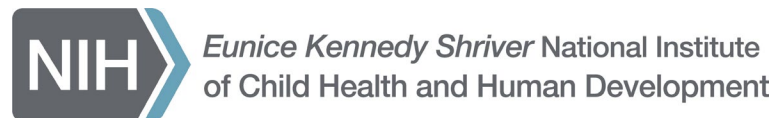


# NICHD COVID-19 Research

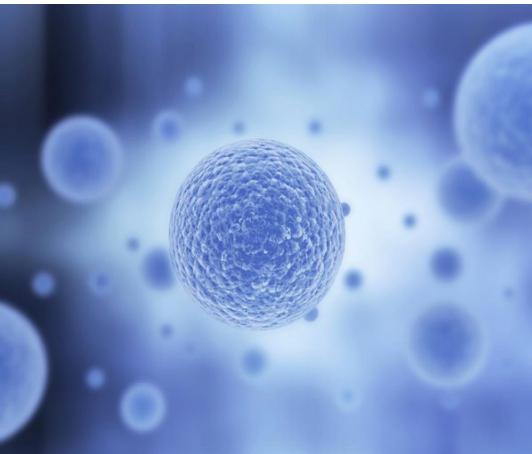
Diana W. Bianchi, M.D.

March 19, 2021



# Mission Statement

**The NICHD leads research and training to understand human development, improve reproductive health, enhance the lives of children and adolescents, and optimize abilities for all.**





# **NICHD COVID-19 Research Children**

# CARING for Children with COVID

*(Collaboration to Assess Risk and Identify loNG-term outcomes for Children with COVID)*



- Two approaches
- Combined resources and networks from 3 NIH ICs to capture data from hospitalized patients with MIS-C
- Trans-NIH effort through RADx initiative to enhance diagnostic and predictive efforts
- [CARING4KidswithCOVID.nih.gov](https://www.caring4kidswithcovid.nih.gov)



