Appendix 1. Supplemental Methods

Setting

The Vaccine Safety Datalink (VSD) is a long-standing collaborative effort between the CDC's

Immunization Safety Office and integrated health care systems (sites) across the US.[1] VSD sites create

standardized, deidentified data files from electronic health records and claims data, which allows

linkage of select demographics, medical event information, and vaccination history. Data for this

analysis were obtained from eight VSD sites (HealthPartners, Marshfield Clinic, Denver Health, and

the Colorado, Northern California, Northwest, Southern California, and Washington regions of Kaiser

Permanente) in six US states (California, Colorado, Minnesota, Oregon, Washington, and Wisconsin).

Previous work showed that the VSD population is representative of the general US population on

several key demographic and socioeconomic variables, including sex, race, ethnicity, and education.[2]

This research was reviewed and approved by the CDC and the institutional review boards of the

participating eight VSD sites with a waiver of informed consent.

Influenza seasons of interest

Influenza vaccination coverage was evaluated retrospectively for six influenza seasons: 2016-17

through 2021-22. Coverage analyses spanned the August 1 through March 31 period of each season;

to be comprehensive in same-season vaccine capture, influenza vaccination July 1 through March 31

was included as described below.

Study population

Each influenza season's eligible population consisted of people ages 18-49 years with a pregnancy spanning at least one day from August 1 through March 31. Pregnancies were identified using a validated VSD algorithm,[3] and patient age was determined as of August 1 each year. The algorithm uses International Classification of Diseases, Tenth Revision (ICD-10), and CPT® codes from inpatient, outpatient, and emergency department visits, supplemented with clinical data and is updated weekly to identify ongoing and completed pregnancies.

For inclusion in a season's analysis, participants were required to be continuously enrolled in the participating VSD health system throughout the August 1 through March 31 period to ensure adequate capture of pregnancy information, vaccination, and clinical characteristics. Pregnancies that ended in spontaneous or induced abortion, pregnancies that ended prior to 14 weeks of gestation regardless of the outcome, and pregnancies for which the VSD algorithm could not identify a pregnancy outcome were excluded from analyses.

People with multiple pregnancies per season were included in all analyses; for those with a vaccine, the pregnancy during which influenza vaccination occurred was included in pregnancy-level analyses of coverage by the timing of pregnancy start relative to the influenza season and of uptake relative to pregnancy stage, as described below. If a person with multiple pregnancies remained unvaccinated, the last pregnancy identified during the influenza season was included in that season's analysis of coverage by timing of pregnancy start. Pregnancies that spanned two influenza seasons were included in both seasons' analyses.

Ascertainment of vaccination status

All influenza vaccines administered in the eligible study population were identified from standardized VSD files (**Appendix 2**). The VSD vaccine files include data from electronic health records and medical and pharmacy claims, and are supplemented at some sites through bidirectional communication with regional or state immunization information systems, with standardized data quality checks and de-duplication of vaccines from multiple sources.[4] Concordance between EMR documentation and self-reported influenza vaccination within the VSD's pregnant population has been shown to be high.[5] Influenza vaccines administered between July 1 and March 31 were included in season-specific analyses, irrespective of the timing of administration relative to pregnancy (i.e., prior to, during, or after pregnancy). Vaccinated was defined as receipt of ≥1 dose in the July 1 through March 31 period; unvaccinated was defined as no documented influenza vaccine doses within the period.

Analyses

Season-specific crude influenza vaccination coverage

For each season, crude influenza vaccination coverage was calculated at the individual level by dividing the number of pregnant people vaccinated between July 1 and March 31 by the total number of pregnant people identified. Each season, coverage was calculated overall and by age group (18-24, 25-34, 35-49 years as of August 1); self-reported race and ethnicity (Hispanic; Asian, non-Hispanic; Black, non-Hispanic; White, non-Hispanic; another race or multiple races, non-Hispanic; unknown or missing); health care utilization (number of in-person clinical encounters between the July 1-June 30 period overlapping the influenza season of interest: <6, 6-10, 11-20, >20 encounters); pregnancy comorbidities or complications (**Appendix 5**); and conditions associated with increased risk of severe

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illness and complication from influenza (hereafter referred to as high-risk conditions; **Appendix 7**).

Both pregnancy comorbidities/complications and high-risk conditions were assessed using ICD-10-CM

diagnosis codes assigned between pregnancy start and end dates. Race and ethnicity were included in

an effort to examine disparities in vaccination coverage, which have been documented previously and

in other populations.

