

## Supplemental Online Content

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### **eReferences**

This supplemental material has been provided by the authors to give readers additional information about their work.

**eAppendix. Overcoming COVID-19 Investigators**

**(Listed in PubMed, and ordered by U.S. State)**

The following study group members were all closely involved with the design, implementation, and oversight of the Overcoming COVID-19 study.

**Alabama:** Children's of Alabama, Birmingham. Michele Kong, MD.

**Arizona:** University of Arizona, Tucson. Mary Glas Gaspers, MD; Katri V. Typpo, MD.

**Arkansas:** Arkansas Children's Hospital, Little Rock. Ronald C. Sanders Jr., MD, MS; Katherine Irby, MD.

**California:** Children's Hospital of Orange County, Orange County. Adam J. Schwarz, MD.

**California:** Miller Children's & Women's Hospital Long Beach, Long Beach. Christopher J. Babbitt, MD.

**California:** Rady Children's Hospital, San Diego. Helen Harvey, MD, MS.

**California:** UCSF Benioff Children's Hospital Oakland, Oakland. Natalie Z. Cvijanovich, MD.

**California:** UCSF Benioff Children's Hospital, San Francisco. Matt S. Zinter, MD

**Colorado:** Children's Hospital Colorado, Aurora. Aline B. Maddux, MD, MSCS; Peter M. Mourani, MD.

**Connecticut:** Connecticut Children's, Hartford. Christopher L. Carroll, MD, MS.

**Connecticut:** Yale New-Haven Children's Hospital, New Haven. John S. Giuliano, Jr., MD.

**Florida:** Holtz Children's Hospital, Miami. Gwenn E. McLaughlin, MD, MSPH.

**Georgia:** Children's Healthcare of Atlanta at Egleston and Scottish Rite, Atlanta. Keiko M. Tarquinio, MD; Preeti Jaggi, MD.

**Illinois:** Advocate Children's Hospital, Chicago. Vinod Havalad, MD; Stacy Ramsingh, MD.

**Illinois:** Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago. Kelly N. Michelson, MD, MPH; Bria M. Coates, MD.

**Indiana:** Riley Hospital for Children, Indianapolis. Courtney M. Rowan, MD, MS.

**Iowa:** University of Iowa Stead Family Children's Hospital, Iowa City. Kari Wellnitz, MD.

**Kentucky:** University of Louisville and Norton Children's Hospital, Louisville. Janice E. Sullivan, MD; Vicki L. Montgomery, MD; Kevin M. Havlin, MD.

**Louisiana:** Children's Hospital of New Orleans, New Orleans. Tamara T. Bradford, MD.

**Maryland:** Johns Hopkins Children's Hospital, Baltimore. Becky J. Riggs, MD; Melania M. Bembea, MD, MPH, PhD.

**Maryland:** University of Maryland Children's Hospital, Baltimore. Ana Lia Graciano, MD.

**Maryland:** Sinai Hospital of Baltimore, Baltimore. Susan V. Lipton, MD, MPH.

**Massachusetts:** Baystate Children's Hospital, Springfield. Kimberly L. Marohn, MD.

**Massachusetts:** Boston Children's Hospital, Boston. Adrienne G. Randolph, MD; Margaret M. Newhams, MPH; Sabrina R. Chen; Cameron C. Young; Suden Kucukak, MD; Jane W. Newburger, MD, MPH; Kevin G. Friedman, MD; Mary Beth F. Son, MD; Janet Chou, MD.

**Massachusetts:** MassGeneral Hospital for Children, Boston. Ryan W. Carroll, MD, MPH; Phoebe H. Yager,

MD; Neil D. Fernandes, MBBS.

**Michigan:** Children’s Hospital of Michigan, Detroit. Sabrina M. Heidemann, MD.

**Michigan:** University of Michigan CS Mott Children’s Hospital, Ann Arbor. Heidi R. Flori, MD, FAAP.

**Minnesota:** University of Minnesota Masonic Children’s Hospital, Minneapolis, Janet R. Hume, MD, PhD.

**Minnesota:** Mayo Clinic, Rochester. Emily R. Levy, MD.

**Mississippi:** Children’s Hospital of Mississippi, Jackson. Charlotte V. Hobbs, MD; Padma Garg, MD; Kengo Inagaki, MD.

**Missouri:** Children’s Mercy Hospital, Kansas City. Jennifer E. Schuster, MD.

**Missouri:** Washington University in St. Louis. Philip C. Spinella MD.

**Nebraska:** Children’s Hospital & Medical Center, Omaha. Melissa L. Cullimore, MD, PhD; Russell J. McCulloh, MD.

**New Jersey:** Cooper University Hospital, Camden. Karen S. Walker, MD.

**New Jersey:** Hackensack University Medical Center, Hackensack. Katharine N. Clouser, MD.

**New Jersey:** Goryeb Children’s Hospital, Morristown. Cecilia Di Pentima, MD.

**New Jersey:** Newark Beth Israel Medical Center, Newark. Rowan F. Walsh, MD

**New Jersey:** Bristol-Myers Squibb Children's Hospital, New Brunswick. Lawrence C. Kleinman, MD, MPH, FAAP; Simon Li, MD, MPH; Steven M. Horwitz, MD.

