Influenza and pertussis vaccination coverage in pregnant women

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Abstract

Background: Pregnant women have an increased risk for complications and hospitalizations when infected with the influenza virus in the second or third trimester. Additionally, infants under six months of age are most vulnerable when contracting pertussis. Immunization against influenza and pertussis during pregnancy provides protection for mother and neonate against influenza and for neonates against pertussis pending protection through infant immunization. In Belgium, a gradual increase in pertussis cases over the past decade was observed. This study was undertaken to document vaccination coverage for influenza and pertussis and factors related to vaccination status in pregnant women.

Methods: 250 pregnant women completed a questionnaire during their third trimester. Vaccination data were collected and reasons for non-vaccination were noted as well as socio-demographic data which are known to influence vaccination coverage.

Results: A documented vaccination coverage of 42.8% for influenza and 39.2% for pertussis was observed. Taking into account doses which were not documented, but administered according to the expectant mother, coverage for influenza would increase to 62% and for pertussis to 46%. The most important reasons for non-vaccination were the absence of a recommendation by medical staff (9.6%) and delay in vaccination (8.4%). The GP was the most important vaccinator. Pregnant women with a lower education and those with a foreign origin were more vulnerable for non-vaccination.

Conclusion: Incomplete documentation is the most important barrier in determining the vaccination status of pregnant women. Immunization during pregnancy needs further integration through vaccination campaigns aimed at both health care providers and pregnant women.

Key words: influenza, pertussis, pregnancy, vaccination coverage, immunization

Abbreviations:

GP General Practitioner

HCP Health Care Provider

Highlights:

- 42.8% of pregnant women had immunization records for influenza and 39.2% for pertussis, while only 23.6% had documentation for both vaccines.
- The coverage increases to 62% for influenza and 46% for pertussis when oral communication was considered in addition.
- Obstetricians and GP are most influential in decision of pregnant women to vaccinate.
- Women with a low education and those of foreign origin are more vulnerable for non-vaccination.

Introduction

Insights in the burden of disease of influenza in pregnant women and studies on the resurgence of pertussis with a particular burden of disease in neonates have increased knowledge and awareness regarding the necessity of immunization of pregnant women against influenza and pertussis.[1-3]

Pregnant women are at increased risk of severe complications and hospitalization when infected with influenza. Physiologic changes in the respiratory, cardiovascular and immune system during pregnancy may contribute to this increased risk [4-6]. In addition, pregnant women who are infected with influenza have an increased risk of adverse pregnancy outcomes such as preterm delivery, small-for-gestational-age infants, lower birth weight babies, and stillbirths [7-9].

Since 2000, there is an increase in cases of pertussis in countries which have used the acellular pertussis vaccine for infant vaccination, including Belgium[10-11]. In particular newborns under 6 months of age are extremely vulnerable and the highest burden of disease occurs in this age group [11]. Infants need at least three doses of acellular pertussis vaccines to gain protection against pertussis by six months of age [12-13]. During the first months of life, maternal antibodies provide primary protection against infectious agents, as the neonate immune system cannot yet elicit adult-like humoral immune responses [14]. Therefore, the main reason to recommend pertussis vaccination during pregnancy is to elicit maternal antibodies in order to protect newborns during the first 6 months after birth [13].

Inactivated influenza vaccines and combined diphtheria-tetanus-acellular pertussis vaccines are considered to be safe when given during pregnancy [2,4-6,15-17]. Studies on effectiveness on reducing influenza in pregnant women and neonates [1,18-19] and pertussis in neonates have shown the added value of immunizing pregnant women [11,20,21]. In 2012 the World Health Organization (WHO) recommended immunization against seasonal flu for pregnant women[22] and in 2014 the Strategic Advisory Group of Experts (SAGE) considered that maternal immunization against pertussis was the most cost-effective complementary

strategy to prevent pertussis-associated infant mortality [23]. The Belgian Superior Health Council also recommends influenza vaccination in pregnant women from the second trimester of pregnancy onwards during the flu season [24]. In 2012, a new action plan regarding influenza vaccination was launched in Flanders, which considers pregnant women to be a specific target group, and aims at a coverage of at least 50% of all pregnant women by 2020 [25]. Additionally, all pregnant women are also advised to be immunized against pertussis between 24–32 weeks of each pregnancy, regardless of whether they received a booster vaccine in the past or not [12].

