

# COVID in Pregnancy

## Pearls and Perils of Management

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# Disclosures

- I have no financial relationships to disclose



# Objectives

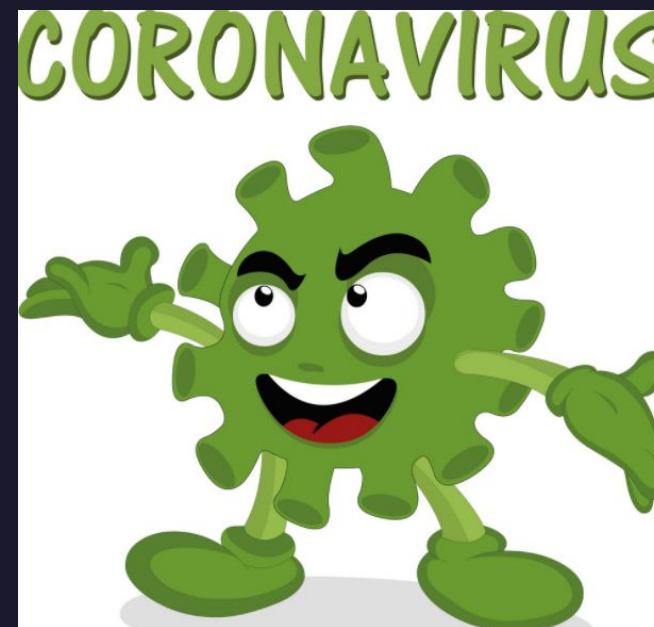
- At the end of this discussion, the participant will be able
  - Describe the viral etiology of SAR2-COVID 19
  - Describe the pathophysiology of the SAR2-COVID
  - Describe the disparities and racial inequities that surround COVID-19
  - Describe the impact of COVID-19 in pregnancy
  - Implement evidenced based guidelines for treatment(including vaccine recommendations)and use of telehealth
  - Address the impact of COVID-19 on offspring





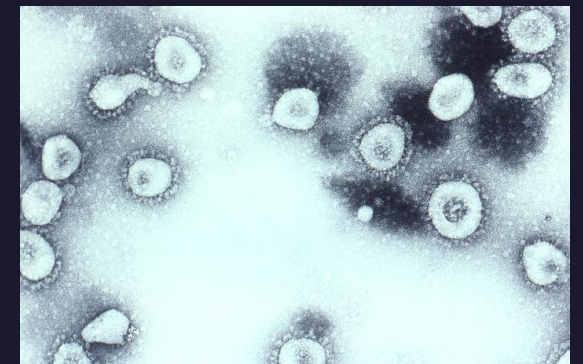
# COVID-19: The Virus

Virology and Pathophysiology



- Coronavirus is group of RNA viruses

- Cause disease in birds and mammals
- One of the largest RNA virus
- Have spikes that project from their surface giving the appearance of a corona



# Subtypes of Coronavirus

- Alpha, Beta, Delta, Gamma
- Most cause mild respiratory symptoms; the common cold
- The most virulent are beta viruses
  - **MERS-CoV**, a beta virus that causes Middle East respiratory syndrome (MERS)-**2002**
  - **SARS-CoV**, a beta virus that causes severe acute respiratory syndrome (SARS)-**2012**
  - **SARS-CoV-2**, which causes COVID-19-**2019**

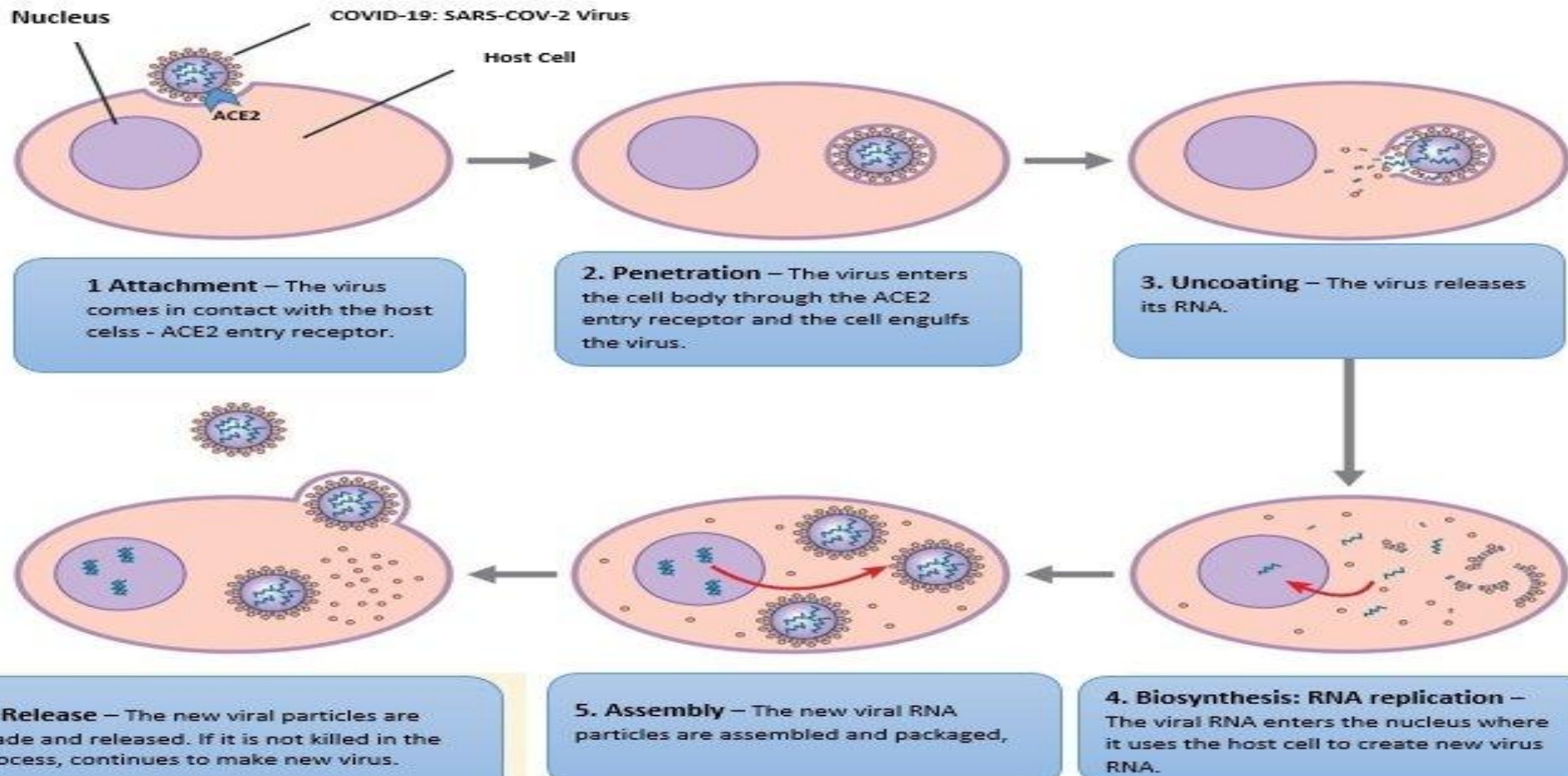


# Timeline for COVID-19

- Nov 19, 2019
  - First case noted in Wuhan
  - Postulated to be from the market
- Dec 1, 2019
  - More cases are seen
- Jan 9, 2020
  - Announced by the WHO (59 cases)
- Jan 20, 2020
  - CDC announces airport screenings
- Jan 21, 2020
  - First US case
- Jan 31, 2020
  - WHO declares global health emergency
- February 3, 2020
  - US declares a global health emergency
  - Issues travel restrictions