**New Jersey:** St. Barnabas Medical Center, Livingston. Shira J. Gertz, MD.

**New Jersey:** The Valley Hospital, Ridgewood. Dennis C. Coffey, MD.

**New York:** Golisano Children’s Hospital, Rochester. Kate G. Ackerman, MD, MPH; Jill M. Cholette, MD.

**New York:** Kings County Hospital, Brooklyn. Michael A. Keenaghan, MD.

**New York:** Division of Pediatric Critical Care, New York University Grossman School of Medicine. Ariel Daube, MD.

**New York:** Maria Fareri Children's Hospital, Westchester. Aalok R. Singh, MD.

**New York:** The Mount Sinai Hospital, New York City. Sheemon P. Zackai, MD; Jennifer K. Gillen, MD.

**New York:** Hassenfeld Children’s Hospital at NYU Langone, New York. Adam J. Ratner, MD, MPH; Heda Dapul, MD; Vijaya L. Soma, MD.

**New York:** Stony Brook University Hospital, Stony Brook. Ilana Harwayne-Gidansky, MD; Saul R. Hymes, MD.

**New York:** SUNY Downstate Medical Center University Hospital, Brooklyn. Sule Doymaz, MD.

**North Carolina:** University of North Carolina at Chapel Hill, Chapel Hill. Stephanie P. Schwartz, MD; Tracie C. Walker, MD.

**Ohio:** MetroHealth Medical Center, Cleveland. Hulya Bukulmez, MD.

**Ohio:** University Hospitals Rainbow Babies and Children's Hospital, Cleveland. Steven L. Shein, MD; Amanda N. Lansell, MD.

**Ohio:** Nationwide Children’s Hospital, Columbus. Mark W. Hall MD, FCCM.

**Ohio:** Akron Children's Hospital, Akron. Ryan A. Nofziger, MD.

**Ohio:** Cincinnati Children's Hospital, Cincinnati. Mary Allen Staat, MD, MPH.

**Pennsylvania:** Children's Hospital of Philadelphia, Philadelphia. Julie C. Fitzgerald, MD, PhD, MSCE.

**Pennsylvania:** Penn State Children's Hospital, Hershey. Neal J. Thomas, MD, MSc.

**Pennsylvania:** St. Christopher's Hospital for Children, Philadelphia. Monica L. Koncicki, MD.

**Pennsylvania:** UPMC Children's Hospital of Pittsburgh. Ericka L. Fink, MD, MS; Joseph A. Carcillo, MD.

**South Carolina:** MUSC Children's Health, Charleston. Elizabeth H. Mack, MD, MS.

**Tennessee:** Monroe Carell Jr. Children's Hospital at Vanderbilt, Nashville. Natasha B. Halasa, MD, MPH.

**Tennessee:** Le Bonheur Children's Hospital, Memphis. Dai Kimura, MD.

**Texas:** Texas Children's Hospital, Houston. Laura L. Loftis, MD.

**Texas:** University of Texas Health Science Center, Houston. Alvaro Coronado Munoz, MD.

**Texas:** University of Texas Southwestern, Children's Medical Center Dallas, Dallas. Cindy Bowens, MD, MSCS; Mia Maamari, MD.

**Utah:** Primary Children's Hospital, Salt Lake City. Hillary Crandall, MD, PhD.

**Washington:** Seattle Children's Hospital, Seattle. Lincoln S. Smith, MD; John K. McGuire, MD.

**Wisconsin:** University of Wisconsin-Madison, Madison. Pelin Cengiz, MD.

**CDC COVID-19 Response Team on Overcoming COVID-19:** Manish M. Patel, MD, MPH; Leora R. Feldstein, PhD, MSc; Erica Billig Rose, PhD MS; Mark W. Tenforde, MD PhD; Ashley M. Jackson MPH; Kimberly Wong

**eTable 1.** Included patients that were published from the Overcoming COVID-19 Public Health Surveillance Registry or included in publications from registry sites in studies that compared COVID-19 to MIS-C, or that reported cardiac outcomes

