Vaccine exposure during pregnancy among privately and publicly insured women in the United States, 2016–2018

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Abstract

Background: Vaccine use during pregnancy affects maternal and infant health. Many women do not receive vaccines recommended during pregnancy; conversely, inadvertent exposure to vaccines contraindicated or not recommended during pregnancy may occur. We assessed exposure to two recommended vaccines and two vaccines not recommended during pregnancy among privately and Medicaid-insured women in the United States.

Methods: This study includes a retrospective cohort of pregnancies in women aged 12–55 years resulting in live birth, spontaneous abortion, or stillbirth identified in the IBM® MarketScan® Commercial, Blue Health Intelligence® Commercial, and IBM MarketScan Multi-State Medicaid Databases from August 1, 2016, to December 31, 2018. Gestational age at vaccination was determined using a validated algorithm. We examined vaccines (1) recommended by the Centers for Disease Control and Prevention Advisory Committee on Immunization Practices (ACIP) (tetanus, diphtheria, and acellular pertussis [Tdap]; inactivated influenza) and (2) not recommended (human papillomavirus [HPV]) or contraindicated (measles, mumps, and rubella [MMR]).

Results: We identified 496,771 (MarketScan Commercial), 858,961 (BHI), and 289,573 (MarketScan Medicaid) pregnancies (approximately 75% aged 20–34 years). Across these three databases, 52.1%, 50.3%, and 31.3% of pregnancies, respectively, received Tdap, most often at a gestational age of 28 weeks, and influenza vaccination occurred in 32.1%, 30.8%, and 18.0% of pregnancies, respectively. HPV vaccination occurred in < 0.2% of pregnancies, mostly in the first trimester among women aged 12–19 years, and MMR was administered in < 0.1% of pregnancies. Use of other contraindicated vaccines per ACIP (e.g., varicella, live attenuated influenza) was rare.

Conclusion: Maternal vaccination with ACIP-recommended vaccines was suboptimal among privately and Medicaid-insured patients, with lower vaccination coverage among Medicaid-insured pregnancies than their privately insured counterparts. Inadvertent exposure to contraindicated vaccines during pregnancy was rare. This study evaluated only vaccinations reimbursed among insured populations and may have limited generalizability to uninsured populations.

Abbreviations: ACIP, Advisory Committee on Immunization Practices; BCBS, Blue Cross Blue Shield; BHI, Blue Health Intelligence; CDC, Centers for Disease Control and Prevention; COBRA, Consolidated Omnibus Budget Reconciliation Act; HCPCS, Healthcare Common Procedure Coding System; HPV, human papillomavirus; ICD-10-CM/PCS, International Classification of Diseases, Tenth Revision, Clinical Modification/Procedure Coding System; MMR, measles, mumps, rubella; NDC, National Drug Code; Tdap, tetanus, diphtheria, and acellular pertussis.

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1. Introduction

Studies have suggested that maternal immunization protects the mother and the infant against vaccine-preventable diseases [1]. Newborns have underdeveloped immune systems in their first few months of life, placing them at risk of morbidity and mortality associated with certain infectious diseases [2–4]. Maternal immunization aims to protect the mother and promote the transfer of
maternal antibodies to infants for protection after birth. Currently, there are no licensed vaccines with a specific indication of passive protection of the infant via maternal immunization during pregnancy. Although the benefits of licensed vaccines routinely recommended for pregnant women, such as tetanus, diphtheria, and acellular pertussis (Tdap) and influenza (excluding the live vaccine), outweigh the risks [1], many women do not receive these vaccines during pregnancy [5–6].

In contrast, some vaccines are deemed as contraindicated or not recommended by professional societies and the Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) [7,8] for administration during pregnancy because of the theoretical risk of fetal transmission or because safety during pregnancy has not been established. Bacille Calmette-Guerin; live attenuated influenza vaccine; measles, mumps, rubella [MMR]; and varicella are contraindicated for maternal use according to ACIP recommendations. Human papillomavirus [HPV] and Zoster are “not recommended” during pregnancy by ACIP. However, given that nearly half of all pregnancies in the United States may be unintended [9], a woman may be exposed to vaccines contraindicated during pregnancy at early gestational stages before knowing she is pregnant.