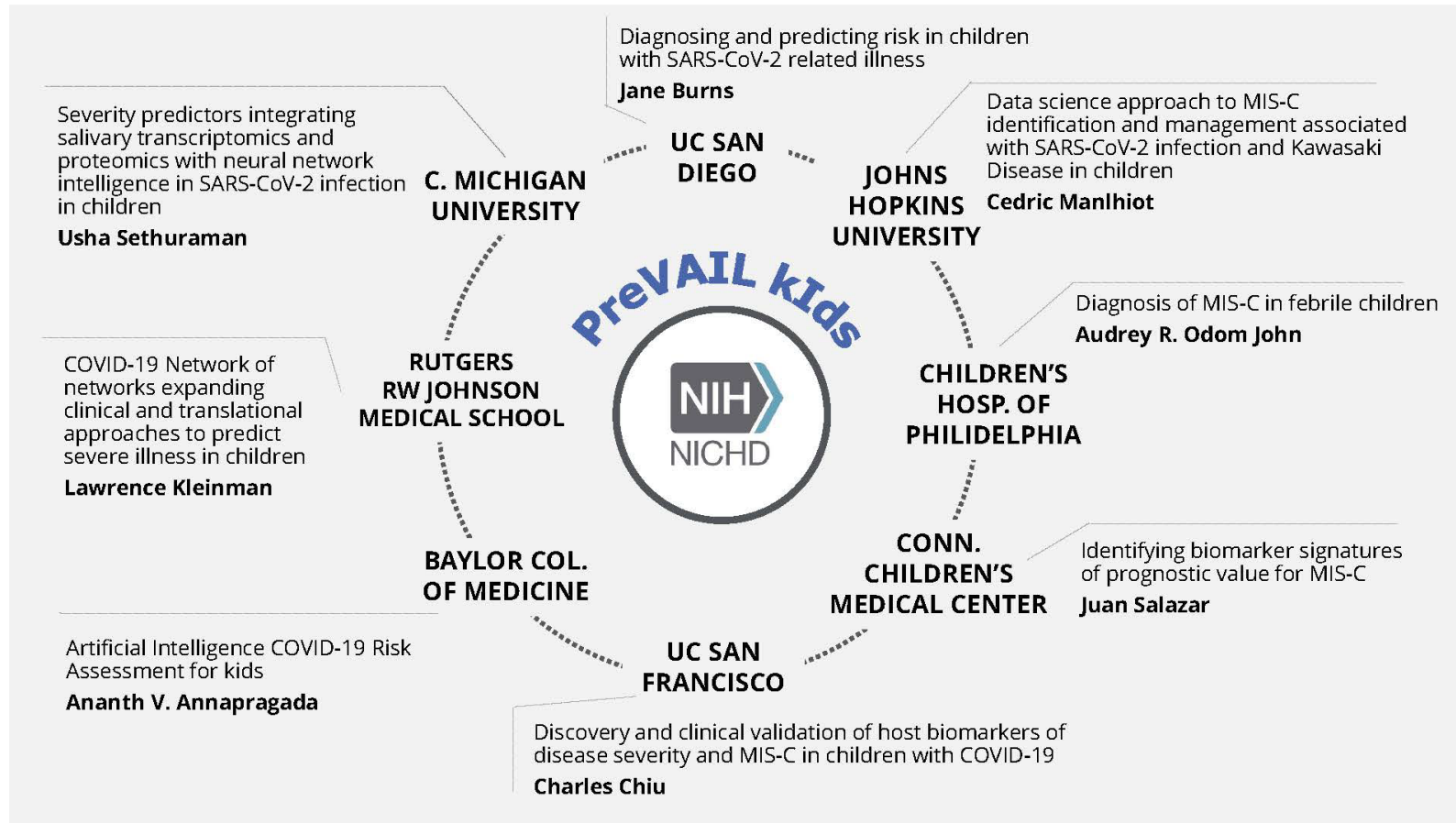
# CARING for Children with COVID

*(Collaboration to Assess Risk and Identify loNG-term outcomes for Children with COVID)*

- Leveraging networks from NICHD, NHLBI, NIAID to create a centralized cohort of children with MIS-C
  - Capitalizes on strengths of each network: immune profiling (NIAID); long-term cardiac effects (NHLBI); PK/PD of drugs used to treat COVID-19 but not labeled for children (NICHD)
  - **Clinical data will be harmonized** across MIS-C cohort studies
  - A large searchable data set with common data elements and widely available measures (including WGS) will be created for **interoperable sharing across different platforms**
  - Aim is to follow children with MIS-C for five years through longitudinal protocol



# Predicting Viral-Associated Inflammatory Disease Severity in Children with Laboratory Diagnostics and Artificial Intelligence (PreVAIL kids)



# Additional Pediatric Studies Led by NICHD

- **Pediatric Trials Network**

- Purpose: Gather information on pharmacokinetics and safety of several drugs not typically used in children to define appropriate dosing of these drugs for COVID-19
- Incorporated opportunistic study of 15 drugs into an existing protocol across nearly 50 study sites

- **Supplemental award to one of NICHD's Intellectual and Developmental Disability Research Centers**

- Provide weekly saliva-based SARS-CoV-2 tests for students, teachers, and staff in 6 special education schools in St. Louis to determine the best implementation strategies using an FDA-approved diagnostic test
- Evaluate the best testing approaches and mitigation strategies to guide the safe return to school for vulnerable children with IDD
- Develop a one-pager and website of best practices to help other school districts bring kids with IDD back to school safely



# Return To School Diagnostic Testing Approaches

## Context

- Impact of returning to school and other service settings goes beyond children's education
- Societal impacts of closed childcare centers, preschools and schools: Disproportionate burden on vulnerable populations

## Goal

- Develop and test COVID-19 diagnostic testing approaches to safely return children and staff to the in-person school setting in underserved and vulnerable communities

## Approach

- Focus on children below the age eligible for vaccination via EUA (age 16); all school personnel
- Advance methods to integrate testing in return to or maintenance of in-person instruction
- Identify effective, scalable, and sustainable testing implementation strategies in a range of settings serving primarily underserved or disadvantaged children and their families





# Post-Acute Sequelae of SARS-CoV-2 Infection (PASC)

- FY 21 COVID relief bill: \$1.15 billion to NIH to support research and clinical trials related to the long-term effects of COVID-19
- **Trans-NIH effort:** Improve understanding of and develop strategies to prevent and treat post-acute manifestations of SARS-CoV-2 infection ***across the lifespan***
  - Specific language in the Research Opportunity Announcement (ROA) to include children in this research effort
  - <https://covid19.nih.gov/sites/default/files/2021-02/PASC-ROA-OTA-Recovery-Cohort-Studies.pdf>
  - <https://covid19.nih.gov/sites/default/files/2021-02/PASC-ROA-OTA-3-Cores.pdf>





# **NICHD COVID-19 Research Pregnant and Lactating People**

# Gestational research assessments for covid-19 (GRAVID)

- Medical records analysis of up to 24,500 women who have given birth at a clinical center within NICHD's [Maternal-Fetal Medicine Units Networks](#) to examine maternal and neonatal outcomes for pregnant women with and without SARS-CoV-2 infection
- Early results analyzing data from 1,200 COVID+ pregnant women showed that pregnant women with severe symptoms of COVID-19 had a higher risk of complications during and after pregnancy.
  - Those with severe symptoms were at higher risk for cesarean delivery, postpartum hemorrhage, hypertensive disorders of pregnancy, and preterm birth.
- Pregnant people outside of the network inquired if they could participate



12 Centers; 39 individual hospital sites

<https://www.nichd.nih.gov/newsroom/news/012821-GRAVID>



# Additional NICHD-supported COVID-19 research

- **Remdesivir clinical trial**

- NIH-funded International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network (NIAID, NICHD, NIMH support)
- Compare remdesivir use in pregnant and non-pregnant people (<https://clinicaltrials.gov/ct2/show/NCT04582266>)
- Assessing drug metabolism and side effects; analyzing umbilical cord blood and breast milk, as applicable



