

Safety of COVID-19 Vaccination in Pregnancy, Interim Data from the Vaccine Safety Datalink

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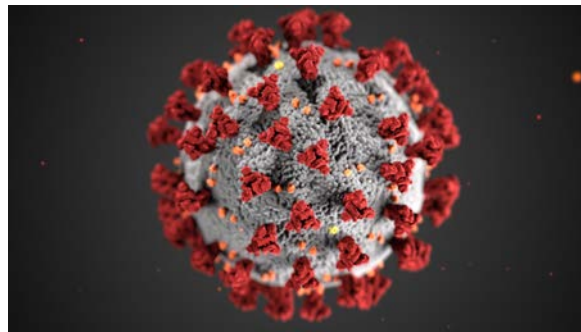
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Advisory Committee on Immunization
Practices

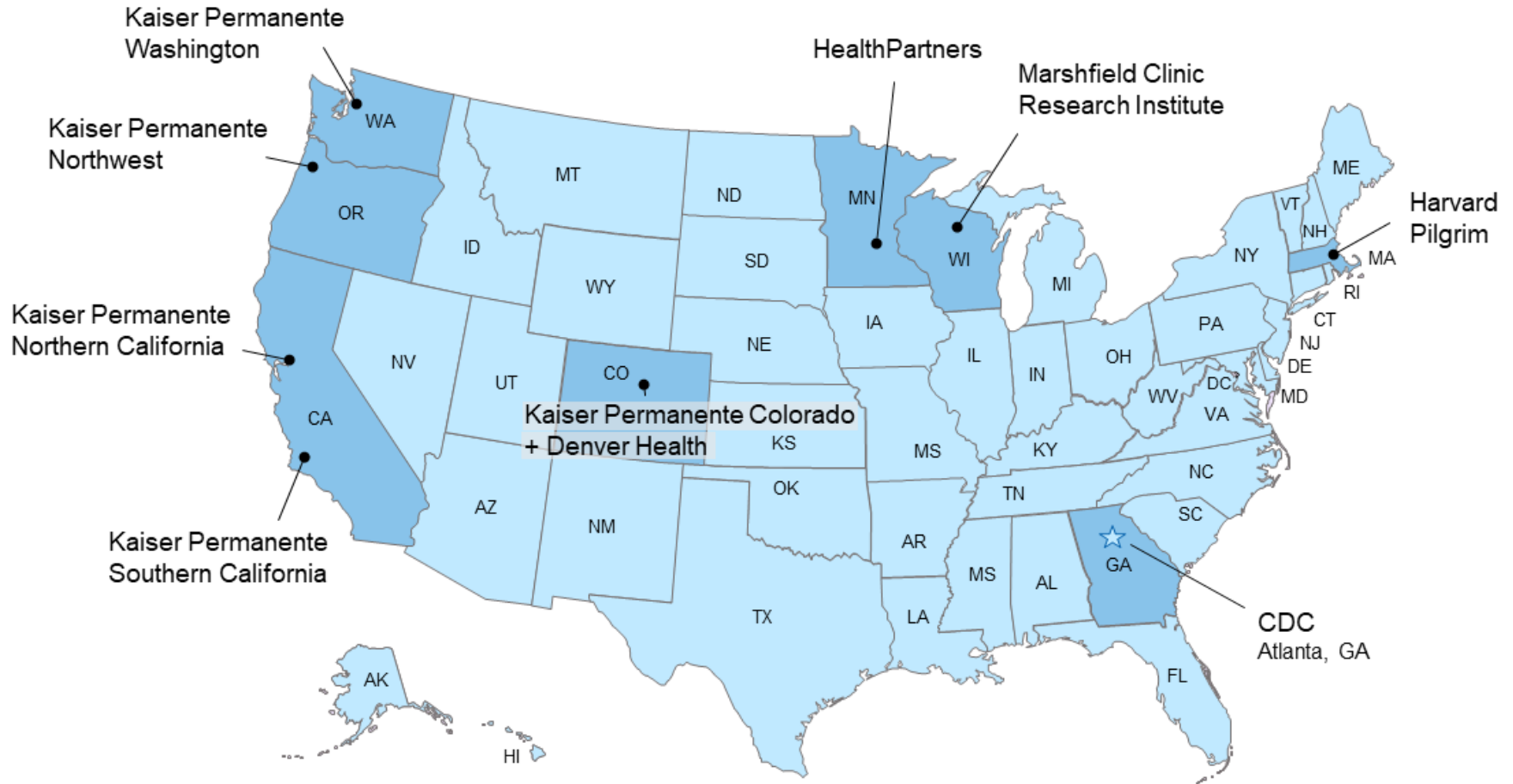
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Overview

- Data from the Vaccine Safety Datalink (VSD)
 - Receipt of COVID-19 vaccines before and during pregnancy
 - Spontaneous abortion following COVID-19 vaccination
 - Stillbirth surveillance



