

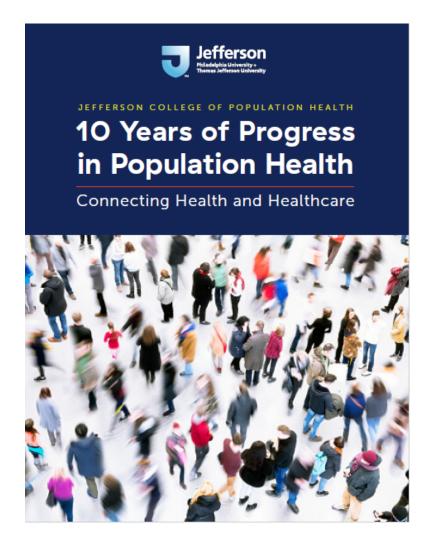


May 18, 2021 | 4:00-5:00 pm ET





#### Jefferson College of Population Health



#### Best Practices for Perinatal Care during COVID-19

#### **Featuring**



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Department of Obstetrics,
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Division of Maternal-Fetal Medicine
and
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#### Presented by



# COVID-19 in Pregnancy

Sarah N. Cross, MD

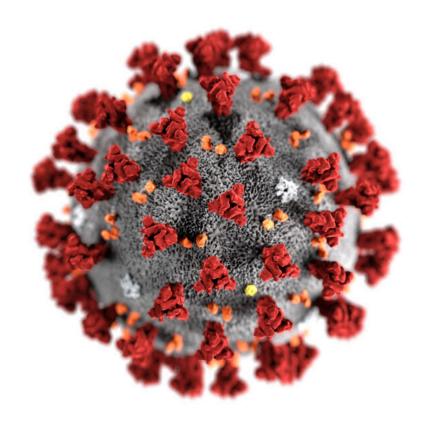
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May 18, 2021

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#### **Disclosures**

None



#### **Objectives**

- Describe the epidemiology of SARS-CoV-2 in pregnancy
- Review pregnancy physiology
- Review outcomes of pregnant patients & neonates
- Outline outpatient management
- Outline admission considerations
- Review the use of COVID-19 therapies in the pregnant patient
- Review the use of obstetric medications in the SARS-CoV-2 positive patient
- Discuss alterations on L&D



#### In The Beginning

Characteristics	COVID-19	SARS	MERS
No. of cases	55	17	12
Age (y)	23-40	27-44	31-39
Maternal complications			
Mortality (%)	0	18	25
Mechanical ventilation (%)	2	35	41



#### **EPIDEMIOLOGY**

**OF COVID-19** 

#### **Epidemiology of SARS-CoV-2**

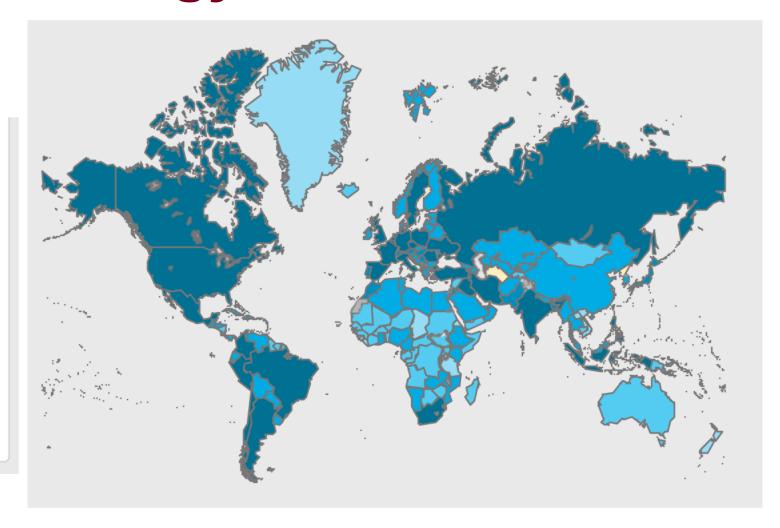
**WORLD** 

434,193 new cases

163,212,543 confirmed cases

> 3,383,979 deaths

**1,264,164,553** vaccine doses administered

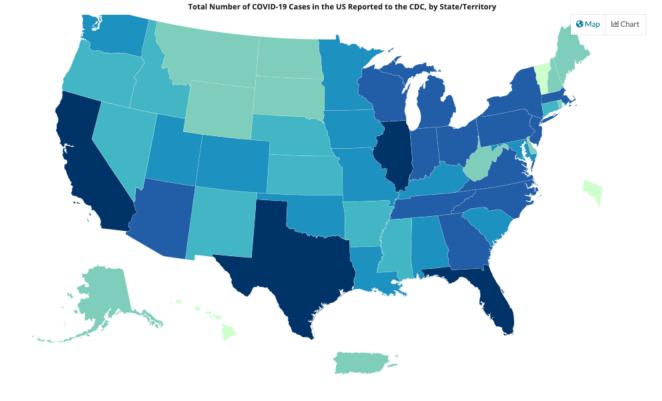




https://covid19.who.int/?gclid=Cj0KCQjw5eX7BRDQARIsAMhYLP\_x6mo5ioClxBI\_-FHptEdlb7Qh7LJfiGTO4HtLIL\_4xJ-el8QLa1caAvd3EALw\_wcB\_ - accessed 5/18/2021

## **Epidemiology of SARS-CoV-2** USA

	People Vaccinated	At Least One Dose	Fully Vaccinated
Total Vaccine Doses	Total	157,827,208	123,828,224
Delivered 344,503,595 Administered 274,411,901 Learn more about the distribution of vaccines.	% of Total Population	47.5%	37.3%
	Population ≥ 12 Years of Age	157,774,165	123,820,066
	% of Population ≥ 12 Years of Age	56.3%	44.2%
	Population ≥ 18 Years of Age	154,478,960	122,238,476
	% of Population ≥ 18 Years of Age	59.8%	47.4%
	Population ≥ 65 Years of Age	46,273,886	39,814,913
	% of Population ≥ 65 Years of Age	84.6%	72.8%
_			
DCC   Data as of: May 17, 2021 6:00am ET. Posted: Monday, May 17, 2021 9:43 PM ET			





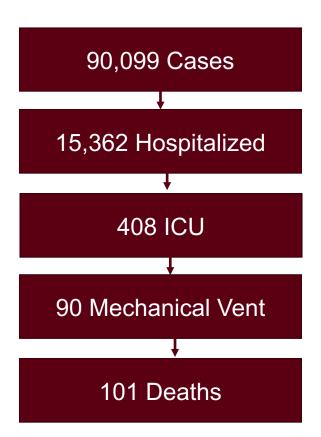


https://covid.cdc.gov/covid-data-tracker/#cases\_casesinlast7days - accessed 5/18/21

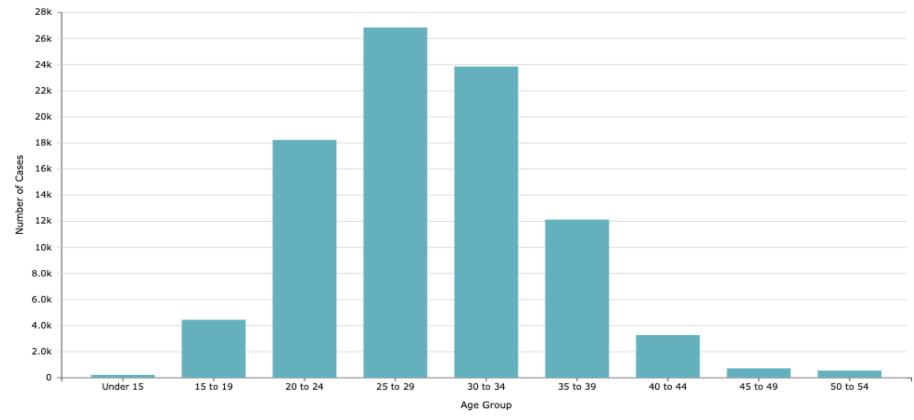


#### **Epidemiology of SARS-CoV-2**

Pregnancy



Pregnant women with COVID-19 by age, United States, January 22, 2020 - May 10, 2021 Data were collected from 90,099 women, and age was available for 90,099 (100%) women.





https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/special-populations/pregnancy-data-on-covid-19.html - accessed 5/18/2021

#### **Epidemiology of SARS-CoV-2**

Pregnancy

Pregnant women with COVID-19 by race/ethnicity, United States, January 22, 2020 - May 10, 2021 Data were collected from 90,099 women, but race/ethnicity was only available for 77,616 (86.1%) women.

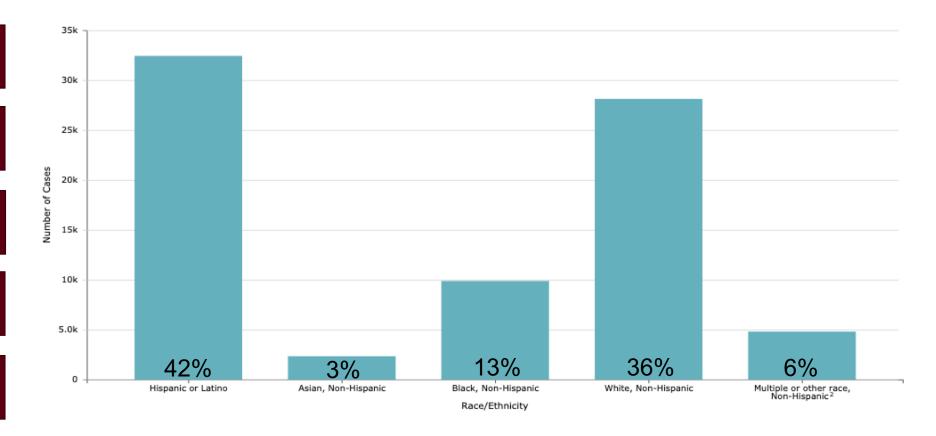


5.9% Asian

13.4% Black Non-H

63.4% White Non-H

2.7% Multiple



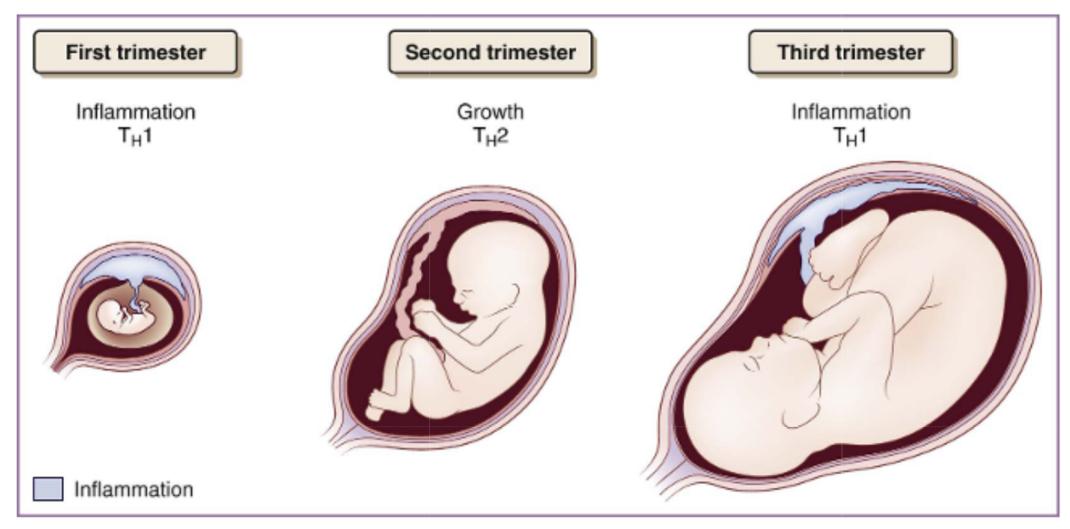
https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/special-populations/pregnancy-data-on-covid-19.html - accessed 5/11/2021