Data on the combined vaccination coverage rate of influenza and pertussis in pregnant women are limited. This article reports the documented vaccination coverage of influenza and pertussis in pregnant women and possible associated socio-demographic factors for (non-)vaccination.

Material and methods

Population and Sampling Procedure

During the influenza season (December 2013 – February 2014), 257 women in their third trimester of pregnancy (≥ 28 weeks) attending the University Hospitals KU Leuven, Belgium for a routine third trimester ultrasound examination, were approached to participate in the study. Seven (2.8%) woman refused, mainly because of language barrier or lack of time, leaving questionnaires of the remaining 250 pregnant women fit for analysis. All participants were Belgian residents.

Survey Procedure

Potential participants were informed about the aim and course of the study by one of the authors. Upon agreement, they were asked to sign the informed consent, and a questionnaire was taken. The questionnaire was based on the questionnaire of the 2008-2012 Flemish coverage study in young children and adolescents, but adjusted for the current target group [26]. The questionnaire and informed consent were available in Dutch, French and English language to include as many patients as possible.

The main part of the survey regarded data on influenza and pertussis vaccination: by whom they were informed or advised on vaccination in pregnancy, vaccination status and, if applicable, date and vaccinator, prior vaccination against influenza and pertussis, willingness to vaccinate their child, and vaccination status of the partner. The questionnaire included several items on socio-demographic background of the participant and her partner (*Table 1*). Obstetric data consisted of gestational age, obstetric history, parity, complications during pregnancy (bleeding, preterm contractions, hyperemesis gravidarum, gestational diabetes, gestational hypertension, infectious diseases and preeclampsia) and medical conditions (diabetes mellitus, cardiopathy, nephropathy, pulmonary condition, immune deficiency).

Only documented vaccination data were taken into account. If not available, the hospital medical files or Vaccinnet, the Flemish vaccination registry, were checked. Finally, the GP of

the participant was contacted to provide still missing data. Data files were anonymised prior to analysis.

Definitions for valid immunizations

Valid immunization for influenza was defined as one dose of inactivated influenza vaccine since October 2013 after 12 weeks of pregnancy [24]. The recommendation for pertussis during pregnancy is one dose of dTap (Boostrix®). All vaccinations after 12 weeks of pregnancy were considered valid even though the recommended timing for this vaccine is between 24 and 32 weeks of gestation [12].

Ethical Approval

The study protocol, questionnaire, and informed consent were approved by the Committee of Medical Ethics of the University Hospital of the KU Leuven. Guidelines of Good Clinical Practice and the Belgian law and local regulations were respected.

Statistical Analysis

A sample size of 250 subjects was proposed to obtain a confidence interval width of approximately 10 percentage points for a coverage rate between 10 and 50%. Estimates of the coverage rates are presented with a 95% confidence interval. Statistical significance of the effect of determinants on coverage rates was tested for each vaccine independently by univariate logistic regression. A test probability of 5% was considered statistically significant. Data were entered in Microsoft Access 2010, and R. version 3.0.2. (R Foundation for Statistical Computing, Vienna, Austria, 2013) was used for the statistical analysis.

Results

Study population

Baseline characteristics of the study population are listed in table 1. Baseline characteristics of the partners were similar compared to pregnant women, except for a slightly older age (35% was over 35 years of age) and more often having a full-time job (91.3%). Most participants were aged between 25-34 years (70.8%), 78.0% were 28 to 32 weeks pregnant, 45.6% were primiparae, and 2% were pregnant of twins. Complications occurred in 12.8% of pregnancies. Most common complications were hyperemesis gravidarum (4.0%), bleeding (2.8%) and preterm contractions (2.8%). Twenty (8.0%) women had a medical condition which could give an increased risk when contracting influenza. All data on our study population were in line with census data on pregnant women in Flanders, except for a lower prevalence of gestational diabetes and hypertension.[27]

Vaccination coverage

In our study population, the documented vaccination coverage rate was 42.8% (n=107 - 95% CI: 36.6%-49.2%) for influenza, and 39.2% (n=98 - 95%CI: 33.2%-45.6%) for pertussis. Documentation for both vaccines was available in 59 women (23.6% - 95% CI: 18.6-29.5%). However, for many women who reported being immunized during the interview no documentation could be retrieved. Vaccination data for influenza were provided by 62 pregnant women, for 27 women, data on flu vaccination were retrieved from the hospital medical records and 18 dates on flu vaccination by the general practitioner of the participants. For pertussis, 53 vaccination dates were obtained from the pregnant women directly, 18 were retrieved from the hospital medical records, 18 provided by the GP and 9 dates were found in Vaccinnet. When all information on both documented and undocumented vaccine doses, are taken into account, coverage rates increase to 62.0% for influenza and to 46.0% for pertussis. For women who received both vaccines, the coverage would increase to 34.4%. Women with

an underlying medical condition had a significantly higher vaccination coverage for both influenza (45.0% vs 38.7%; p<0.05) and pertussis (45.0% vs 42.6%; p<0.01).