Vaccine Safety Datalink



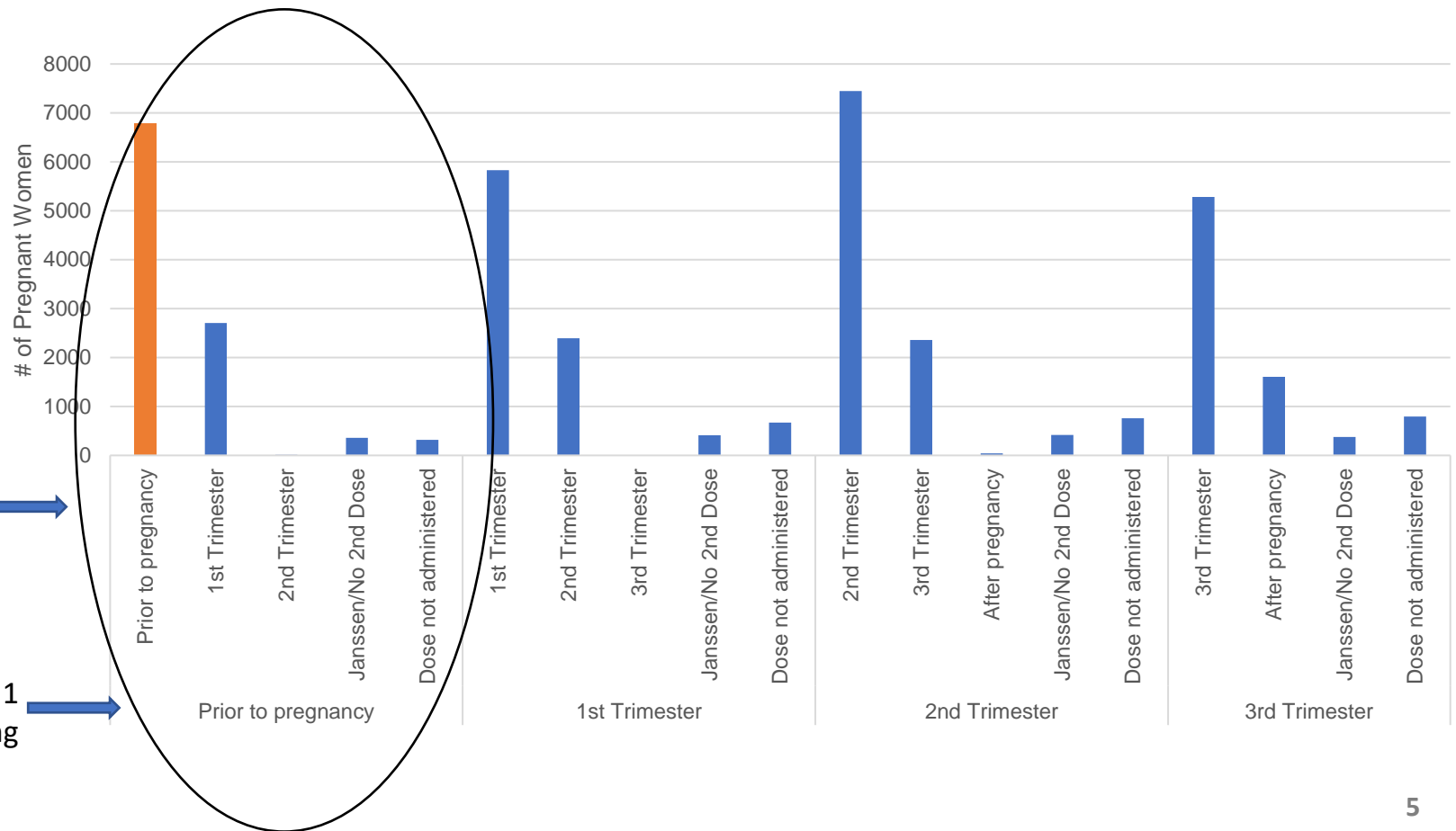
Identifying ongoing pregnancies in the Vaccine Safety Datalink (VSD)

- VSD previously developed and validated pregnancy episode algorithm (PEA) applied to identify completed pregnancies
 - PEA used in prior VSD studies of maternal Tdap and IIV safety
- Dynamic pregnancy algorithm (DPA) developed and validated to identify and date ongoing pregnancies¹
 - DPA incorporates diagnoses and procedure codes from health care visits, clinical variables (e.g., EDD, LMP), updated weekly
 - DPA made our work on safety of COVID-19 vaccine in pregnancy possible

¹Naleway et al. Vaccine Safety Datalink infrastructure enhancements for evaluating the safety of maternal vaccination. Therapeutic Advances in Drug Safety. 2021