Maximum overlapping patients <sup>a</sup>	Pubmed ID	Journal	Type of Patients	Last enrollment
168	PMID: 32598831	N Engl J Med	MIS-C patients from Overcoming COVID-19 U.S. study from 26 states	May 20, 2020
<b>Published reports of cardiac outcomes of MIS-C</b>				
≤ 33	PMID: 32975439	Clin Pediatr	NY site #1	June 8, 2020
≤ 28	PMID: 32890666	J Amer Coll Cardiol	PA site	June 7, 2020
≤ 15	PMID: 32768467	J Pediatr	NY site #2	May 16, 2020
25	PMID: 32855347	Pediatrics	MA site #1	May 30, 2020
11	PMID: 33010855	J Amer Soc Echocardiogr	MA site #2	June 5, 2020
3	PMID: 32941261	Cardiol Rev	NY site #3	May 5, 2020
<b>Published report comparing MIS-C to acute COVID-19 patients</b>				
≤ 76	PMID: 33197493	J Pediatr	4 NY (sites #4-7), 1 CT, 1 NJ	May 22, 2020

Abbreviations: MIS-C, multisystem inflammatory syndrome in children

<sup>a</sup> The 168 patients in the first report may be the same as those in reports that include MIS-C patients listed below it. When exact numbers are not shown (e.g. ≤), investigators were independent and unable to compare patients while maintaining confidentiality, so maximum potential number of overlapping patients are shown, and this number may be less.

**eTable 2.** Methods for evaluating cardiac outcomes

<b>Cardiac outcome definitions</b>	
Receipt of vasopressors outcomes (Figure S2)	<ul style="list-style-type: none"> <li>• CV pSOFA score 0-1 (no dobutamine, dopamine, epinephrine, norepinephrine)</li> <li>• CV pSOFA score 2 (any dobutamine, or dopamine <math>\leq 5</math> mcg/kg/min)<sup>1</sup></li> <li>• CV pSOFA of score 3 (dopamine <math>&gt; 5</math> or epinephrine/norepinephrine <math>\leq 0.1</math> mcg/kg/min)</li> <li>• CV pSOFA of score 4 (dopamine <math>&gt; 15</math> or epinephrine/norepinephrine <math>&gt; 0.1</math> mcg/kg/min)</li> </ul>
Left ventricular ejection fraction impairment on echocardiogram <sup>2</sup>	<ul style="list-style-type: none"> <li>• Normal ejection fraction reported as <math>\geq 55\%</math> or noted as qualitatively normal</li> <li>• Mildly depressed ejection fraction reported as <math>\geq 45\%</math> to <math>&lt; 55\%</math></li> <li>• Moderately depressed ejection fraction reported as <math>\geq 35\%</math> to <math>&lt; 45\%</math></li> <li>• Severely depressed ejection fraction <math>&lt; 35\%</math></li> </ul>
Coronary artery aneurysms (CAA) in left anterior descending (LAD) or right coronary artery (RCA) on echocardiogram <sup>3</sup>	<ul style="list-style-type: none"> <li>• Normal: z score <math>&lt; 2.5</math> or documented visualization of both LAD and RCA and noted normal<sup>a, b</sup></li> <li>• Small: z score <math>\geq 2.5</math> to <math>&lt; 5</math></li> <li>• Medium: <math>\geq 5</math> to <math>&lt; 10</math></li> <li>• Large: <math>\geq 10</math></li> </ul>
Resolved ejection fraction and CAA	<ul style="list-style-type: none"> <li>• Evidence of ejection fraction <math>\geq 55\%</math>, z-score <math>&lt; 2.5</math>, or noted as qualitatively normal</li> </ul>
Unresolved ejection fraction and CAA	<ul style="list-style-type: none"> <li>• Persistently depressed left ventricular ejection fraction on repeat imaging prior to hospital discharge</li> </ul>
CAA that were not evaluable during hospital admission	<ul style="list-style-type: none"> <li>• Unable to assess due to lack of or insufficient imaging</li> <li>• Did not note the z score or given sufficient information to calculate it</li> <li>• Only commented on one artery (RCA or LAD but not both)</li> <li>• Insufficient information presented to assess whether an aneurysm was present, as determined by two cardiologists (JN, KF).</li> </ul>
<b>Denominators for cardiac outcome calculations</b>	
Vasopressors	<ul style="list-style-type: none"> <li>• All patients who were on vasopressors at least one day during hospitalization</li> </ul>
Ejection Fraction	<ul style="list-style-type: none"> <li>• All patients with at least one echocardiogram</li> </ul>
Coronary Artery Aneurysms	<ul style="list-style-type: none"> <li>• For MIS-C patients: all patients with evaluable coronary arteries on at least one echocardiogram</li> <li>• For severe acute COVID-19 patients: all patients with at least one evaluable echocardiogram</li> </ul>

Abbreviations: pSOFA, pediatric severe organ failure assessment; LAD, left anterior descending; RCA, right coronary artery; MIS-C, multisystem inflammatory syndrome in children

<sup>a</sup> Not limited to assessment at origins

<sup>b</sup> Recalculation of z scores by cardiologists (JN, KF) was done for those with z scores of  $\leq 2.5$  using height and weight.