- **SARS-CoV-2 and Breast Milk**

- Investigator initiated work in an existing collaborative network supported by NICHD, NIAID and NIMH
- Active virus is not transmitted to uninfected infant via breast milk
- Human milk contains antibodies directed against SARS-CoV-2
- Might suggest the potential to use milk-derived antibodies for therapeutic use



# Lack of Inclusion in Research Complicates Pandemic Decision Making for Pregnant and Lactating People

- Pregnancy increases risk of hospitalization, need for ICU care, and medical ventilation with COVID-19
- Prevention is key
- Evidence for the utility, safety, and effectiveness of the available vaccines in pregnancy is unknown
- Implementing PRGLAC recommendations could improve the situation faced by pregnant and lactating women

## VIEWPOINT

### Involving Pregnant Individuals in Clinical Research on COVID-19 Vaccines

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**The continued global escalation** of coronavirus disease 2019 (COVID-19) cases is of particular concern for pregnant and lactating individuals. While many cases of COVID-19 are asymptomatic or relatively mild, recent evidence suggests that pregnant people are at increased risk of hospitalization and have a 3-fold adjusted relative risk of needing intensive care (10.5 vs 3.9/1000 cases) and mechanical ventilation (2.9 vs 1.1/1000 cases) compared with age-matched nonpregnant individuals.<sup>1</sup> Pregnant people with laboratory-confirmed severe or critical COVID-19 disease have higher adjusted relative risks of cesarean delivery (1.57 [95% CI, 1.30-1.90]), postpartum hemorrhage (2.04 [95% CI, 1.19-3.47]), hypertensive disorders of pregnancy (1.64 [95% CI, 1.21-2.23]), and preterm birth (3.53 [95% CI, 2.42-5.15]).<sup>2</sup>

These complications are exacerbated in women who are older, have a higher body mass index, and who have medical comorbidities; evidence is emerging that racial and ethnic disparities also are related to morbidity and mortality among pregnant people.<sup>1,2</sup> With the development of COVID-19 vaccines, there is the potential for

been provided for nonpregnant patients. Efforts by the Centers for Disease Control and Prevention through its V-Safe registry<sup>5</sup> as well as industry and the Food and Drug Administration will yield postmarket vaccine surveillance information from pregnant people, including evidence on the effects of the vaccine on pregnancy and infant outcomes. These data will be useful, but in the meantime, pregnant people and their clinicians must make real-time decisions based on little or no scientific evidence.

As noted in 2016, when the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC) was established as part of the 21st Century Cures Act,<sup>6</sup> there is a continuing need to address gaps in knowledge and research related to the development of safe and effective therapies for pregnant and lactating people. COVID-19 provides a clear and urgent example that these gaps remain and provides compelling reasons why the implementation recommendations of this task force need to be carried out. Pregnant people were excluded from participating in clinical trials of COVID-19 vaccines, but there are now being

<https://jamanetwork.com/journals/jama/fullarticle/2776540>



# Some Suggestions from our Viewpoint Article

- Pregnant people are no longer considered as a vulnerable population
- It is not too early to begin preparing now for the next epidemic or pandemic
- If animal studies and initial Phase I safety data are reassuring, make a plan for inclusion of pregnant people
- Create registries (e.g., CDC's V-Safe), use existing networks, share data and biospecimens
- Liability risks to pharma can be mitigated by programs such as the Countermeasures Injury Compensation Program [www.hrsa.gov/cicp](http://www.hrsa.gov/cicp)
  - Provides benefits to pregnant and non-pregnant people who are injured by products designed to treat or prevent public health threats



# Effects of the Pandemic on Trainees and Junior Faculty

- Clinician-scientists may need to do more clinical time because of increased numbers of hospitalized children and colleagues who become ill
- Inability to get to the bench due to shutdowns of physical workspaces
- Decreased recruitment in clinical trials due to decreased non-COVID clinical volume and/or research staff who are unable to be in the physical workspace
- Disproportionate effects on people with families
  - Effects of day care and school closures
  - Productivity in males vs. females
- News is not all bad...virtual workshops have expanded access and opportunities



# Summary

- NICHD is actively involved in designing and funding research opportunities to improve the diagnosis and treatment of SARS-CoV-2 infection in our populations
- Initial approach was to harness and repurpose existing clinical trial network infrastructures
- Over the past year a growing appreciation for the spectrum of disease manifestations in children
- Urgent need for evidence to allow children to return to in-person school safely
- Pregnant and lactating people need to be included in clinical trials
- Attention needs to be paid to the next generation of scientists who have been disproportionately affected by disruption in the physical workspace





# NICHD Vision Statement



**Healthy pregnancies. Healthy children.  
Healthy and optimal lives.**