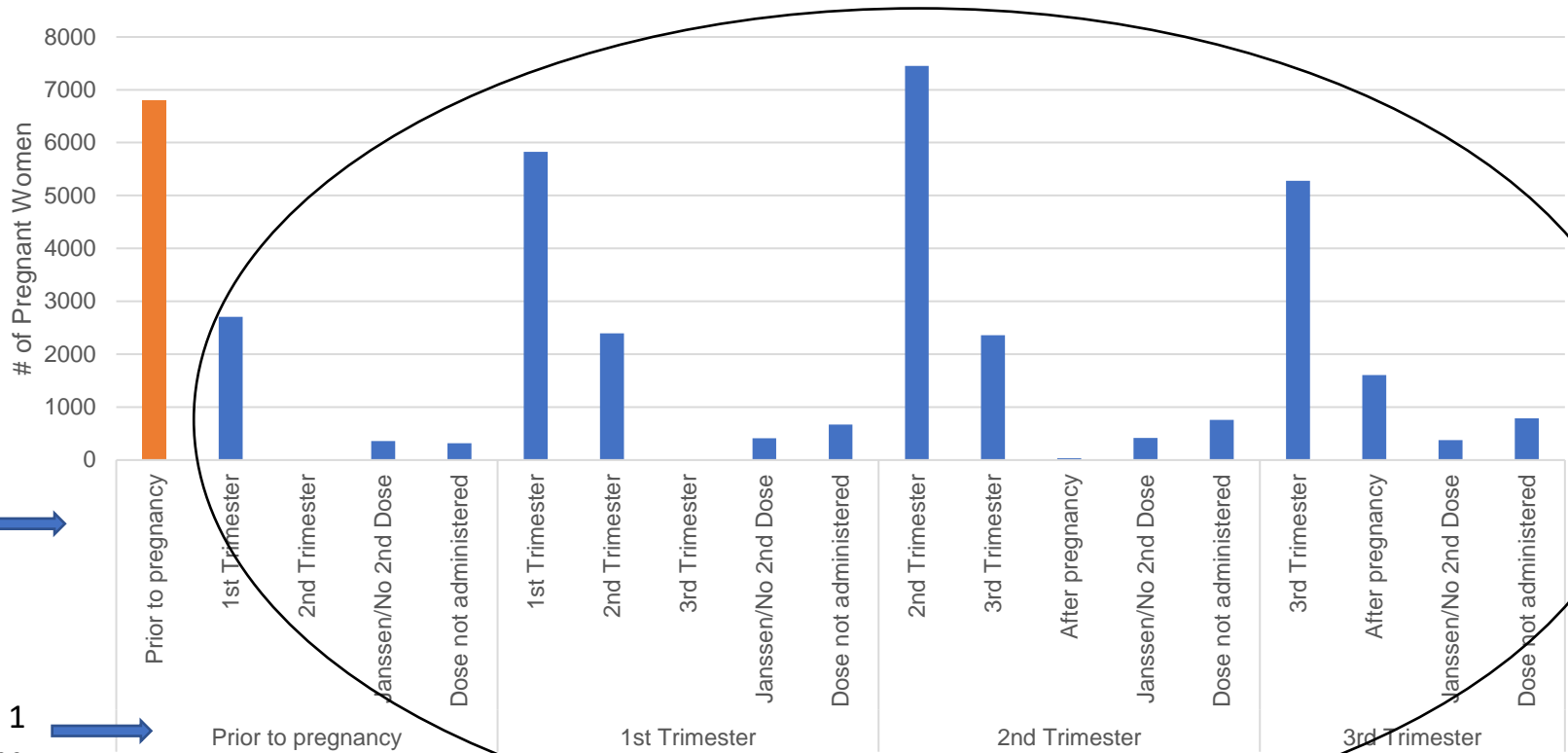
COVID-19 vaccine doses administered and pregnancy in VSD, Dec 14, 2020 – Jul 31, 2021, of 122,998 pregnancies:

- 10,178 pregnancies with ≥ 1 vaccine dose prior to pregnancy
- 6,792 pregnancies with 2 vaccine doses prior to pregnancy



COVID-19 vaccine doses administered and pregnancy in VSD, Dec 14, 2020 – Jul 31, 2021, of 122,998 pregnancies:

- 31,080 pregnancies with ≥ 1 vaccine during pregnancy
- 23,310 pregnancies with 2 vaccine doses during pregnancy



RESEARCH LETTER

Spontaneous Abortion Following COVID-19 Vaccination During Pregnancy

COVID-19 infection during pregnancy can be associated with severe maternal morbidity.¹ In the United States, 1 COVID-19 vaccine has been approved and 2 have been authorized for use for pregnant women. To date, data on maternal COVID-19 vaccine safety come primarily from passive surveillance, and studies lack an unvaccinated comparison group.^{2,3} Spontaneous abortion has been identified as a priority outcome in studies of maternal vaccine safety,⁴ and concerns regarding risks of spontaneous abortion may be a barrier to vaccination during pregnancy. We present findings from case-control surveillance of COVID-19 vaccination during pregnancy and spontaneous abortion.

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Supplemental content

Methods | The Vaccine Safety Datalink is a collaboration between the Centers for Disease Control and Prevention and 9 health systems, representing approximately 3% of the US population.⁵ We applied a validated pregnancy algorithm, which incorporates diagnostic and procedure codes and electronic health record (EHR) data, to identify and assign gestational ages for spontaneous abortions and ongoing pregnancies.⁶ Data from 8 health systems (Kaiser Permanente: Washington, Northwest, Northern California, Southern California, and Colorado; Denver Health; HealthPartners; and Marshfield Clinic, Wisconsin) over seven 4-week surveillance periods from December 15, 2020, through June 28, 2021, were included. Ongoing pregnancies between 6 and 19 weeks' gestation were identified on the last day of each 4-week surveillance period (index date) and contributed data to 1 or more surveillance periods. Spontaneous abortions were assigned to a 4-week surveillance period based on their outcome date;

Table 1. Receipt of COVID-19 Vaccine in Prior 28-Day Window, by Baseline Characteristics and Surveillance Period, December 15, 2020, Through June 28, 2021

