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Kamini Doraivelu Date

Predictors of Tetanus, Diphtheria, Acellular Pertussis and Influenza Vaccination during Pregnancy among Full Term Deliveries in a Medically Underserved Population

By

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Master of Public Health

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Predictors of Tetanus, Diphtheria, Acellular Pertussis and Influenza Vaccination during Pregnancy among Full Term Deliveries at a Tertiary Care Hospital in Atlanta, Georgia

By

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Bachelor of Science, University of Wisconsin-Madison, 2017

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An abstract of a thesis submitted to the Faculty of the Rollins School of Public Health of Emory University in partial fulfillment of the requirements for the degree of

Master of Public Health
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Abstract

Predictors of Tetanus, Diphtheria, Acellular Pertussis and Influenza Vaccination during Pregnancy among Full Term Deliveries in a Medically Underserved Population

By Kamini Doraivelu

OBJECTIVE: To evaluate predictors of vaccination for women that received tetanus, diphtheria, and acellular pertussis vaccination (Tdap), influenza vaccination, and Tdap and influenza vaccinations.

Study Design: In a retrospective cohort study of all full-term (≥37 weeks gestation) deliveries between July 1, 2016 and June 30, 2018 at a single, safety net institution, we used multinomial logistic regression models to compare predictors of vaccination among women who received Tdap only, influenza only, and both Tdap and influenza vaccines.

RESULTS: Among 3,133 full-term deliveries, women were primarily non-Hispanic black (67.5%), between the ages of 21-34 (65.3%), and multiparous (76.0 %). The rates of only influenza and Tdap vaccination were 9.2% and 23.6% respectively; 41.3% of women received both vaccines, and 26.0% of women did not receive either vaccine. In the adjusted model, Hispanic ethnicity and non-Spanish language interpreter use were positively associated with receipt of all types of vaccination. Inadequate and unknown prenatal care adequacy were negative predictors of all types of vaccination. HIV-positive status was negatively associated with influenza vaccination and Tdap and influenza vaccination.

CONCLUSION: Compared to the national rate of both Tdap and influenza vaccination (32.8%), a higher proportion of women received both vaccines in our study population. Vaccine uptake may be affected by race/ethnicity, use of interpreter services, HIV status, and prenatal care adequacy. The lower rate of influenza vaccination, compared to Tdap vaccination, suggests that other factors, such as vaccine hesitancy and mistrust, may differentially impact influenza vaccination uptake in our predominantly minority population. Future provider and public health approaches to vaccine promotion should incorporate appropriate strategies that address vaccine-related beliefs and misconceptions.

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Chapter I: Introduction

Context of Project

Influenza and pertussis infection pose severe risks to pregnant women and their infants [1-3]. Newborns under two months of age, before they are able to get vaccinated, have the highest rates of hospitalization and death due to pertussis [1]. Annual surveillance reports since 2000 show that among pertussis cases, 80% of hospitalizations and 90% of deaths happen in babies under one [4]. Further, during outbreaks, attack rates among newborns less than six months of age can be almost twenty times higher than the attack rate among the general population [5]. Pregnant women with influenza have higher rates of hospital admission [6, 7] and were more likely to be admitted to intensive care units compared to non-pregnant women [8-10]. Additionally, prior research has also suggested that expectant mothers with influenza have an increased risk of premature labor and delivery, contributing to a greater risk of infant morbidity and mortality [4]. Patients who seek care from safety net hospitals, that provide care for medically underserved patients, likely have several barriers that negatively affect their access to medical care, including antenatal Tdap and influenza vaccination.

Problem Statement

The Centers for Disease Control and Prevention (CDC) and American College of Obstetrics and Gynecology (ACOG) both currently recommend that women receive the Tdap vaccine between 27 and 36 weeks gestation of each pregnancy to provide protection to newborns [11]. However, Tdap vaccination rates remain low. Influenza vaccination rates also remain low at 49.1% in 2017 [12], despite the support of both CDC [13] and ACOG [14] for routine

influenza vaccination of pregnant women in all trimesters. Factors associated with Tdap and influenza vaccine refusal in pregnancy include young maternal age [15, 16], absence of public insurance [17], black race [15, 16, 18, 19], and lack of provider recommendation [16, 20, 21], with lack of provider recommendation being the most common reason for absence of antenatal vaccination [4, 5, 18, 22]. However, these findings have not been consistently replicated, and other studies have found no associations between these factors and refusal of antenatal Tdap and influenza vaccination [5, 23, 24]. Several studies have looked at predictors of influenza and Tdap vaccinations separately, however, none have systematically compared differences in predictors of receipt of either or both of the vaccines, particularly in a predominantly non-Hispanic black population with high levels of medical mistrust [18, 25, 26].

Purpose of Project

The objectives of the current study are to determine the predictors of Tdap vaccination, influenza vaccination, and both Tdap and influenza vaccination in an underserved population of women at Grady Memorial Hospital.

Chapter II: Literature Review

Pertussis

Pertussis Infection

Pertussis, also known as whooping cough, is an extremely infectious disease that unvaccinated infants are at an increased risk of contracting. The disease is spread through person-to-person contact, and droplet spread can cause infection. Infected individuals can be contagious for up to two weeks after initial onset of symptoms Pertussis can be separated into early, late, and recovery stages based on symptoms. Earlier symptoms have a clinical presentation similar to the common cold last one or two weeks, with some patients also endorsing a cough or mild fever [27]. In infants, clinical presentation can include apnea. The similar presentation to a cold often makes pertussis difficult to diagnose in the early stages of infection.