#### **PREGNANCY**

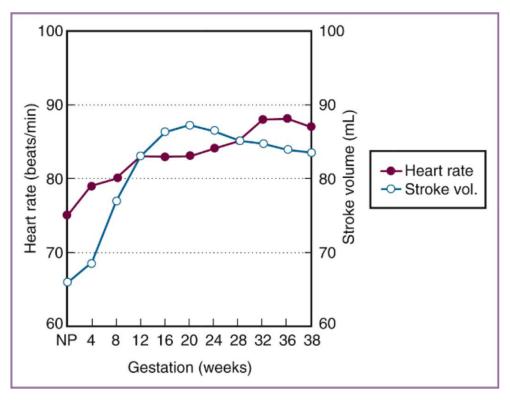
#### **PHYSIOLOGY**

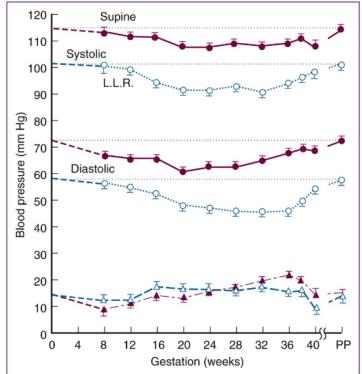
#### **Pregnancy Immunology**





#### Cardiovascular Physiology of Pregnancy





	First Trimester	Second Trimester	
Cardiac output		↑↑35-45%	
Heart rate	↑3-5%	↑10-15%	↑15-20%
Blood pressure	↓10%	↓5%	↑5%
Plasma volume	<b>↑</b>	↑↑40-50%	)

#### Cardiovascular Physiology of Pregnancy

Cardiovascular	Effect
----------------	--------

Increased	Plasma volume by 40 to 50 percent, but erythrocyte volume by only 20 percent	Dilutional anemia results in decreased oxygen carrying capacity
	Cardiac output by 40 percent	Increased CPR circulation demands
	Heart rate by 15 to 20 beats per minute	Increased CPR circulation demands
	Clotting factors susceptible to thromboembolism	
	Dextrorotation of the heart	Increased EKG left axis deviation
	Estrogen effect on myocardial receptors	Supraventricular arrhythmias
Decreased	Supine blood pressure and venous return with aortocaval compression	Decreases cardiac output by 30 percent
	Arterial blood pressure by 10 to 15 mm Hg	Susceptible to cardiovascular insult
	Systemic vascular resistance	Sequesters blood during CPR
	Colloid oncotic pressure (COP)	Susceptible to third spacing
	Pulmonary capillary wedge pressure (PCWP)	Susceptible to pulmonary edema

Uteroplacental		Effect	
Increased	Uteroplacental blood flow by 30 percent of cardiac output	Sequesters blood in CPR	
	Aortocaval compression	Decreases cardiac output by 30 percent	
	Elevation of diaphragm by 4 to 7 cm	Aspiration of gastric contents	
Decreased	Autoregulation of blood pressure	Uterine perfusion decreases with drop in maternal blood pressure	

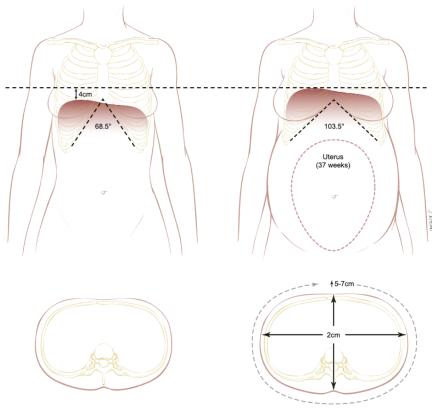


ACOG

#### Respiratory Physiology of Pregnancy

Lung Volume (mL)	Nonpregnant	Pregnant	Change
Total lung capacity (vital capacity + residual volume)	4200	4000	-4%
Vital capacity (total lung capacity – residual volume)	3200	3200	No change
Inspiratory capacity (vital capacity – expiratory reserve volume)	2500	2650	+6%
Tidal volume	450	600	+33%
Expiratory reserve volume (vital capacity – inspiratory capacity)	700	550	-20%
Inspiratory reserve volume (inspiratory capacity – tidal volume)	2050	2050	No change
Residual volume (result: decrease in total lung capacity)	1000	800	-20%
Functional residual capacity (residual volume + expiratory reserve volume)	1700	1350	-20%





**Fig. 1.** Chest wall changes that occur during pregnancy. The subcostal angle increases, as does the anterior-posterior and transverse diameters of the chest wall and the chest wall circumference. These changes compensate for the 4-cm elevation of the diaphragm so that total lung capacity is not significantly reduced.



#### Respiratory Physiology of Pregnancy

	Respiratory	Effect
Increased	Respiratory rate (progesterone-mediated)	Decreased buffering capacity
	Oxygen consumption by 20 percent	Rapid decrease of PaO <sub>2</sub> in hypoxia
	Tidal volume (progesterone-mediated)	Decreased buffering capacity
	Minute ventilation	Compensated respiratory alkalosis
	Laryngeal angle	Failed intubation
	Pharyngeal edema	Failed intubation
	Nasal edema	Difficult nasal intubation
Decreased	Functional residual capacity by 25 percent	Decreases ventilatory capacity
	Arterial PCO <sub>2</sub>	Decreases buffering capacity
	Serum bicarbonate	Compensated respiratory alkalosis



#### **Labor & Delivery Physiology**

	Stage 1 Labor	Stage 2 Labor
Cardiac output	↑30%	↑↑50%

Stroke volume 22% increase

Contractions transfer 300-500 mL of blood from the uterus to the general circulation

·	
Heart rate	During uterine contractions: ↑40-50%
Blood pressure	During uterine contractions: ↑SBP 15-25% ↑DBP 10-15%
Plasma volume	$\uparrow$ $\uparrow$

#### Vaginal Delivery

- 80% increase in CO within 15-20 minutes w/o regional
- 60% increase in CO within 15-20 minutes with regional
- Blood loss ~ 500 mL
- Cesarean Delivery under spinal
  - 47% increase in CO within 2 minutes
  - 39% decrease in SVR
  - Blood loss ~ 1000 mL



#### **Postpartum Physiology**

	Early Postpartum	3–6 months Postpartum
Cardiac output	$\uparrow\uparrow\uparrow60-80\%$ immediately, then rapidly decreases within the first hour	Return to prepregnancy values
Heart rate	↓5–10% within 24 hours; continues to decrease throughout the first 6 weeks	Return to prepregnancy values
Blood pressure	↓SBP 5–10% within 48 hours; may increase again between days 3–6 due to fluid shifts	Return to prepregnancy values
Plasma volume	↑↑↑500 mL due to autotransfusion	Return to prepregnancy values

- Cardiac changes
  - LA dimension increase 1-3 days after birth and normalize by 10 days
  - HR normalizes by 10 days
  - LV dimension decrease gradually over 4-6 months
  - SV, CO, SVR do not completely return to normal until 12 weeks, and sometimes 24 week postpartum



#### **OUTCOMES**

#### **IN PREGNANCY**

#### **CDC Pregnancy Outcomes**

Update: Characteristics of Symptomatic Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status — United States, January 22–October 3, 2020

Early Release / November 2, 2020 / 69

Laura D. Zambrano, PhD¹,\*; Sascha Ellington, PhD¹,\*; Penelope Strid, MPH¹; Romeo R. Galang, MD¹; Titilope Oduyebo, MD¹; Van T. Tong, MPH¹; Kate R. Woodworth, MD¹; John F. Nahabedian III, MS¹; Eduardo Azziz-Baumgartner, MD¹; Suzanne M. Gilboa, PhD¹; Dana Meaney-Delman, MD¹; CDC COVID-19 Response Pregnancy and Infant Linked Outcomes Team (View author affiliations)



TABLE 2. Intensive care unit (ICU) admissions, receipt of invasive ventilation, receipt of extracorporeal membrane oxygenation (ECMO), and deaths among symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 (N = 409,462), by pregnancy status, age, race/ethnicity, and underlying health conditions — United States, January 22—October 3, 2020

	No. (per 1,000 cases) of	f symptomatic women	Risk ratio (95% CI)				
Outcome*/Characteristic	Pregnant (n = 23,434)	Nonpregnant (n = 386,028)	Crude <sup>†</sup>	Adjusted <sup>†,§</sup>			
ICU admission <sup>¶</sup>	ICU admission¶						
All	245 (10.5)	1,492 (3.9)	2.7 (2.4–3.1)	3.0 (2.6–3.4)			
Invasive ventilation††							
ilivasive veridiadioni							
All	67 (2.9)	412 (1.1)	2.7 (2.1–3.5)	2.9 (2.2–3.8)			
ECMO***	1		I				
All	17 (0.7)	120 (0.3)	2.3 (1.4–3.9)	2.4 (1.5–4.0)			
Death <sup>§§§</sup>	,						
All	34 (1.5)	447 (1.2)	1.3 (0.9–1.8)	1.7 (1.2–2.4)			



### Hospitalized pregnant women with COVID-19 can have severe illness

About half of hospitalized pregnant women with COVID-19 had symptoms



Some hospitalized pregnant women who had symptoms had severe outcomes, including

ICU admission

Mechanical ventilation

Death

Slow the spread and protect yourself from COVID-19 during pregnancy











Wear a mask when out in public

Stay 6 feet apart

Wash hands often

Continue receiving prenatal care

COVID-19-Associated Hospitalization Surveillance Network (COVID-NET) among 13 states. Vaccine Safety Datalink (VSD) surveillance of COVID-19 hospitalizations among eight healthcare centers.