	Ongoing pregnancy-periods*		Spontaneous abortions	
	No.	COVID-19 vaccine, No. (%)	No.	COVID-19 vaccine, No. (%)
All	250 944	20 139 (8.0)	13 160	1128 (8.6)
Maternal age group, y				
16-24	37 210	1325 (3.6)	1433	69 (4.8)
25-34	156 166	12 451 (8.0)	6640	493 (7.4)
35-49	57 568	6363 (11.1)	5087	566 (11.1)
Race and ethnicity ^b				
Asian	35 938	4433 (12.3)	2028	262 (12.9)
Black, non-Hispanic	18 790	715 (3.8)	1079	48 (4.4)
Hispanic	86 108	5207 (6.0)	4346	322 (7.4)
White, non-Hispanic	81 834	7571 (9.3)	4272	373 (8.7)
Unknown/other	28 274	2213 (7.8)	1435	123 (8.6)
Gestational age group, wk				
6-8	57 355	5196 (9.1)	5238	482 (9.2)
9-13	88 982	6067 (6.8)	6652	528 (7.9)
14-19	104 607	8876 (8.5)	1270	118 (9.3)
Antenatal visits				
≥1	89 913	6850 (7.6)	3203	244 (7.6)
≥2	161 031	13 289 (8.3)	9957	884 (8.9)
Surveillance periods				
December 15, 2020-January 11, 2021	36 964	711 (1.9)	1767	21 (1.2)
2021				
January 12-February 8	36 981	1696 (4.6)	2097	68 (3.2)
February 9-March 8	37 030	2322 (6.3)	1871	97 (5.2)
March 9-April 5	37 144	4934 (13.3)	1903	204 (10.7)
April 6-May 3	36 191	5654 (15.6)	1864	330 (17.7)
May 4-May 31	34 545	3485 (10.1)	1811	272 (15.0)
June 1-June 28	32 089	1337 (4.2)	1847	136 (7.4)

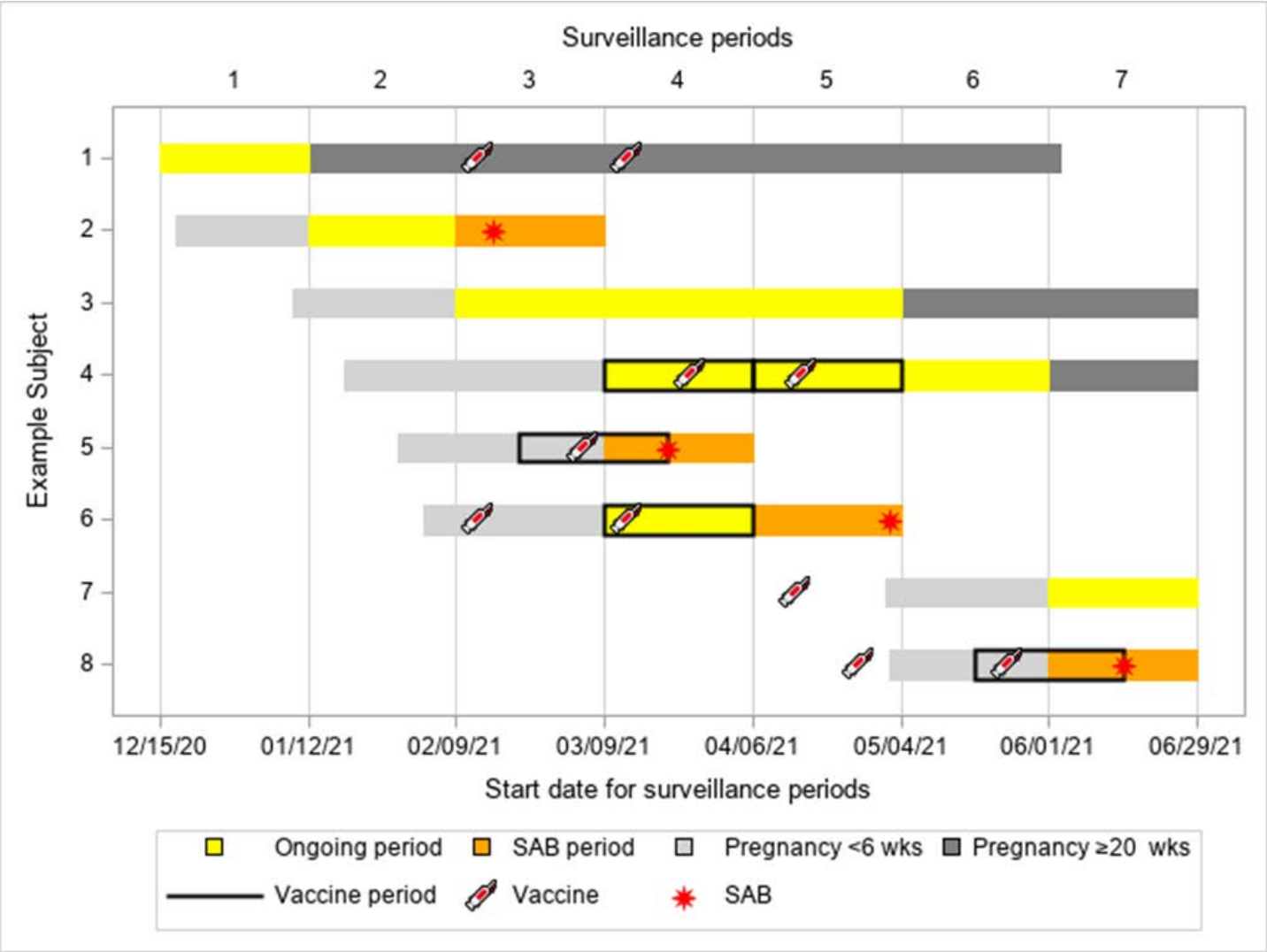
* Four-week surveillance periods included: December 15, 2020, through January 11, 2021; January 12 through February 8, 2021; February 9 through March 8, 2021; March 9 through April 5, 2021; April 6 through May 3, 2021; May 4 through May 31, 2021; and June 1 through June 28, 2021. Unique ongoing pregnancies may be counted in more than one 4-week surveillance period and were identified at the last date of the 4-week period.