Thus, information on vaccine exposure during pregnancy is important for monitoring the safety and effectiveness of vaccines. To our knowledge, there has not yet been a comprehensive study on use of vaccines licensed in the United States during pregnancy. Reported vaccine exposure during pregnancy has been limited primarily to Tdap and influenza in the CDC internet panel survey of pregnant women [5] or to studies using administrative claims data [6,10–11] prior to 2017. Information on unintentional exposure to contraindicated vaccines or vaccines that are not recommended during pregnancy in the United States is sparse and based on data prior to 2010 [12]. Most studies have been limited to manufacturer-maintained pregnancy registries [13–15] or manufacturers’ postmarketing passive safety surveillance [16].

This study focused on the prevalence and timing of exposure to Tdap, influenza, MMR, and HPV vaccines during pregnancy in the United States from 2016 through 2018. We used three large administrative claims databases that include data for individuals that includes recipients of any Food and Drug Administration–regulated biologic as well as women with evidence of a potential pregnancy. Because these databases contain deidentified data and are fully compliant with U.S. privacy laws and regulations (i.e., the Health Insurance Portability and Accountability Act), this study was exempt from institutional review board approval.

2. Methods

2.1. Study population

This study included a retrospective cohort of pregnancies ending between August 2016 and December 2018 that resulted in live birth, spontaneous abortion, or stillbirth among women aged 12–55 years at the time of the outcome. To be included, the women had to be continuously enrolled in medical benefits during pregnancy, with no coverage gaps exceeding 45 days. Three administrative databases were used as the primary data sources for this study: IBM® MarketScan® Commercial Database, Blue Health Intelligence® (BHI®) database, and IBM MarketScan Multi-State Medicaid Database.

The MarketScan Research Databases capture person-specific clinical services, expenditures, and enrollment across inpatient, outpatient, prescription drug, and carve-out services. The data span more than two decades and come from a selection of large employers, health plans, and government and public organizations. The MarketScan Commercial Database includes more than 200 million active employees, early retirees, Consolidated Omnibus Budget Reconciliation Act (COBRA) continues, and dependents insured by employer-sponsored plans. The MarketScan Multi-State Medicaid Database contains the pooled healthcare experience of more than 48 million Medicaid enrollees from multiple states. In this study, the Medicaid data evaluated consisted of populations from nine states.

The BHI National Data Repository contains confirmed medical and pharmacy claims from millions of unique individuals enrolled in individual, group, fully insured, and self-insured Blue Cross Blue Shield (BCBS) commercial medical insurance plans that cover a broad cross-section of the U.S. population. The BHI database used in this study contains detailed enrollment, demographic, and claims information across all 50 states for a subpopulation of 30 million individuals that includes recipients of any Food and Drug Administration–regulated biologic as well as women with evidence of a potential pregnancy. Because these databases contain deidentified data and are fully compliant with U.S. privacy laws and regulations (i.e., the Health Insurance Portability and Accountability Act), this study was exempt from institutional review board approval.

2.2. Pregnancy outcome and timing algorithm

Pregnancy outcomes and gestational age at the time of the outcome were determined using a validated hierarchical algorithm [17]. In short, the algorithm identifies live births, spontaneous abortions, and stillbirths using the World Health Organization’s International Classification of Diseases, Tenth Revision, Clinical Modification/Procedure Coding System (ICD-10-CM/PCS) and Healthcare Common Procedure Coding System (HCPCS) codes on claims (Appendix A). Pregnancy start date is estimated by the presence of diagnosis codes specifying gestational age (in weeks, trimester, or preterm/full-term status), the timing of assisted reproductive technology procedures (e.g., intrauterine insemination), and the timing of prenatal screening tests (e.g., nuchal translucency, glucose tolerance screening) (Appendix A). If multiple estimates of gestational age are present, a pregnancy start date is determined using claims with the highest clinical accuracy. For example, the timing of assisted reproductive technology procedures and gestational age determined during the first trimester ultrasound are considered to be evidence with higher accuracy than evidence recorded on other prenatal encounters, such as timing of prenatal cell-free DNA screening, gestational age recorded in trimesters, and timing of glucose tolerance tests. A pregnancy episode is defined as the period between the estimated pregnancy start date and the time of the pregnancy outcome. The gestational age at vaccine exposure was based on the time difference between the receipt of the first vaccine dose and the estimated pregnancy start date, which may be further classified into trimesters (first trimester: 0–13 6/7 weeks; second trimester: 14 0/7–27 6/7 weeks; third trimester: ≥28 0/7 week). A small percentage of pregnancies were excluded because of conflicting coding of outcome types or because a gestational age estimate could not be determined using information in the claims according to the algorithms.

