

Multisystem Inflammatory Syndrome in Children (MIS-C) and Impact on Kids

Pei-Ni Jone, MD

Professor of Pediatrics, Pediatric Cardiology, University of Colorado

Director of Kawasaki Disease Clinic

Director of 3D Echocardiography, Children's Hospital Colorado



Children's Hospital Colorado



April 21, 2022



Affiliated with

University of Colorado
Anschutz Medical Campus



Children's Hospital
Colorado

Pei-Ni Jone, MD

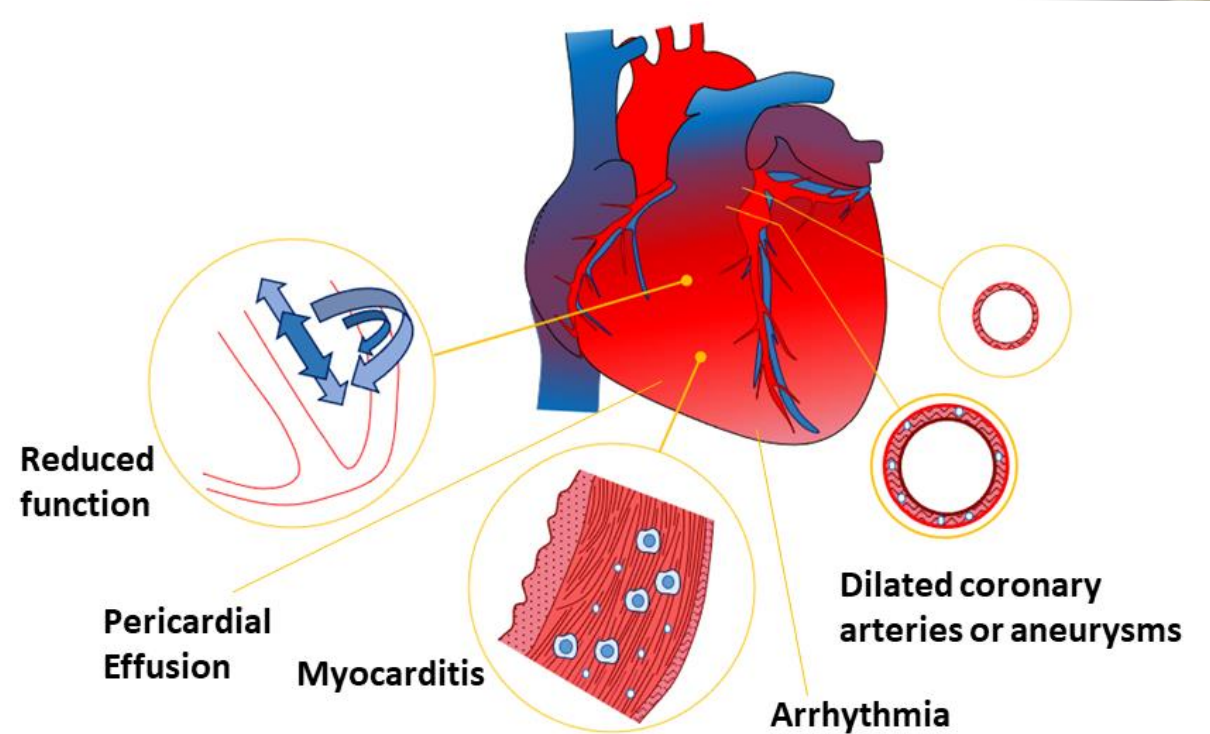
Financial Disclosure

- I have no relevant financial relationships with any commercial interests

MIS-C and Impact on Kids

Learning Objectives

- Define MIS-C
 - Epidemiology
 - Pathophysiology
- Describe Diagnosis of MIS-C
 - Clinical Presentation
 - Laboratory Presentation
 - Imaging Studies
- Summarize Treatment of MIS-C
- Outcomes of MIS-C



Jone PN, John A, Oster ME, Allen K, Tremoulet AH, Saarel EV, Lambert LM, Miyamoto SD, de Ferranti SD. SARS-CoV-2 Infection and Associated Cardiovascular Manifestations and Complications in Children and Young Adults: A Scientific Statement From the American Heart Association. *Circulation*. 2022 Apr 11:101161CIR0000000000001064.

MIS-C – CASE DEFINITION

CDC Definition – 4 criteria

1. Age <21 years
2. Clinical Presentation include:
 - a. Fever >38C for >24 hours
 - b. Laboratory evidence of inflammation
 - c. Multisystem involvement (2 or more organ system involvement)
 - Cardiovascular (eg, shock, elevated troponin, elevated BNP, abnormal echocardiogram, arrhythmia)
 - Respiratory (eg, pneumonia, ARDS, pulmonary embolism)
 - Renal (eg, AKI, renal failure)
 - Neurologic (eg, seizure, stroke, aseptic meningitis)
 - Hematologic (eg, coagulopathy)
 - Gastrointestinal (eg, abdominal pain, vomiting, diarrhea, elevated liver enzymes, ileus, gastrointestinal bleeding)
 - Dermatologic (eg, erythroderma, mucositis, other rash)
 - d. Severe illness requiring hospitalization
3. No Alternative plausible diagnosis
4. Recent or current SARS-CoV2 infection or exposure

WHO Definition – 6 criteria

1. Age 0-19 years
2. Fever for ≥ 3 days
3. Clinical signs of multisystem (at least 2):
 - a. Rash, bilateral nonpurulent conjunctivitis, or mucocutaneous inflammation signs (oral, hands, feet)
 - b. Hypotension or shock
 - c. Cardiac dysfunction
 - d. Coagulopathy
 - e. Acute GI symptoms
4. Elevated markers of inflammation
5. No other causes of inflammation
6. Evidence of SARS-CoV 2 infection or exposure

MIS-C Criteria	RCPCH (Royal College Paediatrics and Child Health)	CDC	WHO (World Health Organization)
Age	All children (age not defined)	<21 years	0–19 years
Fever	Persistent fever ($\geq 38.5^{\circ}\text{C}$)	Temperature $\geq 38.0^{\circ}\text{C}$ for ≥ 24 hours <i>or</i> subjective fever for ≥ 24 hours	Fever for ≥ 3 days
Clinical symptoms	Both of the following: 1.single or multiorgan dysfunction; <i>and</i> 2.additional features	Both of the following: 1.severe illness (hospitalized); <i>and</i> 2. ≥ 2 organ systems involved	At least 2 of the following: 1.rash, conjunctivitis, and mucocutaneous inflammation; 2.hypotension or shock; 3.cardiac involvement; 4.coagulopathy; 5.acute GI symptoms
Inflammation	All 3 of the following: 1.neutrophilia; <i>and</i> 2.increased CRP; <i>and</i> 3.lymphopenia	Laboratory evidence of inflammation including, but not limited to, 1 or more of the following: 1. \uparrow CRP; 2. \uparrow ESR; 3. \uparrow fibrinogen; 4. \uparrow procalcitonin; 5. \uparrow D-dimer; 6. \uparrow ferritin; 7. \uparrow LDH; 8. \uparrow IL-6; 9.neutrophilia; 10.lymphopenia; 11.hypoalbuminemia	Elevated inflammation markers, including any of the following: 1. \uparrow ESR; 2. \uparrow CRP; 3. \uparrow procalcitonin
Link to SARS-CoV-2	Positive or negative by PCR	Current or recent findings of the following: 1.positive by PCR; 2.positive by serology; 3.positive by antigen test; <i>or</i> 4.COVID-19 exposure within prior 4 weeks	Evidence of COVID-19 by the following: 1.positive by PCR; 2.positive by antigen test; 3.positive by serology; <i>or</i> 4.likely COVID-19 contact
Exclusion	Other infections	No alternative diagnosis	No obvious microbial cause

MIS-C Clinical Pathway - CHCO



Christina Osborne MD
Infectious Disease



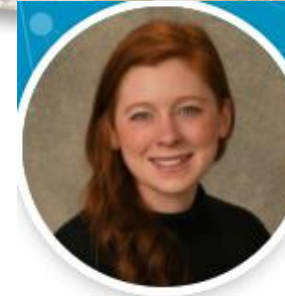
Pei-Ni Jone MD
Cardiology



Marion Sills MD
Emergency Medicine



Eva Nozik MD
PICU



Kaleigh Ogawa RN
Clinical Effectiveness



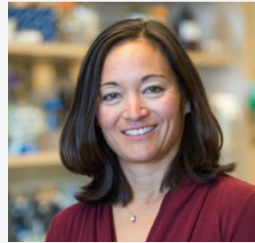
Justin Lockwood MD
Hospital Medicine



Samuel Dominguez MD
Infectious Disease



Melanie Everitt MD
Cardiology



Shelley Miyamoto MD
Cardiology

Multisystem Inflammatory Syndrome in Children (MIS-C) associated with Coronavirus Disease COVID-19

Updated as of 09-10-2021

Initial Assessment for Patients with Suspected MIS-C

Does patient have current fever ≥ 3 days and ≥ 2 of the following clinical criteria:

- Rash or bilateral non-purulent conjunctivitis or signs of mucocutaneous inflammation (erythema and/or swelling of hands and feet, strawberry tongue, red lips)
- Acute gastrointestinal problems (diarrhea defined as 3 or more watery stools (Bristol 6 or 7) in a 24-hour period, vomiting, and/or abdominal pain)
- Hypotension or shock
- Neurological symptoms: headache, neck stiffness, neck pain, altered mental status

[CHCO MIS-C Clinical Case Definition](#)
(adapted from [CDC](#) and [WHO](#) definitions)

Diagnostic Timeout

Given the broad case definition.



Robert Fuhlbrigge MD
Rheumatology



Leigh Anne Bakel MD
Hospital Medicine



Clinical Case Definition (CHCO), combination of CDC and WHO definitions

Children and adolescents <21 years of age with **FEVER greater than or equal to 3 days AND TWO of the following:**

1. Rash or bilateral non-purulent conjunctivitis or signs of mucocutaneous inflammation (erythema and/or swelling of hands and feet, strawberry tongue, red lips)
2. Acute gastrointestinal problems (diarrhea, vomiting, and/or abdominal pain)
3. Hypotension or shock
4. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary artery abnormalities (including echocardiogram findings or elevated troponin or NT-pro BNP)
5. Evidence of coagulopathy (by PT, PTT, elevated D-dimer)

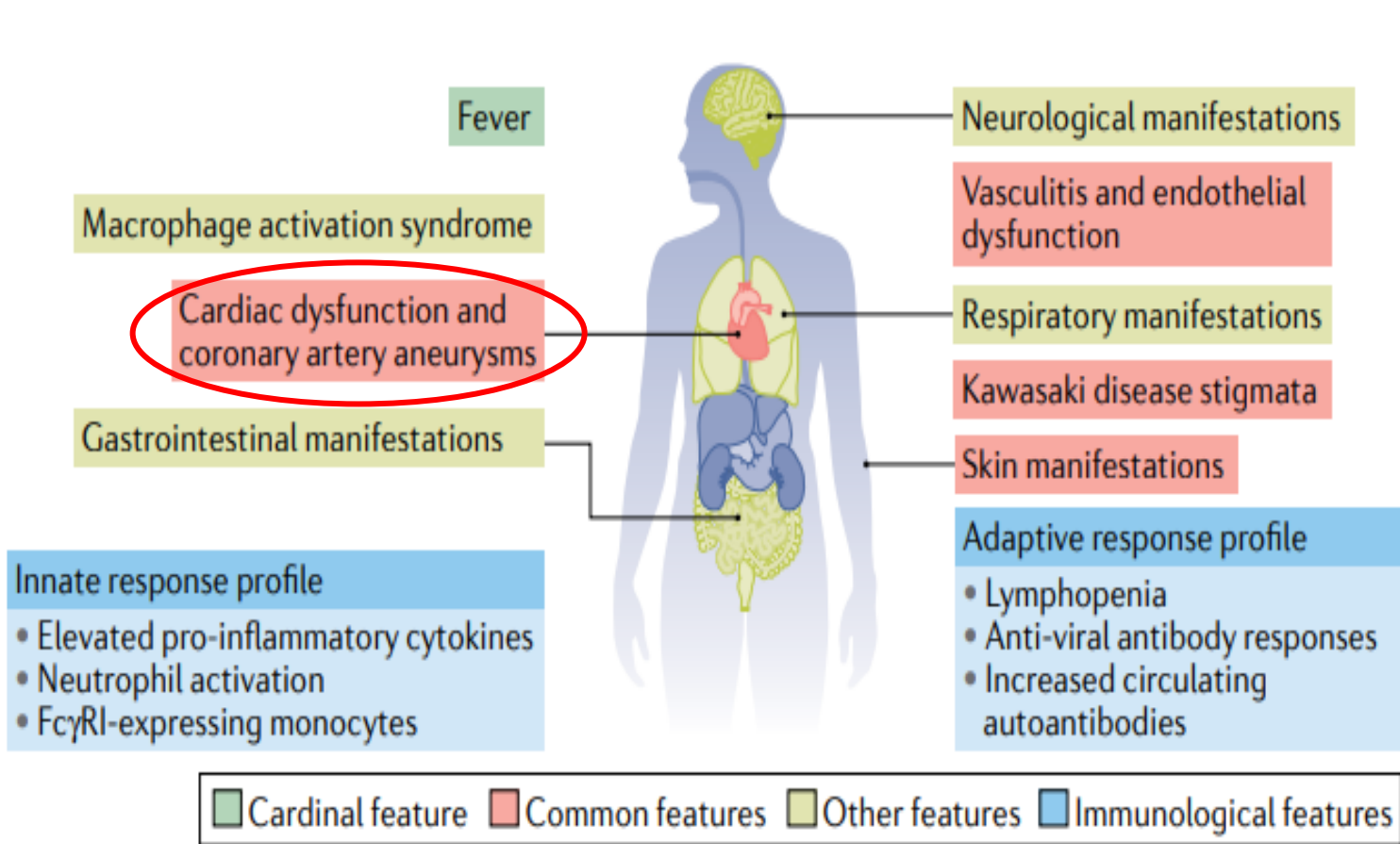
AND elevated markers of inflammation

Including 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

AND no other obvious microbial cause of inflammation including bacterial sepsis, local bacterial infection (e.g. urinary tract infection, osteomyelitis, etc.), or staphylococcal and streptococcal toxic shock syndromes