^b Race and ethnicity came from electronic health data, based on self-report. Race and ethnicity is included as both COVID-19 vaccine uptake and rates of spontaneous abortion vary by race and ethnicity.

COVID-19 vaccine in pregnancy and spontaneous abortion (SAB) surveillance

- Identified SABs and ongoing pregnancies 6–19 weeks' gestation
 - SABs assigned to a 4-week surveillance period
 - Ongoing pregnancies, including pregnancy time prior to SAB, assigned to ≥ 1 surveillance periods
- Using GEE, odds of exposure to COVID-19 vaccine in 28 days prior to SAB compared to odds of exposure to COVID-19 vaccine among ongoing pregnancies in 28 days prior to index date
 - Adjusting for gestational age, maternal age, receipt of prenatal care, race/ethnicity, and VSD site

Example of how SABs and ongoing pregnancies classified across seven surveillance periods



Kharbanda et al. Spontaneous Abortion Following COVID-19 Vaccination During Pregnancy. JAMA. 2021 Sep 8. doi: 10.1001/jama.2021.15494.

COVID-19 vaccines received during pregnancy

(Dec 15, 2020 – Jun 28, 2021, for 105,446 unique pregnancies <20 weeks' gestation)

Seven surveillance periods (Dec 15, 2020 – Jun 28, 2021)	Ongoing Pregnancies N (%)	Spontaneous abortions N (%)
All included pregnancies	92,286	13,160
Vaccine type		
Janssen / J&J	480 (0.5)	48 (0.4)
Moderna	5638 (6.1)	675 (5.1)
Pfizer	7463 (8.1)	804 (6.1)

COVID-19 vaccines in prior 28 days

(Dec 15, 2020 – Jun 28, 2021, 264,104 pregnancy-periods)

	Ongoing pregnancy-periods		Spontaneous abortions	
	N	COVID-19 vaccination	N	COVID-19 vaccination
		n (%)		n (%)
All pregnancy-periods*	250,944	20,139 (8.0)	13,160	1128 (8.6)
6–8 weeks gestation	57,355	5196 (9.1)	5238	482 (9.2)
9–13 weeks gestation	88,982	6067 (6.8)	6652	528 (7.9)
14–19 weeks gestation	104,607	8876 (8.5)	1270	118 (9.3)
16–24 years	37,210	1325 (3.6)	1433	69 (4.8)
25–34 years	156,166	12,451 (8.0)	6640	493 (7.4)
35–49 years	57,568	6363 (11.1)	5087	566 (11.1)

*Individual pregnancies may contribute data for more than one surveillance period, pregnancies <20 weeks' gestation included

COVID-19 vaccines in prior 28 days

(Dec 15, 2020 – Jun 28, 2021, 264,104 pregnancy-periods)

	Ongoing pregnancy-periods		Spontaneous abortions	
	N	COVID-19 vaccination	N	COVID-19 vaccination
		n (%)		n (%)
Hispanic	86,108	5207 (6.0)	4346	322 (7.4)
White, non-Hispanic	81,834	7571 (9.3)	4272	373 (8.7)
Asian	35,938	4433 (12.3)	2028	262 (12.9)
Unknown / other	28,274	2213 (7.8)	1435	123 (8.6)
Black, non-Hispanic	18,790	715 (3.8)	1079	48 (4.4)
<= 1 antenatal visits	89,913	6850 (7.6)	3203	244 (7.6)
>= 2 antenatal visits	161,031	13,289 (8.3)	9957	884 (8.9)

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	N	COVID vaccination	N	COVID vaccination
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Dec 15, 2020–Jan 11, 2021	36,964	711 (1.9)	1767	21 (1.2)
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Apr 6, 2021–May 3, 2021	36,191	5654 (15.6)	1864	330 (17.7)
May 4, 2021–May 31, 2021	34,545	3485 (10.1)	1811	272 (15.0)
Jun 1, 2021–Jun 28, 2021	32,089	1337 (4.2)	1847	136 (7.4)

*Individual pregnancies may contribute data for more than one surveillance period, pregnancies <20 weeks' gestation included

