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RESEARCH ARTICLE



Trends in influenza vaccination and its determinants among pregnant French women between 2015 and 2020: A single-center study

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ABSTRACT

In 2016, only 7% of French women had received an influenza vaccination during their pregnancy. In this vaccine-averse country, the possibility of reaching the rates of 50% observed in other countries remains unknown. To measure the rate of influenza vaccination in a French university maternity. To study its evolution and determinants over the last 5 years. Single-center observational study of all women who gave birth during March 2020 in this maternity. Comparison with rates observed in 2015 in the same conditions. Of the 337 women included in the study, 202 received a vaccination during pregnancy (59.9%). After logistic regression, the factors significantly associated with achieving vaccination were the offer of vaccination during pregnancy, odds ratio (ORa) 26.2 [7.0; 98.2]; previous vaccination, ORa 20.3 [9.6; 42.6]; high education level, ORa 2.9 [1.3; 6.2]; delivery of a CERFA government reimbursement form, ORa 2.5 [1.3; 4.8]; a vaccination offer made by a general practitioner, ORa 2.1 [1.0; 4.4] and not by a hospital midwife, ORa 0.3 [0.1; 0.6]. The rate of vaccination increased from 35% to 59.9% between 2015 and 2020 ($p < .001$), with a significant increase in the offer of vaccination during pregnancy (+14.6%) - especially by a general practitioner (+17.2%) - and in the rate of women with earlier vaccination (+13.6%). In France, vaccination rates above 50% are possible at a center level. A proposal of vaccination during pregnancy - especially by the general practitioner - seems to be a determining factor in this development.

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Introduction

In France, influenza is an acute respiratory viral infection that is epidemic, causing approximately 10,000 deaths each year.¹ It can affect pregnant women, with a higher risk of complications than for nonpregnant women.^{2,3} During the 2009 H1N1 influenza pandemic, 5% of deaths occurred in pregnant women, even though they represented only about 1% of the population.² Although the reason for this increase in mortality is still debated, there is no doubt about an increase in severe forms of influenza in pregnant women.³

Influenza vaccination is the best strategy to overcome this susceptibility of pregnant women to influenza, thereby preventing complications. In 2012, the World Health Organization identified pregnant women as a priority group for national influenza vaccination programs.⁴ In the same year, the French health authorities recommended that all pregnant women be vaccinated.⁵ This recommendation was all the more legitimate because the data concerning vaccine safety are reassuring⁶ and vaccination reduces the risk of neonatal influenza by the passive transmission of maternal antibodies through the placenta.^{7,8}

In France, the dissemination of this 2012 national recommendation did not reach the desired effect because only 7.4% of pregnant French women declared that they had been vaccinated against influenza in 2016, with this rate ranging from 4.5% to

11.6% depending on the region.⁹ Aware of the difficulties in disseminating a new vaccination among pregnant women in our country, our center has attempted to study the factors linked to the uptake of vaccination.^{10,11} After having shown that it was possible to reach 35% of women vaccinated in 2015, we recently set ourselves the goal of knowing the evolution of vaccination in 2020 among women who give birth in our center and analyzing the determinants of this evolution.

Materials and methods

This is a single-center observational study of all women who gave birth during March 2020 in our university type 3 maternity hospital. The methodology used was the same as the one used in 2015 in our center¹⁰ but over a much shorter period (2015: seven months from November to June, our study in 2020: only the month of March). Eligible women were all pregnant women who had given birth in our maternity hospital between March 1 and 31 March 2020. Women were excluded from the study if they were minors, if they did not speak or read French, if they had an egg allergy that contraindicated vaccination.

Data were collected directly from a self-administered questionnaire given to all women during their stay in the maternity hospital after delivery (Appendix). The questionnaire asked

about pregnant women's knowledge of influenza infection and its potential consequences for the mother and the fetus, as well as about the influenza vaccine, its benefits and adverse effects.¹⁰ It also included questions on influenza vaccination before and during pregnancy, as well as sources of information, modalities of vaccination offer, motivations and reluctance to be vaccinated as well as simple sociodemographic data (age, level of education). A 10-point Likert scale was used to assess each of the women's perceptions of influenza and the vaccine, which was then transformed into a four-point variable ("very low 0–1, low 2–3, medium 4–7, high 8–9"). To obtain the best contrasts in the analyses, dichotomization into only two classes was performed near the median ($\geq 4/9$ or $7/9$, as appropriate). The CEROG (Committee for Ethics in Research in Gynecology and Obstetrics), approved the study (CEROG OBS 2014-11-01).

