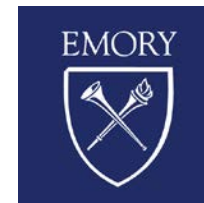


Management of Severe MIS-C and Pediatric COVID-19

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Disclosures

- Clinical investigator in Emory Children's Center Vaccine Research Center (ECC-VRC) and Vaccine Treatment and Evaluation Unit (VTEU)
 - Institution has received funds to conduct clinical research unrelated to this talk from BioFire Inc, GSK, Janssen, MedImmune, Micron, Merck, Moderna, Novavax, PaxVax, Pfizer, Regeneron, Sanofi-Pasteur
- Co-inventor of patented RSV vaccine technology unrelated to this talk, which has been licensed to Meissa Vaccines, Inc.

Management of Severe MIS-C

CDC MIS-C Case Definition



- An individual aged <21 years presenting with feverⁱ, laboratory evidence of inflammationⁱⁱ, and evidence of clinically severe illness requiring hospitalization, with multisystem (≥ 2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); **AND**
- No alternative plausible diagnoses; **AND**
- 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
 - ⁱFever $\geq 38.0^{\circ}\text{C}$ for ≥ 24 hours, or report of subjective fever lasting ≥ 24 hours
 - ⁱⁱIncluding, but not limited to one or more of the following: an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, d-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes and low albumin

Who is affected by MIS-C?

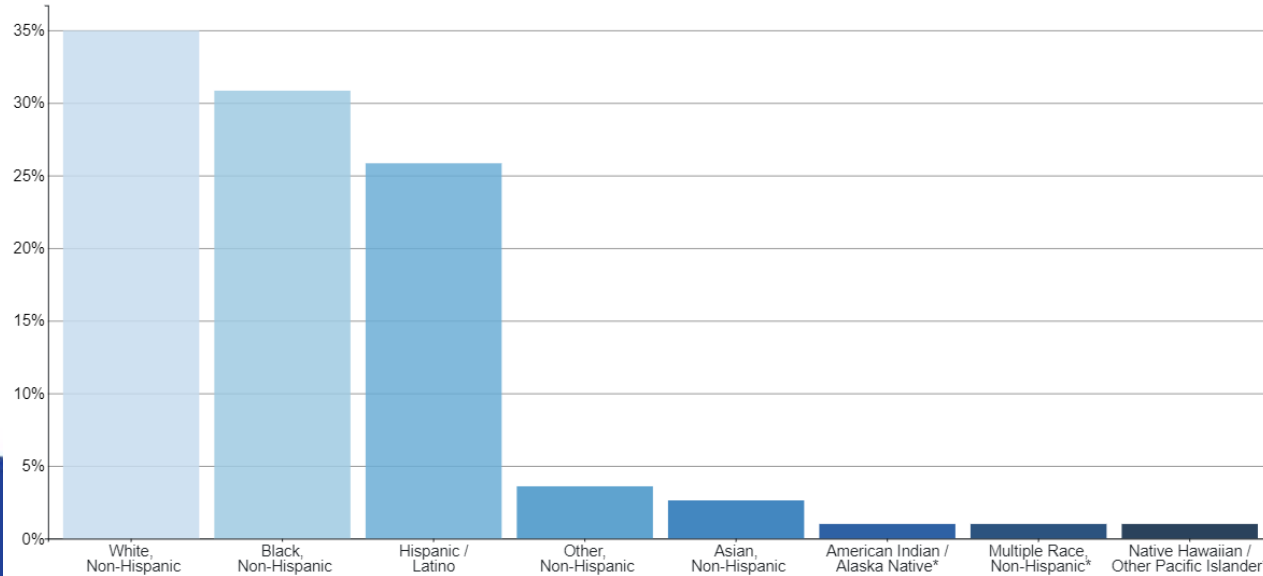
TOTAL MIS-C PATIENTS MEETING CASE DEFINITION*

