KNOWLEDGE, ATTITUDES AND PRACTICES ON INFLUENZA VACCINE DURING PREGNANCY IN QUITO, ECUADOR.

Carlos-Espartaco Erazo[a], Sofia Arriola[b], Carlos-Vinicio Erazo[c], Mario J. Grijalva[a, d], Ana-Lucía Moncayo[a].

Author Affiliation (s):

[a] Center for Research on Health in Latin America, School of Biological Sciences, College of Exact and Natural Sciences, Pontificia Universidad Católica del Ecuador, Quito, Ecuador

[b] Influenza Division, Centers for Disease Control and Prevention, Atlanta, GA, USA

[c] College of Medicine, Pontificia Universidad Católica del Ecuador, Quito, Ecuador.

[d]Infectious and Tropical Disease Institute, Department of Biomedical Sciences, Heritage College of Osteopathic Medicine, Ohio University, USA

Corresponding author: Ana-Lucía Moncayo, Center for Research on Health in Latin America, School of Biological Sciences, College of Exact and Natural Sciences, Pontificia Universidad Católica del Ecuador, Calle Pambacienda s/n and San Pedro del Valle, campus Nayón, Quito-Ecuador.

E-mail: amoncayo708@puce.edu.ec

Running head: Influenza vaccine uptake in pregnant women

ABSTRACT

Background: Vaccination is the most effective way to prevent infection and severe outcomes caused by influenza viruses in pregnant women and their children. In Ecuador, the coverage of seasonal influenza vaccination in pregnant women is low.

Objective: The aim of this study was to assess the knowledge, attitudes, practices, and factors associated with the uptake of the influenza vaccination in women in Quito-Ecuador during pregnancy.

Methods: A cross-sectional study enrolled 842 women who delivered at three main public gynecological-obstetric units of the Metropolitan District of Quito. A questionnaire regarding demographics, antenatal care, risk conditions and knowledge, attitudes and practices related to influenza vaccination was administered. We examined factors associated with vaccination using log-binomial regression models.

Results: A low vaccination rate (36.6%) against influenza was observed among pregnant women. The factors associated with vaccination included the recommendations from health providers (adjusted PR: 15.84; CI 95% 9.62-26.10), belief in the security of the influenza vaccine (adjusted PR: 1.53; CI 95% 1.03-2.37) and antenatal care (adjusted PR: 1.21; CI 95% 1.01-1.47). The most common reasons for not vaccinating included the lack of recommendation from health care providers (73.9%) and lack of access to vaccine (9.0%).

Conclusions: Our results show that recommendations by a health provider and antenatal care affected vaccination coverage, reflecting their importance for vaccination campaign success. Therefore, health educational programs aimed to pregnant women and antenatal care providers have the most potential to increase influenza vaccination rates. It is necessary develop further studies to understand the barriers for health care providers regarding influenza vaccination in Ecuador.

Keywords: influenza vaccine, pregnant women, health providers, Quito, Ecuador

1. INTRODUCTION

Globally, approximately 3-5 million cases of serious illness from influenza virus occur every year and 290,000-650,000 of these results in death (1). In May 2009, the first cases of pandemic influenza A (pH1N1) were detected in Ecuador. Between 2011-2014, 1,872 laboratory-confirmed influenza cases were reported in the country of which 40% were influenza A (H3N2) and 39,6% were influenza A (H1N1)pdm09 (2). In 2016, there was an increase in the circulation of influenza during the wet season (December to June). By April 2016 (epidemiological week 17), 469 positive cases of laboratory-confirmed influenza were detected and 75.3% were by influenza A (H1N1)pdm09 (3). The influenza activity also increased from November 2017 to March 2018 (epidemiological week 47-10) reporting 1,280 cases of influenza, and 1,133 (88.5%) were by influenza A (H1N1)pdm09 (case-fatality rate of 9.1%) (4). Historically (2013-2016), the case-fatality rate in Ecuador has fluctuated between 9% and 13% (4). The seasonality of influenza activity in Ecuador follows that of temperate climatic regions in the Southern hemisphere, primary peak between beginning of July and end of August and the secondary peak on late January (2,5).

Pregnant women and infants under six months are among the population subgroups considered to be at high risk for serious influenza-related morbidity and mortality, as illustrated during the 1928 and 2009-2010 influenza A (H1N1) pandemics (6). Influenza

vaccination is the most effective way to prevent influenza virus infection and hence its severe outcomes (7). According to this evidence and the vaccine safety and effectiveness, the World Health Organization (WHO), in 2012, recommended that countries should considered pregnant women as a priority group for vaccination (8). Maternal influenza immunization has been recommended to protect pregnant women from severe outcomes related to influenza virus infection (6,9–11), and recent data show an additional benefit in infants of immunized women up to 6 months of age (12–14).

The Ministry of Public Health (MOPH) of Ecuador incorporated the seasonal influenza vaccine to its national vaccination schedule in 2006 and priority groups were included progressively according to WHO recommendations. The MOPH provides inactivated vaccine from northern hemisphere annually through campaigns (December to February) and free of charge. In addition, the vaccine is offered in health services during the season until exhaustion of the vaccine or its expiration (5). In May 2016, an additional vaccination campaign focusing on priority groups was developed due to an outbreak presented earlier that month. The importance of annual influenza vaccination is highlighted in different media and healthcare centers as well as on MOPH's website. Despite these efforts, Ecuador has reported low coverage rates of the influenza vaccine in pregnant women (55% in 2015-2016 and 43% in 2016-2017) (5,15).

Many studies have tried to determine the factors influencing coverage of vaccination against influenza during pregnancy. Different authors have highlighted that vaccination recommendation by health professionals is the main reason why pregnant women chose to be vaccinated against influenza (16–19). Other studies have identified additional

influences such as: socio-economic characteristics, fear of side effects, doubts about the security and effectiveness of the vaccine, fear of needles/pain or under-estimation of personal risk (20–24).

Currently, in Ecuador, there is not available data on the factors affecting vaccination among pregnant women. Therefore, this study aimed to assess knowledge, attitudes and practices of pregnant women regarding influenza vaccination in Quito, Ecuador and to determine the influencing factors associated with vaccination during 2015-2016 campaign. The results of this study may help health authorities to plan and implement policies to improve influenza vaccination coverage among pregnant women.

2. MATERIALS AND METHODS

2.1. Study design and setting

In Ecuador, two influenza vaccination campaigns were carried out for all priority groups, including pregnant women (December to February 2015-2016 and May 2016). We carried a cross-sectional survey on the knowledge, attitudes and practices regarding the influenza vaccination during pregnancy from September 2016 to January 2017 in three public hospitals in Quito, the capital of Ecuador. Quito sits at an altitude of 2,850 meters above sea level and has 2,239,191 inhabitants being the second most populous city in Ecuador (25).