After the early stage passes (one or two weeks after initial infection), the clinical presentation is more differentiated from a cold making it easier to diagnose. Symptoms during the later stage including fits of numerous, quick coughs with a “whoop” sound after them, emesis during or after bouts of coughing, and exhaustion [27]. Finally, the recovery stage, which can last several weeks, is accompanied by milder and less frequent coughing fits.

Pertussis can cause severe complications and illness in infants, especially in unvaccinated or under-vaccinated infants. Roughly half of infants under the age of one who contract Pertussis require hospitalization [28]. Among the infants that require hospitalization for pertussis infection, complications include pneumonia (23%), convulsions (1.1%), apnea (61%), encephalopathy (0.3%), and even death (1%) [28].

Pertussis Vaccination

The most effective way to prevent pertussis is through vaccination. The Centers for Disease Control and Prevention (CDC) and American College of Obstetrics and Gynecology (ACOG) both currently recommend that women receive the Tdap vaccine during the third trimester of each pregnancy to provide protection to newborns [11]. The recommended window to receive the Tdap vaccination during pregnancy is between 27 and 36 weeks of gestation, with maximum maternal antibody transfer occurring when the vaccination is administered earlier in this window [29]. Maternal antibodies for Pertussis are highest two weeks after receiving the Tdap vaccination and conferral of these antibodies to the baby can take even more time, so earlier administration within the window of the Tdap vaccination is preferred [29]. Infants are not able to get the DTaP vaccination until they are 2 months old, so maternal antibodies may protect against pertussis until infants can be vaccinated. A recent study found that, compared to receiving Tdap after birth, receiving Tdap in the recommended stage of pregnancy is 85% more effective at preventing disease in infants younger than the vaccination age [29].

Annual surveillance reports since 200 show that among pertussis cases, 80% of hospitalizations and 90% of deaths happen in babies under one year of age [4]. Further, during outbreaks, attack rates among newborns less than six months of age can be twenty times higher than the attack rate among the general population [5]. However, Tdap vaccination rates remain low – during the 2017-2018 flu season only 54.4% of pregnant women with a live birth had received the Tdap vaccination during their pregnancy [2].

Influenza

Influenza infection

The clinical symptoms of influenza infection typically include fever, runny nose, sore throat, cough, myalgias, chills, and fatigue; occasionally some individuals also experience vomiting and diarrhea, while others may not have a fever with respiratory symptoms [30]. Fever, which is a typical symptom of influenza infection, has been associated with neural tube defects and other detrimental outcomes in developing babies [31]. During pregnancy, systemic changes in the heart, lung, and immune systems make pregnant women more susceptible to severe courses of influenza illness. Pregnant women with influenza have higher rates of hospital admissions [6, 7] and were more likely to be admitted to intensive care units compared to non-pregnant women [8-10]. Additionally, research has suggested that expectant mothers with influenza have an increased risk of premature labor and delivery, contributing to a greater risk of infant morbidity and mortality [4].

Influenza Vaccination

Given the increased risk of complications that pregnant women face, vaccination against influenza protects pregnant women from complications from influenza. The CDC [13] and ACOG [14] both support routine influenza vaccination of pregnant women in all trimesters. Per their recommendations, pregnant women should receive the flu shot, not the nasal spray flu vaccine which is a live attenuated influenza vaccine [31]. A study from 2018 demonstrated that pregnant women that received the flu shot were approximately 40% less likely to be hospitalized secondary to influenza infection [32]. Aside from the maternal protection the influenza vaccination provides, babies will also be protected by maternal antibodies during the pregnancy. Infants are not able to receive the influenza vaccination until they are six months old, but maternal vaccination during pregnancy can provide protection until vaccination age is reached [31].

The influenza vaccination is safe for pregnant women, which is supported by extensive scientific research. However, one study found that there was an increased risk of spontaneous abortion 28 days after receiving the most recent vaccine in women who received two consecutive influenza vaccinations in 2010-2011 and 2011-12. Although, several studies have shown that there is no elevated risk of spontaneous abortion secondary to receipt of influenza vaccination during pregnancy, the CDC is investigating the credibility of these findings. Despite this study, both ACOG and the CDC have maintained their vaccination recommendations.

Despite the protection from influenza infection that vaccination provides for both mother and child, typically more than half of all pregnant women remain unvaccinated in any given influenza season. In fact, data collected by the CDC from November 2017 found that 49.1% of pregnant patients had been vaccinated against influenza before or during their pregnancy [12], which is substantially lower than the Healthy People 2020 objective of 80% seasonal influenza vaccination rate for pregnant women [33]. Although the benefits of vaccinating pregnant women against influenza have been demonstrated by numerous studies, some women still remain reluctant to get vaccinated during pregnancy [15]. One of the greatest contributing factors to this reluctance concern about vaccine safety even though influenza vaccination in pregnancy has been recommended by both ACOG and the CDC.

Predictors of Antenatal Vaccination

General Predictors of Vaccination

Barriers to vaccination that have been consistently replicated include concerns regarding the safety and necessity of vaccination. Some Prior research has demonstrated that predictors associated with Tdap and influenza vaccine refusal include young maternal age, absence of

public insurance, black race, lack of provider recommendation, and premature delivery, with lack of provider recommendation being the most common reason for absence of antenatal vaccination [4, 22, 34]. However, these findings have not been consistently replicated, and other studies have found no association between these factors and refusal of antenatal Tdap and influenza vaccination [23, 24, 34].

A recent study suggested that there is a significant association between Tdap acceptance in patients that receive the influenza vaccine [24]. According to a 2018 retrospective cross-sectional study, patients who were willing to get the influenza vaccine were more open to receiving other preventative vaccinations [24]. Further, there is evidence that influenza vaccination receipt in the last year is associated with a greater likelihood of receiving Tdap vaccination.