AND evidence of COVID-19 (RT-PCR positive, positive serologies) OR likely contact with persons with COVID-19

MIS-C – Clinical Features



Distinction between MISC and KD

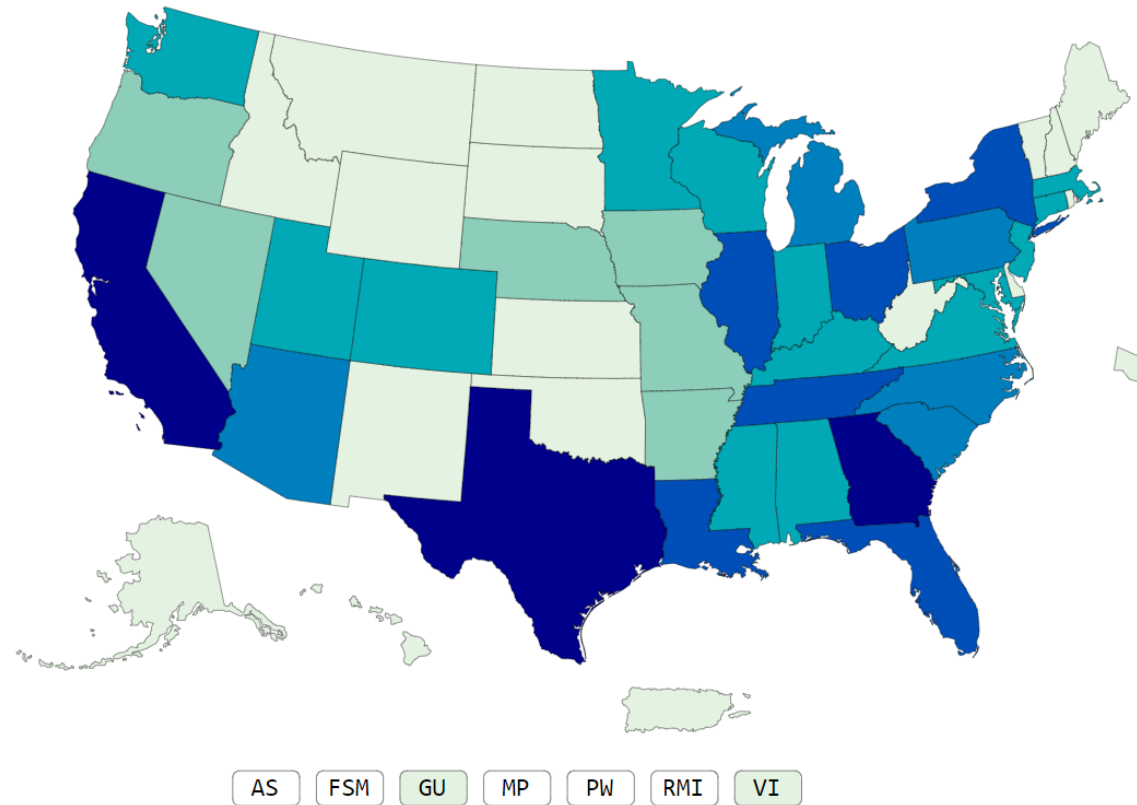
MISC – exposure/testing SARS

- Older children and Adolescents (mean age 9.3 ± 0.4 years)
- Black and Hispanics, Asians small percentage
- GI presentation (abdominal pain) – very common
- Myocardial dysfunction and shock occur more commonly (60.2%)
- Inflammatory markers are more elevated (higher CRP, ferritin, and D-dimer)
- Absolute lymphocytes and platelet counts are lower in MISC compared to KD

KD

- Infants and young children (<5 years)
- Large percentage of Asian
- GI symptoms are less common
- KD shock is only in 5%
- CRP 4, sed rate >40

Reported MIS-C Case Ranges by Jurisdiction, on or before March 28, 2022*



Reported
MIS-C Cases

- No case reported
- 1-49 cases
- 50-99 cases
- 100-199 cases
- 200-299 cases
- 300-399 cases
- 400+ cases

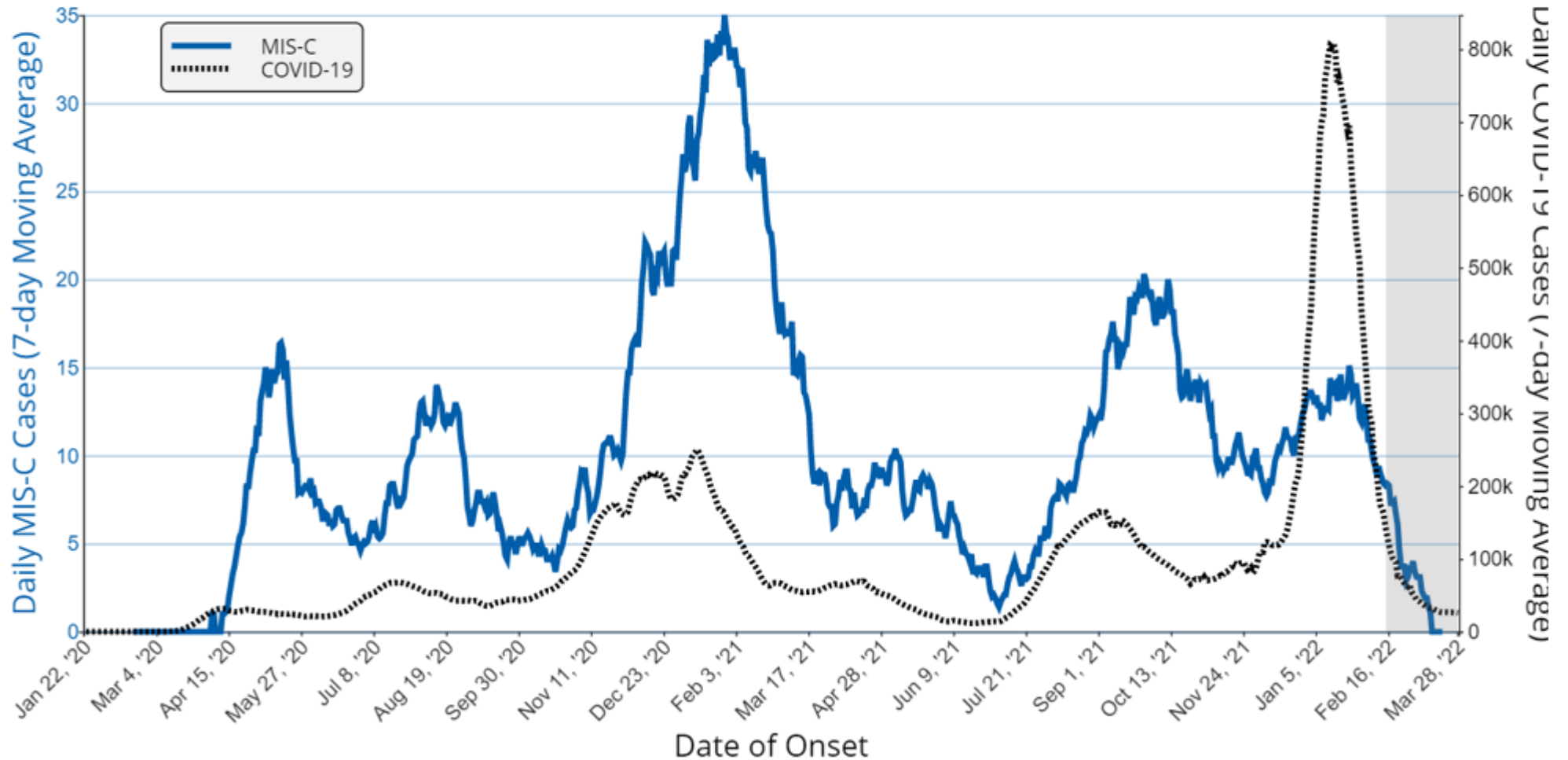
***Incidence is 3 in 10,000**

<https://www.cdc.gov/mis/cases/index.html>

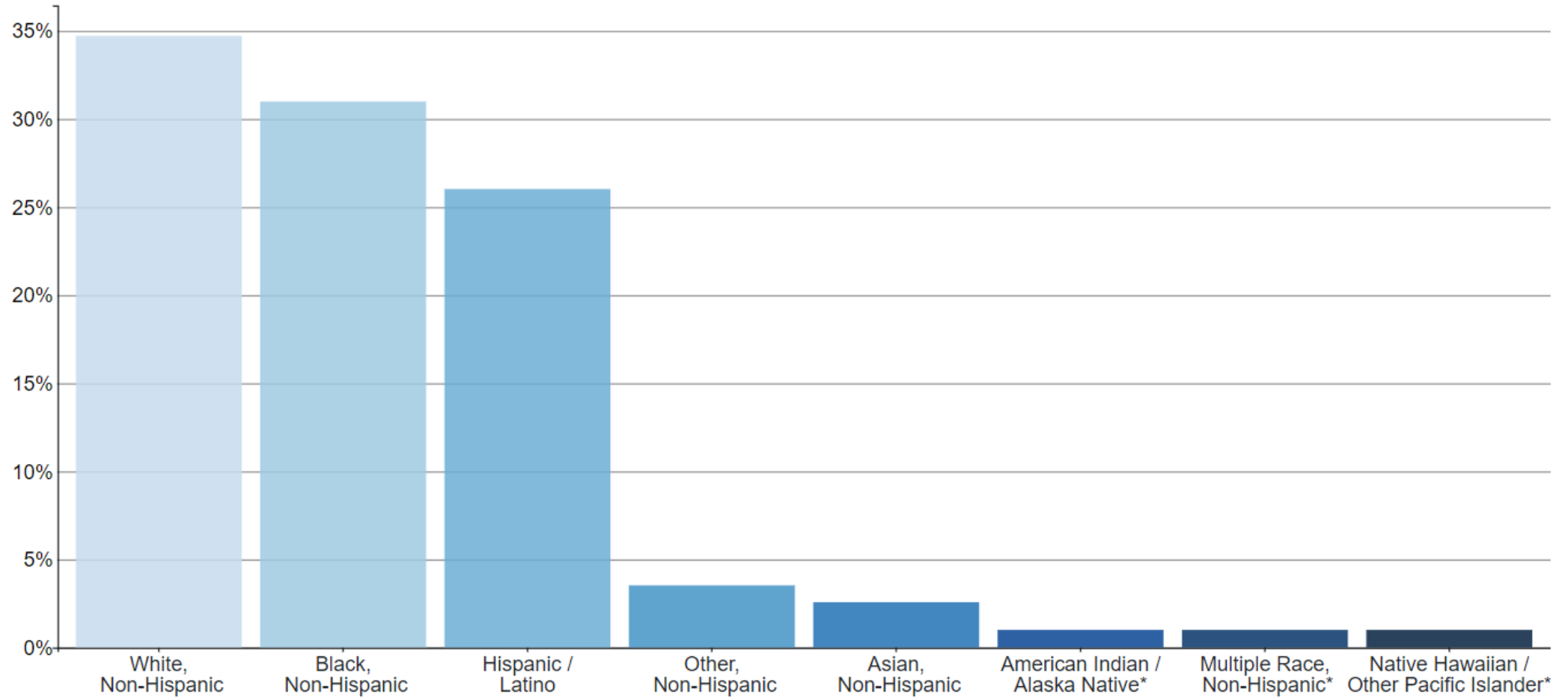
*Payne AB, Gilani Z, Godfred-Cato S, et al. ; MIS-C Incidence Authorship Group. Incidence of multisystem inflammatory syndrome in children among US persons infected with SARS-CoV-2. JAMA Netw Open. 2021;4:e2116420.