2.2. Sampling

The three public hospitals chosen (Hospitals Luz Elena Arizmendi, Hospital Isidro Ayora and Hospital Pablo Arturo Suárez) had the highest number of births in 2015 and

each hospital is located in a specific area of the city (south, center and north, respectively). In these hospitals, women in immediate postpartum period between 18 and 50 years old were recruited. We interviewed a sample of 854 women (Hospital Luz Elena Arismendi, n=168; Hospital Isidro Ayora, n= 536 and Hospital Pablo Arturo Suárez, n=150 women) with probability of selection proportional to the number of live births reported for each health care facility in 2015. This sample size provided 80% power to detect a 10% difference in survey responses to questions about knowledge, attitudes and practices between vaccinated and unvaccinated women (assuming 50% of surveyed women are vaccinated, a 10% non-response rate and alpha = 0.05). Women who did not reside within the Metropolitan District of Quito were excluded from the study.

2.3. Procedure

Signed informed consent was obtained from each eligible women interested in enrolling prior to administration of survey. A modified survey from the study "Policies, knowledge, attitudes and practices of the use of seasonal influenza vaccine, oseltamivir and palivizumab in Guatemala, 2016" (Centers for Disease Control and Prevention, Atlanta, GA, USA and University del Valle de Guatemala- Cooperative Agreement; unpublished data) was applied by trained interviewers. The survey included questions on demographics, educational level, employment, antenatal care, high-risk conditions, knowledge (influenza, influenza vaccine and severity of influenza), attitudes (perception of vaccine safety and effectiveness) and practices (uptake of influenza vaccine) about influenza vaccine, influenza vaccine during pregnancy, reasons for not receiving vaccination, health provider recommendation and offer of the vaccine. In order to validate the questionnaire, a team of experts (Influenza Division, CDC, Atlanta, USA)

reviewed the items to ensure clarity and adequacy of comprehension prior to administration. Field validation was then carried out and the survey instrument was adjusted accordingly. Self-reported data about influenza vaccination was corroborated through vaccination cards and medical records. The survey was applied by trained interviewers.

2.4. Statistical analysis

For the analysis of the data, the vaccination report of the mother was used. Age was categorized in four groups: 18-24, 25-30, 31-35, ≥36. Patients were classified as high obstetric risk if they reported having diagnosis of bronchitis, asthma, chronic obstructive pulmonary disease, cystic fibrosis, diabetes, HIV, cardiovascular disease, chronic kidney disease or stroke. We calculated the percentage of women that were vaccinated against influenza by provider recommendation and offer of influenza vaccination. Among unvaccinated persons, we categorized main reasons reported for not being vaccinated into 4 main groups: access issues, not wanting or needing the vaccine, concern with safety, lack of offer / recommendation of the vaccine. We also assessed the categorized main reported reasons for not being vaccinated by demographic characteristics, education, number of children, antenatal care, and high-risk conditions. Finally, we analyzed the relationship of receipt of influenza vaccination with predictors for vaccination (age, educational level, marital status, employment, antenatal care, number of children, high-risk conditions, gestational age at birth, recommendation or offer of vaccination by health care provider, and knowledge and attitudes about vaccination) by bivariate and multivariate analysis (log-binomial regression). We present unadjusted and adjusted prevalence ratios (PRs) with 95% confidence intervals. Data were analyzed using STATA® software (version 14.0).

2.5. Ethical considerations

Signed informed consent was obtained from all participants, following protocols approved by the Institutional Review Board of Pontifical Catholic University of Ecuador (CEISH-164-2016) and Direction of Intelligence for Health of the Ministry of Public Health of Ecuador (MSP-DIS-2016-0143-O).

3. RESULTS

3.1. Characteristics of study population

A total of 854 pregnant women were invited to participate in the survey. Of those invited, 12 (1.4%) were excluded because they were not residents of Quito city and only arrived at selected hospitals for delivery.

The characteristics of the sample are described in Table 1. Almost three-quarters of participants in this survey were between 18 and 30 years old, 86% were mixed-race women and 58% finished high school. The majority of women were married or cohabited with a partner (79%), 44.2% were homemakers and approximately two thirds (65%) of women reported having at least one other child prior to this pregnancy. Nearly all women (98.7%) reported attending at least one antenatal visit and 81% reported more than four antenatal visits. Only 8% of women reported having chronic diseases.

3.2. Vaccine coverage

The percentage of women who reported having been vaccinated against influenza at any time in their pregnancy was 36.6% and vaccination data was confirmed with the

vaccination card and/or medical records in 67% of vaccinated women (Table 1). Sixty percent of women have been vaccinated during the second trimester of pregnancy.

3.3 Influenza and influenza vaccine knowledge and attitudes

Knowledge about the severity of influenza and the existence of a vaccine was higher among women who reported having been vaccinated compared to those who reported not having been vaccinated ($p = 0.017$ and $p < 0.001$, respectively, Figure 1A and 1B). Vaccinated women perceived that the influenza vaccine is safe (95.8% vs 71.7%, respectively) and effective (68.5% vs. 61.4%, respectively) in a higher proportion than unvaccinated women ($p<0.001$ y $p=0.030$, respectively, Figure 1C and 1D).

3.4. Reasons for not receiving influenza vaccination

Among the four categories (e.g. access, not wanting/needing the vaccine, safety concerns and lack of recommendation/offer of the vaccine), the most frequent reason identified as a barrier to vaccination among pregnant women was the lack of recommendation/offer of the vaccine by the health provider (73.9%). Other reasons in smaller proportion were lack of access (9.0%), concern with the safety of the vaccine (6.2%), not wanting/needing the vaccine (3.7%) and other causes (7.3%) (Table 2). The most common reasons for non-vaccination among women with complete basic education or higher were also related to not having received a recommendation/offer of the vaccine by the health care provider, vaccine safety concerns and other reasons, whereas for women without any educational level or with incomplete basic education, not wanting/needing the vaccine and access barriers were the most common reason for non-vaccination. ($p= 0.001$, Table 2).

3.5. Provider recommendation and offer of influenza vaccination

Among women who indicated that their health care provider recommended and offered the influenza vaccine, 82.7% reported having been vaccinated for influenza since the end of 2015. Among those who reported that their health care provider recommended but did not offer vaccination against influenza, 15.0% reported having been vaccinated for influenza. Finally, 4.3% of the respondents who did not receive either a recommendation or an influenza vaccination offer reported having been vaccinated ($p < 0.001$, Figure 2).

