Welcome! We will begin shortly.

“Update 2022: COVID-19, Multisystem Inflammatory Syndrome in Children, and the Heart”

Jane W. Newburger, M.D., M.P.H.
Associate Cardiologist-in-Chief for Academic Affairs, Boston Children’s Hospital;
Commonwealth Professor of Pediatrics, Harvard Medical School

Dongngan Truong, M.D., M.S.
Associate Professor of Pediatrics, The University of Utah and Primary Children’s Hospital

Introduction by Victoria Pemberton, M.S., RNS, CCRC, Program Officer, NHLBI/PHN
Upcoming Q & A Session

Please send us your questions via the Q & A pod directed to All Panelists

You may use the Chat pod for general commentary or to request technical assistance
“Update 2022: COVID-19, Multisystem Inflammatory Syndrome in Children, and the Heart”

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Prevention SIG Webinar Series
January 26, 2022

Update 2022: COVID-19, the Multisystem Inflammatory Syndrome in Children, and the Heart

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Boston Children’s Hospital

Dongngan T. Truong, M.D., M.S.C.I.
University of Utah and Primary Children’s Hospital
Disclosures and Conflicts of Interest (COI)

- Jane Newburger:
  - Grant Support: NIH, CDC
  - Co-PI for Planned NHLBI Pediatric Heart Network-Pfizer Partnership to Study Vaccine-Associated Myocarditis after COVID-19 Vaccine
  - Chair, Independent Events Adjudication Committees for trials sponsored by Bristol-Myers Squibb, Pfizer, Novartis
  - Member, Steering Committee, Enoble Trial (sponsor: Daiichi Sankyo)

- Dongngan Truong:
  - Grant Support: NIH
  - Co-PI for Planned NHLBI Pediatric Heart Network-Pfizer Partnership to Study Vaccine-Associated Myocarditis after COVID-19 Vaccine
Learning Objectives

• Review the epidemiology of COVID-19 and MIS-C in children.
• Identify the cardiovascular manifestations and management of MIS-C.
• Review the NHLBI MUSIC study.
• Review the current understanding of myocarditis temporally related to COVID-19 vaccination
WHO MAP JAN 7, 2022

- ~299 million cases
- ~5.5 million deaths
- ~9 billion vaccine doses administered
Burden of COVID-19 Among Children (12/30/21)

• Positive US cases in children: ~7.9 million

• COVID-19 is much milder in children than adults:
  • 17% of confirmed cases since pandemic onset
  • 18% of confirmed cases in last week.
  • 10,484 cases per 100,000 children in the population
  • 0.1% - 1.6% of children with COVID-19 are hospitalized

• Mortality rate in children 0.00% to < 0.02% in state reporting
Original Investigation | Pediatrics

Underlying Medical Conditions Associated With Severe COVID-19 Illness Among Children

Lyudmyla Kompaniayets, PhD; Nickolas T. Agathis, MD; Jennifer M. Nelson, MD; Leigh Ellyn Preston, DrPH; Jean Y. Ko, PhD; Brook Belay, MD; Audrey F. Pennington, PhD; Melissa L. Danielson, MSPH; Carla L. DeSisto, PhD; Jennifer R. Chevinsky, MD; Lyna Z. Schieber, DPhil, MD; Hussain Yusuf, MD; James Baggs, PhD; William R. MacKenzie, MD; Karen K. Wong, MD; Tegan K. Boehmer, PhD; Adi V. Gundlapalli, MD, PhD; Alyson B. Goodman, MD

Abstract

IMPORTANCE Information on underlying conditions and severe COVID-19 illness among children is limited.

OBJECTIVE To examine the risk of severe COVID-19 illness among children associated with underlying medical conditions and medical complexity.

Key Points

Question Among children with a COVID-19 diagnosis, what conditions are common, and which are associated with severe COVID-19 illness?

Findings In this cross-sectional study of 43,665 patients aged 18 years or...
**Figure 2. Association Between Medical Complexity and Risk of Hospitalization or Severe Illness When Hospitalized in the Sample**

*Kompaniyets et al, JAMA Open, 2021*

**A** Hospitalization

<table>
<thead>
<tr>
<th>Chronic disease</th>
<th>Risk ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No chronic disease</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>Noncomplex chronic disease</td>
<td>2.91 (2.63-3.23)</td>
</tr>
<tr>
<td>Complex chronic disease</td>
<td>7.86 (6.91-8.95)</td>
</tr>
</tbody>
</table>

**B** Severe illness when hospitalized

<table>
<thead>
<tr>
<th>Chronic disease</th>
<th>Risk ratio (95% CI)</th>
</tr>
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<tbody>
<tr>
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<td>Complex chronic disease</td>
<td>2.86 (2.47-3.32)</td>
</tr>
</tbody>
</table>
The Emergence of a New Syndrome in Children

March 2020

April-May 2020 – Worldwide Alert

April 2020

Boroughs of New York
CDC Case Definition for Multisystem Inflammatory Syndrome in Children Associated with COVID-19 (MIS-C)

- **Age** <21 years
- **Fever** ≥38°C for ≥24 hours
- Laboratory evidence of inflammation
- Evidence of clinically severe illness requiring hospitalization, with multisystem (≥2) organ involvement based on clinical judgment from record review, discharge dx, lab or diagnostic tests.
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms
- No plausible alternative explanation.
TIMING OF MIS-C IN RELATION TO COVID-19

Laboratory Confirmed COVID-19 cases, London

Dr. Mike Levin, Imperial College London
TIMING OF MIS-C IN RELATION TO COVID-19

MIS-C IN NY

MIS-C IN USA

Temporal Relationship between MIS-C and Covid-19 Activity in Persons <21 Yr of Age
MIS-C CDC Update, 01/03/22