Total: 7880 cases
Death: 66 cases

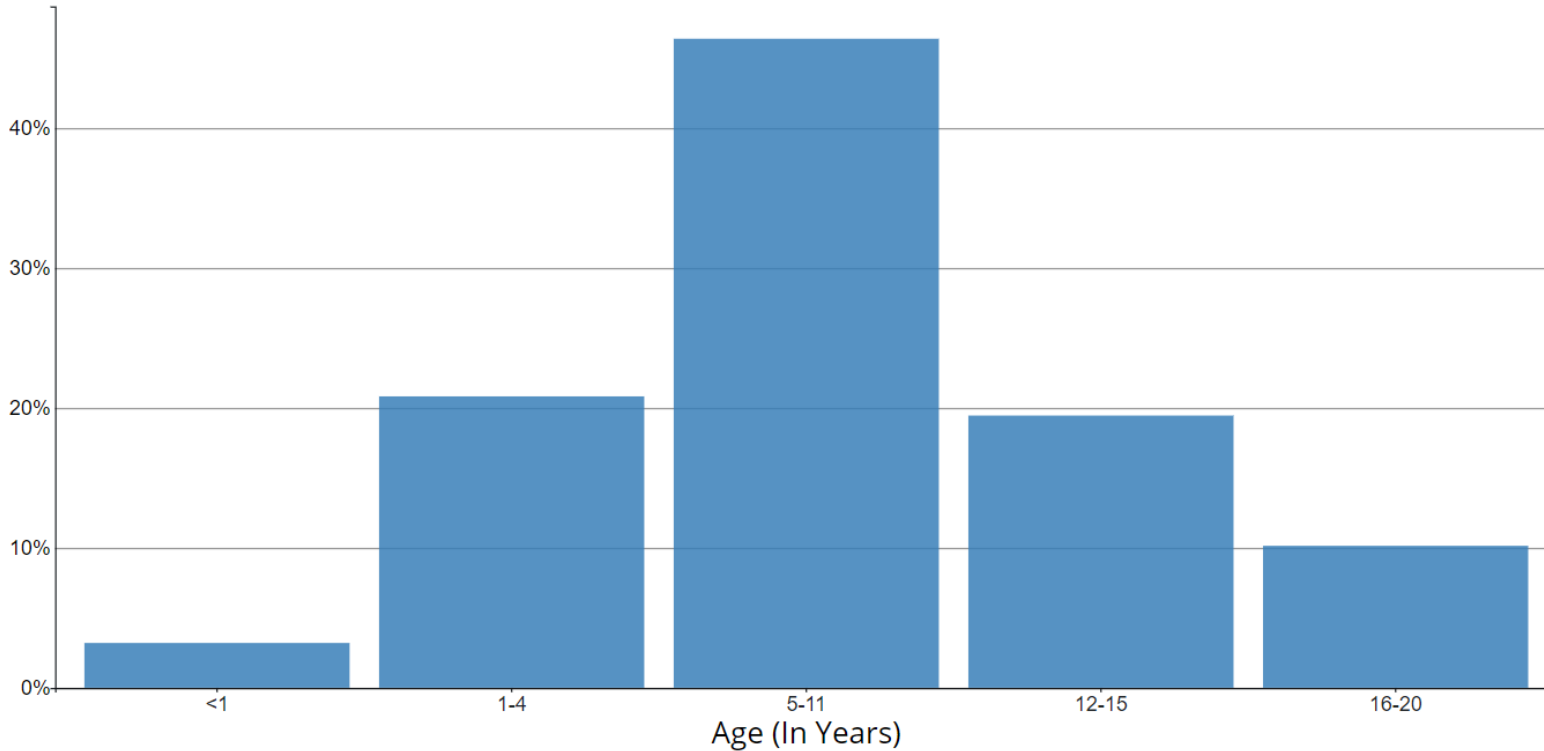
Daily MIS-C Cases and COVID-19 Cases Reported to CDC (7-Day Moving Average)



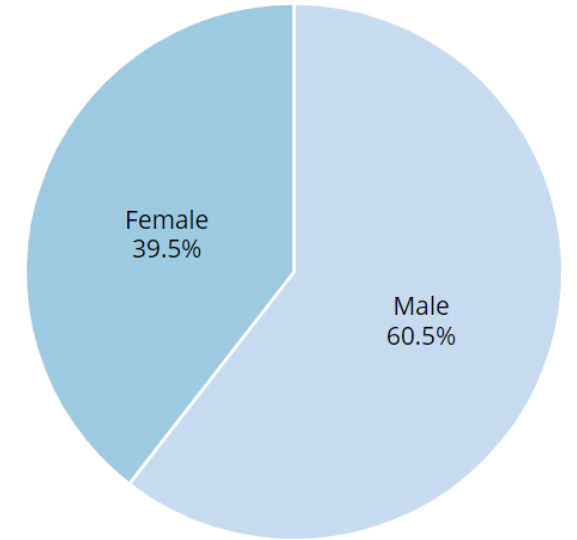
MIS-C Patients by Race & Ethnicity



MIS-C Patients By Age Group



MIS-C Patients By Sex



- MIS-C median age = 9 years.
- 1/2 MIS-C between 5-13 years
- 61% of reported patients were male



CDC summary statistics – MIS-C

- The median age was 9 years.
- Half of children with MIS-C were between the ages of 5 and 13 years.
- 57% of the reported patients with race/ethnicity information available occurred in children who are Hispanic/Latino (1,943 patients) or Black, Non-Hispanic (2,303 patients).
- 98% of patients had a positive test result for SARS CoV-2, the virus that causes COVID-19. The remaining 2% of patients had contact with someone with COVID-19.
- 61% of reported patients were male.

Pathophysiology??

- Hyperinflammatory response
 - High levels of interleukin-1 β (IL-1 β), IL-6, IL-8, IL-10, IL-17, interferon- γ and differential T and B cell subset lymphopenia
 - Cytokine storm
 - Macrophage activation syndrome
 - Appears distinct from KD
- Mechanisms of Myocardial Injury is unknown
 - Injury from systemic inflammation
 - Acute viral myocarditis
 - hypoxia

MIS-C Clinical Presentation

Clinical Symptoms	Frequency (%)
•Persistent fevers (median duration 4 to 6 days)	100
•Gastrointestinal symptoms (abdominal pain, vomiting, diarrhea)	60 to 100
•Rash	45 to 76
•Conjunctivitis	30 to 81
•Mucous membrane involvement	27 to 76
•Neurocognitive symptoms (headache, lethargy, confusion)	29 to 58
•Respiratory symptoms (tachypnea, labored breathing)	21 to 65
•Sore throat	10 to 16
•Myalgias	8 to 17
•Swollen hands/feet	9 to 16
•Lymphadenopathy	6 to 16

MIS-C (Belay Study = 1733 patients)

Table 1. Characteristics of Patients With MIS-C by Age Group, United States, March 2020 to January 2021

Variable	All MIS-C cases (N = 1733), No. (%)	Age, No. (%), y ^a					P value ^b
		0-4 (n = 445)	5-9 (n = 588)	10-14 (n = 451)	15-17 (n = 191)	18-20 (n = 55)	
Sex ^c							
Signs and symptoms							
Abdominal pain ^e	1153 (66.5)	187 (42)	475 (80.8)	330 (73.2)	123 (64.4)	37 (67.3)	<.001
Vomiting	1114 (64.3)	233 (52.4)	426 (72.4)	305 (67.6)	121 (63.4)	27 (49.1)	<.001
Diarrhea	931 (53.7)	218 (49)	331 (56.3)	246 (54.5)	105 (55)	30 (54.5)	.22
Rash	963 (55.6)	303 (68.1)	354 (60.2)	221 (49)	65 (34)	20 (36.4)	<.001
Conjunctival hyperemia	929 (53.6)	248 (55.7)	362 (61.6)	250 (55.4)	58 (30.4)	10 (18.2)	<.001
Cough	490 (28.3)	111 (24.9)	131 (22.3)	145 (32.2)	76 (39.8)	27 (49.1)	<.001
Shortness of breath ^e	475 (27.4)	67 (15.1)	141 (24)	153 (33.9)	84 (44)	29 (52.7)	<.001
Chest pain or tightness ^e	252 (14.5)	6 (1.3)	57 (9.7)	100 (22.2)	66 (34.6)	23 (41.8)	<.001
ICU admission	1009 (58.2)	197 (44.3)	349 (59.4)	300 (66.5)	129 (67.5)	32 (58.2)	<.001
Died	24 (1.4)	6 (1.3)	3 (0.5)	4 (0.9)	5 (2.6)	6 (10.9)	<.001

MIS-C Clinical Findings

Clinical Findings	Frequency (%)
•Shock	32 to 76
•Criteria for complete Kawasaki disease met	22 to 64
•Myocardial dysfunction (by echocardiogram or elevated troponin/BNP)	51 to 90
•Arrhythmia	12
•Acute respiratory failure requiring noninvasive or invasive ventilation	28 to 52
•Acute kidney injury	8 to 52
•Serositis (small pleural, pericardial, and ascitic effusions)	24 to 57
•Hepatitis or hepatomegaly	5 to 21
•Encephalopathy, seizures, coma, or meningoencephalitis	6 to 7

MIS-C (Belay Study = 1733 patients)

Table 1. Characteristics of Patients With MIS-C by Age Group, United States, March 2020 to January 2021

Variable	All MIS-C cases (N = 1733), No. (%)	Age, No. (%), y ^a					P value ^b
		0-4 (n = 445)	5-9 (n = 588)	10-14 (n = 451)	15-17 (n = 191)	18-20 (n = 55)	
Clinical findings							
Hypotension	880 (50.8)	160 (36)	297 (50.5)	283 (62.7)	109 (57.1)	29 (52.7)	<.001
Shock	638 (36.8)	110 (24.7)	210 (35.7)	207 (45.9)	88 (46.1)	22 (40)	<.001
Cardiac dysfunction ^f	484 (31.0)	76 (18.8)	175 (32.4)	141 (34.7)	74 (43.3)	17 (41.5)	<.001
Myocarditis	300 (17.3)	41 (9.2)	96 (16.3)	93 (20.6)	53 (27.7)	17 (30.9)	<.001
Coronary artery dilatation or aneurysm ^f	258 (16.5)	74 (18.3)	90 (16.7)	65 (16)	22 (12.9)	6 (14.6)	.61
Pericardial effusion ^f	365 (23.4)	102 (25.2)	129 (23.9)	85 (20.9)	38 (22.2)	11 (26.8)	.60
Pneumonia ^g	330 (19)	53 (11.9)	98 (16.7)	103 (22.8)	55 (28.8)	20 (36.4)	<.001
ARDS	115 (6.6)	22 (4.9)	32 (5.4)	33 (7.3)	17 (8.9)	10 (18.2)	.01
Pleural effusion ^h	171 (10.3)	35 (8.2)	68 (12)	44 (10.1)	18 (9.7)	6 (12)	.40
SARS-CoV-2 testing							
PCR positive ⁱ	893 (51.5)	218 (49)	274 (46.6)	242 (53.7)	118 (61.8)	39 (70.9)	<.001
Received serology and tested positive ⁱ	1432 (82.6)	371 (83.4)	513 (87.2)	373 (82.7)	141 (73.8)	32 (58.2)	<.001
Treatment							
IVIG ^k	1395 (80.5)	368 (82.7)	492 (83.7)	376 (83.4)	129 (67.5)	29 (52.7)	<.001
Steroids	1230 (71)	278 (62.5)	412 (70.1)	359 (79.6)	141 (73.8)	38 (69.1)	<.001

MIS-C Laboratory Findings

Abnormal blood cell counts

- Lymphocytopenia – 80 to 95 percent
- Neutrophilia – 68 to 90 percent
- Mild anemia – 70 percent
- Thrombocytopenia – 31 to 80 percent

Elevated Inflammatory Markers

- C-reactive protein (CRP) – 90 to 100 percent
- Erythrocyte sedimentation rate (ESR) – 75 to 80 percent
- D-dimer – 67 to 100 percent
- Fibrinogen – 80 to 100 percent
- Ferritin – 55 to 76 percent
- Procalcitonin – 80 to 95 percent
- Interleukin-6 (IL-6) – 80 to 100 percent

MIS-C Laboratory Findings

Elevated Cardiac Markers

- Troponin – 50 to 90 percent
- BNP or N-terminal pro-BNP (NT-pro-BNP) – 73 to 90 percent