MMWR



CDC.GOV

Systematic Review

# Adverse Pregnancy Outcomes Among Individuals With and Without Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)

A Systematic Review and Meta-analysis

Benjamin J. F. Huntley, MD, Isabelle A. Mulder, Daniele Di Mascio, MD, William S. Vintzileos, MD, Anthony M. Vintzileos, MD, Vincenzo Berghella, MD, and Suneet P. Chauhan, MD, Hon DSc



	SARS-CoV-2 Test Result			
Maternal Outcome*	Positive	Negative	$P^{\dagger}$	
Death <sup>13,14,16–18,‡</sup>	3/559 (0.5)	8/3,155 (0.3)	.23	
Respiratory support <sup>14,17,18,§</sup>	6/179 (3.4)	0/1,592 (0.0)	≤.001	
ICU admission <sup>13,14,17,18</sup>	8/425 (1.9)	3/2,355 (0.1)	<.001	
Hypertensive disease <sup>13–15,18</sup>	42/510 (8.2)	227/2,354 (9.6)	.39	
Antepartum or postpartum hemorrhage 13,15-17	24/605 (4.0)	138/2,772 (5.0)	.27	
Transfusion of at least one unit PRBC18	0/32 (0.0)	1/129 (0.8)	.87	
Intrapartum fever <sup>14,17,18,  </sup>	12/179 (6.7)	73/1,592 (4.6)	.15	
Postpartum fever <sup>14,17,18,  </sup>	13/179 (7.3)	35/1,592 (2.2)	≤.001	
Maternal postpartum readmission to the hospital 13,14,17,18	4/425 (0.9)	19/2,355 (0.8)	.15	
Maternal sepsis <sup>18</sup>	1/32 (3.1)	0/129 (0.0)	.13	
Maternal venous thromboembolism <sup>18</sup>	0/32 (0.0)	0/129 (0.0)	_	



	SARS-CoV-2 Test Result				
Outcome	Positive (n=728 Fetuses, 432 Neonates)	Negative (n=3,836 Fetuses, 2,400 Neonates)	<b>P</b> *		
Fetal death (20 wk or more) <sup>13–18,†</sup> Neonatal death (from birth to 27 d) <sup>13,14,17,18,‡</sup>	8/728 (1.1) 0/432 (0.0)	44/3,836 (1.1) 5/2,400 (0.2) <sup>§</sup>	.60 .90		

#### **SARS-CoV-2 Test Result**

Outcome	Positive	Negative	<b>P</b> *	
Live birth <sup>13–18,†</sup>	720	3,798	_	
Preterm birth before 37 wk <sup>13–18,‡§</sup>	95/714 (13.3)	446/3,759 (11.9)	.31	
Operative vaginal delivery <sup>13,15,16,18</sup>	34/567 (6.0)	149/2,296 (6.5)	.85	
Nonoperative vaginal delivery <sup>13,15,16,18</sup>	366/567 (64.6)	1,425/2,296 (62.1)	.75	
Vaginal delivery, unspecified 14,17	94/147 (63.9)	1,042/1,463 (71.2)	.30	
Cesarean delivery <sup>13–18</sup>	220/714 (30.8)	1,142/3,759 (30.4)	.28	
Nonreassuring fetal status <sup>17,18</sup>	5/102 (4.9)	27/734 (3.7)	.49	
Labor indications <sup>17,18</sup>	14/102 (13.7)	58/734 (7.9)	.52	
Scheduled repeat <sup>17,18</sup>	9/102 (8.8)	86/734 (11.7)	.57	
Multiple gestation <sup>17,18</sup>	3/102 (2.9)	12/734 (1.6)	.32	
Malpresentation <sup>17,18</sup>	1/102 (1.0)	23/734 (3.1)	.31	
Other <sup>17,18</sup>	9/102 (8.8)	50/734 (6.8)	.87	



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## Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis

John Allotey, <sup>1,2</sup> Elena Stallings, <sup>3,4</sup> Mercedes Bonet, <sup>5</sup> Magnus Yap, <sup>6</sup> Shaunak Chatterjee, <sup>6</sup> Tania Kew, <sup>6</sup> Luke Debenham, <sup>6</sup> Anna Clavé Llavall, <sup>6</sup> Anushka Dixit, <sup>6</sup> Dengyi Zhou, <sup>6</sup> Rishab Balaji, <sup>6</sup> Siang Ing Lee, <sup>1</sup> Xiu Qiu, <sup>7,8,9</sup> Mingyang Yuan, <sup>1,7</sup> Dyuti Coomar, <sup>1</sup> Jameela Sheikh, <sup>6</sup> Heidi Lawson, <sup>6</sup> Kehkashan Ansari, <sup>2</sup> Madelon van Wely, <sup>10</sup> Elizabeth van Leeuwen, <sup>11</sup> Elena Kostova, <sup>10</sup> Heinke Kunst, <sup>12,13</sup> Asma Khalil, <sup>14</sup> Simon Tiberi, <sup>12,13</sup> Vanessa Brizuela, <sup>5</sup> Nathalie Broutet, <sup>5</sup> Edna Kara, <sup>3</sup> Caron Rahn Kim, <sup>5</sup> Anna Thorson, <sup>5</sup> Ramón Escuriet, <sup>15</sup> Olufemi T Oladapo, <sup>5</sup> Lynne Mofenson, <sup>16</sup> Javier Zamora, <sup>2,3,4</sup> Shakila Thangaratinam, <sup>2,18</sup> on behalf of the PregCOV-19 Living Systematic Review Consortium



#### Studies included

(64 676 pregnant and recently pregnant women with covid-19; 569 981 non-pregnant reproductive aged women with covid-19)

Prevalence of covid-19 (73 studies)

Risk factors for covid-19 and complications (108 studies)

Clinical manifestations of covid-19 (82 studies)

Covid-19 related outcomes (92 studies)

Pregnancy related maternal and perinatal outcomes (95 studies)



	recently pregnant	women with coronavirus diseas	Se 2019 (COVIG-19)		
		Women (No with even	t/No in group (%))		
Outcomes	No of studies	Pregnant women with covid-19 Comparison group		Odds ratio (95% CI)	l <sup>2</sup> (%)
Comparison group: non-pregnant wom	en of reproductive	age with covid-19			
All cause mortalitv	8	103/34047 (0.3)	3388/567 075 (0.6)	0.96 (0.79 to 1.18)	0
CU admission	7	616/34035 (1.8)	9568/567 073 (1.7)	2.13 (1.54 to 2.95)	71.2
nvasive ventilation	6	270/34001 (0.8)	3280/567 043 (0.6)	2.59 (2.28 to 2.94)	0
ECMO	2	17/30 446 (0.1)	120/431 490 (0.0)	2.02 (1.22 to 3.34)	0
Oxygen through nasal cannula	2	8/48 (16.7)	49/106 (46.2)	0.21 (0.04 to 1.13)	65.7
ARDS	1	0/17 (0)	0/26 (0)	1.51 (0.03 to 79.93)	NE
Major organ failure	1	0/17 (0)	0/26 (0)	1.51 (0.03 to 79.93)	NE
Comparison group: pregnant women w	ithout covid-19				
Maternal outcomes:					
All cause mortality	8*	8/1195 (0.7)	8/3625 (0.2)	2.85 (1.08 to 7.52)	0
ICU admission	7*	64/1508 (4.2)	4/3482 (0.1)	18.58 (7.53 to 45.82)	0
Preterm birth <37 weeks	18	147/1184 (12.4)	572/7365 (7.8)	1.47 (1.14 to 1.91)	18.6
Caesarean section	21*†	669/1854 (36.1)	4221/11842 (35.6)	1.12 (0.91 to 1.38)	57.6
Perinatal outcomes:					
Stillbirth	9*	9/1039 (0.9)	26/4755 (0.5)	2.84 (1.25 to 6.45)	0
Neonatal death	8*	4/970 (0.4)	5/3316 (0.2)	2.77 (0.92 to 8.37)	0
Admission to neonatal unit	10*	329/1285 (25.6)	519/4588 (11.3)	4.89 (1.87 to 12.81)	96.2
Abnormal Apgar score at 5 minutes	6	13/662 (2.0)	46/2823 (1.6)	1.38 (0.71 to 2.70)	0
Fetal distress	2	11/77 (14.3)	13/263 (4.9)	2.37 (0.77 to 7.31)	0

ICU=intensive care unit; ECMO=extracorporeal membrane oxygenation; ARDS=acute respiratory distress syndrome; NE=not estimable. The denominator is number of pregnancies for all outcomes.

†Includes Gulersen et al 2020<sup>60</sup> with historical comparative cohort (50 women).



Allotey et al, 2020

<sup>\*</sup>Includes UK Obstetric Surveillance System<sup>44</sup> study with historical comparative cohort (694 women).

