250; 22%
Pharmacist	4/250; 1.6%	Pharmacist	55/250; 22%
Hospital	8/250; 3.2%	Hospital	135/250; 54%
Web	30/250; 12%	Web	45/250; 18%
Social media	8/250; 3.2%	Social media	35/250; 14%
Television, radio, magazines	12/250; 4.8%	Television, radio, magazines	55/250; 22%
Friends or acquaintances	37/250; 14.8%	Friends or acquaintances	30/250; 12%
Others	4/250; 1.6%	Others	0/250
No-one	117/250; 46.8%	No-one	24/250; 9.6%

HCP: health care provider; MMR: measles, mumps and rubella; OB/GYN Obstetrician/gynecologist.
[a] Diseases: Endocrine disease (n=9), obesity (n=8), chronic respiratory diseases (n=6), oncological pathology (n=4), diabetes mellitus (n=3), autoimmune disorder and antiphospholipid antibody syndrome (n=2), hemoglobinopathy (n=2), genetic disorders (n=2), dermatological diseases (n=2), kidney disease (n=2), urologic disease (n=1), thromboembolism and/or thrombophilia (n=1), asthma (n=1), congenital coagulation disorder (n=1), hiatal hernia (n=1), inflammatory bowel disease (n=1), liver disease (n=1), chronic infectious disease (n=1), neurological and/or psychiatric disorder (n=1), cardiovascular disease (n=1).
[b] Before pregnancy.

pregnancy (OR= 3.51; 95% CI: 1.99-6.22), having received influenza vaccination in the last 5 years (OR= 2.97; 95% CI: 1.52-5.77), having received informations about the vaccines recommended during pregnancy from one or more sources (OR= 9.34; 95% CI: 4.49-19.43), having correct knowledge about VPDs (OR= 5.07; 95% CI: 2.74-9.36), correct knowledge about vaccines (OR= 2.54; 95% CI: 1.41-4.57).

A first logistic regression was completed to determine the relationship between the pregnant women background variables and their uptake of influenza vaccination during pregnancy (Table 2). Model 1 shows that pregnant women who had received influenza vaccination in the last 5 years and information about the vaccines recommended during pregnancy from one or more sources, were 144 and 16 times more likely respective to having received influenza vaccination during pregnancy. The explanatory power of the model is high, accounting for 63% of the variance. Model 2 adds the correct knowledges about VPDs and vaccination in pregnancy, VPDs and vaccines, and this increases the explanatory power of the model accounting for around 72% of the variance. Two factors had significant association with uptake of influenza vaccination: having received influenza vaccination in the last 5 years and having knowledge about VPDs. Model 3 adds having highest level of education attained, pregnancy cared for by a private OB/GYN, and current pathologies, as well as having received prenatal exams and both rubella and varicella test. This increases the explanatory power of the model but not in a significant way.

A second logistic regression was completed to determine the relationship between the pregnant women background variables and their uptake of Tdap vaccination during pregnancy (Table 3). Model 1 shows that pregnant women who had received influenza vaccination in the last 5 years and

Table 2 - Multivariate logistic regression of determinants of pregnant women's uptake of influenza vaccination

	Model 1			Model 2			Model 3		
Variable	B	SE	aOR	B	SE	aOR	B	SE	aOR
Constant	-7.440	1.434	.001	-9.086	1.866	.000	-9.159	2.143	.000
Influenza vaccination in the last 5 years	4.972***	1.059	144.375	5.230***	1.147	186.770	5.180***	1.186	177.625
Information received from one or more sourcesa	2.780*	1.092	16.122	2.422	1.238	11.623	2.364	1.408	10.635
Correct knowledge about VPDs and vaccination in pregnancy				1.282	.769	3.603	1.220	.849	3.388
Correct knowledge about VPDs				1.902*	.793	6.698	1.897*	.889	6.669
Correct knowledge about vaccines				.314	.842	1.369	-.049	.946	.952
Highest level of education attained							.237	.882	1.267
Prenatal exams							.539	.998	1.715
Both rubella and varicella test							.727	1.019	2.069
Pregnancy cared for by a private OB/GYN							-.083	1.199	.920
Current pathologies							-1.094	1.495	.335
-2LL	63.204			49.932			46.624		
	χ^2 =81.012, df = 2, p< .001			χ^2 =13.272, df = 3, p= .004			χ2 =3.308, df = 5, p= .653		
Nagelkerke pseudo r2	63.1%			71.7%			73.7%		
Hosmer & Lemeshow test	p= .965			p= 3.905			p= .998		
Classification accuracy	93.6%			96%			97.2%		

OB/GYN Obstetrician/gynecologist; VPDs: vaccine-preventable diseases.
[a] Information received about the vaccines recommended during pregnancy.
*p < .05, **p < .01, ***p< .001.