Adjusted Odds Ratios for receipt of COVID-19 vaccine in 28 days prior to SAB, Dec 15, 2020 – Jun 28, 2021

	aOR (95% CI)
Full population	1.02 (0.96–1.08)
By gestational age strata	
6–8 weeks	0.94 (0.86–1.03)
9–13 weeks	1.07 (0.99–1.17)
14–19 weeks	1.08 (0.89–1.29)
By vaccine type	
mRNA-1273, Moderna	1.03 (0.94–1.11)
BNT162b2, Pfizer-BioNTech	1.03 (0.95–1.11)

aOR = adjusted odds ratio; SAB= spontaneous abortion

GEE models adjusted for gestational age group, study month, site, maternal age group, number of antenatal visits, and race/ethnicity and accounted for repeated ongoing pregnancies

Limitations, summary and next steps

- Limitations
 - Spontaneous abortion cases not chart confirmed
 - Unable to adjust for some potential confounders
- **Among women with spontaneous abortions, adjusted odds of COVID-19 vaccine exposure were not increased in the prior 28 days, compared to women with ongoing pregnancies**
- Future individually matched case-control study planned, with all spontaneous abortion cases chart confirmed

Monthly surveillance for stillbirths following COVID-19 vaccination

- Potential stillbirth cases with COVID-19 vaccine exposures identified each month
- To increase sensitivity, included SABs at 18–19 weeks' gestation
- All potential cases chart reviewed by sites
- All potential cases adjudicated by Yale OB team
- For confirmed stillbirths, using adjudicated date and gestational age at fetal demise, evaluated timing of COVID-19 vaccine exposures

Monthly surveillance for stillbirths following COVID-19 vaccination (Dec 2020 – Jul 2021, 11,300 live births in VSD during this period received COVID-19 vaccine during pregnancy)

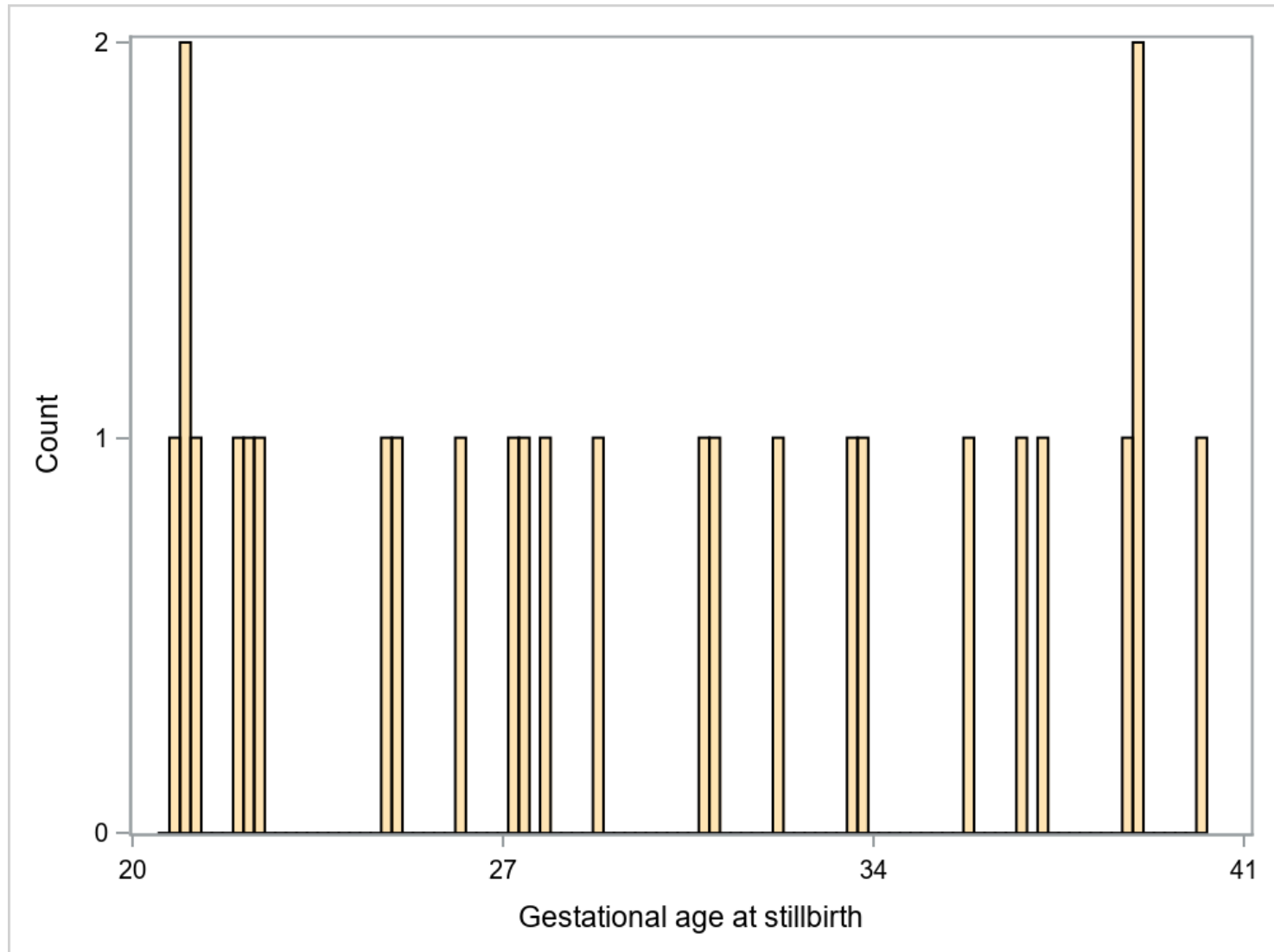
Outcome date	Stillbirths or late SABs* (N)	Stillbirths or late SABs with COVID-19 vaccine* (N)	Excluded** (N)	Confirmed stillbirths with COVID-19 vaccine exposure during pregnancy (N)
December 2020	47	0	.	0
January 2021	108	3	3	0
February 2021	97	7	6	1
March 2021	89	8	5	3
April 2021	104	20	12	8
May 2021	90	22	16	6
June 2021	94	25	20	5
July 2021	41	7	4	3
Dec 2020 – Jul 2021	670	92	66	26***