Vaccine Hesitancy and Medical Mistrust

Even with a much smaller vaccination window for Tdap (given between 27-36 weeks of gestation) compared to influenza vaccination (given in any trimester), rates of Tdap vaccination are higher than influenza vaccination. One prior study demonstrated that women were less likely to refuse Tdap vaccination than influenza vaccination during pregnancy [21]. This could be related to maternal hesitation and perceptions surrounding the importance of influenza and Tdap vaccines.

One study reports that women perceive the influenza vaccine as being unsafe during pregnancy [19]. Another study reports that pregnant women are more likely to receive the Tdap vaccine, compared to the influenza vaccine [21], because they believed pertussis was more serious during pregnancy [1]. Additionally, there is a tendency for educational pamphlets and media to portray that influenza vaccination is necessary for maternal protection, and that Tdap

vaccination is necessary for infant protection [35]. This, combined with the perception that Pertussis poses a greater risk to the baby, may be significant positive predictors for receipt of Tdap vaccination [35].

Prior research on trust and maternal vaccination has shown that people are less likely to trust in the influenza vaccine [21] than the Tdap vaccine [18], because of skepticism surrounding the efficacy of the influenza vaccine [18,19,21]. Some people that have been vaccinated still get influenza each season for several reasons [36], making people doubt the efficacy of the vaccine. Influenza infection can happen in vaccinated individuals if exposure to influenza happened two weeks before vaccination, or if the infleunza that the individual was exposed to is a different strain of virus than what the vaccination protects against [36]. Since the influenza vaccination is recommended yearly, people are less likely to believe that the vaccine is actually medically necessary [18, 19]. Rather, there is a tendency to believe that influenza vaccine is merely recommended annually as a mechanism to maximize profits of pharmaceutical companies [19, 21]. The perceived effectiveness of the influenza vaccine is a predictor of influenza vaccination status.

Although provider recommendations can be an important influencing factor for patients to accept vaccines [21], the level of trust in healthcare providers differs by race [18]. Prior studies have found that African Americans are more skeptical of vaccinations, especially the influenza vaccine [25], and of healthcare providers than non-Hispanic whites [26]. African Americans may have greater medical distrust as a result of experiences of discrimination and racial biases [18]. Several studies have demonstrated that as a result of racism in the health care system, African American patients are less likely to trust research, physicians, and the healthcare system as a whole [18].

Chapter III: Manuscript

Title Page

Predictors of Tetanus, Diphtheria, Acellular Pertussis and Influenza Vaccination during Pregnancy among Full Term Deliveries in a Medically Underserved Population

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I have been involved in this project from the data collection stage. I helped abstract information from the medical charts of all of the patients in this cohort over the summer of 2018. I subsequently performed the quantitative data analysis beginning in fall of 2018. I was also responsible for performing all analyses and writing and preparing the manuscript for publication, including the creation of all tables.

Abstract

OBJECTIVE: To evaluate predictors of vaccination for women that received tetanus, diphtheria, and acellular pertussis vaccination (Tdap), influenza vaccination, and Tdap and influenza vaccinations.

Study Design: In a retrospective cohort study of all full-term (≥37 weeks gestation) deliveries between July 1, 2016 and June 30, 2018 at a single, safety net institution, we used multinomial logistic regression models to compare predictors of vaccination among women who received Tdap only, influenza only, and both Tdap and influenza vaccines.

RESULTS: Among 3,133 full-term deliveries, women were primarily non-Hispanic black (67.5%), between the ages of 21-34 (65.3%), and multiparous (76.0 %). The rates of only influenza and Tdap vaccination were 9.2% and 23.6% respectively; 41.3% of women received both vaccines, and 26.0% of women did not receive either vaccine. In the adjusted model, Hispanic ethnicity and non-Spanish language interpreter use were positively associated with receipt of all types of vaccination. Inadequate and unknown prenatal care adequacy were negative predictors of all types of vaccination. HIV-positive status was negatively associated with influenza vaccination and Tdap and influenza vaccination.

CONCLUSION: Compared to the national rate of both Tdap and influenza vaccination (32.8%), a higher proportion of women received both vaccines in our study population. Vaccine uptake may be affected by race/ethnicity, use of interpreter services, HIV status, and prenatal care adequacy. The lower rate of influenza vaccination, compared to Tdap vaccination, suggests that

other factors, such as vaccine hesitancy and mistrust, may be differentially impacting influenza vaccination uptake in our predominantly non-Hispanic black population. Future provider and public health approaches to vaccine promotion should incorporate appropriate strategies that address vaccine-related beliefs and misconceptions.

I. Introduction

Influenza and pertussis infection can pose severe risks to pregnant women and their infants [1-3]. Newborns under two months of age, before they are able to get vaccinated, have the highest rates of hospitalization and death due to Pertussis [1]. Annual surveillance reports since 200 show that among pertussis cases, 80% of hospitalizations and 90% of deaths happen in babies under one [4]. Further, during outbreaks, attack rates among newborns less than six months of age can be almost twenty times higher than the attack rate among the general population [5]. Pregnant women with influenza have higher rates of hospital admissions [6,7] and were more likely to be admitted to intensive care units compared to non-pregnant women [8-10]. Additionally, prior research has also suggested that expectant mothers with influenza have an increased risk of premature labor and delivery, contributing to a greater risk of infant morbidity and mortality [4].

The Centers for Disease Control and Prevention (CDC) and American College of Obstetrics and Gynecology (ACOG) both currently recommend that women receive the Tdap vaccine between 27 and 36 weeks gestation of each pregnancy to provide protection to newborns [11]. However, Tdap vaccination rates remain low – during the 2017-2018 influenza season only 54.4% of pregnant patients with a live birth had received the Tdap vaccination during their pregnancy [2]. Influenza vaccination rates also remain low at 49.1% in 2017 [12], despite the support of both CDC [13] and ACOG [14] for routine influenza vaccination of pregnant women in all trimesters.