Table 3 - Multivariate logistic regression of determinants of pregnant women's uptake of Tdap vaccination

	Model 1			Model 2			Model 3		
Variable	***B***	**SE**	**aOR**	***B***	**SE**	**aOR**	***B***	**SE**	**aOR**
Constant	-3.902	.600	.020	-4.314	.654	.013	-5.022	.804	.007
Information received from one or more sourcesa	3.191***	.617	24.303	2.846***	.634	17.221	2.876***	.658	17.744
Influenza vaccination in the last 5 years	1.416***	.405	4.119	1.211**	.427	3.358	1.272**	.447	3.569
Correct knowledge about VPDs and vaccination in pregnancy				.921*	.387	2.511	.796	.420	2.216
Correct knowledge about VPDs				.715	.408	2.044	.887*	.426	2.427
Correct knowledge about vaccines				.206	.389	1.229	.099	.402	1.104
Varicella vaccination before pregnancy							.403	.836	1.496
Both rubella and varicella test							.561	.485	1.753
MMR vaccination before pregnancy							.623	.655	1.865
Participation in childbirth education classes during current pregnancy							.546	.401	1.727
Planned current pregnancy							.210	.471	1.233
-2LL	195.546			182.422			172.604		
	χ^2= 75.295, df = 2, *p*< .001			χ^2 = 13.124, df= 3, *p*= .004			χ^2 = 9,818, df= 5, *p*= .081		
Nagelkerke pseudo r2	39.3%			45%			49.1%		
Hosmer & Lemeshow test	*p*= .994			*p*= .797			*p*= .672		
Classification accuracy	81.2%			81.6%			82%		

MMR: measles, mumps and rubella; VPDs: vaccine-preventable diseases.
a Information received about the vaccines recommended during pregnancy.
*p < .05, **p < .01, ***p< .001.

information about the vaccines recommended during pregnancy from one or more sources were 4 and 24 times more likely respective to having received Tdap vaccination during pregnancy. The explanatory power of the model accounts for 39% of the variance. Model 2 adds the correct knowledges about VPDs and vaccination in pregnancy, VPDs and vaccines, and this increases the explanatory power of the model accounting for around 45% of the variance. Three factors had significant association with uptake of influenza vaccination during pregnancy: information received about the vaccines recommended during pregnancy from one or more sources, influenza vaccination in the last 5 years, correct knowledge about VPDs and vaccination in pregnancy. Model 3 adds having received varicella vaccination before pregnancy, both rubella and varicella test, MMR vaccination before pregnancy, as well as having participated in childbirth education classes during current pregnancy and planned current pregnancy. This increases the explanatory power of the model but not in a significant way.

A third logistic regression was completed to determine the relationship between the pregnant women background variables and their correct knowledge about VPDs and vaccination in pregnancy (Table 4). Model 1 shows that pregnant women who had received information about the vaccines recommended during pregnancy from one or more sources and had correct knowledge about VPDs were 10 and 4.5 times more likely respective to having correct knowledge about VPDs and vaccination in pregnancy. The explanatory power of the model accounts for 37% of the variance. Model 2 adds the nationality and the highest level of education attained. The explanatory power of the model accounts for 41% of the variance. Three factors were found to be associated with correct knowledge about VPDs and vaccination in pregnancy: having received information about the vaccines recommended during pregnancy from one or more sources, having correct knowledge about VPDs, and the nationality. Model 3 adds having participated in childbirth education classes during current pregnancy and its explanatory power accounts for 43% of the variance. Three factors were found to be associated with correct knowledge about VPDs and vaccination in pregnancy: having received information about the vaccines recommended during pregnancy from one or more sources, having correct knowledge about VPDs, and having participated in childbirth education classes during current pregnancy. Model 4 adds having influenza vaccination in the last 5 years, planned current pregnancy and having received both rubella and varicella test. This increases the explanatory power of the model but not in a significant way.