- Number of cases: 6,431
- Total deaths: 55 (0.9%)
- Percent male: 61%
- + test for SARS-CoV-2: 98%
- Half between ages 5 -13 years

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hispanic/Latino</td>
<td>27.4%</td>
</tr>
<tr>
<td>Black Non-Hispanic</td>
<td>31.9%</td>
</tr>
<tr>
<td>White Non-Hispanic</td>
<td>32.5%</td>
</tr>
<tr>
<td>Other Non-Hispanic</td>
<td>3.5%</td>
</tr>
<tr>
<td>Asian Non-Hispanic</td>
<td>2.6%</td>
</tr>
<tr>
<td>Multiple Races, Non-Hispanic</td>
<td>&lt;1.0%</td>
</tr>
<tr>
<td>American Indian/Alaskan Native</td>
<td>&lt;1.0%</td>
</tr>
<tr>
<td>Native Hawaiian/Pacific Islander</td>
<td>&lt;1.0%</td>
</tr>
</tbody>
</table>
• Population incidence: 5.1 per 1 million person-months

• Compared with White persons, higher rate in
  • Black persons: aIRR = 9.26
  • Hispanic/Latino: aIRR = 8.92
  • Asian/Pacific Islander: aIRR = 2.94
• Population MIS-C incidence: 5.1 per 1 million person-months

• Compared with White persons, higher rate in
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  • Asian/Pacific Islander: aIRR = 2.94

• MIS-C incidence: 316 per million SARS-CoV-2 infections

• Compared with White persons, higher rate in
  • Black persons: aIRR = 5.62
  • Hispanic/Latino: aIRR = 4.26
  • Asian/Pacific Islander: aIRR = 2.88
Multisystem Inflammatory Syndrome in U.S. Children and Adolescents


Published online June 29, 2020
### Treatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous Immunoglobulin (IVlg)</td>
<td>77%</td>
</tr>
<tr>
<td>Second dose IVlg</td>
<td>21%</td>
</tr>
<tr>
<td>Systemic Steroids</td>
<td>49%</td>
</tr>
<tr>
<td>IL-6 Inhibitors (tocilizumab and siltuximab)</td>
<td>8%</td>
</tr>
<tr>
<td>IL-1Ra Inhibitor (anakinra)</td>
<td>13%</td>
</tr>
<tr>
<td>Systemic Anticoagulation</td>
<td>47%</td>
</tr>
</tbody>
</table>

### Highest Level of Care

<table>
<thead>
<tr>
<th>Level</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ward</td>
<td>20%</td>
</tr>
<tr>
<td>Intensive Care Unit</td>
<td>80%</td>
</tr>
<tr>
<td>Intensive Care Interventions</td>
<td></td>
</tr>
<tr>
<td>ECMO</td>
<td>4%</td>
</tr>
<tr>
<td>Mechanical Ventilation</td>
<td>20%</td>
</tr>
<tr>
<td>Vasoactive Support</td>
<td>48%</td>
</tr>
</tbody>
</table>

### Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Hospitalization</td>
<td>7 days</td>
</tr>
<tr>
<td>Still Hospitalized May 20, 2020</td>
<td>70%</td>
</tr>
<tr>
<td>Discharged Alive</td>
<td>70%</td>
</tr>
<tr>
<td>Died</td>
<td>2%</td>
</tr>
</tbody>
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## Symptoms Vary According to Age Group

<table>
<thead>
<tr>
<th>Symptom Category</th>
<th>0–5 Years (N=31)</th>
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<tr>
<td>Dermatologic or mucocutaneous</td>
<td>87.1</td>
<td>78.6</td>
<td>61.5</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>74.2</td>
<td>83.3</td>
<td>80.8</td>
</tr>
<tr>
<td>KD or atypical KD</td>
<td>48.4</td>
<td>42.9</td>
<td>11.5</td>
</tr>
<tr>
<td>Myocarditis</td>
<td>38.7</td>
<td>50.0</td>
<td>73.1</td>
</tr>
<tr>
<td>Neurologic</td>
<td>12.9</td>
<td>38.1</td>
<td>38.5</td>
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**Percent of Patients**

- **0 to 38.4**
- **38.5 to 46.2**
- **46.3 to 66.1**
- **66.2 to 79.0**
- **79.1 to 100**

*Dufort et al, NEJM, 2020*
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**Percent of Patients**

- 0 to 38.4
- 38.5 to 46.2
- 46.3 to 66.1
- 66.2 to 79.0
- 79.1 to 100

*Dufort et al, NEJM, 2020*
Non-Cardiovascular Involvement

- Gastrointestinal symptoms
- Hematologic symptoms
- Coagulopathy
- DVT/PE
- Mucocutaneous
- Respiratory symptoms
- Musculoskeletal
- Neurologic complications
- Guillain Barré
- ADEM
Cardiovascular Involvement

- Any cardiovascular involvement: 80%
- Elevated troponin: 50%
- BNP > 400: 73%
- LV ejection fraction < 55%: 38%
- Coronary aneurysms ≥ 2.5: 8%
- ECMO: 4%

Feldstein LR, NEJM, 2020
Multisystemic Inflammatory Syndrome in Children

Pathophysiology

- Cardiomyocyte Invasion
- Dysregulated Inflammatory Response
- Endothelial Injury and Hypercoagulability
- Microvascular Injury
- SARS CoV2 Infection

Clinical Manifestation

- Multisystem Involvement:
  1. Shock/Cardiac
  2. Gastrointestinal
  3. Coagulopathy
  4. Lung (mild)
  5. Renal
  6. Mucocutaneous