All data were recorded with Excel software (Excel 2013, Microsoft®, Washington, DC, USA) and analyzed with Epi Info software (Epi Info version 7.2.2.6, CDC, Atlanta, GA, USA). Numbers are accompanied by percentages in parentheses. All comparisons were qualitative and used the chi-square test, or Fisher's exact test in the case of small numbers. To better understand the factors associated with influenza vaccination during pregnancy, a logistic regression of the use of influenza vaccination during pregnancy was carried out on all the factors associated with this use at the 0.05 threshold in univariate analysis. The adjusted odds ratios were given with their 95% confidence intervals. All differences were considered significant if $p < .05$.

Results

A total of 534 women gave birth in our center between March 1 and 31 March 2020 and 363 women received the questionnaire and responded (68.0%) (Figure 1). Of these, 17 were secondarily excluded: 13 because they did not speak or read French, three because they were minors and one because of an allergy to egg proteins. Finally, 9 questionnaires were unusable regarding vaccination during pregnancy and 337 women were included in the study.

Of these women, 202 reported having been vaccinated against influenza during pregnancy (59.9%, 95%CI [54.5; 65.2]). The factors significantly related to the existence of an influenza vaccination in a univariate analysis and after logistic regression are presented in Table 1. Women with a higher level of education were more likely to report having been vaccinated (64.3% vs 45.7%, odds ratio (ORa) 2.9 [1.3; 6.2]), as were those who had been previously vaccinated against influenza (84.8% vs 34.3%, ORa 20.3 [9.6; 42.6]). Women who reported having been offered a vaccination during pregnancy were significantly more likely to be vaccinated than those who had not (66.0% vs 10.8%, ORa 26.2 [7.0; 98.2]), especially when offered by a general practitioner (76.7% vs 53.8%, ORa 2.1 [1.0; 4.4]). On the other hand, having been offered the vaccine by a hospital midwife was associated with a lower frequency of influenza vaccination (42.8% vs 64.4%, ORa 0.3 [0.1; 0.6]). Finally, women who received the French government CERFA reimbursement form during pregnancy were more likely to

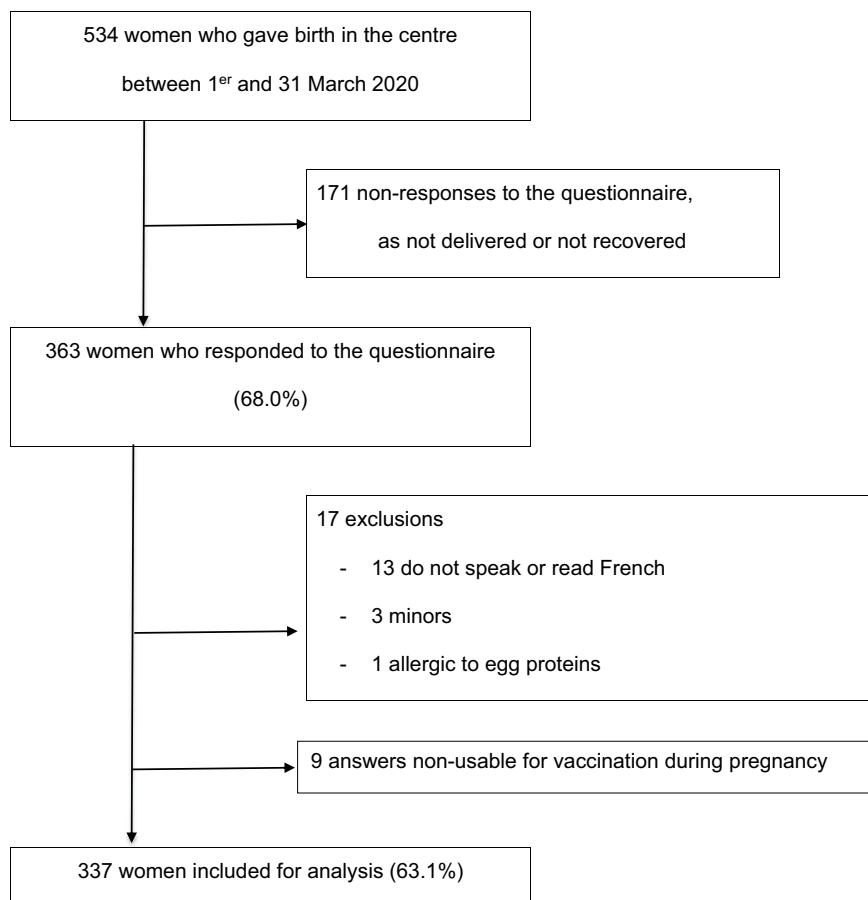


Figure 1. Flow chart.