Factors associated with Tdap and influenza vaccine in pregnancy include maternal age [15,16], public insurance [17], race [15,16,18,19], and provider recommendation [16,20,21], with

lack of provider recommendation being the most common reason for absence of antenatal vaccination [4,5,18,22]. However, these findings have not been consistently replicated, and other studies have found no associations between these factors and refusal of antenatal Tdap and influenza vaccination [5,23,24]. Recent studies have also suggested that there is a significant association between Tdap acceptance in patients who receive the influenza vaccine [24].

Even though the timing for Tdap vaccination is more restrictive than the influenza vaccination since influenza vaccination can be given in all three trimesters, rates of Tdap vaccination are marginally higher than influenza vaccination. Some prior studies attribute the lower rate of influenza uptake to greater distrust in the influenza vaccine as a result of skepticism surrounding vaccine efficacy [15,18,21]. This distrust in the influenza vaccination, is higher among African American mothers compared to Caucasian mothers [18]. Pregnant women are also more likely to refuse influenza vaccination [21] because of the perception that the influenza vaccine is necessary for self-protection, compared to the Tdap vaccine which is as necessary for protection of the baby [25]. Additionally, influenza vaccination rates may be lower due to misconceptions surrounding the safety and side-effects of the vaccine [19,21], and the perception of low susceptibility to influenza [19].

The objectives of the current study are to determine the predictors of Tdap vaccination, influenza vaccination, and both Tdap and influenza vaccination in an underserved population of women at Grady Memorial Hospital. Several studies have looked at predictors of influenza and Tdap vaccinations separately, however, none have systematically compared differences in predictors of receipt of either or both of the vaccines, particularly in a predominantly non-Hispanic black population. Our primary hypothesis is that the rate of influenza vaccination in our

population will be lower than the rate of Tdap vaccination in our population because of differences in underlying predictors for Tdap and influenza vaccinations.

II. Materials and Methods

We conducted a retrospective cohort study of pregnant women who delivered at Grady Memorial Hospital under the supervision of Emory University clinicians. Grady Memorial Hospital is the only public hospital in Atlanta, Georgia and offers medical care to a diverse body of patients, including many individuals who are indigent, underinsured, or uninsured [24]. All women who delivered between July 1, 2016 and June 30, 2018 were included.

Two data sources were used to identify all women with deliveries during the study period- the Emory Medical Care Foundation database and a delivery record maintained in the labor and delivery suite. Delivery was defined as the birth of one or more fetuses after 20 weeks of gestation, regardless of the viability of the fetus. Medical record numbers corresponding to a patient without a delivery, deliveries outside of the study period, and deliveries attended by non-Emory University providers at Grady Memorial Hospital were excluded.

Medical charts for identified patients were each reviewed for demographic information, including age, race, ethnicity, language and use of interpretive services, insurance status, education, and zip code of residence. Clinical characteristics including history of chronic diseases, parity, and prior obstetrical history were abstracted. Information about all clinical encounters in the current pregnancy (e.g. prenatal care visits, triage visits, hospital admissions) and prenatal care adequacy were also recorded. Prenatal care adequacy was defined using the Kotelchuck Index or Adequacy of Prenatal Care Utilization (APNCU) Index [26,27]. We were not able to determine prenatal care adequacy for patients that received prenatal care outside of Grady, so they were defined as ‘transfer of care.’ Study data were collected and managed using

Research Electronic Data Capture (REDCap) electronic data capture tools hosted at Emory University.

Influenza vaccination was defined as electronically documented receipt of influenza vaccine of any type during pregnancy. Tdap vaccination was defined as electronically documented receipt of Tdap vaccine during 27-36 weeks of gestation. Tdap vaccinations occurring before pregnancy, outside of the vaccination window, or immediately after delivery were documented as 'no Tdap' because of current CDC and ACOG recommendations for timing of the vaccine [12]. Provider offer or recommendation of Tdap and Influenza vaccination and reported reasons for vaccine refusal were recorded from review of prenatal care notes. If no offer or recommendation was documented in the medical chart, then it was assumed that the provider did not offer or recommend the vaccinations.

Rate of influenza vaccination in the pregnant population was calculated by dividing the number of influenza vaccinations in our sample by the number of deliveries after 37 weeks of gestation. The rate of Tdap vaccination in the pregnant population was calculated by dividing the number of Tdap vaccinations in our sample by the number of deliveries after 37 weeks of gestation. Deliveries prior to 37 weeks of gestation were excluded from analysis in order to allow all women the opportunity to receive vaccination during the recommended window [28].

To identify predictors of prenatal Tdap only, influenza only, and both Tdap and influenza vaccination, multinomial logistic regression models were used to estimate unadjusted and adjusted odds ratios (aOR), as well as corresponding 95% confidence intervals (CIs). Logistic regression models were used to estimate adjusted and unadjusted odds ratios as well as 95% confidence intervals (CIs) for the association between Tdap and influenza vaccinations. Both associations were adjusted for maternal age, smoking during pregnancy, race/ethnicity, parity,

prenatal care adequacy, and prior history of chronic medical conditions (asthma, HIV, diabetes, hypertension, obesity). These factors were selected *a priori* for inclusion as they have been previously identified in the literature as predictors of maternal vaccination. P values of <0.05 were considered statistically significant. Statistical analyses were conducted using Statistical Analysis Software (SAS) (SAS Institute Inc., Cary, NC), version 9.4.

The study was approved by the institutional review board at Emory University and the Grady Research Oversight Committee.

