American Journal of
Preventive Medicine

RESEARCH BRIEF

Maternal Immunization in the U.S.: A Nationwide Retrospective Cohort Study

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Introduction: At present, pregnant women in the U.S. are recommended to receive tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) and influenza vaccines. This study assessed maternal coverage of these 2 vaccinations.

Methods: Data for this retrospective cohort study were extracted from 2 large administrative claims databases, the MarketScan Commercial and Multi-State Medicaid Databases, for 2009–2017 and analyzed in 2018. Women aged 15–44 years on the date of pregnancy end were included. Pregnancies with gestational age of less than 23 weeks were excluded from the Tdap vaccination endpoint owing to the optimal recommended gestational age for Tdap vaccination. Multivariable logistic regression models identified predictors of vaccination.

Results: The Tdap vaccination subpopulation included 1,421,452 Commercial and 523,635 Medicaid pregnancies; the influenza vaccination subpopulation included 1,862,705 Commercial and 628,079 Medicaid pregnancies. There were marked increases in vaccination coverage from 2010 to 2017: from 1.0% to 56.3% (Commercial) and from 0.5% to 31.4% (Medicaid) for Tdap, and from 14.7% to 31.3% (Commercial) and from 9.7% to 17.5% (Medicaid) for influenza. The likelihood of Tdap/influenza vaccination increased significantly with receipt of the other vaccine and more pregnancy-related healthcare visits.

Conclusions: Although maternal Tdap and influenza vaccination coverage increased substantially from 2010 to 2017 among large, geographically diverse U.S. cohorts, coverage remained suboptimal, potentially putting newborns at risk of pertussis and influenza. Strategies to increase maternal vaccination coverage could target women identified to have a reduced likelihood of vaccination: those who are younger, black, residing in rural areas, with multiple gestation, and a prepregnancy inpatient admission.

Am J Prev Med 2019;57(3):e87–e93.

INTRODUCTION

Pertussis and influenza infection can cause severe illness in newborns,[1,2] but infant vaccination against these diseases is not recommended until the ages of 2 and 6 months, respectively.[3] The U.S. Advisory Committee on Immunization Practices has recommended immunization with the tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine since 2012,[4] and influenza vaccination since 2004,[5,6] during each pregnancy. Despite these recommendations, in a 2017–2018 Centers for Disease Control and Prevention (CDC) survey, only 54.4% and 49.1% of pregnant women self-reported receiving Tdap and influenza vaccinations, respectively.[7] However, these estimates may be subject to recall, nonresponse, or social desirability bias.[7] Other estimates of maternal

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0749-3797/$36.00
https://doi.org/10.1016/j.amepre.2019.04.013

immunization are from surveys/interviews[8−18] or limited to selected states[17−26] or years before 2015.[27−29]

This study assessed Tdap and influenza vaccination coverage in large, geographically diverse cohorts, for commercially and Medicaid-insured women separately during 2010−2017, and assessed select characteristics that influenced the likelihood of maternal immunization.

METHODS

Study Sample

Data were extracted from the MarketScan Commercial and Multi-State Medicaid Databases for 2009−2017 and analyzed in 2018. The former contains the inpatient, outpatient, and prescription drug claims experience of several million employees and their dependents,[30] and the latter reflects the healthcare service use of individuals covered by Medicaid programs.

Measures

This retrospective cohort study identified pregnancies using diagnosis or procedure codes indicating a pregnancy end on an inpatient or outpatient claim between January 2010 and April 2017. Vaccination coverage is the proportion of vaccinated pregnancies and was measured according to various maternal demographic and clinical characteristics. Tdap and influenza vaccinations were assessed for each year during 2010−2017 and for each season from 2009−2010 through 2016−2017, respectively.

Statistical Analysis

Multivariable logistic regression was used to estimate the likelihood of vaccination, controlled for demographics, clinical characteristics, and healthcare resource use and costs (baseline all-cause and pregnancy-related). Data are presented as AORs and 99% CIs. Owing to the large cohort sizes, the threshold to detect a statistically significant association was $p<0.01$; it was predefined that an OR ≤0.85 or ≥1.15 indicated a potentially clinically meaningful association. SAS, version 9.4 (SAS Institute, Cary, NC) was used for all analyses. Additional methodology details are described in Appendix 1 (available online).