Discussion and conclusions

The main goal of the present study was to estimate vaccination coverage with influenza and Tdap vaccines during pregnancy. Data revealed a maternal influenza vaccine coverage rate of 8.1% (95% CI: 5-11.8), a percentage in line with those obtained from other Italian studies, while Tdap vaccine coverage rate of 23.2% (95% CI: 18-28.4%) calculated in the present study is slightly higher than that found by other Italian studies (7-11). Anyway, contrary to international vaccination data, Italy shows a significant low vaccination rate in pregnant population, and this can be associated with multiple factors.

The vast majority of women were cared for by an OB/GYN during pregnancy, and only 4 women were attended by a midwife. However, only about 32% of the sample received information on vaccination during pregnancy from an OB/GYN, 20% from a midwife, and 18% from the general practitioner. Furthermore, most of the

Table 4 - Multivariate logistic regression of determinants of pregnant women's correct knowledge about VPDs and vaccination in pregnancy

	Model 1			Model 2			Model 3			Model 4		
Variable	***B***	**SE**	**aOR**	***B***	**SE**	**aOR**	***B***	**SE**	**aOR**	***B***	**SE**	**aOR**
Constant	-3.270	.446	.038	-4.857	.783	.008	-4.803	.787	.008	-4.897	.810	.007
Information received from one or more sources[a]	2.303***	.408	10.004	2.384***	.417	10.846	2.223***	.425	9.236	2.129***	.429	8.404
Correct knowledge about VPDs	1.513***	.360	4.541	1.479***	.380	4.390	1.609***	.392	4.999	1.563***	.393	4.774
Correct knowledge about vaccines	.591	.346	1.805	.488	.356	1.629	.511	.362	1.667	.457	.366	1.580
Nationality				1.639*	.679	5.148	1.263	.702	3.536	1.140	.716	3.128
Highest level of education attained				.257	.356	1.293	.118	.368	1.125	.085	.374	1.088
Participation in childbirth education classes during current pregnancy							.870*	.369	2.388	.921*	.374	2.511
Influenza vaccination in the last 5 years										.586	.423	1.797
Planned current pregnancy										.240	.424	1.271
Both rubella and varicella test										.055	.428	1.057
-2LL	223.285			213.752			208.080			205.815		
	$\chi^2 = 74.391$, df = 3, $p < .001$			$\chi^2 = 9{,}533$, df = 2, $p = .009$			$\chi^2 = 5.672$, df = 1, $p = .017$			$\chi^2 = 2.265$, df = 3, $p = .519$		
Nagelkerke pseudo r2	37%			41%			43.3%			44.2%		
Hosmer &Lemeshow test	$p = .697$			$p = .925$			$p = .381$			$p = .764$		
Classification accuracy	78.3%			79.1%			80.7%			80.3%		

VPDs: vaccine-preventable diseases.
[a] Information received about the vaccines recommended during pregnancy.
*p < .05, **p < .01, ***p< .001.

sample stated that it would like to receive information about vaccines in pregnancy from an OB/GYN, followed by the general practitioner and the midwife. Only 31% of the sample had undergone the rubella test before pregnancy, 21% the varicella test, 31% MMR vaccine, 7% varicella vaccine, 6% both MMR and varicella vaccine. Only 18% of women had been influenza-vaccinated in the last 5 years and 84% had had influenza infection in the last 5 years.

In the present study, most women first became aware about the Tdap and/or influenza vaccines given in pregnancy during a meeting with an OB/GYN and a minority during the meeting with a midwife or other HCP. A 2016-2017 UK study described that many women first became aware about the pertussis vaccination in pregnancy during a meeting with a midwife (23). Several reasons could explain this difference, but probably the most relevant is simply that in Italy pregnancies are almost exclusively followed by an OB/GYN and women's opportunities to meet midwives are mainly at the time of childbirth.

The present study showed that both having received an influenza vaccination in the last 5 years, and having a correct knowledge related to VPDs were major determinants of pregnant women's uptake of influenza vaccination. In addition, having received information about the vaccines recommended during pregnancy from one or more sources; having received influenza vaccination in the last 5 years, having correct knowledge about VPDs and vaccines in general and during pregnancy appeared as major determinant factors in pregnant women's uptake of Tdap vaccination. Furthermore, data showed that having received information about the vaccines recommended during pregnancy from one or more sources (HCP and not), having correct knowledge about VPDs and participated in childbirth education classes during pregnancy seem to predict pregnant women's correct knowledge about VPDs and vaccination in pregnancy, independently from others factors.