**eTable 3.** Number of patients aged <21 years with MIS-C and severe acute COVID-19 illness by site number and state

<b>State</b>	<b>MIS-C (n = 539)</b>	<b>Severe Acute COVID-19 (n = 577)</b>
Alabama	16	20
Arizona	4	3
Arkansas	11	10
California 1	1	5
California 2	7	12
California 3	4	7
California 4	8	9
California 5	0	1
Colorado	10	53
Connecticut 1	6	9
Connecticut 2	14	16
Florida	8	24
Georgia	29	2
Illinois 1	4	15
Illinois 2	4	0
Indiana	9	6
Iowa	3	9
Kentucky	8	7
Louisiana	9	4
Maryland 1	17	24
Maryland 2	3	1
Maryland 3	1	0
Massachusetts 1	35	29
Massachusetts 2	10	1
Massachusetts 3	2	0
Michigan 1	1	7
Michigan 2	16	0
Minnesota 1	13	5
Minnesota 2	1	7
Mississippi	10	17
Missouri 1	5	5
Missouri 2	14	18
Nebraska	4	0
New Jersey 1	4	8
New Jersey 2	9	1
New Jersey 3	1	0
New Jersey 4	9	0
New Jersey 5	14	9

New Jersey 6	1	0
New Jersey 7	1	0
New York 1	1	0
New York 2	19	17
New York 3	2	3
New York 4	18	44
New York 5	17	1
New York 6	15	0
New York 7	12	0
New York 8	2	0
North Carolina	12	23
Ohio 1	11	28
Ohio 2	0	5
Ohio 3	3	0
Ohio 4	2	4
Pennsylvania 1	18	3
Pennsylvania 2	5	2
Pennsylvania 3	3	2
Pennsylvania 4	2	0
South Carolina	9	19
Tennessee 1	8	21
Tennessee 2	1	0
Texas 1	31	17
Texas 2	7	36
Texas 3	2	1
Utah	1	0
Washington	12	6
Wisconsin	0	1

Abbreviations: MIS-C, multisystem inflammatory syndrome in children



**eTable 4.** SARS-CoV-2 test results and severe organ system involvement of patients (diagnosed within first 24 hours of admission) aged <21 years with MIS-C and severe acute COVID-19 illness

	<b>MIS-C n = 539 (48%)</b>	<b>Severe Acute COVID-19 n = 577 (52%)</b>
<b>SARS-CoV-2 test results</b>		
RT-PCR positive	281 (52)	577 (100)
Antibody positive	409 (76)	43 (7)
Antibody positive, RT-PCR negative	241 (45)	0 (0)
RT-PCR positive and antibody positive	168 (31)	43 (7)
RT-PCR positive and antibody negative	19 (5)	29 (5)
Antibody test not performed	102 (19)	505 (88)
<b>Respiratory</b>	432 (80)	459 (80)
Respiratory insufficiency / failure <sup>a</sup>	303 (56)	292 (51)
High flow nasal cannula	114 (21)	121 (21)
Non-invasive ventilation (CPAP / BiPAP)	41 (8)	33 (6)
Invasive mechanical ventilation	95 (18)	82 (14)
Pleural effusions	148 (27)	45 (8)
Infiltrates on chest X-ray	197 (37)	220 (38)
<b>Cardiovascular<sup>b,c</sup></b>	359 (67)	68 (12)
Vasopressor support	244 (45)	50 (9)
Ejection fraction <35%	38 (8)	6 (5)
Ejection fraction 35 to <45%	39 (8)	1 (1)
Ejection fraction 45 to <55%	95 (19)	6 (5)
LAD or RCA z score $\geq 2.5$	57 (13)	1 (1)
BNP $\geq 1,000^d$	111 (21)	17 (3)
Elevated troponin <sup>e</sup>	158 (29)	10 (2)
Arrhythmia	46 (9)	4 (1)
ECMO	16 (3)	7 (1)
<b>Gastrointestinal</b>	50 (9)	42 (7)
Appendicitis	6 (1)	22 (4)
Hepatitis or hepatomegaly	27 (5)	14 (2)
Pancreatitis	17 (3)	7 (1)
Gallbladder hydrops or edema	11 (2)	1 (0)
<b>Hematologic/thrombotic<sup>c</sup></b>	256 (47)	159 (28)
Deep vein thrombosis/pulmonary embolism	11 (2)	8 (1)
Platelet count <50,000/ $\mu$ L	9 (2)	8 (1)
Severe anemia <sup>f</sup>	17 (3)	23 (4)
Absolute lymphocyte count <1 $\times 10^3$ cells/ $\mu$ L	226 (42)	137 (24)
Absolute neutrophil count <0.5 $\times 10^3$ cells/ $\mu$ L	5 (1)	11 (2)
<b>Renal</b>	17 (3)	6 (1)
Acute kidney injury <sup>g</sup>	9 (2)	0 (0)
Renal failure requiring dialysis	9 (2)	8 (1)
<b>Neurologic<sup>h</sup></b>	66 (12)	115 (20)
Seizures	9 (2)	34 (6)

