Title: Pertussis vaccination during pregnancy: vaccine coverage associated with four different models of vaccine delivery in a quasi-experimental multicenter observational study

Authors: Yinan Li (BSc, MScPH candidate)^{1,2}, Nicholas Brousseau (MD, MSc)^{3,4}, Maryse Guay (MD, MSc)^{5,6}, Ève Dubé (PhD)^{3,4}, Zineb Laghdir (MSc)², Isabelle Boucoiran (MD, MSc)^{2,7}, Bruce Tapiéro (MD)^{2,8}, Caroline Quach (MD, MSc)^{9,10}

Institutional affiliations:

¹ Department of Epidemiology, Biostatistics & Occupational Health, McGill University, Montreal, Quebec, Canada ² CHU Sainte-Justine Research Center, Montreal, Quebec, Canada

³ Direction des risques biologiques et de la santé au travail, Institut national de la santé publique du Québec, Quebec City, Quebec, Canada

⁴ CHU de Quebec Research Center, Université Laval, Quebec City, Quebec, Canada

⁵ Research Center, Hôpital Charles-Lemoyne, Longueuil, Quebec, Canada

⁶ Département des sciences de la santé communautaire, Université de Sherbrooke, Sherbrooke, Quebec, Canada

⁷ Department of Obstetrics & Gynecology, School of Public Health, Université de Montréal, Montreal, Quebec, Canada

⁸ Infectious Diseases Division, Department of Pediatrics, CHU Sainte-Justine, Montreal, Quebec, Canada
⁹ Department of Microbiology, Infectious Diseases and Immunology, Université de Montréal, Montreal, Quebec, Canada

¹⁰ Infection Prevention and Control, Clinical Department of Laboratory Medicine, CHU Sainte-Justine, Montreal, Quebec, Canada

Corresponding Author

Caroline Quach

B.17.102 – 3175, chemin de la Côte Ste-Catherine, Montreal, Quebec, Canada, H3T 1C5 Tel: (514)-345-4931, ext. 7430 Email: c.quach@umontreal.ca

Funding statement

This work was funded by Quebec Ministry of Health and Social Services (Ministère de la Santé et des Services sociaux).

Data sharing statement

Data presented in this manuscript are available upon request after project completion to other investigators who are not on public servers.

Declaration of author(s) competing interests

Bruce Tapiéro received research grants from Merck, GSK, Pfizer, and Sanofi. All other authors have no competing interests to declare.

Acknowledgements

The authors thank Maryline Vivion, Marie-Claude Gariépy, Josiane Rivard and all people who contributed to data collection. They also thank all the study participants and regional collaborators who made this project possible.

Keywords

Immunization, Infectious diseases, Obstetrics and gynecology, Pertussis, Pregnancy, Public Health, Vaccine coverage, Vaccine delivery, Whooping cough

Word count: 2468 words

Abstract

Background:

Vaccination of all pregnant women with an acellular pertussis-containing vaccine (Tdap) is recommended in Canada since 2018. The evaluation of delivery models for efficient maternal Tdap administration was considered a priority. We aimed to compare the vaccine coverage (VC) for four delivery models in Quebec.

Methods:

In this quasi-experimental multicenter observational study, 1000 women <21 weeks of pregnancy were recruited in four Quebec regions. Four vaccine delivery models were compared: 1) Local Community Service Centres (CLSCs, baseline), 2) family medicine group (FMG), 3) obstetrics clinic, and 4) the oral glucose challenge test (OGCT). Vaccination status was determined from a self-reported questionnaire, the Quebec Immunization Registry, and/or medical charts. Model-specific and global VC was compared between models and logistic regression was used to adjust for socio-demographic variables.

Results:

Overall, 946 women were eligible for analyses. Vaccination at the FMG achieved highest model-specific VC (67.8%; 95%CI, 60.5%-74.4%), not significantly different from the CLSC model (63.8%; 95%CI, 57.6%-69.6%). For global VC, the FMG (86.5%; 95%CI, 80.6%-90.9%) and obstetrics models (85.9%; 95%CI, 80.9%-89.7%) achieved significantly higher VC than the CLSC model (66.3%; 95%CI, 60.1%-71.9%). The OGCT model did not improve global VC (61.8%; 95%CI, 56.1%-67.2%).

Interpretation:

Compared with CLSCs, global VC was improved when Tdap was offered in the FMG or obstetrics clinic providing prenatal care. Recommendation of vaccination from health professionals involved in pregnancy follow-up and offering the vaccine may be a key factor in optimizing VC. Additional analyses focused on vaccine acceptability and costs for model implementation are underway.

Page 8 of 31

Introduction

Pertussis infection and complications can be severe in young infants.[1,2] From 2006 to 2015 in Canada, infants less than one year of age had the highest hospitalization rates (33.6 cases per 100,000 population).[1] Infants <two months of age, who have not started their primary vaccination against pertussis, accounted for nearly half of special care unit admissions (40.5%).[1] Administration of the tetanus-diphtheria-acellular pertussis (Tdap) vaccine during pregnancy increases trans-placental transfer of maternal antibodies and provides direct protection of the infants.[1,3,4,5] In 2018, the National Advisory Committee on Immunization (NACI) recommended the systematic vaccination of all pregnant women against pertussis, at every pregnancy.[4] As of May 2018, the province of Quebec has recommended maternal Tdap immunization, ideally between 26 and 32 weeks of every pregnancy.[6] Many countries, including the United States [7-11], the United Kingdom [12], Belgium [13,14], New Zealand [15,16], and Switzerland [17], have recommended maternal Tdap immunization routinely in every pregnancy. Public Health England reported that, in 2019-2020, maternal Tdap vaccine coverage (VC) was ~70%.[12] Nevertheless, VC has been suboptimal in several countries [7-14,16-20], such as in the United States, where VC was ~57% in 2019-2020.[11] The modalities of Tdap vaccination implementation are major factors influencing VC.[13,18,20,21]

In Canada, there has not yet been a maternal pertussis immunization program that is integrated into existing medical care. A previous study conducted in Quebec identified challenges to successfully implement maternal Tdap vaccination.[21] Vaccination is rarely available in clinics offering prenatal care and is mainly offered in local public health clinics (Local Community Service Centres, CLSCs) by appointment. However, the study did not conclude on a specific model for efficient Tdap delivery.[21] Studies showed that Tdap VC improved when offering vaccination in traditional prenatal care settings by general practitioners or obstetrics clinics.[9,12] Gestational diabetes screening was also identified as a possible vaccination venue but has not been well studied.[21-23] As a follow-up to the previous study

[21], we aimed to assess and compare the VC associated with four province-based implementation models of maternal Tdap vaccine delivery, namely vaccination at 1) CLSCs, 2) family medicine group (FMG), 3) obstetrics clinic, and 4) the oral glucose challenge test (OGCT).