Table 2 | Maternal characteristics associated with severe coronavirus disease 2019 (covid-19) and all cause death in pregnant and recently pregnant women with a diagnosis of covid-19

and outcomes Age ≥35 years: Severe disease ICU admission Invasive ventilation Maternal death	No of studies  7 7	Total No of women	With outcome	Without outcome	Odds ratio (95% CI)	I2 (%)
Severe disease ICU admission Invasive ventilation Maternal death					J = = = . =	1 (70)
ICU admission Invasive ventilation Maternal death						
Invasive ventilation Maternal death	7	3561	811*	2750*	1.83 (1.27 to 2.63)	43
Maternal death		31710	348*	31362*	2.11 (1.69 to 2.63)	0
	3	718	18*	700*	1.72 (0.60 to 4.97)	17
Marchaile en militar	3	31710	176*	31525*	0.91 (0.22 to 3.72)	93
Multiparity:						
Severe disease	4	278	17/159 (10.7)	12/119 (10.1)	1.11 (0.50 to 2.46)	0
ICU admission	3	815	34/501(6.8)	17/314 (5.4)	1.34 (0.72 to 2.50)	0
Invasive ventilation	1	350	1/216 (0.5)	0/134 (0)	1.87 (0.08 to 46.30)	NE
Body mass index ≥30:						
Severe disease	5	3367	787*	2580*	2.37 (1.83 to 3.07)	0
ICU admission	4	31456	339*	31117*	2.71 (1.10 to 6.63)	63
Invasive ventilation	2	485	12*	4473*	6.61 (1.98 to 22.02)	0
Maternal death	3	31085	113*	30972*	2.27 (1.20 to 4.31)	0
Non-white ethnicity:					, , , , , , , , , , , , , , , , , , ,	
Severe disease	4	2263	375/1638 (22.9)	140/625 (22.4)	0.94 (0.57 to 1.57)	35
ICU admission	4	31543	306/23996 (1.3)	158/7547 (2.1)	1.66 (1.20 to 2.29)	26
Invasive ventilation	1	669	20/134 (14.9)	39/535 (7.3)	2.23 (1.25 to 3.97)	NE
Maternal death	3	31 469	110/24124 (0.5)	36/7345 (0.5)	1.61 (1.05 to 2.47)	0
Any comorbidity:		31407	110/24124 (0.5)	20/1 242 (0.2)	1.01 (1.03 to 2.47)	
Severe disease	3	2634	226/730 (31.0)	382/1904 (20.1)	1.81 (1.49 to 2.20)	0
ICU admission	5	31512	106/6639 (1.6)	226/24873.9)	1.70 (1.34 to 2.15)	0
Invasive ventilation	3	715	7/71 (9.9)	11/644(1.7)	5.26 (1.76 to 15.68)	0
Maternal death	2	30 639	19/6493 (0.3)	33/24146 (0.1)	2.53 (0.78 to 8.17)	50
Chronic hypertension:		30 639	19/6493 (0.3)	33/24 146 (0.1)	2.53 (0.78 to 8.17)	50
, , , , , , , , , , , , , , , , , , , ,		050	25/64/440	430/303/0000	2.00 (4.47 + 2.70)	
Severe disease	2	858	25/61 (41.0)	178/797 (22.3)	2.00 (1.14 to 3.48)	0
ICU admission	5	31 433	15/262 (5.7)	319/31171(1.0)	4.72 (2.37 to 9.41)	13
Invasive ventilation	2	484	5/24 (20.8)	7/460 (1.5)	63.82 (9.69 to 420.45)	0
Maternal death	3	31 011	7/249 (2.8)	81/30762 (0.3)	4.25 (1.82 to 9.95)	0
Pre-existing diabetes:						
Severe disease	3	3333	97/248 (39.1)	696/3085 (22.6)	2.12 (1.62 to 2.78)	0
ICU admission	6	31 473	36/638 (5.6)	306/30835 (1.0)	4.67 (1.94 to 11.22)	38
Invasive ventilation	2	482	2/12 (16.7)	9/470 (1.9)	18.61 (0.26 to 1324.16)	78
Maternal death	2	30723	11/620 (1.8)	41/30 103 (0.1)	14.88 (4.19 to 52.81)	53
Asthma:						
Severe disease	4	3332	39/148 (26.4)	717/3184 (22.5)	1.43 (0.85 to 2.38)	28
ICU admission	1	100	2/9 (22.2)	8/91 (8.8)	2.96 (0.53 to 16.74)	NE
Maternal death	3	889	5/39 (12.8)	63/850 (7.4)	1.68 (0.66 to 4.24)	0
Smoking:						
Severe disease	3	776	5/23 (21.7)	141/753 (18.7)	1.67 (0.64 to 4.40)	0
ICU admission	2	142	1/4 (25.0)	17/138 (12.3)	2.92 (0.35 to 24.23)	0
Maternal death	1	308	0/10 (0)	7/298 (2.3)	1.85 (0.10 to 34.60)	NE
Gestation ≥28 weeks:						
Severe disease	3	289	29/227 (12.8)	16/62 (25.8)	0.56 (0.27 to 1.17)	0
Maternal death	1	721	46/495 (9.3)	23/226 (10.2)	0.90 (0.53 to 1.53)	NE
Gestational diabetes:				, , ,		
Severe disease	4	973	18/88 (20.5)	148/885 (16.7)	1.23 (0.70 to 2.14)	0
ICU admission	2	777	11/81 (13.6)	31/696 (4.5)	3.27 (1.55 to 6.89)	0
Invasive ventilation	1	350	0/32 (0)	0/318 (0)	_	NE
Pre-eclampsia:	-	,,,,	0, 22 (0)	0, 510 (0)		112
Severe disease	4	274	4/16 (25.0)	18/258 (7.0)	4.21 (1.27 to 14.00)	0
ICU admission	1	42	6/6 (100.0)	2/36 (5.6)	179.40 (7.69 to 4186.05)	NE NE



<sup>\*</sup>Includes one or more studies with continuous measurement of risk factor.

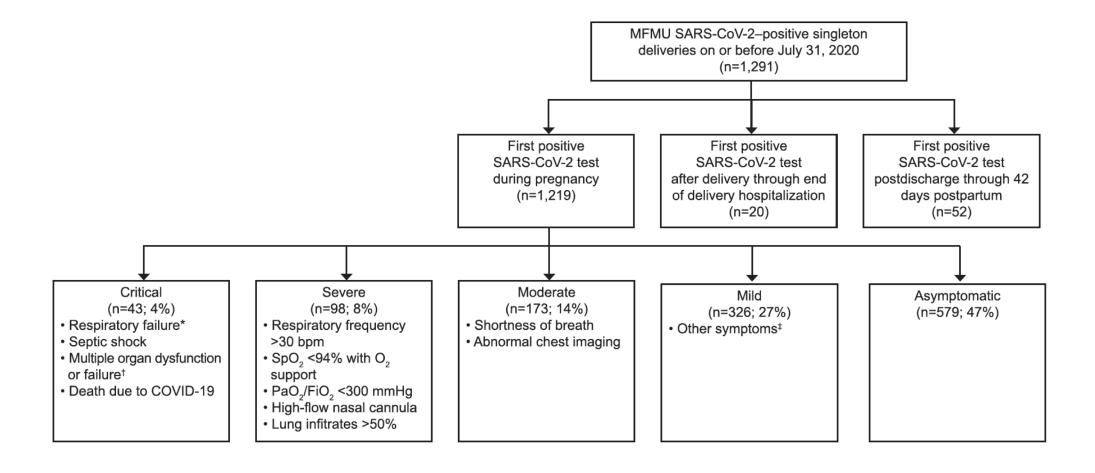
Original Research

## Disease Severity and Perinatal Outcomes of Pregnant Patients With Coronavirus Disease 2019 (COVID-19)

Torri D. Metz, MD, MS, Rebecca G. Clifton, PhD, Brenna L. Hughes, MD, Grecio Sandoval, MA, George R. Saade, MD, William A. Grobman, MD, MBA, Tracy A. Manuck, MD, MS, Menachem Miodovnik, MD, Amber Sowles, BSN, RN, Kelly Clark, BSN, RN, Cynthia Gyamfi-Bannerman, MD, MS, Hector Mendez-Figueroa, MD, Harish M. Sehdev, MD, Dwight J. Rouse, MD, Alan T.N. Tita, MD, PhD, Jennifer Bailit, MD, MPH, Maged M. Costantine, MD, Hyagriv N. Simhan, MD, and George A. Macones, MD, for the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Maternal-Fetal Medicine Units (MFMU) Network\*



#### **MFMU Pregnancy Outcomes**





#### Table 3. Perinatal Outcomes by Coronavirus Disease 2019 (COVID-19) Severity

#### MFMU Pregnancy Outcomes

	Critical–Severe (n=141)		Mode	rate–Mild (r	Asymptomatic			
Outcome		RR (95% CI)	aRR* (95% CI)		RR (95% CI)	aRR* (95% CI)	Asymptomatic (ref) (n=579)	<i>P</i> for Trend <sup>†</sup>
Maternal death	6 (4.3)			0			0	<.001
Venous thromboe- mbolism <sup>‡</sup>	8 (5.7)			1 (0.2)			0	<.001
Maternal ICU admission	50 (35.5)	68.4 (21.7–216)	57.5 (17.8– 186.3)	6 (1.2)	2.32 (0.58– 9.23)	2.07 (0.51– 8.34)	3 (0.5)	<.001
Cesarean birth	84 (59.6)	1.75 (1.47–2.09)	•	169 (33.9)	1.00 (0.84– 1.18)	0.94 (0.81– 1.09)	197 (34.0)	<.001
Postpartum hemorrhage§	21 (14.9)	2.05 (1.26–3.35)	2.02 (1.18–3.45)	45 (9.0)	1.24 (0.83– 1.86)	1.21 (0.78– 1.87)	42 (7.3)	.008
Hypertensive disorders of pregnancy	57 (40.4)	2.15 (1.65–2.79)	1.61 (1.18–2.20)	119 (23.8)	1.27 (1.01– 1.60)	1.24 (0.98– 1.58)	109 (18.8)	<.001
Fetal or neonatal death	6 (4.3)			11 (2.2)			11 (1.9)	.15
Fetal loss at less than 20 wk	3			6			4	
Fetal loss at 20 wk or later	1			4			5	
Neonatal death	2			1			2	
Preterm birth (less than 37 wk)	59 (41.8)	3.51 (2.61–4.72)	3.53 (2.42–5.14)	76 (15.2)	1.28 (0.94– 1.73)	1.36 (0.97– 1.91)	69 (11.9)	<.001
Spontaneous	10 (16.9)			30 (39.5)			35 (50.7)	
Indicated	49 (83.1)			46 (60.5)			34 (49.3)	
Live birth	137			489			570	
SGA (less than the 10th	11 (8.0)	0.81 (0.44–1.51)	1.22 (0.63–2.37)	59 (12.2)	1.23 (0.87– 1.74)	1.48 (1.02– 2.16)	56 (9.9)	.93
percentile) Birth weight (g)	2,841±726.1	$-364 (-479 \text{ to } -249)^{\P}$	$-385 (-510 \text{ to} -261)^{\P}$	3,174±600.1	$-32 (-106 \text{ to } 43)^{\P}$	-61 (-138 to 15)¶	3,205±603.9	<.001
NICU admission#	69 (50.4)	3.15 (2.45–4.06)	,	94 (19.2)	1.20 (0.93– 1.56)	1.24 (0.93– 1.66)	91 (16.0)	<.001