Coverage by timing of pregnancy start relative to the influenza season

In each of the six seasons, we calculated influenza vaccination coverage at the pregnancy level,

according to the calendar month of the pregnancy start date relative to the influenza season of

interest. In these analyses, crude coverage was calculated by dividing the number of pregnant people

vaccinated between July 1 and March 31 by the total number of pregnant people with a pregnancy

start in a given calendar month. Each season, eligible pregnancies had start dates as early as January

preceding an influenza season (i.e., with estimated dates of delivery in August/September of a season

of interest) and as late as March of the season of interest (i.e., with estimates dates of delivery in the

subsequent season).

Uptake of influenza vaccine relative to pregnancy stage

Among those vaccinated, we examined the timing of same-season vaccine receipt relative to

pregnancy: before pregnancy, during pregnancy by trimester (<14, 14-27, >27 weeks of gestation), at

delivery (+/- 3 days of pregnancy end date), and after pregnancy.

Appendix 2. **CVX Codes Used to Identify Influenza Vaccines**

CVX code	Description
111	influenza, live, intranasal
135	Influenza, high dose seasonal
140	Influenza, seasonal, injectable, preservative free
141	Influenza, seasonal, injectable
144	influenza, seasonal, intradermal, preservative free
149	influenza, live, intranasal, quadrivalent
15	influenza, split (incl. purified surface antigen)
150	influenza, injectable, quadrivalent, preservative free
151	influenza nasal, unspecified formulation
153	Influenza, injectable, MDCK, preservative free
155	influenza, recombinant, injectable, preservative free
158	influenza, injectable, quadrivalent
16	influenza, whole
161	Influenza, injectable, quadrivalent, preservative free, pediatric
166	influenza, intradermal, quadrivalent, preservative free
168	influenza, trivalent, adjuvanted
171	Influenza, injectable, MDCK, preservative free, quadrivalent
185	influenza, recombinant, quadrivalent, injectable, preservative free
186	Influenza, injectable, MDCK, quadrivalent, preservative
194	Influenza, Southern Hemisphere
197	influenza, high-dose, quadrivalent
200	influenza, Southern Hemisphere, pediatric, preservative free
201	influenza, Southern Hemisphere, preservative free
202	influenza, Southern Hemisphere, quadrivalent, with preservative
205	Influenza vaccine, quadrivalent, adjuvanted
88	influenza, unspecified formulation
125	Novel Influenza-H1N1-09, nasal
126	Novel Influenza-H1N1-09, preservative-free
127	Novel influenza-H1N1-09
128	Novel Influenza-H1N1-09, all formulations

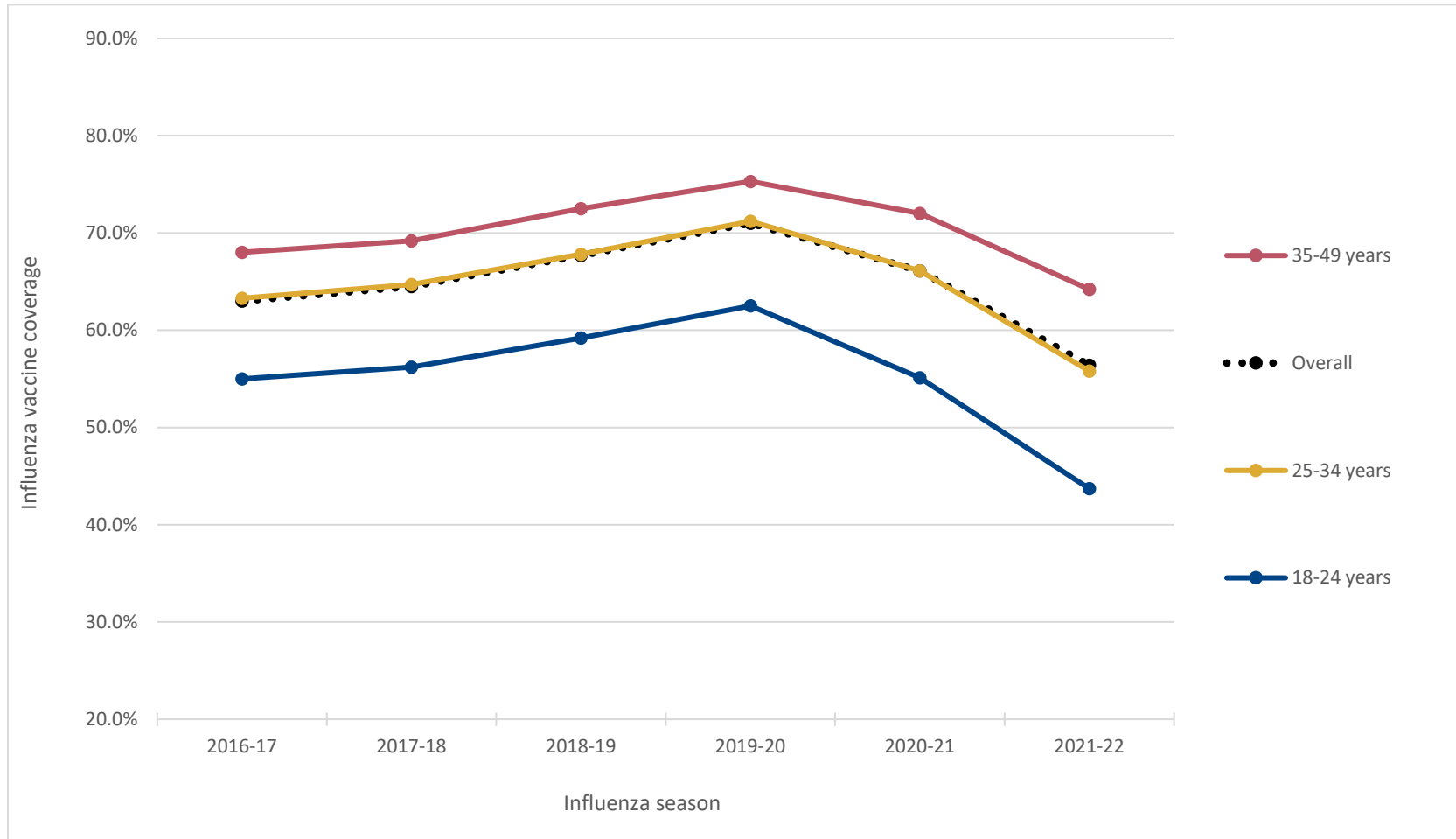| 123 | Influenza, H5N1-1203 |
| 160 | Influenza A monovalent (H5N1), Adjuvanted-2013 |