2.3. Vaccine identification

Vaccines were identified by the presence of HCPCS codes and National Drug Codes (NDCs) in medical and drug reimbursement claims for dispensed prescriptions, respectively, during the pregnancy episode. An exposure to a type of vaccine was defined as having at least one dose of the vaccine of interest during the pregnancy episode.

We focused on vaccines (1) recommended by ACIP: Tdap and inactivated influenza; (2) not recommended: HPV; and (3) con-
trainindicated for use in pregnancy per ACIP: MMR. [18]. The MMR II vaccine is also contraindicated for use in pregnant women in the MMR II package insert [18]. With respect to influenza, we also examined maternal exposures to different types of vaccines by manufacturing process (i.e., egg based, recombinant, cell based), dose strength (i.e., standard, high), additional ingredients (i.e., non-adjuvanted, adjuvanted), and the number of antigens (i.e., quadrivalent, trivalent). A list of NDCs and HCPCS codes used to identify influenza vaccines is provided in Appendix B. Negative controls for influenza vaccines that are pandemic formulations or were no longer available on the market during 2016–2018 also were examined to ensure that their prevalence was low, signaling unlikely misclassification of vaccine exposure due to billing errors (Appendix C). Appendix D provides codes for the other vaccines of interest.

In secondary analyses, we assessed exposure to other vaccines that either have been recommended in special circumstances or do not contain specific pregnancy-related recommendations per ACIP. These vaccines are also listed in Appendix D.

2.4. Statistical analyses

The characteristics of the study population were described by reporting the median gestational age at outcome, counts and proportions by pregnancy outcome type (preterm live birth [<37 weeks of gestation], full-term live birth [37 + weeks of gestation], stillbirth, spontaneous abortion), maternal age (defined as age at pregnancy outcome of 12–19, 20–34, 35–44, or 45–55 years), and geographic location (census region: metropolitan and non-metropolitan areas) [19–20]. We calculated the proportion of pregnancies exposed to the above vaccines at any time during pregnancy as well as by trimester using the date of first vaccine dose. For the overall and first trimester results, the denominator included all pregnancy episodes. For second and third trimester results, the denominators were limited to pregnancies that reached the second and third trimesters, respectively. For Tdap vaccines, we also reported timing of vaccinations by estimated gestational age in weeks to assess adherence to the recommended Tdap vaccination schedule for pregnant women. Proportions of vaccine-exposed pregnancies stratified by maternal age were also reported. Supplemental analyses estimated vaccination rates per person-months of pregnancy to account for differences in gestational lengths across age groups and outcome types (Appendix E).

3. Results

3.1. Study population characteristics

A total of 496,771 (MarketScan Commercial, 858,961 (BHI), and 289,573 (MarketScan Medicaid) pregnancies were identified with pregnancy outcomes occurring between August 2016 and December 2018 (Table 1). Approximately 72–76% of pregnancies were among women aged 20 to 34 years at the time of the pregnancy outcome across all three databases; however, a greater proportion of Medicaid pregnancies were among women aged 12–19 years (16.5%) than among commercially insured women (1.7–2.5%), and fewer were among women aged 35 years or older. Among the commercially insured populations in the MarketScan and BHI databases, more women resided in the South (45.6% and 40.2%, respectively) than in other regions and in metropolitan areas (89.5% and 90.1%, respectively). Most pregnancies (73–78%) resulted in a full-term live birth. The median length of the pregnancies was 38 weeks.

