

Inclusion of Pregnant Women in Clinical Trials

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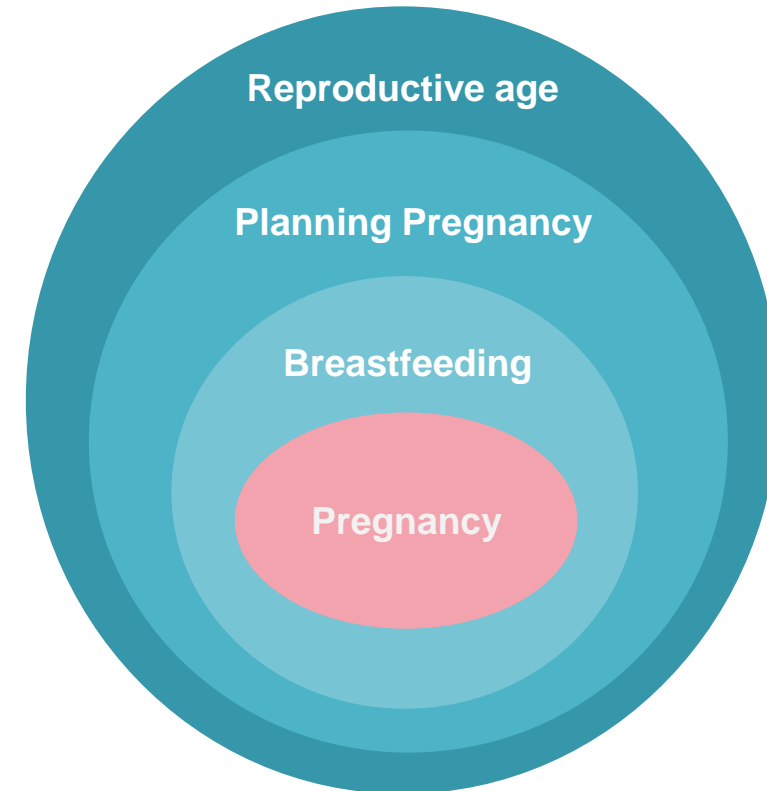


Overview

- Scope of the problem
- Informed consent in pregnancy
- COVID-19 as Case Study
 - Impact of COVID-19 in Pregnancy
 - Therapeutic trials in pregnant vs. non-pregnant women
 - Vaccine trials in pregnant vs. non-pregnant women
 - Potential harm by exclusion

Scope of the Problem

- **About 6 million pregnancies in the United States every year**
- **In addition, many more women are planning pregnancy or actively breastfeeding**



Why are Pregnant Women Excluded?

Pregnant women have been excluded:

- Because of potential for birth defects
- Labeled as a “vulnerable population”

“Vulnerable Population”

- Usually applies to populations with compromised decision-making capacity
- For example: small children, adults with limited cognitive ability

There is nothing about the state of pregnancy that renders pregnant women incapable of offering valid research consents or refusals.

Example: COVID19 Vaccine Trials

Vaccine trials not only excluded pregnant women, but also excluded anyone who could become pregnant or was actively breastfeeding

Accessed at <https://clinicaltrials.gov/ct2/show/NCT04470427>

ClinicalTrials.gov Identifier: NCT04470427

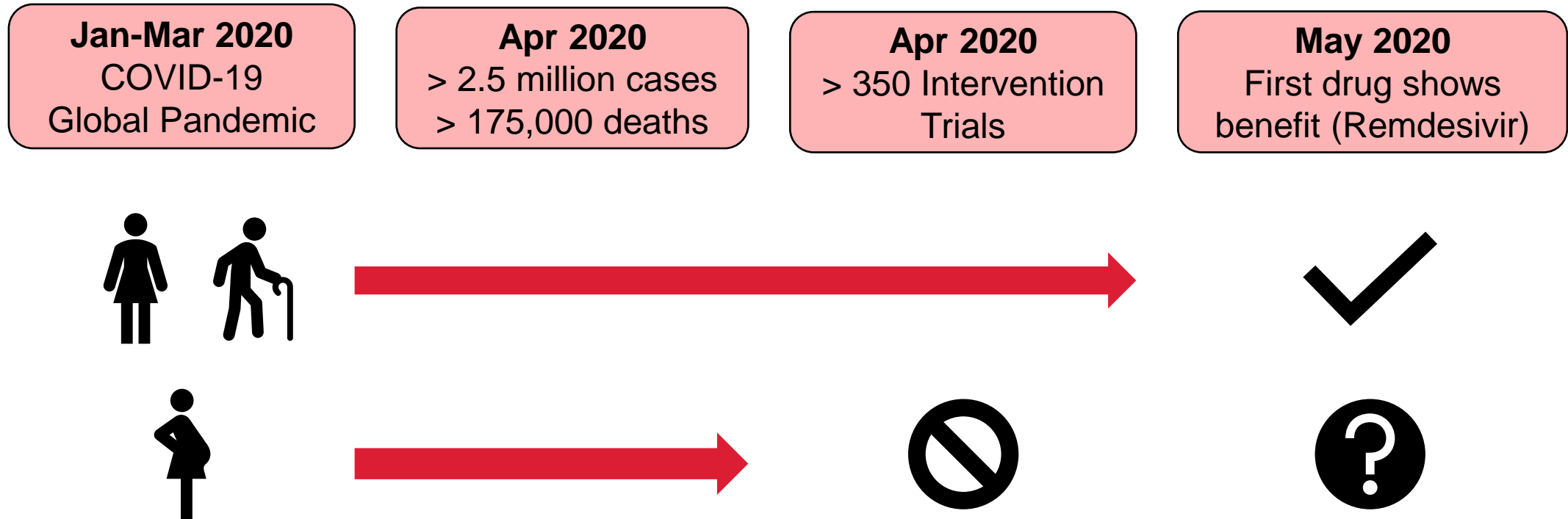
A Study to Evaluate Efficacy, Safety, and Immunogenicity of mRNA-1273 Vaccine in Adults Aged 18 Years and Older to Prevent COVID-19