RESULTS

The eligible Tdap vaccination cohorts included 1,421,452 Commercial and 523,635 Medicaid pregnancies; the eligible influenza vaccination cohorts included 1,862,705 and 628,079 pregnancies, respectively. Maternal demographic and clinical characteristics are shown in Appendix Table 1 (available online). From 2010 to 2017, Tdap vaccination coverage increased dramatically in the Commercial (1.0% ≥ 56.3%) and Medicaid (0.5% ≥ 31.4%) cohorts (Figure 1). During this period, influenza vaccination coverage also increased in the Commercial (14.7% ≥ 31.3%) and Medicaid (9.7% ≥ 17.5%) cohorts.

Women received Tdap immunizations within the recommended 27−36 weeks gestation[4] for 89.1% and 88.8% of pregnancies in the Commercial and Medicaid cohorts, respectively. Tdap was administered at a mean gestational age of 31 (SD=5) weeks in both cohorts, influenza at 21 (SD=11) weeks (Commercial) and 23 (SD=10) weeks (Medicaid).

Coverage increased with increasing age up to 30−34 years, then declined among older women (Table 1). In the Medicaid cohort, coverage varied by race/ethnicity, with lowest coverage among black women. Across the U.S. Census divisions, West North Central had the highest coverage for Tdap (32.7%), whereas New England had the highest coverage for influenza (28.9%) vaccines, and West South Central had the lowest coverage for Tdap (18.5%) and influenza (19.9%) vaccines (Appendix Figure 2, available online). The most common prescriber type at time of Tdap/influenza vaccination was obstetricians/gynecologists for the Commercial cohort, whereas in the Medicaid cohort, a range of provider types were involved (Figure 2).

Two factors were statistically significant and potentially clinically meaningful in all analyses: likelihood of vaccination increased with receipt of the other vaccine during pregnancy (ORs=3.39−5.19) and reduced with no pregnancy-related visits (ORs=0.23−0.40) (Appendix Table 2, available online). Other notable factors that increased the likelihood of vaccination included Hispanic origin and ≥11 versus 1−5 pregnancy-related visits, whereas age 15−19 years versus 30−34 years, black race, residence in rural areas, multiple gestation, and inpatient admission during baseline had the opposite effect.

DISCUSSION

In a large population of U.S. pregnant women, maternal Tdap vaccine coverage increased substantially after the 2012 recommendation to vaccinate during every pregnancy,[4] consistent with increases reported in other studies[15,18,20,27−29]; however, coverage remains suboptimal. Despite the recommendation of influenza vaccination for all pregnant women since 2004,[5] influenza coverage by the end of the study was far below the *Healthy People 2020* target of 80%.[31] Maternal Tdap vaccination coverage estimates in the Commercial cohort of this study are in agreement with a recent CDC survey[7] among those with private/military insurance (2017, 56.3%; 2017−2018, 58.8%). However, 2016−2017 influenza vaccination coverage in the current Commercial cohort was lower than the CDC's estimates[13] (31.3% vs 59.3%), although the latter included prepregnancy vaccination (~30% of recipients), which likely accounts for this difference. Coverage in the current Medicaid cohort was lower than among those with public insurance in the CDC surveys (Tdap, 31.4% in 2017 vs 50.8% in 2017−2018[7]; influenza, 17.5% in

Table 1. Maternal Immunization Coverage for Pregnancies With End Dates During January 2010 Through April 2017