Table 1. Patient characteristics and factors related to influenza vaccination Adjusted ORs – logistic regression – were calculated only for variables significantly associated with receiving an influenza vaccination during pregnancy 2015–2021.

			<i>p</i>	ORa [CI 95]
High level of education (≥ Bachelor's degree)	Yes	170/264 (64.3)	.005	2.9 [1.3; 6.2]
	No	32/70 (45.7)		
Age >35 years	Yes	65/110 (59.1)	.80	
	No	123/203 (60.6)		
Consultation at the maternity during the first trimester	Yes	83/147 (56.4)	.17	
	No	115/180 (63.8)		
Any previous influenza vaccination before pregnancy	Yes	145/171 (84.8)	<.001	20.3 [9.6; 42.6]
	No	57/166 (34.3)		
Viewing a video for vaccination in the waiting room	Yes	25/39 (64.1)	.58	
	No	175/294 (59.5)		
Vaccination proposal during pregnancy	Yes	198/300 (66.0)	<.001	26.2 [7.0; 98.2]
	No	4/37 (10.8)		
Vaccination proposal by a general practitioner	Yes	69/90 (76.7)	<.001	2.1 [1.0; 4.4]
	No	133/247 (53.8)		
Vaccination proposal by a private midwife	Yes	57/88 (64.8)	.28	
	No	145/249 (58.2)		
Vaccination proposal by a hospital midwife	Yes	30/70 (42.8)	<.001	0.3 [0.1; 0.6]
	No	172/267 (64.4)		
Vaccination proposal by a hospital obstetrician-gynecologist	Yes	56/86 (65.1)	.26	
	No	146/251 (58.2)		
Vaccination proposal by another liberal health professional	Yes	34/53 (64.1)	.50	
	No	168/284 (59.1)		
Vaccination proposal by a non-health professional	Yes	98/175 (56.0)	.12	
	No	104/162 (64.2)		
Delivery of the CERFA government reimbursement form by a professional	Yes	123/170 (72.3)	<.001	2.5 [1.3; 4.8]
	No	73/153 (47.7)		

have received the vaccine than those who did not (72.3% vs 47.7%, ORa 2.5 [1.3; 4.8]).

Women's reported reluctance and perception differed significantly between vaccinated and unvaccinated women (Table 2). Vaccinated women were more likely to perceive influenza as a common disease, potentially serious for the mother and the infant. They were more likely to be aware of the recommended nature of the vaccination. As a corollary, vaccinated women were less likely to fear for their baby's health, or their health, and less likely to feel they lacked information about the benefits and risks of the vaccine. These women were less reluctant to vaccinate in general. They were less likely to perceive complications from the flu vaccine as frequent and potentially serious for their own or their baby's health. Under these conditions, flu vaccination was perceived as certainly useful by 89.5% of vaccinated women but only 30.5% of unvaccinated women ($p < .001$).

In our center, the evolution of influenza vaccination and its determinants were studied by comparing women who gave birth between November 2014 and June 2015 with those who gave birth in March 2020 (Table 3). During this period, we observed a 35.5% to 59.9% increase in the rate of influenza vaccination during pregnancy (+24.3%, 95%CI [19.8; 29.3]). This increase remained statistically significant if the analysis was restricted to women who gave birth in March 2015 and March 2020 (+21.4% [17.3; 26.0]). Among the determinants of vaccination during pregnancy whose evolution could be compared between the two periods, three of them increased very significantly between 2015 and 2020: the vaccine offered during pregnancy (from 74.4% to 89.0%, +14.6%, 95%CI [11.0; 18.8]), being previously vaccinated for influenza (from 36.8% to 50.1%, +13.3%, 95%CI [10.0; 17.5]) and offer of vaccination by a general practitioner, which showed the greatest increase between the two periods (from 9.5% to 26.7%,

+17.2%, 95%CI [13.3; 21.7]). Conversely, neither the percentage of pregnant women with a high educational level nor that of women who received a French government CERFA reimbursement form varied significantly between 2015 and 2020. Finally, our data indicated a significant decrease in the rate of refusal of vaccination after the vaccination offer between 2015 and 2020 (from 53.0% to 34.0%, −19.0%, 95%CI [−14.7; −23.9]).