Cardiac Manifestation

- Sudden Cardiac Death
- Elevated C-reactive Protein/Inflammatory Markers
- Elevated BNP and Troponin

- Fever

- Ventricular Dysfunction

- Coronary Dilation and Aneurysms

- EKG and Conduction Abnormalities

Alsaied T, et al, Circulation, 2021
Valverde, n=286 (Europe/55 centers)
Feldstein, n=186 (US/26 States)
Dufort, n=99 (New York Department of Health)
Whitaker n=58 (UK)
Belhadjer n=35 (Switzerland/France)
Kaushik n=33 (NYC)
Grimaud n=20 (France)
Toubiana n=21 (France)
Cheung n=17 (NYC)
Verdoni n=10 (Italy)
Riphagen n=8 (UK)

Alsaied T, et al, Circulation, 2020
Resolution of decreased left ventricular ejection fraction

172/503 pts, 34.2%

- EF <35%
- EF 35% to <45%
- EF 45% to <55%

Median, 4 (IQR, 3-8) days of observation
Log-rank P = .88

Feldstein et al, JAMA, 2021
Diastolic Dysfunction

- 28 patients with MIS-C, 20 healthy control, 20 Kawasaki disease patients
- Diastolic dysfunction was found in all MIS-C patients, even those with normal systolic function
- Patients with myocardial injury (elevated troponin) were more affected
- Diastolic dysfunction persisted after normalization systolic function

Matsubara et al. JACC, 2020
Resolution of coronary artery aneurysms

57/424 pts, 13.4%

Median, 6 (IQR, 3-18) days of observation

Feldstein et al, JAMA, 2021
Cardiac MRI after MIS-C (20 patients)

• Mean time to CMR 20 days (range 11-29 days)

• Myocardial edema in 10 patients (50%)
  • Global increase T2 weighted imaging most common (n=6), followed basal septal segments (n=3)
  • Global MR strain analysis demonstrated impaired systolic strain indices in all pts

• Myocardial scar with late gadolinium enhancement in 1 patient (5%)

• EF and strain did not correlate with persistent myocardial edema, scarring, age or timing presentation
Arrhythmias and ECG changes

- 7-60% patients with MIS-C
- ECG changes
  - Non-specific ST segment changes
  - Prolonged QTc interval
- Atrial arrhythmias
  - Atrial ectopy
  - Atrial fibrillation
- Ventricular arrhythmias
  - Ventricular ectopy
  - NSVT/VT, some requiring resuscitation and ECMO
- AV block
  - 1st, 2nd, 3rd degree AV block
  - Often preceded by PR prolongation
How do we manage MIS-C?
French consortium studied 111 children with MIS-C
Propensity score analysis for children treated with IVIG versus IVIG + Steroids
Primary outcome was fever at 48 hours
Secondary outcomes: second line treatments, hemodynamic support, LVEF and PICU stay
IVIG + Steroids led to improved outcomes
• French consortium studied 111 children with MIS-C
• Propensity score analysis for children treated with IVIG versus IVIG + Steroids
• Primary outcome was fever at 48 hours
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• IVIG + Steroids led to improved outcomes

| Table 2. Primary and Secondary Analyses in the Propensity Score-Matched Cohorts |
|---|---|---|---|---|
| Outcomes | After propensity score matching |
| | No. (%) | Absolute risk difference between groups (95% CI) [reference: IVIG alone] | Odds ratio (95% CI) [reference: IVIG alone] |
| Primary outcome | | | |
| Treatment failure<sup>a</sup> | 3 (9) | IVIG and methylprednisolone (n = 32) | 0.25 (0.09 to 0.70) |
| | 24 (38) | IVIG alone (n = 64) | -0.28 (-0.48 to -0.08) |
| | | | 0.008 |
| Secondary outcomes | | | |
| Second-line treatment<sup>b</sup> | 3 (9) | IVIG and methylprednisolone (n = 32) | 0.19 (0.06 to 0.61) |
| | 20 (31) | IVIG alone (n = 64) | -0.02 (-0.40 to 0.04) |
| | | | 0.004 |
| Hemodynamic support<sup>c</sup> | 2 (6) | IVIG and methylprednisolone (n = 32) | 0.21 (0.06 to 0.76) |
| | 15 (23) | IVIG alone (n = 64) | -0.17 (-0.34 to -0.004) |
| | | | 0.01 |
| LVEF <55%<sup>c</sup> | 2/12 (17) | IVIG and methylprednisolone (n = 32) | 0.20 (0.06 to 0.66) |
| | 14/40 (35) | IVIG alone (n = 64) | -0.18 (-0.35 to -0.01) |
| | | | 0.007 |
| Duration of PICU stay, median (IQR), d | 4 (2 to 5) | IVIG and methylprednisolone (n = 32) | Reduction of days: -2.4 (-4.0 to -0.7) |
| | 6 (4 to 8.5) | IVIG alone (n = 64) | |
| | | | 0.005 |
IVIG + glucocorticoids as initial treatment on Day 0 was associated with
- less cardiovascular dysfunction 2 or more days later; and
- less adjunctive therapies 1 or more days later

“We found no evidence that recovery from MIS-C differed after primary treatment with IVIG alone, IVIG plus glucocorticoids, or glucocorticoids alone.”
Cohort Differences

• Inclusion criteria: OC-19 participants were adjudicated and met CDC definition. BATS included suspected cases.

• OC-19 patients were much sicker (47% on vasopressors, 41% with LV dysfunction, 18% on mechanical ventilation) than BATS patients (12% on vasopressors, 12% with LV dysfunction, 1.5% on mechanical ventilation).