3.6. Relationship between determinants and vaccination

Number of antenatal care visits, knowledge about vaccine safety and having received recommendation (with or without offer of the vaccine) by health care personnel was associated with vaccination during pregnancy in both the bivariate and multivariate analysis ($p < 0.005$; Table 3). Specifically, the vaccination rate was 1.67 times higher in women who reported having five or more antenatal controls during pregnancy than in women who reported having fewer than five controls and the association was maintained after adjustment by other predictors (adjusted PR 1.21, 95% CI 1.01-1.47). Women who perceived vaccination against influenza as safe had higher vaccination rates than those who did not (adjusted PR 1.53, 95% CI 1.03-2.37). Finally, women who reported receiving recommendation but were not offered vaccination and those who reported receiving both recommendation and were offered vaccination had 3.17 (95% CI 1.57-6.40) and 15.84 (95% CI 9.62-26.10) greater likelihood of having received the vaccine compared to women who did not receive a recommendation/offer.

4. DISCUSION

Our study found a low influenza vaccination rates in pregnant women in Quito-Ecuador and identified some barriers that could contribute to low vaccination coverage. Those women who were vaccinated knew about the severity of influenza, about the existence of a vaccine, and perceived vaccination against influenza as safe and effective. Our study also suggests that the main barrier for not receiving the vaccine is the lack of recommendation/offer regarding influenza vaccine by health care provider. Among the determinants, recommendation/offer of vaccine increases the likelihood of pregnant women vaccination. Other factors associated with vaccination were knowledge about vaccine safety and more than five antenatal care visits.

The vaccination rate reported in this study (36.6%) is lower than those reported for Ecuador in 2015-2016 (55%) and 2016-2017 (43%) (5) and for those reported by other countries of the region, such as Venezuela (41%) and Bolivia (49%) for 2015. The highest coverages were reported by Chile (72%), Colombia (72%) and Brazil (83%) (15). In Ecuador, the coverage of all vaccines (including the influenza vaccine) indicates a gradual decrease since 2013 (5). The Evaluation of National Strategy of Immunizations (5) revealed two elements related to this fact: 1) the Immunization Program underwent a transition, becoming part of the National Immunization Strategy. This fact implied a disaggregation of functions between different actors without an effective articulation of actions; and 2) the lack of budget allocation in a sustainable manner for operational activities of vaccination strategy. Given these facts and the results of our study, there is an urgent need to implement a contingency plan to improve

short-term vaccination coverage and reduce the risk of transmission of vaccine-preventable diseases in Ecuador.

Our results are in agreement with previous studies that show that a compelling recommendation from a provider is one of the most important factors in a pregnant woman's decision to undergo vaccination (19,26–32). Indeed, our study identified that the lack of recommendation was a barrier for vaccination among pregnant women. Knowledge about influenza and vaccination by health workers has an impact on the decisions made regarding the vaccination of their patients and themselves. Studies show that maternal care providers with high levels of knowledge and positive attitudes consistently discuss and recommend influenza vaccine to their patients in greater proportion than other health providers (33,34). Similarly, health professionals who know the national guidelines on influenza vaccination are more likely to discuss and recommend the vaccine than those who do not know them (35). To our knowledge, there are no studies in Ecuador on the knowledge and attitudes of health workers regarding the influenza vaccine. Other studies demonstrate that health care workers are often reluctant to receive a vaccine (36,37), have concerns about side effects, demonstrate a lack of faith in its efficacy and have concerns in the severity of the disease (38,39). Understanding health provider barriers is vitally important because it is not possible to overcome vaccination barriers among pregnant women if health providers themselves are not fully convinced about benefits of maternal immunization. Therefore, working to promote practices related to the recommendation and offer of influenza vaccination among health care providers will be crucial to improving vaccination coverage during pregnancy.

In our study, women who reported perceiving the influenza vaccine as safe and effective had the highest vaccination rates and vaccine safety concern was a reason for not receiving vaccination among 6.2% of non-vaccinated women. Lack of knowledge due to insufficient information about the safety of the influenza vaccine has previously been linked to lower vaccination rates (20,21,40). The vaccine is considered safe throughout pregnancy and during lactation, and has been administered to pregnant women for many years without having observed adverse effects (6,41). Therefore, efforts are needed to educate pregnant women and the population in general regarding the safety and effectiveness of the influenza vaccine in order to improve vaccination coverage at this risk group.

Scheminske *et al*. showed high vaccination rates in women who practice healthy behaviors during pregnancy (42). In our study, having five or more antenatal visits, as a proxy for healthy behaviors, increase the probability of vaccination which is in accordance to other studies (43–45). Antenatal check-ups are essential to promoting the benefits of influenza vaccination and to offering the vaccine to pregnant women (46). If women receive few antenatal care visits and/or present late for antenatal care, it may be useful to offer influenza vaccination over a longer period of time, rather than a single 2-month campaign in order to improve vaccine coverage. In addition, influenza vaccination may also serve as an inducement to seek antenatal care if offered as part of a focused antenatal care package. Altogether, different strategies of vaccine delivery to pregnant women need to be evaluated in order to inform policy decisions in countries where influenza circulation is not confined to a single seasonal peak.

Our study showed different reasons for not to being vaccinated according to educational level of women. The main reasons for not to being vaccinated among illiterate women or with incomplete basic education was not need/want the vaccine and lack of access to vaccination. Studies have shown that people who have a higher education level and/or household income are more likely to receive preventive health services because they may have more knowledge about the importance of health-preventive care and the effectiveness of preventive strategies and more access to health-related services (47,48).

Care is required in interpreting the findings of this study for potential limitations. Firstly, it is difficult to precisely determine temporal sequence between the dependent and independent variables in cross-sectional studies. Second, the study sample was not randomly selected but rather a convenience sample, which makes generalization difficult and affects the external validity. Finally, thirty percent of vaccinated women lacked documentation of influenza vaccine status and self-report of vaccination could be affected by social desirability and forgetfulness; however, analysis of a subsample that included only those with written documentation of vaccination showed similar findings (data not shown).

5. CONCLUSION

In conclusion, the low rate of vaccination of pregnant women in Quito supports the need to develop health educational programs in order to improve the level of knowledge about seasonal influenza and on the efficacy and safety of vaccination among this population. Furthermore, it is necessary to further study health provider barriers regarding influenza vaccination in Ecuador. Our data indicate that education and

training of health care providers is needed to enhance their role as vaccinators, which could potentially increase the number of those willing to recommend and offer vaccination. Finally, other methods of vaccine delivery need to be evaluated, such as year-round antenatal care distribution or to incorporate influenza vaccination into other programs that focus on the most vulnerable pregnant women in tropical countries where influenza circulation is not confined to a single seasonal peak.

Author constributions

Carlos-Espartaco Erazo: Md. Erazo participated in data collection, analysis and interpretation of the data, and the drafting of the manuscript.

Sofia Arriola: PhD. Arriola participated in the design of the study and scientific technical advice.