Vaccinator

For influenza, 63.2% of vaccinated women received the vaccine from their GP, 27.7% received the vaccine at work from the occupational medical officer and 9% received the vaccine from an obstetrician. For pertussis, 75.9% of vaccinated woman received the vaccine from the GPs, 20.5% from an obstetrician, and 3.6% at work.

Reasons for vaccination

Reasons given for vaccination were highly similar for influenza and pertussis (*Table 2*).

In those who were not vaccinated against influenza, 24 (9.6%) cited the absence of a recommendation from their GP or obstetrician as main reason. For pertussis, 32 women (12.8%) cited pertussis vaccination during a previous pregnancy as reason for not being vaccinated.

Socio-demographic determinants of vaccination status

Potential socio-demographic determinants of the expectant mother and her partner are presented in *Table 3*. Age and work situation of the women and their partner, marital status or family income did not influence coverage rates for influenza or pertussis.

Coverage rates were significantly higher in women of Belgian origin compared to women of European (other than Belgian, p<0.05) and non-European origin (p<0.01), except for pertussis in European women. Comparable results were obtained for the origin of the partner.

Influenza coverage rates were higher in higher educated women (p<0.01) and partners (p<0.001), but no significant differences were found for pertussis.

Women previously vaccinated against influenza had a higher vaccination rate during the current pregnancy (62.2% vs 37.8%), but this did not reach statistical significance due to the small number of subjects (n = 45) for whom this information was available (p=0.1). On the

contrary, out of 32 women who were vaccinated against pertussis during a previous pregnancy against pertussis, only 7 (21.9%) were revaccinated during the current pregnancy. Women of whom the partner recently received a pertussis vaccine, had also a significant higher coverage (47.7% vs 33.6%) ($p<0.001$). Almost 97% (n=242) of the participants intended to comply with Belgian recommendations for infant immunization, regardless of whether they received the pertussis vaccine or not.

Information about vaccines

Of the 250 women surveyed, 173 (69.2%) were aware of vaccination campaigns for pregnant women, 188 (75%) received information about flu vaccination, and 183 (73.2%) received information on pertussis vaccination. Vaccination coverage was higher in women who received information on influenza vaccination (50.5% vs. 19.3% - $p<0.001$) and pertussis vaccination (50.8% vs. 7.5% - $p<0.001$). For influenza vaccination, receiving information from the GP had the highest impact (60.6% coverage) compared to 47.1% if information was given by the obstetrician and 50.0% by midwife. Information on pertussis provided by an obstetrician resulted in a higher coverage (56.6%) compared to information given by a midwife (55.6%) or GP (44.9%).

Discussion

This study is one of few surveys studying the coverage rates and influencing factors of both influenza and pertussis immunization during pregnancy. The documented coverage rate among pregnant women was 42.8% for influenza and 39.2% for pertussis. In comparison to other countries for which coverage rates in pregnant women are available these rates are acceptable, given the fact that recommendations are fairly recent. However, the goal of 50% documented influenza vaccination coverage set by the Flemish government in 2012 has not yet been reached [25]. The coverage rate for pertussis is lower compared to influenza, but information campaigns to stimulate immunization of pregnant women have mainly focussed on influenza, whereas the recommendation for vaccination against pertussis is more recent. Since the recent increase in pertussis cases in the general population as well as in children below one year of age, the Flemish community has started a campaign to raise awareness for pertussis vaccination during pregnancy for pregnant women and treating physicians such as GPs and obstetricians.

Vaccination against influenza in pregnant women seems to increase worldwide. Studies in Australia partially confirmed this positive trend with coverage rates of 30% in 2010, 40% in 2011 (Melbourne) [28] but the coverage dropped to 25% in 2012 (Sydney) [29]. Studies in the US showed similar trends with coverage rates of 38% in 2008-2009 and 63% in 2011-2012 [30].

