Pediatric COVID-19 Research Programs

AAP Town Hall

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NIH Eunice Kennedy Shriver National Institute of Child Health and Human Development
Active Pediatric COVID-related Research Programs

• CARING for Children with COVID
  • MIS-C Cohorts
  • PreVAIL kids
• Safe Return to School Diagnostic Testing
• RECOVER
CARING for Children with COVID
The CARING for Children with COVID program is led by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) and National Heart, Lung, and Blood Institute (NHLBI) in collaboration with the National Institute of Allergy and Infectious Diseases (NIAID). This program leverages the clinical networks of NICHD, NHLBI, and NIAID to research SARS-CoV-2 infection in children and related conditions, including **multisystem inflammatory syndrome in children (MIS-C)**.

More information about the clinical networks **is available in the following sections** and more details about the research they are conducting is available on the **Research page**.
CARING for Children with COVID
(Collaboration to Assess Risk and Identify Long-term outcomes for Children with COVID)

- **TWO APPROACHES**
- Leverages resources and Networks from three NIH Institutes to capture data from hospitalized patients with MIS-C
- Trans-NIH effort through RADx-Rad Program to enhance diagnostic and predictive efforts
- [CARING4KidswithCOVID.nih.gov](http://CARING4KidswithCOVID.nih.gov)

**CARING for Children with COVID**

- **MUSIC**
  - NHLBI
- **POPS02**
  - NICHD
- **PRISM**
  - NIAID
- **PreVAIL**
  - klds
• Observational study
  • 1,685 screened and 1074 children with MIS-C enrolled at 33 sites
• Primary Focus
  • Left ventricular dysfunction
  • Coronary artery aneurysms
• Assessment of all other organ dysfunction, inflammation, and major medical events
• 5-year follow-up
• Observational study, MIS-C and pediatric COVID
  • ~205 enrolled, ~123 MIS-C, 20 sites
• Focus on inflammatory pathways
• Interim status of baseline specimen collection
  • ~862 specimens from ~167 participants
  • PBMC, plasma, serum
• 327 Pre-treatment specimens from 69 participants (38 COVID/31 MIS-C)
• 535 Post-treatment specimens from 98 participants (27 COVID, 71 MISC)
Pharmacokinetic study of medications used to treat COVID-19 in children
  - Expanded to study MIS-C
  - Observational study – 34 sites
    - ~460 SARS-CoV-2 positive
    - ~120 with MIS-C
  - 114 treated with remdesivir; 47 less than 12 years of age; PK data pending
Multisystem Inflammatory Syndrome (MIS-C)

Health Department-Reported Cases of Multisystem Inflammatory Syndrome in Children (MIS-C) in the United States

<table>
<thead>
<tr>
<th>TOTAL MIS-C PATIENTS MEETING CASE DEFINITION*</th>
<th>TOTAL MIS-C DEATHS MEETING CASE DEFINITION</th>
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<tbody>
<tr>
<td>5,526</td>
<td>48</td>
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Last updated with cases reported to CDC on or before November 1, 2021
Predicting Viral-Associated Inflammatory disease severity in children with Laboratory diagnostics and artificial Intelligence (PreVAIL klds)

*Note that- MIS-C is identified as a form of post acute sequelae of COVID-19 also know as Long COVID

Develop translational tools to understand the spectrum of pediatric SARS-CoV-2 illness, rapidly diagnose and characterize MIS-C associated with SARS-CoV-2, and predict the longitudinal risk of disease severity after exposure to and/or infection by SARS-CoV-2

- Genetics; Omics; Other biomarkers
- Viral Dynamics and Immune Profiling Studies
- Digital Health Platforms Leveraged for Children
- Artificial Intelligence

- Milestone-driven award (R61/R33); up to 4 years
Predicting Viral-Associated Inflammatory disease severity in children with Laboratory diagnostics and artificial Intelligence

PreVAIL kids

Severities predictors integrating salivary transcriptomics and proteomics with neural network intelligence in SARS-CoV-2 infection in children
Usha Sethuraman

COVID-19 Network of networks expanding clinical and translational approaches to predict severe illness in children
Lawrence Kleinman

Artificial Intelligence COVID-19 Risk Assessment for kids
Ananth V. Annapragada

Data science approach to MIS-C identification and management associated with SARS-CoV-2 infection and Kawasaki Disease in children
Cedric Manlhiot

Diagnosis of MIS-C in febrile children
Audrey R. Odom John

Identifying biomarker signatures of prognostic value for MIS-C
Juan Salazar

Discovery and clinical validation of host biomarkers of disease severity and MIS-C in children with COVID-19
Charles Chiu
Domestic and International Enrollment Scope

Planned Geographic Locations$^1$ of Cohorts in the Continental United States (CONUS)

Geographic Locations of Cohorts Outside CONUS (OCONUS)