Methods

Setting and participants

We used a quasi-experimental multicenter study design with non-equivalent control groups of pregnant women, taking place in four health regions of Quebec (Montréal, Montérégie, Capitale-Nationale and Mauricie). From April to October 2019, women <21 weeks of pregnancy were recruited during a follow-up visit where their pregnancy was followed (Montérégie, Capitale-Nationale and Mauricie) or during their appointment for prenatal screening at the 11-13 weeks (Montréal). Eligible participants were 18 years of age and over, spoke French or English, provided a valid email address, were <21 weeks of pregnancy at recruitment and delivered a live birth.

Vaccine delivery models

Four models of vaccine delivery were implemented in the four Quebec health regions where participants were recruited. Vaccine administration ran from May 2019 to March 2020.

Local Community Service Centres (CLSCs) Model

In Montérégie, participants were recruited at a FMG clinic and were referred to their CLSC for vaccine administration by a nurse. CLSCs offer community healthcare services and serve specific geographical area.[21] This model is the current standard for Tdap vaccination in Quebec and served as the baseline model.[21]

Family Medicine Group (FMG) Model

Page 10 of 31

In Montérégie and Capitale-Nationale, participants were offered Tdap vaccination at the FMG where they were followed by a team of family physicians and nurses. Three FMG served as the recruitment and vaccination sites for this model, with each one following 200 – 400 pregnancies annually.

Obstetrics Model

In Mauricie, participants received Tdap vaccination in a high-speed obstetrics follow-up clinic, where approximately 1200 pregnancies are followed annually. Tdap was recommended by the obstetrician and offered by a nurse at a separately scheduled appointment in the same clinic.

Oral Glucose Challenge Test (OGCT) Model

In Montreal, participants are screened for gestational diabetes between weeks 24 – 28 of gestation through an OGCT (50 – 75g of glucose) at a hospital. Women were offered Tdap vaccination during the wait hour of the same appointment or after blood procurement. Women with preexisting diabetes were referred to CLSCs for vaccination.

Variables

Socio-demographic and contact information was collected through a paper questionnaire at recruitment. An online questionnaire on self-reported vaccination status, date and place of vaccination, was filled by participants at week 35 of pregnancy. Vaccination records from the Quebec Immunization Registry were checked to validate vaccination status. When possible, medical charts were reviewed to validate vaccination status for women who indicated unknown vaccination status or did not answer the questionnaire and for whom a proof of vaccination could not be found in the provincial registry. Medical charts were reviewed for all models, except for the CLSC model, due to logistical constraints. A pregnant woman was considered to be vaccinated when she self-reported as vaccinated in the online

questionnaire, provided a date and for whom non-vaccination was not documented in the medical chart, or when there was a vaccination proof in the registry or the medical chart.

Statistical analysis

The required sample size was calculated to be 250 per vaccine delivery model to detect a 15% difference in VC between models (55% vs. 70%).

The primary outcome, model-specific VC, was computed as the proportion of women who received Tdap vaccination within a specific vaccine delivery model out of all women eligible for each model (x100). The secondary outcome, global VC, was computed as the proportion of women vaccinated with Tdap (regardless of vaccination place) out of all eligible women for each model (x100). Comparisons of VC for each model to the baseline model were performed using the Chi-Squared test (α =5%, two-sided tests). Multivariable logistic regression was used to adjust for socio-demographic characteristics and compute adjusted odds ratios (OR) of vaccination for each model. All analyses were performed using RStudio version 1.1.463 (Boston, MA, USA).

Additional sensitivity analyses and VC calculated using aggregated data collected for the OGCT model are provided in the Supplementary Appendix.

Ethics approval

The Centre hospitalier universitaire Sainte-Justine Research Ethics Board reviewed the study protocol and approved the research project.

Results

Participation rate

In total, 1000/1336 (75%) invited women agreed to participate (CLSC model, 251/257(98%); FMG model, Overall: 187/223 (84%), FMG 1: 50/60 (83%), FMG 2: 54/77 (70%), FMG 3: 83/86 (96%); Obstetrics model, 263/519 (51%); OGCT model, 299/337 (89%)). Overall, 946 women were eligible after the exclusion of 54 women (14 based on age or gestational age, 16 miscarried, 3 who later refused to participate, 9 with duplicate information, 11 with missing information, and 1 no longer residing in Quebec).

Determination of vaccination status

We obtained questionnaire response on vaccination status for 619/946 (65.4%) participants and 503 (81.3%) of them self-reported as vaccinated. Using the Quebec Immunization Registry, we found a proof of vaccination for 174 additional women, including for 4 women who self-reported as non-vaccinated in the questionnaire. Furthermore, we found 23 additional doses by reviewing medical charts. We finally identified proof of non-vaccination for 4 women who self-reported as vaccinated within the OGCT model.

Therefore, 696/946 women (73.6%) received a Tdap vaccine during their pregnancy (Figure 1).

Participants' characteristics

The median maternal age was 31 years. A large proportion of women were born in Canada (71.2%), Francophone (79.8%), and married (89.0%). Approximately half had university level education (53.4%) and were in their first pregnancy (43.5%). Participants significantly differed in socio-demographic characteristics across models (Table 1), with the OGCT model having more non-Canadian born, non-Francophones and with a higher education level. For the FMG model consisting of 3 recruitment sites, characteristics are summarized in Table S1.