8,210

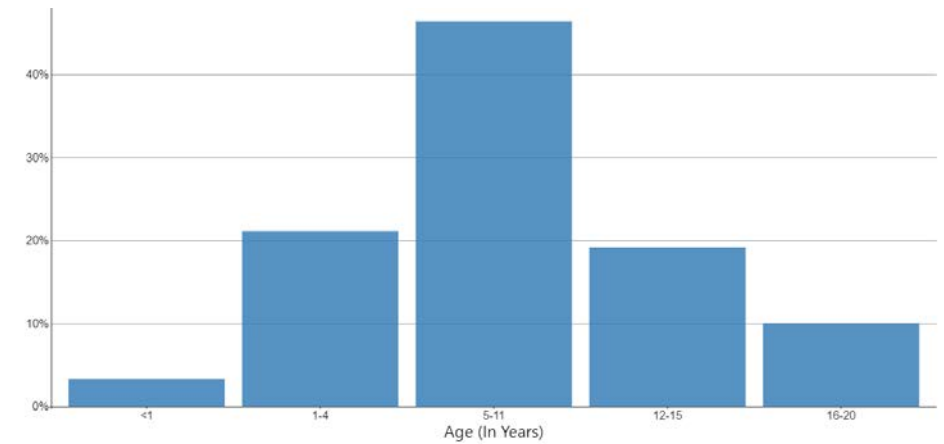
TOTAL MIS-C DEATHS MEETING CASE DEFINITION