In Europe, data on the vaccination coverage during pregnancy is limited, as only one study from the UK was published, in which the coverage varied between 14.9% and 21.6% for influenza [31].

Intentions of pregnant women to accept vaccination in pregnancy are more frequently recorded. Varan et al reported that 57% of Mexican pregnant women were willing to accept a pertussis vaccine if offered, and over 80% would accept it if recommended by an obstetrician. However, only 16% had ever heard of pertussis [32]. An Australian study confirmed this trend for pertussis [33]. In our study, the main reasons cited for receiving the influenza vaccine

during pregnancy were recommendation by a health care provider (HCP), to protect the baby, to prevent influenza and information from friends, media and family. Reasons given for not being vaccinated against influenza are safety concerns regarding the unborn child and the lack of information or recommendation. Our data thus confirm concerns regarding vaccination given by pregnant women worldwide [18,27,32-36]. A large number of studies on the safety of influenza and pertussis immunization during pregnancy published to date show no evidence for an increase in adverse reactions in pregnant women or their offspring, nor an adverse outcome of pregnancy for either vaccine.[2,3,15-20] Even though the vaccination coverage for pertussis was lower compared to influenza, the reasons for not being vaccinated were similar for both vaccines. Also, there is no evidence that mothers in our study prioritised protection of the baby over their own protection as was shown in a recent on behaviours and attitudes of pregnant women towards vaccination [37]. Nevertheless, yearly influenza vaccination is well established, whereas booster vaccines for pertussis, particularly the recommendation of a booster during every pregnancy, is novel. This could explain why women who received a pertussis booster during a previous pregnancy were less likely to be vaccinated during the current pregnancy.

The most important socio-demographic determinant of a lower vaccination coverage for both vaccines was the origin of participants and their partner, particularly in non-Europeans. This is in line with the factors that influence infant and adolescent vaccination coverage rates in Flanders, and is possibly due to a poor understanding of the local language, and the resulting difficulties to comprehend information on vaccinations given by HCPs [38].For influenza, a higher education of women and partners is associated with a higher coverage. This is probably due to better access to information on the vaccine and its advantages. In contrast, knowledge about the pertussis vaccination seems to be similar for every educational degree.

As physicians are the most trusted source of information and their recommendation has the highest impact, the treating physician should take every opportunity to promote immunization against influenza and pertussis in pregnant women. Increased access to vaccination services

in non-traditional settings has been used as a strategy in pursuit of national vaccination coverage objectives in other countries [39]. For pregnant women, midwives could have an important role in giving information on immunization during pregnancy, since they monitor women during pregnancy. In our study, information given by midwives resulted in a higher vaccination coverage for both influenza and pertussis. However, midwives have also been instructed for many years to use as little medication as possible in pregnant women. Therefore reluctance to implement the recommendation regarding vaccination cannot be excluded, and additional training of midwives may be necessary to overcome these barriers and to promote vaccination during pregnancy.

One other reason for the relatively low coverage rates in our study, could be that obstetricians recommended vaccination against influenza and pertussis, but do not administer the vaccines themselves. In Belgium, the GP is considered the primary vaccinator for adults, and pregnant women are therefore referred to their GP for vaccination. However, it has been shown that pregnant women whose HCPs both recommend and offer influenza vaccination are more likely to be vaccinated (73.6%) compared to those who only received a recommendation (47.9%) and those who received neither recommendation or offer (11.1%) [40]. Moreover, for pertussis it is important that vaccines during pregnancy are given prior to 32 weeks to reach higher titers of neonatal antibodies, which results in longer protection [41,42].

In this study only 250 participants were sampled in a single university hospital in Flanders. Further research in several Belgian hospitals is recommended to confirm whether these results can be extrapolated to the entire country. Another limitation is the large difference between documented and assumed coverage rates. Despite our efforts to trace written proof for all vaccines, this information could not be retrieved for all given doses. Therefore, the (documented) coverage rates presented here should be considered as a minimum. If oral communication on vaccination would be taken into account, coverage would increase to 62% for influenza and 46% for pertussis. We explicitly choose for a face-to-face survey because written and telephone surveys tend to overrate the actual vaccination coverage due to recall