Metz et al, 2021



## PRESENTATION & MANAGEMENT

#### IN PREGNANCY

#### Signs & Symptoms of COVID-19 in Pregnancy

Clinical manifestation	Studies	No of events/ total	Proportion (95% CI)	Proportion (95% CI)	l²(%) (P value)	Range
Clinical manifestations						
Symptoms						
Fever	53	8033/39 429	<del></del>	0.40 (0.31 to 0.49)	99.2 (0.00)	(0.05-0.78)
Cough	53	10 379/39 641	<del></del>	0.41 (0.33 to 0.50)	99.1 (0.00)	(0.03-0.83)
Dyspnoea	42	5408/39014	<b>-</b>	0.21 (0.15 to 0.28)	98.7 (0.00)	(0.00-0.62)
Myalgia	22	5196/34663	<b></b>	0.19 (0.12 to 0.27)	98.4 (0.00)	(0.00-0.67)
Ageusia	10	83/776	<del></del>	0.14 (0.06 to 0.24)	89.6 (0.00)	(0.03-0.55)
Diarrhoea	29	2236/38 206	•••	0.08 (0.06 to 0.10)	93.4 (0.00)	(0.00-0.53)
Laboratory findings						
Raised WCC	13	159/580	<del></del>	0.26 (0.14 to 0.40)	90.9 (0.00)	(0.00-0.65)
Lymphopaenia	27	659/1833	<b></b>	0.33 (0.25 to 0.41)	90.4 (0.00)	(0.00-0.90)
Thrombocytopaenia	13	91/1383	<b>-\( -</b>	0.06 (0.02 to 0.10)	86.3 (0.00)	(0.00-0.35)
Abnormal LFTs	12	99/641	<b></b>	0.13 (0.06 to 0.21)	84.8 (0.00)	(0.00-0.36)
Raised PCT	5	60/261	<b>\</b>	0.21 (0.00 to 0.59)	96.6 (0.00)	(0.00-0.97)
Raised CRP	10	298/637	<del></del>	0.49 (0.36 to 0.62)	89.5 (0.00)	(0.10-0.71)
Radiological findings						
Ground glass appearance	14	338/569	<del></del>	0.69 (0.46 to 0.87)	96.3 (0.00)	(0.09-1.00)
Any CT abnormality	24	694/2120	<b>—</b>	0.64 (0.47 to 0.80)	98.2 (0.00)	(0.02-1.00)



#### **Severity Scale in Pregnancy**

Severity	Criteria
Asymptomatic/pre-symptomatic/ presumptive infection	Positive COVID-19 test result with no symptoms
Mild disease	Flu-like symptoms (e.g. fever, cough, myalgias and anosmia) without dyspnea, SOB or abnormal chest imaging
Moderate disease	Evidence of lower respiratory tract disease with clinical assessment (dyspnea, PNA on imaging, abnormal blood gas, refractory fever of $\geq 102.2F$ not alleviated with acetaminophen), while maintain an $O_2$ saturation of $\geq 93\%$ on room air at sea level
Severe disease	Respiratory rate > 30 bpm, hypoxia with oxygen saturation of $\leq$ 93%, ratio of arterial partial pressure of O <sub>2</sub> /fraction of inspired O <sub>2</sub> <300, or >50% lung involvement on imaging
Critical disease	Multi-organ failure or dysfunction, shock, respiratory failure requiring mechanical ventilation or high-flow nasal cannula



### **Admission Considerations**

#### **OUTPATIENT**

- Asymptomatic
- Mild symptoms and no co-morbidities

#### **INPATIENT**

- Moderate to severe signs and symptoms or O<sub>2</sub> saturation <95% (including exertional)
- With co-morbidities:
  - Uncontrolled hypertension
  - Inadequately controlled diabetes
  - Chronic renal disease
  - Chronic cardiopulmonary disease
  - Immunosuppressed states
- With fever >102.2F despite
   acetaminophen raising concern for
   secondary hemophagocytic
   lymphohistiocytosis or cytokine storm



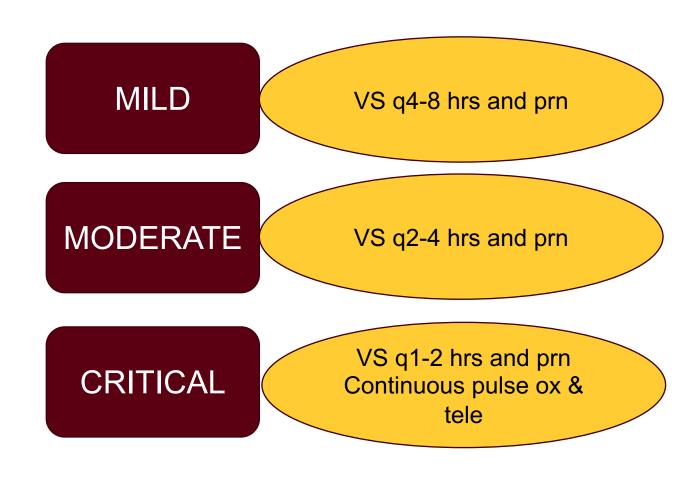
# **Outpatient Management**

- Televisits to check on symptom severity, unless in person care is indicated
- Ideally home vital sign monitoring, especially pulse-oximetry
- Symptoms worsen in second week
- Review calling guidelines



# Inpatient Management

- Based on severity of illness
- Vital signs
  - Temperature
  - Heart rate
  - Respiratory rate
  - Blood pressure
  - Pulse oximetry
- Electronic fetal monitoring/tocometry as indicated





### **SOFA Score**

Maximum SOFA Score	Mortality
0-6	<10%
7-9	15-20%
10-12	40-50%
13-14	50-60%
15	>80%
15-24	>90%

TABLE 1			
Sequential Organ	<b>Failure</b>	<b>Assessment</b>	score

	Score				
Organ system	0	1	2	3	4
Respiratory	_				
PaO <sub>2</sub> /F <sub>1</sub> O <sub>2</sub>	≥400 mm Hg (53.3 kPa)	<400 mm Hg (53.3 kPa)	<300 mm Hg (40 kPa)	<200 mm Hg (26.7 kPa) with respiratory support	<100 mm Hg (13.3 kPa) with respiratory support
Coagulation					
Platelets	$\geq$ 150 $\times$ 10 <sup>3</sup> / $\mu$ L	<150	<100	<50	<20
Hepatic					
Bilirubin	<1.2 mg/dL (20 µmol/L)	1.2—1.9 mg/dL (20—32 μmol/L)	2.0—5.9 mg/dL (33—101 μmol/L)	6.0—11.9 mg/dL (102—204 µmol/L)	>12 mg/dL (204 <i>µ</i> mol/L)
Cardiovascular					
MAP	≥70 mm Hg	<70	Dopamine $<$ 5 $\mu$ g/kg per minute or any dose of dobutamine	Dopamine 5.1—15 $\mu$ g/kg per minute or epinephrine $\leq$ 0.1 $\mu$ g/kg per minute or norepinephrine $\leq$ 0.1 $\mu$ g/kg per minute	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1
Central nervous system: Glasgow Coma Scale score	15	13—14	10—12	6—9	<6
Renal	Serum creatinine <1.2 mg/dL (110 μmol/L)	Serum creatinine 1.2—1.9 mg/dL (110—170 $\mu$ mol/L)	Serum creatinine 2.0—3.4 mg/dL (171—299 $\mu$ mol/L)	Serum creatinine $3.5-4.9 \text{ mg/dL}$ $(300-440 \mu\text{mol/L})$ or urine output $<500 \text{ mL/d}$	Serum creatinine $>$ 5.0 mg/dL (440 $\mu$ mol/L) or urine output $<$ 200 mL/d

 $F_1O_2$ , fraction of inspired oxygen; MAP, mean arterial pressure;  $PaO_2$ , partial pressure of oxygen.



Reproduced, with permission, from Vincent et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med 1996;22:707-10.

Society for Maternal-Fetal Medicine. Sepsis during pregnancy and the puerperium. Am J Obstet Gynecol 2019.

### **ICU Admission Considerations**

#### Figure 1. Algorithm for Intensive Care Unit Admission

Hospitalized obstetric patient with COVID-19

#### Presence of any of the following:

- Inability to maintain oxygen saturation ≥95% (pulse oximetry) with supplemental oxygen/rapidly escalating supplemental oxygen need.
- Hypotension (mean arterial pressure MAP <65) despite appropriate fluid resuscitation (~500-1000 mL bolus of crystalloid fluids, eg, lactated Ringer's solution).
  - For patients with COVID-19 in acute resuscitation, a conservative fluid strategy should be considered to avoid concomitant fluid overload and worsening pulmonary edema.
  - Further, we recommend judicious fluid administration and starting maintenance intravenous fluids in the setting of clear hypovolemia and NPO status.
- Evidence of new end-organ dysfunction (eg, altered mental status, renal insufficiency, hepatic insufficiency, cardiac dysfunction, etc.).



### **Intubation Considerations**

- Individualized
- When oxygen requirements are (to maintain saturation of 95%):
  - Greater than 15 L/min (by nasal cannula or mask)
  - Greater than 40-50 L/min (by high flow nasal cannula)
  - Greater than 60% FiO<sub>2</sub> by Venturi mask
- Inability to protect airway due to altered mental status



### **COVID-19 THERAPIES**

### **IN PREGNANCY**

# **COVID-19 Therapies in Pregnancy**

Medication	COVID-19 Recommendation	Pregnancy Recommendation
Remdesivir	<ul> <li>Hospitalized patients with SpO2 ≤94% or those who require supplemental oxygen</li> <li>Mechanically ventilated</li> <li>ECMO</li> </ul>	Offered to those meeting criteria, no known fetal toxicity
Dexamethasone 6 mg PO or IV daily for up to 10 days	<ul><li>Patients who require supplemental oxygen</li><li>Mechanically ventilated</li></ul>	Offered to those meeting criteria, benefit of mortality outweighs fetal exposure
Convalescent plasma		Not contraindicated
Enoxaparin, heparin		Not contraindicated
Azithromycin, ceftriaxone, cefepime, meropenem, piperacillin-tazobactam, linezolid, vancomycin	Superimposed bacterial pneumonia	Not contraindicated



# **Antibody Therapy**

- Monoclonal antibodies
- Bamlanivimab & etesevimab
- EUA for moderate-severe
   COVID-19 in outpatients at high
   risk for progressing to severe
   COVID and/or hospitalization

- Polyclonal antibodies
- Casirivimab and imdevimab
- EAU for moderate-severe COVID-19 in outpatients

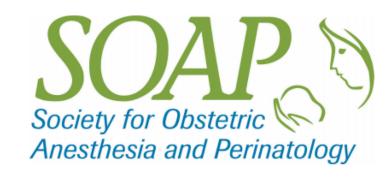


### LABOR & DELIVERY

# CONSIDERATIONS FOR COVID-19

# Rethinking L&D





Society for Maternal-Fetal Medicine and Society for Obstetric and Anesthesia and Perinatology Labor and Delivery COVID-19 Considerations