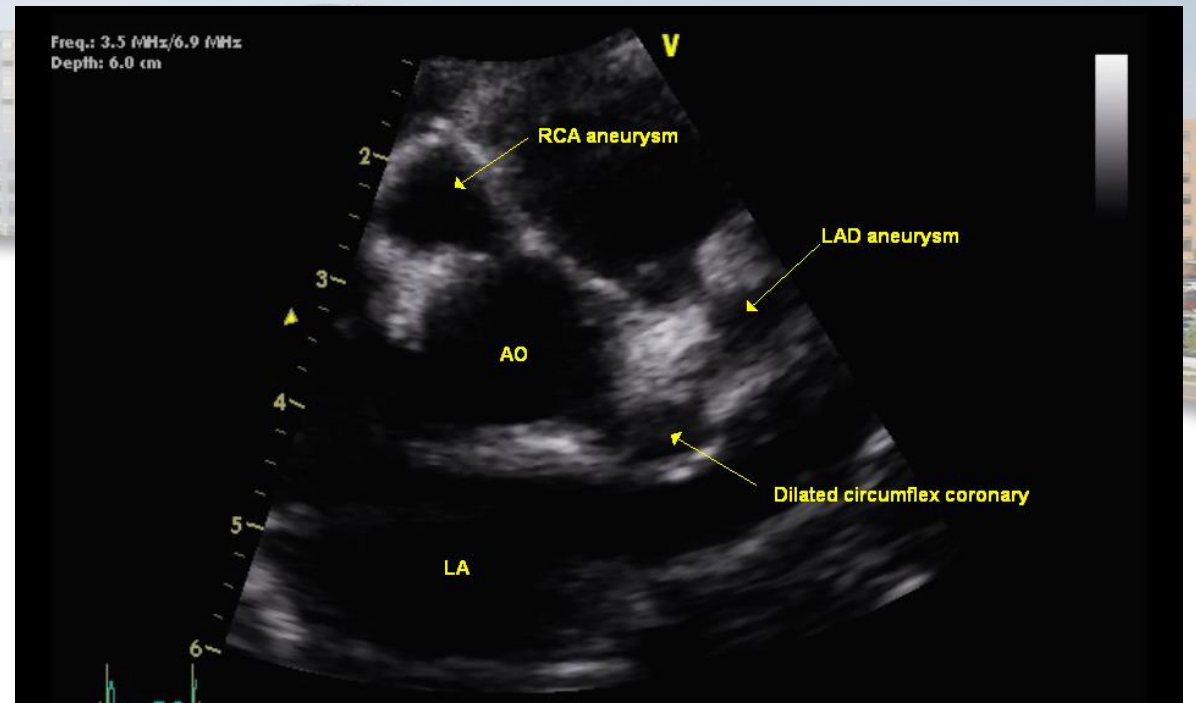
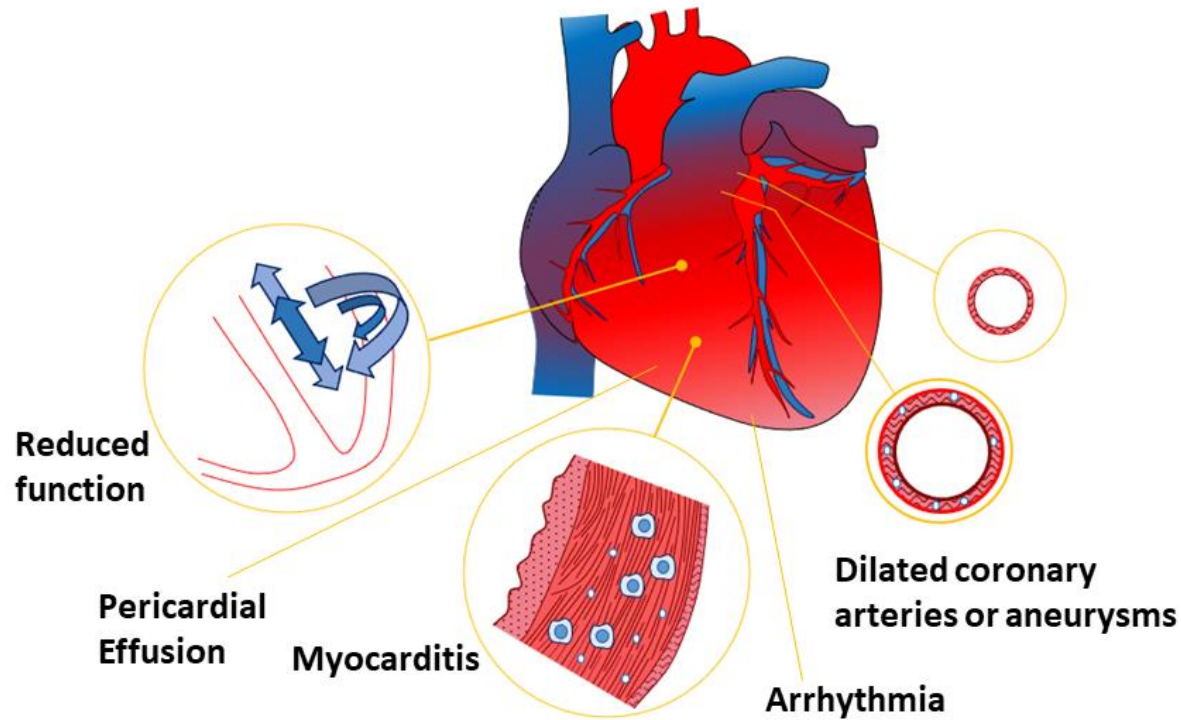
Other Markers

- Hypoalbuminemia – 48 to 95 percent
- Mildly elevated liver enzymes – 62 to 70 percent
- Elevated lactate dehydrogenase – 10 to 60 percent
- Hypertriglyceridemia – 70 percent

MIS-C (Belay Study = 1733 pts)

- 2-5 weeks after COVID-19 (in 18-20 age group – can present as early as 7 days)
- GI symptoms of abdominal pain, vomiting, diarrhea (66%)
- Rash (55.6%)
- Conjunctival hyperemia (53.6%)
- Hypotension or shock with 60% admitted to the ICU
- 0-4 years of age fewer complications and less ICU admissions (44%)
- Myocarditis, cardiac dysfunction, and coronary artery dilation ~30%

MIS-C EKG and Echo



Jone PN, John A, Oster ME, Allen K, Tremoulet AH, Saarel EV, Lambert LM, Miyamoto SD, de Ferranti SD. SARS-CoV-2 Infection and Associated Cardiovascular Manifestations and Complications in Children and Young Adults: A Scientific Statement From the American Heart Association. *Circulation*. 2022 Apr 11:101161CIR0000000000001064.

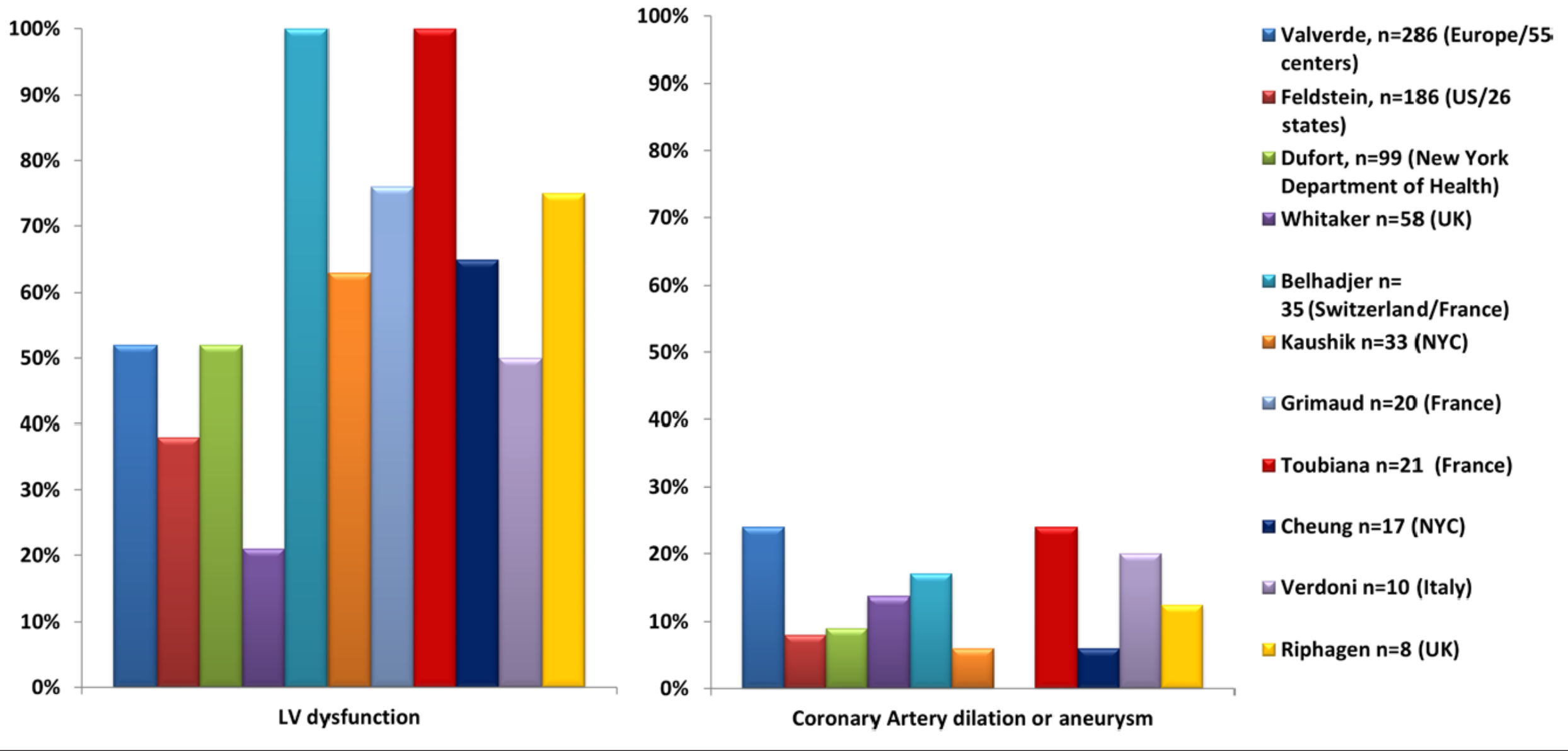


Figure 2. Percentage of ventricular dysfunction and coronary artery dilation or aneurysms in different studies. The studies by Belhadjer and Toubiana only included patients with left ventricular dysfunction. LV indicates left ventricle; and NYC, New York City.

MIS-C Treatment (1733 patients)

Table 1. Characteristics of Patients With MIS-C by Age Group, United States, March 2020 to January 2021

Variable	All MIS-C cases (N = 1733), No. (%)	Age, No. (%), y ^a					P value ^b
		0-4 (n = 445)	5-9 (n = 588)	10-14 (n = 451)	15-17 (n = 191)	18-20 (n = 55)	
Treatment							
IVIG ^k	1395 (80.5)	368 (82.7)	492 (83.7)	376 (83.4)	129 (67.5)	29 (52.7)	<.001
Steroids	1230 (71)	278 (62.5)	412 (70.1)	359 (79.6)	141 (73.8)	38 (69.1)	<.001

- Intravenous immunoglobulin
- Infliximab – for coronary artery dilation
- Aspirin
- IL – 1 receptor antagonist (Anakinra)
- Steroids

MIS-C Treatment – Overcoming COVID-19

- IVIG versus IVIG + steroids (58 US centers, 518 MIS-C patients)
- Primary outcome: LV dysfunction or shock needing vasopressors on or after day 2
- Secondary outcome: components of primary outcome, receipt of adjunctive treatment on or after day 1, and persistent fever on or after day 2)