Abbreviations: MIS-C, multisystem inflammatory syndrome in children; ; SARS-CoV-2, severe acute respiratory syndrome coronavirus; CPAP, continuous positive airway pressure; BiPAP, bilevel positive airway pressure; LAD, left anterior descending; RCA, right coronary artery; BNP, B-type natriuretic peptide; ECMO, extracorporeal membrane oxygenation

<sup>a</sup> Defined as requiring any supplemental oxygen.

<sup>b</sup> Denominator for ejection fraction is patients with echocardiograms (MIS-C: n=503, severe acute COVID-19: n=111) and for coronary artery aneurysms is evaluable echocardiograms (MIS-C: n=424, severe acute COVID-19: n=111).

<sup>c</sup> All laboratory values are within the first day of admission.

<sup>d</sup> B-type natriuretic peptide values missing for 69 MIS-C, 107 COVID-19.

<sup>e</sup> Elevated troponin missing for 278 MIS-C, 530 COVID-19.

<sup>f</sup> Severe anemia was defined as hemoglobin <7 g/dL among children <59 months of age, otherwise hemoglobin <8 g/dL.

<sup>g</sup> Definition of acute kidney injury in Table S1.

<sup>h</sup> Diagnosed by a neurologist.

**eTable 5.** Demographics and clinical characteristics of 18 hospitalized patients who died aged <21 years with COVID-19 related illness

	MIS-C	Age category (years)	Sex	Race/ethnicity	Obesity <sup>a</sup>	Clinically documented underlying conditions	ECMO	Days from illness onset to death <sup>b</sup>	Primary listed cause of death
<b>Patient 1</b>	Yes	1-5	Male	Unknown	No	None	Yes	Unknown	Brain death/severe brain injury
<b>Patient 2</b>	Yes	6-12	Male	Hispanic or Latino	No	Hypertension, oncologic	No	52	Primary respiratory
<b>Patient 3</b>	Yes	6-12	Male	Black or African American	Yes	Asthma	No	7	Primary respiratory
<b>Patient 4</b>	Yes	6-12	Male	Black or African American	No	Asthma, other chronic lung disease	No	14	Primary respiratory
<b>Patient 5</b>	Yes	6-12	Male	Asian	Yes	None	No	6	Brain death/severe brain injury
<b>Patient 6</b>	Yes	1-5	Female	White	No	Oncologic (neuroblastoma)	Yes	Unknown	Other
<b>Patient 7</b>	Yes	6-12	Female	Hispanic or Latino	No	None	No	3	Brain death/severe brain injury
<b>Patient 8</b>	Yes	13-21	Female	Hispanic or Latino	No	Cerebral palsy, neuromuscular scoliosis	Yes	11	Primary respiratory
<b>Patient 9</b>	Yes	13-21	Female	Black or African American	Yes	None	Yes	12	Primary cardiac

<b>Patient 10</b>	Yes	13-21	Female	Hispanic or Latino	Yes	Genetic syndrome	Yes	21	Multiorgan failure
<b>Patient 11</b>	No	<1	Male	White	No	None	No	1	Brain death/severe brain injury
<b>Patient 12</b>	No	1-5	Male	Black or African American	No	Severe congenital heart disease	Yes	16	Primary cardiac
<b>Patient 13</b>	No	6-12	Male	Black or African American	No	Immune deficiency with enteropathy, asthma	No	Unknown	Primary respiratory
<b>Patient 14</b>	No	13-21	Male	Hispanic or Latino	No	None	No	19	Primary respiratory
<b>Patient 15</b>	No	13-21	Female	Hispanic or Latino	Yes	Chronic lung disease, neurologic (spastic quadriplegia)	No	31	Brain death/severe brain injury
<b>Patient 16</b>	No	13-21	Female	Hispanic or Latino	No	Asthma	No	Unknown	Multiorgan failure
<b>Patient 17</b>	No	13-21	Female	Black or African American	Yes	Hypertension, diabetes	Yes	39	Multiorgan failure
<b>Patient 18</b>	No	13-21	Female	Hispanic or Latino	No	Chronic lung disease, hypertension post lung transplant, immunocompromised, hematologic	No	9	Primary respiratory

Abbreviations: BMI, body-mass index; MIS-C, multisystem inflammatory syndrome in children; ECMO, extracorporeal membrane oxygenation

<sup>a</sup> A patient was considered to have obesity by either clinician diagnosed obesity or BMI-based obesity (defined as BMI >95<sup>th</sup> percentile for age and sex based on national reference standards), only calculated in children ≥2.