	Commercial, *n/N* (%)		Medicaid, *n/N* (%)	
Characteristic	**Tdap**	**Influenza**	**Tdap**	**Influenza**
Overall	328,361/1,421,452 (23.1)	411,834/1,862,705 (22.1)	81,501/523,635 (15.6)	90,912/628,079 (14.5)
Age at pregnancy end, years				
14–19	5,982/43,740 (13.7)	9,285/65,485 (14.2)	13,316/111,748 (11.9)	18,402/130,791 (14.1)
20–24	32,033/156,889 (20.4)	34,792/217,055 (16.0)	27,013/175,737 (15.4)	29,596/204,951 (14.4)
25–29	81,793/372,559 (22.0)	100,982/465,338 (21.7)	23,353/136,409 (17.1)	24,123/163,502 (14.8)
30–34	129,928/521,720 (24.9)	163,378/648,509 (25.2)	12,457/69,282 (18.0)	12,865/86,124 (14.9)
35–39	65,666/267,932 (24.5)	84,918/364,045 (23.3)	4,563/25,632 (17.8)	4,919/34,577 (14.2)
40–44	12,959/58,612 (22.1)	18,479/102,273 (18.1)	799/4,827 (16.6)	1,008/8,134 (12.4)
Health plan type				
Comprehensive/indemnity	3,656/12,945 (28.2)	3,525/16,978 (20.8)	33,575/223,650 (15.0)	41,397/260,012 (15.9)
EPO/PPO	195,113/871,829 (22.4)	250,936/1,138,588 (22.0)	387/521 (74.3)	242/679 (35.6)
POS/POS with capitation	22,464/107,704 (20.9)	30,794/142,411 (21.6)	180/7,453 (2.4)	880/8,721 (10.1)
HMO	43,142/200,297 (21.5)	54,099/266,428 (20.3)	47,348/291,836 (16.2)	48,369/358,428 (13.5)
CDHP/HDHP	60,280/176,569 (34.1)	60,285/229,725 (26.2)	—	—
Other/unknown	3,706/52,108 (7.1)	12,195/68,575 (17.8)	11/175 (6.3)	24/239 (10.0)
Race/ethnicity				
White	—	—	40,013/255,784 (15.6)	46,144/303,107 (15.2)
Black	—	—	28,503/209,242 (13.6)	31,333/251,417 (12.5)
Hispanic	—	—	3,881/19,258 (20.2)	4,837/22,920 (21.1)
Other/unknown	—	—	9,104/39,351 (23.1)	8,598/50,635 (17.0)
Geographic region				
Northeast	51,515/237,387 (21.7)	77,542/338,626 (22.9)	—	—
North Central	81,776/321,376 (25.4)	97,436/406,456 (24.0)	—	—
South	116,499/559,836 (20.8)	150,723/716,679 (21.0)	—	—
West	75,310/287,585 (26.2)	81,402/380,748 (21.4)	—	—
Unknown	3,261/15,268 (21.4)	4,731/20,196 (23.4)	—	—
Population density				
Urban	294,996/1,235,400 (23.9)	361,829/1,630,281 (22.2)	—	—
Rural	30,130/171,369 (17.6)	45,304/212,950 (21.3)	—	—
Unknown	3,235/14,683 (22.0)	4,701/19,474 (24.1)	—	—

Note: n indicates number of pregnancies with vaccination, and *N* indicates total number of pregnancies.
CDHP, consumer-driven health plan; EPO, exclusive provider organization; HDHP, high deductible health plan; POS, point of service; PPO, preferred provider organizations; Tdap, tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