Comparison of model-specific vaccine coverage

To compare model performance, we evaluated model-specific VC considering only doses delivered within each model. For the baseline CLSC model, 96.3% of women who had received their Tdap did so within the CLSC vaccine delivery model (referral to the nearest CLSCs). The CLSC model-specific VC was 63.8% (95%CI, 57.6%-69.6%) (Table 2 and Figure 2). In comparison, under the FMG model, 78.4% of vaccinated women were vaccinated in their corresponding FMG clinic, and the FMG model-specific VC was 67.8% (95%CI, 60.5%-74.4%), which did not significantly differ from baseline. The Obstetrics model showed a significantly lower model-specific VC at 35.3% (95%CI, 29.5%-41.5%), since only 41.1% of vaccinated women actually received their vaccine in that obstetrics clinic. Finally, the OGCT model-specific VC was 44.1% (95%CI, 38.5%-49.9%), which was significantly lower compared to baseline. 71.4% of vaccinated women received the Tdap vaccine during the OGCT.

After adjusting for maternal age, country of birth (Canada vs. other), education, language and the number of prior children, compared to the CLSC model, the OR of receiving the Tdap vaccine within each vaccine delivery model was 1.26 (95%Cl, 0.82-1.94) for the FMG model, 0.30 (95%Cl, 0.20-0.44) for the Obstetrics model, and 0.46 (95%Cl, 0.32-0.67) for the OGCT model.

VC was also calculated using aggregated data for all women who presented for their OGCT, regardless of recruitment status, which did not modify the overall VC associated with this model (Supplemental Appendix).

Comparison of global vaccine coverage

To compare overall vaccine uptake, we evaluated global VC considering all doses administered regardless of vaccination place. For the baseline CLSC model, global Tdap VC was 66.3% (95%CI, 60.1%-71.9%). In comparison, a significantly higher VC was achieved by the FMG model (86.5%; 95%CI, 80.6%-90.9%) and the Obstetrics model (85.9%; 95%CI, 80.9%-89.7%). However, the OGCT model was not

associated with a statistically significant difference in global VC compared to the baseline model (61.8%; 95% CI, 56.1%-67.2%).

Overall, maternal age above the median age of 31 years (p=0.008) and nulliparity (p<0.001) were significantly associated with higher likelihood of vaccination. Being born in Canada (p=0.070), having completed a university level education (p=0.098), and being a Francophone (p=0.071) were positively associated with Tdap vaccination without these associations being significant.

The overall adjusted OR of receiving the Tdap vaccine was 4.05 for the FMG model (95% CI, 2.36-7.22), 3.37 for the Obstetrics model (95% CI, 2.11-5.49), and 0.92 for the OGCT model (95% CI, 0.62-1.37), compared to the CLSC model.

Interpretation

Referring patients to public health clinics (CLSC model) is the current standard model for maternal Tdap vaccination in Quebec. Under this model, model-specific and global VC was moderately good but not optimal (63.8% and 66.3%, respectively). The CLSC model was highly utilized by participants and thus resulted in similar or higher model-specific VC compared to other delivery models. Nevertheless, the FMG and Obstetrics model achieved significantly higher global VC (86.5% and 85.9%, respectively), a difference of approximately 20 percentage points compared with the CLSC model.

A previous study [21] reported that vaccination would be facilitated if offered in FMG clinics where pregnancies are followed. In our study, model-specific VC was similar for the FMG model and the CLSC model (~65%), but global VC increased to 85% for the FMG model when considering all vaccination venues. Pregnant women were most likely to receive Tdap when it was recommended and offered by their family physician, which could be explained by a stronger perceived importance of vaccination from family physician/nurse offering prenatal care. High maternal Tdap VC was also observed in studies from Belgium and the UK, where the main vaccinators were general practitioners [12,13]. In our context, high

VC of the FMG model suggested potential benefits of integrating vaccination in the prenatal care, as offered in FMG clinics.

The obstetrics clinic offering Tdap vaccination during pregnancy follow-up also achieved significantly higher global VC (around 20 percentage points) compared to the CLSC model. A vaccine offer within the clinic may increase accessibility to Tdap vaccination and emphasize its importance. Maternal pertussis immunization recommendation from healthcare professionals traditionally involved in pregnancy, including obstetricians, has been associated with higher VC.[9,13] Interestingly, within our Obstetrics model, 41% of vaccinated women received their vaccine at the obstetrics clinic. It was likely that women decided to be vaccinated at their CLSC for reasons such as geographical accessibility, or limited appointment availability: the nurse offering Tdap vaccination only worked two days/week. Results could be different with another obstetric clinic organization.

The impact of offering Tdap vaccination at the time of gestational diabetes screening had not been well studied. Our study showed that this strategy did not improve VC – model-specific or global. Suboptimal model-specific VC could be explained in part by the timing of the vaccine offer (before 26 weeks of gestation) or because the OGCT was perceived as an ordeal in itself. Diabetic and pre-diabetic women who were not present for an OGCT appointment were referred to CLSC, although the exclusion of these women did not improve the model-specific VC. Nevertheless, women utilized the OGCT model better than the obstetrics clinic, as a higher percentage (71.4%) of vaccinated women received their vaccine during their OGCT. This may highlight benefits of opportunistic vaccination services at the OGCT appointment, which overlaps with the ideal time for maternal pertussis immunization [21-23]. Future research is needed to evaluate strategies combining physician/obstetrician referral for OGCT and offering of Tdap during an OGCT appointment. Integration of Tdap vaccination with other prenatal

Page 16 of 31

services should also be considered, which could refer women to other resources if they miss this vaccination opportunity.

Limitations

In the present study, strengths include the quasi-experimental study design, which is effective at evaluating vaccine delivery interventions [24], and the validation of vaccination history. Limitations include the fact that participation rate was lower for the Obstetrics model. For one of the recruitment site, participation rate was high (96%) and very high VC was also obtained. Medical charts were not reviewed for the CLSC model, but after a sensitivity analysis (Supplementary Appendix; Table S2) addressing this issue, conclusions remained similar to the primary analysis. Participants differed in socio-demographic characteristics at baseline, which might have influenced their likelihood of Tdap vaccination. We accounted for these differences in our multivariable models. Finally, our sample recruited for the OGCT model may not be representative of the pregnant women population who access prenatal care services in the province or the country, since the hospital where this model was implemented serves a large urban multiethnic catchment area and is the referral center for high risk pregnancies.