3.2. Tdap and influenza

3.2.1. Tdap vaccine exposure

Among the commercially insured populations in the MarketScan and BHI databases, respectively, 52.1% and 50.3% of all pregnancies received Tdap (for pregnancies ending in live birth: 59.5% and 57.9%, data not shown), with the highest proportions observed in the third trimester (Table 2, Fig. 1). For pregnancies that reached 28 weeks in the two commercial databases, respectively, 43.8% and 42.5% received Tdap in the third trimester. The proportion of pregnancies with a Tdap vaccination was higher among women aged 20–44 years than among women in the youngest or oldest age groups (Table 2). Accounting for different gestational lengths, incidence rates of Tdap vaccine exposure varied across age groups in a similar pattern as reported above (Supplemental Table E1). The same age variation pattern mostly persisted in Tdap vaccine exposures after further stratifying by pregnancy outcome (Supplemental Table E2).

Among the MarketScan Medicaid population, 31.3% of the pregnancies received the Tdap vaccination (for pregnancies ending in live birth: 33.6%, data not shown). However, consistent with the commercial populations, the highest proportion of Tdap vaccination occurred during the third trimester (24.4%) (Table 2, Fig. 1). Similarly, a greater proportion of women aged 20–34 (32.0%) and 35–44 (28.7%) years received the Tdap vaccine compared with women aged 45–55 years (14.9%); however, the proportion was similar for younger women aged 12–19 years (29.5%). A consistent variation pattern by age was observed for the Tdap vaccination rates per 1,000 person-months of pregnancy and after stratifying by pregnancy outcome (Supplemental Table E2).

For both the commercial and Medicaid populations, among full-term live birth pregnancies vaccinated for Tdap, 89–92% received Tdap between the recommended range of 27 and 36 weeks (Fig. 1).

3.2.2. Influenza vaccine exposure

In the commercial MarketScan and BHI populations, 32.1% and 30.8% of all pregnancies received the influenza vaccine, respectively, with only marginal differences in proportions vaccinated by trimester (Table 2). Similar to what we observed for the Tdap vaccine, the proportion of pregnancies with an influenza vaccination was higher among women aged 20–44 years than among women in the youngest and oldest age groups (Table 2). Rates of influenza vaccination per 1,000 person-months of pregnancy varied across age groups in a similar pattern (Supplemental Table E1). Influenza vaccination rates per 1,000 person-months of pregnancy stratified by pregnancy outcome are provided in Supplemental Table E2.

In the MarketScan Medicaid population, 18.0% of all pregnancies received the influenza vaccine. Similar to the commercial populations, only marginal differences in influenza vaccination rates were observed by trimester (Table 2). The proportion of pregnancies that received the influenza vaccine was consistent across age groups, ranging from 16.7% to 18.8%. This consistency across age groups generally persisted in the vaccination rates per 1,000 person-months of pregnancy and stratifications by pregnancy outcome (Supplemental Tables E1 and E2).

For pregnancies during which the influenza vaccine was administered, the most common types of influenza vaccines were egg based (89.0%, 90.1%, and 92.4%), standard dose (99.8%, 99.5%, and 99.3%), non-adjuvanted (99.9%, 99.5%, and 99.4%), and quadrivalent (75.7%, 75.5%, and 77.8%) for the MarketScan Commercial, BHI, and MarketScan Medicaid populations, respectively (Table 3).

3.3. MMR and HPV

3.3.1. MMR

Across all populations examined, MMR and HPV vaccinations were administered in <1% of pregnancies (Table 4). Among the commercially insured populations of the MarketScan and BHI databases, 13.1 and 12.1 per 10,000 pregnancies received MMR, respectively. MMR vaccination was most commonly administered after 28 weeks, including the day of delivery (12.3 and 11.3 per 10,000 pregnancies that reached 28 weeks). Most of the maternal MMR exposures occurred on the pregnancy outcome date (82.5% and 79.1%, data not shown). Exposure to the MMR vaccine during pregnancy varied slightly by age, ranging for the two commercial populations between 7.9 and 9.1 (35–44 years) and 13.2 and 14.6 (20–34 years) per 10,000 pregnancies.