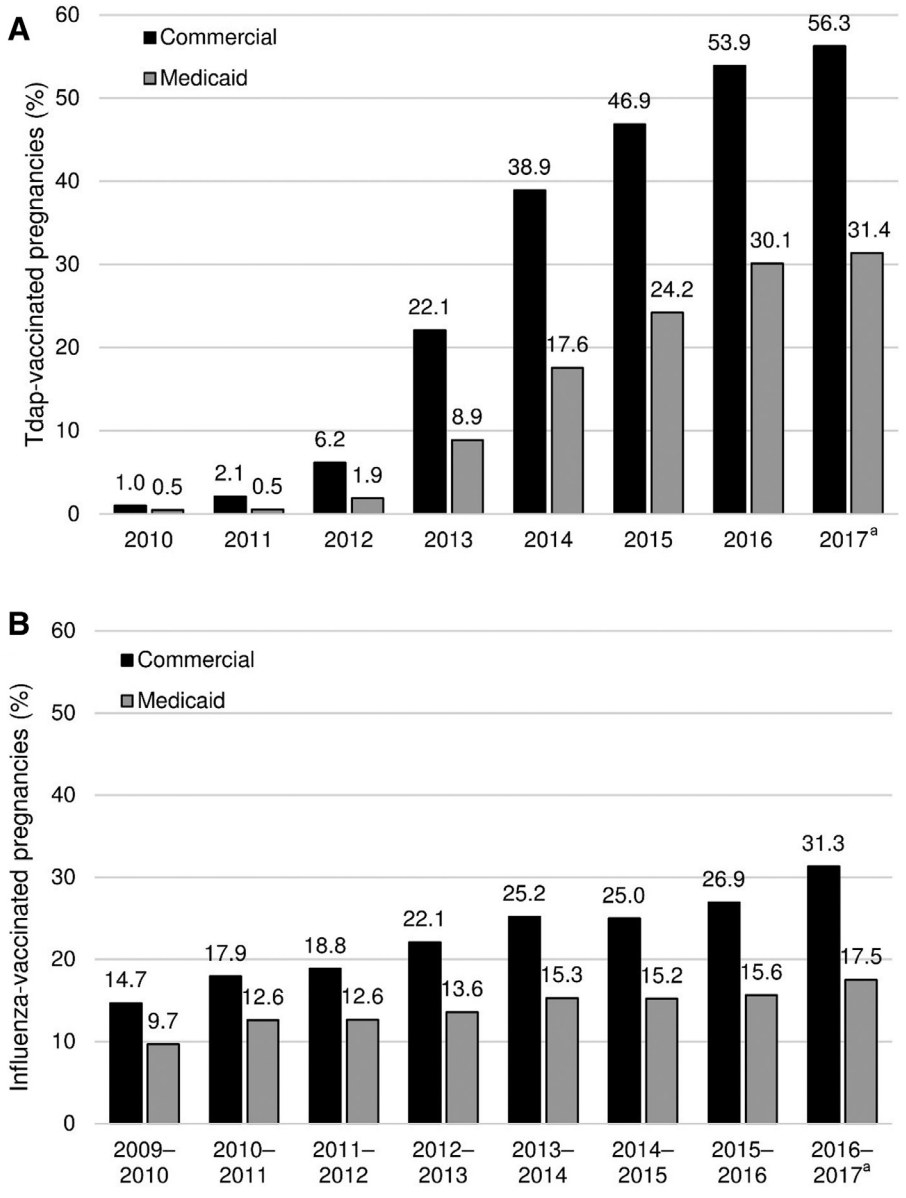

Figure 1. (a) Tdap and (b) influenza maternal immunization coverage by calendar year and influenza season, respectively.
Note: Only influenza vaccinations administered during the influenza season (September–May) of pregnancy end were included. Tdap and influenza vaccines were co-administered (on the same date) in 7.2% and 10.4% of pregnancies in the Commercial and Medicaid Tdap cohorts, respectively. [a]Only partial year data were available for 2017 at the time of data extraction (January–April). Tdap, tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

2016 vs 47.6% in 2017[13]), although, as above, prepregnancy vaccinations were included in the CDC survey. These discrepancies are likely because of the different methodologies, including that claims data do not capture vaccinations provided in free clinics. Vaccination coverage discrepancies by insurance type have also been observed in other studies.[7,13,19,21,24]

Tdap coverage varied from 20.8% in the South to 26.2% in the West. Similarly, Kriss et al.[16] reported that Tdap coverage was lowest in the South and highest in the West. Conversely, Butler and colleagues[28] reported that Tdap coverage was highest in the South and lowest in the Northeast. However, it should be noted that the 2 previous studies were soon after[16] or spanned[28] the 2012 recommendation to provide Tdap during every pregnancy.[4]

In both cohorts, immunizations were administered by a range of providers, highlighting the need for all providers to act upon the maternal immunization recommendations, as provider recommendations are strongly influential on maternal vaccine uptake.[7,13]

The factors most associated with vaccination were as follows: receipt of the other vaccine, Hispanic origin, and