Carlos Erazo: MPH. Erazo participated in design of the study and data collection instruments, and interpretation of the data.

Mario J. Grijalva: PhD. Grijalva participated in the drafting and revision of the manuscript

Ana-Lucía Moncayo: PhD. Moncayo participated in the design of the study, the analysis and interpretation of the data, and the drafting and revision of the manuscript.

Funding

This study was supported by Pontificia Universidad Católica del Ecuador (Grant number M13398). The funder had no role in the study design, collection, analysis or interpretation of data, writing of the report or decision to submit the article for publication.

Conflict of interest

The authors have not conflicts of interest.

Acknowledgments

Thanks to the Influenza Division of the Centers for Diseases Control and Prevention (CDC) for their scientific technical advice. Also, we are grateful to the health care providers, the administrative staff and the participating patients of the Hospital Luz Elena Arizmendy, Hospital Isidro Ayora and Hospital Pablo Arturo Suárez for their co-operation

References

1. World Health Organization. Influenza (Seasonal) [Internet]. WHO Media Centre; 2016 [cited 2018 Feb 21]. Available from: http://www.who.int/mediacentre/factsheets/fs211/en/
2. Caini S, Alonso WJ, Balmaseda A, Bruno A, Bustos P, Castillo L, et al. Characteristics of seasonal influenza A and B in Latin America: Influenza surveillance data from ten countries. Shaman J, editor. PLoS One [Internet]. Public Library of Science; 2017 Mar 27 [cited 2017 Jun 8];12(3):e0174592. Available from: http://dx.plos.org/10.1371/journal.pone.0174592
3. World Health Organization. Influenza Laboratory Surveillance Information [Internet]. FluNet. 2018. Available from: http://apps.who.int/flumart/Default?ReportNo=2
4. Ministerio de Salud Pública del Ecuador. Influenza Actualización Epidemiológica SE 47, 2017 - SE 10. 2018. 2018; Available from: http://www.salud.gob.ec/wp-content/uploads/2016/03/gaceta-influenza.pdf
5. Ministerio de Salud Pública del Ecuador. Evaluación de la Estrategia Nacional de Inmunizaciones [Internet]. 2017 [cited 2017 Oct 12]. Available from: http://www.paho.org/ecu/index.php?option=com_docman&view=download&category_slug=inmunizaciones&alias=673-evaluacion-de-la-estrategia-nacional-de-inmunizaciones-ecuador-2017&Itemid=599
6. Somerville LK, Basile K, Dwyer DE, Kok J. The impact of influenza virus infection in pregnancy. Future Microbiol [Internet]. 2018;13(2):263–74. Available from: http://www.futuremedicine.com/doi/10.2217/fmb-2017-0096
7. Cox NJ, Subbarao K. Influenza. Lancet [Internet]. 1999 [cited 2017 May 31];354(9186):1277–82. Available from: http://www.sciencedirect.com/science/article/pii/S0140673699012416
8. World Health Organization. Vaccines against influenza WHO position paper – November

2012. Wkly Epidemiol Rec [Internet]. 2012;47(87):461–76. Available from: http://www.who.int/wer/2012/wer8747.pdf?ua=1

9. Katz MA, Gessner BD, Johnson J, Skidmore B, Knight M, Bhat N, et al. Incidence of influenza virus infection among pregnant women: a systematic review. BMC Pregnancy Childbirth [Internet]. 2017 [cited 2017 Jun 10];17 (1):155. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5450114/pdf/12884_2017_Article_1333.pdf

10. Vojtek I, Dieussaert I, Doherty TM, Franck V, Hanssens L, Miller J, et al. Maternal immunization: Where are we now and how to move forward? Ann Med [Internet]. Informa UK Limited, trading as Taylor & Francis Group; 2018;0(0):1–36. Available from: https://www.tandfonline.com/doi/full/10.1080/07853890.2017.1421320

11. Thompson MG, Li DK, Shifflett P, Sokolow LZ, Ferber JR, Kurosky S, et al. Effectiveness of seasonal trivalent influenza vaccine for preventing influenza virus illness among pregnant women: A population-based case-control study during the 2010-2011 and 2011-2012 influenza seasons. Clin Infect Dis. 2014;58(4):449–57.

12. Nunes MC, Cutland CL, Jones S, Downs S, Weinberg A, Ortiz JR, et al. Efficacy of maternal influenza vaccination against all-cause lower respiratory tract infection hospitalizations in young infants: Results from a randomized controlled trial. Oxford Univ Press [Internet]. 2017 [cited 2017 Jun 10];65(7):1066–1071. Available from: https://oup.silverchair-cdn.com/oup/backfile/Content_public/Journal/cid/PAP/10.1093_cid_cix497/1/cix497.pdf

13. Eick AA, Uyeki TM, Klimov A, Hall H, Reid R, Santosham M, et al. Maternal influenza vaccination and effect on influenza virus infection in young infants. Arch Pediatr Adolesc Med [Internet]. 2011;165(2):104–11. Available from: https://www.researchgate.net/publication/47336544_Maternal_Influenza_Vaccination_and_Effect_on_Influenza_Virus_Infection_in_Young_Infants

14. Zaman K, Roy E, Arifeen SE, Rahman M, Raqib R, Wilson E, et al. Effectiveness of maternal influenza immunization in mothers and infants. N Engl J Med [Internet]. 2008;359(15):1555–64. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18799552

15. Pan American Health Organization; World Health Organization. Influenza Vaccine Coverage in countries and territories of the Americas [Internet]. World Health Organization; 2016 [cited 2018 Feb 27]. Available from: http://ais.paho.org/imm/InfluenzaCoverageMap.asp

16. Yuen CYS, Tarrant M. A Comprehensive Review of Influenza and Influenza Vaccination During Pregnancy. J Perinat Neonatal Nurs [Internet]. 2014;28(4):261–70. Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00005237-201410000-00007

17. Arriola CS, Vasconez N, Thompson M, Mirza S, Moen AC, Bresee J, et al. Factors associated with a successful expansion of influenza vaccination among pregnant women in Nicaragua. Vaccine [Internet]. Elsevier Ltd; 2016;34(8):1086–90. Available from: http://dx.doi.org/10.1016/j.vaccine.2015.12.065

18. Jung EJ, Noh JY, Choi WS, Seo Y Bin, Lee J, Song JY, et al. Perceptions of influenza vaccination during pregnancy in Korean women of childbearing age. Hum Vaccin Immunother [Internet]. Taylor & Francis; 2016;12(8):1997–2002. Available from: https://www.tandfonline.com/doi/full/10.1080/21645515.2015.1119347

19. Stark LM, Power ML, Turrentine M, Samelson R, Siddiqui MM, Paglia MJ, et al. Influenza Vaccination among Pregnant Women: Patient Beliefs and Medical Provider Practices. Infect Dis Obstet Gynecol. Hindawi Publishing Corporation; 2016;2016:3281975.