Discussion

Our study showed that the reported rate of influenza vaccination immediately after delivery by women in our center was close to 60% in 2020. The vaccine offer – especially from a general practitioner – and the existence of a previous vaccination were the main factors related to the achievement of vaccination during pregnancy. Our study showed that these factors improved very significantly between 2015 and 2020, probably explaining much of the increase in vaccination coverage in our center during this period.

The response rate of 68% observed in our study is a weakness of our study because this rate is 10% lower than that observed in 2015 in our maternity with the same questionnaire.¹⁰ However, our study was carried out in March 2020, at the beginning of the health crisis linked to COVID-19, with a reorganization of the activities linked to containment from 13 March 2020. Finally, this is a fairly usual response rate for this type of survey, with rates ranging from 31% to 89% depending on the study considered.^{12–14} Although surveyed at the time of the COVID pandemic onset, the decision whether or not to get the influenza vaccine had been made by women during the winter vaccination campaign (between 4.5 and 1 month before the onset of the pandemic, almost a year before COVID vaccination began 19). In these

Table 2. Pregnant women's reluctance and perceptions of influenza and influenza vaccination.

	Vaccinated n = 202	Not vaccinated n = 137	p
Perception of illness (Likert scale)			
Perceived as frequent ($\geq 7/9$)	134 (67.7)	66 (33.3)	.001
Potentially at risk of serious maternal complications ($\geq 7/9$)	174 (86.1)	97 (72.9)	.01
Potentially at risk of serious complications in infants ($\geq 7/9$)	144 (71.3)	79 (59.0)	.035
Knowledge of recommended vaccination	181 (89.6)	104 (77.0)	<.001
Vaccine reluctance			
Fear for the baby's health	12 (5.9)	25 (18.5)	<.001
Fear for one's own health	9 (4.4)	22 (16.3)	<.001
Little information on benefits and risks	4 (2.0)	32 (23.7)	<.001
More against vaccines in general	9 (4.4)	34 (25.2)	<.001
Other	3 (1.5)	34 (25.2)	<.001
Perception of complications of the flu vaccine (Likert scale)			
– Perceived as frequent ($\geq 4/9$)	57 (29.5)	70 (58.8)	<.001
Potentially serious in the mother ($\geq 4/9$)	82 (42.3)	74 (61.7)	<.001
Potentially serious in infants ($\geq 4/9$)	73 (38.6)	72 (62.6)	<.001
Perceived usefulness of the vaccine			
Certainly useful	179 (89.5)	40 (30.5)	<.001
Can be useful	17 (8.5)	78 (59.5)	
Not necessary	3 (1.5)	10 (7.6)	
Contraindicated	1 (0.5)	3 (2.3)	

Table 3. Evolution of influenza vaccination, its determinants and the refusal rate after vaccination proposal between 2015 and 2020 in our center.

	2015 n = 2045	2020 n = 337	p	Significant developments % [IC95]
Vaccination during pregnancy	725/2045 (35.5)	202/337 (59.9)	<.001	+24.3 [19.8; 29.3]
<i>Delivery in March only</i>	140/364 (38.5)	202/337 (59.9)	<.001	+21.4 [17.3; 26.0]
Determinants of vaccination during pregnancy				
High level of education (\geq Bachelor's degree)	1589 (77.8)	264 (79.1)	.64	
Any previous influenza vaccination before pregnancy	749 (36.8)	169 (50.1)	<.001	+13.3 [10.0; 17.5]
Vaccination proposal during pregnancy	1512 (74.4)	300 (89.0)	<.001	+14.6 [11.0; 18.8]
Vaccination proposal by the general practitioner	143 (9.5)	90 (26.7)	<.001	+17.2 [13.3; 21.7]
Submission of the CERFA gov ⁿ t reimbursement form	1005 (50.0)	170 (52.6)	.38	
Refusal of the patient after vaccination proposal	801/1512 (53.0)	102/300 (34.0)	<.001	–19.0 [–14.7; –23.9]

conditions, we believe that the risk of bias related to COVID 19 was very low in our study.