<sup>b</sup> Illness day 1 was defined as date of first COVID-19 symptoms.

**eTable 6.** Multivariable analyses examining of the association between patient baseline demographic and clinical characteristics and diagnosis of MIS-C versus severe COVID-19.<sup>a,b</sup>

Characteristic	Unadjusted risk difference (95%CI)	P-value	Adjusted risk difference (95%CI) <sup>c</sup>	P-value
<b>Age</b>				
0 to 5 y	0 (ref)		0 (ref)	
6 to 12 y	0.21 (0.14 to 0.28)	<0.001	0.23 (0.17 to 0.30)	<0.001
13 to 20 y	-0.10 (-0.17 to -0.03)	0.005	0.01 (-0.05 to 0.08)	0.67
<b>Race/ethnicity<sup>d</sup></b>				
White, non-Hispanic	0 (ref)		0 (ref)	
Black, non-Hispanic	0.21 (0.12 to 0.30)	<0.001	0.18 (0.10 to 0.26)	<0.001
Hispanic or Latino	0.05 (-0.03 to 0.14)	0.24	0.02 (-0.06 to 0.10)	0.68
<b>Sex</b>				
Male	0 (ref)		0 (ref)	
Female	-0.05 (-0.11 to 0.01)	0.12	-0.05 (-0.10 to 0.004)	0.07
<b>≥1 underlying medical conditions</b>				
No	0 (ref)		0 (ref)	
Yes	-0.31 (-0.37 to -0.26)	<0.001	-0.31 (-0.36 to -0.25)	<0.001
<b>Clinical group by complication</b>				
Respiratory without cardiovascular	0 (ref)		0 (ref)	
Respiratory and cardiovascular	0.57 (0.52 to 0.62)	<0.001	0.49 (0.43 to 0.54)	<0.001
Cardiovascular without respiratory	0.38 (0.31 to 0.46)	<0.001	0.28 (0.19 to 0.36)	<0.001
Mucocutaneous without respiratory or cardiovascular	0.36 (0.27 to 0.44)	<0.001	0.23 (0.13 to 0.33)	<0.001
Other without respiratory, cardiovascular, or mucocutaneous	-0.13 (-0.23 to -0.03)	0.009	-0.20 (-0.28 to -0.11)	<0.001
<b>Lab value within first 48 hours</b>				
Neutrophil to lymphocyte ratio >5	0.29 (0.23 to 0.35)	<0.001	0.23 (0.17 to 0.29)	<0.001
Platelets <150 × 10 <sup>3</sup> /μL	0.28 (0.22 to 0.34)	<0.001	0.26 (0.20 to 0.32)	<0.001
C-reactive protein >100 mg/L	0.40 (0.33 to 0.46)	<0.001	0.31 (0.25 to 0.37)	<0.001

Abbreviations: 95%CI, 95% confidence interval; COVID-19, coronavirus disease 2019; MIS-C, multisystem inflammatory syndrome in children

<sup>a</sup> A risk difference >0 represents a higher relative risk of MIS-C compared to COVID-19.

<sup>b</sup> Risk difference models generated using adjrr function in Stata <sup>4</sup>

<sup>c</sup> The primary outcome is diagnosis of MIS-C vs COVID-19. Associations were adjusted for age group (0-5 years, 6-12 years, 13-20 years), race/ethnicity (White non-Hispanic, Black non-Hispanic, Hispanic of any race, Other non-Hispanic), sex, one or more versus no underlying medical conditions, and US census region (Northeast, South, Midwest, West).

<sup>d</sup> Other non-Hispanic race/ethnicity, which included patients documented as having other, unknown, or mixed race, not shown in the table.