Conclusions

This study identified that vaccination in FMG clinics providing prenatal care improved VC, despite it being non-significantly higher than the current standard of practice at CLSCs – when only considering vaccine doses administered within the FMG clinic (model-specific VC). Overall however, the addition of a vaccine offer in FMG and obstetrics clinics was associated with significantly higher VC than the CLSC model, while vaccination at an OGCT appointment did not have a significant impact on VC. Recommendation of vaccination from health professionals involved in routine pregnancy follow-up and offering the vaccine may be the key factor in optimizing VC. This work and additional analyses on

vaccine acceptability, as well as costs of vaccination strategies will be important to understand for the

successful implementation of universal maternal pertussis vaccination in Quebec and elsewhere.

References

[1] Brophy J, Baclic O, Tunis MC on behalf of the National Advisory Committee on Immunization (NACI). Summary of the NACI Update on Immunization in Pregnancy with Tetanus Toxoid, Reduced Diphtheria Toxoid and Reduced Acellular Pertussis (Tdap) Vaccine. Can Commun Dis Rep [Internet]. 2018 Mar 1 [cited 2020 Aug 10]; 44(3/4): 91-4. Available from: <u>https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2018-44/issue-3-4-march-1-2018/article-5-update-immunization-pregnancy-vaccine-2018.html doi: https://doi.org/10.14745/ccdr.v44i34a04</u>

[2] Abu-Raya B, Bettinger JA, Vanderkooi OG, Vaudry W, Halperin SA, Sadarangani M et al. (2020).
Burden of Children Hospitalized With Pertussis in Canada in the Acellular Pertussis Vaccine Era, 1999-2015. J Pediatric Infect Dis Soc [Internet]. 2020 Jun [cited 2020 Aug 10]; 9(2): 118–27. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7192396/ doi: https://www.ncbi.nlm.nih.gov/ doi: https://www.ncbi.nl

[3] Public Health Agency of Canada. Pertussis vaccine: Canadian Immunization Guide [Internet]. Ottawa, Canada: Public Health Agency of Canada; 2018 [updated 2018 Apr 9; cited 2020 Aug 10]. Available from: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunizationguide-part-4-active-vaccines/page-15-pertussis-vaccine.html

[4] Fleurant-Ceelen A, Tunis M, House A, on behalf of the National Advisory Committee on Immunization (NACI). What is new in the Canadian Immunization Guide: November 2016 to November 2018. Can Commun Dis Rep [Internet]. 2018 Dec 6 [cited 2020 Aug 10]; 44(12): 331-5. Available from: https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-diseasereport-ccdr/monthly-issue/2018-44/issue-12-december-6-2018/article-6-updates-to-canadianimmunization-guide.html doi: https://doi.org/10.14745/ccdr.v44i12a06

[5] Abu Raya B, Edwards KM, Scheifele DW, Halperin SA. Pertussis and influenza immunisation during pregnancy: a landscape review. Lancet Infect Dis [Internet]. 2017 Jul 1 [cited 2020 Aug 10]; 17(7): e209– e222. Available from: <u>https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(17)30190-1/fulltext</u> doi: 10.1016/S1473-3099(17)30190-1

[6] Gouvernement du Québec. Whooping cough. Quebec: Gouvernement du Québec; [updated 2019 Jun 20; cited 2020 Aug 18]. Available from: https://www.quebec.ca/en/health/health-issues/a-z/whooping-cough/#c6954

[7] Koepke R, Kahn D, Petit AB, Schauer SL, Hopfensperger DJ, Conway JH, et al. Pertussis and influenza vaccination among insured pregnant women—Wisconsin, 2013–2014. MMWR Morb Mortal Wkly Rep [Internet]. 2015 Jul 17 [cited 2020 Aug 10]; 64(27): 746-50. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4584586/ [8] Barber A, Muscoplat MH, Fedorowicz A. Coverage with Tetanus, Diphtheria, and Acellular Pertussis
 Vaccine and Influenza Vaccine Among Pregnant Women - Minnesota, March 2013-December 2014.
 MMWR Morb Mortal Wkly Rep [Internet]. 2017 Jan 20 [cited 2020 Aug 10]; 66(2): 56–9. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5657652/ doi: 10.15585/mmwr.mm6602a4

[9] Kerr S, Van Bennekom CM, Liang JL, Mitchell AA. Tdap Vaccination Coverage During Pregnancy -Selected Sites, United States, 2006-2015. MMWR Morb Mortal Wkly Rep [Internet]. 2017 Oct 20 [cited 2020 Aug 10]; 66(41): 1105–8. Available from:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5689095/ doi: 10.15585/mmwr.mm6641a3

[10] Ghaswalla P, Poirrier JE, Packnett ER, Irwin DE, Gray SR, Buck PO. Maternal Immunization in the U.S.: A Nationwide Retrospective Cohort Study. Am J of Prev Med [Internet]. 2019 Sep 1 [cited 2020 Aug 10]; 57(3): e87–e93. Available from: <u>https://www.ajpmonline.org/article/S0749-3797(19)30207-7/fulltext</u> doi: 10.1016/j.amepre.2019.04.013

[11] Razzaghi H, Kahn KE, Black CL, Lindley MC, Jatlaoui TC, Fiebelkorn AP, et al. Influenza and Tdap Vaccination Coverage Among Pregnant Women - United States, April 2020. MMWR Morb Mortal Wkly Rep [Internet]. 2020 Oct 2 [cited 2020 Oct 5]; 69(39):1391-7. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7537555/ doi: 10.15585/mmwr.mm6939a2

[12] Public Health England. Pertussis vaccination programme for pregnant women: vaccine coverage in England, January to March 2020 and 2019-20 annual coverage. Health Protection Report [Internet] 2020 May 26 [cited 2020 Aug 10]; 14(10): 1-9. Available from:

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/88 7216/hpr1020_prtsss-vc.pdf

[13] Maertens K, Braeckman T, Top G, Van Damme P, Leuridan E. Maternal pertussis and influenza immunization coverage and attitude of health care workers towards these recommendations in Flanders, Belgium. Vaccine [Internet]. 2016 Nov 11 [cited 2020 Aug 10]; 34(47): 5785-91. Available from: https://www.sciencedirect.com/science/article/pii/S0264410X16308829?via%3Dihub doi: 10.1016/j.vaccine.2016.09.055

[14] Laenen J, Roelants M, Devlieger R, Vandermeulen C. Influenza and pertussis vaccination coverage in pregnant women. Vaccine [Internet]. 2015 Apr 27 [cited 2020 Aug 10]; 33(18): 2125-31. Available from: <u>https://www.sciencedirect.com/science/article/pii/S0264410X15003084?via%3Dihub</u> doi: 10.1016/j.vaccine.2015.03.020

[15] Griffin JB, Yu L, Watson D, Turner N, Walls T, Howe AS, et al. Pertussis Immunisation in Pregnancy Safety (PIPS) Study: A retrospective cohort study of safety outcomes in pregnant women vaccinated with Tdap vaccine. Vaccine [Internet]. 2018 Aug 16 [cited 2020 Aug 10]; 36(34): 5173–9. Available from: <u>https://www.sciencedirect.com/science/article/pii/S0264410X18309411?via%3Dihub</u> doi: 10.1016/j.vaccine.2018.07.011

1	
2 3	[16] Deverall EJ, Gilmore B, Illing S, Peiris-John R. Pertussis vaccination uptake in pregnancy: lessons to
4	be learned from an integrated healthcare approach. NZ Med J [Internet]. 2018 Apr 13 [cited 2020 Aug
5 6	10]; 131(1473): 42-7. Available from: https://www.nzma.org.nz/journal-articles/pertussis-vaccination-
7	uptake-in-pregnancy-lessons-to-be-learned-from-an-integrated-healthcare-approach
8	
9 10	[17] Erb ML, Erlanger TE, Heininger U. Child-parent immunization survey: How well are national
11	immunization recommendations accepted by the target groups? Vaccine: X [internet]. 2019 Apr 11
12	[cited 2020 Aug 10]; 1: 100013. Available from:
13 14	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6668236/ doi: 10.1016/j.jvacx.2019.100013
15	[18] Amirthalingam G, Andrews N, Campbell H, Ribeiro S, Kara E, Donegan K, et al. Effectiveness of
16	maternal pertussis vaccination in England: an observational study. Lancet [Internet]. 2014 Oct 25 [cited
17 18	2020 Aug 10]; 384(9953): 1521-8. Available from:
19	https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(14)60686-3/fulltext doi:
20	10.1016/S0140-6736(14)60686-3
21 22	
23	[19] Brillo E, Tosto V, Giardina I, Buonomo E. Maternal tetanus, diphtheria, and acellular pertussis (Tdap)
24	and influenza immunization: an overview. J Matern Fetal Neonatal Med [Internet]. 2019 Oct 24 [cited
25 26	2020 Aug 10]; 1-30. Available from:
27	https://www.tandfonline.com/doi/full/10.1080/14767058.2019.1680633 doi:
28	10.1080/14767058.2019.1680633
29 30	[20] Ahluwalia IB, Ding H, D'Angelo D, Shealy KH, Singleton JA, Liang J, et al. Tetanus, diphtheria,
31	pertussis vaccination coverage before, during, and after pregnancy - 16 States and New York City, 2011.
32	MMWR Morb Mortal Wkly Rep [Internet]. 2015 May 22 [cited 2020 Aug 18]; 64(19): 522–6. Available
33 34	from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4584571/
35	
36	[21] Brousseau N, Gagnon D, Vivion M, Poliquin V, Boucoiran I, Tapiéro B, et al. Expected challenges of
37 38	implementing universal pertussis vaccination during pregnancy in Quebec: a cross-sectional survey.
39	CMAJ open [Internet]. 2018 Sep 20 [cited 2020 Aug 10]; 6(3): E391-7. Available from:
40	http://cmajopen.ca/content/6/3/E391.long doi: 10.9778/cmajo.20180040
41 42	[22] National Advisory Committee on Immunization (NACI). Update on Immunization in Pregnancy with
43	Tetanus Toxoid, Reduced Diphtheria Toxoid and Reduced Acellular Pertussis (Tdap) Vaccine [Internet].
44	Ottawa, Canada: Public Health Agency of Canada; 2018 Feb [updated 2019 Oct 9; cited 2020 Aug 10].
45 46	Available from: https://www.canada.ca/en/public-health/services/publications/healthy-living/update-
47	immunization-pregnancy-tdap-vaccine.html
48	
49 50	[23] Committee on Obstetric Practice & Immunization and Emerging Infections Expert Work Group.
51	(2017). Committee Opinion No. 718: Update on Immunization and Rregnancy: Tetanus, Diphtheria, and
52	Pertussis Vaccination. Obstet Gynecol [Internet]. 2017 [cited 2020 Aug 18]; 130(3): e153-7. Available
53 54	from: <u>https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2017/09/update-on-</u> immunization-and-pregnancy-tetanus-diphtheria-and-pertussis-vaccination
55	<u>ווווועוווצמנוסוו-מווע־טרפוומונע־נכנמוועז-עוטווכוומ-מווע־טבו נעצאא־אמנטוומנוטוו</u>
56 57	
57 58	
59	
60	For Peer Review Only

[24] Lopez Bernal JA, Andrews N, Amirthalingam G. The use of quasi-experimental designs for vaccine evaluation. Clin Infect Dis [Internet]. 2019 May 2 [cited 2020 Aug 10]; 68(10): 1769-76. Available from: https://academic.oup.com/cid/article/68/10/1769/5140188 doi: 10.1093/cid/ciy906

Table 1. Baseline socio-demographic characteristics from the recruitment questionnaire