• Different study endpoints
  • CO-19 – LV dysfunction or shock
  • BATS – composite of inotropic support or mechanical ventilation or death OR reduction in disease severity score
Guidelines
First tier treatments in hospitalized patients:
  - High-dose IVIG (2 gm/kg based upon ideal body weight to max 100 gm) and IV methylprednisolone 1-2mg/kg/day.
    - If LV dysfunction, IVIG may be given as 1 gm/kg daily over 2 days.

Refractory MIS-C despite IVIG and low-moderate dose glucocorticoids:
  - IV pulse dose steroids (10-30 mg/kg/day) for non-responders, especially if they require high-dose or multiple inotropes and/or vasopressors.
  - Anakinra (4 mg/kg/day IV or SC) for treatment of MIS-C refractory to IVIG and steroids, with features of MAS, or with contraindications to long-term steroids.
  - Infliximab (5-10 mg/kg/day IV X 1 dose) may be considered an alternative biologic agent to anakinra or in patients with contraindications to long-term use of steroids.

Serial laboratory testing and cardiac assessment guide immunomodulatory treatment and tapering
Patients often require a 2-3-week taper of immunomodulatory medications
WHO issues guidelines on the treatment of children with multisystem inflammatory syndrome associated with COVID-19

23 November 2021 | News release | Geneva, Switzerland | Reading time: Less than a minute (171 words)


MIS-C is a rare but serious condition where children with COVID-19 develop inflammation affecting different organs of the body. Children with this condition need specialized care, and may need to be admitted to intensive care.

Conditional recommendation for steroids.
Level of evidence – very low

Media Contacts

WHO Media inquiries
Telephone: +41 22 791 2222
Email: mediaenquiries@who.int
Cardiac Management of MIS-C
Alsaied et al. Circulation, 2021

• Baseline Cardiac Testing: ECG, BNP, troponin, echo

• During Active Disease Course:
  • EKG q 1-2 days
  • Trend BNP and troponin daily if abnormal
  • Repeat echo as clinically indicated

• Outpatient F/U
  • Echo and ECG at 1-2 weeks, 4-6 weeks
  • Continue to follow BNP and troponin if not normalized
  • Holter monitors for patients with EKG/conduction abnormalities
Cardiac Management of MIS-C
Alsaied et al. Circulation, 2021

- For patients with history of LV dysfunction
  - Echo/EKG at one year or sooner
  - Exercise restrictions considered for 3-6 months
  - MRI can be considered in acute phase or at 3-4 mo

- For patients with coronary artery aneurysms
  - Follow in accordance with KD guidelines
  - CT may be indicated if coronaries can not be well imaged in larger patients in whom aneurysms are suspected.
"An ounce of prevention is worth a pound of cure."
Benjamin Franklin
Multisystem Inflammatory Syndrome in Children by COVID-19 Vaccination Status of Adolescents in France

<table>
<thead>
<tr>
<th>COVID-19 vaccination status(^a)</th>
<th>No. of patients with MIS-C (N = 33)</th>
<th>Hazard ratio (95% CI)(^b)</th>
<th>(P) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unvaccinated</td>
<td>26</td>
<td>1 [Reference]</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>One dose</td>
<td>7</td>
<td>0.09 (0.04-0.21)</td>
<td></td>
</tr>
</tbody>
</table>

Sensitivity analysis: fully vaccinated ≥14 d after first dose\(^c\)

| Unvaccinated                       | 28                                | 1 [Reference]               | <.001       |
| One dose                           | 5                                 | 0.07 (0.03-0.18)            |             |

Sensitivity analysis: fully vaccinated ≥28 d after first dose\(^c\)

| Unvaccinated                       | 31                                | 1 [Reference]               | <.001       |
| One dose                           | 2                                 | 0.03 (0.01-0.12)            |             |

Sensitivity analysis: fully vaccinated ≥42 d after first dose\(^c\)

| Unvaccinated                       | 31                                | 1 [Reference]               | <.001       |
| One dose                           | 2                                 | 0.04 (0.01-0.16)            |             |

Levy et al, JAMA, 2021
Effectiveness of BNT162b2 (Pfizer-BioNTech) mRNA Vaccination Against Multisystem Inflammatory Syndrome in Children Among Persons Aged 12–18 Years — United States, July–December 2021

Laura D. Zambrano, PhD1,2,*; Margaret M. Newhams, MPH2,4; Samantha M. Olson, MPH1; Natasha B. Halasa, MD3; Ashley M. Price, MPH1; Julie A. Boom, MD4; Leila C. Sahni, PhD4; Satoshi Kamidani, MD5; Keiko M. Tarquinio, MD6; Aline B. Maddux, MD7; Sabrina M. Heidemann, MD8; Samina S. Bhumbra, MD9; Katherine E. Bline, MD10; Ryan A. Nozfiger, MD11; Charlotte V. Hobbs, MD12; Tamara T. Bradford, MD13; Natalie Z. Cvijanovich, MD14; Katherine Irby, MD15; Elizabeth H. Mack, MD16; Melissa L. Cullimore, MD17; Pia S. Pannaraj, MD18; Michele Kong, MD19; Tracie C. Walker, MD20; Shira J. Gertz, MD21; Kelly N. Michelson, MD22; Melissa A. Cameron, MD23; Kathleen Chiotos, MD24; Mia Maamari, MD25; Jennifer E. Schuster, MD26; Amber O. Orzel, MPH2; Manish M. Patel, MD1; Angela P. Campbell, MD1,3; Adrienne G. Randolph, MD2,27,4; Overcoming COVID-19 Investigators