20. Vila-Candel R, Navarro-Illana P, Navarro-Illana E, Castro-Sánchez E, Duke K, Soriano-Vidal FJ, et al. Determinants of seasonal influenza vaccination in pregnant women in Valencia, Spain. BMC Public Health [Internet]. 2016 [cited 2017 Jun 10];16:1173.

Available from: http://download.springer.com/static/pdf/726/art%253A10.1186%252Fs12889-016-3823-1.pdf?originUrl=http%3A%2F%2Fbmcpublichealth.biomedcentral.com%2Farticle%2F10.1186%2Fs12889-016-3823-1&token2=exp=1497117088~acl=%2Fstatic%2Fpdf%2F726%2Fart%25253A10.1186%2525

21. Napolitano F, Napolitano P, Angelillo IF. Seasonal influenza vaccination in pregnant women: knowledge, attitudes, and behaviors in Italy. BMC Infect Dis [Internet]. 2017 [cited 2017 Jun 10];17:48. Available from: http://download.springer.com/static/pdf/687/art%253A10.1186%252Fs12879-016-2138-2.pdf?originUrl=http%3A%2F%2Fbmcinfectdis.biomedcentral.com%2Farticle%2F10.1186%2Fs12879-016-2138-2&token2=exp=1497116961~acl=%2Fstatic%2Fpdf%2F687%2Fart%25253A10.1186%25252Fs

22. Wilson RJ, Paterson P, Jarrett C, Larson HJ. Understanding factors influencing vaccination acceptance during pregnancy globally: A literature review. Vaccine [Internet]. Elsevier Ltd; 2015;33(47):6420–9. Available from: http://www.sciencedirect.com/science/article/pii/S0264410X15011731?via%3Dihub

23. Thompson MG, Gaglani MJ, Naleway A, Ball S, Henkle EM, Sokolow LZ, et al. The expected emotional benefits of influenza vaccination strongly affect pre-season intentions and subsequent vaccination among healthcare personnel. Vaccine [Internet]. 2012;30(24):3557–65. Available from: http://www.sciencedirect.com/science/article/pii/S0264410X12004549

24. Bali NK, Ashraf M, Ahmad F, Khan UH, Widdowson M-A, Lal RB, et al. Knowledge, attitude, and practices about the seasonal influenza vaccination among healthcare workers in Srinagar, India. Influenza Other Respi Viruses [Internet]. 2013;7(4):540–5. Available

from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84879119470&partnerID=tZOtx3y1

25. Instituto Nacional de Estadística y Censos I. Fascículo provincial Pichincha. Fascículo Prov Pichincha [Internet]. 2010;0–7. Available from: http://www.ecuadorencifras.gob.ec/fasciculos-provinciales/

26. Arriola CS, Mercado-Crespo MC, Rivera B, Serrano-Rodriguez R, Macklin N, Rivera A, et al. Reasons for low influenza vaccination coverage among adults in Puerto Rico, influenza season 2013-2014. Vaccine [Internet]. Elsevier Ltd; 2015;33(32):3829–35. Available from: http://www.sciencedirect.com/science/article/pii/S0264410X15009081

27. Bödeker B, Walter D, Reiter S, Wichmann O. Cross-sectional study on factors associated with influenza vaccine uptake and pertussis vaccination status among pregnant women in Germany. Vaccine [Internet]. Elsevier Ltd; 2014;32(33):4131–9. Available from: http://dx.doi.org/10.1016/j.vaccine.2014.06.007

28. Blanchard-Rohner G, Meier S, Ryser J, Schaller D, Combescure C, Yudin MH, et al. Acceptability of maternal immunization against influenza: The critical role of obstetricians. J Matern Neonatal Med. 2012;25(9):1800–9.

29. Moniz M, Beigi R. Clinical experiences, challenges, and opportunities in vaccine acceptance. Hum Vaccines Immunother [Internet]. 2014;10(9):2574–5. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4977442/pdf/khvi-10-09-970901.pdf

30. Laenen J, Roelants M, Devlieger R, Vandermeulen C. Influenza and pertussis vaccination coverage in pregnant women. Vaccine [Internet]. Elsevier Ltd; 2015;33(18):2125–31. Available from: http://dx.doi.org/10.1016/j.vaccine.2015.03.020

31. Myers KL. Predictors of maternal vaccination in the United States: An integrative review of the literature. Vaccine [Internet]. Elsevier Ltd; 2016;34(34):3942–9. Available from: http://dx.doi.org/10.1016/j.vaccine.2016.06.042

32. Wiley KE, Massey PD, Cooper SC, Wood NJ, Ho J, Quinn HE, et al. Uptake of influenza

vaccine by pregnant women: A cross-sectional survey. Med J Aust. 2013;198(7):373–5.

33. Englund JA. Maternal immunization with inactivated influenza vaccine: Rationale and experience. Vaccine. 2003;21(24):3460–4.

34. Martinello RA, Jones L, Topal JE. Correlation between healthcare workers' knowledge of influenza vaccine and vaccine. Infect Control Hosp Epidemiol. 2014;24(11):845–7.

35. Tong A, Biringer A, Ofner-Agostini M, Upshur R, McGeer A. A Cross-Sectional Study of Maternity Care Providers' and Women's Knowledge, Attitudes, and Behaviours Towards Influenza Vaccination During Pregnancy. J Obstet Gynaecol Canada [Internet]. Elsevier Masson SAS; 2008;30(5):404–10. Available from: http://dx.doi.org/10.1016/S1701-2163(16)32825-0

36. Aguilar-Díaz F del C, Jiménez-Corona ME, Ponce-de-León-Rosales S. Influenza vaccine and healthcare workers. Arch Med Res. 2011;42(8):652–7.

37. Seale H, Wang Q, Yang P, Dwyer DE, Wang X, Zhang Y, et al. Influenza vaccination amongst hospital health care workers in Beijing. Occup Med (Chic Ill). 2010;60(5):335–9.

38. Willis BC, Wortley P. Nurses' attitudes and beliefs about influenza and the influenza vaccine: A summary of focus groups in Alabama and Michigan. Am J Infect Control. 2007;35(1):20–4.