			No. (%)*			
-		Vaccine delive	ry models			
Characteristic	CLSC n = 246 (26.0%)	FMG n = 171 (18.1%)	Obstetrics n = 241 (25.5%)	OGCT n = 288 (30.4%)	Total N = 946†	p‡
Median maternal age, year (IQR)	30 (6)	30 (6)	30 (7)	32 (7)	31 (7)	< 0.00
Born in Canada						
Yes	191 (77.6%)	129 (75.4%)	211 (87.5%)	143 (49.6%)	674 (71.2%)	
No	47 (19.1%)	34 (19.9%)	19 (7.9%)	141 (49.0%)	241 (25.5%)	< 0.00
No response	8 (3.3%)	8 (4.7%)	11 (4.6%)	4 (1.4%)	31 (3.3%)	
Marital Status						
Married	221 (89.8%)	158 (92.4%)	197 (81.7%)	266 (92.4%)	842 (89.0%)	
Other	23 (9.4%)	11 (6.4%)	38 (15.8%)	20 (6.9%)	92 (9.7%)	0.003
No response (Prefer not to answer & no response)	2 (0.8%)	2 (1.2%)	6 (2.5%)	2 (0.7%)	12 (1.3%)	0.005
Level of education			0/			
University	126 (51.2%)	88 (51.5%)	93 (38.6%)	198 (68.7%)	505 (53.4%)	
Other (College or less)	119 (48.4%)	82 (47.9%)	148 (61.4%)	88 (30.6%)	437 (46.2%)	< 0.00
No response (Prefer not to answer & no response)	1 (0.4%)	1 (0.6%)	0 (0%)	2 (0.7%)	4 (0.4%)	
Language						
French	190 (77.2%)	150 (87.7%)	226 (93.8%)	189 (65.6%)	755 (79.8%)	
Other	56 (22.8%)	21 (12.3%)	15 (6.2%)	99 (34.4%)	191 (20.2%)	< 0.00
Number of previous children		66 (38.6%)	93 (38.6%)	119 (41.3%)	411 (43.5%)	0.005

1 child or more prior to this pregnancy	113 (45.9%)	105 (61.4%)	147 (61.0%)	168 (58.3%)	533 (56.3%)	
No response	0 (0%)	0 (0%)	1 (0.4%)	1 (0.4%)	2 (0.2%)	
Diabetes						
Yes	9 (3.7%)	7 (4.1%)	6 (2.5%)	21 (7.3%)	43 (4.5%)	
No	234 (95.1%)	162 (94.7%)	232 (96.3%)	264 (91.7%)	892 (94.3%)	0.242
Unknown (Do not know + no response)	3 (1.2%)	2 (1.2%)	3 (1.2%)	3 (1.0%)	11 (1.2%)	0.242
Type of health professional following the pregnancy						
Family physician	136 (55. <mark>3</mark> %)	114 (66.7%)	3 (1.2%)	7 (2.4%)	260 (27.5%)	
Obstetrician	95 (38.6%)	25 (14.6%)	232 (96.3%)	267 (92.7%)	619 (65.4%)	
Other (including multiple health professionals)	11 (4.5%)	26 (15.2%)	5 (2.1%)	14 (4.9%)	56 (5.9%)	< 0.001
No response	4 (1.6%)	6 (3.5%)	1 (0.4%)	0 (0%)	11 (1.2%)	

Note: CLSC = local community service centre, FMG = family medicine group, OGCT = oral glucose challenge test, IQR = interquartile range.

*Unless otherwise specified.

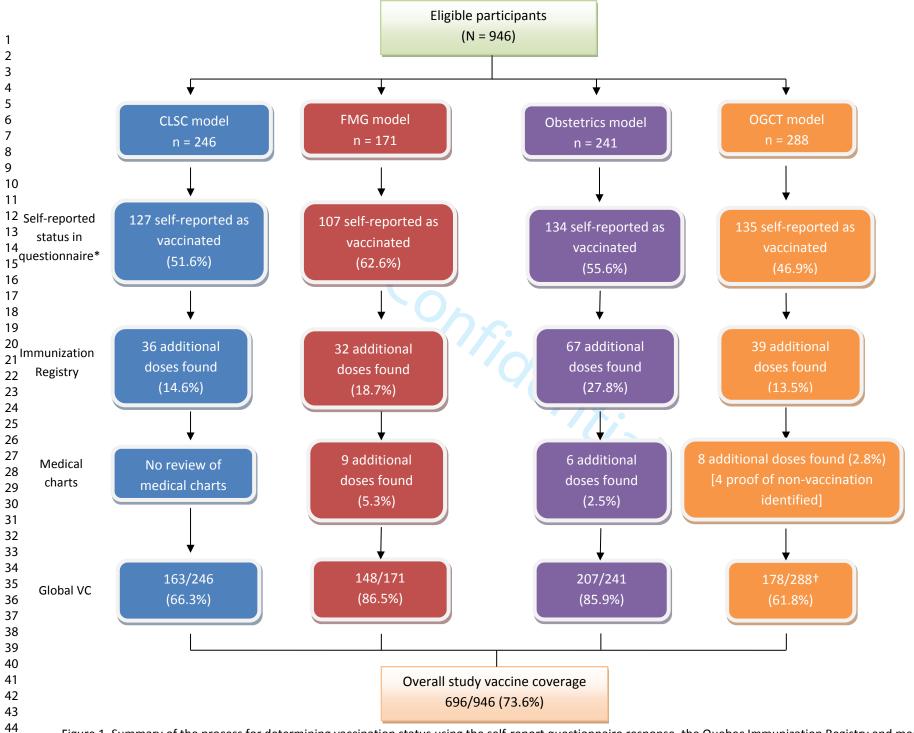
[†]946 women were eligible after exclusion of 54 women who did not meet the inclusion criteria.

‡Comparison of participants' characteristics across the four vaccine delivery models using Kruskal-Wallis test, Pearson's Chi Squared test or by Monte Carlo simulation for cells with expected count <5.

1 2 3 4 5 6 7 8	_
9 10 11 12 13 14	
15 16 17 18 19 20	
21 22 23 24 25 26	
27 28 29 30 31 32	
33 34 35 36 37 38	
39 40 41 42 43 44	

Table 2. Tdap vaccine coverage, model-specific and global.