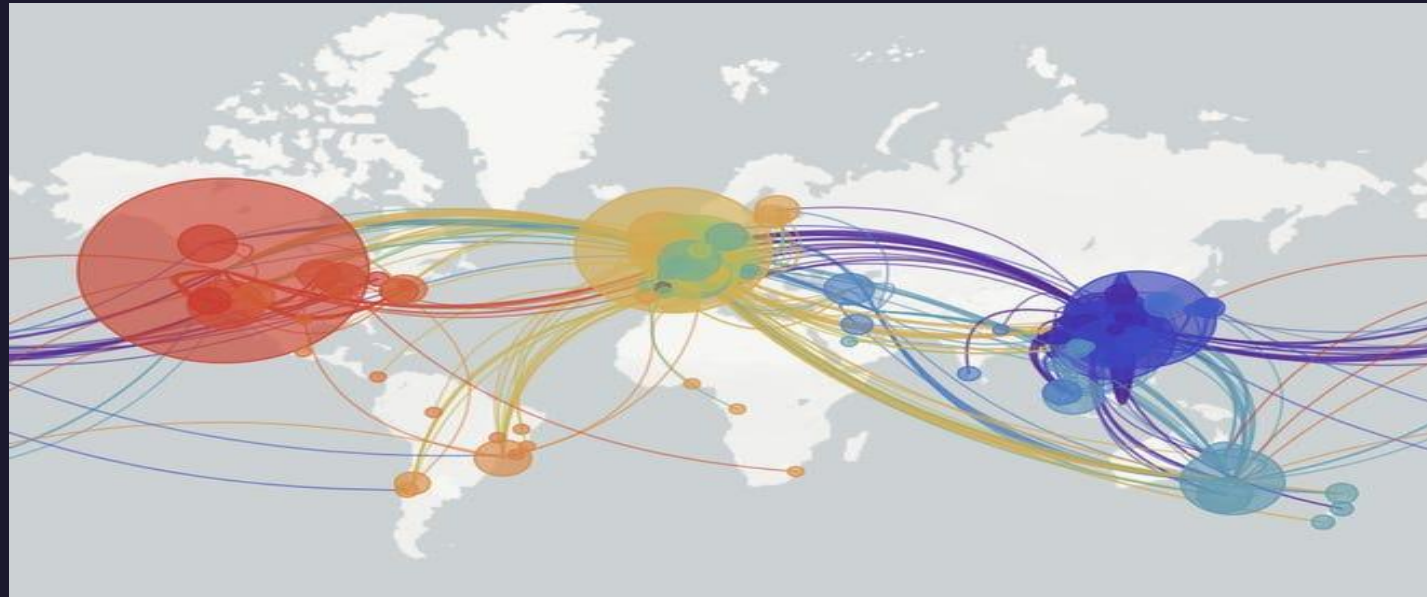
# Lifecycle of the coronavirus



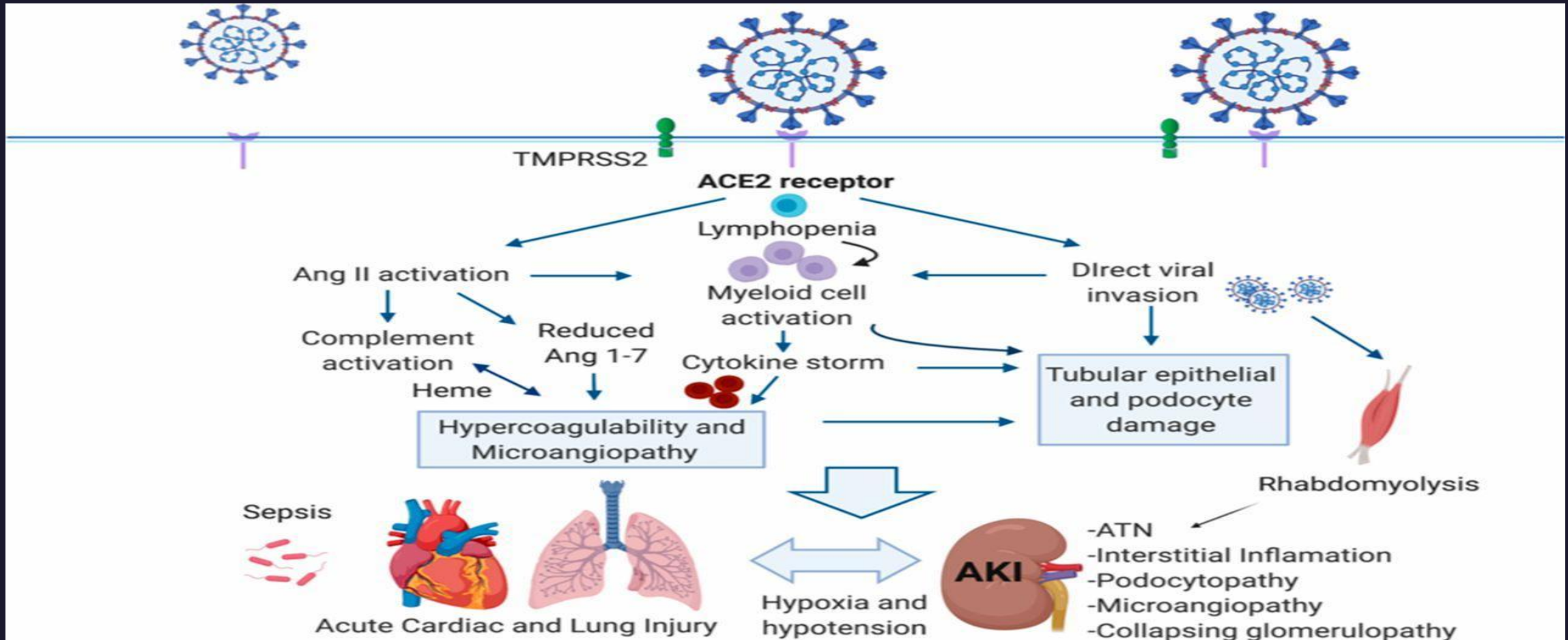


# COVID-19 Subtypes

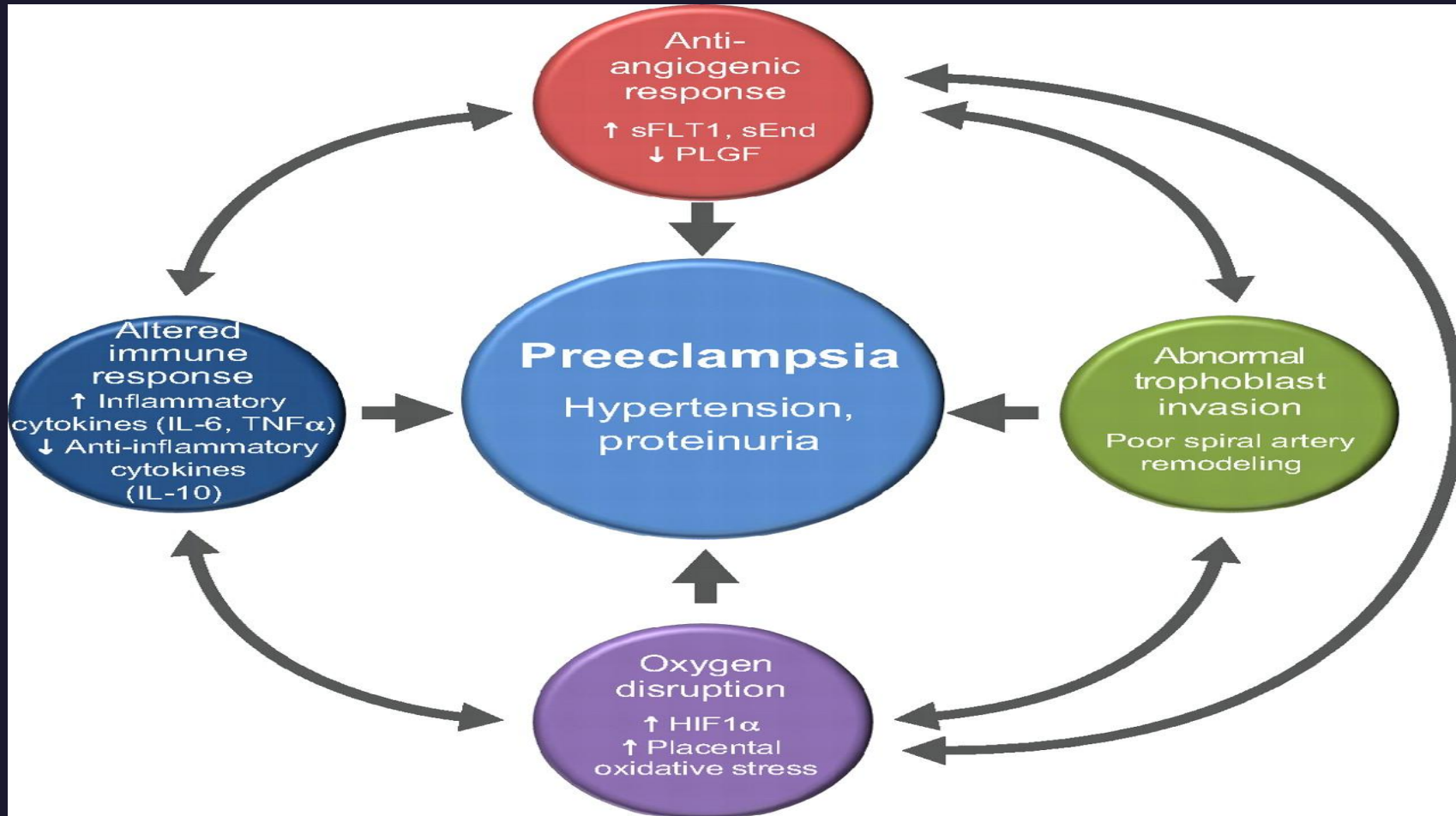
- Up to 8-10 different strains
- May explain differences in outbreaks and symptoms



# Pathophysiology of COVID-19



# Pathophysiology of Preeclampsia



# Symptoms of infection with COVID-19

occur 2-14 days post exposure

- Fever or chills
- Cough
- Shortness of breath or difficulty breathing
- Fatigue
- Muscle or body aches
- Diarrhea
- Headache
- New loss of taste or smell
- Sore throat
- Congestion or runny nose
- Nausea or vomiting



# Long term symptoms of COVID-19

- Common

- Fatigue
- Shortness of breath
- Cough
- Joint pain
- Chest pain

- Less Common

- Difficulty with thinking and concentration
- Depression
- Muscle pain
- Headache
- Intermittent fever
- Fast-beating or pounding heart

CDC 2020

# Severe long term complications

- Cardiovascular

- Cardiomyopathy

- Respiratory

- Chronic Lung Injury

- Renal

- Chronic renal disease

- Dermatologic

- Skin Changes/rash

- Hair loss

- Neurological

- Stroke

CDC, 2020



# Racial Inequities in COVID-19





# Racial Disparities in COVID outcomes

Rate ratios compared to White, Non-Hispanic persons	American Indian or Alaska Native, Non-Hispanic persons	Asian, Non-Hispanic persons	Black or African American, Non-Hispanic persons	Hispanic or Latino persons
Cases <sup>1</sup>	1.8x	0.6x	1.4x	1.7x
Hospitalization <sup>2</sup>	4.0x	1.2x	3.7x	4.1x
Death <sup>3</sup>	2.6x	1.1x	2.8x	2.8x

CDC, 2020

# Hospitalizations and Death as related to age

	Hospitalization <sup>1</sup>	Death <sup>2</sup>
0-4 years	4x lower	9x lower
5-17 years	9x lower	16x lower
18-29 years	Comparison Group	Comparison Group
30-39 years	2x higher	4x higher
40-49 years	3x higher	10x higher
50-64 years	4x higher	30x higher
65-74 years	5x higher	90x higher
75-84 years	8x higher	220x higher
85+ years	13x higher	630x higher

# Why are people of color more likely to be affected?

- Front line exposures
  - Clerks
  - Janitors
  - Public transportation
  - Healthcare
- Chronic Illness
  - Diabetes
  - High blood pressure
  - Heart Disease
- Obesity
- Poor diet
- Genetics