III. Results

From July 1, 2016 to June 30, 2018, we identified 3727 women with a delivery by Emory health care providers at Grady Memorial Hospital. Our final analytic cohort for the analysis of vaccination predictors consisted of 3133 women with a delivery after 37 weeks of gestation. As shown in Table 1, approximately 65% of our sample were between the ages of 21-34, 67% were non-Hispanic black, and 76% were multiparous. Of women who were identified as being born outside of the United States, Mexico, Guatemala, and Ethiopia were the most common countries of origin (data not shown). Roughly 23% of the study population were Hispanic, and Spanish was the most common language requiring an interpreter. Very few women had history of diabetes mellitus and HIV, while approximately 7% had hypertension and 9% had a history of asthma. Ten percent of women used tobacco products during pregnancy. Medicare and Medicaid paid for most deliveries (88%).

In our study population, the total rates of only influenza vaccination and Tdap vaccination were 9.2% and 23.6%, respectively; the rate of Tdap vaccination (64.8%) was markedly higher than the rate of influenza vaccination (50.5%). The rate of both Tdap and

influenza vaccination was 41.3%, and 26.0% of women did not receive Tdap or influenza vaccines. Among non-Hispanic black women, 31% did not receive Tdap or influenza vaccination. Among women who had at least one prenatal care visit at GMH and did not receive both Tdap and influenza vaccinations, the provider did not offer either vaccine to 61.9% of these women.

In adjusted multivariate regression analyses, women who received the influenza vaccine were 3.7 (95% CI: 3.1-4.4) times more likely to also receive the Tdap vaccine (data not shown). As shown in Table 2, Hispanic race/ ethnicity was generally associated with increased odds of influenza vaccination and Tdap vaccination. Non-Hispanic other race/ethnicity was positively associated with receipt of both Tdap and influenza vaccinations. Women who used interpreter services for a language other than Spanish had significantly higher odds of Tdap vaccination only and both Tdap and influenza vaccination. HIV+ status was negatively associated with influenza vaccination only and both Tdap and influenza vaccinations. Women with inadequate prenatal care and women with unknown prenatal care adequacy had lower odds of antenatal influenza and Tdap vaccination.

IV. Comment

The rate of both antenatal Tdap and influenza vaccination (41.3%) in our study population is higher than the national rates reported by the CDC in the 2017-2018 influenza season, which was roughly 32.8%. This higher rate of vaccination may be related to practices in place at Grady including universal provider recommendation of Tdap and influenza vaccination with standing orders, maintaining clinic stock of both vaccines, and provision of both vaccinations at no additional cost to patients. Maternal race and ethnicity, use of language

interpretive services for a language other than Spanish, HIV+ status, and prenatal care adequacy were all found to be predictors of vaccination. Additionally, receiving the influenza vaccine also predicted receipt of Tdap vaccination.

Our finding that Hispanic ethnicity is a predictor of antenatal Tdap vaccination builds upon previously reported data which found that women who accepted the Tdap vaccine were more likely to be Hispanic, compared to black and white women [29]. Conversely, a retrospective cohort study of pregnant women enrolled in Medicaid found that there were no significant differences in rates of Tdap between white and Hispanic women [30]. However, this study included infants delivered prior to 36 weeks gestation limiting direct comparison to our study findings. Additionally, our study population is primarily African American women with only a small subset of white women, making direct comparison difficult due to community level differences that can contribute to differing rates of vaccination. Our finding that use of non-Spanish language interpreter services was positively associated with Tdap vaccination only and Tdap and influenza vaccinations is novel.

According to a 2018 retrospective cross-sectional study, patients who were willing to get the influenza vaccine were more open to receiving other preventive vaccinations [24]; our results provide further support for this finding. Additionally, this association between Tdap and influenza vaccination may demonstrate that a preferential attitude towards preventative measures, such as vaccination, greatly impacts decision to vaccinate [17]. Even with a much smaller vaccination window for Tdap, between 27-36 weeks of gestation, rates of Tdap vaccination are much higher than influenza vaccination in our study population. This could be related to maternal hesitation and perceptions surrounding the importance of influenza and Tdap vaccines.

Some women may perceive the influenza vaccine as being unsafe during pregnancy [19]. Moreover, pregnant women are more likely to receive the Tdap vaccine than the influenza vaccine [21], because they believed pertussis was more serious than influenza during pregnancy [1]. Additionally, some portray influenza vaccination is necessary for maternal protection and Tdap vaccination for infant protection [25]. This, combined with the perception that Pertussis poses a greater risk to the baby, may be important predictors for receipt of Tdap vaccination [25].

Prior research on trust and maternal vaccination has shown that people are less likely to trust in the influenza vaccine [21] than the Tdap vaccine [18], because of skepticism surrounding the efficacy of the influenza vaccine [18,19,21]. Although provider recommendations can be an important influencing factor for patients to accept vaccines [21], level of trust in healthcare providers also differs by race [18]. Prior studies have found that African Americans are more skeptical of vaccinations, especially the influenza vaccine [31], and of healthcare providers than non-Hispanic whites [32]. African Americans may have greater medical distrust as a result of experiences of discrimination and racial biases [18]. While recommending influenza vaccination during pregnancy, healthcare providers should be conscious of vaccine hesitancy, and address misinformation and negative perceptions about the influenza vaccination [32-34].

Attending regular prenatal care visits increases the likelihood that vaccinations are offered or recommended by the provider and accepted by the patient. Antenatal Tdap is usually administered between 27 and 36 weeks of gestation, so if a patient is not able to access prenatal care during this window then the likelihood of vaccine receipt is greatly reduced. We were not able to evaluate external factors that impact access to care, such as education and transportation. Future research should focus on determining how these barriers to care impact vaccination rates, and mechanisms to improve these barriers.