				N	1odel-specific			Glo	bal	
Vaccine delivery models	Vaccinated within model	Vaccinated outside model	Proportion vaccinated within model	Model-specific VC [95% CI]	OR* [95% CI]	aOR† [95% CI]	Global VC [95% Cl]	Absolute VC difference	OR* [95% CI]	aOR† [95% CI]
CLSC (n = 246)	157	6	157/163 (96.3%)	157/246 (63.8%) [57.6%, 69.6%]	1 (Reference)	1 (Reference)	163/246 (66.3%) [60.1%, 71.9%]	Reference	1 (Reference)	1 (Reference)
FMG (n = 171)	116	32	116/148 (78.4%)	116/171 (67.8%) [60.5%, 74.4%]	1.20 [0.79, 1.81]	1.26 [0.82, 1.94]	148/171 (86.5%) [80.6%, 90.9%]	20.2%	3.28 [1.99, 5.57]	4.05 [2.36, 7.22]
Obstetrics (n = 241)	85	122	85/207 (41.1%)	85/241 (35.3%) [29.5%, 41.5%]	0.31 [0.21, 0.45]	0.30 [0.20, 0.44]	207/241 (85.9%) [80.9%, 89.7%]	19.6%	3.10 [1.99, 4.91]	3.37 [2.11, 5.49]
OGCT (n = 288)	127	51	127/178 (71.4%)	127/288 (44.1%) [38.5%, 49.9%]	0.45 [0.31, 0.63]	0.47 [0.32, 0.68]	178/288 (61.8%) [56.1%, 67.2%]	4.5%	0.82 [0.58, 1.17]	0.92 [0.62, 1.37]
od *O †A	ds ratio, aOR dds ratios cal djusted odds	= adjusted odd culated from u	ds ratio. Inivariate logisti ed from multiva	FMG = family med			cose challenge t			



3

5

6

Figure 1. Summary of the process for determining vaccination status using the self-report questionnaire response, the Quebec Immunization Registry and medical charts. 45 Note: CLSC = local community service centre, FMG = family medicine group, OGCT = oral glucose challenge test.

46 *Questionnaire response rate: CLSC model: 159/246 (64.6%); FMG model: 122/171 (71.3%); Obstetrics model: 142/241 (58.9%); OGCT model: 196/288 (68.1%). 47

+ For the OGCT model, the global vaccine coverage was adjusted to 178/288 after identifying a proof of non-vaccination for 4 women who self-reported as vaccinated.

Page 24 of 31

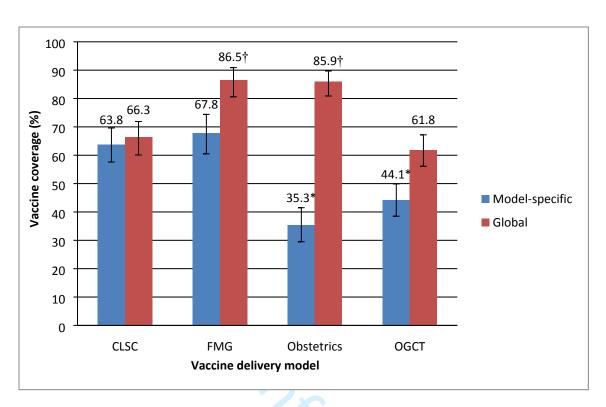


Figure 2. Model-specific and global vaccine coverage of the four vaccine delivery models.

*The model-specific vaccine coverage of the Obstetrics and OGCT model were significantly lower compared to model-specific vaccine coverage of the baseline CLSC model (p<0.001).

[†]The global vaccine coverage of the FMG and Obstetrics model were significantly higher compared to the global vaccine coverage of the baseline CLSC model (p<0.001).

Supplementary Appendix

Table of Contents

Supplementary Methods2
Vaccination at OGCT (aggregated data)2
Sensitivity Analyses2
Supplementary Results
Vaccination at OGCT (aggregated data)3
Sensitivity Analyses
Supplementary Tables
Table S14
Table S26
Table S37

Supplementary Methods

Vaccination during the oral glucose challenge test (aggregated data)

For the oral glucose challenge test (OGCT) model, VC was calculated using aggregated data collected daily at the blood procurement centre for all women, regardless of their recruitment in the study. Results were compared to the baseline VC of the primary analysis.

Sensitivity Analyses

Sensitivity analyses were performed to test the robustness of the results. Since no medical charts were reviewed for the CLSC model, an analysis was performed assuming as vaccinated women who indicated unknown vaccination status or who did not answer the self-reported questionnaire and for whom information in the Immunization Registry was unavailable. This led to a higher VC for the CLSC model which was again compared with VC of other models. A second sensitivity analysis was performed for the OGCT model where we excluded pregnant women who were known diabetes by their medical charts.

Supplementary Results

Vaccination during OGCT

The aggregated data showed that, among recruited women who attended the OGCT in the participating site, 99/210 (47.1%; 95%CI, 40.5%-53.9%) were vaccinated during or after the OGCT waiting hour. Tdap VC was significantly lower than the baseline model-specific VC (63.8%; p<0.001). Regardless of recruitment status, 290/802 (36.2%; 95%CI, 32.9%-39.5%) of women who came to their OGCT received the Tdap vaccine during their appointment.

Sensitivity analyses

For the CLSC model where medical charts were not reviewed, we found 17 women who indicated unknown vaccination status or who did not answer the self-reported questionnaire, for whom there was no information available in the Immunization Registry. Assuming that these 17 women would have been vaccinated in a CLSC, the analysis showed that the model-specific VC of the FMG model remained similar to the CLSC model (p=0.528), and the FMG model (p=0.001) and the obstetrics model (p<0.001) still achieved significantly higher global VC than the CLSC model (Table S2).

A second analysis was performed for the OGCT model specifically after the exclusion of 19 diabetic and pre-diabetic women who were not present at the OGCT during which the Tdap vaccine was offered (Table S3). Comparisons of the model-specific and global VC to the baseline again aligned with our primary analysis results.