The 60% vaccination rate we observed appears high and even surprising insofar as pregnant French women usually appear to be poorly vaccinated against influenza, unlike pregnant women in countries with the same standard of living.¹⁵ As early as the 2009 H1N1 pandemic, the policy of systematically vaccinating pregnant French women resulted in a vaccination coverage of only 29.3%¹⁶ whereas some countries or areas observed rates of 50% or more at the same time (Norway, Finland, Quebec, USA).¹⁶ In a routine epidemic situation, the latest French data indicated a coverage rate of 7.4% in 2016, whereas some countries measured rates of around 50% at the same time (Belgium,¹³ USA,¹⁷ England.¹⁸

This high rate of 60% vaccination coverage observed in our center is very encouraging. However, we are aware of the single-center nature of these results, which may not be generalizable to our region or country. However, the evolution of the rate from 35% to 60% that we observed in 5 years in our center was obtained quite easily, with some instructive elements. First, our results confirm the essential role of the vaccine offer.^{19–21} The existence of a vaccine proposal was the factor most closely linked to the completion of a vaccination in 89% of the women at our center in 2020. In our center itself, this factor has clearly and significantly increased between 2015 and 2020. The other lesson from our study concerns the role of general practitioners, whose vaccine offer was associated with a doubling of

the chances of vaccination in our study, after adjusting for other factors related to vaccination rates. Several studies confirm this essential role of general practitioners in vaccination, whether for pregnant women^{15,22} or nonpregnant women.²³ In our center, this is the factor that has increased the most between 2015 and 2020. Conversely, the significant decrease in the rate of vaccination when women were offered vaccination by a hospital midwife is a reminder that the reluctance of professionals greatly determines the attitude of pregnant women.^{12,20,21} Moreover, some studies indicate that midwives feel less legitimate to give vaccination advice than other health professionals during pregnancy, and are more reluctant to vaccinate pregnant women.^{12,13,24,25}

Finally, our data rather support the theory of the “multichannel” approach developed in 2013 by Stockport et al.²⁶ Although we were not aware of this theory at the time of our study, it is possible that the “multichannel” approach we had toward flu vaccination explained the rapid increase in the vaccine offer and then in the vaccine coverage observed in our center. Our action included a “nonmilitant” awareness campaign to relay the 2012 national recommendations, the broadcasting of a video in the waiting room reminding pregnant women of the importance of flu vaccination, the availability of CERFA government reimbursement forms in all consultation rooms from mid-October onward (start of the winter season), and the inclusion of flu vaccination as a “reminder” in the interinstitutional pregnancy monitoring file.

In the end, our results are extremely encouraging for us as health professionals. On the one hand, the latest known flu vaccination rate is 7.4% in France.⁹ On the other hand, they indicate that high rates of influenza vaccination are possible among pregnant French women, despite their fears of the effects of the vaccine on their babies and themselves, fears that are found in our center as in other countries.^{20–21–29} On the other hand, and above all, our results indicate that acceptance of the vaccine offer has clearly increased between 2015 and 2020, whereas the refusal rate has clearly and significantly decreased. This is an essential secondary result. For us, everything seems to have happened until 2015 as if the lower the vaccine offer, the higher the refusal rate, in a kind of “vicious circle.” At the national level, only a quarter of pregnant French women declared at that time that they had received a vaccination proposal during their pregnancy, and 70% of women who had received this offer refused the vaccination.¹⁵ In these conditions, the vaccination offer might appear to some doctors as a waste of time due to “a battle lost in advance.” Moreover, in our center, the fear of refusal was cited in 2015 as the main reason for not offering vaccination and concerned more than half of the doctors, with a “no offer/nonacceptance vicious circle.” Finally, the results of our study, showing an increase in vaccine offers from 74.4% to 89.0% concurrent with a decrease in refusals from 53.0% to 34.0%, may indicate the end of this vicious circle.

Conclusion

Although we thought it would be difficult – if not impossible – to increase the vaccination coverage of pregnant women in our French maternity hospital, an increase from 35% to 60% was possible without pressure in five years. The “multichannel” strategy we adopted, based on different sources of information and different prescribers – including general practitioners – seemed to us to be the key to breaking the vicious circle we were in. We hope that this experience can be extended to other maternity hospitals in our country and that it will lead to the adoption of flu vaccination in France and in other countries in Europe and the world that are experiencing the same difficulties.