# Social Determinants of Health

## Unequal Care



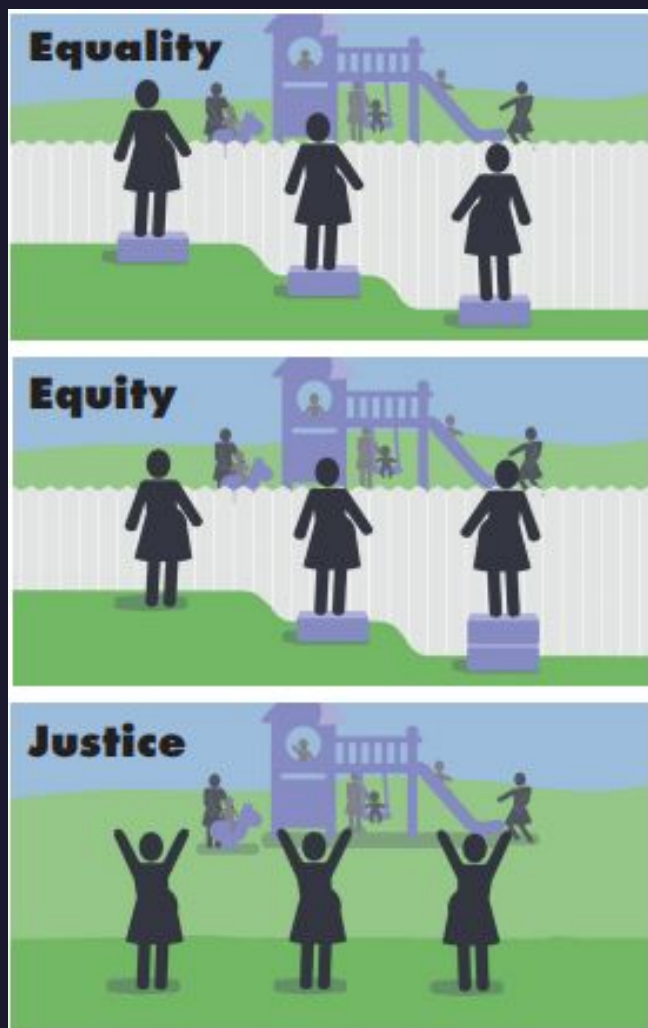
### Explicit bias

- Expressed directly
- Aware of bias
- Operates consciously
- Example -- "I like whites more than Latinos."

### Implicit bias

- Expressed indirectly
- Unaware of bias
- Operates sub-consciously
- Example -- sitting further away from a Latino than a white individual.





## Provide Equitable Care

- ☐ Recognize racism is at the root of inequities
- ☐ Screen for social determinants of health
- ☐ Ask about:
  - ability to safely social distance
  - availability of cleaning supplies
  - access to internet/data for virtual visits
  - Screen more frequently for IPV and safety
- ☐ Identify key community resources:
  -  Food banks or pantries
  -  Housing assistance
  -  Infection mitigation supplies (e.g. masks, sanitizer)
  -  Intimate partner violence services
- ☐ Provide information in the language that your patient speaks, reads, or understands.
- ☐ Increase capacity for care for vulnerable populations (i.e. increase provider, nursing, social service resources)

# **Meharry leader says medical college 'somehow' didn't get first wave of COVID-19 vaccines**

- Despite the fact they staffed ALL of the testing sites in Nashville
- Despite the fact, that their president, who is an international expert in infectious disease who sits of the FDA Board for emergency release and served as a member and resource for the Metro Task Force
- Despite the fact, the hospital is Nashville's only safety net hospital



# Dr Susan Moore: Dies of COVID-19

Had to ask for appropriate treatment

Was denied pain medications

Was told her chest X-ray was negative

Went to another hospital, but died after admission

Leaves son and 2 parents with dementia

Hospital states” they will have diversity training”

USA Today, Dec 2020







Help!!

My patient has COVID



# Our Case

32 year old G1 presents with complaints of SOB, cough and headache. She reports that her partner is an essential worker and has been going to work every day

On exam, her temperature is 102 F and she is breathing 38 times per minute. BP is 145/106. HR is 120 bpm

What are the steps in management and treatment of this patient???

# Maternal Presentation of COVID

- Cough
- Fever
- Shortness of breath
- Preeclampsia-like syndrome
  - May be associated with hyper-inflammatory state
- Postpartum Hemorrhage

# COVID Testing

- COVID PCR

- Takes at least 24 hours for results
- 90-95% detection rate

- COVID Rapid Antigen testing

- 15 minutes
- About 70-75% accurate

- Antibody testing  
~80%

# Workup for COVID

- Chest x-ray
  - Ground glass appearance in lower lung fields
- CBC, Comprehensive metabolic panel
  - Leukopenia
  - Thrombocytopenia
  - Elevated liver function test
- D-dimer
  - Elevated, greater than 1000
- BNP
  - May be elevated in myocardial dysfunction
- Ferritin
  - Elevated in severe cases
- C-reactive protein
  - May be elevated, difficult to interpret in pregnancy
- Procalcitonin?
  - Elevated ; unchanged in pregnancy



# Physiologic Changes in Pregnancy



# Physiologic Changes

- **Hyperventilation**

- Begins in the 1st trimester
- Increases by 48% at term
  - Stimulated by progesterone
- Due to an increase in minute ventilation which increases 20% to 40% above baseline





# Physiologic Changes

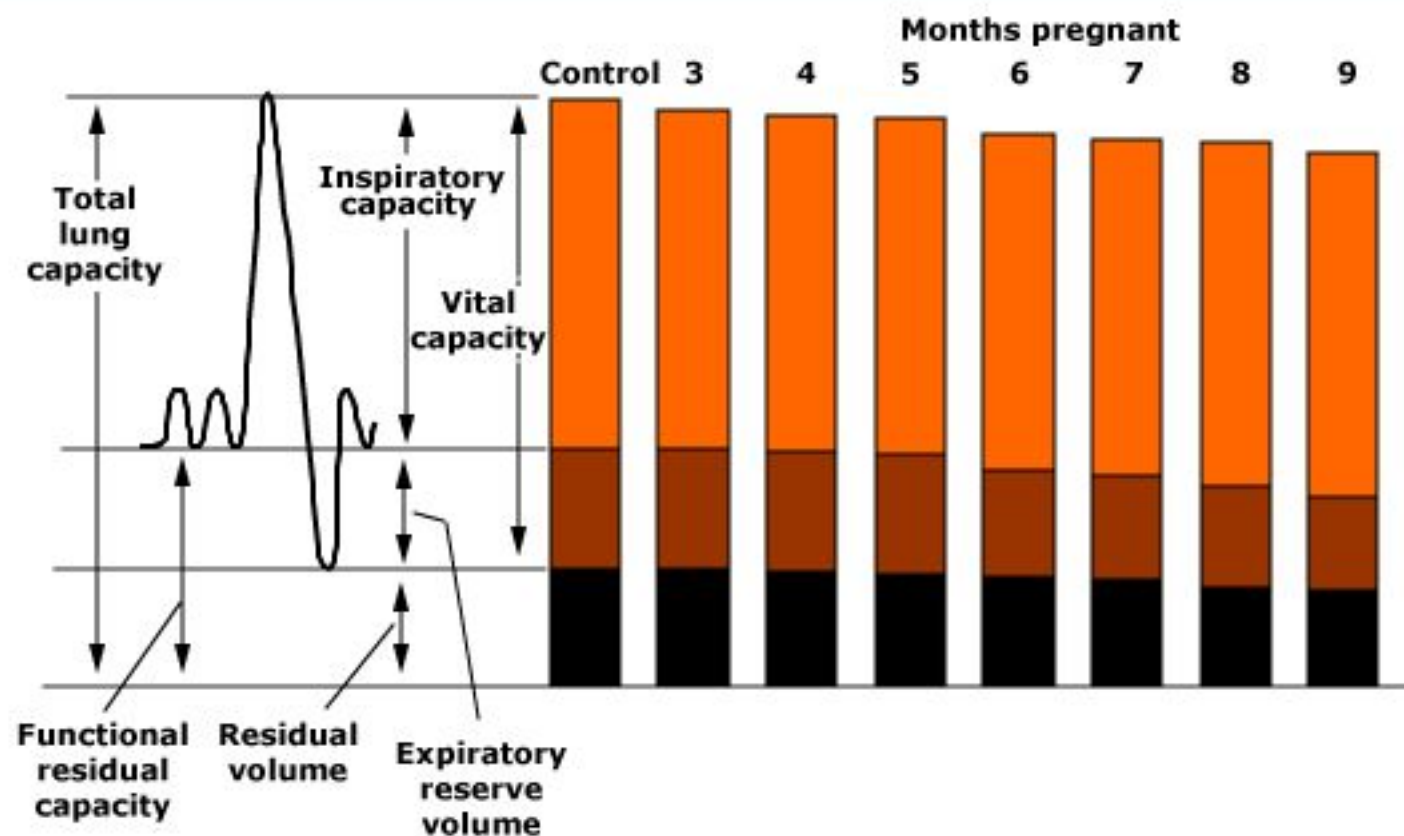
- Oxygen consumption increased by 20%
- FEV<sub>1</sub> remains unchanged
- Tidal volume is increased
- Decreased in functional residual capacity by 18%
- Pulmonary vascular resistance decreases by 34%
- Colloid osmotic pressure decreases by 14%

# Physiologic Changes

- Respiratory Alkalosis
  - Compensated renal acidosis, pH remains unchanged
  - Resting arterial CO<sub>2</sub> tension about 30 mmHg or less
  - Resting arterial O<sub>2</sub> tension about 105 mm Hg
  - Shift of oxygen dissociation curve to the right