Late SABs = spontaneous abortions estimated to occur at 18- or 19-weeks' gestation

*Based on automated pregnancy algorithm; **Exclusions due to: SAB (n=41) ongoing pregnancy (n=2), live birth (n=10), ectopic pregnancy (n=1) therapeutic abortion (n=9), and records not available (n=3);

***Consistent with expected background rates

Gestational age at stillbirth in weeks



Mean = 29.5 weeks (sd=6.6 weeks); Range = 20 - 40 weeks (n=26)

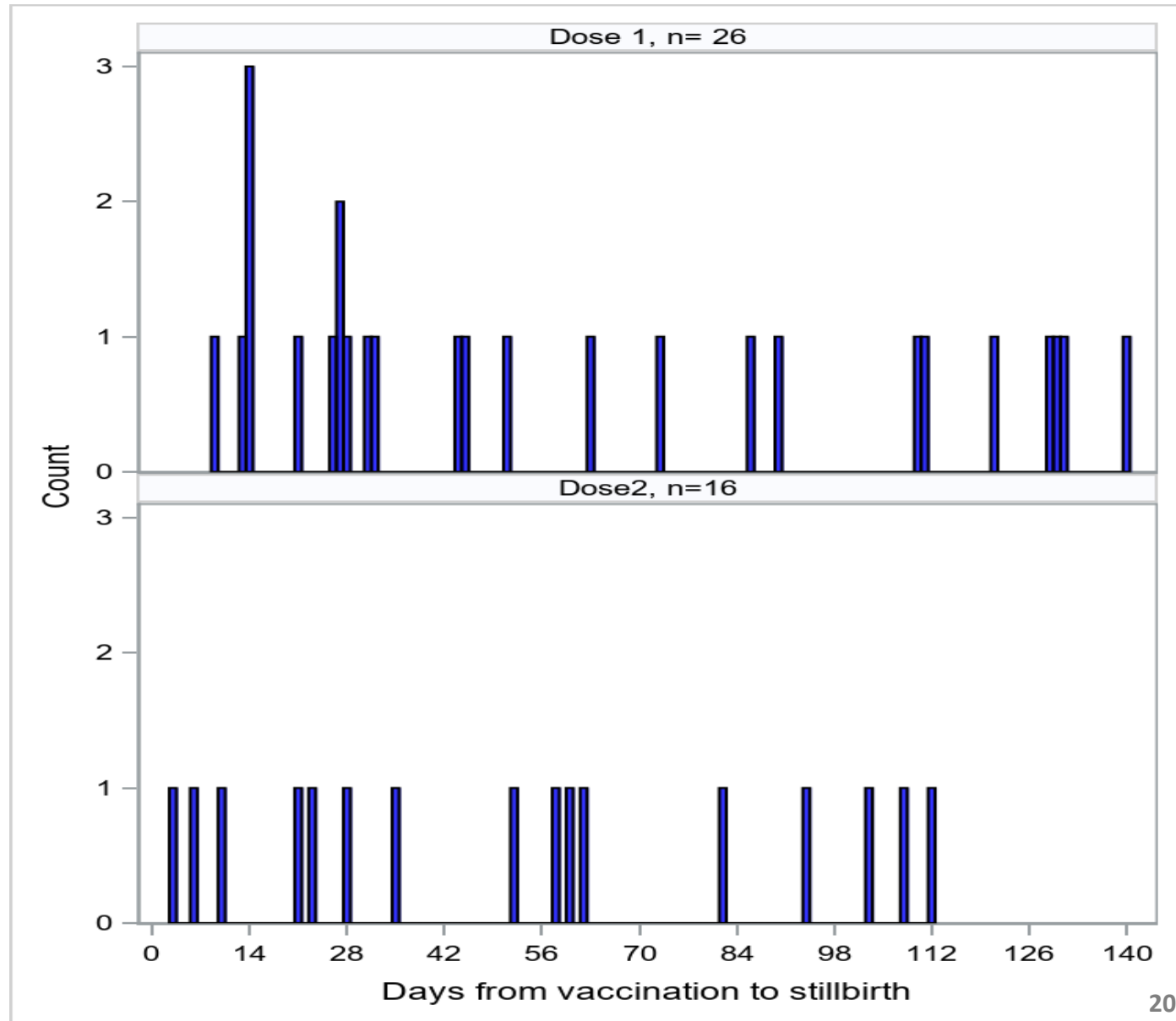
Pregnancy or birth complications associated with stillbirth in cases with COVID-19 vaccine exposure (n=26)