68

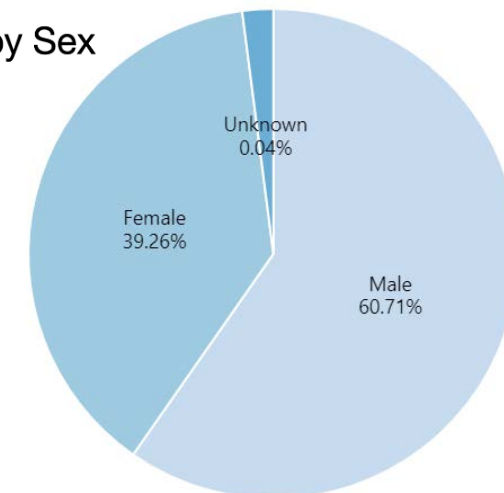
MIS-C Patients by Race & Ethnicity



MIS-C Patients by Age Group



MIS-C Patients by Sex



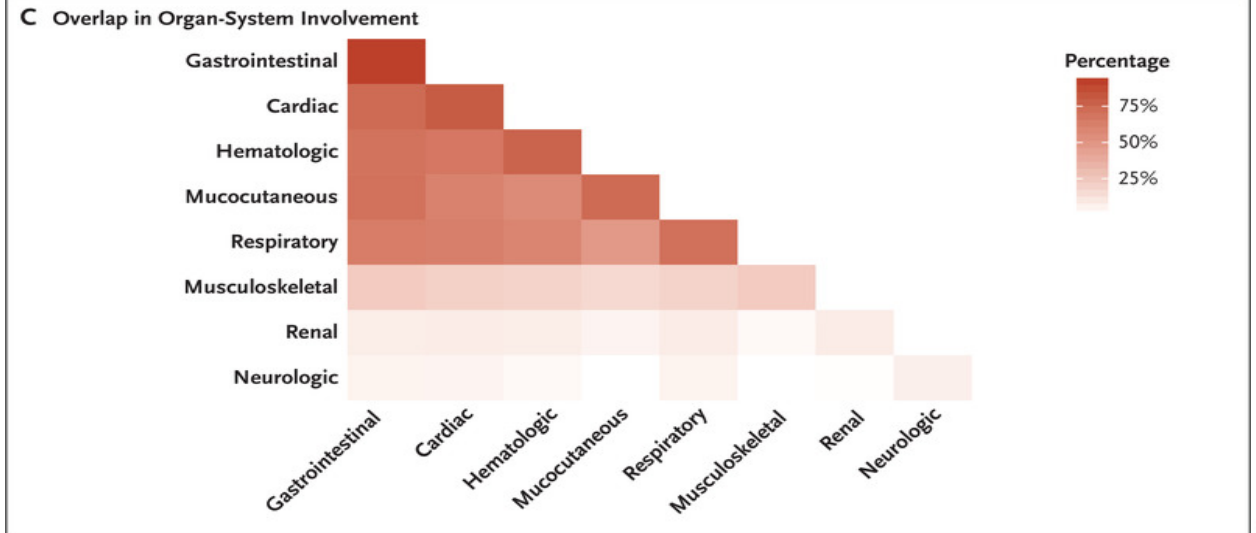
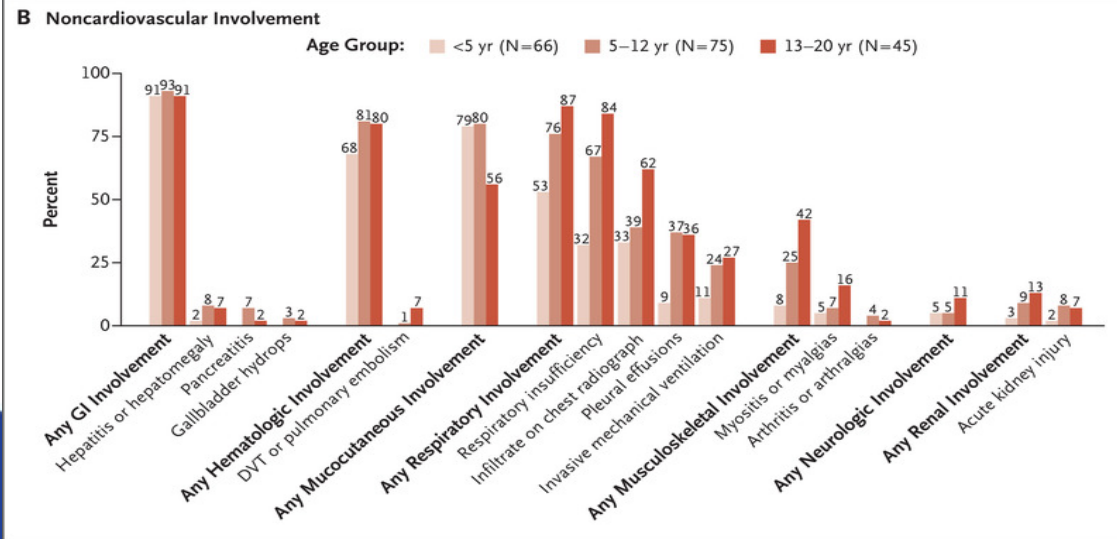
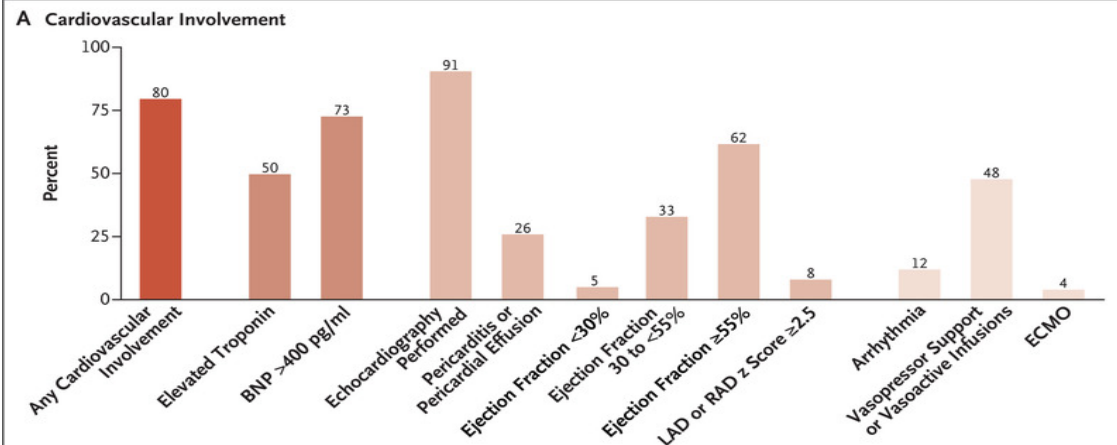
MIS-C Clinical Features

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Multisystem Inflammatory Syndrome in U.S. Children and Adolescents

Highest level of care — no. (%)				
Ward	11 (15)	5 (9)	22 (40)	38 (20)
Intensive care unit	62 (85)	53 (91)	33 (60)	148 (80)
Extracorporeal membrane oxygenation	6 (8)	1 (2)	1 (2)	8 (4)
Mechanical ventilation	23 (32)	8 (14)	6 (11)	37 (20)



Treatment of MIS-C

- **Best Available Treatments Study (BATS)**

- Observational cohort
- 614 children from 32 countries
 - IVIG alone: 246
 - IVIG + steroids: 208
 - Steroids alone: 99
- Primary outcomes:
 - Inotropic support or mechanical ventilation by day 2 or death;
 - Reduction in disease severity by day 2
- Results: No difference in recovery