1Centers for Disease Control and Prevention, Atlanta, Georgia
2Georgia Department of Public Health, Atlanta, Georgia
3University of Kentucky, Lexington, Kentucky
4University of North Carolina, Chapel Hill, North Carolina
5Washington University School of Medicine, St. Louis, Missouri
6University of Texas Southwestern Medical Center, Dallas, Texas
7Mayo Clinic, Rochester, Minnesota
8University of Michigan, Ann Arbor, Michigan
9Johns Hopkins Children’s Center, Baltimore, Maryland
10University of Rochester School of Medicine and Dentistry, Rochester, New York
11Children’s Hospital of Philadelphia, Philadelphia, Pennsylvania
12University of Alabama at Birmingham, Birmingham, Alabama
13University of Medicine and Dentistry of New Jersey, Newark, New Jersey
14University of California, San Francisco, California
15University of Missouri, Columbia, Missouri
16University of California, Los Angeles, Los Angeles, California
17Wright State University, Dayton, Ohio
18University of Mississippi Medical Center, Jackson, Mississippi
19Children’s Hospital of Wisconsin, Milwaukee, Wisconsin
20East Carolina University, Greenville, North Carolina
21Massachusetts General Hospital, Boston, Massachusetts
22Texas Children’s Hospital, Houston, Texas
23Children’s Hospital of Philadelphia, Pennsylvania
24University of Kansas Medical Center, Kansas City, Kansas
25University of Illinois at Chicago, Chicago, Illinois
26University of California, San Francisco, California
27University of North Carolina, Chapel Hill, North Carolina
# TABLE 1. (Continued) Characteristics of multisystem inflammatory syndrome in children case-patients and controls aged 12–18 years — 24 pediatric hospitals, 20 U.S. states,* July 1–December 9, 2021

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (N = 283)</th>
<th>MIS-C case-patients (n = 102)</th>
<th>Controls (n = 181)</th>
<th>p-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Laboratory test results††</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RT-PCR or antigen-positive, antibody not performed</td>
<td>11 (3.9)</td>
<td>11 (10.8)</td>
<td>0 (—)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>RT-PCR or antigen-positive, antibody-positive</td>
<td>12 (4.2)</td>
<td>12 (11.8)</td>
<td>0 (—)</td>
<td></td>
</tr>
<tr>
<td>Antibody positive only</td>
<td>76 (26.9)</td>
<td>76 (74.5)</td>
<td>0 (—)</td>
<td></td>
</tr>
<tr>
<td>Pre-admission results available only</td>
<td>3 (1.1)</td>
<td>3 (2.9)</td>
<td>0 (—)</td>
<td></td>
</tr>
<tr>
<td><strong>Fully vaccinated§§</strong></td>
<td>70 (24.7)</td>
<td>5 (4.9)</td>
<td>65 (35.9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Median interval from receipt of second vaccine dose to reference hospitalization date, days (IQR)¶¶</td>
<td>84 (51–122)</td>
<td>63 (48–89)</td>
<td>88 (52–122)</td>
<td>0.37</td>
</tr>
</tbody>
</table>

* Data from the Centers for Disease Control and Prevention’s COVID-19 Vaccine Safety and Effectiveness Surveillance System, which includes information from 24 pediatric hospitals in 20 U.S. states.

†† Based on data available as of December 9, 2021.

§§ Includes both doses of the Moderna or Pfizer/BioNTech vaccine.

¶¶ IQR = interquartile range.
TABLE 1. (Continued) Characteristics of multisystem inflammatory syndrome in children case-patients and controls aged 12–18 years — 24 pediatric hospitals, 20 U.S. states,* July 1–December 9, 2021

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (N = 283)</th>
<th>MIS-C case-patients (n = 102)</th>
<th>Controls (n = 181)</th>
<th>p-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory test results**</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RT-PCR or antigen-positive, antibody not performed</td>
<td>11 (3.9)</td>
<td>11 (10.8)</td>
<td>0 (—)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>RT-PCR or antigen-positive, antibody-positive</td>
<td>12 (4.2)</td>
<td>12 (11.8)</td>
<td>0 (—)</td>
<td></td>
</tr>
<tr>
<td>Antibody positive only</td>
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<td>76 (74.5)</td>
<td>0 (—)</td>
<td></td>
</tr>
<tr>
<td>Pre-admission results available only</td>
<td>3 (1.1)</td>
<td>3 (2.9)</td>
<td>0 (—)</td>
<td></td>
</tr>
<tr>
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<td>70 (24.7)</td>
<td>5 (4.9)</td>
<td>65 (35.9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Median interval from receipt of second vaccine dose to reference hospitalization date, days (IQR)**</td>
<td>84 (51–122)</td>
<td>63 (48–89)</td>
<td>88 (52–122)</td>
<td>0.37</td>
</tr>
</tbody>
</table>
TABLE 3. Effectiveness* of 2 doses of Pfizer-BioNTech vaccine against multisystem inflammatory syndrome in children among hospitalized patients aged 12–18 years — 24 pediatric hospitals, 20 U.S. states, † July–December 2021

<table>
<thead>
<tr>
<th>Control groups</th>
<th>MIS-C case patients</th>
<th>Control patients</th>
<th>Adjusted VE, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All controls</td>
<td>5/102 (4.9)</td>
<td>65/181 (35.9)</td>
<td>91 (78–97)</td>
</tr>
<tr>
<td>Test-negative</td>
<td>5/102 (4.9)</td>
<td>34/90 (37.8)</td>
<td>92 (77–97)</td>
</tr>
<tr>
<td>Syndrome-negative</td>
<td>5/102 (4.9)</td>
<td>31/91 (34.1)</td>
<td>89 (70–96)</td>
</tr>
<tr>
<td><strong>Sensitivity analysis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MIS-C case patients with serologic evidence present†</td>
<td>5/88 (5.7)</td>
<td>61/161 (37.9)</td>
<td>90 (75–96)</td>
</tr>
</tbody>
</table>