The proportion of pregnancies with an MMR vaccination was lower in the Medicaid population (4.0 per 10,000 pregnancies) than in the MarketScan Commercial (13.1 per 10,000 pregnancies) and BHI (12.1 per 10,000 pregnancies) populations described above. For women with Medicaid, the MMR exposure was highest among women aged 35–44 years (8.5 per 10,000 pregnancies) compared with other age groups (<4 per 10,000 pregnancies). Exposure rates per 10,000 person-months of pregnancy for MMR vaccinations varied in similar patterns across age groups to those based on proportions (Supplemental Table E3). In contrast to the commercial populations, only 21% of the MMR vaccine exposure occurred on the pregnancy outcome date (82.5% and 79.1%, data not shown). Exposure to the MMR vaccine during pregnancy was higher in the Medicaid population (15.5 per 10,000 pregnancies) compared with 6.4 and 6.6 per 10,000 pregnancies noted above in the MarketScan Commercial and BHI populations. The age and trimester distributions of HPV vaccination were similar in the Medicaid and commercial populations. Exposure rates per 10,000 person-months of pregnancy for HPV vaccinations varied in similar patterns across age groups to those based on the exposure proportions per 10,000 pregnancies as reported above (Supplemental Table E3).

3.3.2. HPV

In the MarketScan Commercial and BHI databases, respectively, 6.4 and 6.6 per 10,000 pregnancies received the HPV vaccine, which was most often administered during the first trimester (5.4 and 5.7 per 10,000 pregnancies). Maternal exposure to HPV vaccination was much higher among women aged 12–19 years than among women aged 20+ years (73.6 and 99.7 per 10,000 vs<7 per 10,000 in the MarketScan Commercial and BHI databases, respectively).

Exposure to HPV vaccination during pregnancy was higher in the Medicaid population (15.5 per 10,000 pregnancies) compared with 6.4 and 6.6 per 10,000 pregnancies noted above in the MarketScan Commercial and BHI populations. The age and trimester distributions of HPV vaccination were similar in the Medicaid and commercial populations. Exposure rates per 10,000 person-months of pregnancy for HPV vaccinations varied in similar patterns across age groups to those based on the exposure proportions per 10,000 pregnancies as reported above (Supplemental Table E3).

3.4. Other vaccines

Use of other contraindicated vaccines was rare. For instance, across the MarketScan Commercial, BHI, and MarketScan Medicaid populations, respectively, maternal exposure to varicella was 1.7, 1.8, and 5.8 per 10,000 pregnancies. Exposure to live attenuated influenza (contraindicated per ACIP), zoster, and bacille Calmette-Guerin was under 0.1 per 10,000 pregnancies in all populations. Use of other vaccines without a specific routine recommendation (e.g., Hepatitis A) for pregnant women with commercial insurance or Medicaid was below 1% (data not shown).

4. Discussion

In our large study of pregnancies identified in two nationwide commercial insurance databases and one public insurance (Medicaid) database, we observed low coverage of two vaccines that are recommended for nearly all pregnancies (Tdap and influenza vaccines), particularly in the Medicaid-insured population. Our observations are consistent with reported Tdap and influenza vaccinations received during pregnancy identified through self-reported internet panel surveys [5] and via reimbursement claims in other insured populations [6,10–11,21] but slightly lower than
coverage reported by others (e.g., state registry and insurance claims [22] and single hospital site electronic health records [23]). Our study only includes influenza vaccinations during pregnancy, whereas some estimates closer to 50% are based on coverage of pregnancies through vaccination before and during pregnancy [5]. On the other hand, inadvertent exposure to contraindicated vaccines per ACIP and vaccines that are not recommended for use during pregnancy was very rare, occurring in <1% of pregnancies in our study, but this finding aligns with vaccine administration identified in the electronic health records of health maintenance organizations [12].