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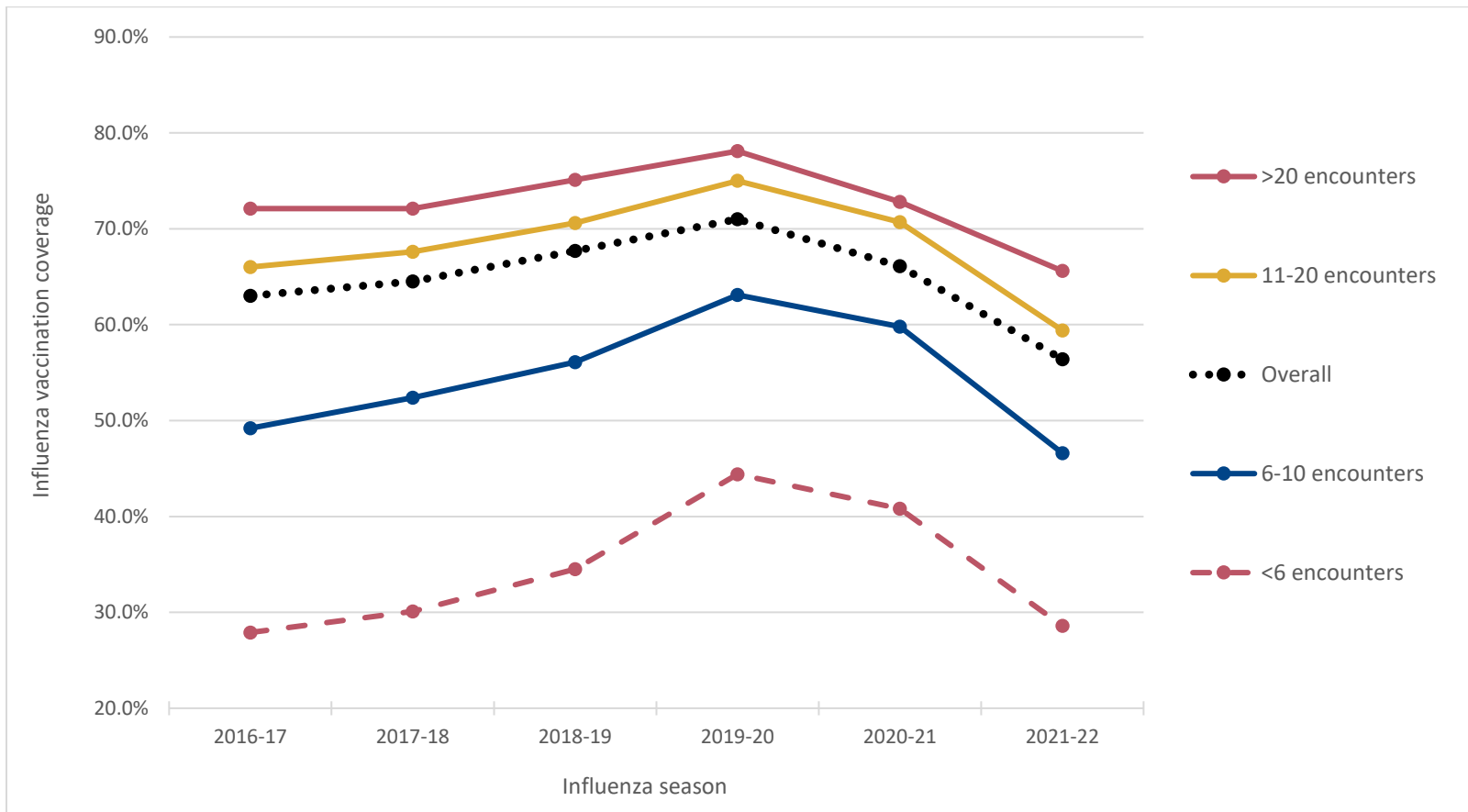The authors provided this information as a supplement to their article.