Zambrano et al, MMWR, 2022
Return to Play after Coronavirus Infection

- Return to play guidelines have been released by the AAP, ACC, and other organizations
  - Graduated return to play protocols
- Reasonable to treat pediatric patients who have had MIS-C as if they had myocarditis.
- If cardiac abnormalities acutely, patient should be restricted for 3-6 months
- Only resume activities when/if ECG, echo, Holter, CPET, CMR have normalized.
MIS-C
What We Don’t Know About the Heart

• To date, there are limited data on:
  • MIS-C-associated coronary aneurysms or heart function using standardized assessments in Core Labs (echo, MRI)
  • Long-term cardiac outcomes
  • Association of heart complications with clinical and laboratory risk factors or treatments
NHLBI’s MUSIC Study

Long-Term Outcomes after the Multisystem Inflammatory Syndrome In Children
Overarching Goals

• To characterize the occurrence and time course of
  • Cardiac outcomes: coronary abnormalities, ventricular dysfunction, and arrhythmias/conduction disturbances
  • Systemic organ dysfunction
  • Inflammatory response
  • Major medical events

• To develop clinical risk stratification models
• To provide phenotyping for correlation with basic/translational mechanistic studies
Study Design

- Observational cohort study
- Research funding available for echoes and CMRs not ordered by primary provider.
- Annual medical history forms for up to 5 years.
- Adjudication Committee to review MIS-C diagnoses (specialists in Rheumatology, ID, and Cardiology).
Recruitment

• Enrollment of at least 600 subjects

• Participants can be enrolled any time in the first year after MIS-C onset

• Prospective cases can be enrolled as early as during hospitalization

• For retrospective cases or those in whom consent could not be obtained during hospitalization, we will send a letter and opt out card (English or Spanish), then after 2 weeks, phone, text, or email to discuss study

• Written consent and assent in-person OR virtual

• Waiver of consent for inclusion of routine clinical data if:
  ▪ 3 unsuccessful attempts to reach patient/family
  ▪ Death before consent can be obtained
NHLBI’s MUSIC Study

Long-Term Outcomes after the Multisystem Inflammatory Syndrome In Children
Primary Outcomes

• Worst-ever LVEF by 6-month visit
• Maximum z score of the proximal LAD or RCA (zMax) by 6-month visit
Secondary Cardiac Outcomes

1. Coronary Outcomes
   a. Proximal LAD or RCA z score of ≥2.5 on any echocardiogram
   b. Occurrence of aneurysms by Japanese Ministry of Health criteria
   c. Individual z scores for LMCA, RCA and LAD

2. Ventricular Function Outcomes
   a. LV size and function (LVEDV z score, LVEF, LVSF)
   b. % with LVEF<55%, and with LVEF 45-54%, 35-44%, and <35% on any echo.
   c. LV strain (global circumferential and longitudinal)
   d. Qualitative assessment of RV systolic function and RV strain (global longitudinal)
   e. LV diastolic function, i.e., tissue Doppler imaging and mitral valve (MV) inflow

3. Valve regurgitation: presence and degree of mitral and aortic regurgitation

4. Presence and size of pericardial effusion

5. Arrhythmias and conduction system disturbances

6. MRI outcomes of LVEF, RVEF, valvar regurgitation, % and distribution of LGE, abnormal T2-weighted imaging (%), elevated T2 (%), elevated native T1 (%), elevated ECV (%), coronary artery dilation/aneurysm (%), and overall interpretation of CMR as abnormal, equivocal, or normal
Secondary Non-Cardiac Outcomes

1. Other organ abnormalities by medical history: Immunologic, rheumatologic, renal, pulmonary, hematologic, gastrointestinal, dermatologic or neurologic
2. Laboratory markers of inflammation
3. Admission to ICU
4. Hospital length of stay
5. Symptom duration
6. Major medical events (e.g., stroke, renal replacement therapy, plasma exchange, ECMO, VAD)
7. Mortality
<table>
<thead>
<tr>
<th>Question</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has the participant experienced any symptoms, clinical findings, or diagnoses related to this organ system since the last visit?</td>
<td>Yes  No</td>
</tr>
<tr>
<td>If yes, has the participant been evaluated by a rheumatologist since the last visit?</td>
<td>Yes  No</td>
</tr>
<tr>
<td>Has the participant experienced any of the following symptoms, clinical findings, or diagnoses since the last visit? (choose all that apply)</td>
<td>Joint pain and/or swelling  Muscle weakness or muscle pain  Post-exertional fatigue  Systemic lupus/mixed connective tissue disease  Juvenile idiopathic arthritis/psoriatic arthritis  Vasculitis (such as Henoch-Schonlein Purpura)  Other, specify</td>
</tr>
<tr>
<td>If joint pain or swelling, how many joints were involved (choose best answer; please note that each joint is counted separately. For example, if both the right and left shoulder joints are involved, that would count as 2 joints)?</td>
<td>&lt; 5 joints  5 or more joints</td>
</tr>
<tr>
<td>If joint pain or swelling, was there medical treatment?</td>
<td>Yes  No</td>
</tr>
<tr>
<td>What medications were used for joint pain or swelling (choose all that apply)</td>
<td></td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>□ NSAIDS</td>
<td></td>
</tr>
<tr>
<td>□ Oral steroids</td>
<td></td>
</tr>
<tr>
<td>□ Steroid injection</td>
<td></td>
</tr>
<tr>
<td>□ Methotrexate</td>
<td></td>
</tr>
<tr>
<td>□ Infliximab (Remicade), Etanercept (Enbrel)</td>
<td></td>
</tr>
<tr>
<td>□ Adalimumab (Humira)</td>
<td></td>
</tr>
<tr>
<td>□ Tocilizumab (Actemra)</td>
<td></td>
</tr>
<tr>
<td>□ Other</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other medication used for joint pain or swelling:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other rheumatologic condition, specify</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>
## Neurologic