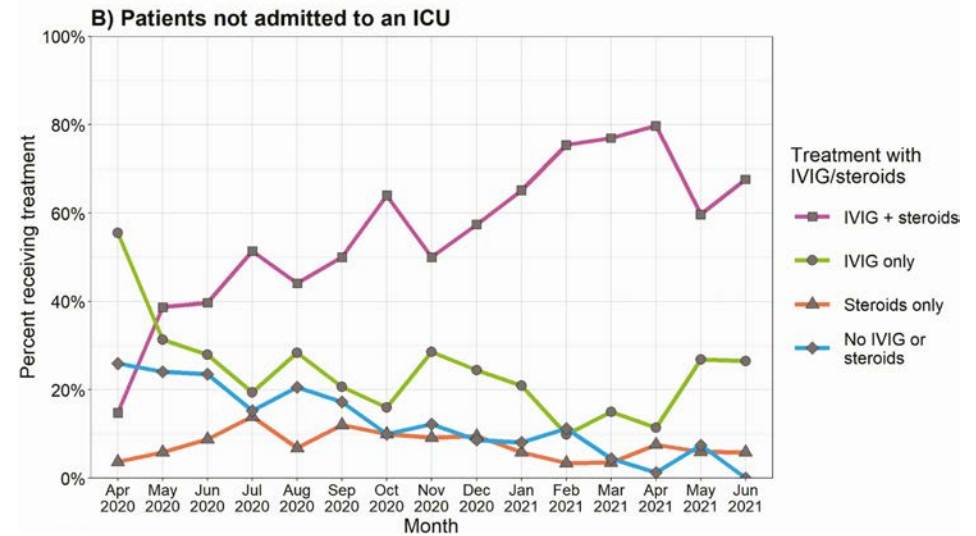
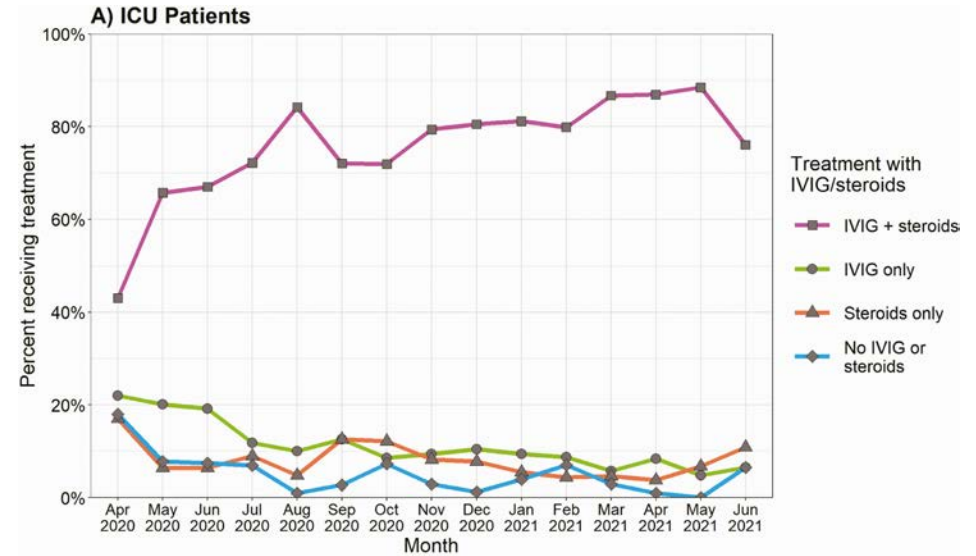
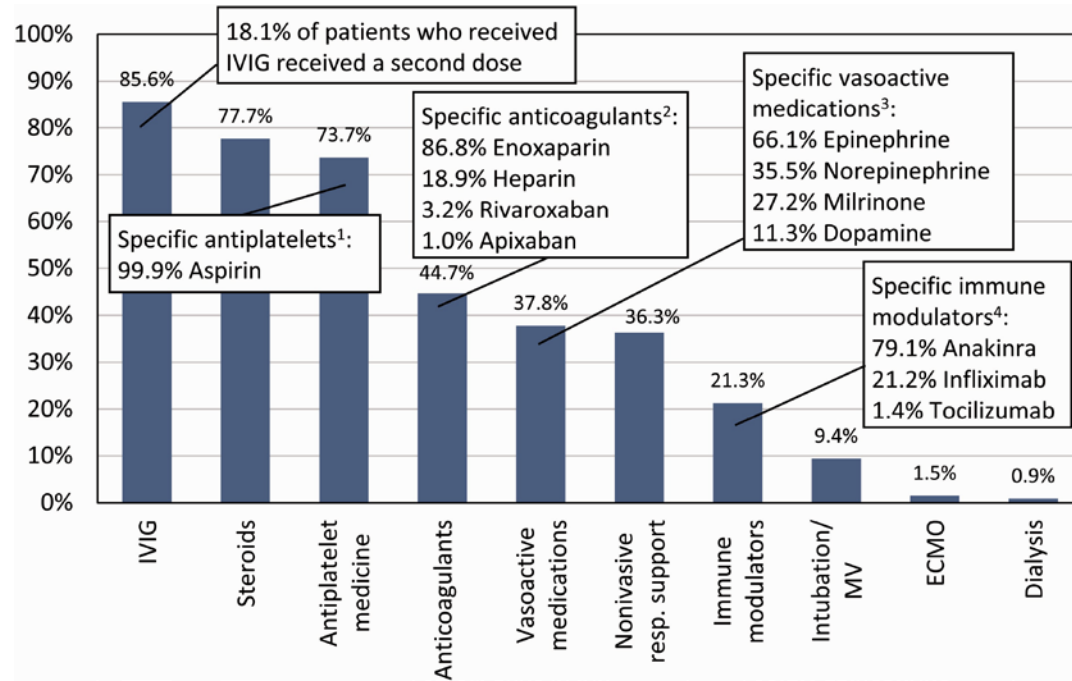
McArdle AJ, et. al. *NEJM*, July 1, 2021.