Appendix 3. Influenza vaccination coverage among pregnant people, overall and by age group: 2016-2017 through the 2021-2022 influenza seasons.

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Appendix 4. Influenza vaccination coverage among pregnant people, by health care utilization strata: 2016-2017 through the 2021–2022 influenza seasons.

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The authors provided this information as a supplement to their article.

Appendix 5. Pregnancy Comorbidities and Complications[*]

Pregnancy comorbidities and complications	ICD-10-CM code(s)[†]
Hypertension (pre-existing hypertension complicating pregnancy, gestational hypertension, pre-eclampsia, or eclampsia)	O10.0*, O10.11*, O10.12, O10.13, O10.21*, O10.22, O10,23, O10.3*, O10.4*, 010.9*, O11* - O16*
Diabetes (pre-existing diabetes in pregnancy or gestational diabetes)	O24.0*, O24.1*, O24.3*, O24.4*, O24.8*, O24.9*
Liver and biliary tract disorders in pregnancy	O26.6*
Pregnancy related renal disease	O26.83*
Obesity complicating pregnancy	O99.21*
Diseases of nervous system complicating pregnancy	O99.35*
Disease of respiratory system complicating pregnancy	O99.51*
Diseases of digestive system complicating pregnancy	O99.61*
Alcohol or drug use complicating pregnancy	O99.31*, O99.32*
Tobacco smoking complicating pregnancy	O99.33*

[*] Identified via the ICD-10-CM codes listed, assigned between pregnancy start and end dates.

[†] Use of asterisk in code list indicates that all sub-codes were included.

Appendix 6. Influenza Vaccination Coverage Among Pregnant People, by Presence of Pregnancy Comorbidities and Complications:2016-2017 through the 2021-2022 Influenza Seasons[*]

	2016-17	2017-18	2018-19	2019-20	2020-21	2021-22
Hypertension	64.2%	65.5%	68.3%	71.7%	66.3%	62.2%
Diabetes	67.2%	67.9%	71.3%	74.0%	69.2%	64.4%
Liver and biliary tract disorders in pregnancy	66.2%	67.3%	70.2%	73.0%	66.4%	63.5%
Pregnancy related renal disease	59.2%	69.7%	68.6%	70.7%	65.2%	61.2%
Obesity complicating pregnancy	63.1%	65.1%	67.4%	70.6%	65.7%	58.2%
Diseases of nervous system complicating pregnancy	62.3%	64.8%	68.4%	68.7%	67.2%	61.3%
Disease of respiratory system complicating pregnancy	64.4%	66.9%	69.1%	72.9%	65.6%	59.3%
Diseases of digestive system complicating pregnancy	65.5%	66.1%	67.2%	72.3%	66.3%	61.6%
Alcohol or drug use complicating pregnancy	51.8%	51.8%	53.0%	58.1%	49.4%	45.2%
Tobacco smoking complicating pregnancy	50.7%	50.8%	51.7%	56.0%	47.5%	41.2%
Any comorbidity or complication	63.2%	64.8%	67.6%	71.0%	66.1%	59.5%
No comorbidity or complication	62.8%	64.1%	67.8%	70.9%	66.0%	53.8%

[*] Eligible pregnancies spanned ≥1 day during the August 1 through March 31 period of an influenza season and met enrollment criteria. All same-season influenza vaccines administered between August 1 and March 31, including prior to, during, or after pregnancy, were included in coverage estimates. Pre-defined pregnancy comorbidities and complications were identified using ICD-10-CM diagnoses in the electronic health record during the pregnancy and are defined in Supplemental Table 2.