Complication	n (%)
One or more complications associated with stillbirth	25 (96)
Umbilical cord or placental complication (e.g., true knot, tight nuchal cord, placenta <10%)	19 (73)
Obstetric complication (e.g., placental abruption, chorioamnionitis)	18 (69)
Maternal comorbidity (e.g., hypertension, diabetes)	16 (62)
Fetal condition (e.g., congenital CMV)	7 (27)
Multiple gestation pregnancy with complications	1 (4)

Timing between COVID-19 vaccination and stillbirth, by dose

Dose 1 (n=26)
Range = 8 - 140 days

Dose 2 (n=16)
Range = 3 - 112 days

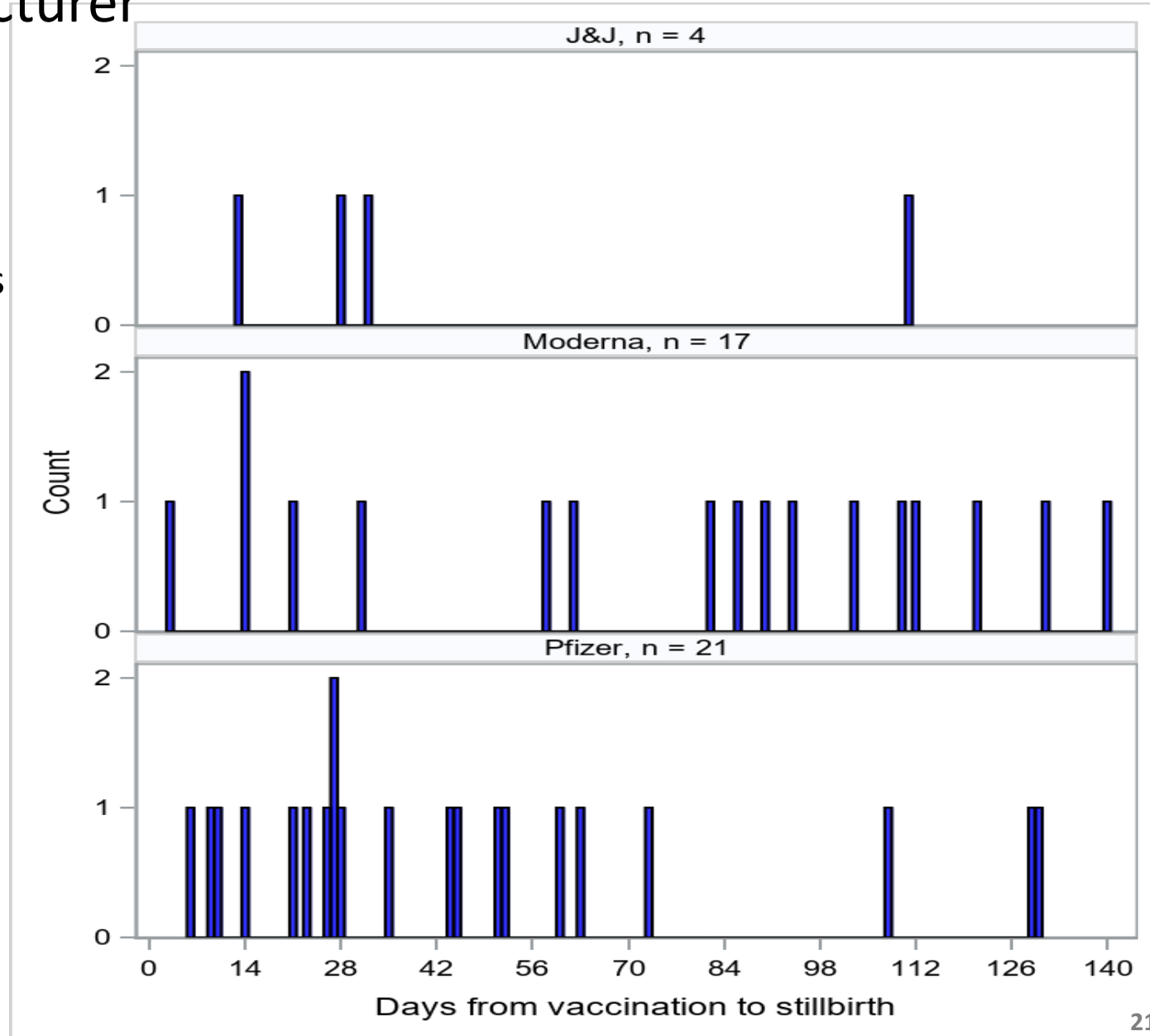


Timing between vaccination and stillbirth, by manufacturer

J&J (n=4)
Range = 13 - 111 days

Moderna (n=17)
Range = 3 - 140 days

Pfizer (n=21)
Range = 6 - 129 days



Limitation, summary and next steps

- Limitation
 - Stillbirth surveillance is descriptive, no comparison group
- **Monthly stillbirth surveillance with chart review and adjudication has identified 26 stillbirths following COVID-19 vaccination from Dec 2020 – Jul 2021**
 - Nearly all cases with known stillbirth risk factors
 - No concerning patterns identified related to timing of vaccine exposure or stillbirth etiology
- Future case-control study planned

Our Team

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- Mike Jackson
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- Simon Hambidge
- Jim Donahue