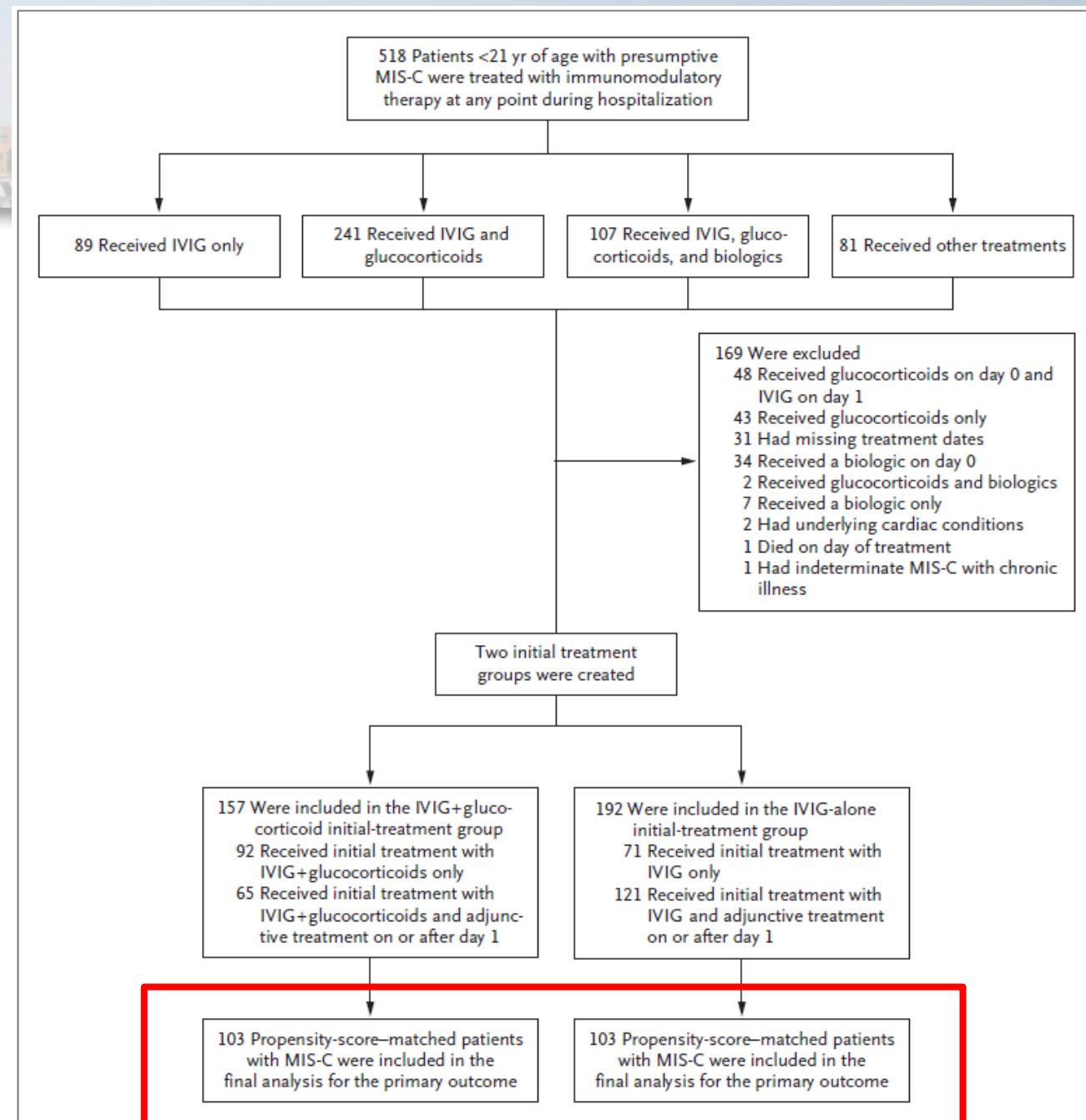


Figure 1. Patients with MIS-C Treated with Immunomodulatory Therapies in the Overcoming COVID-19 Surveillance Registry.



MIS-C Treatment – Overcoming COVID-19

Children's Hospital Colorado

Analytic Approach and Outcomes

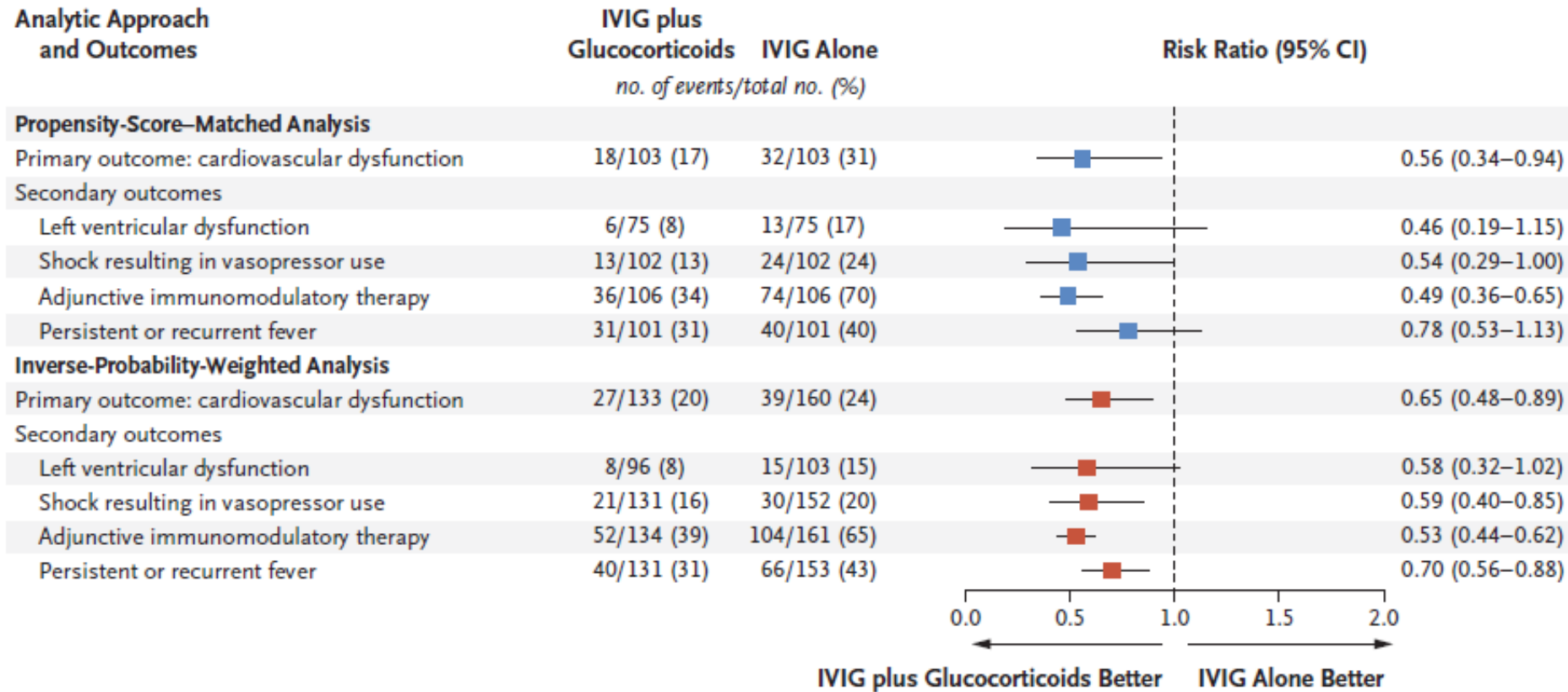


Figure 3. Associations between Initial Treatment with IVIG plus Glucocorticoids, or with IVIG Alone, and Clinical Outcomes.

Cardiovascular dysfunction was based on a composite of left ventricular dysfunction or shock that resulted in the use of vasopressors on or after day 2 after initial treatment. Left ventricular dysfunction was defined as an LVEF below 55%. Medications that met the study criterion of vasopressor use were dobutamine, dopamine, epinephrine, norepinephrine, or a combination of these. Adjunctive immunomodulatory therapy included a second dose of IVIG, glucocorticoids, or biologic treatment on or after day 1. Persistent or recurrent fever was defined as a body temperature of higher than 38.0°C on or after day 2.

- Initial Treatment with IVIG + steroids was associated with lower risk of new or persistent CV dysfunction than IVIG alone.
- Less use of adjunctive therapy.
- Fever and ICU stay were not lower.

Son et al. MIS-C – initial therapy and outcomes. N Engl J Med. 2021 Jul 1;385(1):23-34.



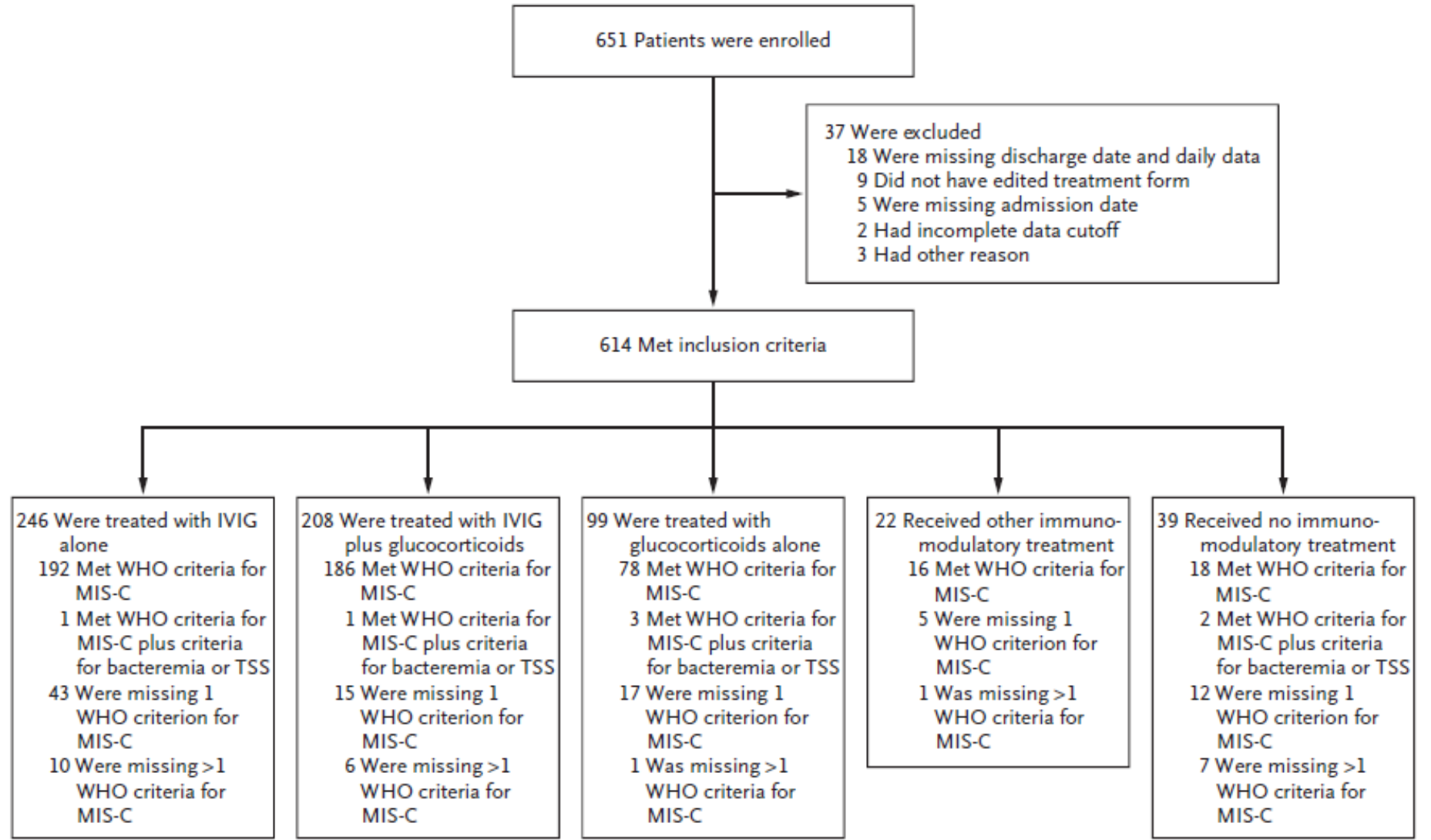
MIS-C Treatment – BATS (Best Available Treatment Study)

- 32 countries (614 MIS-C patients)
- IVIG versus IVIG + Steroids versus Steroids
- Primary outcome
 - Composite of inotropic support or mechanical ventilation by day 2 or later or death
- Secondary outcome
 - Reduction in disease severity on an ordinal scale by day 2
 - Treatment escalation and the time until reduction in organ failure and inflammation.