### **Labor & Delivery Changes for All Patients**

- Universal COVID testing
- Masking
- Room restrictions
- Oxygen for fetal resuscitation
- Prevention of postpartum hemorrhage
- Huddles
- Visitor restrictions
- Infection prevention and special precautions
- Ask all patients every time the call if they have symptoms



### **Labor & Delivery Considerations for COVID-19**

- Levels of Care
- Cohorting
- Rooms
- Dedicated OR
- PPE
- Triage/ER
- Team huddle
- Cesarean planning
- Nitrous oxide
- Water births



# **Laboring Patient**

- Patient to wear a mask during labor and as tolerated at the time of delivery
- Recommended that OB provider be in house
- Supplemental oxygen for maternal indications as needed
- Judicious use of IVF (<75 cc per hour if needed)</li>
- Continuous electronic fetal monitoring, close monitoring of the category II tracing
- Strong recommendation for early epidural to prevent need for GETA
- Internal monitors, artificial rupture of membranes per OB indications
- Operative vaginal delivery as indicated, consider performing in the OR to avoid an emergent transfer to the OR
- Counsel patients on possible delay in emergencies due to need for team to don/doff PPE
- Delayed cord clamping as per usually guidelines



### **Cesarean Patient**

- Early notification of anesthesiology and neonatology staff
- Limit number of staff/providers in the room
- Strong preference for neuraxial anesthesia
- Discuss timing and amount of IVF prior to spinal anesthesia
- Follow all PPE and aerosolizing procedure policies
- STAT cases



### **Obstetric Medications in COVID-19**

Medication	Mild Disease	Moderate-Severe Disease
Antenatal corticosteroids	Assuming no steroids for COVID:  • <34 weeks, give as indicated  • ≥34 weeks, do not give Assuming steroids for COVID:  • See right	<ul> <li>Assuming steroids for COVID:</li> <li>&lt;34 weeks</li> <li>Dexamethasone 6 mg IV q12 x 4 doses then</li> <li>Dexamethasone 6 mg PO/IV daily per protocol for up to 10 days</li> <li>Recommend against switching to another type of steroid</li> <li>≥34 weeks</li> <li>Dexamethasone 6 mg PO/IV daily per protocol for up to 10 days</li> </ul>
Magnesium sulfate	If clinically indicated with close cardiopulmonary monitoring. Monitor renal function and magnesium levels, consider bolus only if mild respiratory distress. Monitor UOP strict I & O Q 2hours	Individualize depending on maternal status, indication for use and gestational age, more neuroprotection at <28 weeks. Discuss with consultants (e.g. ICU)
Tocolysis	Consider as indicated, avoiding indomethacin if possible (prefer nifedipine). Stronger consideration if indication for hospitalization is not COVID-19 and/or patient is <28 weeks	Not recommended
NSAIDS	Standard use, maximize acetaminophen	Maximize acetaminophen, check current guidelines
Enoxaparin/heparin	Prophylactic dosing postpartum and for antepartum hospitalizations	Dosing per ICU guidelines



# **Delivery Timing**

- Patients presenting for indicated delivery who test positive should not be rescheduled due to the risk of a less controlled delivery and/or worsening disease with on-going pregnancy
- In asymptomatic or mildly symptomatic patients at <39 weeks without another indication for delivery consider expectant management until 14d after the positive PCR OR until 7d after the onset of symptoms and 3d after resolution of symptoms
- In an asymptomatic or mildly symptomatic patient at ≥39 weeks delivery can be considered to decreased the risk of worsening maternal status
- In the critically ill patient delivery timing is individualized and requires
  multidisciplinary planning. In the very preterm severely hypoxemic patient all
  options, including pronging and ECMO should be considered.



## Postpartum Considerations

- Be judicious with fluids
- Monitor I&O, especially in the first 24-48 hours postpartum
- Specific duration of hospitalization depends on severity of symptoms and should be individualized
- Review newborn cares
- Ambulatory oxygen saturation (in room) prior to discharge
- Consider discharge with pulse oximeter and blood pressure cuff
- Calling guidelines including anticipatory guidance on natural course of symptoms (worsen in the second week)
- Review self-quarantining at home
- Consider waiting six weeks to initiate estrogen-containing birth control, especially in symptomatic patients
- Follow institution recommendations on use of anticoagulation
- Consider telehealth visit



# **Infant Cares/Feeding**

- Early and close contact between the mother and neonate has many well-established benefits
- The ideal setting for a healthy, term newborn while in the hospital is in the mother's room.
  - Risk of a neonate acquiring SARS-CoV-2 from its mother is low.
  - No difference in risk of SARS-CoV-2 infection whether a neonate is cared for in a separate room or remains in the mother's room.
- Potential risk of transmission via contact with infectious respiratory secretions from the mother, caregiver, or other person with SARS-CoV-2 infection.
  - All caregivers should practice infection prevention and control measures (i.e., wearing a mask, practicing hand hygiene) before and while caring for a neonate.
  - Test babies for SARS-CoV-2
- Patients may feel uncomfortable with potential risk, each should discuss whether she would like the neonate to be in her room or a separate location.
  - Healthcare providers should respect autonomy in the medical decision-making process.



### PERINATAL INFECTION?

# VERTICAL TRANSMISSION?

### **Infant Outcomes**

Table 1. Maternal and Infant Characteristics, by Maternal Severe Acute Respiratory Syndrome Coronavirus 2 Status

	SARS-CoV-2 positive, n (%) or mean (SD), n = 179	SARS-CoV-2 negative, n (%) or mean (SD), n = 84	<i>P</i> value
Gestational age at birth <sup>b</sup>	38.3 ± 2.6	38.2 ± 2.8	.77
Preterm birth <sup>b</sup>	21 (13.9)	9 (16.1)	.69
Birthweight, grams <sup>c</sup>	$3211 \pm 738$	3198 ± 831	.99
Delivered vaginally	106 (59.2)	50 (59.5)	.79
Primiparous mothers	79 (44.1)	32 (38.1)	.36
Female infant <sup>d</sup>	42 (52.5)	17 (39.5)	.17
Birth defect	2 (1.1)	1 (1.2)	.96
Breast milk after birth	148 (83.1)	77 (91.7)	.07
NICU admission	31 (17.3)	13 (15.5)	.71
Abnormal newborn exam	3 (1.7)	1 (1.2)	.76
Infant positive for SARS-CoV-2	2 (1)	0 (0)	.17
Fast or difficulty breathing <sup>d</sup>	11 (13.8)	3 (7.0)	.26
Upper respiratory infection <sup>e</sup>	2 (5.0)	1 (6.3)	.85
Apnea <sup>e</sup>	0 (0)	2 (4.7)	.052
Rooming in with mother <sup>d</sup>	57 (71.3)	34 (79.1)	.35
Breastfeeding at 6–8 weeks <sup>e</sup>	35 (87.5)	14 (87.5)	1.00

### **SET-NET**

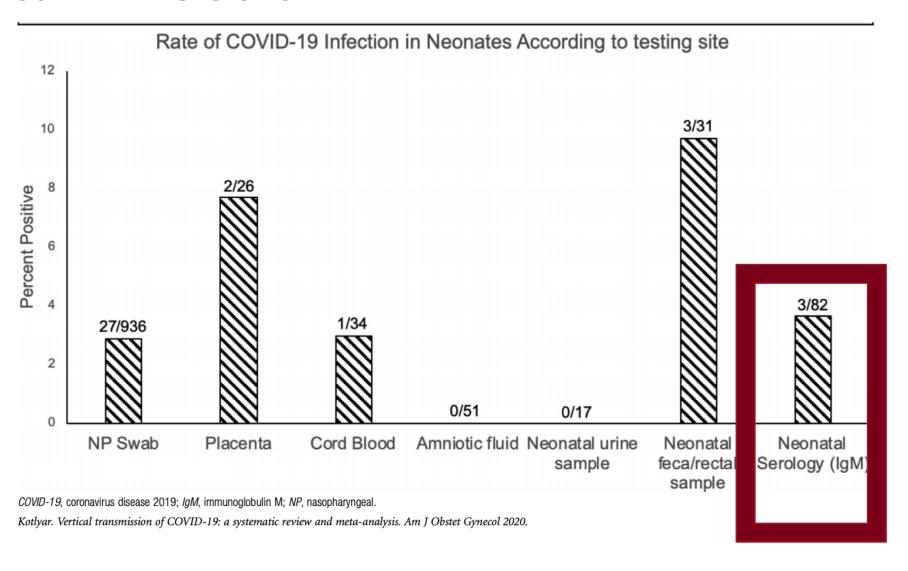
TABLE 3. Characteristics of laboratory-confirmed infection among infants born to pregnant women with laboratory-confirmed SARS-CoV-2 infection — SET-NET, 13\* jurisdictions, March 29-October 14, 2020

	No. of infants (%) [Total no. of infants with available information]			
	Total	Total Not tested or missing data†		RT-PCR negative results
Characteristic	N = 2,869 (100.0)	N = 2,259 (78.7)	N = 16 (0.6)§	N = 594 (20.7)
Maternal symptom status	[1,871]	[1,475]	[13]	[383]
Asymptomatic	231 (12.3)	127 (8.6)	4 (30.8)	100 (26.1)
Symptomatic	1,640 (87.7)	1,348 (91.4)	9 (69.2)	283 (73.9)
Timing of maternal infection¶	[1,851]	[1,440]	[14]	[398]
≤7 days before delivery	740 (40.0)	456 (31.7)	11 (84.6)	273 (68.6)
8–10 days before delivery	77 (4.2)	56 (3.9)	1 (7.7)	20 (5.0)
>10 days before delivery	1,034 (55.9)	928 (64.4)	1 (7.7)	105 (26.4)
Median (IQR) days from mother's first positive test to delivery	17 (2–53)	28 (3-63)	1 (0-4)	2 (0–12)
Maximum days from mother's first positive test to delivery	191	191	12	132
Gestational age at birth	[2,692]	[2,085]	[16]	[591]
Term (≥37 wks)	2,349 (87.3)	1,849 (88.7)	8 (50)	492 (83.2)
Late preterm (34–36 wks)	237 (8.8)	168 (8.1)	3 (18.8)	66 (11.2)
Moderate to very preterm (<34 wks)	106 (3.9)	68 (3.3)	5 (31.3)	33 (5.6)
Infant ICU admission of term infants** n/N (%)	276/2,315 (11.9)	202/1,818 (11.1)	1/8 (12.5)	73/489 (14.9)