Within our study, approximately half of commercially insured pregnant women and merely a third of Medicaid-insured women received the Tdap vaccine. ACIP recommends that pregnant women receive one dose of the Tdap vaccine during each pregnancy, irrespective of their history of receiving the vaccine. ACIP

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**Table 2**

Proportions of Tdap and influenza vaccinations for women whose pregnancy ended in live birth, spontaneous abortion, or stillbirth at 12–55 years old, August 2016 through December 2018.

<table>
<thead>
<tr>
<th>Vaccination Type, Age Group, and Timing of Vaccination</th>
<th>MarketScan Commercial</th>
<th>BHI Commercial</th>
<th>MarketScan Medicaid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tdap, overall</td>
<td>496,771</td>
<td>858,961</td>
<td>289,573</td>
</tr>
<tr>
<td>Age at pregnancy outcome, years</td>
<td>Total Pregnancies</td>
<td>% Vaccinated (95% CI)</td>
<td>Total Pregnancies % Vaccinated (95% CI)</td>
</tr>
<tr>
<td>12–19</td>
<td>12,644</td>
<td>40.6 (39.8–41.5)</td>
<td>14,647</td>
</tr>
<tr>
<td>20–34</td>
<td>374,672</td>
<td>53.3 (52.3–53.3)</td>
<td>624,274</td>
</tr>
<tr>
<td>35–44</td>
<td>107,724</td>
<td>49.6 (49.3–49.9)</td>
<td>216,023</td>
</tr>
<tr>
<td>45–55</td>
<td>1,731</td>
<td>32.6 (30.4–34.8)</td>
<td>4,017</td>
</tr>
<tr>
<td>Timing of vaccination</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First trimester</td>
<td>496,771</td>
<td>0.4 (0.3–0.4)</td>
<td>858,961</td>
</tr>
<tr>
<td>Second trimester</td>
<td>446,492</td>
<td>14.4 (14.3–14.5)</td>
<td>753,467</td>
</tr>
<tr>
<td>Third trimester</td>
<td>439,716</td>
<td>43.8 (43.7–44.0)</td>
<td>742,329</td>
</tr>
<tr>
<td>Influenza, overall</td>
<td>496,771</td>
<td>32.1 (32.0–32.2)</td>
<td>858,961</td>
</tr>
<tr>
<td>Age at pregnancy outcome, years</td>
<td>Total Pregnancies</td>
<td>% Vaccinated (95% CI)</td>
<td>Total Pregnancies % Vaccinated (95% CI)</td>
</tr>
<tr>
<td>12–19</td>
<td>496,771</td>
<td>26.2 (25.5–27.0)</td>
<td>14,647</td>
</tr>
<tr>
<td>20–34</td>
<td>374,672</td>
<td>32.0 (31.8–32.1)</td>
<td>624,274</td>
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<td>107,724</td>
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<td></td>
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<td>439,716</td>
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</tr>
</tbody>
</table>

Abbreviations: BHI = Blue Health Intelligence; CI = confidence interval; Tdap = tetanus, diphtheria, and acellular pertussis.

Note: Timing of vaccination was based on the first exposure if multiple vaccinations occurred during the same pregnancy episode. Data exclude FluMist.

a The denominator is pregnancies that reached the second trimester.

b The denominator is pregnancies that reached the third trimester.

Sources: IBM MarketScan Commercial and Multi-State Medicaid Databases; Blue Health Intelligence database.