$^1$ Numbers reflect active and IRB-pending PreVAIL kids enrollment sites in each state
PreVAIL kids Prospective and Retrospective Enrollments – October 2021

**Prospective Enrollment Summary**

- 4,587 enrolled as of October, 2021
- 3,653 Participant Target

**Legend**

- Actual Accruals trendline
- Target Accruals trendline

**Retrospective Enrollment Summary**

- Chiu: 1,286
- Burns: 3,206
- Annapragada: 27,971
- Salazar: 41
- Manlhiot: 1,271
PreVAIL kids-associated Publications and Presentations

**BY THE NUMBERS**

30
Published articles from the cohort

6
Presentations by PIs
Safe Return to School Diagnostic Testing
NIH-funded COVID-19 testing initiative aims to safely return children to in-person school

NIH COVID-19 testing initiative funds additional research projects to safely return children to in-person school
Geographic Distribution of Projects

PHASE I SITES
- Yakima Valley, WA
- Salt Lake City, UT
- HI (Multiple Cities)
- Los Angeles, CA
- San Diego, CA

PHASE II SITES
- NB (Multiple Counties)
- Madison, WI
- Rochester, NY
- Kansas City, MO
- St. Louis, MO
- Iredell County, NC
- MD (Multiple Counties)
- Durham, NC
- Miami, FL
- AZ (Multiple Cities)
- Shiprock NM
Return to School Diagnostic Testing Initiative

Goals

• Provide evidence for the effectiveness, sustainability, and scalability of COVID-19 testing approaches and mitigation strategies in school settings in underserved and vulnerable communities

• Provide information to understand the social, behavioral, and ethical implications of implementation of COVID-19 testing within identified communities

Approach

• Emphasis on children and adolescents below the age eligible for vaccination via Emergency Use Authorization (age 12+) and all school personnel

• Advance methods to integrate testing in return to or maintenance of in-person instruction
Investigator Workshop

Goals

• Bring together RADX-UP Return to School Phase I and Phase II awardees/investigative teams and others conducting school-based research on COVID-19 diagnostic testing to learn from each other and define the current state of their research projects supporting the safe return of children to in-person school

Videocast and Executive Summary posted on RADx-UP website
Preliminary Results

- COVID-19 testing is feasible and acceptable in the school setting across a range of populations and settings

- After implementing a testing program for students and staff after SARS-CoV-2 exposure, there was increased access to testing (37% increase) and the number of days in quarantine for students/staff decreased overall (28% moved from >10 days to <10 days)

- Low rates of within-school transmission were observed with COVID-19 testing and mitigation strategies in place
  *Note: Data gathered before Delta variant became dominant

- Both surveillance and post-exposure testing are important strategies to return and keep students in school, especially for those children with disabilities who may not be able to effectively use other mitigation methods
Building the Evidence for Safe Return to School During the COVID-19 Pandemic
Alison N. Cernich, PhD; Sonia Lee, PhD; Diana W. Bianchi, MD
RECOVER
Post-Acute Sequelae of SARS-CoV-2 Infection (PASC)

These children had COVID-19. Now they have long-haul symptoms.
Their medical scans and blood tests are normal. So why are they still feeling sick months after infection?

By Ariana Eunjung Cha, The Washington Post
March 18, 2021
RECOVER: Researching COVID to Enhance Recovery

We're building a nationwide study population to support research on the long-term effects of COVID-19. Join the search for answers.

LEARN MORE

RECOVER Website – www.recovercovid.org
NIH builds large nationwide study population of tens of thousands to support research on long-term effects of COVID-19

The National Institutes of Health awarded nearly $470 million to build a national study population of diverse research volunteers and support large-scale studies on the long-term effects of COVID-19. The NIH REsearching COVID to Enhance Recovery (RECOVER) Initiative made the parent award to New York University (NYU) Langone Health, New York City, which will make multiple sub-awards to more than 100 researchers at more than 30 institutions and serves as the RECOVER Clinical Science Core. This major new award to NYU Langone supports new studies of COVID-19 survivors and leverages existing long-running large cohort studies with an expansion of their research focus. This combined population of research participants from new and existing cohorts, called a meta-cohort, will comprise the RECOVER Cohort. This funding was supported by the American Rescue Plan.

RECOVER – Research Questions

• What are the clinical spectrum of and biology underlying recovery from acute SARS-CoV-2 infection over time?

• For those patients who do not fully recover, what is the incidence/prevalence, natural history, clinical spectrum, and underlying biology of this condition?

• Are there distinct phenotypes of patients who have prolonged symptoms or other sequelae including risk and resiliency factors?

• Does SARS-CoV-2 infection initiate or promote the pathogenesis of conditions or findings that evolve over time to cause organ dysfunction or increase the risk of developing other disorders?