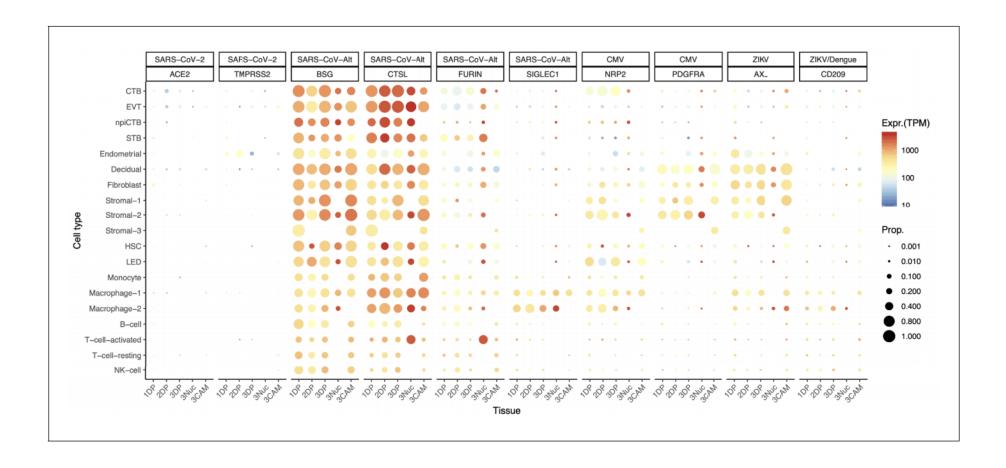
woodworth et al, 2020 58

### **Perinatal Infection**





# **Placental Receptors**





### **Breast Milk**

- Some studies show no evidence of SARS-CoV-2 in breast milk
- Some studies do show SARS-CoV-2 in breast milk
  - Unclear if this is live and therefore transmissible virus
- No evidence thus far of transmission via breast milk
- Multiple on-going studies
- No current contraindication to breastfeeding



### **COVID-19 VACCINES**

### **IN PREGNANCY**



## Society for Maternal-Fetal Medicine (SMFM) Statement: SARS-CoV-2 Vaccination in -Pregnancy

12-1-20

Although preventive measures (universal masking, physical distancing, hand hygiene, and prompt testing with isolation and contact tracing) can significantly decrease SARS-CoV-2 transmission, the consensus among experts is that only an effective COVID-19 vaccine will end the pandemic.<sup>1,2</sup> Vaccination represents the most promising strategy for combatting COVID-19 through primary prevention.

Despite the categorization of pregnancy as a high-risk condition for severe COVID-19, hospitalization, and mortality, <sup>3-6</sup> pregnancy remains an exclusion for participation in vaccine trials. The Society for Maternal-Fetal Medicine (SMFM) and other leading organizations, including the National Academy of Medicine, have consistently advocated for the inclusion of pregnant and lactating women in vaccination trials, particularly when the following criteria are met: (1) pregnancy poses increased susceptibility to or severity of a disease; (2) the best approach to protect the infant is through passive placental antibody transfer, which provides the most efficient and direct protection to the newborn before an infant can be vaccinated, and (3) there is an active outbreak.<sup>7-9</sup> Ultimately, the existing practice of "protection by exclusion" is harmful and has been characterized as clinical experimentation on pregnant women, as vaccines are distributed and adminstered without the safeguards of research protocols in place.<sup>10,11</sup> Furthermore, there is no biological plausibility for the exclusion of lactating women from these trials.



https://s3.amazonaws.com/cdn.smfm.org/media/2591/SMFM Vaccine Statement 12-1-20 (final).pdf - accessed 3/17/2021

# Vaccinating Pregnant and Lactating Patients Against COVID-19



- ACOG recommends that COVID-19 vaccines should not be withheld from pregnant individuals.
- COVID-19 vaccines should be offered to lactating individuals similar to nonlactating individuals.
- While a conversation with a clinician may be helpful, it should not be required prior to vaccination, as this may cause unnecessary barriers to access.
- Vaccines currently available under EUA have not been tested in pregnant women. Therefore, limited safety data specific to use in pregnancy is

- Individuals considering a COVID-19 vaccine should have access to available
  information about the safety and efficacy of the vaccine, including information
  about data that are not available. A conversation between the patient and their
  clinical team may assist with decisions regarding the use of vaccines
  approved under EUA for the prevention of COVID-19 by pregnant patients.
   Important considerations include:
  - · the level of activity of the virus in the community
  - the potential efficacy of the vaccine
  - the risk and potential severity of maternal disease, including the effects of disease on the fetus and newborn
  - the safety of the vaccine for the pregnant patient and the fetus.



https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/12/vaccinating-pregnant-and-lactating-patients-against-covid-19 - accessed 3/17/2021

# J&J Vaccine in Pregnancy

 Women under age 50 including pregnant individuals can receive any FDAauthorized COVID-19 vaccine available to them. However, they should be aware of the rare risk of TTS (thrombosis with thrombocytopenia syndrome) after receipt of the Janssen COVID-19 vaccine and that other FDA-authorized COVID-19 vaccines are available (i.e., mRNA vaccines).

Medical details about the cases that were presented at the ACIP meeting are as follows:

- 3 had obesity
- 1 had hypothyroidism
- 1 had asthma
- 1 had hypertension
- 1 was currently taking estrogen/progesterone

None had preexisting coagulation disorders. None were pregnant or postpartum. One of the patients died; three remain hospitalized; and two have been discharged to home.

https://www.acog.org/news/news-releases/2021/04/acog-statement-on-johnson-johnson-covid-19-vaccine - accessed 4/29/2021



https://s3.amazonaws.com/cdn.smfm.org/media/2865/JJ Pause 04-19-21 UPDATE.pdf - accessed 4/19/2021

# Vaccine Safety in Pregnancy

The NEW ENGLAND JOURNAL of MEDICINE

#### ORIGINAL ARTICLE

### Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons

Tom T. Shimabukuro, M.D., Shin Y. Kim, M.P.H., Tanya R. Myers, Ph.D., Pedro L. Moro, M.D., Titilope Oduyebo, M.D., Lakshmi Panagiotakopoulos, M.D., Paige L. Marquez, M.S.P.H., Christine K. Olson, M.D., Ruiling Liu, Ph.D., Karen T. Chang, Ph.D., Sascha R. Ellington, Ph.D., Veronica K. Burkel, M.P.H., Ashley N. Smoots, M.P.H., Caitlin J. Green, M.P.H., Charles Licata, Ph.D., Bicheng C. Zhang, M.S., Meghna Alimchandani, M.D., Adamma Mba-Jonas, M.D., Stacey W. Martin, M.S., Julianne M. Gee, M.P.H., and Dana M. Meaney-Delman, M.D., for the CDC v-safe COVID-19 Pregnancy Registry Team\*



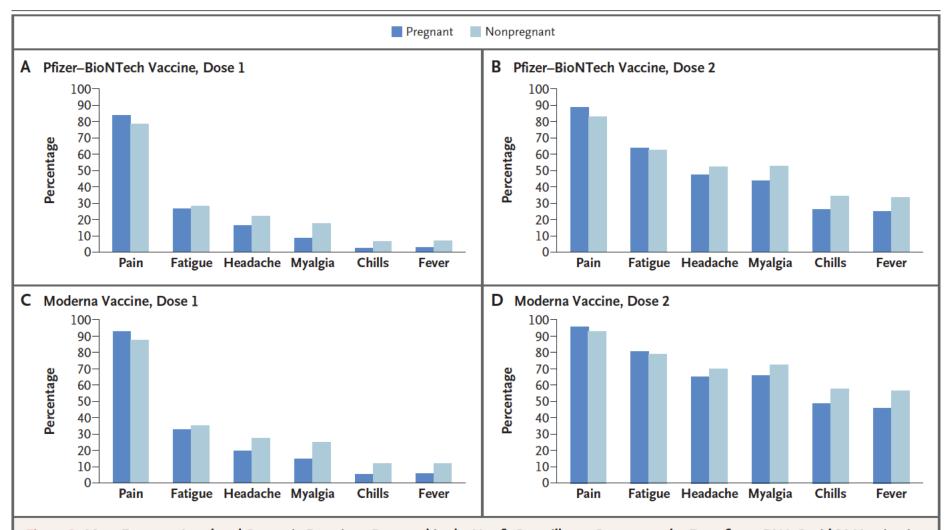


Figure 1. Most Frequent Local and Systemic Reactions Reported in the V-safe Surveillance System on the Day after mRNA Covid-19 Vaccination. Shown are solicited reactions in pregnant persons and nonpregnant women 16 to 54 years of age who received a messenger RNA (mRNA) coronavirus disease 2019 (Covid-19) vaccine — BNT162b2 (Pfizer–BioNTech) or mRNA-1273 (Moderna) — from December 14, 2020, to February 28, 2021. The percentage of respondents was calculated among those who completed a day 1 survey, with the top events shown of injection-site pain (pain), fatigue or tiredness (fatigue), headache, muscle or body aches (myalgia), chills, and fever or felt feverish (fever).