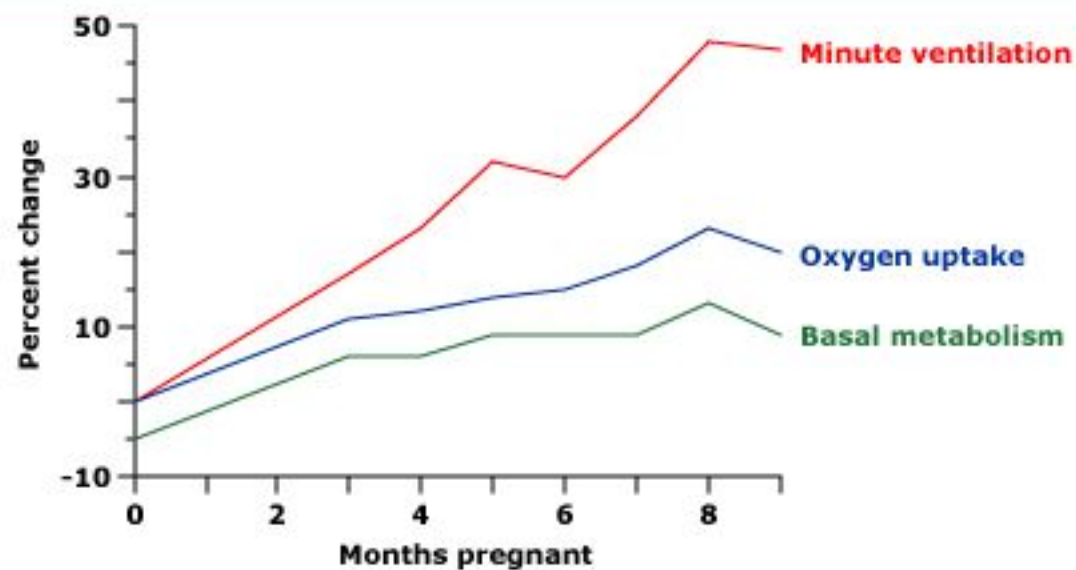
## Changes in pulmonary function tests during pregnancy



Serial measurements of lung volume compartments during pregnancy. Functional residual capacity decreases approximately 20 percent during the latter half of pregnancy, due to a decrease in both expiratory reserve volume and residual volume.

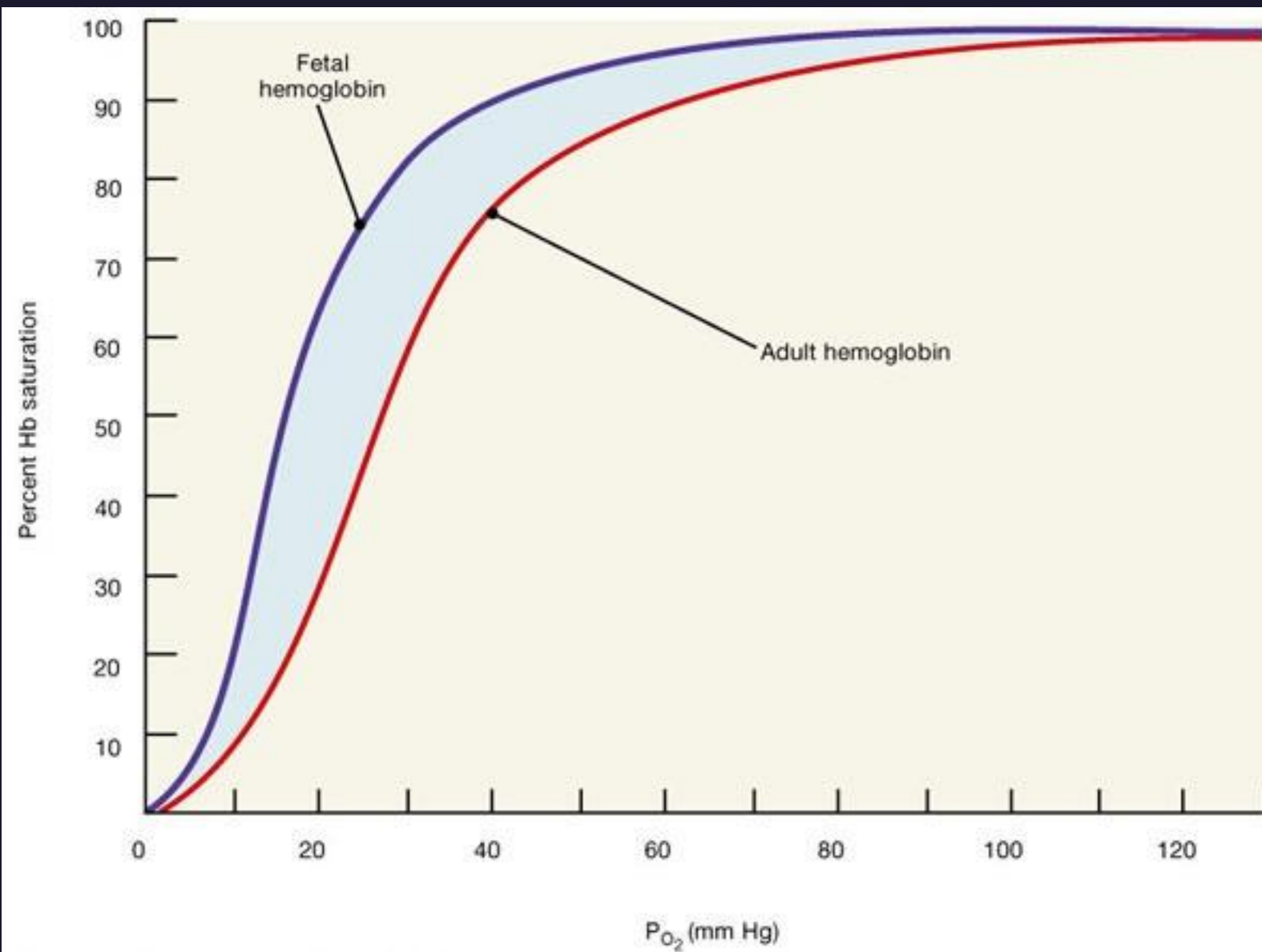
*Redrawn from Prowse, CM, Gaensler, EA, Anesthesiology 1965; 26:381.*

## Changes in ventilation during pregnancy



Time course of percent increases in minute ventilation, oxygen uptake, and basal metabolism during pregnancy.

*Redrawn from Prowse, CM, Gaensler, EA, Anesthesiology 1965; 26:381.*



# When to Admit the Pregnant Patient with COVID

Patient can not maintain oxygen saturation of at least 95%

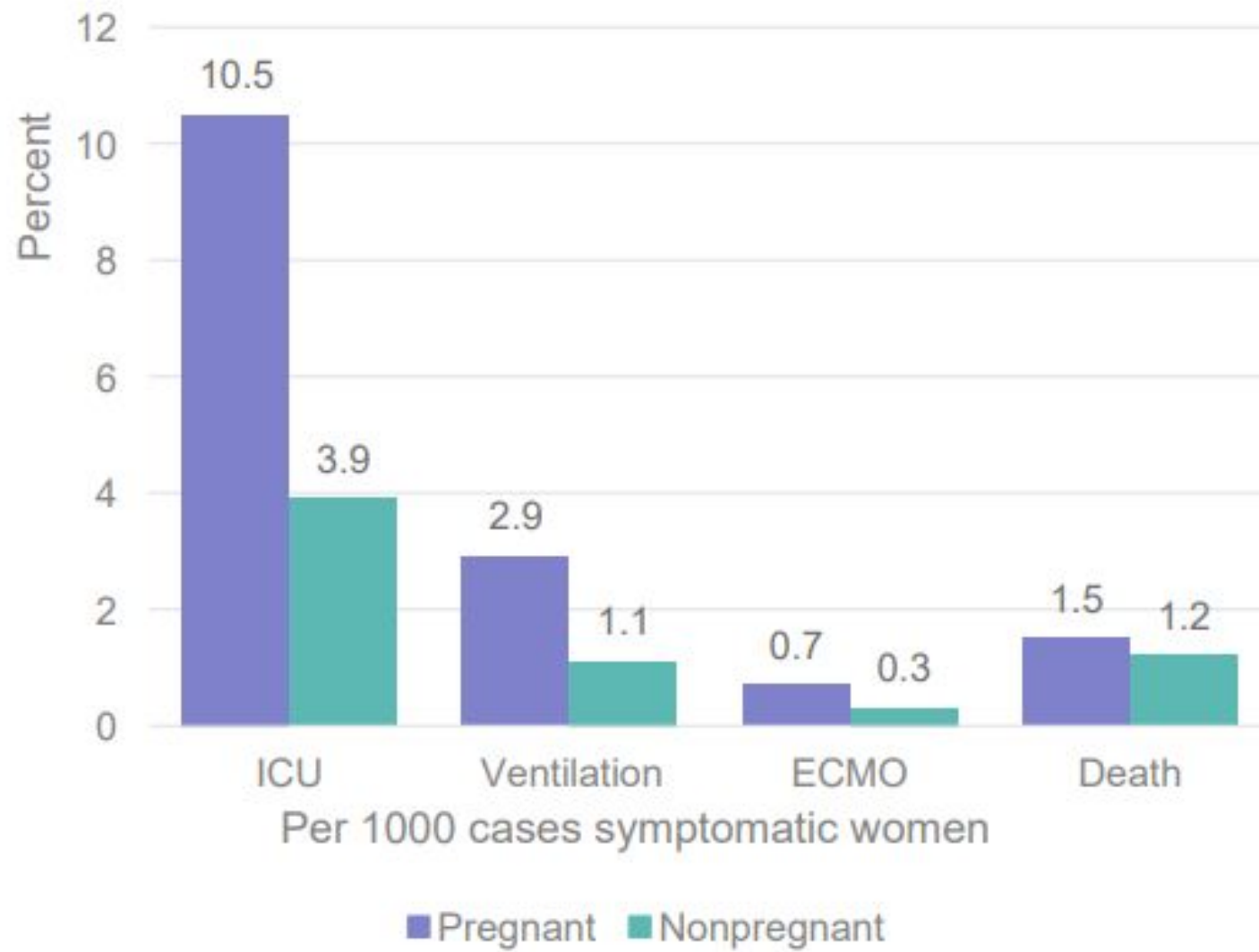
Respiratory rate greater than or equal to 30-35

Chronic illnesses-i.e. asthma, diabetes, hypertension

Fetal or other obstetrical concerns

- MMWR, 2020
  - Over 8,000 patients with COVID-19 in the US.
  - Hospital admission rate was 6x higher in pregnant women than in non-pregnant women
  - Pregnant women are more likely to end up in the ICU (aRR-1.5) and require mechanical ventilation(aRR-1.7)
  - No change in mortality over non pregnant women





# Treatment

- Supportive care
  - Oxygen therapy
    - High Flow Nasal cannula
    - Noninvasive positive pressure ventilation
    - Mechanical Ventilation



# Case Study(continued)

The patient is placed on oxygen by nasal cannula but cannot maintain her saturations at 95% without at least 3L. She is breathing ~28-32 times per minute

What are your next steps??