MIS-C Treatment – BATS Consortium

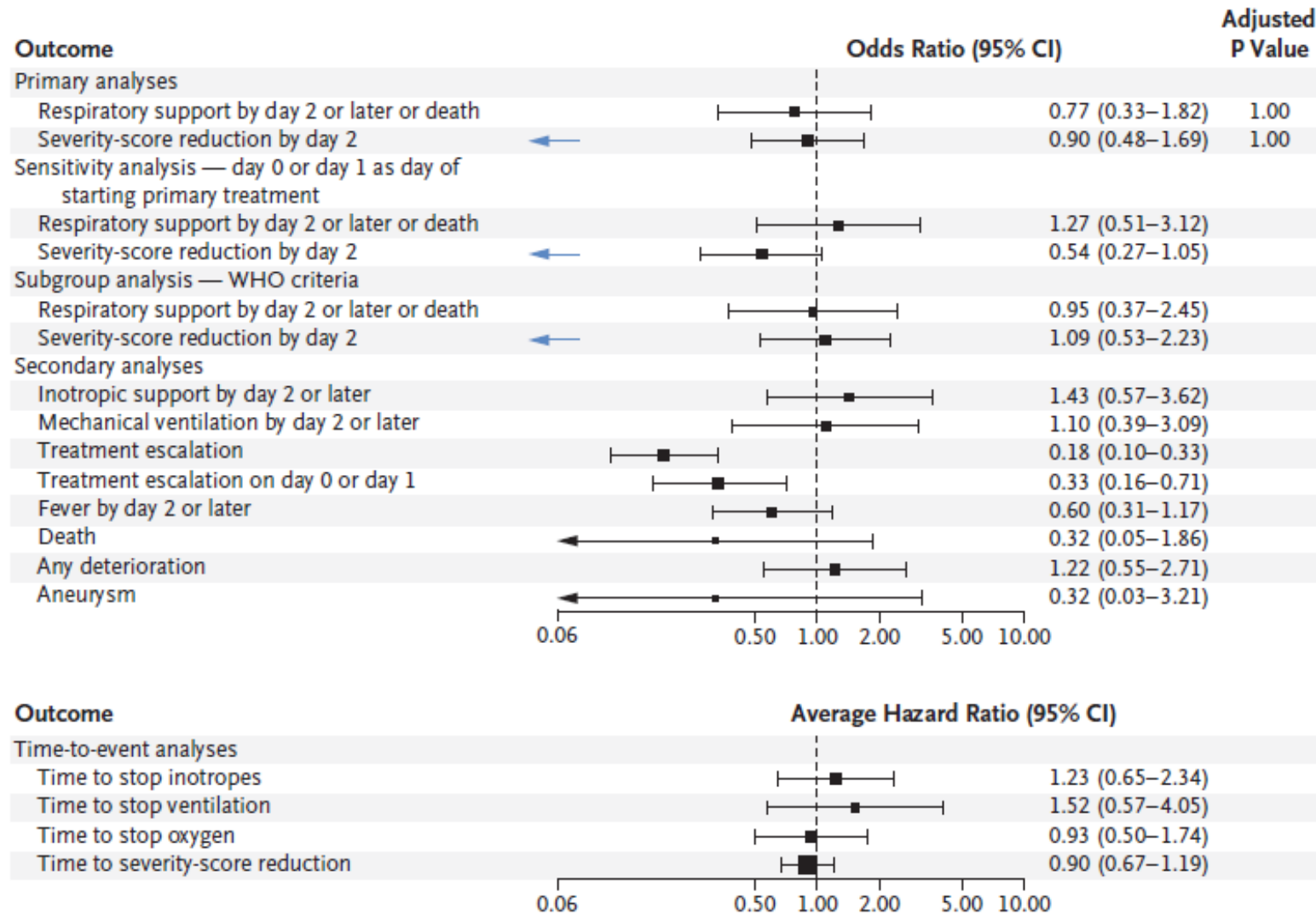
A Primary Therapy Groups





MIS-C Treatment – BATS Consortium

A Comparison of IVIG plus Glucocorticoids versus IVIG Alone



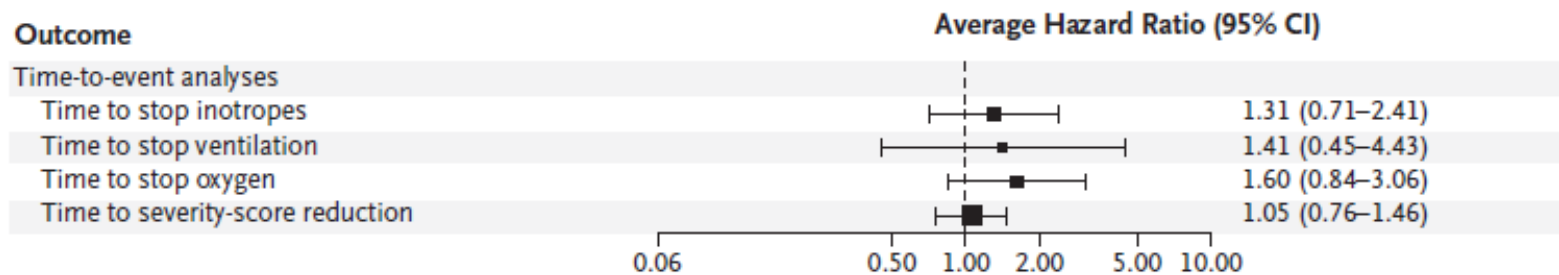
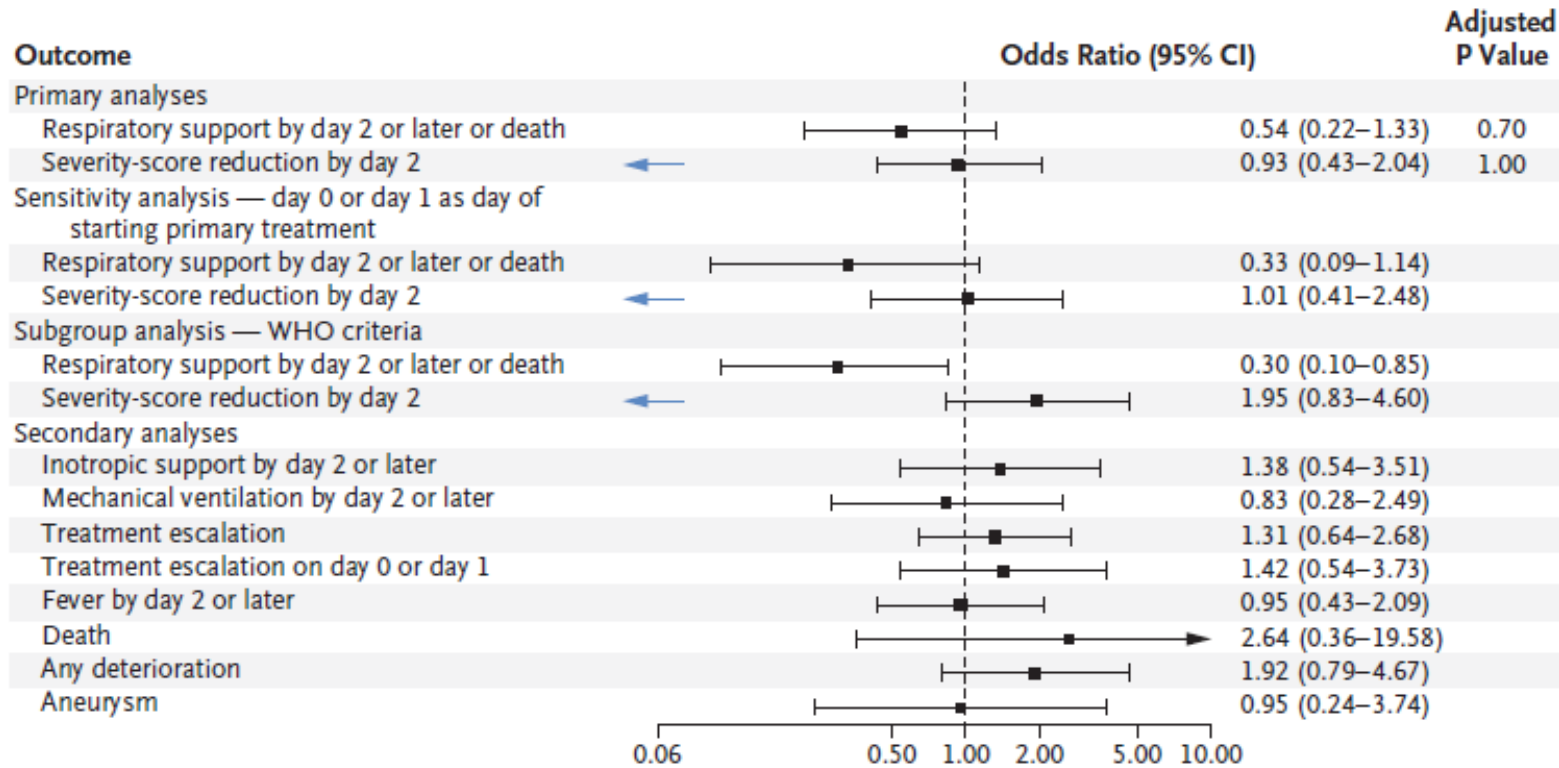
- IVIG versus IVIG+steroids
- No difference found



MIS-C Treatment – BATS Consortium

Children's Hospital Colorado

B Comparison of Glucocorticoids Alone versus IVIG Alone



- IVIG versus steroids
- No difference found

MIS-C Treatment – Denver Study

IVIIG Compared to IVIG Plus Infliximab in Multisystem Inflammatory Syndrome in Children



Lyndsey D. Cole, MD^{1*}; Christina M. Osborne, MD^{2*}; Lori J. Silveira, PhD³; Suchitra Rao, MBBS, MSCS⁴; Justin M. Lockwood, MD, MSCS⁵; Megan J. Kunkel, BS³; Christine E. MacBrayne, PharmD⁶; Heather R. Heizer, PA⁷; Marsha S. Anderson, MD⁷; Pei-Ni Jone, MD⁸; Samuel R. Dominguez, MD, PhD⁷

*Contributed equally as co-first authors



MIS-C Treatment – Denver Study

Clinical Presentation of MIS-C (n=72)

- Median age = 8.5 years
- Male (58%)
- Hispanic/Latino (48%)
- Underlying Medical Condition (22%)
- Median day of fever at initial treatment = 5 days
- PICU admission (58%)
- Fever (100%)
- Gastrointestinal (94%)
- Cardiac (100%)
- Respiratory (64%)
- Neurologic (88%)
- Rash (76%)
- Conjunctivitis (90%)



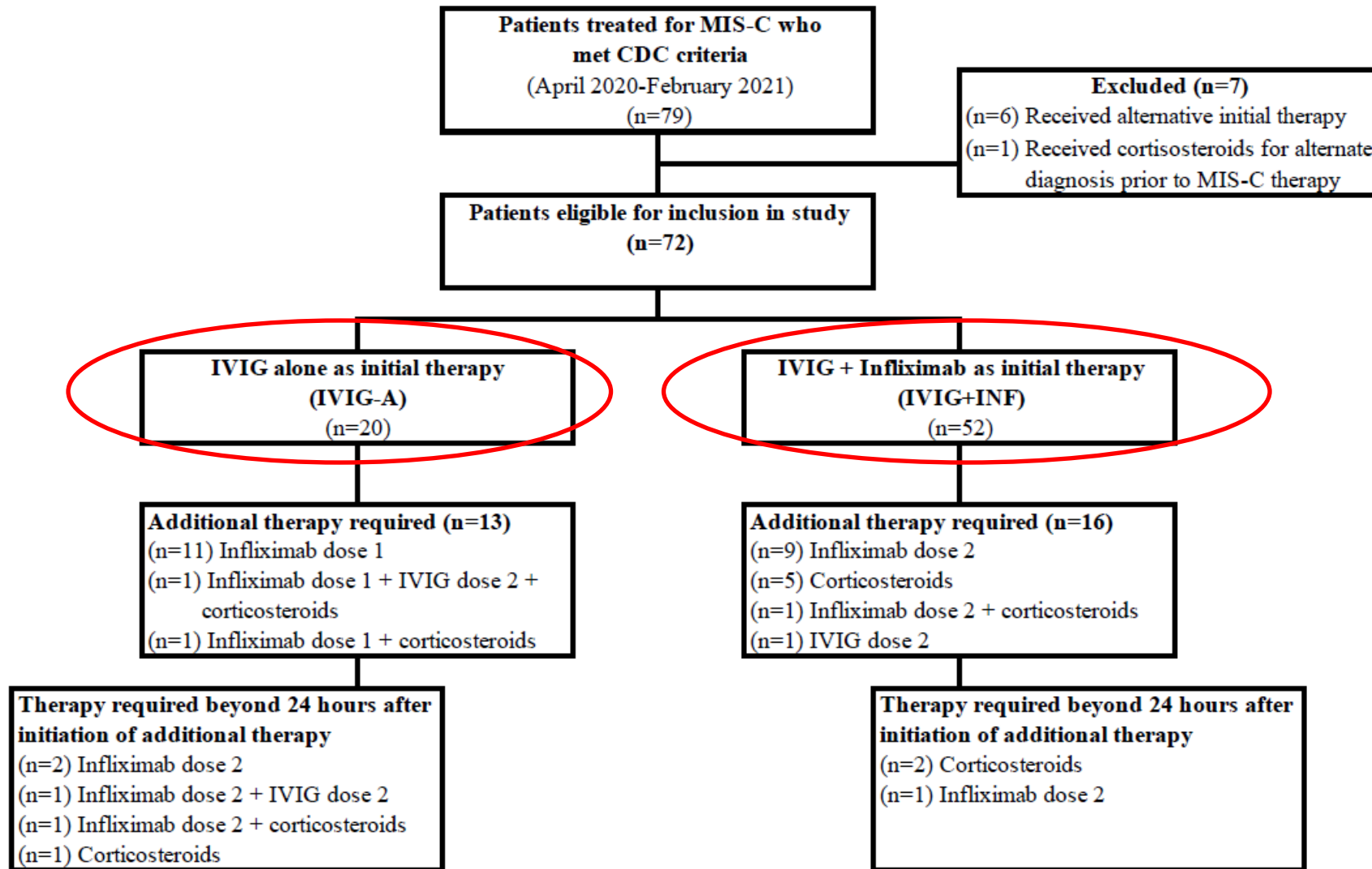
MIS-C Treatment – Denver Study

Laboratory Characteristics (n=72)

- SARS-CoV-2 PCR+ (36%)
- SARS-CoV-2 IgG+ (89%)
- Lymphopenia (69%)
- Thrombocytopenia (53%)
- Hyponatremia (63%)
- Hypoalbuminemia (39%)
- Median CRP = 16.9 mg/dL
- Median ESR = 36 mm/hr
- Median NT-proBNP = 1750 pg/mL

MIS-C Treatment – Denver Study

Figure 1: Study schematic for patients diagnosed with MIS-C by CDC guidelines who received treatment. Alternative initial therapies included IVIG plus corticosteroids, infliximab, and/or anakinra



Cole L et al. IVIG compared to IVIG plus infliximab in Multisystem Inflammatory Syndrome in Children. Pediatrics 2021 Sep 22:e2021052701.