Supplementary Tables

Table S1. Baseline socio-demographic characteristics from the recruitment questionnaire (Family medicine group model).

-		No. (%)*		
		Recruitment site		
Characteristics	FMG 1	FMG 2	FMG 3	p†
	n = 48 (28.1%)	n = 42 (24.6%)	n = 81 (47.4%)	•
Median maternal age (IQR)	31 (8)	29 (5)	30 (5)	0.125
If born in Canada (%)				
Yes	24 (50.0%)	34 (81.0%)	71 (87.7%)	
No	22 (45.8%)	8 (19.0%)	4 (4.9%)	<0.001
No response	2 (4.2%)	0 (0%)	6 (7.4%)	
Marital Status (%)				
Married	45 (93.8%)	38 (90.5%)	75 (92.6%)	
Other	3 (6.2%)	3 (7.1%)	5 (6.2%)	0.979
No response (Prefer not to answer + no response)	0 (0%)	1 (2.4%)	1 (1.2%)	
Level of education (%)		9/		
University	29 (60.4%)	23 (54.8%)	36 (44.4%)	
Other (College or less)	19 (39.6%)	18 (42.9%)	45 (55.6%)	0.111
No response (Prefer not to answer + no response)	0 (0%)	1 (2.4%)	0 (0%)	
Language (%)				
French	35 (72.9%)	38 (90.5%)	77 (95.1%)	-0.004
Other	13 (27.1%)	4 (9.5%)	4 (4.9%)	<0.001
Number of infants (%)				
First Pregnancy	14 (29.2%)	19 (45.2%)	33 (40.7%)	0.254
1 child or more prior to this pregnancy	34 (70.8%)	23 (54.8%)	48 (59.3%)	0.254
Diabetes (%)				

Yes	1 (2.1%)	1 (2.4%)	5 (6.2%)	
No	47 (97.9%)	39 (92.9%)	76 (93.8%)	0.087
Unknown (Do not know + no response)	0 (0%)	2 (4.8%)	0 (0%)	
Type of health professional following the pregnancy (%)				
Family physician	30 (62.5%)	25 (59.5%)	59 (72.8%)	
Obstetrician	10 (20.8%)	5 (11.9%)	10 (12.4%)	0.000
Other (including multiple health professionals)	6 (12.5%)	8 (19.0%)	12 (14.8%)	0.099
No response	2 (4.2%)	4 (9.5%)	0 (0%)	

Note: FMG = family medicine group, IQR = interquartile range.

*Unless otherwise specified.

 + P-values calculated from Kruskal-Wallis test and Pearson's Chi Squared test. For cells with expected count <5, p-values are computed by Monte Carlo simulation.

Table S2. Sensitivity analyses of the Tdap vaccine coverage, considering higher	r vaccine coverage for the CLSC model*
---	--

	N	Iodel-specific			Global	
Vaccine delivery models	Model-specific VC [95% Cl]	OR [†] [95% CI]	aOR [‡] [95% CI]	Global VC [95% CI]	OR⁺ [95% CI]	aOR [‡] [95% CI]
CLSC	174/246 (70.7%)	1	1	180/246 (73.2%)	1	1
(n = 246)	[64.8%, 76.1%]	(Reference)	(Reference)	[67.3%, 78.3%]	(Reference)	(Reference
FMG	116/171 (67.8%)	0.87	0.95	148/171 (86.5%)	2.36	2.98
(n = 171)	[60.5%, 74.4%]	[0.57, 1.33]	[0.61, 1.48]	[80.6%, 90.9%]	[1.42, 4.04]	[1.72, 5.34
Obstetrics	85/241 (35.3%)	0.23	0.23	207/241 (85.9%)	2.23	2.57
(n = 241)	[29.5%, 41.5%]	[0.15, 0.33]	[0.15, 0.34]	[80.9%, 89.7%]	[1.42, 3.57]	[1.59, 4.21
OGCT	127/288 (44.1%)	0.33	0.33	178/288 (61.8%)	0.59	0.63
(n = 288)	[38.5%, 49.9%]	[0.23, 0.47]	[0.22, 0.48]	[56.1%, 67.2%]	[0.41, 0.86]	[0.42, 0.94

Note: CLSC = local community service centre, FMG = family medicine group, OGCT = oral glucose challenge test, VC = vaccine coverage, OR = odds ratio, aOR = adjusted odds ratio.

*The sensitivity analyses assumed that 17 additional participants would have been vaccinated in the CLSC model.

[†]Odds ratios calculated from univariate logistic regression.

^{*}Adjusted odds ratios calculated from multivariable logistic regression, adjusting for maternal age, country of birth (Canada vs. other), education, language and the number of prior children

	Mod	del-specific	Global			
Vaccine delivery models	Model-specific VC [95% CI]	OR⁺ [95% CI]	aOR [‡] [95% CI]	Global VC [95% Cl]	OR⁺ [95% CI]	aOR [‡] [95% CI]
CLSC (n = 246)	157/246 (63.8%) [57.6%, 69.6%]	1 (Reference)	1 (Reference)	163/246 (66.3%) [60.1%, 71.9%]	1 (Reference)	1 (Reference
OGCT	127/269 (47.2%)	0.51	0.50	174/269 (64.7%)	0.93	0.99
(n = 269)	[41.3%, 53.2%]	[0.36, 0.72]	[0.34, 0.73]	[58.8%, 70.2%]	[0.65, 1.34]	[0.66, 1.4

Table S3. Sensitivity analyses of the Tdap vaccine coverage, excluding some women from the Oral Glucose Challenge Test model*

Note: CLSC = local community service centre, OGCT = oral glucose challenge test, VC = vaccine coverage, OR = odds ratio, aOR = adjusted odds ratio.

*The sensitivity analysis was done after the exclusion of 19 women diagnosed with gestational diabetics or pre-gestational diabetics. Comparisons of VC, ORs, and aORs were against the baseline CLSC model of the primary analysis.

[†]OR = Odds ratios calculated from univariate logistic regression.

[‡]aOR = Adjusted odds ratios calculated from multivariable logistic regression, adjusting for maternal age, country of birth (Canada vs. other), education, language and the number of prior children.