- **Overcoming COVID-19 Study**

- Observational cohort
- 598 children from 58 U.S. centers
 - IVIG alone: 103
 - IVIG + steroids: 103
- Primary outcomes:
 - LV dysfunction or shock (vasopressor use) on/after day 2
- Results:
 - **Lower risk of cardiovascular dysfunction on/after day 2 with IVIG + steroids vs IVIG alone (17% vs. 31%, RR 0.56, 95% CI, 0.34 to 0.94).**

Son MBF, et. al. *NEJM*, July 1, 2021.

Treatment of MIS-C



MIS-C Management: Diagnostic Testing

- EKG and echocardiogram
- SARS-CoV-2 RT-PCR and IgG
- CBCd, CMP
- ESR, CRP, DIC screen, ferritin
- Troponin, BNP
- Blood culture
- Urinalysis with reflex to culture
- Other infectious work-up*

MIS-C Management: Treatments & Interventions

- Isolation considerations
- Respiratory and circulatory support
- Antibiotics if concern for sepsis
- Anti-inflammatory
 - Our center's approach:
 - Methylprednisolone 1 mg/kg Q12 hrs (max 60 mg)
 - Consider IVIG 2 g/kg x 1 dose (max 100 g) if Kawasaki features
 - For refractory disease, consult Rheumatology, consider pulse steroids vs other immunomodulators
- Anti-coagulation for VTE prophylaxis based on risk
- Anti-platelet: Aspirin 3-5 mg/kg (max 81 mg) daily
- Gastric protection: Famotidine

Management of Severe Pediatric COVID-19

Treatment options for severe pediatric COVID-19

- **Remdesivir**

- **Mechanism:** inhibits viral RNA-dependent RNA polymerase
- Approved in children ≥ 28 days of age who weigh ≥ 3 kg
- Prioritized for pts with severe rather than critical COVID-19
- **Our center's approach:** Recommend for all children requiring high-flow oxygen or noninvasive ventilation due to COVID-19
- **Dosing:**
 - For children ≥ 3 to < 40 kg – 5 mg/kg intravenous (IV) loading dose on day 1, followed by 2.5 mg/kg IV Q 24 hrs
 - For children ≥ 40 kg – 200 mg IV loading dose on day 1, followed by 100 mg IV Q 24 hrs
- Usual duration 5 days, can be extended to 10 days
- Co-administer with a steroid
- Common adverse effects: nausea, vomiting, transaminase elevations

Treatment options for severe pediatric COVID-19

- **Dexamethasone**
 - **Mechanism:** glucocorticoid
 - RECOVERY trial in adults showed reduced mortality, especially in mechanically ventilated patients
 - Less data available in children
 - **Our center's approach:** Recommend for all hospitalized patients receiving supplemental oxygen, ventilation, ECMO
 - **Dose:** 0.15 mg/kg IV/PO Q 24 hrs up to 10 days
 - Patient should receive gastric protection while on steroids and anticoagulation

Treatment options for severe pediatric COVID-19

- **Baricitinib:**

- **Mechanism of action:** Janus kinase inhibitor, immunomodulatory
- FDA EUA for patients ≥ 2 years of age who are hospitalized with COVID-19 and require oxygen or ventilator support
- In adult studies, the combination of baricitinib + remdesivir appeared to modestly improve the time to recovery and mortality
- Limited data about risks and benefits in children
- **Our center's approach:** Administer if high-flow oxygen with rapidly increasing oxygen requirements
- Administered in combination with steroids +/- remdesivir
- **Dosing:** 2-9 years: 2 mg PO daily. ≥ 9 years: 4 mg PO daily.
- Adverse effects include venous thromboembolism, cytopenias, transaminase elevation, secondary infections