Appendix 7. Conditions Associated With Increased Risk of Severe Illness and Complication From Influenza [*]

Condition	ICD-10-CM code(s) [†]
Cardiac disease	A52.0*, I01*, I02*, I05* - I09*, I11*, I13*, I20* - I28*, I31*, I33* - I44*, I46*, I48*, I50* - I52*, I97.0-1*, M31*, P29.0*, Q20* - 28*, Q89.3*, R00.1*, Z94.1*, Z95*, Z98.61*
Cerebrovascular disease	H34.0*, I60* - I69*
Chronic pulmonary disease	A15*, A31.0*, B39* - B41*, B44*, B45*, B46.0*, D86.0*, E84*, E88.01*, J18.2*, J40* - J47*, J60* - J70*, J80* - J82*, J84* - J86*, J95.0*, J96*, J98.1*, J99*, M35.1*, M35.3*, P25* - P28*, Q33*, T86.3*, T86.8*, Z94.2*
Diabetes	E08* - E14*
Endocrine disorders	E00*, E03*, E05*, E06*, E15*, E16*, E20* - E29*, E31*, E32*, E34*
Hemoglobinopathies	D55*, D56.0-2*, D56.4*, D56.5*, D56.9*, D57.0-2*, D57.4*, D57.8*, D58* - D61*, D64.0*, D64.0-4*, D64.8*, D65* - D68*
Immunosuppressive disorders	B20*, B59*, B97.3*, D47.Z1*, D70* - D73*, D76*, D80*- D84*, D89*, M05* - M08*, M30*, M32* - M35.0*, M35.9*, Q89.0*, T45.1X1, Z21*, Z48.2*, Z51.0 – Z51.1*, Z94*
Liver disease	B18*, I81*, I85*, I86.4*, I98.2*, K70* - K77*, K79.9*, Z94.4*
Long-term steroid or aspirin use	Z79.5*, Z79.82*
Malignancy	C00* - C26*, C30* - C34*, C37* - C41*, C43* - C49*, C4A*, C50* - C58*, C60* - C79*, C7A*, C7B*, C80* - C86*, C88*, C90* - CC97*, D03*, D46*, Z85*
Morbid obesity	E66.01*, E66.2*, Z68.4*
Neurological/ Musculoskeletal disorders	A17.0*, E75.02*, E75.19*, E75.4*, F01* - F03*, F71* - F73*, F84.2*, G10* - G14*, G20* - G21*, G23* - G26*, G30* - G32*, G35* - G37*, G40*, G45* - G46*, G60* - G64*, G70* - G71*, G73*, G80* - G83*, G90.3*, G91*, G93* - G95*, G99.2*, H49.81*, M12.0*, M36.0*, P91*,

	Q00* - Q07*, Q76* - Q79*, Q85*, Q87.4*, Q90* - Q93*, Q96*, R41*, R53.2*, R54*
Non-diabetic metabolic disorders	E70* - E72*, E74*, E75.2*, E76* - E80*, E83*, E85*, E88*, E89.1*, E89.6*
Peptic ulcer disease	K25* - K28*
Peripheral vascular disease	I70* - I77*, I79*, K55.1*, K55.8-9*, Z95.8-9*
Renal disease	I12*, N01* - N08*, N11*, N14* - N19*, N25* - N26*, N28*, Q60*, Z49*, Z91.15*, Z94.0*, Z99.2*

[*] Identified via the ICD-10-CM codes listed, assigned between pregnancy start and end dates.

[†] Use of an asterisk in code list indicates that all sub-codes were included.

Appendix 8. Influenza Vaccination Coverage Among Pregnant People, by Presence of Conditions Associated With Increased Risk of Severe Illness and Complication From Influenza: 2016-2017 through the 2021-2022 Influenza Seasons[*]

|	2016-17	2017-18	2018-19	2019-20	2020-21	2021-22
Cardiac disease	64.4%	65.6%	68.5%	71.7%	65.8%	58.3%
Cerebrovascular disease	58.9%	66.4%	58.9%	71.5%	65.2%	59.1%
Chronic Pulmonary disease	64.3%	65.1%	67.7%	71.3%	66.1%	59.2%
Diabetes Mellitus	72.8%	72.9%	74.7%	75.9%	72.5%	65.6%
Non-diabetes metabolic disorder	69.6%	71.3%	74.7%	75.2%	72.1%	64.0%
Endocrine disorders	67.4%	69.2%	72.4%	75.3%	71.1%	63.8%
Hemoglobinopathies	64.7%	66.4%	68.8%	71.4%	65.5%	59.8%
Immunosuppressive disorders	63.4%	66.4%	69.4%	72.9%	65.8%	58.4%
Liver disease	67.5%	69.8%	72.1%	73.8%	69.4%	64.3%
Long-term steroid or aspirin use	67.6%	69.3%	69.4%	73.4%	68.4%	65.0%
Malignancy	68.9%	67.1%	70.9%	75.7%	68.6%	65.8%
Morbid obesity	63.1%	66.1%	67.8%	70.5%	65.3%	59.0%
Neurological/Musculoskeletal disorders	64.0%	64.9%	67.9%	70.0%	65.1%	58.2%
Peripheral vascular disease	65.6%	69.5%	70.6%	75.5%	72.0%	62.5%
Renal disease	64.2%	67.2%	67.7%	74.4%	67.5%	59.0%
Any condition	65.1%	66.4%	69.3%	72.4%	67.3%	60.5%
No condition	61.9%	63.4%	66.8%	70.1%	65.3%	54.5%