MIS-C Denver Study






Dual Therapy Research Clinical Impact

IVIG Compared to IVIG Plus Infliximab in Multisystem Inflammatory Syndrome in Children.

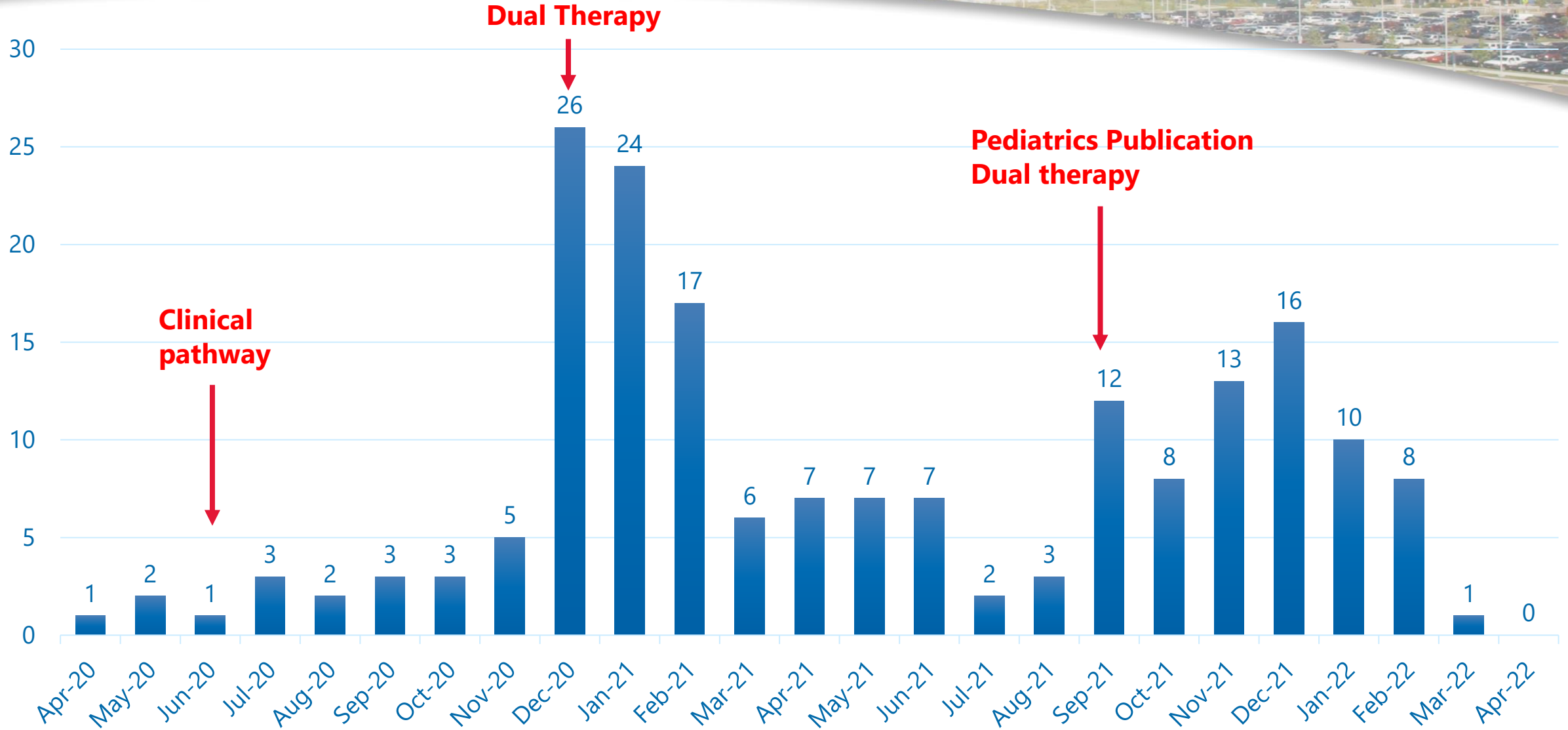


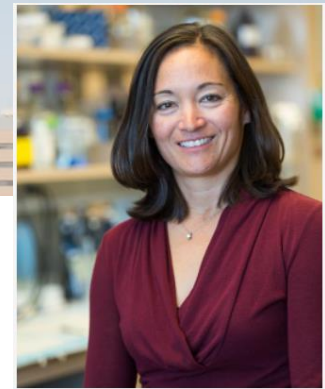
Cole LD, Osborne CM, Silveira LJ, Rao S, Lockwood JM, Kunkel MJ, MacBrayne CE, Heizer HR, Anderson MS, Jone PN, Dominguez SR.

- **Decreased requirement of additional therapy**
- **Decreased development of heart dysfunction**
- **Rapid decline of inflammation**
- **Decreased length of ICU stay**

IVIG vs dual therapy	IVIG alone	IVIG + infliximab
 Required additional therapy	65%	31%
 Developed left ventricle dysfunction	20%	4%
 CRP fall at 24 hours	0%	-46%
 CRP fall at 48 hours	-5%	-70%
 Median length of stay	3.3 days	1.8 days

CHCO MIS-C Cases = 187





AHA Journals

Journal Information


All Issues

Subjects

Features

Resources & Educ

[Home](#) > [Circulation](#) > [Ahead of Print](#) > [SARS-CoV-2 Infection and Associated Cardiovascular Manifestations and Complications in Children and Young Adults: A Sci...](#)

 FREE ACCESS

REVIEW ARTICLE

 PDF/EPUB


 Tools  Share

Jump to

SARS-CoV-2 Infection and Associated Cardiovascular Manifestations and Complications in Children and Young Adults: A Scientific Statement From the American Heart Association

Pei-Ni Jone, Anitha John, Matthew E. Oster, Kiona Allen, Adrianna H. Tremoulet, Elizabeth V. Saarel, Linda M. Lambert, Shelley D. Miyamoto, Sarah D. de Ferranti and

on behalf of the American Heart Association Leadership Committee and Congenital Cardiac Defects Committee of the Council on Lifelong Congenital Heart Disease and Heart Health in the Young; Council on Hypertension, and Council on Peripheral Vascular Disease

See fewer authors 

Originally published 11 Apr 2022 | <https://doi.org/10.1161/CIR.0000000000001064> | Circulation. 2022;0:10.1161/CIR.0000000000001064





Jone PN, John A, Oster ME, Allen K, Tremoulet AH, Saarel EV, Lambert LM, Miyamoto SD, de Ferranti SD. SARS-CoV-2 Infection and Associated Cardiovascular Manifestations and Complications in Children and Young Adults: A Scientific Statement From the American Heart Association. Circulation. 2022 Apr 11:101161CIR0000000000001064.

MIS-C Outcomes: Ventricular Function

Journal of the American Heart Association

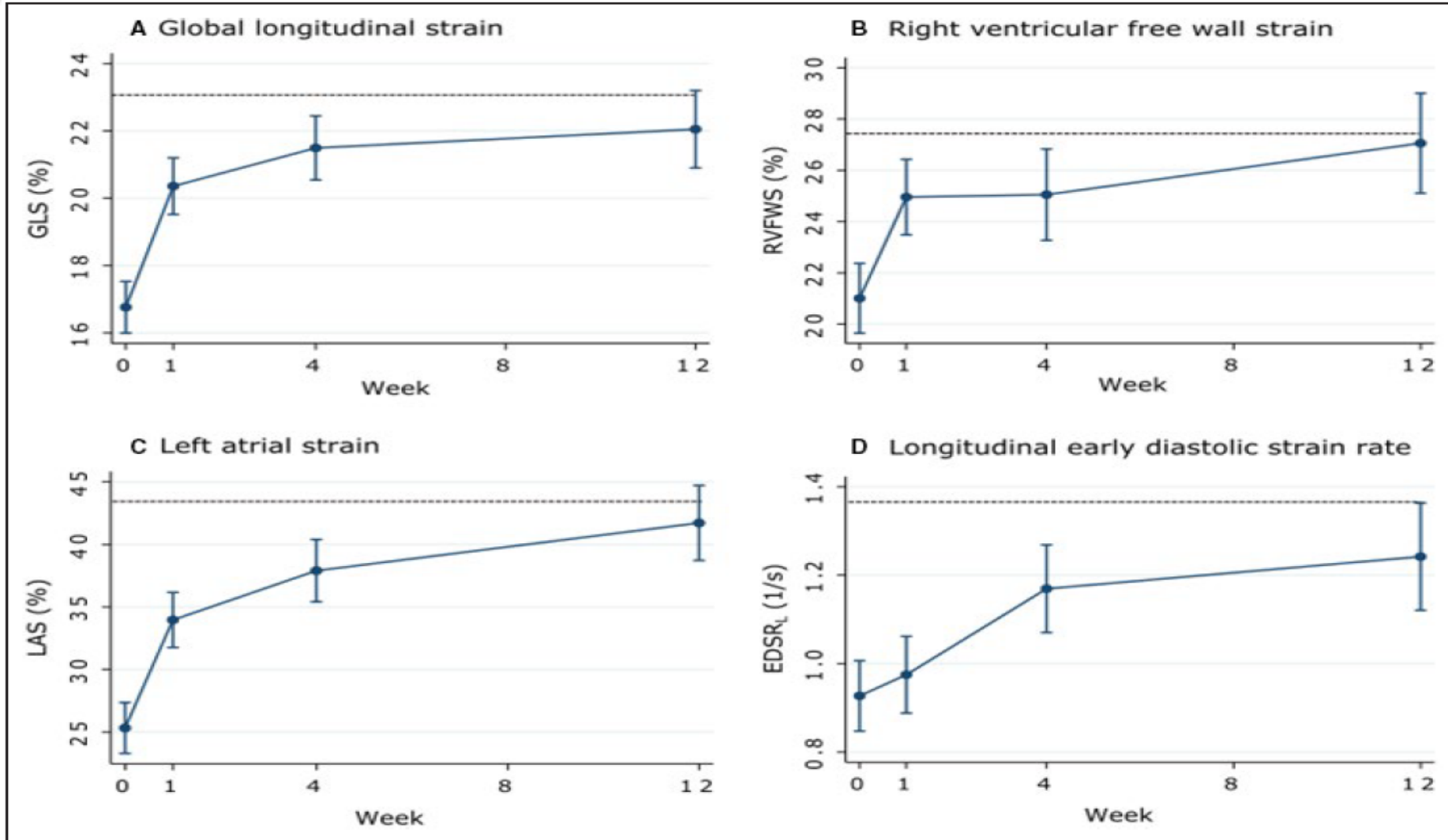
ORIGINAL RESEARCH

Longitudinal Assessment of Cardiac Outcomes of Multisystem Inflammatory Syndrome in Children Associated With COVID-19 Infections