Several studies have estimated that women with a higher level of education attained, and prior knowledge about vaccination or VPDs were more likely to be vaccinated for influenza during pregnancy (8, 24). In line with this view, multivariate analyses have shown that several factors could contribute to a below-par vaccination rate: poor influenza or Tdap-related knowledge and/or their potential risks (25), and disbelief regarding efficacy and safety profile of influenza/Tdap vaccines (26-28). Additionally, some studies have found that a previous history of influenza vaccination drastically improves the chances of vaccine uptake in subsequent pregnancies (31, 32), as supported by the current study.

Moreover, Tarrant et al. indicated that having an already vaccinated relative helps build a positive perception towards vaccination in pregnancy (27). Interactive sessions with HCPs are also associated with better vaccine uptake among pregnant women (7, 31-33), as supported by the current study. Other researches revealed that a positive attitude from HCPs can enhance the overall prevalence of vaccination in pregnancy. On this way, the lack of vaccination recommendation by HCPs can reduce the chances of pregnant women getting vaccinated (34, 35). Furthermore, the HCP's own level of education as well as their self-confidence in vaccines seem to be crucial aspects when advising the patients about the vaccines (9, 33).

The present study has some limitations. First of all, the sample may not be representative of the entire Italian population. Secondly, although the sample size was adequate for the primary objectives, a larger sample would have been useful for the secondary objectives in order to give more accurate results. Finally, although the questionnaire was constructed in accordance with other questionnaires and pilot tested,

the instrument had not been validated.

In conclusion, this study found that very few women are subject to recommended Tdap and influenza vaccinations during pregnancy and more than half of the participants remembered not receiving any information about it from an HCP. Many women would have been vaccinated with Tdap and influenza vaccines if they had been informed. According to the women themselves, it seems important that the information is provided by an HCP and focuses on recommended vaccines in pregnancy, health problems due to diseases prevented by these vaccines, their effectiveness and side effects.

Therefore, information seems to play a major role in choosing to get vaccinated in pregnancy with Tdap and influenza vaccines. HCPs should take every opportunity to inform women and recommend vaccines during pregnancy.

Ethics

The research was carried out according to the World Medical Association Declaration of Helsinki. It does not report any experiment, or research on identifiable human material or data because it is an observational survey conducted through an anonymous questionnaire. Therefore it did not need any approval by an Ethical Committee

Riassunto

Vaccino dTpa e Vaccino antinfluenzale in gravidanza: uno studio trasversale

Premessa. La letteratura sostiene che vi sia un rischio aumentato di complicanze per le donne incinte e i neonati che sviluppano la pertosse o l'influenza. I vaccini antidifterite, tetano, pertosse acellulare (dTpa) e antinfluenzale sembrano ridurre questo rischio tant'è che diversi paesi si stanno impegnando ad incrementare le immunizzazioni materne, ma sfortunatamente non tutti questi Paesi conoscono i livelli di copertura vaccinale di questa popolazione e i fattori che motivano essa alla vaccinazione.

Disegno dello studio È stata condotta un'indagine trasversale.

Metodi. Abbiamo condotto quest'indagine per stimare nelle donne a termine di gravidanza: 1) la copertura vaccinale materna, 2) la ricezione di informazioni, 3) il possesso di conoscenze circa i vaccini dTpa e antinfluenzale, 4) i fattori che potrebbero spingere le gestanti a vaccinarsi. In aggiunta, sono stati analizzati i determinanti dell'assorbimento dei vaccini e delle corrette conoscenze circa le malattie prevenibili con vaccino, le vaccinazioni in gravidanza.

Risultati. Delle 250 donne incluse nello studio, solo 58 (23,2%, 95% Intervallo di Confidenza (IC): 18-28,4%) e 21 (8,1%, 95% CI: 5-11,8%) hanno dichiarato di aver ricevuto rispettivamente i vaccini dTpa e antinfluenzale durante l'attuale gravidanza. Le più citate ragioni per le quali si sarebbero potute vaccinare sono state: l'aver avuto conoscenza dei problemi di salute causate dalle infezioni prevenute dai vaccini dTpa e antinfluenzale, la consapevolezza che questi vaccini sono raccomandati in gravidanza, la conoscenza della loro efficacia e/o degli eventi avversi, l'essere stato informato sui vaccini da un professionista sanitario.