* Eligible pregnancies spanned ≥1 day during the August 1 through March 31 period of an influenza season and met enrollment criteria. All same-season influenza vaccines administered between August 1 and March 31, including prior to, during, or after pregnancy, were included in coverage estimates. Pre-defined conditions associated with increased risk of severe illness and complication from influenza were identified using ICD-10-CM diagnoses in the electronic health record during the pregnancy and are defined in Supplemental Table 3. Coverage estimates for pregnant people with peptic ulcer disease are not displayed due to low numbers.

Appendix 9. Influenza vaccination coverage among pregnant people, by month of pregnancy start: 2016-2017 through the 2021–2022 influenza seasons.
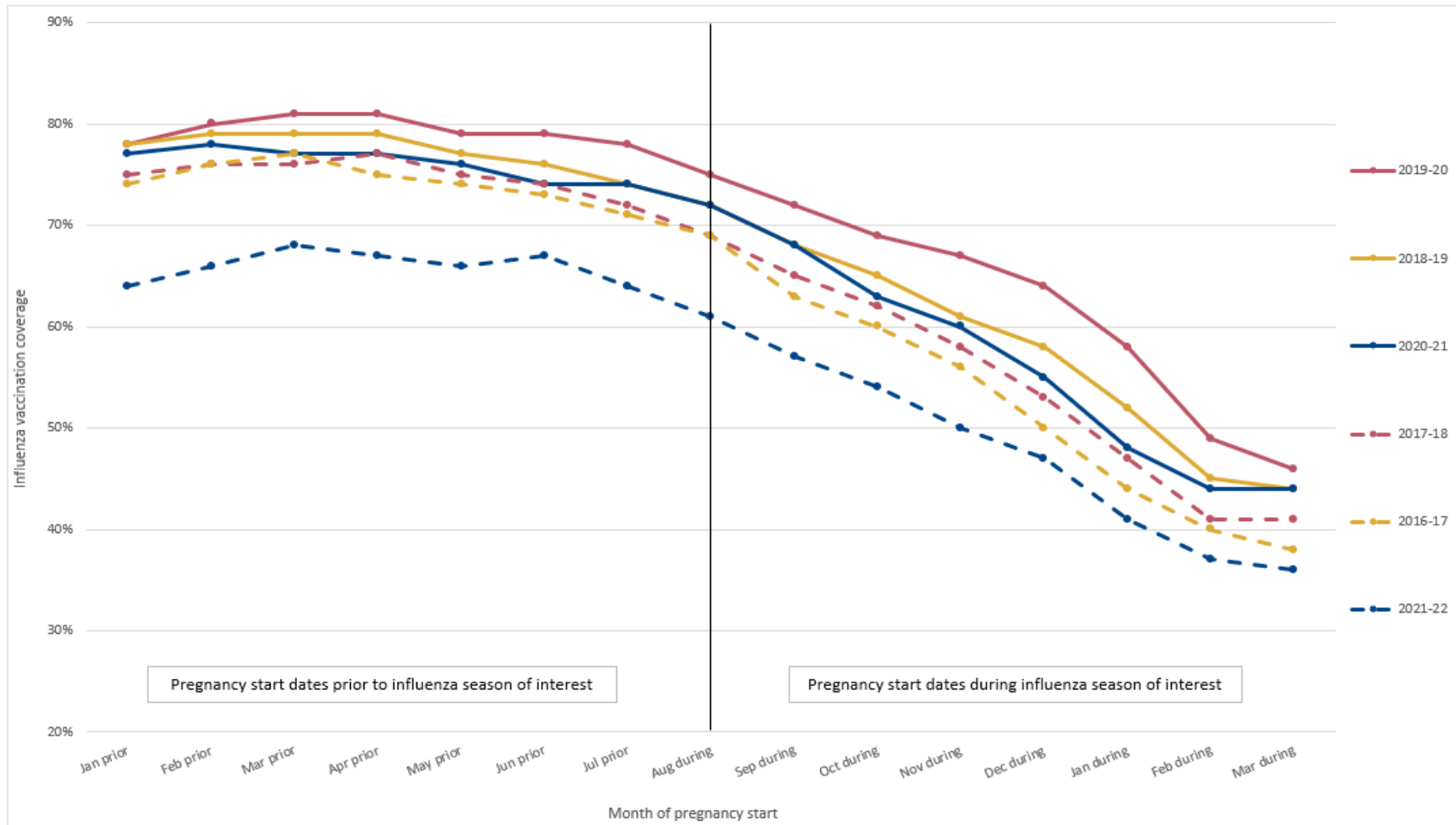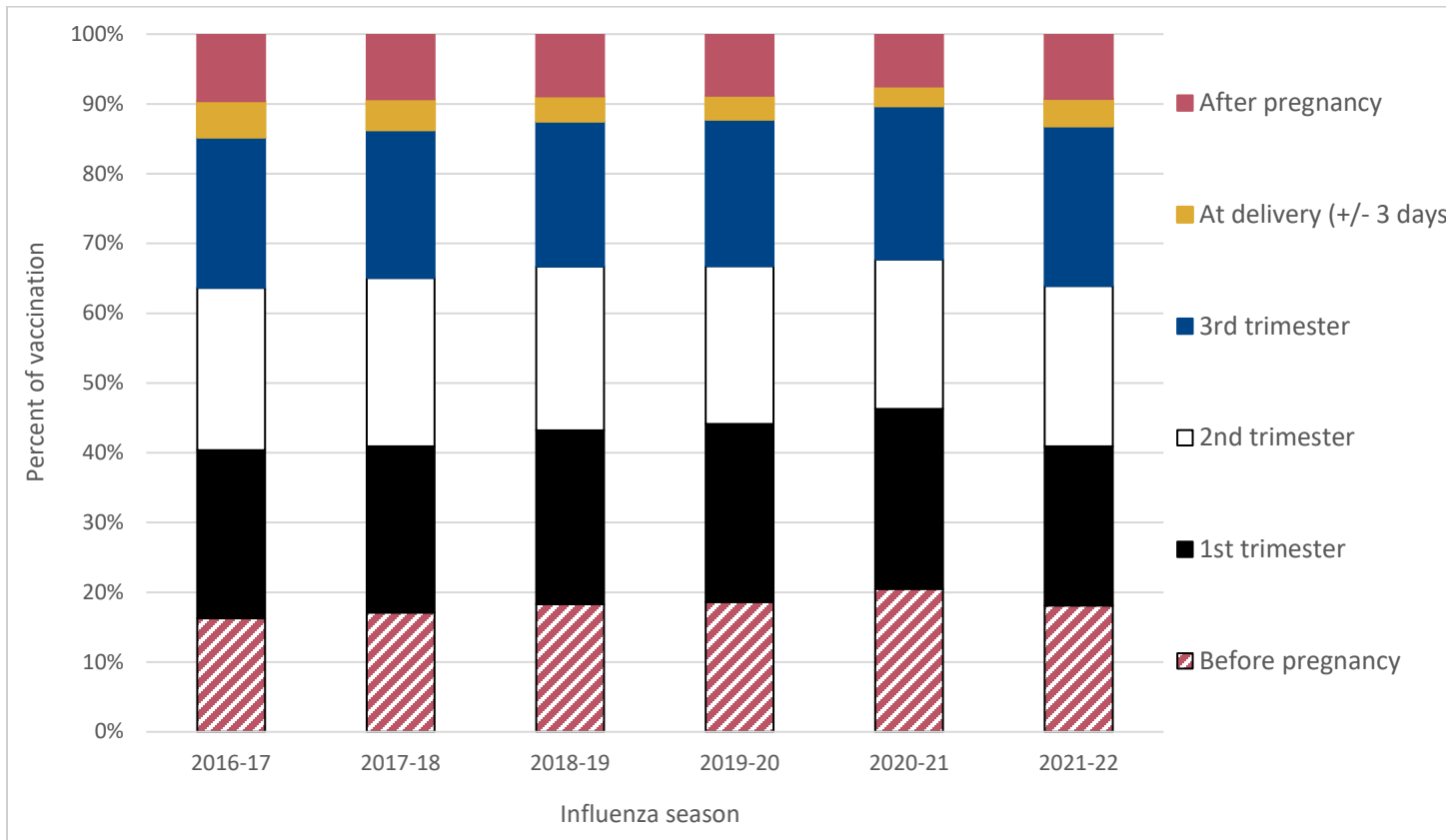

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Appendix 10. Timing of influenza vaccine receipt among vaccinated pregnant people, by influenza season.

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Appendix 11. Comprehensive Discussion

This large retrospective analysis found that from the 2016-17 through 2019-20 influenza seasons influenza vaccination coverage increased in the VSD population of pregnant people, peaking at an overall crude coverage of 71.0% in 2019-20. However, coverage fell in the 2020-21 season and declined even more in the 2021-22 season, to a low of 56.4% overall. We identified differences in coverage across demographic and clinical characteristics, with the lowest coverage estimates among younger (18-24-year-old) and non-Hispanic Black pregnant people, and those with fewer medical encounters.