Importantly, a key limitation of our data is that we were not able to determine prenatal care adequacy for about 15% of the patients in our population. This was because these women received prenatal care from providers outside of Grady Health System. We found that these women had significantly lower vaccination rates than women with adequate prenatal care. Transferring prenatal care might be a unique negative predictor of antenatal vaccination and/or women that received care at several sites might be less likely to receive adequate prenatal care, however there is currently a gap in the literature to support these hypotheses.

Our study has a few other limitations. First, the rates of antenatal vaccination rates may underestimate actual rates of antenatal vaccination uptake because we were not able to account for women that received vaccinations at outside facility that were not documented in Georgia Registry of Immunization Transactions and Services (GRITS), or if they were vaccinated outside the state of Georgia. Additionally, our interpretation of provider offer of vaccination is limited by documentation in EMR. Finally, due to the nature of our data, we were not able to examine or control for social determinants of health that were not regularly documented in the EMR like education, socioeconomic status, marital status, and employment status. Strengths of our study include examining a large cohort of pregnant patients where the majority are insured by Medicaid and Medicare. We were also able to account for influenza vaccination in two distinct ways, including EMR documentation and GRITS documentation.

The lower rate of influenza vaccination, compared to Tdap vaccination rate, demonstrates that other factors, such as vaccine hesitancy and mistrust, may be differentially impacting influenza vaccination uptake. Further research is needed to understand this difference in Tdap and influenza vaccination uptake. Our findings suggest that barriers to accessing adequate prenatal care-including transportation, insurance status, and lack of social support- should

continue to be examined and addressed, especially among underserved patient populations. Future approaches to increasing antenatal vaccination must be considered with input among public health programs and providers of prenatal care in order to identify and overcome barriers to vaccination among pregnant women.

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VI. Tables and Figures

Table 1: Demographic and Clinical Characteristics of Pregnancies Resulting in Delivery, July 1, 2016 – June 30, 2018

	Total Study Population (n= 3133)	No Tdap or Flu Vaccines	Flu Only	Tdap Only	Both Flu & Tdap Vaccines
Age at delivery					
<21	631 (20.14)	189 (23.25)	61 (21.11)	145 (19.65)	236 (18.25)
21-34	2045 (65.27)	515 (63.35)	191 (66.09)	480 (65.04)	859 (66.43)
>34	457 (14.59)	109 (13.41)	37 (12.80)	113 (15.31)	198 (15.31)
Race/ethnicity					
Non-Hispanic white	81 (2.61)	28 (3.50)	10 (3.48)	16 (2.19)	27 (2.11)
Non-Hispanic black	2090 (67.46)	639 (79.78)	203 (70.73)	499 (68.36)	749 (58.52)
Non-Hispanic other	198 (6.39)	34 (4.24)	12 (4.18)	51 (6.99)	101 (7.89)
Hispanic	729 (23.53)	100 (12.48)	62 (21.60)	164 (22.47)	403 (31.48)
Interpreter Use					
None	2363 (75.42)	700 (86.10)	229 (79.24)	548 (74.25)	886 (68.52)
Spanish	506 (16.15)	64 (7.87)	39 (13.49)	121 (16.40)	282 (21.81)
Other language	264 (8.43)	49 (6.03)	21 (7.27)	69 (9.35)	125 (9.67)
Parity					
0	750 (23.95)	199 (24.51)	70 (24.22)	180 (24.39)	301 (23.28)
1	236 (7.54)	41 (5.05)	26 (9.00)	68 (9.21)	101 (7.81)
2	775 (24.74)	186 (22.91)	70 (24.22)	173 (23.44)	346 (26.76)
3 or more	1371 (43.77)	386 (47.54)	123 (42.56)	317 (42.95)	545 (42.15)
Chronic medical conditions					
Hypertension	229 (7.31)	62 (7.63)	19 (6.57)	40 (5.42)	108 (8.35)
Diabetes Mellitus	65 (2.07)	11 (1.35)	8 (2.77)	9 (1.22)	37 (2.86)
Asthma	274 (8.75)	84 (10.33)	30 (10.38)	59 (7.99)	101 (7.81)
HIV+	63 (2.01)	22 (2.71)	2 (0.69)	15 (2.03)	24 (1.86)
Tobacco use in pregnancy	313 (10.23)	115 (14.41)	31 (11.03)	65 (9.00)	102 (8.10)
Prenatal care					
Transfer of care	468 (14.96)	284 (35.06)	46 (15.97)	78 (10.57)	60 (4.64)
Inadequate	1345 (43.00)	392 (48.40)	130 (45.14)	325 (44.04)	498 (38.54)
Intermediate	515 (16.46)	61 (7.53)	48 (16.67)	125 (16.94)	281 (21.75)
Adequate	638 (20.40)	63 (7.78)	48 (16.67)	171 (23.17)	356 (27.55)
Adequate plus	162 (5.18)	10 (1.23)	16 (5.56)	39 (5.28)	97 (7.51)
Primary insurance type					
Self-pay	199 (6.35)	77 (9.47)	21 (7.27)	38 (5.15)	63 (4.87)
Medicare/Medicaid	2772 (88.48)	688 (84.62)	257 (88.93)	654 (88.62)	1173 (90.72)
Commercial	162 (5.17)	77 (9.47)	21 (7.27)	38 (5.15)	63 (4.87)

Table 2: Relative Odds of Tdap and Influenza Immunization during Pregnancy for Full Term Deliveries by Selected Demographic Characteristics, Clinical Characteristics, Prenatal Care Adequacy, and Insurance Status