Conclusioni. La copertura dei vaccini dTpa e antinfluenzale tra le donne gravide è bassa in Italia, comunque il presente studio ha mostrato che le donne sono disponibili a vaccinarsi durante la gravidanza quando adeguatamente informate da un da un professionista sanitario sui vaccini raccomandati.

References

1. World Health Organization (WHO). Immunization safety surveillance: guidelines for immunization programme managers on surveillance of adverse events following immunization. 3rd ed. Manila: World Health Organization. Regional Office for the Western Pacific, 2016.
2. Centers for Disease Control and Prevention (CDC). Influenza (flu). Adressing concerns pregnant women might have about influenza vaccine safety. Washington, DC: CDC, 2019 [updated 2019 Oct 22; cited 2020 Nov 19]. Available on: https://www.cdc.gov/flu/professionals/vaccination/vaccination-possible-safety-signal.html [Last accessed: 2021 October 15].
3. Ministero della Salute. Circolare 21 novembre 2018. Vaccinazioni raccomandate per le donne in età fertile e in gravidanza - *ERRATA CORRIGE* [cited 2019 July 29]. Available on: http://www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2018&codLeg=66751&parte=1%20&serie=null [Last accessed: 2021 October 15].

4. Conferenza Stato-Regioni 22 febbraio 2012. Schema di intesa tra il Governo, le Regioni e le Province autonome di Trento e di Bolzano sul documento recante Piano Nazionale Prevenzione Vaccinale 2012-2014 [cited 2019 Nov 12]. Available on: http://www.trovanorme.salute.gov.it/norme/dettaglioAtto?id=42048&articolo=2 [Last accessed: 2021 October 15].
5. Conferenza Stato-Regioni 19 gennaio 2017. Schema di intesa tra il Governo, le Regioni e le Province autonome di Trento e di Bolzano sul documento recante Piano nazionale della prevenzione vaccinale 2017-2019 [cited 2019 June 22]. Available on: http://archivio.statoregioni.it/dettaglioDoc50a5.html?idprov=18027&iddoc=56289&tipodoc=5&CONF=CSR [Last accessed: 2021 October 15].
6. Ministero della Salute. Circolare 12 novembre 2019. Vaccinazioni raccomandate per le donne in età fertile e in gravidanza. Aggiornamento novembre 2019 [cited 2020 Oct 1]. Available on: http://www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2019&codLeg=71540&parte=1%20&serie=null. [Last accessed: 2021 October 15].
7. Maurici M, Dugo V, Zaratti L, et al. Knowledge and attitude of pregnant women toward flu vaccination: a cross-sectional survey. J Matern Fetal Neonatal Med. 2016 Oct; **29**(19): 3147-50. doi: 10.3109/14767058.2015.1118033. Epub 2015 Dec 15.
8. Napolitano F, Napolitano P, Angelillo IF. Seasonal influenza vaccination in pregnant women: knowledge, attitudes, and behaviors in Italy. BMC Infect Dis. 2017 Jan 9; **17**(1): 48. doi: 10.1186/s12879-016-2138-2.