Eligibility Criteria

Female participants of childbearing potential may be enrolled in the study if the participant fulfills all the following criteria:

- Has a negative pregnancy test at Screening and on the day of the first dose (Day 1).
- Has practiced adequate contraception or has abstained from all activities that could result in pregnancy for at least 28 days prior to the first dose (Day 1).
- Has agreed to continue adequate contraception through 3 months following the second dose on Day 29.
- Is not currently breastfeeding.

COVID19 as a Case Study



COVID19 as a Case Study



Feb 25, 2020

NIH Clinical Trial of Remdesivir to Treat COVID-19 Begins

May 22, 2020



The NEW ENGLAND
JOURNAL of MEDICINE

Remdesivir for the Treatment of Covid-19



Jan-Jun 2020

CDC Report:

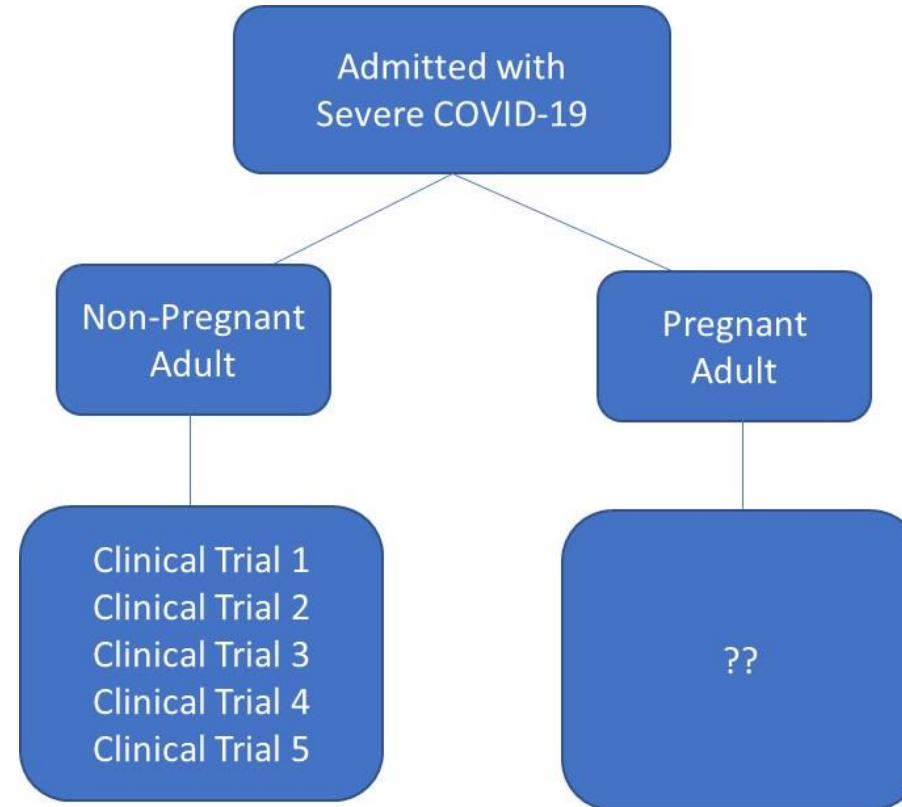
- 21% of SARS-CoV2 infections in reproductive age women
- 9% were pregnant
- Increased hospitalization, ICU admission, mechanical ventilation

COVID-19 in Pregnancy: Early Pandemic

Treatment of pregnant women early in the COVID-19 Pandemic?