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Appendix.**Questionnaire for patients following a birth**

Answer the 5
questions THEN
if a grey box is
checked in
question a):
STOP

- a) In order to participate in this study, we need to know certain information:
- are you over 18 years old? ☐ yes ☐ no
 - do you read French ☐ yes ☐ with difficulty ☐ not at all
 - are you allergic to egg proteins? ☐ no ☐ yes
 - do you agree to complete this questionnaire? ☐ yes ☐ no
- b) What is your level of education?
- ☐ Primary ☐ Secondary or technical ☐ Baccalaureate or higher
- c) When did you have your first pregnancy follow-up consultation at Jeanne de Flandre centre?
- ☐ 1st trimester ☐ 2nd trimester ☐ 3rd trimester
- d) What is the name of the person who followed you in our centre (at least twice)?.
- 1) In your opinion, **influenza** is a disease: (*for each proposition, circle the number that corresponds to your opinion*)
- | | |
|---------------------|---------------------|
| Very rare | Very frequent |
| 0 1 2 3 4 5 6 7 8 9 | 0 1 2 3 4 5 6 7 8 9 |
| Never serious | Always severe |
| 0 1 2 3 4 5 6 7 8 9 | 0 1 2 3 4 5 6 7 8 9 |
- 2) Do you think that influenza can cause **serious complications** during pregnancy **in the mother**?
- ☐ Yes ☐ No ☐ I don't know
- If so, can you give an example?
- 3) Do you think that the flu can cause **serious complications** during pregnancy **for the baby**?
- ☐ Yes ☐ No ☐ I don't know
- If so, can you give an example?
- 4) In your opinion, flu **vaccination** during **pregnancy** is:
- ☐ Contra indicated ☐ Not useful ☐ May be useful ☐ Definitely useful
- 5) In your opinion, flu **vaccination** during **pregnancy** is:
- ☐ Mandatory ☐ Neither mandatory nor recommended
- ☐ Recommended by health authorities ☐ I don't know
- 6) Have you ever been **vaccinated against the flu**?
- ☐ Yes, outside of pregnancy ☐ No
- ☐ Yes, in a previous pregnancy ☐ I do not know
- 7) What were your **sources of information** about flu **vaccination**?
- (Multiple answers possible)
- ☐ Health professionals (doctor, midwife, nurse, pharmacist ...)
- ☐ Media (radio, television, newspapers and magazines, internet, billboards, ...)
- ☐ Discussion forums (Chat, associations of people ...)
- ☐ Surroundings (family, friends ...)
- ☐ Official health authorities (HAS, Inpes, Ansm ...)
- ☐ Video shown in the waiting room of the Jeanne de Flandre hospital
- ☐ Other
- 8) **Which** of these **sources was the** reason for your decision (to vaccinate or not)?.
- 9) **During this pregnancy**, were you **offered the flu vaccination**?
- ☐ Yes ☐ No
- If so, who suggested it to you?
- ☐ Obstetrician gynecologist of Jeanne de Flandre ☐ General practitioner
- ☐ Midwife in Jeanne de Flandre ☐ Liberal midwife
- ☐ Other:
- 10) During your pregnancy, did you watch a **video about flu vaccination** in the hospital waiting room?
- ☐ Yes ☐ No
- If so, did it influence your choice? ☐ Yes ☐ No
- 11) During the pregnancy, were you given the **form for reimbursement of** the vaccination by the social security (free voucher)?
- ☐ Yes ☐ No

12) Did you get a flu **shot** during **this pregnancy**?

☐ Yes ☐ No ☐ I don't know

If yes,

⇒by whom?

⇒at what point in the pregnancy did you receive the vaccination?

☐ 1st trimester (0–3 months) ☐ 2nd trimester (4–6 months) ☐ 3rd trimester (7–9 months)

⇒what were your arguments? (*several answers possible*)

- ☐ The vaccine protects me
☐ The vaccine protects my baby
☐ I have received sufficient information about the benefits of the vaccine
☐ I am rather “for” vaccines in general
☐ The vaccine is fully reimbursed
☐ Other:

If not,

⇒What were your reservations? (*several answers possible*)

- ☐ I didn't know there was a vaccine
☐ I was afraid for my baby's health
☐ I was afraid for my health
☐ I didn't get enough information about the benefits and risks
☐ I am rather “against” vaccines
☐ Other:

13) Which **person** helped you most in making **your choice**?

☐ GP ☐ Gynaecologist/midwife ☐ Gynaecologist/midwife ☐ Friend/family ☐ Other

14) In your opinion, the flu **vaccine** can cause **complications** in**the mother**:

(*circle the number that corresponds to your opinion*)

Very rare Very frequent

0 1 2 3 4 5 6 7 8 9

Never serious Always serious

0 1 2 3 4 5 6 7 8 9

15) In your opinion, the flu **vaccine** can cause **complications** in**the baby**:

Very rare Very common

0 1 2 3 4 5 6 7 8 9

Never serious Always serious

0 1 2 3 4 5 6 7 8 9

A BIG THANK YOU FOR YOUR PARTICIPATION