39. Dvalishvili M, Mesxishvili D, Butsashvili M, Kamkamidze G, McFarland D, Bednarczyk RA. Knowledge, attitudes, and practices of healthcare providers in the country of Georgia regarding influenza vaccinations for pregnant women. Vaccine [Internet]. Elsevier Ltd; 2016;34(48):5907–11. Available from: http://dx.doi.org/10.1016/j.vaccine.2016.10.033

40. Mayet AY, Al-Shaikh GK, Al-Mandeel HM, Alsaleh NA, Hamad AF. Knowledge, attitudes, beliefs, and barriers associated with the uptake of influenza vaccine among pregnant women. Saudi Pharm J SPJ Off Publ Saudi Pharm Soc [Internet]. Elsevier; 2017 Jan [cited 2017 Jun 10];25(1):76–82. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28223865

41. World Health Organization. Vacunación antigripal de las mujeres durante el embarazo [Internet]. 2017 [cited 2018 Feb 21]. Available from: http://www.who.int/vaccine_safety/committee/topics/influenza/pregnancy/es/

42. Scheminske M, Henninger M, Irving SA, Thompson M, Williams J, Shifflett P, et al. The Association Between Influenza Vaccination and Other Preventative Health Behaviors in a Cohort of Pregnant Women. Heal Educ Behav [Internet]. SAGE Publications Inc; 2014 Dec 12;42(3):402–8. Available from: https://doi.org/10.1177/1090198114560021

43. Mendoza-Sassi RA, Cesar JA, Cagol JM, Duarte IA, Friedrich LM, Santos VK Dos, et al. 2010 A(H1N1) vaccination in pregnant women in Brazil: identifying coverage and associated factors. Cad Saude Publica. 2015;31(6):1247–56.

44. Blondel B, Mahjoub N, Drewniak N, Launay O, Goffinet F. Failure of the vaccination campaign against A(H1N1) influenza in pregnant women in France: Results from a national survey. Vaccine. 2012;30(38):5661–5.

45. Maher L, Hope K, Torvaldsen S, Lawrence G, Dawson A, Wiley K, et al. Influenza vaccination during pregnancy: Coverage rates and influencing factors in two urban districts in Sydney. Vaccine [Internet]. Elsevier Ltd; 2013;31(47):5557–64. Available from: http://dx.doi.org/10.1016/j.vaccine.2013.08.081

46. Mak DB, Regan AK, Joyce S, Gibbs R, Effler P V. Antenatal care provider's advice is the key determinant of influenza vaccination uptake in pregnant women. Aust New Zeal J Obstet Gynaecol [Internet]. 2015 Apr [cited 2017 Mar 8];55(2):131–7. Available from: http://doi.wiley.com/10.1111/ajo.12292

47. Christenson B, Lundbergh P. Comparison between cohorts vaccinated and unvaccinated against influenza and pneumococcal infection. Epidemiol Infect [Internet]. 2002;129(3):515–24. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2869913/pdf/12558334.pdf

48. Worasathit R, Wattana W, Okanurak K, Songthap A, Dhitavat J, Pitisuttithum P. Health

education and factors influencing acceptance of and willingness to pay for influenza vaccination among older adults. BMC Geriatr [Internet]. BMC Geriatrics; 2015;15(1):1–14. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4620638/pdf/12877_2015_Article_137.pdf

Figures and Tables

Table 1. Characteristics of study population (postpartum women) in Quito, Ecuador, 2016-2017 (n = 842).

Participant characteristics	n (%)
Age	
18-24	363 (43.1%)
25-30	260 (30.9%)
31-35	123 (14.6%)
≥36	96 (11.4)
Race	
White	27 (3.4%)
Mixed	723 (85.8%)
Indigenous	54 (6.4%)
Black	30 (3.5%)
Other	8 (0.9%)
Education	
Complete higher education or graduate degree	83 (9.9%)
Complete high school or incomplete higher education	407 (48.3%)
Complete basic education or incomplete high school	222 (26.4%)
Illiterate or incomplete basic education	130 (15,4%%)
Marital status	
Married	288 (34.2%)
Cohabited with a partner	376 (44.7%)
Separated / Widowed / Divorced - Never Married or Unmarried	178 (21.1%)
Employment	
Public or private employee	175 (20.8%)
Independent worker	172 (20.4%)
Homemaker	372 (44.2%)
Student	119 (14.1%)
Unemployed	4 (0.5%)
Number of children (prior to this pregnancy)	
0	295 (35.0%)
1-2	459 (54.5%)
3-6	88 (10.5%)
Number of antenatal visits	
0	11 (1.3%)
1 to 4	150 (17.8%)
≥5	681 (80.9%)
Gestational age at birth	
24-36 weeks	122 (14.5%)
37-42 weeks	720 (85.5%)
High-risk conditions	
No	775 (92.0%)
Yes	67 (8.0%)
Received influenza vaccination (self-reported)*	
Yes	308 (36.6%)
Confirmed with vaccination card	206 (66.9%)
No	534 (63.4%)

Received influenza vaccination (vaccination card/medical records)**	
Yes	206 (24.5%)
No	636 (75.5%)

*Vaccination reported by the women used for analysis; **Vaccination confirmed by vaccination card/medical records

Table 2. Main reasons for not receiving the influenza vaccine during pregnancy (n = 520), Quito, Ecuador, 2016-2017.

	All n (%)	Main reason					
		Concern about vaccine safety n (%)	Do not need / do not want n (%)	Access barriers n (%)	Did not receive recommendation / offer n (%)	Other reasons* n (%)	*p*-value ǂ
All	520 (100)**	32 (6.2)	19 (3.7)	47 (9.0)	384 (73.9)	38 (7.3)	
Age							0.509
18-24	226 (43.5)	19 (59.4)	9 (47.4)	17 (36.2)	169 (44.0)	12 (31.6)	
25-30	159 (30.6)	8 (25.0)	4 (21.1)	18 (38.3)	117 (30.5)	12 (31.6)	
31-35	77 (14.8)	2 (6.2)	4 (21.0)	9 (19.1)	54 (14.1)	8 (21.0)	
≥36	58 (11.1)	3 (9.4)	2 (10.5)	3 (6.4)	44 (11.4)	6 (15.8)	
Education							**0.001**
Complete higher education or graduate degree	60 (11.5)	2 (6.3)	1 (5.3)	3 (6.4)	47 (12.2)	7 (18.4)	
Complete high school or incomplete higher education	244 (46.9)	16 (50.0)	6 (31.6)	21 (44.7)	180 (46.9)	21 (55.3)	
Complete basic education or incomplete high school	134 (25.8)	13 (40.6)	5 (26.3)	7 (14.9)	103 (26.8)	6 (15.8)	
Illiterate or incomplete basic education	82 (15.8)	1 (3.1)	7 (36.8)	16 (34.0)	54 (14.1)	4 (10.5)	
Number of children (prior to this pregnancy)							0.065
None	188 (36.2)	17 (53.1)	4 (26.3)	12 (25.5)	146 (38.0)	8 (21.0)	
1-2	285 (54.8)	12 (37.5)	12 (63.2)	29 (61.7)	208 (54.2)	24 (63.2)	
3-6	47 (9.0)	3 (9.4)	2 (10.5)	6 (12.8)	30 (7.8)	6 (15.8)	
Number of antenatal visits							0.621
≤4	117 (22.5)	7 (21.9)	6 (31.6)	13 (27.7)	85 (22.1)	6 (15.8)	
≥ 5	403 (77.5)	25 (78.1)	13 (68.4)	34 (72.3)	299 (78.9)	32 (84.2)	
High-risk conditions							0.615
No	472 (90.8)	28 (87.5)	19 (100)	42 (89.4)	349 (90.9)	37 (89.5)	
Si	48 (9.2)	4 (12.5)	0 (0)	5 (10.6)	35 (9.1)	4 (10.5)	

ǂ x^2 test or Fisher's test,

This table refers to the following question from the survey: "of the reasons you listed, what is the main reason you will not get a flu vaccination this flu season?