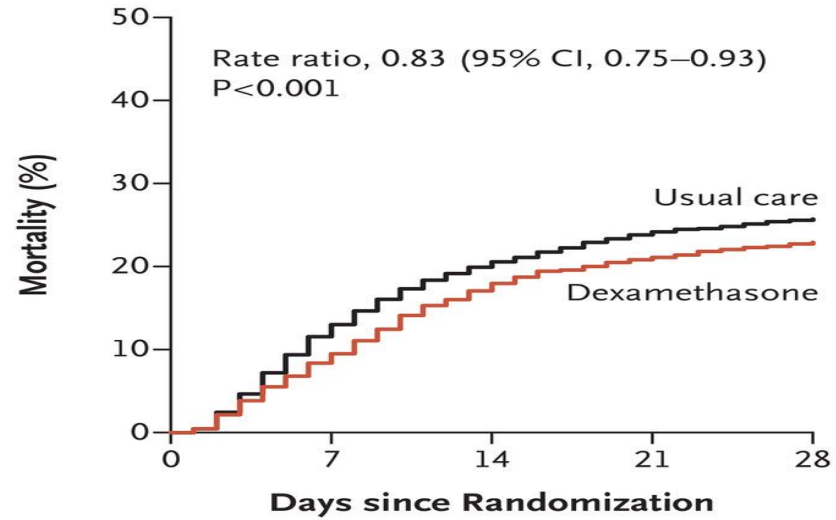


# Treatment

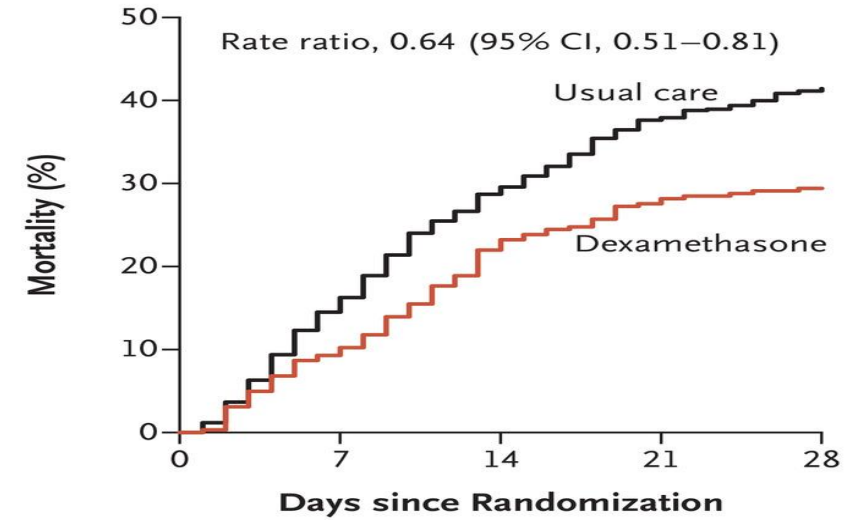
- Dexamethasone
  - Dosing-6mg daily for up to 10 days
  - RECOVERY STUDY
    - Double blind randomized placebo trial
    - Lower 28 day mortality in those needing respiratory support

NEJM, July 2020

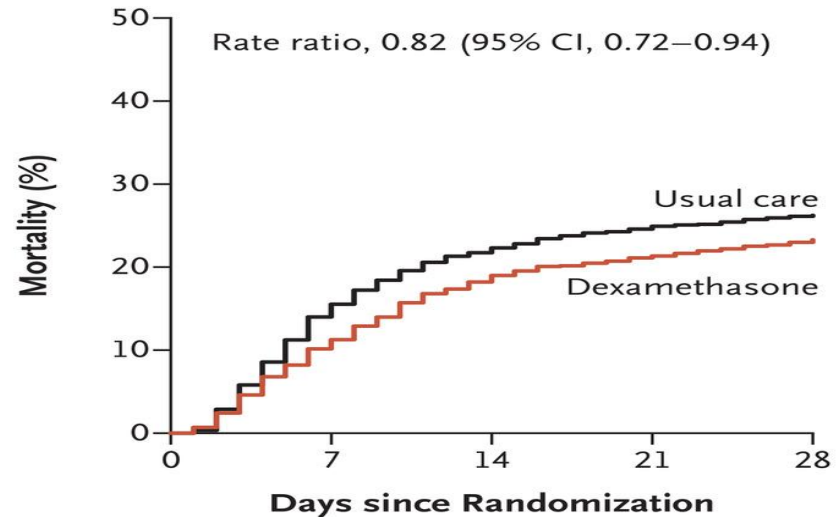


**A All Participants (N=6425)****No. at Risk**

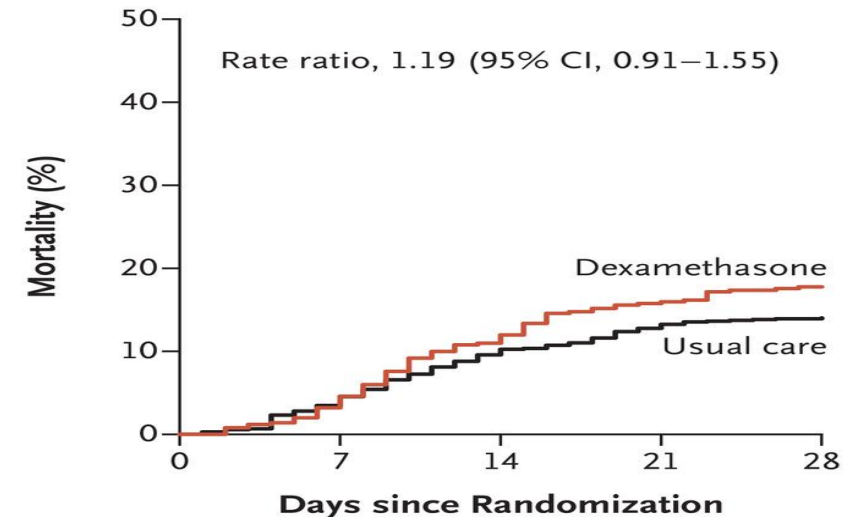
Usual care	4321	3754	3427	3271	3205
Dexamethasone	2104	1903	1725	1659	1621

**B Invasive Mechanical Ventilation (N=1007)****No. at Risk**

Usual care	683	572	481	424	400
Dexamethasone	324	290	248	232	228

**C Oxygen Only (N=3883)****No. at Risk**

Usual care	2604	2195	2018	1950	1916
Dexamethasone	1279	1135	1036	1006	981

**D No Oxygen Received (N=1535)****No. at Risk**

Usual care	1034	987	928	897	889
Dexamethasone	501	478	441	421	412

# Treatment

- Convalescent plasma

- Small randomized studies show some benefit; other studies do not
- Should be started when patient has an oxygen requirement
- Data suggest patients receiving plasma may form antibodies earlier than those who do not



# Treatment

- Remdesivir
  - Inhibitor of the viral RNA-dependent , RNA polymerase
  - Shown to be effective against SARS-CoV-1 and MERS-CoV
  - Initially used for compassionate care in special groups
    - Pregnancy and children less than 18 years of age
    - Required release and request from the FDA
  - Has been used successfully in pregnancy