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has the participant experienced any symptoms, clinical findings, or diagnoses related to this organ system since the last visit?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Has the participant been evaluated by a neurologist since the last visit?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Has the participant experienced any of the following symptoms, clinical findings, or diagnoses since the last visit (choose all that apply)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Headaches frequent or severe enough to impact school attendance or activities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Seizures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Cerebrovascular accident (TIA or stroke)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Choreaathetoid movements</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Coma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Decreased vision</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Decreased hearing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Decreased sense of taste</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Decreased sense of smell</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Difficulty concentrating</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ &quot;Mental slowness&quot; or &quot;COVID fog&quot;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Limb numbness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Limb paresthesia/tingling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Iritis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Uveitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Ataxia (or loss of balance or accuracy of reach)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Change in mood</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Guillain-Barre</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Limb weakness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Other</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>If cerebrovascular accident (TIA or stroke), what type (choose all that apply)?</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Transient ischemic attack (TIA)</td>
</tr>
<tr>
<td>□ Ischemic stroke</td>
</tr>
<tr>
<td>□ Hemorrhagic stroke</td>
</tr>
<tr>
<td>□ Mixed ischemic and hemorrhagic</td>
</tr>
<tr>
<td>□ Unknown type</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>If limb weakness, please specify if</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Unilateral</td>
</tr>
<tr>
<td>□ Bilateral</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other neurologic condition, please specify</th>
</tr>
</thead>
</table>
Core Laboratories

- Echo Core Lab
  - Kevin Friedman, MD, PI

- MRI Core Lab
  - Michael Taylor, MD, PI
  - Andrew Powell, MD, Co-PI

- Biorepository
  - Mark Russell, MD
<table>
<thead>
<tr>
<th>Variable</th>
<th>Day 1</th>
<th>Discharge</th>
<th>2 wks</th>
<th>6 wks</th>
<th>3 mo</th>
<th>6 mo</th>
<th>Years 1-5</th>
</tr>
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<tbody>
<tr>
<td>Demographics</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Medical History</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>PROMIS Global Health</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Echo</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X*</td>
<td>X**</td>
</tr>
<tr>
<td>EKG</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Cardiac MRI and ETT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X***</td>
</tr>
<tr>
<td>Clinical Labs</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X*</td>
<td></td>
</tr>
<tr>
<td>WGS, other research Labs</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

* ≥6-mo echo and labs optional if all earlier echoes normal; ** if abnormal echo at 6 months, repeat ≥ annually until 2 consecutive normal echoes; *** All with history mod-severe LV dysfunction by protocol; CMR Core Lab will read any CMR for any indication.
Informed Consent and Data Sharing

• Allows us to share clinical and genetic data broadly

• Allows Electronic Health Record review
Center Data Warehouses

• Benefits of using center data warehouses: decreased coordinator burden, increased accuracy, and analytics

• Paul Avillach (BCH) is conducting a pilot study of BCH and Utah data warehouses to analyze completeness of collection of data elements

• If successful, CDW extraction will extend to other MUSIC centers with data warehouses
STUDY UPDATE: Screening/Enrollment
MUSIC Demographics (1/14/2022)

% Children According to Race and Ethnicity

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>HISPANIC OR LATINO</td>
<td>26%</td>
</tr>
<tr>
<td>BLACK, NON-HISPANIC</td>
<td>26%</td>
</tr>
<tr>
<td>WHITE, NON-HISPANIC</td>
<td>30%</td>
</tr>
<tr>
<td>OTHER, NON-HISPANIC</td>
<td>9%</td>
</tr>
<tr>
<td>UNKNOWN</td>
<td>10%</td>
</tr>
</tbody>
</table>

*Race categories were non-exclusive

Male: 60%  Female: 40%

Years of Age:
- < 1: 1%
- 1-4: 18%
- 5-9: 34%
- 10-14: 29%
- 15-20: 13%

COVID MUSIC STUDY
Understanding MIS-C

NIH National Heart, Lung, and Blood Institute
Pediatric Heart Network
CORE LAB UPDATES

BIOREPOSITORY
SAMPLES RECEIVED

- 280 Child
  (192 blood, 88 saliva)
- 207 Mother
  (73 blood, 134 saliva)
- 84 Father
  (26 blood, 58 saliva)
- 50 complete trios

ECHO LAB

- 867 echos received
  (592 reviewed and finalized)
- Reminder to update echo
  form in REDCap when sent.