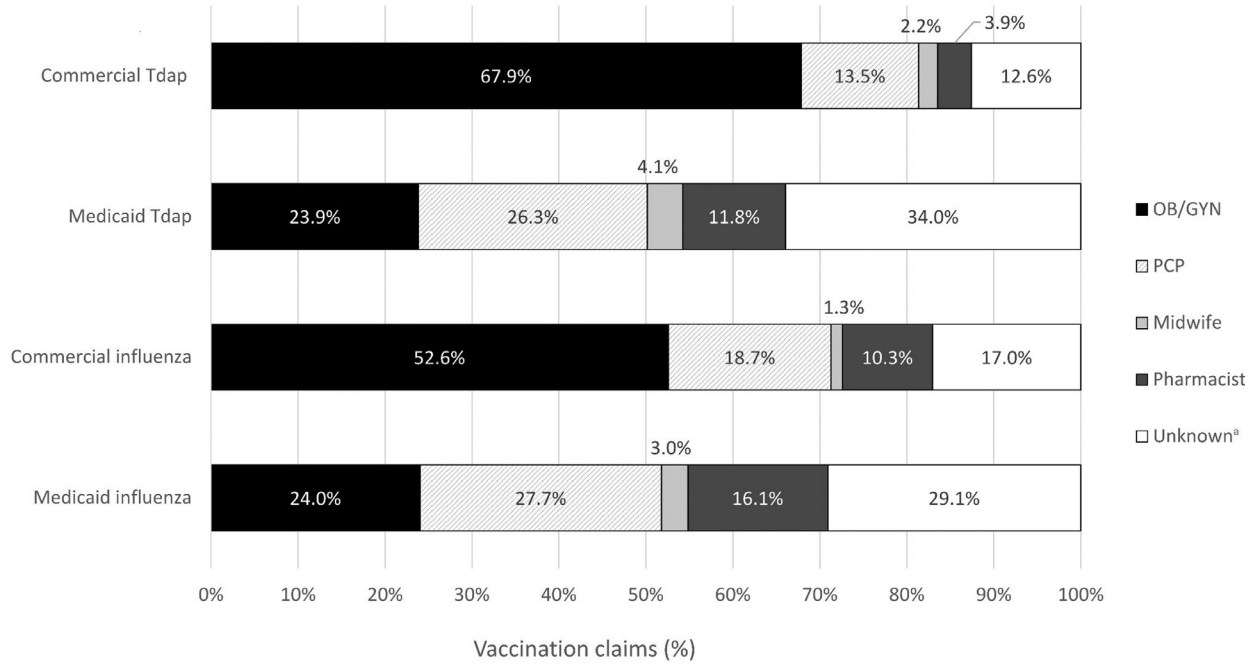

Figure 2. Overall distribution of provider type for Tdap and influenza vaccination for the Commercial and Medicaid cohorts.
[a]Includes vaccination claims where provider's specialty was missing or unspecified (e.g., multi-specialty practice group or public health agency).
OB/GYN, obstetrician/gynecologist; PCP, primary care physician; Tdap, tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

more pregnancy-related visits, consistent with previously reported positive predictors.[7,13,19,21,24,25] Conversely, no pregnancy-related visits, younger age (15–19 years), multiple gestation, and an inpatient admission during baseline generally reduced the likelihood of vaccination. The association between the number of visits and maternal immunization emphasizes the need for providers of pregnant women to recommend and offer vaccination at every opportunity to ensure higher vaccination coverage among pregnant women.

Strengths of this study include the large number of women, inclusion from geographic regions across the U.S., use of vaccination records from claims data rather than self-reported surveys, and separate Commercial and Medicaid analyses.

Limitations

Limitations include potential data coding and data entry error in claims; limited generalizability to women who are uninsured, self-insured, or have intermittent insurance coverage; and inability of claims databases to capture vaccinations administered in free clinics or to those eligible under the Vaccines for Children program.

CONCLUSIONS

This study's findings showed suboptimal maternal Tdap and influenza vaccination coverage among large, geographically diverse cohorts in the U.S. These results also highlighted the beneficial impact of the receipt of 1 vaccination on receipt of the other and emphasized the need for providers to recommend and offer vaccination at every opportunity. Strategies to increase maternal vaccination coverage could be targeted toward pregnant women identified to have a reduced likelihood of vaccination: those who are younger, black, residing in rural areas, with multiple gestation, and a prepregnancy inpatient admission. Future studies are warranted to understand barriers to maternal immunization and determine interventions to increase vaccination uptake, particularly among pregnant women with characteristics associated with lower likelihood of vaccination.

ACKNOWLEDGMENTS

GlaxoSmithKline Biologicals SA funded this study (GSK study identifier: HO-17-18109) and was involved in all stages of study conduct, including critical review of the analyzed data. GlaxoSmithKline Biologicals SA also paid all costs associated with the development and publication of this manuscript. The authors would like to thank Hervé Akpo (GSK, Belgium) for his support on this study analysis. The authors also thank the Business & Decision Life Sciences platform for editorial assistance and publications coordination, on behalf of GSK. Amandine Radziejwoski coordinated publications development and editorial support. Writing support was provided by Jenny Lloyd (Compass Healthcare Communications Ltd.).

All authors participated in the design or implementation or analysis, and interpretation of the study; and the development of this manuscript. All authors had full access to the data and gave final approval before submission.

Parinaz Ghaswalla, Jean-Etienne Poirrier, and Philip O. Buck are employees of the GSK group of companies and hold shares in the GSK group of companies. Elizabeth Packnett, Debra E. Irwin, and Stephani Gray are employees of IBM Watson Health. IBM Watson Health receives funding from a variety of sources to conduct studies.

No other conflicts of interest were reported by the authors of this paper.

SUPPLEMENTAL MATERIAL

Supplemental materials associated with this article can be found in the online version at https://doi.org/10.1016/j.amepre.2019.04.013.

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