Anderson J, et al. Case Rep Women's Health. 2020 May 16;27

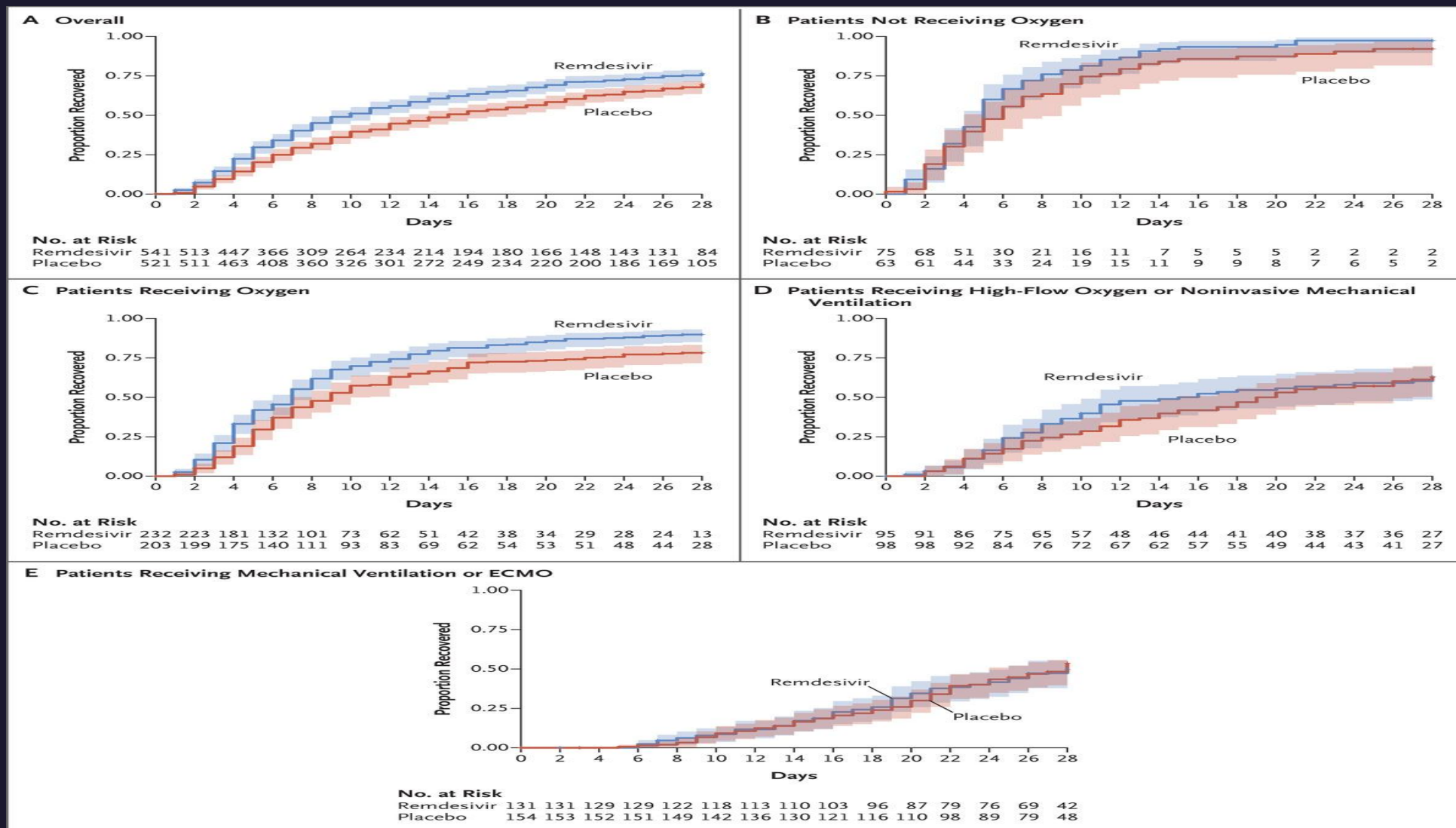
# Treatment

- Remdesivir
  - ACTT-1 trial
  - 1062 patients; 1:1 randomized control trial
  - Remdesivir more likely than placebo to shorten recovery time (OR-1.5)
  - Decrease incidence of respiratory tract infection
    - Begel et al. Remdesivir for the Treatment of Covid-19—Final Report NEJM 383(19):1813-1825

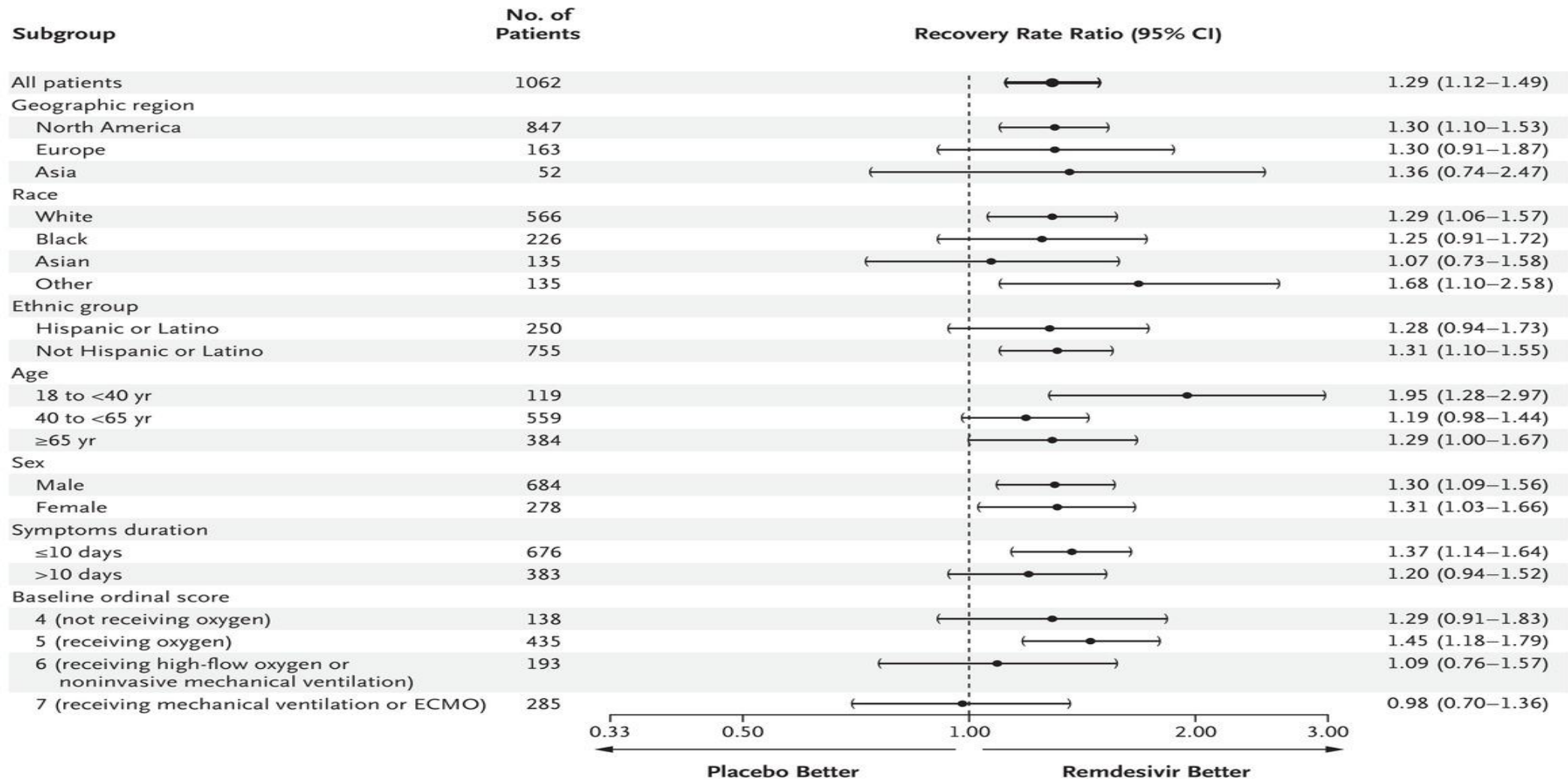




# Kaplan–Meier Estimates of Cumulative Recoveries.



# Time to Recovery According to Subgroup.



# Treatment

- Anticoagulation

- Essential for treatment
- Dose-40mg to 60 mg bid
- Controversial
  - Should patients who have COVID continue anticoagulation during pregnancy and postpartum?
  - MY OPINION IS YES!!!!



# Newer Therapies

- Monoclonal antibodies (Bamlanivimab)
  - Emergency use on Nov 9, 2020
  - Can be used during pregnancy
  - Used for mild-moderate COVID infection
  - Has not been shown to change outcome in severe disease
- Oral medication (Molnupiravir)
  - Blocks transmission of COVID within 24 ours
  - Still in clinical trials

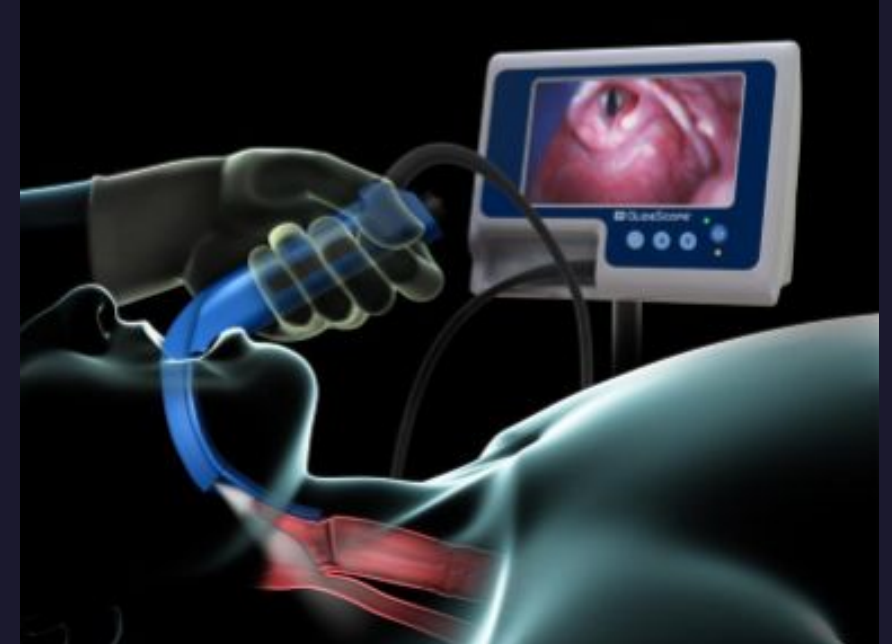
# Respiratory Failure

- Evaluation
  - Examine the patient
  - Assess oxygen saturation
    - Less than 95% in pregnancy is concerning
  - Assess ventilation
    - Remember Type 2 failure
  - Assess respiratory rate
    - $\geq 30$



# Things to consider with Intubation

- Placement of ET tube
  - Laryngeal edema and need for a smaller size tube
  - Video laryngoscope
  - Failure 8x more likely in pregnancy



# Clinical Key Questions ????

- Does the patient appear to be becoming **unstable**
- What are your **available resources**
- Can the patient **maintain** adequate oxygenation using your current therapy
- What is the status of the **fetus**
- Does the patient have a **full stomach**

# Things to Consider

- Maternal stabilization or need for transport
  - Consider early intubation and airway protection
- Fetal intervention—yes or no





- Remember structural issues unique to pregnancy
  - Heavier chest wall due to breast enlargement
    - Patient positioning-prone positioning is not contraindicated and may be helpful



# Strategies for Mechanical Ventilation in Pregnancy

Parameter	
Tidal Volume	5-8 ml/kg PBW
Inspiratory Rate	60 L/min
Respiratory Rate	15-18 breaths/min
Oxygen Saturation Goal	> or=95%
Carbon dioxide Goal	Avoid hypercapnia, mild hypercapnia <50 may be ok
PEEP	5 mm Hg
Peak pressure limit	30-35 cmH2O