Table 4. Pregnancy Loss and Neonatal Outcomes in Published Studies and V-safe Pregnancy Registry Participants.					
Participant-Reported Outcome	Published Incidence*	V-safe Pregnancy Registry†			
	%	no./total no. (%)			
Pregnancy loss among participants with a completed pregnancy					
Spontaneous abortion: <20 wk <sup>15-17</sup>	10–26	104/827 (12.6)‡			
Stillbirth: ≥ 20 wk <sup>18-20</sup>	<1	1/725 (0.1)§			
Neonatal outcome among live-born infants					
Preterm birth: <37 wk <sup>21,22</sup>	8–15	60/636 (9.4)¶			
Small size for gestational age <sup>23,24</sup>	3.5	23/724 (3.2)			
Congenital anomalies <sup>25</sup> **	3	16/724 (2.2)			
Neonatal death <sup>26</sup> ††	<1	0/724			

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/vsafepregnancyregistry.html



# **Immunity**

# COVID-19 vaccine response in pregnant and lactating women: a cohort study

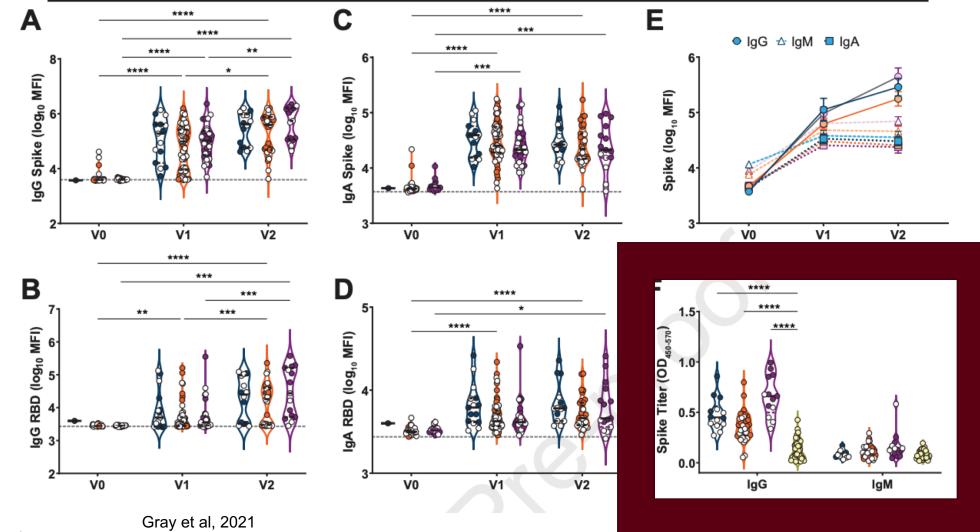
Kathryn J Gray <sup>1</sup>, Evan A Bordt <sup>2</sup>, Caroline Atyeo <sup>3</sup>, Elizabeth Deriso <sup>4</sup>, Babatunde Akinwunmi <sup>1</sup>, Nicola Young <sup>5</sup>, Aranxta Medina Baez <sup>5</sup>, Lydia L Shook <sup>6</sup>, Dana Cvrk <sup>5</sup>, Kaitlyn James <sup>5</sup>, Rose De Guzman <sup>5</sup>, Sara Brigida <sup>5</sup>, Khady Diouf <sup>1</sup>, Ilona Goldfarb <sup>5</sup>, Lisa M Bebell <sup>7</sup>, Lael M Yonker <sup>8</sup>, Alessio Fasano <sup>8</sup>, S Alireza Rabi <sup>9</sup>, Michal A Elovitz <sup>10</sup>, Galit Alter <sup>11</sup>, Andrea G Edlow <sup>12</sup>



## **Immunity**

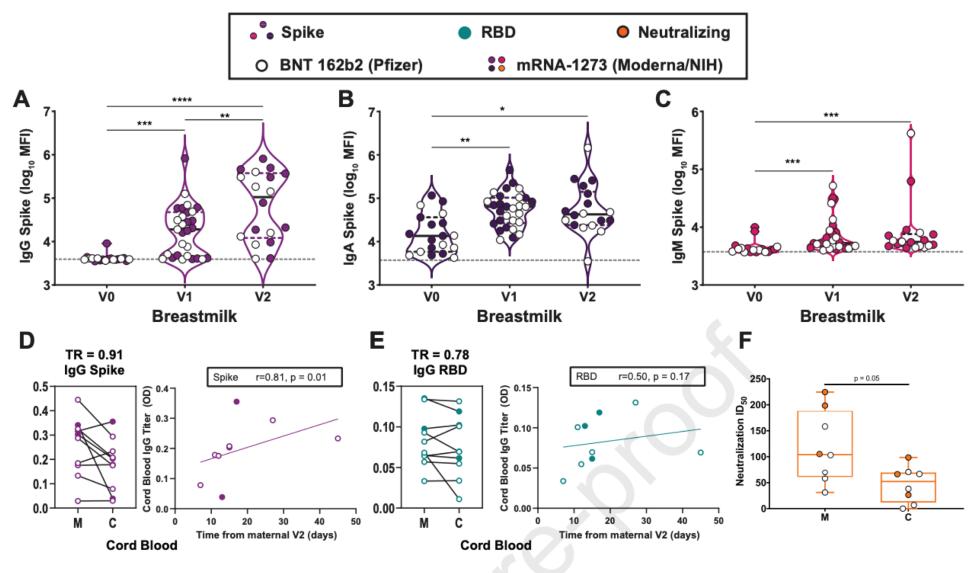
- Non-Pregnant
- Pregnant
- Lactating
- Natural Infection Pregnant

- O BNT 162b2 (Pfizer)
- mRNA-1273 (Moderna/NIH)



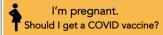


# **Immunity**





# https://foamcast.org/covidvacpregnancy/



For most people, getting the COVID vaccine as soon as possible is the safest choice.

Although pregnant people were not included in the studies, data is emerging on people who are pregnant and got a vaccine.

The information below will help you make an informed choice about whether to get a COVID vaccine while you are pregnant or trying to get pregnant.

#### Your options:

Get a COVID vaccine as soon as it is available



#### Understanding COVID in pregnancy:

#### COVID is dangerous. It is more dangerous in pregnancy.

- Pregnant COVID patients are 5 times more likely to end up in the intensive care unit than non-pregnant COVID patients.1
- Preterm birth may be more common.<sup>2</sup>
- Pregnant people are more likely to die of COVID than other people with COVID who are the same age.3,4

HEALTH



#### What are the benefits of getting the COVID Vaccine?

#### The COVID vaccines prevent moderate and severe COVID.

Getting a vaccine will prevent you from aetting very sick with COVID.

#### The COVID vaccines may reduce spread.

The vaccine may help keep you from giving COVID to people around you. As COVID infections go up in our communities, your risk of getting - and giving - COVID goes up too.

These vaccines have no live virus<sup>5</sup> and do NOT contain ingredients that are known to be harmful to pregnant people or to the

Many vaccines are routinely given in pregnancy and are safe (for example: tetanus, diphtheria, and flu).

#### What are the risks and unknowns of getting the COVID Vaccine?

- · Each vaccine was tested in over 20,000 people, and there were no serious side
- We do not know if the vaccines work as well in pregnancy as they do in nonpregnant people.



- We know that in studies done by Moderna and Johnson & Johnson, there were no adverse effects on female reproduction or fetal development. 6,7
- · So far, the mRNA vaccines have been given to over 30,000 pregnant people in the US who registered with the CDC.8
- · Of those pregnancies, 275 have been reported as complete. The number of miscarriages in people who got the vaccine (15%) was about the same as we see in pregnant people who have NOT gotten a COVID vaccine (10-25 %).8
- · Birth defects were seen in the same number of people as in the general population who have NOT gotten a COVID vaccine (3-4%). 8

#### People getting the vaccine will probably have some side effects.

This is a normal response by the immune system. These effects are more common after the second dose and in the mRNA vaccines but were not more common in pregnancy. The most common side effects are:6,7,8

- arm pain (~84%)
   muscle pain (~38%) fatigue (~62%)
  - chills (~32%)
- fever (~14%) joint pain (~24%)

Of every 100-500 people who get a vaccine, 1 will get a high fever (over 102°F). A persistent high fever during the first trimester might increase the risk of fetal abnormalities or miscarriage.

 The CDC recommends using acetaminophen during pregnancy if you have a high fever. Another option is to delay your COVID vaccine until after the first trimester.

#### What do the experts recommend?

The CDC recommends the COVID vaccines for adults.9 However, because there are no studies of pregnant people yet, there are no clear recommendations for pregnant people. This is standard for a new drug and early research of the vaccines in pregnancy is reassuring.

The Society for Maternal-Fetal Medicine strongly recommends that pregnant individuals have access to COVID vaccines, and that each person talk to their doctor or midwife about their own personal choice.<sup>10</sup>

The American College of Obstetricians and Gynecologists recommends that the COVID vaccine should not be withheld from pregnant individuals.11

The World Health Organization states the mRNA vaccine can be given to people who breastfeeding without stopping breastfeeding after vaccination. They recommend that pregnant people at high risk of exposure to COVID or with medical problems may be vaccinated in consultation with their health care provider. 12

#### What else should I think about to help me decide?

Make sure you understand as much as you can about COVID and about the

Ask a trusted source, like your midwife or doctor.

f you want more information on specific vaccines and references, scan the QR code

#### Think about your own personal risk.

Look at the columns below and think about your risk of getting COVID (left) and think about your safety - are you able to stay safe (right)?

and...

If you are not at

You always wear a

☐ You and the people

you live with can

pregnancy

socially distance from

others for the whole

■ Your community does

NOT have high or

increasing COVID

☐ You think the vaccine

itself will make you

very nervous (you are

the unknown risks than

about getting COVID)

more worried about

You have had a severe

... it might make

allergic reaction to a

sense for you to wait

for more information.

higher risk for COVID

#### The risks of getting sick from COVID are

- You have contact with people outside your
- ☐ You are 35 years old or
- You are overweight
- medical problems like diabetes, high blood pressure, or heart disease
- You are a smoker
- You are a racial or ethnic minority, or your community has a high rate of COVID infections
- You are a healthcare worker1
- it probably makes sense to get the vaccine.

University of Massachusetts UMASS. Medical School

Updated March 17, 2021

#### Summary

- COVID seems to cause more harm in pregnant people than in people of the same age who are not pregnant.
- The risks of getting an mRNA COVID vaccine during pregnancy are thought to be small but are not totally known.
- 3. You should consider your own personal risk of getting COVID. If your personal risk is high, or there are many cases of COVID in your community, it probably makes sense for you to get a vaccine while pregnant.
- 4. Whether to get a COVID vaccine during pregnancy is your choice

Do you have more questions? Call your doctor or midwife to talk about your decision

Was this decision aid helpful? Please take a moment to give us feedback about this decision aid at https://is.gd/COVIDVac

#### Tell the CDC about your experience with the vaccine

If you get the vaccine, you will get a "V-safe information sheet." Consider registering so we can better counsel people in the future.

Intended Use: This decision aid is intended for use by pregnant people who are considering getting a COVID-19 vaccine. It was created by the Shared Decision-Making: COVID Vaccination in Pregnancy working group at the University of Massachusetts Medical School - Baystate. This group consists of experts in the fields of OB/GYN, Maternal-Fetal Medicine, Shared Decision-Making and risk communication, Emergency Medicine, and COVID-19

This decision aid can be reproduced and distributed without

Translations, references, more info available at: http://foamcast.org/COVIDvacPregnancy

https://foamcast.org/wp-content/uploads/2021/03/English-Decision-Aid.pdf - accessed 3/17/21

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FAIRVIEW

A collaboration among the University of Minnesota,
University of Minnesota Physicians and Fairview Health Services

# **Questions?**

Thank you!









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