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**Fig. 1.** Number of pregnancy episodes with Tdap vaccine exposure by gestational age and by pregnancy outcome from August 2016 through December 2018 across data sources. Abbreviations: BHI = Blue Health Intelligence; Tdap = tetanus, diphtheria, and acellular pertussis. Note: Timing of vaccination was based on the first exposure if multiple vaccinations occurred during the same pregnancy episode. The dotted lines mark 27 weeks and 36 weeks, the Advisory Committee on Immunization Practices’ recommended range of gestational age for maternal Tdap vaccination. Data ranging from 500 to 10,000 are not shown to ensure that the distributions for rarer pregnancy outcomes (spontaneous abortion and stillbirth) are visible. Sources: IBM MarketScan Commercial and Multi-State Medicaid Databases; Blue Health Intelligence database.
recommends that the Tdap vaccine be administered at 27–36 weeks of gestation, preferably during the earlier part of this period [24], which is thought to maximize protection via transplacental passage of maternal antibodies. Healy and colleagues reported that this subsequently protects infants younger than 2 months old during a period when the level of maternal antibodies is highest [25]. Additionally, Healy et al. (2018) suggest that earlier Tdap administration from gestational ages of 27 to 32 weeks may confer higher protection to infants [26]. In this study, more than 80% of Tdap vaccinations occurred within the ACIP-recommended time frame of 27–36 weeks of gestation and more than 70% received Tdap during 27–32 weeks of gestation.

Seasonal influenza remains a priority for public health. Although influenza vaccination has been recommended for all pregnant women since 2004, the observed coverage in this study—based on reimbursed claims of approximately 30% of commercially insured pregnancies and 18% of Medicaid-insured pregnancies—is far from the Healthy People 2020 goal of increasing the coverage of seasonal influenza vaccination to 80% [27]. Our findings are consistent with survey-based results (36.8%) [5] and a study that used MarketScan data from 2009 to 2017, partially overlapping with this study [6].

Across databases, women aged 1–19 and 45–55 years had lower vaccination rates for both Tdap and influenza compared with...
women in the 20–34 and 35–44 age categories. This finding highlights the need for targeted outreach to women in the youngest and oldest age groups, who already have higher risk pregnancies with respect to some maternal and infant outcomes [28,29]. Medicaid-covered women had lower vaccination proportions for both Tdap and influenza than their privately insured counterparts across all ages. The association between type of insurance and Tdap and influenza vaccine coverage is consistent with patterns that have been previously reported [6,22]. The reported maternal vaccination proportions and rates in this study may be underestimated because non-reimbursed vaccines were not captured. Nonetheless, overall maternal vaccination of flu and Tdap was low in the present study. Kahn et al. reported several reasons preventing women from receiving vaccination during pregnancy [5].

The most common reason for not receiving Tdap was patients’ lack of knowledge about the need to receive Tdap during every pregnancy, whereas the most common reason for not receiving influenza vaccine was the belief that it is ineffective [5].

Inadvertent exposure to contraindicated vaccines seems to be very rare. Among the commercially insured populations, maternal exposure to MMR occurred most often after 28 weeks of gestation, with most vaccinations administered on the delivery or outcome date, indicating possible postpartum exposure only. These were likely MMR vaccinations after delivery while mothers were still in the hospital, given that ACIP recommends immediate postpartum administration of MMR vaccines for women who lacked presumptive evidence of immunity to rubella or measles [18].

In this study population, maternal exposure to vaccines not recommended by ACIP was rare, with HPV vaccination being the most common. HPV exposure for both commercially and Medicaid-insured pregnant women was highest between ages 12 and 19 years and in the first trimester. This was expected because HPV vaccine is recommended for children and adults aged 9 through 26 years [30]. Incidental exposure to HPV vaccines in the younger age group was more likely to occur during the first trimester, probably before women knew they were pregnant. The overall HPV vaccine exposure was more than twofold higher in the Medicaid-insured than in the commercially insured women. This is likely due to the higher proportion of younger mothers among the Medicaid population, who had much higher incidental HPV exposures than other age groups. However, among women aged 12–19 years, the proportion of pregnancies exposed to HPV vaccine was similar between the Medicaid and the two commercially insured populations (73 [Medicaid] vs 74 [MarketScan commercial] and 100 [BHl] per 10,000 pregnancies), which is comparable to the maternal exposure to quadrivalent HPV vaccine reported in the Vaccine Safety Datalink database (0.4% and 0.7% among women aged 12–27 years [31,32]). However, both studies were conducted on data from prior to 2015.