# Principles of ECMO

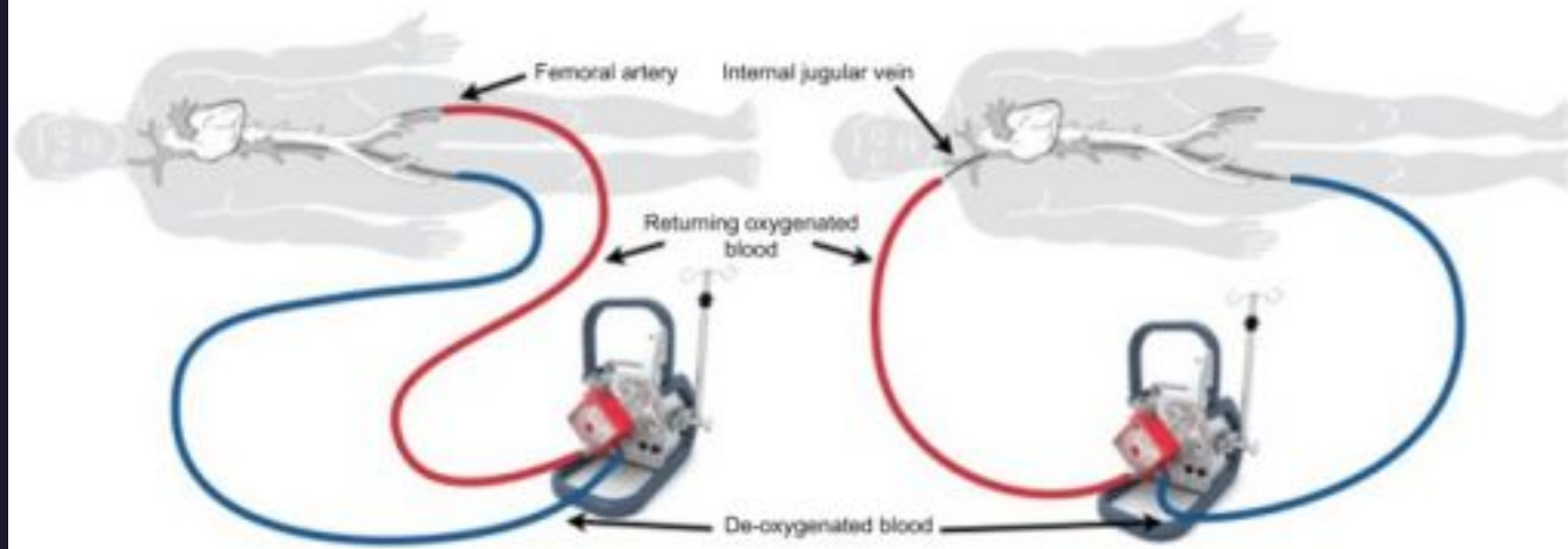
- Basic principle

- De-saturated blood is drained via venous CO<sub>2</sub> is removed, O<sub>2</sub> added through an “extracorporeal” device (an oxygenator), and the blood is then returned to systemic circulation via another vein (VV) or artery (AV)



VA-ECMO

VV-ECMO



# ECMO Outcomes

- 18 patients
  - 4 were pregnant
- Median maternal age-32.6 years
- Median gestational age-32 weeks
- Maternal survival
  - 16 out of 18-(88.9%)
- Fetal survival-(77%); 100% if viable
- 4 patients delivered on ECMO

• Agerstrand et al, (Ann Thorac Surg 2016;102:774–9)

# Viral pneumonia in pregnancy

- **Increased mortality rates when compared to the general population**
  - 2009-H1N1
    - 32% admission rate; 4x more likely to be admitted
    - 6 maternal deaths
  - SARS
    - Maternal death-18%
  - MERS
    - Maternal Death-25%
  - COVID-19
    - Maternal death-1.2%



# When should I delivery the fetus?

- Consider delivery after 34 weeks gestation if prolonged illness is expected
  - Some case reports suggest 28 weeks with COVID
  - Individualized care
- No data to suggest delivery improves maternal outcomes
  - 10 patients
  - Delivery reduced oxygen requirements by 28%
  - No change in lung compliance



Tomlinson MW, et al. Obstet Gynecol. 1998;91:108-11.

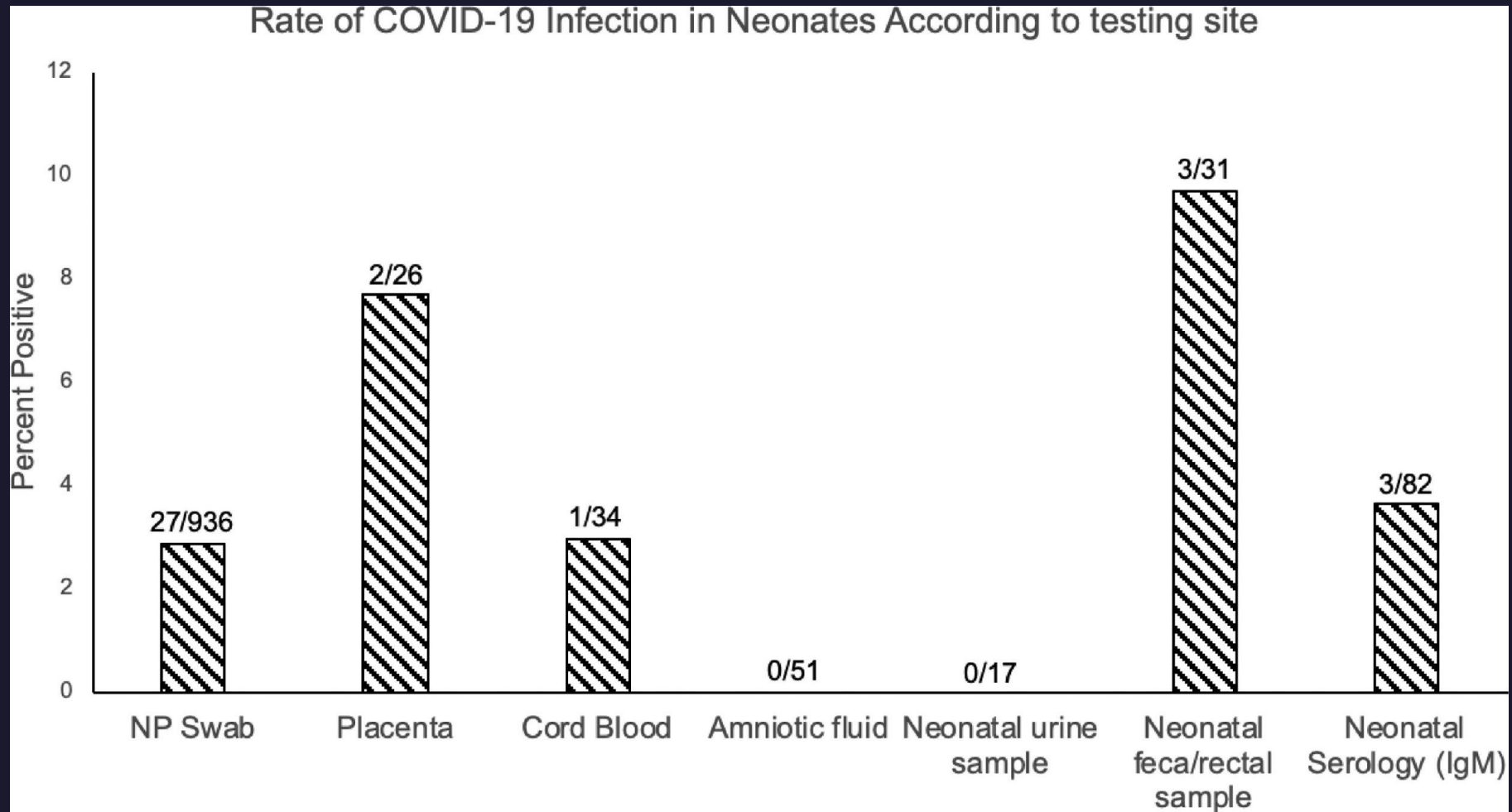
# Fetal outcomes

- Lancet 2020
  - 9 patients delivered by C/S-Wuhan
  - No transplacental transmission
  - No maternal deaths
  - No increase in respiratory complications
- Arch Pathol Lab Med 2020.
  - 38 cases
  - No transplacental passage
  - No increase in maternal respiratory symptoms



# Fetal Outcomes

- Preterm labor and delivery-21%
- Cesarean section for severe COVID-28%
- Stillbirth-1.9%
- Neonatal Death-0.8%
- Recovered COVID patients
  - Possible IUGR
- Management
  - Consider antenatal testing in recovered patients
- No consistent documentation of transplacental or vertical transmission