bias [43,44]. It might be that for pregnant women recall bias is less applicable since recall is only necessary for the last 6 months. Nevertheless, immediate registration of all administered vaccines in the available electronic vaccination database would largely facilitate the retrieval of vaccination dates and thus increase the accuracy of future coverage estimates. A vaccination register, Vaccinnet, is in use since 1999 for the registration of community-based vaccination of infants and school-aged children by well-baby clinics and school health centers. Even though this register has since been open to Flemish inhabitants, registration of adult vaccination is still limited. From July 2014 onwards, one dose of the combined diphtheria-tetanus-acellular pertussis vaccine is available free of charge for all adults (including pregnant women) on the condition that the vaccine is registered in Vaccinnet. This might improve the documented data on pertussis vaccination during pregnancy. A final limitation of our study is it was conducted during pregnancy and not after delivery. The survey itself could have triggered our study subjects to comply with recommendations, but this could not be measured with the present study design. A survey immediately after delivery might pick-up vaccines given after 32 weeks of pregnancy.

A strength of this study was the high response (98%) and the fact that our population matched with census data. Only seven women refused to participate because of lack of time or a language barrier. Survey forms were available in different languages to maximize the response, and all participants were interviewed by only one of us (JL), which increased the consistency of the data. Moreover, all vaccination data were double-checked against medical files from the hospital or GP.

To improve uptake of recommended vaccines in pregnant women, HCPs (obstetricians, GP's and midwives) should receive clear guidelines and more information on the benefits and safety of vaccination during pregnancy. Based on the results of our study, special attention for women with a lower education or foreign origin is recommended.

Conclusion

The documented vaccination coverage in pregnant women is 42.8% for influenza and 39.2% for pertussis, but only 23.6% received both vaccines. These estimates should be considered as a minimum, as only documented vaccination was taken into account.

While counseling, treating physicians should pay special attention to vulnerable groups, such as pregnant women with a lower educational level and foreign origin. Midwives could be involved in informing pregnant women on the benefits of vaccination during pregnancy. Registration of all administered vaccines in the register could improve documented coverage rates.

345 Table 1: Characteristics of participants and current pregnancy
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Characteristic	Pregnant women n=250 n (%)	
Age (years)		
< 25	19	(7.6)
25-34	177	(70.8)
≥ 35	54	(21.6)
Origin[1]		
Belgian	191	(76.4)
European	24	(9.6)
Non-European	35	(14.0)
Education[2]		
Lower education	29	(11.6)
Secondary school (completed)	59	(23.6)
Higher education (Bachelor, Master, PhD)	162	(64.8)
Work Situation		
Job (full-time, independent)	146	(58.4)
Part-time job	52	(20.8)
No job (student, paid leave, housewife/man, disabled or job-seeking)	52	(20.8)
Marital status		
Cohabiting	111	(44.4)
Married	122	(48.8)
Single	10	(4.0)
Other	7	(2.8)
Family income (euros)[3]		
< 1500	9	(3.6)
1500 – 3000	73	(29.2)
> 3000	131	(52.4)
No data	37	(14.8)
Gestational age (weeks)		
28 - 32	195	(78.0)
> 32	55	(22.0)
Parity		
First pregnancy	114	(45.6)
Second pregnancy or higher parity	136	(54.4)
Current pregnancy		
Singleton	245	(98.0)
Twin	5	(2.0)
Pregnancy complications		
No	218	(87.2)
Yes	32	(12.8)
Pre-existing medical condition		
No	230	(92.0)
Yes	20	(8.0)

347 [1] Origin: based on the country of origin of the women, their partners and their parents. If the woman or one or both
348 parents was of non-Belgian origin then the subject was considered of non-Belgian origin. If the birth country
349 was located within the 27 countries of the European Union, then the subject was assigned as European. All
350 other countries were regarded as non-European. Similar classification was done for the partner.
351 [2] Education: lower education = no secondary school diploma; Secondary school = completed secondary school
352 with diploma; Higher education = continued education beyond secondary school.
353 [3] Family income was determined as the total amount of money available monthly that could be spent, including
354 alimony, wages and social security allowance.