**eTable 7.** Characteristics and outcomes of all enrolled patients <21 years with COVID-19 related illness by severe outcome group

Characteristic, No. (%)	Severe cardiorespiratory involvement (n = 353)	Severe cardiovascular involvement without respiratory (n = 74)	Severe respiratory involvement without cardiovascular (n = 538)	Mucocutaneous involvement without severe cardiorespiratory involvement (n = 51)	Hematologic, neurologic, or gastrointestinal severe involvement only (n = 100)
Age, median (IQR), y	10.1 (6.4, 14.7)	8.3 (3.5, 10.3)	10.9 (2.2, 16.4)	3.4 (1.3, 11.2)	7.7 (0.1, 13.6)
Male sex	209 (59)	40 (54)	294 (55)	26 (51)	50 (50)
One or more underlying conditions <sup>a</sup>	136 (39)	16 (22)	321 (60)	9 (18)	43 (43)
Black, non-Hispanic	130 (37)	20 (27)	132 (25)	14 (27)	14 (14)
<b>Clinical diagnosis</b>					
MIS-C	302 (86)	57 (77)	130 (24)	38 (75)	12 (12)
Severe COVID-19	51 (14)	17 (23)	408 (76)	13 (25)	88 (88)
<b>Positive SARS-CoV-2 test</b>					
RT-PCR positive	203 (58)	42 (57)	495 (92)	23 (45)	95 (95)
Antibody positive	244 (69)	55 (74)	112 (21)	31 (61)	10 (10)
Antibody positive, RT-PCR negative	139 (39)	31 (42)	36 (7)	20 (39)	4 (4)
RT-PCR positive and antibody positive	102 (29)	23 (31)	72 (13)	9 (18)	5 (5)
RT-PCR positive and antibody negative	17 (5)	2 (3)	25 (5)	0 (0)	4 (4)
Antibody test not performed	90 (26)	17 (23)	399 (74)	15 (29)	86 (86)
<b>Laboratory values within first 48 hours</b>					
BNP median (IQR), pg/mL	917 (212, 2830.7)	1079 (279, 2348)	85.5 (30, 296.8)	85.4 (22.4, 197.7)	142 (37, 348)
BNP ≥400 pg/mL	170 (48)	40 (54)	30 (6)	4 (8)	2 (2)
BNP ≥1000 pg/mL	120 (34)	31 (42)	6 (1)	1 (2)	0 (0)
CRP, median (IQR), mg/L	175 (92, 256)	138.1 (82.0, 205.5)	52.5 (15, 137.6)	61.1 (21, 146.3)	10.1 (2.0, 58.7)
NLR, median (IQR)	8.5 (4.6, 15.6)	5.3 (2.9, 9.6)	3.2 (1.4, 6.8)	3.0 (1.2, 4.8)	1.9 (0.6, 5.7)
Platelets, median (IQR), × 10 <sup>3</sup> /μL	155 (108, 217)	198 (126.5, 288)	228 (168, 315)	233 (161, 342)	256 (204, 341)
<b>Cardiac outcomes</b>					
Ejection Fraction 45 to <55%	76 (22)	15 (20)	8 (1)	0 (0)	2 (2)
Ejection Fraction 35 to <45%	32 (9)	8 (11)	0 (0)	0 (0)	0 (0)

Ejection Fraction <35%	43 (12)	1 (1)	0 (0)	0 (0)	0 (0)
Coronary artery aneurysm	46 (13)	11 (15)	0 (0)	0 (0)	0 (0)
Vasopressor therapy	268 (76)	23 (31)	3 (1)	0 (0)	0 (0)
<b>Respiratory outcomes</b>					
Abnormal chest x-ray with 24 hours	173 (49)	0 (0)	244 (45)	0 (0)	0 (0)
Non-invasive mechanical ventilation	164 (46)	1 (1)	213 (40)	0 (0)	2 (2)
Invasive mechanical ventilation	117 (33)	0 (0)	61 (11)	0 (0)	1 (1)
<b>Other organ system involvement</b>					
Gastrointestinal	47 (13)	3 (4)	17 (3)	4 (8)	21 (21)
Hematologic	199 (56)	25 (34)	147 (27)	15 (29)	29 (29)
Neurologic	65 (18)	3 (4)	56 (10)	6 (12)	51 (51)
<b>Presenting signs/symptoms</b>					
Constitutional	342 (97)	71 (96)	470 (87)	50 (98)	75 (75)
Gastrointestinal	306 (87)	65 (88)	347 (64)	41 (80)	59 (59)
Upper respiratory	122 (35)	18 (24)	195 (36)	15 (29)	19 (19)
Lower respiratory	177 (50)	25 (34)	351 (65)	11 (22)	27 (27)
Neurologic	161 (46)	24 (32)	175 (33)	13 (25)	31 (31)
Mucocutaneous	209 (59)	46 (62)	114 (21)	51 (100)	0 (0)
<b>Critical outcomes</b>					
ICU admission	316 (90)	49 (66)	245 (46)	17 (33)	24 (24)
ICU length of stay, median (IQR), d	5 (3, 9)	3 (2, 4)	3 (2, 7)	2 (1, 3)	3 (1.5, 5)
Death	17 (5)	0 (0)	1 (0)	0 (0)	0 (0)

Abbreviations: CXR, chest x-ray; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; IQR, interquartile range; SARS-CoV-2, severe acute respiratory syndrome coronavirus; RT-PCR, real-time reverse transcriptase polymerase chain reaction; BNP, B-type natriuretic peptide; CRP, C-reactive protein; NLR, neutrophil to lymphocyte ratio

<sup>a</sup> Underlying conditions excluded body mass index (BMI)-based obesity (defined as BMI >95<sup>th</sup> percentile for age and sex based on national reference standards).