CMR LAB

- 85 CMRs received;
  73 reviewed
- Please use MUSIC ID
  number with visit identifier
during anonymization.
Summary

The MUSIC longitudinal cohort study will:

1. Contribute important new information on acute cardiac findings and long-term cardiac health status following MIS-C
2. Facilitate surveillance for abnormalities in other systemic organs and overall well-being
3. Provide a unique framework including phenotype for basic and translational research studies
4. Facilitate creation of a clinical care pathway for children with suspected or confirmed MIS-C
RECOVER Components: A Comprehensive and Complementary Approach

RECOVER Core Elements
- Clinical Science Core
- Data Resource Core
- Biorepository Core

Meta-Cohort Elements
- RECOVER Enrolling Cohorts
- EHR/Health Systems Studies
- Autopsy-Based Studies

Data Resource Elements
- Clinical
- Imaging
- Mobile and Digital Health
- EHR / Other Real-World Data
- Pathology
RECOVER Components: A Comprehensive and Complementary Approach

RECOVER Core Elements

Clinical Science Core  Data Resource Core  Biorepository Core

Meta-Cohort Elements

Data Resource Elements

Clinical  Imaging  Mobile and Digital Health  EHR / Other Real-World Data  Pathology

NIH National Heart, Lung, and Blood Institute
Myocarditis Temporally Related to COVID-19 Vaccination
COVID-19 Vaccine

• May 2020: Plans for Operation Warp Speed
• December 11, 2020: Emergency Use Authorization (EUA) for Pfizer-BioNTech COVID-19 mRNA vaccine for ≥16 years old
  • May 10, 2021: EUA for 12-15 year-olds
• April 2021: Cases of myocarditis in men <30 years old following Pfizer-BioNTech’s COVID-19 mRNA vaccine
COVID-19 Vaccine

• May 2020: Plans for Operation Warp Speed
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• May 10, 2021: EUA for 12-15 year-olds
• April 2021: Cases of myocarditis in men <30 years old following Pfizer-BioNTech’s COVID-19 vaccine
Symptomatic Acute Myocarditis in Seven Adolescents Following Pfizer-BioNTech COVID-19 Vaccination

Mayme Marshall, MD, Ian D. Ferguson, MD, Paul Lewis, MD, MPH, Preeti Jaggi, MD, Christina Gagliardo, MD, James Steward Collins, MD, Robin Shaughnessy, MD, Rachel Caron, BA, Cristina Fuss, MD, Kathleen Jo E. Corbin, MD, MHS, Leonard Emuren, MBBS, PhD, Erin Faherty, MD, E. Kevin Hall, MD, Cecilia Di Pentima, MD, MPH, Matthew E. Oste, MD, MPH, Elijah Paintsil, MD, Saira Siddiqui, MD, Donna M. Timchak, MD, Judith A. Guzman-Cottrill, DO

E-published June 4, 2021
What We Know

• Typically post mRNA vaccination
• Predominantly male
• Typically after 2\textsuperscript{nd} dose, within 7 days of vaccination
• Symptoms
  • Chest pain
  • SOB
  • Palpitations
  • Fatigue

• 18.7% ICU
• 1.4% Vasoactive support
• No ECMO or death
• 70% with ECG changes
• 19% LVEF <55%
• 77% had abnormal CMR
  • 99% Late gadolinium enhancement
  • 72% myocardial edema
• Hospital LOS: 2 days (1-10 days)
### Rare Event: VAERS Data

Reporting Rates of Myocarditis (per 1 million doses administered) after Pfizer-BioNTech COVID-19 vaccination, 7-day risk interval

<table>
<thead>
<tr>
<th>Age group</th>
<th>Males</th>
<th></th>
<th>Females</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dose 1</td>
<td>Dose 2</td>
<td>Dose 1</td>
<td>Dose 2</td>
</tr>
<tr>
<td>5–11 years</td>
<td>0.0</td>
<td>4.3</td>
<td>Not calculated†</td>
<td>2.0</td>
</tr>
<tr>
<td>12–15 years</td>
<td>4.8</td>
<td>45.7</td>
<td>1.0</td>
<td>3.8</td>
</tr>
<tr>
<td>16–17 years (included for reference)</td>
<td>6.1</td>
<td>70.2</td>
<td>0.0</td>
<td>7.6</td>
</tr>
</tbody>
</table>

37,810,998 total 1\textsuperscript{st} and 2\textsuperscript{nd} vaccine doses administered
In Conclusion

• Nearly 2 years after the start of the pandemic, we know a bit more about COVID-19 and MIS-C
  • Incidence
  • Some data on therapies
  • Short-term effects on the heart

• There are still many things we do not know
  • Risk factors
  • Best therapies
  • Long-term outcomes

• Vaccination appears to prevent MIS-C

• Myocarditis following COVID-19 vaccination is a rare event
  • Highest reporting risk in teen-age males
  • Mild clinical course; long-term outcomes needed
MUSIC Study Leadership Team

MUSIC Study Leaders
- Jane Newburger (BCH)
- Dongngan Truong (Primary Children’s)

MUSIC Small Working Group
- Audrey Dionne (BCH)
- Matthew Elias (CHOP)
- Brian McCrindle (Sick Kids)
- Matthew Oster (Emory)
- Lara Shekerdemian (TCH)

Echo Core Lab: Kevin Friedman
MRI Core Lab: Michael Taylor, Andrew Powell
Biorepository: Mark Russell
Lead Coordinators: David Garuba, Tonia Morrison

NHLBI: Gail D. Pearson, Vicki Pemberton
PHN Chair: Lynn Mahony
HealthCore
- Felicia Trachtenberg
- Julie Miller
- Kerri Hayes
- Amanda Marshall

- Adrienne Randolph
- Manish Patel
- Mary Beth Son (CARRA)
<table>
<thead>
<tr>
<th>Participating Centers (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boston Children’s</td>
</tr>
<tr>
<td>Atlanta</td>
</tr>
<tr>
<td>Lurie Children’s</td>
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<td>Nemours/duPont</td>
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<td>Duke</td>
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<td>Phoenix Children’s</td>
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Questions?

Thank You
Q & A Session

Please send us your questions via the Q & A pod directed to All Panelists
Thank You!

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