# Breastfeeding and Lactation

Table 1 Options for infant feeding and measures for a mother with COVID-19			
	Option A	Option B	Option C
Main points	<ul style="list-style-type: none"> <li>• Direct breastfeeding</li> <li>• Infant cared for by mother (rooming-in) or HCP/caregiver</li> </ul>	<ul style="list-style-type: none"> <li>• Expressed human milk</li> <li>• Infant cared for by HCP/caregiver</li> </ul>	<ul style="list-style-type: none"> <li>• No breastfeeding and mother's own milk is not provided</li> </ul>
Risks to breastfeeding	<ul style="list-style-type: none"> <li>• Nil</li> </ul>	<ul style="list-style-type: none"> <li>• Limited mother–infant contact</li> <li>• Difficulty in establishing latching</li> <li>• Strain on healthcare resources</li> </ul>	<ul style="list-style-type: none"> <li>• Limited mother–infant contact</li> <li>• Difficulty in establishing lactation</li> </ul>
Examples of situations	<ul style="list-style-type: none"> <li>• Mother is asymptomatic but swab positive</li> <li>• Infant positive for SARS-CoV-2</li> <li>• Established breastfeeding (infection in the first month postpartum)</li> </ul>	<ul style="list-style-type: none"> <li>• Mother is symptomatic with need for respiratory support</li> </ul>	<ul style="list-style-type: none"> <li>• Mother is critically ill</li> <li>• Parents, informed decision is not to breastfeed</li> <li>• Safe milk substitute available (human donor milk or infant formula)</li> </ul>
Specific measures: Infant managed as person under investigation (PUI) for up to 14 days from maternal last positive swab, with surveillance, and separated from vulnerable nonimmune persons			
Disposition of mother and infant	<ul style="list-style-type: none"> <li>• Scenario 1: mother–infant rooming in and cares for infant, or</li> <li>• Scenario 2: safe distancing of 2 m between mother and infant, and infant cared by HCP/caregiver. Consider use of physical barriers (e.g., curtain/isolette)</li> </ul>	<ul style="list-style-type: none"> <li>• Scenario 1: Safe distancing of 2 m between mother and infant, and infant cared by HCP/caregiver. Consider use of physical barriers (e.g., curtain/isolette) or</li> <li>• Scenario 2: Isolation of mother and infant until mother is no longer infectious</li> </ul>	<ul style="list-style-type: none"> <li>• Isolation of mother and infant until mother is no longer infectious</li> </ul>
Infant feeding	Scenario 1: breastfeeding with IPC practices Scenario 2: mother to have contact with infant only during breastfeeding and breastfeed with IPC practices	Mother expresses human milk with IPC practices <ul style="list-style-type: none"> <li>• Wears facemask and performs hand and breast hygiene</li> <li>• Proper pump cleaning</li> <li>• Dedicated breast pump</li> </ul>	<ul style="list-style-type: none"> <li>• Support continuity of human milk production by expressing</li> <li>• Resume breastfeeding or human milk feeding at appropriate timing</li> <li>• Alternative sources: donor human milk or infant formula</li> </ul>
Handling of human milk	As routine practice	Disinfect outer surface of milk containers	Store or discard (as per joint HCP and parents' decision)



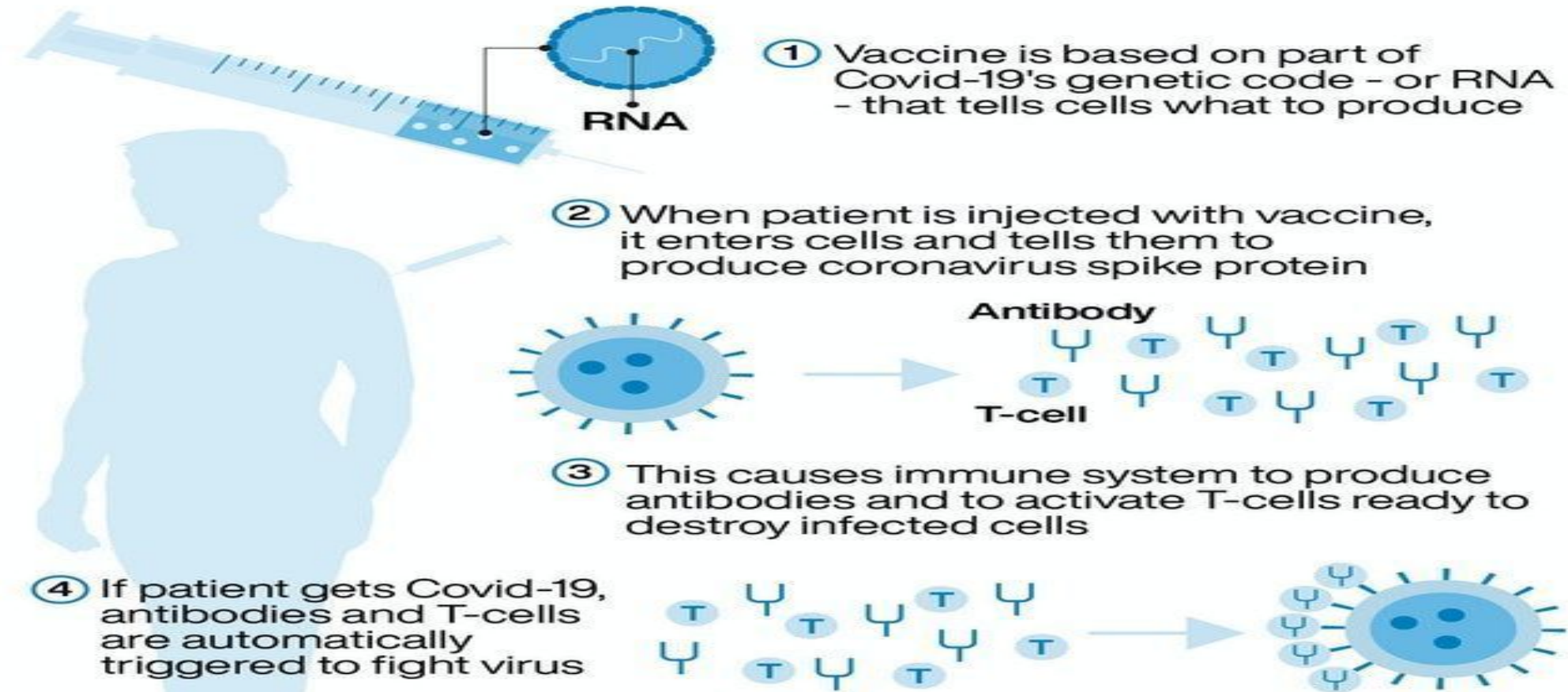
Oh Doctor, what about  
vaccine???





# How was the COVID Vaccine Developed

## How the RNA vaccine would work



PA graphic. Source: Nature

# How effective is the vaccine

- Vaccine is touted as more than 90% affected
  - This means if 10% of the unvaccinated group get the disease but only 1% of the vaccinated group get the disease
  - Better than the flu vaccine
  - Disease course will be lessened
  - Important in pregnant patients where T-cell function is compromised



# Vaccine Counseling

SMFM strongly recommends that pregnant and lactating people have access to the COVID-19 vaccines and that they engage in a discussion about potential benefits and unknown risks with their healthcare providers regarding receipt of the vaccine.

Vaccination is available during pregnancy. Counseling today was based on available data on vaccine safety with the lack of data related to fetal risk, risk of the pregnant person for SAR-CoV-2 infection acquisition, and their individual risk for severe disease.

The patient is aware that pregnant and lactating women were excluded from vaccine trials and that further studies are ongoing, and safety data will become available in the coming months.

We discussed that recent data indicates that pregnancy is an independent risk factor for COVID-19 disease severity, with an increased risk of ICU admission, mechanical ventilation, extracorporeal membrane oxygenation (ECMO), and death among pregnant patients with symptomatic COVID-19 infection compared with symptomatic nonpregnant patients. Although the absolute risk of severe morbidity and mortality remains low, reports have demonstrated a 3-fold increased risk for ICU admission.

# Vaccine Counseling

Recent data also indicate that there may be an increased rate of preterm birth and stillbirth among pregnant symptomatic and asymptomatic patients with SARS-CoV-2 infection.

The patient understand that because it is not a live vaccine there is no risk of genetic modification to people receiving the vaccine.

Fetal risk:

The risk from mRNA vaccines is thought to be low due to the expected degradation of mRNA in the circulation.

The Advisory Committee on Immunization Practices (ACIP) reports that preclinical studies have been reassuring. We discussed that decision-making needs to balance these theoretical risks with the risks associated with delayed vaccination and the possibility of maternal SARS-CoV-2 infection.

After our conversation, the patient wishes to consider her options





# Other Considerations



# PPE for the Caregiver

**TABLE 2**

**Personal protective equipment (PPE)<sup>a</sup> for healthcare workers caring for a patient with COVID-19 in pregnancy**

<b>Risk</b>	<b>Examples of clinical encounters in obstetrics</b>	<b>Recommended PPE<sup>a</sup> for staff attending to patient with COVID-19</b>
Low risk	<ul style="list-style-type: none"><li>Any transient encounter &gt;2 meters/6 feet away from patient</li></ul>	<ul style="list-style-type: none"><li>None; standard precautions and surgical mask suffice</li></ul>
Moderate risk	<ul style="list-style-type: none"><li>Obstetric (including vaginal) examination</li><li>Ultrasonography (including vaginal scans)</li><li>Vaginal or cesarean delivery</li></ul>	<ul style="list-style-type: none"><li>Surgical cap</li><li>Gloves</li><li>Face shield or goggles</li><li>Gown with long sleeves</li><li>Surgical mask or N95/FFP2 respirator</li></ul>
High risk	<ul style="list-style-type: none"><li>Use of supplemental oxygen<sup>b</sup> in labor: nasal cannula, face mask, air-entrainment mask, or non-rebreather mask</li><li>Maternal collapse: cardiopulmonary resuscitation<sup>b</sup> and endotracheal intubation<sup>b</sup></li></ul>	<ul style="list-style-type: none"><li>Surgical cap</li><li>Gloves</li><li>Face shield or goggles</li><li>Gown with long sleeves</li><li>N95/FFP2 respirator or PAPR with HEPA filter (consider if the healthcare worker herself is pregnant)</li></ul>

# Telehealth in COVID

- May help provide care for patients and avoid exposure
- Used in our resident system for patients with COVID, O2 saturation monitor
- Our practice (MFM) sees about 20% of patients by telehealth
  - Diabetes follow up
  - Hypertension management
  - Provider spacing
- Helps to identify patients that may need hands-on care

# Key Points



- Sars-CoV 2 or COVID-19 is a novel RNA virus
- Pregnant patients are at increased risk for respiratory compromise and an ICU admission
- Racial disparities exist in outcome and treatment
- The treatment for COVID-19 in pregnancy is similar to the non-pregnant states



# Key Points



- Fetal monitoring is recommended for patients who have recovered from COVID during pregnancy
- Patients admitted to the ICU should be managed by a multi-disciplinary team with special attention to the physiological changes in pregnancy
- Vaccination is not contraindicated in pregnancy, however, given our limited data a detailed discussion between the patient and her caregiver is advised.
- While there is limited guidance, it is the opinion of the speaker that anticoagulation should be continued as an outpatient in patients affected by COVID-19

# Thank you



# Evaluation Link for CME Credit

[https://redcap.link/COVID in Pregnancy](https://redcap.link/COVID%20in%20Pregnancy)





# Selected References

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