**eTable 8.** Demographics and clinical characteristics of hospitalized patients <21 years diagnosed with MIS-C by RT-PCR and SARS-CoV-2 antibody test result

<b>MIS-C</b>	<b>RT-PCR positive, SARS-CoV-2 antibody negative n = 19</b>	<b>RT-PCR positive, SARS-CoV-2 antibody positive n = 168</b>	<b>RT-PCR negative, SARS-CoV-2 antibody positive n = 230</b>
<b>Age</b>	4.7 (1.4, 9.7)	8.4 (4.9, 13.3)	8.7 (4.7, 12.3)
<b>Sex, female</b>	7 (37)	74 (44)	97 (42)
<b>Race/ethnicity<sup>a</sup></b>			
White, non-Hispanic	3 (16)	21 (13)	23 (10)
Black, non-Hispanic	4 (21)	55 (33)	95 (41)
Hispanic or Latino	8 (42)	69 (41)	63 (27)
Other, non-Hispanic	2 (11)	9 (5)	9 (4)
Unknown race/ethnicity	3 (16)	17 (10)	41 (18)
<b>At least one underlying condition</b>	10 (53)	47 (28)	63 (27)
<b>Obese<sup>b</sup></b>	6 (32)	55 (33)	74 (32)
<b>Initial laboratory value within 48 hours of admission</b>			
CRP >100 mg/L	6 (35)	99 (66)	171 (76)
NLR>5	5 (28)	101 (64)	149 (67)
BNP or pro-BNP ≥400 mg/mL	6 (50)	83 (62)	99 (55)
<b>Clinical outcomes</b>			
ICU admission	12 (63)	126 (75)	171 (74)
Vasopressors	7 (36)	72 (44)	118 (51)
Mechanical ventilation	7 (36)	28 (17)	33 (14)
Meets Kawasaki disease criteria <sup>c</sup>	0 (0)	22 (13)	35 (15)

Abbreviations: RT-PCR, real-time reverse transcriptase polymerase chain reaction; CRP, C-reactive protein; NLR, neutrophil-to-lymphocyte ratio; BNP, brain natriuretic peptide SARS-CoV-2, severe acute respiratory syndrome coronavirus.

<sup>a</sup> Race and ethnicity categories are not mutually exclusive

<sup>b</sup> Patient was considered to have obesity by either clinician diagnosed obesity or body mass index (BMI)-based obesity (defined as BMI >95<sup>th</sup> percentile for age and sex based on national reference standards), only calculated in children ≥2.

<sup>c</sup> Met criteria for complete or incomplete Kawasaki disease criteria (complete: 4-5 criteria and incomplete: 2-3 with laboratory criteria).<sup>3</sup>

**eTable 9.** Evaluation of coronary artery aneurysms in MIS-C patients (N=538)<sup>a</sup> <21 years

LAD or RCA shows aneurysm	57 (13.4% of evaluable) <sup>b</sup>
<b>No CAA<sup>c</sup></b>	
Patients with normal z scores LAD and RCA	295 (69.6% of evaluable)
Patients qualitatively no aneurysms LAD and RCA	72 (17.0% of evaluable)
<b>Total evaluable</b>	424 (78.8% of total)
<b>Unable to determine</b>	114 (21.2% of total patients)
Insufficient data on echocardiogram to determine <sup>d</sup>	80 (14.9% of total patients)
No echocardiograms during hospitalization	34 (6.3% of total patients)
<b>Total patients<sup>a</sup></b>	538

Abbreviations: CAA, coronary artery aneurysm; LAD, left anterior descending; MIS-C, multisystem inflammatory syndrome in children; RCA, right coronary artery.

<sup>a</sup> Excludes 1 patient that had an aneurysm but was at risk due to baseline cardiomyopathy.

<sup>b</sup> Denominator for coronary artery aneurysms is based on evaluable echocardiograms (n=424)

<sup>c</sup> Could have dilation z score 2 to <2.5.

<sup>d</sup> 9 (2%) of these had echocardiogram post-discharge that were normal.

## eReferences

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