	Tdap Unadjusted Odds Ratio (95% CI)	Flu Unadjusted Odds Ratio (95% CI)	Tdap & Flu Unadjusted Odds Ratio (95% CI)	Tdap Adjusted Odds Ratio (95% CI)	Flu Adjusted Odds Ratio (95% CI)	Tdap & Flu Adjusted Odds Ratio (95% CI)
Age at delivery						
<21	0.82 (0.64-1.06)	0.87 (0.62-1.21)	**0.75 (0.60-0.93)**	0.80 (0.60-1.08)	0.80 (0.54-1.18)	0.82 (0.62-1.08)
21-34	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
>34	1.11 (0.83-1.49)	0.92 (0.61-1.38)	1.09 (0.84-1.41)	1.21 (0.88-1.66)	1.00 (0.65-1.54)	1.00 (0.74-1.35)
Race/ethnicity						
Non-Hispanic white	0.73 (0.39-1.37)	1.12 (0.54-2.35)	0.82 (0.48-1.41)	0.92 (0.48-1.79)	1.25 (0.57-2.76)	1.08 (0.59-1.98)
Non-Hispanic black	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
Non-Hispanic other	**1.92 (1.23-3.01)**	1.11 (0.57-2.19)	**2.53 (1.69-3.79)**	1.44 (0.86-2.41)	0.94 (0.45-2.00)	**1.72 (1.06-2.79)**
Hispanic	**2.10 (1.60-2.76)**	**1.95 (1.37-2.78)**	**3.44 (2.70-4.38)**	**1.66 (1.21-2.27)**	**1.81 (1.21-2.71)**	**2.66 (2.00-3.55)**
Interpreter Use						
None	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
Spanish	**2.42 (1.75-3.34)**	**1.86 (1.22-2.85)**	**3.48 (2.61-4.65)**	1.50 (0.91-2.46)	1.02 (0.54-1.92)	1.46 (0.93-2.30)
Other language	**1.80 (1.23-2.64)**	1.31 (0.77-2.23)	**2.02 (1.43-2.85)**	**1.54 (1.02-2.33)**	1.21 (0.69-2.12)	**1.85 (1.25-2.72)**
Parity						
0	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
1	**1.83 (1.19-2.84)**	**1.80 (1.03-3.16)**	**1.63 (1.09-2.44)**	1.53 (0.95-2.45)	1.51 (0.83-2.75)	1.42 (0.90-2.23)
2	1.03 (0.77-1.37)	1.07 (0.73-1.58)	1.23 (0.96-1.58)	0.89 (0.65-1.22)	1.01 (0.67-1.53)	1.11 (0.83-1.48)
3 or more	0.91 (0.71-1.17)	0.91 (0.65-1.27)	0.93 (0.75-1.17)	0.74 (0.55-1.00)	0.79 (0.53-1.18)	0.76 (0.57-1.01)
Chronic Medical Conditions						
Hypertension	0.69 (0.46-1.05)	0.85 (0.50-1.45)	1.10 (0.80-1.53)	0.53 (0.33-0.84)	0.64 (0.36-1.14)	0.83 (0.57-1.23)
Diabetes Mellitus	0.90 (0.37-2.19)	2.08 (0.83-5.21)	**2.15 (1.09-4.24)**	1.00 (0.39-2.58)	2.39 (0.91-6.32)	1.97 (0.89-4.34)
Asthma	0.75 (0.53-1.07)	1.01 (0.65-1.56)	**0.74 (0.54-0.99)**	0.81 (0.56-1.18)	1.10 (0.70-1.74)	0.91 (0.65-1.27)
HIV	0.75 (0.38-1.45)	0.25 (0.06-1.07)	0.68 (0.38-1.22)	0.50 (0.25-1.03)	**0.19 (0.04-0.82)**	**0.43 (0.22-0.86)**
Tobacco use in pregnancy	**0.59 (0.43-0.81)**	0.74 (0.48-1.12)	**0.52 (0.39-0.70)**	0.77 (0.54-1.09)	0.90 (0.58-1.41)	0.78 (0.57-1.08)

Prenatal care						
Transfer of care	**0.10 (0.07-0.15)**	**0.21 (0.13-0.35)**	**0.04 (0.03-0.06)**	**0.10 (0.07-0.15)**	**0.20 (0.12-0.33)**	**0.04 (0.03-0.06)**
Inadequate	**0.31 (0.22-0.42)**	**0.44 (0.29-0.67)**	**0.23 (0.17-0.30)**	**0.33 (0.24-0.46)**	**0.45 (0.29-0.70)**	**0.24 (0.18-0.33)**
Intermediate	**0.76 (0.50-1.15)**	1.03 (0.61-1.76)	0.82 (0.56-1.20)	0.74 (0.48-1.13)	1.03 (0.60-1.77)	0.81 (0.55-1.20)
Adequate	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
Adequate plus	1.44 (0.68-3.05)	2.10 (0.88-5.04)	1.72 (0.85-3.47)	1.69 (0.78-3.66)	2.19 (0.88-5.43)	1.71 (0.83-3.53)
Primary Insurance						
Self-pay	**0.52 (0.29-0.90)**	1.19 (0.53-2.68)	0.69 (0.41-1.15)	0.76 (0.41-1.41)	1.65 (0.71-3.83)	1.17 (0.65-2.08)
Medicaid/ Medicare	0.99 (0.65-1.51)	1.63 (0.83-3.19)	1.44 (0.97-2.13)	1.01 (0.64-1.61)	1.51 (0.76-3.01)	1.36 (0.87-2.15)
Private	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*

Chapter IV: Conclusion and Recommendations

The rate of both antenatal Tdap and influenza vaccination (41.3%) in our study population is higher than the national rates reported by the CDC in the 2017-2018 influenza season, which was roughly 32.8%. This higher rate of vaccination may be related practices in place at Grady including universal provider recommendation of Tdap and influenza vaccination with standing orders, maintaining clinic stock of both vaccines, and provision of both vaccinations at no additional cost to patients. Maternal race and ethnicity, use of language interpretive services for a language other than Spanish, HIV+ status, and prenatal care adequacy were all found to be predictors of vaccination. Additionally, receiving the influenza vaccine also predicted receipt of Tdap vaccination.