++Access barriers: "Vaccine unavailability (n = 23)", "The health center is far from my home or opens at times that are not suitable for me (n=11), "Sick when shot was available (n = 6)", and other reasons related to access.

*Most common other reasons were: "Don´t know", "I had already been vaccinated before pregnancy".

**14 people did not answer the question

Table 3. Determinants of vaccination during pregnancy in Quito-Ecuador, 2016-2017.

Variable	All n = 842	Vaccinated n=308 n (%)	Crude PR CI 95%	Adjusted PR CI 95%
Age				
18-24	363	131 (36.1)	1.0	1.0
25-30	260	98 (37.7)	1.04 (0.85-1.29)	0.99 (0.86-1.15)
31-35	123	42 (34.2)	0.95 (0.71-1.25)	0.89 (0.72-1.11)
≥36	96	37 (38.5)	1.07 (0.80-1.42)	1.01 (0.84-1.22
Race				
White	27	8 (29.6)	1.0	1.0
Afro-Ecuadorian	30	13 (43.3)	1.46 (0.72-2.98)	0.95 (0.68-1.33)
Mixed	723	270 (37.3)	1.26 (0.70-2.27)	0.87 (0.65-1.17)
Indigenous	54	15 (27.8)	0.94 (0.45-1.93)	0.74 (0.48-1.15)
Other	8	2 (25.0)	0.84 (0.22-3.20)	0.60 (0.22-1.64)
Education				
Complete higher education or graduate degree	83	23 (27.1)	1.0	1.0
Complete secondary education or incomplete higher education	407	157 (38.6)	1.39 (0.96-2.01)	1.27 (0.99-1.64)
Basic education complete or incomplete high school	222	82 (36.9)	1.33 (0.90-1.96)	1.30 (0.99-1.71)
Illiterate or incomplete basic education	130	46 (35.4)	1.28 (0.84-1.94)	1.39 (0.90-1.84)
Marital status				
Married	288	107 (37.2)	1.0	1.0
Cohabited with a partner	376	144 (38.3)	1.03 (0.84-1.26)	0.99 (0.87-1.13)
Separated / Widowed / Divorced - Never Married or Unmarried	178	57 (32.0)	0.86 (0.66-1.12)	0.95 (0.77-1.17)
Employment				
Housewife	172	58 (33.7)	1.0	1.0
Student	119	38 (31.9)	1.16 (0.91-1.47)	1.00 (0.86-1.17)
Unemployed	4	1 (25.0)	0.97 (0.72-1.29)	0.95 (0.77-1.17)
Public or private employee	175	61 (34.9)	0.92 (0.66-1.28)	0.88 (0.69-1.12)
Independent worker	372	150 (40.3)	0.72 (0.13-3.97)	0.82 (0.44-1.52)
Number of children				
0	88	37 (42.1)	1.0	1.0
1-2	459	169 (36.8)	1.06 (0.87-1.30)	0.90 (0.79-1.03)
3-6	295	102 (34.6)	1.22 (0.91-1.63)	1.03 (0.81-1.32)

Antenatal Care				
≤4	161	38 (23.6)	1.0	1.0
≥ 5	681	270 (39.7)	**1.67 (1.25-2.25)**[†]	**1.21 (1.01-1.47)**[†]
Gestational age at birth				
<37 weeks	122	37 (30.3)	1.0	1.0
≥37 weeks	720	271 (37.6)	1.24 (0.93-1.65)	1.08 (0.91-1.28)
High-risk conditions				
No	775	290 (37.4)	1.0	1.0
Yes	67	18 (26.9)	0.72 (0.48-1.08)	0.91 (0.69-1.20)
Distance to health center (minutes)				
>30 minutes	35	9 (25.7)	1.0	1.0
15-30 minutes	102	35 (34.3)	1.33 (0.71-2.49)	0.75 (0.54-1.05)
0-15 minutes	696	262 (37.6)	1.46 (0.83-2.59)	0.79 (0.57-1.08)
Knowledge regarding influenza vaccine				
No	54	25 46.3)	1.0	1.0
Yes	721	268 (37.2)	0.80 (0.59-1.09)	0.91 (0.73-1.12)
Do not know/no answer	67	15 (22.4)	0.48 (0.28-0.82)	0.90 (0.63-1.28)
Knowledge about the transmission of the disease				
No	87	34 (39.1)	1.0	1.0
Yes	666	251 (37.7)	0.96 (0.73-1.28)	1.10 (0.91-1.32)
Do not know/no answer	89	23 (25.8)	0.66 (0.43-1.03)	1.23 (0.93-1.63)
Knowledge about the existence of vaccine				
No	17	3 (17.7)	1.0	1.0
Yes	767	301 (39.2)	2.22 (0.79-6.24)	0.69 (0.25-1.91)
Do not know/no answer	58	4 (6.9)	0.39 (0.10-1.58)	0.55 (0.17-1.82)
Perception about vaccine safety				
No	32	6 (18.8)	1.0	1.0
Yes	678	295 (43.5)	**2.32 (1.12-4.80)**[†]	**1.53 (1.03-2.37)**[†]
Do not know/no answer	132	7 (5.3)	0.28 (0.10-0.78)	0.65 (0.33-1.28)
Perception about vaccine effectiveness				
No	72	29 (40.2)	1.0	1.0
Yes	539	211 (39.2)	0.97 (0.72-1.31)	0.87 (0.61-1.2)
Do not know/no answer	231	68 (29.4)	0.73 (0.52-1.03)	0.86 (0.68-1.09)

Recommendation and offer of vaccine				
No recommendation/non-offer	397	17 (4.3)	1.0	1.0
Recommendation / non-offer	80	12 (15.0)	**3.50 (1.74-7.05)**†	**3.17 (1.57-6.40)**†
Recommendation / offer	336	278 (82.7)	**19.32 (12.1-30.85)**†	**15.84 (9.62-26.10)**†

† p-value < 0.05.