9. Prospero E, Galmozzi S, Paris V, et al. Factors influencing refusing of flu vaccination among pregnant women in Italy: Healthcare workers' role. Influenza Other Respir Viruses. 2019 Mar; **13**(2): 201-7. doi: 10.1111/irv.12600. Epub 2019 Jan 8.
10. Galmozzi S, Zocco G, D'Alleva A, Carli V, Rasori SP, D'Errico MM. Vaccinazione antinfluenzale in gravidanza: uno studio pilota nelle Marche. Bollettino Epidemiologico Nazionale (BEN) [Internet]. 2018 Nov [cited 2019 May 22]. Available on: https://www.epicentro.iss.it/ben/2018/novembre/vaccinazione-antinfluenzale-gravidanza-marche [Last accessed: 2021 October 15].
11. Rizzo C, Canessa C, Chini L, et al. Le vaccinazioni in gravidanza: uno strumento fondamentale per la prevenzione dell'influenza e della pertosse nelle mamme e nei neonati. Milan, IT: Società Italiana di Allergologia e Immunologia Pediatrica (SIAIP), 2018 June 26 [cited 2019 August 2]. Available on: https://www.siaip.it/site/search/gravidanza [Last accessed: 2021 October 15].
12. American Academy of Family Physicians, American College of Nurse-Midwives, American College of Obstetricians and Gynecologists, Association of Women's Health Obstetric and Neonatal Nurses. Maternal Immunization Task Force. Immunization for Pregnant Women: A Call to Action. Washington, DC: American College of Obstetricians and Gynecologists; 2020 [cited 2020 Nov 14]. Available on: https://www.aafp.org/dam/AAFP/documents/patient_care/immunizations/2020_Maternal_%20Immunization_Call_to_%20Action.pdf [Last accessed: 2021 October 15].
13. Royal College of Obstetricians & Gynaecologists, The Royal College of Midwives, Royal College of Paediatrics and Child Health, Royal College of Anaesthetists. Coronavirus (COVID-19). Infection in Pregnancy. Information for healthcare professionals Version 12: Published Wednesday 14 October 2020. London: Royal College of Obstetricians and Gynaecologists, 2020 [cited 2000 Nov 14]. Available on: https://www.rcm.org.uk/media/4383/2020-10-14-coronavirus-covid-19-infection-in-pregnancy-v12.pdf [Last accessed: 2021 October 15].
14. WHO Strategic Advisory Group of Experts. WHO SAGE Seasonal Influenza Vaccination. Recommendations during the COVID-19. Interim guidance. 21 Sep 2020. World Health Organization, 2020 [cited 2020 Nov 14]. Available on: https://www.who.int/news/item/21-09-2020-who-sage-seasonal-influenza-vaccination-recommendations-during-the-covid-19-pandemic [Last accessed: 2021 October 15].
15. National Health Service (NHS). Pregnancy and coronavirus. UK: NHS, 2020 [updated 2020 Nov 12; cited 2020 Nov 14]. Available on: https://www.nhs.uk/conditions/coronavirus-covid-19/people-at-higher-risk/pregnancy-and-coronavirus/ [Last accessed: 2021 October 15].
16. Ministero della Salute. Circolare 4 giugno 2020 Prevenzione e controllo dell'influenza:

raccomandazioni per la stagione 2020-2021 [cited 2020 Nov 2]. Available on: https://www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2020&codLeg=74451&parte=1%20&serie=null [Last accessed: 2021 October 15].
17. Ministero della Salute. Decreto 17 settembre 2018. Istituzione dell'Anagrafe nazionale vaccini [cited 2020 Apr 15]. Available on: https://www.gazzettaufficiale.it/eli/id/2018/11/05/18A07050/sg#:~:text=Il%20presente%20decreto%20istituisce%20e,in%20relazione%20al%20Calendario%20vaccinale [Last accessed: 2021 October 15].
18. Fleiss JL, Levin B, Paik M. Statistical Methods for Rates and Proportions. 3rd ed. New York: John Wiley & Sons, 2003.
19. Azienda Ospedaliera di Perugia. Relazione annuale anno 2019. Giugno 2020 [cited 2020 May 1]. Available on: https://www.ospedale.perugia.it/MC-API/Risorse/StreamRisorsa.ashx?guid=d3e6065c-40ff-4503-9192-ac7e398e6175 [Last accessed: 2021 November 6].
20. Istat. Popolazione residente-bilancio: Umbria [cited 2000 Nov 18]. Available on: http://dati.istat.it/Index.aspx?QueryId=18980 [Last accessed: 2021 November 6].
21. Ministero della Salute. Influenza. Dati copertura vaccinale [updated 2020 Sep 11; cited 2020 Sep 24]. Available from: http://www.salute.gov.it/portale/influenza/dettaglioContenutiInfluenza.jsp?lingua=italiano&id=679&area=influenza&menu=vuoto [Last accessed: 2021 September 24].
22. Yudin MH, Salaripour M, Sgro MD. Pregnant women's knowledge of influenza and the use and safety of the influenza vaccine during pregnancy. J Obstet Gynaecol Can. 2009 Feb; 31(2): 120-5. doi: 10.1016/s1701-2163(16)34095-6.
23. Clarke RM, Paterson P, Sirota M. Determinants of satisfaction with information and additional information-seeking behaviour for the pertussis vaccination given during pregnancy. Vaccine. 2019 May 6; 37(20): 2712-20. doi: 10.1016/j.vaccine.2019.04.008. Epub 2019 Apr 8.
24. D'Alessandro A, Napolitano F, D'Ambrosio A, Angelillo IF. Vaccination knowledge and acceptability among pregnant women in Italy. Hum Vaccin immunother. 2018 Jul 3; **14**(7): 1573-9. 10.1080/21645515.2018.1483809. Epub 2018 Jun 20.
25. Eppes C, Wu A, You W, Cameron KA, Garcia P, Grobman W. Barriers to influenza vaccination among pregnant women. Vaccine. 2013 Jun 12; **31**(27): 2874-8. doi: 10.1016/j.vaccine.2013.04.031. Epub 2013 Apr 24.
26. Yuen CY, Tarrant M. Determinants of uptake of influenza vaccination among pregnant women - a systematic review. Vaccine. 2014 Aug 6; **32**(36): 4602-13. doi: 10.1016/j.vaccine.2014.06.067. Epub 2014 Jul 2.
27. Tarrant M, Wu KM, Yuen CY, Cheung KL, Chan VH. Determinants of 2009 A/H1N1 influenza vaccination among pregnant women in Hong Kong. Matern Child Health J. 2013 Jan; **17**(1): 23-32. doi: 10.1007/s10995-011-0943-1.
28. Fridman D, Steinberg E, Azhar E, Weedon J, Wilson TE, Minkoff H. Predictors of H1N1 vaccination in pregnancy. Am J Obstet Gynecol. 2011 Jun; **204**(6 Suppl 1): S124-7. doi: 10.1016/j.ajog.2011.04.011. Epub 2011 Apr 15.
29. Fisher BM, Scott J, Hart J, Winn VD, Gibbs RS, Lynch AM. Behaviors and perceptions regarding seasonal and H1N1 influenza vaccination during pregnancy. Am J Obstet Gynecol. 2011 Jun; **204**(6 Suppl 1): S107-S11. doi: 10.1016/j.ajog.2011.02.041. Epub 2011 Feb 22.
30. Blanchard-Rohner G, Siegrist CA. Vaccination during pregnancy to protect infants against influenza: why and why not? Vaccine. 2011 Oct 6; **29**(43): 7542-50. doi: 10.1016/j.vaccine.2011.08.013. Epub 2011 Aug 4.
31. Bartolo S, Deliege E, Mancel O, et al. Determinants of influenza vaccination uptake in pregnancy: a large single-Centre cohort study. BMC Pregnancy Childbirth. 2019 Dec 19; **19**(1): 510. doi: 10.1186/s12884-019-2628-5.
32. Barrett T, McEntee E, Drew R, et al. Influenza vaccination in pregnancy: vaccine uptake, maternal and healthcare providers' knowledge and attitudes. A quantitative study. BJGP Open. 2018 Aug 8; **2**(3): bjgpopen18X101599. doi: 10.3399/bjgpopen18X101599.
33. Ugezu C, Essajee M. Exploring patients' awareness and healthcare professionals' knowledge and attitude to pertussis and influenza vaccination during the antenatal periods in Cavan Monaghan general hospital. Hum Vaccin Immunother. 2018 Apr 3; **14**(4): 978-83. doi: 10.1080/21645515.2017.1419110. Epub 2018 Feb 22.
34. Offeddu V, Tam CC, Yong TT, et al. Coverage and determinants of influenza vaccine among

pregnant women: a cross-sectional study. BMC Public Health. 2019 Jul 5; **19**(1): 890. doi: 10.1186/s12889-019-7172-8.
35. Quattrocchi A, Mereckiene J, Fitzgerald M, Cotter S. Determinants of influenza and pertussis vaccine uptake in pregnant women in Ireland: A cross-sectional survey in 2017/18 influenza season. Vaccine. 2019 Oct 8; **37**(43): 6390-6. doi: 10.1016/j.vaccine.2019.09.008. Epub 2019 Sep 9.

Corresponding author: Valentina Tosto, Centre for Research in Perinatal and Reproductive Medicine, University of Perugia, 06156 Perugia, Italy
e-mail: tosto.valentina@libero.it