34-year-old with first pregnancy at 28 weeks gestation

- Fever, cough shortness of breath
- +SARS-CoV2
- Viral pneumonia
- Requires supplemental oxygen



Compassionate Use Medications

Pregnant women with Severe COVID-19 treated with Off-Label or Compassionate-Use medications



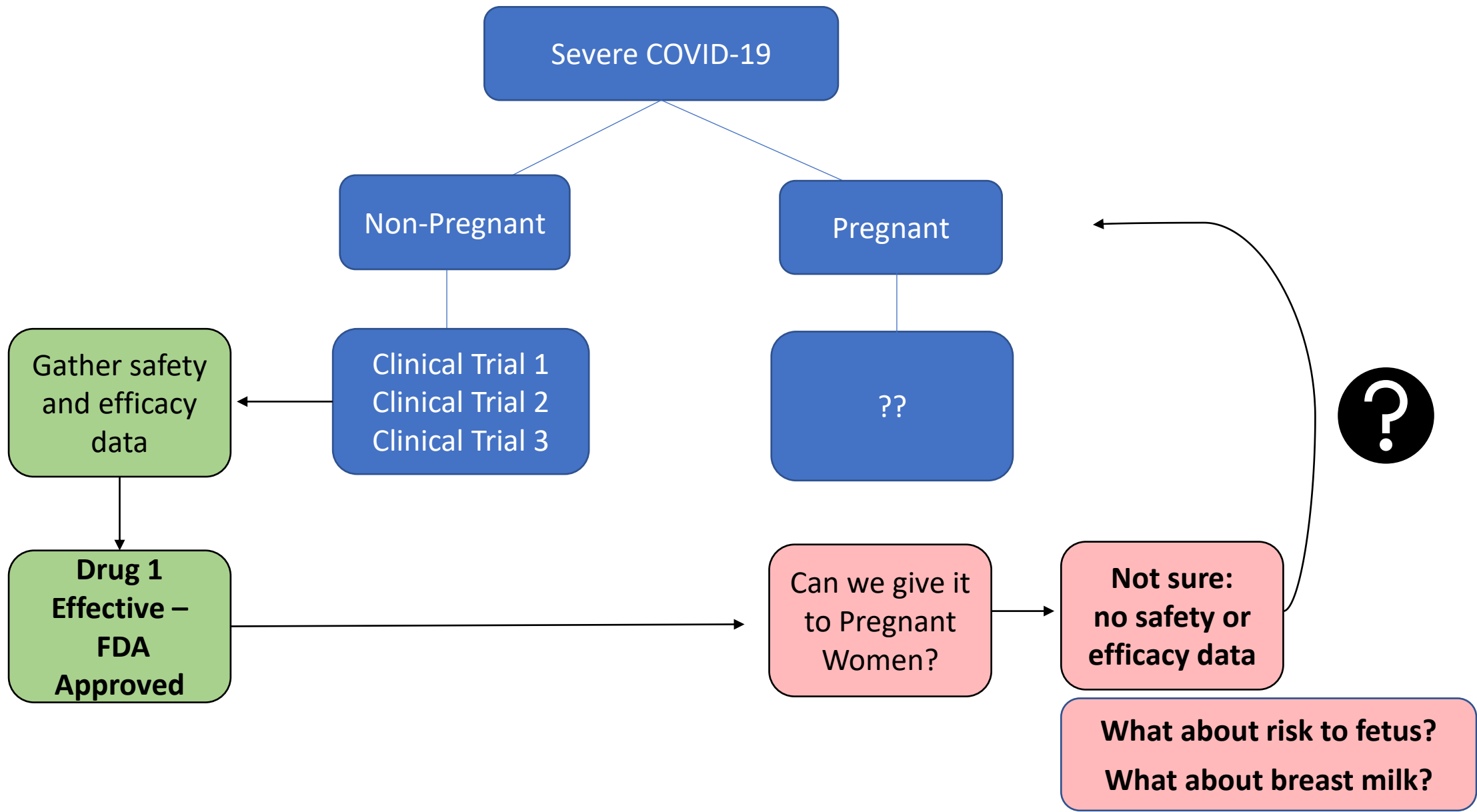
Off-Label

- Quick and easy (e.g., Hydroxychloroquine)
- But often no data on safety or efficacy
- No data collection or monitoring



Compassionate Use

- Long, complex process (e.g., Remdesivir)
- **2-3 days**
- But some data collection and follow-up