This retrospective study reported maternal vaccination rates in two large nationwide commercial insurance databases and one Medicaid database, including more than a million pregnancies during 2016–2018. An extensive list of vaccines available on the U.S. market during the study period was examined, including both vaccines recommended for maternal use and vaccines not recommended or contraindicated during pregnancy. This study identified pregnancies using a set of validated algorithms developed for their applications in ICD-10-CM/PCS-coded claims data—the type of data evaluated in this study. The use of these algorithms allowed for more precise ascertainment of the pregnancy outcomes and the exposure timing in weeks of gestational age. With these strengths, this study provides a comprehensive view of recommended and incidental maternal vaccine exposures in a large subset of the U.S. population. Although the focus of this study is vaccine exposure, it is worth noting that large claims databases have also been used extensively for evaluation of medication safety in pregnancy [33]. Claims databases may cover millions of individuals and contain information on health plan enrollment, demographics, inpatient and outpatient healthcare encounters (date of service, diagnoses, and procedures), and outpatient pharmacy dispensing. Passive surveillance systems, such as the Vaccine Adverse Event Reporting System (VAERS), are critical in early monitoring of potential safety issues warranting further investigation. However, they lack the appropriate denominator to estimate incidence rates of exposures and adverse events. Claims databases allow researchers to follow a well-defined insured population longitudinally. Although unreimbursed encounters may not be reflected in the data, claims accurately capture exposures and outcomes based on reimbursed services. Many claims databases also have mother-infant linkage to allow further evaluation of infant outcomes after maternal vaccine exposure.

Future studies may further examine risk factors contributing to disparities in maternal vaccination rates using large national claims databases. Factors related to maternal vaccination disparities have been previously studied in smaller pregnant populations limited to certain regions [34,35]. Evidence generated from large national databases may inform targeted campaigns among specific populations. Monitoring the uptake and safety of new vaccines among pregnant women will continue to be critical to inform clinicians, policymakers, and patients. To date, several COVID-19 vaccines of different platforms (novel mRNA or viral vector) have been authorized by the Food and Drug Administration on the U.S. market and have been deployed broadly. Millions of women of childbearing age have received COVID-19 vaccines. Future studies may build on our work by monitoring COVID-19 vaccination rates and postmarket safety around the time of pregnancy in large claims databases.

This study has several limitations. First, vaccinations in claims data reflect only those that were reimbursed. As a result, maternal vaccination proportions and rates reported in this study may be underestimates. For example, flu vaccination events occurring at worksites or vaccinations received by Medicaid beneficiaries through programs outside of Medicaid were not captured in the data. Second, this study evaluated maternal vaccination patterns in two privately insured populations. However, we could not assess whether the two populations were independent. Although both data systems contain claims and enrollment data on their own set of unique individuals, the MarketScan Commercial Database may include women covered under BCBS commercial medical insurance plans; hence, potential overlap between the two populations may exist. Because of the limited information available on insurance plan composition in the MarketScan data, we cannot assess whether such overlap exists and, if so, the extent of it. However, as evidenced by the population size difference (858,961 vs 496,771 pregnancies identified in the BHI and MarketScan data, respectively), the two populations likely represent different patient mixes. Third, this is a descriptive study. Variations in outcome-specific vaccination rates were not adjusted for other potential risk factors and should not be interpreted as measures of association. Finally, the study findings may have limited generalizability to all pregnancies. The algorithms used to identify the pregnant populations rely on billing codes in the administrative data. A small percentage of pregnancies were excluded because of conflicting coding of outcome types or because a gestational age estimate could not be determined using information in the claims. Claims-based algorithms cannot comprehensively capture all spontaneous abortions, especially those that occur early during pregnancy before the pregnancy is detected by the mother. Therefore, maternal exposures to the vaccines of interest reported in this study may not be generalizable to those pregnancies not captured.
5. Conclusion

Maternal vaccination rates for ACIP-recommended vaccines (Tdap and influenza) were lower than recommended among privately insured patients and were particularly low for Medicaid-insured patients. Tdap vaccination during pregnancy mostly occurred during the earlier part of the gestational period of 27–36 weeks, complying with the ACIP recommendation. Inadvertent exposure to contraindicated vaccines and vaccines not recommended during pregnancy was rare.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2021.08.091.

References