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356 Table 2: Reasons cited for receiving or not receiving vaccination (several answers were possible)
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	Influenza N=250		Pertussis N=250	
	n (%)		n (%)	
Reasons cited for receiving vaccination during pregnancy				
Obstetrician recommended it	89	(35.6)	83	(33.2)
I want to protect my baby	82	(32.8)	77	(30.8)
I want to protect myself	59	(23.6)	25	(10.0)
GP recommended it	53	(21.1)	36	(14.4)
I think all pregnant women should get it	9	(3.6)	13	(5.2)
I normally get the influenza/pertussis vaccine	8	(3.2)	8	(3.2)
Information from family/friends/media	7	(2.8)	10	(4.0)
High risk work environment	6	(2.4	11	(4.4)
I want to prevent influenza/pertussis	5	(2.0)	7	(2.8)
Other reasons	0	(0.0)	10	(4.0)
Reasons cited for NOT receiving vaccination during pregnancy				
Vaccination was not recommended	24	(9.6)	30	(12.0)
The vaccination was delayed	21	(8.4)	35	(14.0)
I don’t believe vaccines are safe and effective	17	(6.8)	11	(4.4)
Other reasons	13	(5.2)	32	(12.8)
Concerns about the safety for my baby	8	(3.2)	8	(3.2)
An adverse reaction in the past	8	(3.2)	4	(1.6)
Careless/oblivion	6	(2.4)	5	(2.0)
Concerned about adverse reaction	6	(2.4)	1	(0.4)
GP or obstetrician advised against it	3	(1.2)	2	(0.8)

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361 Table 3: Influenza and pertussis vaccination coverage according to socio-demographic characteristics
362 (univariate analysis)
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Characteristic	Influenza			Pertussis		
	Coverage (%)	OR	95% CI	Coverage (%)	OR	95% CI
Age (yrs)						
<25	21.1	0.33	(0.09–0.95)	31.6	0.78	(0.26-2.07)
25-34	44.6			37.3		
≥35	44.4	0.99	(0.53-1.83)	48.1	1.56	(0.84-2.89)
Marital status						
Cohabiting/Married	44.2			39.5		
Single	30.0	0.54	(0.11-2.00)	20.0	0.38	(0.06-1.57)
Other	14.3	0.21	(0.1-1.26)	57.1	2.04	(0.44-10.57)
Origin pregnant women						
Belgian	49.2			42.9		
European	**20.8**	**0.27**	**(0.09-0.71)***	37.5	0.80	(0.32-1.88)
Non-European	**22.9**	**0.31**	**(0.12-0.68)****	**20.0**	**0.33**	**(0.13-0.76)***
Origin partner						
Belgian	48.7			43.5		
European	**19.0**	**0.25**	**(0.07-0.70)***	28.6	0.52	(0.18-1.34)
Non-European	**23.1**	**0.32**	**(0.11-0.78)***	23.1	0.39	(0.14-0.96)
Education pregnant women						
Low education	17.2	0.51	(0.15-1.49)	24.1	0.40	(0.14-1.05)
Secondary school (completed)	28.8			44.1		
High education (Bachelor, Master, PhD)	**52.5**	**2.73**	**(1.46-5.29)****	40.1	0.85	(0.47-1.56)
Education partner						
Low education	34.8	1.49	(0.53-4.00)	43.5	0.85	(0.33-2.18)
Secondary school (completed)	26.3			47.4		
High education (Bachelor, Master, PhD)	**53.9**	**3.27**	**(1.80-6.12)*****	35.5	0.61	(0.35-1.08)
Work pregnant women						
Job (full-time or independent)	46.6			41.8		
Part-time job	40.4	0.78	(0.40-1.47)	42.3	1.02	(0.53-1.93)
No job (student, paid leave, housewife, disabled or job-seeking)	34.6	0.61	(0.21-0.93)	30.0	0.56	(0.28-1.10)
Work partner						
Job (full-time, part-time or independent)	44.5			40.6		

No job (student, paid leave, houseman, disabled or job-seeking)	18.2	0.28	(0.04-1.10)	27.3	0.55	(0.12-1.95)
Income (euros)						
< 1500	22.2	0.46	(0.07-2.06)	22.2	0.55	(0.08-2.47)
1500-3000	38.4			34.2		
> 3000	50.4	1.63	(0.91-2.94)	43.5	1.48	(0.82-2.70)
No data	29.7	0.68	(0.28-1.56)	37.8	1.17	(0.51-2.65)

Logistic regression: *p<0.05; **p<0.01; p<0.001

Conflict of interest

JL No conflicts of interest to report.

CV Acts as principal and sub-investigator of clinical trials for different vaccine manufacturers for which the university receives grants.

MR No conflicts of interest to report

RD Acts as principal and sub-investigator of clinical trials for different vaccine manufacturers for which the hospital and university receives grants.

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