Our finding of a decrease in influenza vaccine coverage in pregnant people in the 2020-21 season differs from results in the literature. Lumbreras Areta, et al. reported an increase in coverage among pregnant people in Switzerland between the 2019-20 and the 2020-2021 season, from 37% to 49.8%.[6] That their study saw an increase in influenza vaccination while our US population saw a decrease could reflect lower baseline coverage in that population, differences in health care access or care seeking during the first year of the COVID-19 pandemic, vaccine hesitancy, and/or differences in public health and media messaging about influenza and vaccination more generally between the countries. Notably, however, the overall 2020-21 coverage estimate in our population (56.4%) was 6.6% higher than the estimate reported from the Swiss study.[6]

We observed the lowest influenza coverage in our study period in the 2021-22 influenza season. The pattern was consistent across age and race and ethnicity groups, as well as by clinical

characteristics. Our 56.4% overall crude coverage estimate was similar to the April 2022 internet panel survey, which found that 49.6% of pregnant people surveyed reported receipt of a same-season influenza vaccine prior to or during their pregnancy.[7] Our higher estimate is likely due in part to our inclusion of post-pregnancy vaccination, which accounted for 7.5-9.6% of vaccination each season.

Our analysis included coverage estimates by a health care utilization proxy, examining coverage by the number of clinical encounters between July 1 and June 30 overlapping each season. We found that influenza vaccination coverage increased with increased health care utilization. The population with high health care utilization likely overlaps with the groups of pregnant people with pregnancy comorbidities/complications or high-risk conditions, where higher coverage estimates were also identified. Because encounter type was not distinguished, this may also reflect pregnancy start dates that allow for more prenatal visits in a given July 1 through June 30 period, as higher number of prenatal care visits has been shown to be associated with increased odds of influenza vaccination.[8] It is also possible that the VSD has more comprehensive capture of influenza vaccination outside the health care system for people with more health care encounters.

We also examined how pregnancy start dates may impact influenza vaccine uptake. Pregnancies starting in the late winter and spring prior to the influenza season of interest -- and thus in the second or third trimester when influenza vaccine is routinely offered in the fall -- had consistently higher coverage than those starting during the influenza season of interest. This

could be due to differences in health care utilization patterns in different stages of pregnancy,

possible worry about early pregnancy exposure, or providers not following the any-trimester

ACIP recommendation. Our coverage estimates for late-season pregnancies are similar to

general US population estimates among adults ages 18-49 years: the 2021-22 coverage among

pregnancies starting in March 2022 was only 1.3 percentage points lower than the general

population National Immunization Survey estimate (35.8% versus 37.1%).[9]

This study is subject to several limitations. First, the findings are not generalizable to all

pregnant people in the United States; it is possible that continuously enrolled VSD members

may have fewer barriers to care and/or more access to vaccination, and our population was

limited to pregnancies resulting in a live birth. Further, while the VSD has been shown to be

representative of the general US population on several key demographic and socioeconomic

variables,[2] it is not geographically representative of the United States and regional variations in

vaccine uptake exist. Second, vaccination status may be misclassified in the VSD, and coverage

underestimated if pregnant people receive vaccinations outside the participating delivery

systems or immunization registry catchment area.[4] Third, it is possible that demographic or

clinical characteristics may be misclassified within the electronic medical record. Fourth,

because our inclusion criteria allowed for any duration of pregnancy within the August 1

through March 31 period each season, pregnancy length within the season differed, thus

creating different possible windows for pre-, during, and post-pregnancy vaccination. Because

all vaccination was included in coverage estimates, irrespective of timing relative to pregnancy,

and the study population was required to have health system enrollment throughout the season, this limitation should have minimal impact on most estimates; however, it could impact the specific pregnancy-timing analyses. Fifth, the granularity of our available race data was limited, and we were unable to report coverage estimates for races other than Asian, Black, and White; while a small proportion of our total, the "another race or multiple races" grouping is very heterogenous. Finally, we did not validate the pregnancies identified by the VSD algorithm for this analysis; it is possible that the algorithm may result in some misclassification of pregnancy outcomes and dates. However, our previous validation work has shown that a high proportion of pregnancies identified by the algorithm are confirmed through medical record review.[3]

Our findings provide insight into recent trends in influenza vaccination coverage among pregnant people and include estimates by age group, race and ethnicity, presence of pregnancy comorbidities or high-risk conditions for severe disease from influenza, and month of pregnancy start date. The persistent disparities in coverage, coupled with decreases in coverage in recent seasons shown here have important public health ramifications. Continued efforts to improve vaccination coverage in the pregnant population, especially in specific sub-populations with lower vaccination coverage, such as younger and non-Hispanic Black pregnant people, are essential.

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