CI: Confidence interval; PR: Prevalence Ratio

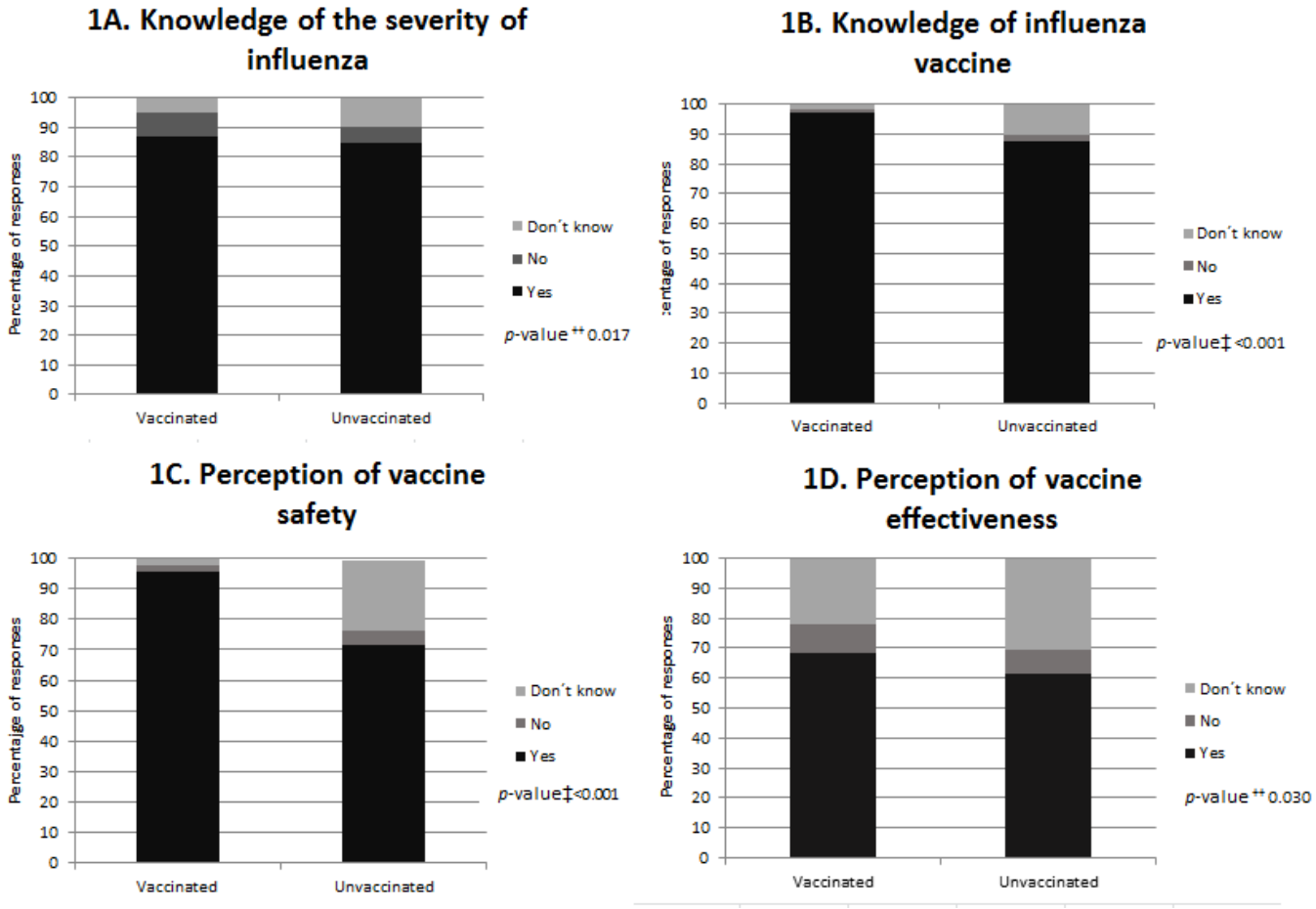

Figure 1. Knowledge and attitudes of women with regard to influenza and influenza vaccine according to the vaccination status (n = 842), Quito-Ecuador, 2016-2017. Bars represent numbers in percentages. This figure refers to the following questions from the survey: (1A) “Can influenza cause serious illness?”; (1B) “There is a vaccine to prevent influenza?”; (1C) “Are flu vaccines safe for me and my child during pregnancy?”; (1D) “Can the flu vaccine protect against severe influenza?”. $^{++}X^2$ test; ‡Fisher’s exact test.

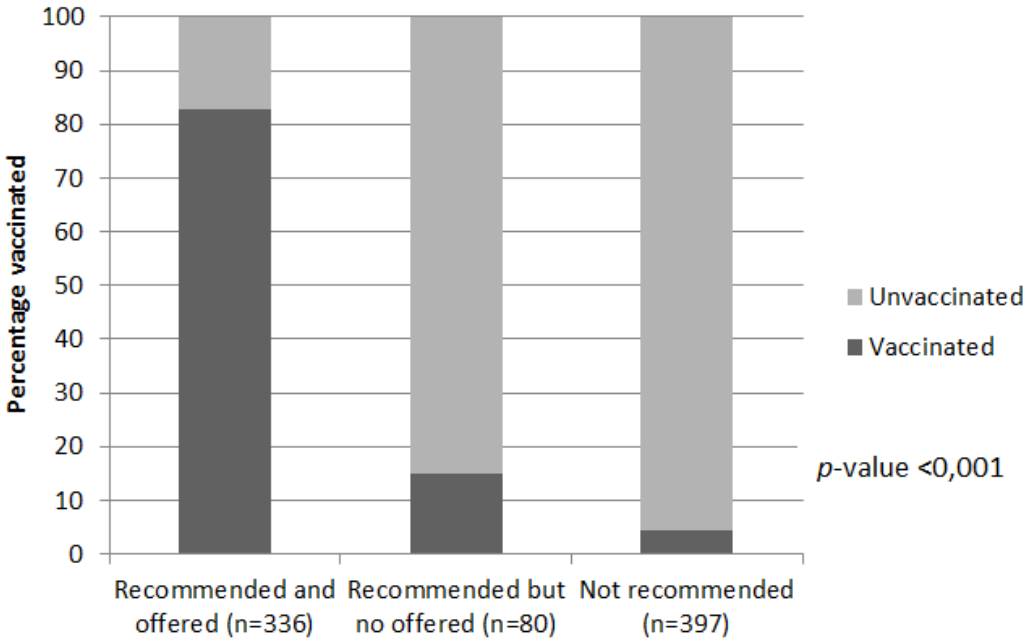

Figure 2. Vaccination against influenza during pregnancy according to the recommendation or offer of the vaccine by health personnel (n = 813). Quito-Ecuador, 2016-2017. Bars represent numbers in percentage.