Treatment of COVID-19 in Pregnancy

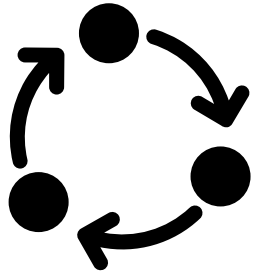


Pregnancy Dilemma

- Pregnant women excluded from clinical trials
- Pregnant women must wait until trials are completed in non-pregnant adults
- Even when new drug approved – use of drug in pregnancy is questioned due to lack of data
- Pregnancy data then gathered retrospectively to assess benefit
- Such data is then questioned as “low-quality”



COVID-19 Vaccine Trials



Pregnancy Cycle repeated

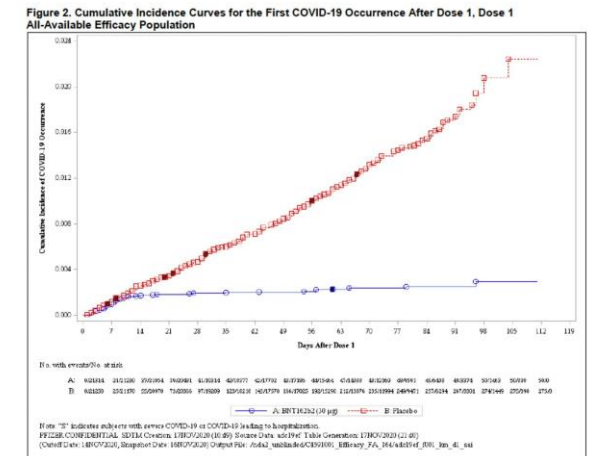
Pregnant women excluded from both mRNA trials (Moderna and Pfizer)

Vaccines Effective!
Both FDA Approved

Can we give it to Pregnant Women?

Not sure: no safety or efficacy data

What about risk to fetus?
What about breast milk?

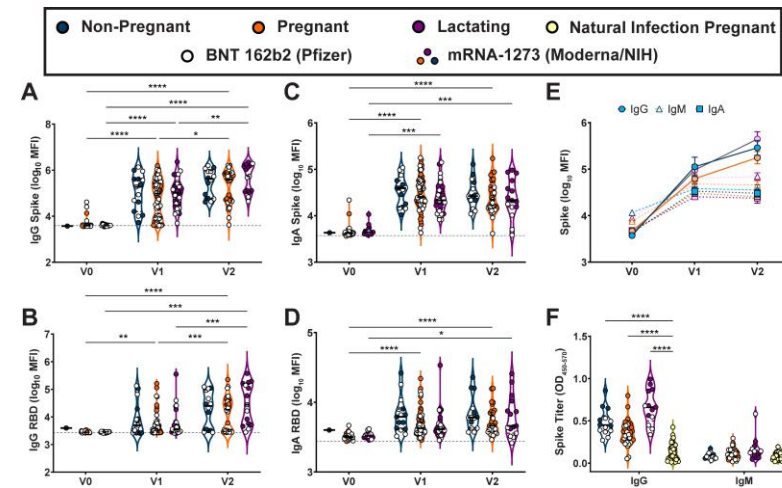


Pregnancy Researchers to the Rescue

Once mRNA vaccines became available, the CDC and researchers around the country, raced to gather vaccine data in women who were pregnant or lactating

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

Kathryn J. Gray, MD PhD, Evan A. Bordt, PhD, Caroline Atyeo, BS, Elizabeth Deriso, PhD, Babatunde Akinwunmi, MD MPH MMSc, Nicola Young, BA, Aranxta Medina Baez, BS, Lydia L. Shook, MD, Dana Cvrk, CNM, Kaitlyn James, PhD, MPH, Rose De Guzman, PhD, Sara Brigida, BA, Khady Diouf, MD, Ilona Goldfarb, MD MPH, Lisa M. Bebell, MD, Lael M. Yonker, MD, Alessio Fasano, MD, S. Alireza Rabi, MD, Michal A. Elovitz, MD, Galit Alter, PhD, Andrea G. Edlow, MD, MSc



My Experience and Conclusions

- Sought out clinical trials for pregnant women with Severe COVID-19 but few were available
- Treated with Compassionate-Use Remdesivir and off-label medications, some benefit but this was approach was suboptimal
- Launched clinical trial with an existing drug to treat pregnant women with Severe COVID-19
- I found that pregnant and postpartum women had a strong desire to participate in clinical trials for COVID-19, following Informed Consent

“If we don’t figure out a way to include pregnant women in more clinical trials and investigate the safety of new therapies, there’s going to be a huge gap in care. Medical innovations are happening rapidly, and pregnant women are getting left behind.”

Richard Burwick, MD, MPH