Our finding that Hispanic ethnicity is a predictor of antenatal Tdap vaccination builds upon previously reported data from a retrospective cohort study in Dallas, which similarly found that women who accepted the Tdap vaccine were more likely to be Hispanic, compared to black and white women [37]. However, an important limitation of these data was that receipt of antenatal Tdap was defined as receipt of Tdap at or after 32 weeks of gestation [37] and might limit direct comparison to our study findings. Conversely, a retrospective cohort study in Michigan of pregnant women enrolled in Medicaid found that there were no significant differences in rates of Tdap between white and Hispanic women [25]. However, a limitation of this study is that they do not account for immortal time bias by including infants delivered prior to 36 weeks gestation, so this might limit direct comparison to our study findings. Tdap vaccination is recommended at 27-36 weeks of gestation, but this creates a setting where pregnancies have to “survive” until 27-36 weeks in order to be offered the Tdap vaccine [26]. So, the time to vaccination is “immortal” because women that deliver before the end of the

vaccination window do not have equal opportunity to be offered the Tdap vaccination [26]. Additionally, our study population is primarily African American women with only a small subset of white women, making direct comparison difficult due to community level differences that can contribute to differing rates of vaccination.

Our finding that use of non-Spanish language interpreter services was positively associated with Tdap vaccination only and Tdap and influenza vaccinations is novel. One prior study found that antenatal vaccination rates were higher among English and Spanish speaking women, and English as a second language was a negative predictor of antenatal vaccination [22].

Recent studies have suggested that there is a significant association between Tdap acceptance in patients that also receive the influenza vaccine [24]. According to a 2018 retrospective cross-sectional study, patients who were willing to get the influenza vaccine were more open to receiving other preventive vaccinations [24]; our results provide further support for this finding. Even with a much smaller vaccination window for Tdap, between 27-36 weeks of gestation, rates of Tdap vaccination are much higher than influenza vaccination in our study population. This could be related to maternal hesitation and perceptions surrounding the importance of influenza and Tdap vaccines.

One previous study found that in their population of pregnant women, almost half viewed the influenza vaccine as being unsafe during pregnancy, and they were more likely to receive the Tdap vaccine than an influenza vaccine because they believed pertussis was more serious during pregnancy [1]. Prior research on trust in the influenza vaccine has also shown that people are less likely to trust in the influenza vaccine than the Tdap vaccine [18]. This lack of trust in the influenza vaccination may be related to the skepticism surrounding the efficacy of the vaccine. Since the influenza vaccine is updated yearly and the vaccine's efficacy is lower than other

vaccines, people are less likely to believe that the vaccine is clinically necessary and more likely to believe that the yearly recommendation garners increased profits for the industry. Prior studies have also found that African Americans are more skeptical of vaccinations, especially the influenza vaccine [26], and healthcare providers than non-Hispanic whites [38].While recommending influenza vaccination during pregnancy, healthcare providers should be conscious of vaccine hesitancy, and address misinformation and negative perceptions about the influenza vaccination [38-40].

Attending regular prenatal care visits increases the likelihood that vaccinations are offered or recommended by the provider and accepted by the patient. Antenatal Tdap is usually administered between 27 and 36 weeks of gestation, so if a patient is not able to access prenatal care during this window then the likelihood of vaccine receipt is greatly reduced. We were not able to evaluate external factors that impact access to care, such as education status, transportation. Future research should focus on determining how these barriers to care impact vaccination rates, and mechanisms to improve these barriers.

Importantly a key limitation of our data was that we were not able to determine prenatal care adequacy for roughly 15% of the patients in our population. This was because these women received prenatal care from providers outside of Grady Health System. We found that these women had significant lower vaccination rates compared to women with adequate prenatal care. Transferring prenatal care might be a unique negative predictor of antenatal vaccination and/or women that received care at several sites might be less likely to receive adequate prenatal care, however there is currently a gap in the literature to support these hypotheses.

There are a few other limitations for our study. First, the rates of antenatal vaccination rates may be underestimating actual rates of antenatal vaccination uptake because we were not

able to account for women that received vaccinations at outside facility that were not documented in GRITS, or if they were vaccinated outside the state of Georgia. Additionally, our interpretation of provider offer of vaccination is limited by documentation in EMR. Finally, due to the nature of our data, we were not able to examine or control for SDH that were not regularly documented in the EMR like education, socioeconomic status, marital status, and employment status. Strengths of our study include examining a large cohort of pregnant patients where the majority are insured by Medicaid and Medicare. We were also able to account for influenza vaccination in two distinct ways, including EMR documentation and GRITS documentation.

The lower rate of influenza vaccination, compared to Tdap vaccination rate, demonstrates that other factors, such as vaccine hesitancy and mistrust, may be differentially impacting influenza vaccination uptake. Further research is needed to understand this difference in Tdap and influenza vaccination uptake. Our findings suggest that barriers to accessing adequate prenatal care-including transportation, insurance status, and lack of social support- should continue to be examined and addressed, especially among underserved patient populations. Future approaches to increasing antenatal vaccination must be considered with input among public health programs and providers of prenatal care in order to identify and overcome barriers to vaccination among pregnant women.

Chapter V. References

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