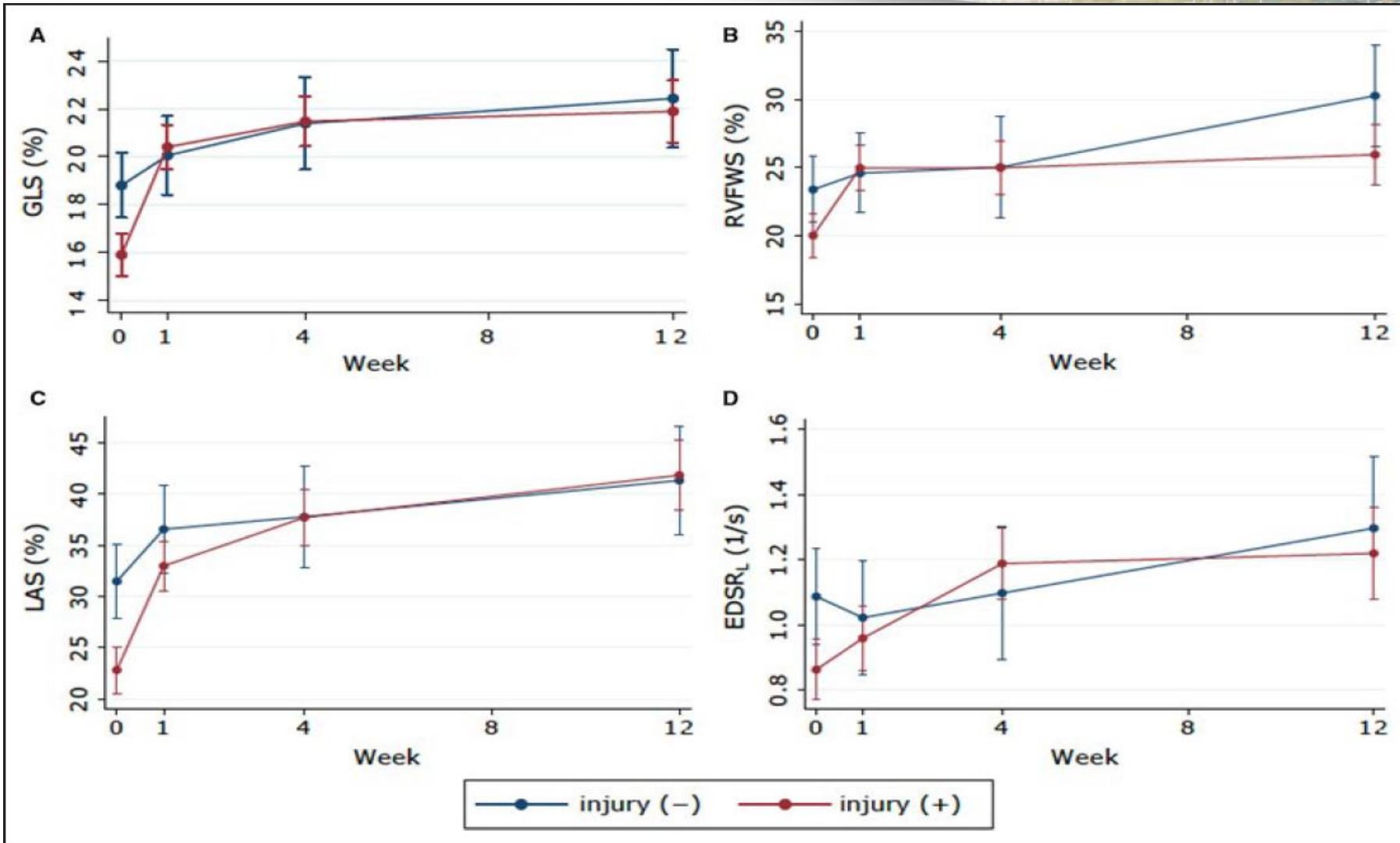
Daisuke Matsubara, MD, PhD; Joyce Chang , MD, MSCE; Hunter L. Kauffman, BS; Yan Wang , RDCS; Sumekala Nadaraj, MD; Chandni Patel , MD; Stephen M. Paridon, MD; Mark A. Fogel, MD; Michael D. Quartermain, MD; Anirban Banerjee , MD

- 60 MIS-C patients compared to 60 controls
- MIS-C patients were followed acute, subacute, and 3 months
- Cardiac function recovered

MIS-C Outcomes: Ventricular Function

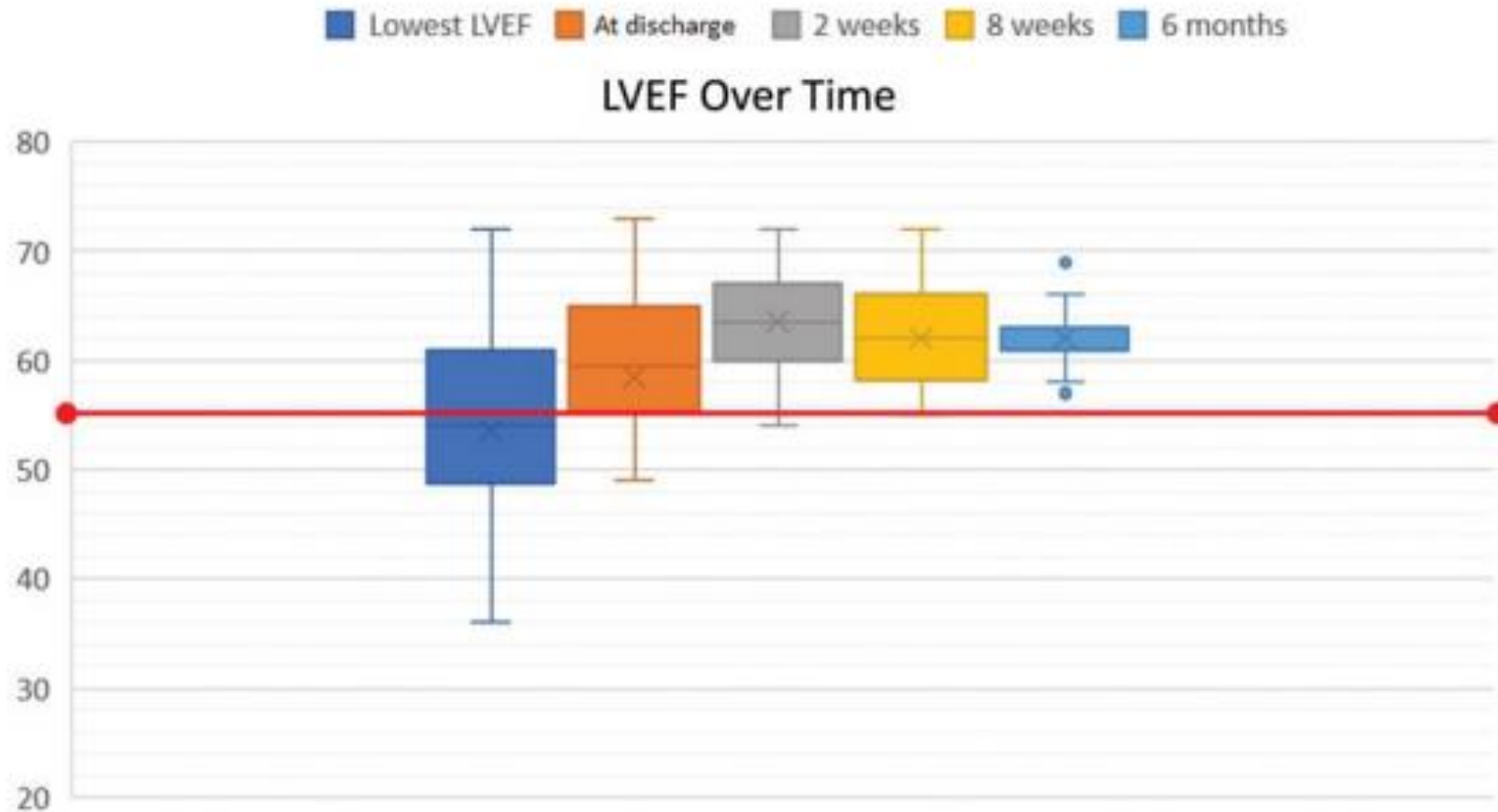


MIS-C Outcomes: Ventricular Function



Myocardial injury was in 23 patient with elevated BNP and troponin.

MIS-C Outcomes: Ventricular Function



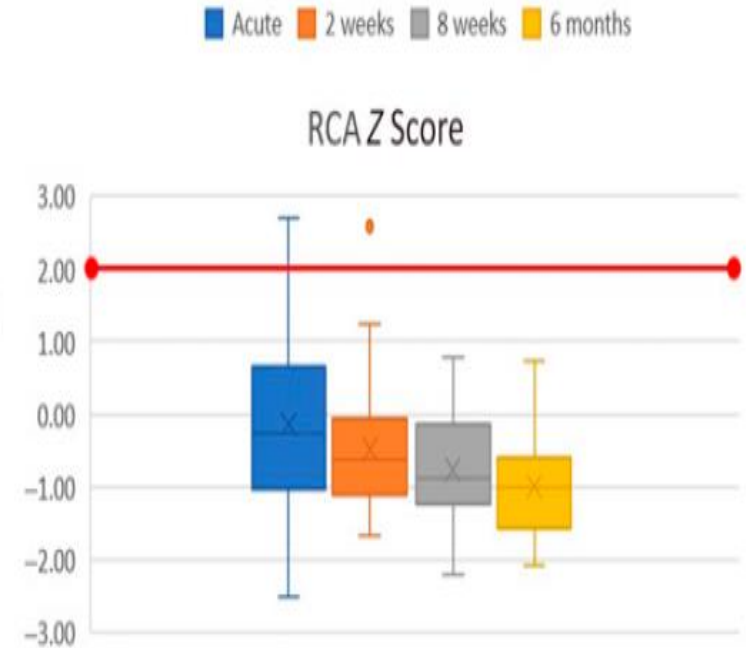
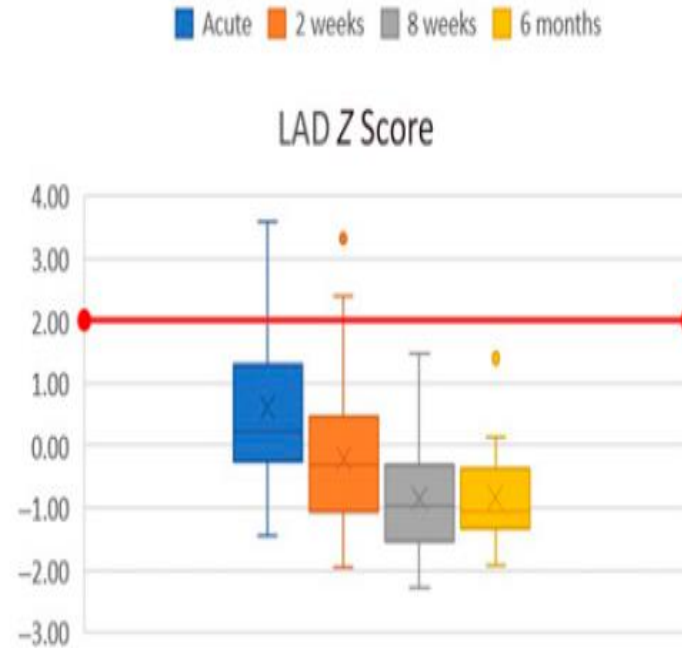
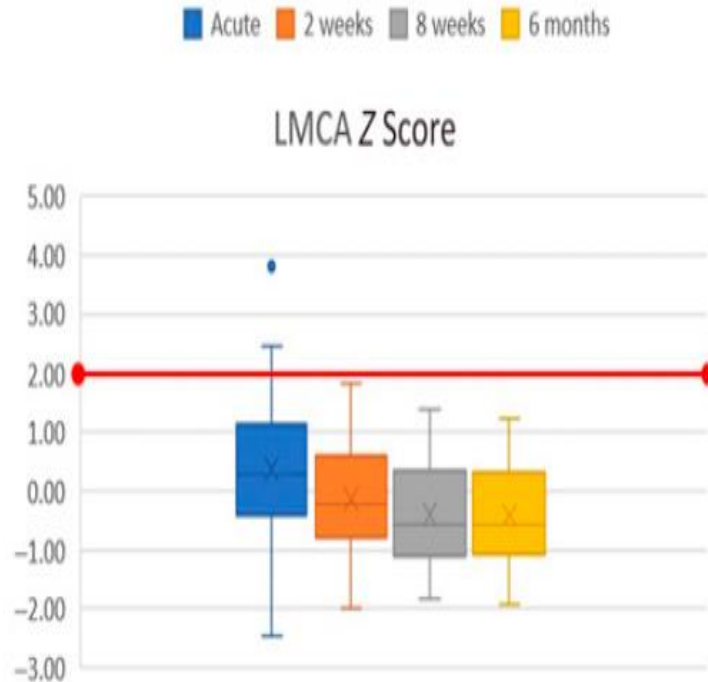
MIS-C Outcomes: Coronary findings

TABLE 2 Echocardiographic Abnormalities Present on Admission and on Follow-up at 2 Weeks, 8 Weeks, and 6 Months

Echocardiogram Findings	Acute (<i>n</i> = 50)	2 wk (<i>n</i> = 47)	8 wk (<i>n</i> = 42)	6 mo (<i>n</i> = 24)
Any coronary abnormality, <i>n</i> (%)	26 (52)	13 (27)	5 (14)	0
LMCA z score	0.38 ± 1.1	−0.14 ± 0.92	−0.40 ± 0.88*	−0.41 ± 0.92*
LAD z score	0.62 ± 1.24	−0.21 ± 1.12	−0.85 ± 0.82*	−0.84 ± 0.72*
RCA z score	−0.14 ± 1.25	−0.48 ± 0.84	−0.77 ± 0.76*	−0.99 ± 0.78*
LAD/RCA z score ≥2.5, <i>n</i> (%)	8 (16)	2 (4)	0	0
LAD/RCA z score 2–2.49, <i>n</i> (%)	4 (8)	1 (2)	0	0
Lack of tapering (z score <2), <i>n</i> (%)	14 (28)	10 (21)	5 (14)	0
Any LV systolic dysfunction, <i>n</i> (%)	26 (52)	1 (2)	0	0
LVEF (mean, SD)	54 ± 9	64 ± 4	62 ± 4*	62 ± 3*
Mild (LVEF 45%–54%), <i>n</i> (%)	15 (30)	1 (20)	0	0
Moderate (LVEF 35%–44%), <i>n</i> (%)	11 (22)	0	0	0
Severe (LVEF <35%), <i>n</i> (%)	0	0	0	0
Diastolic dysfunction, <i>n</i> (%)	16 (32)	5 (11)	4 (9)	1 (4)

* Significant difference (*P* < .05).

MIS-C Outcomes: Coronary findings



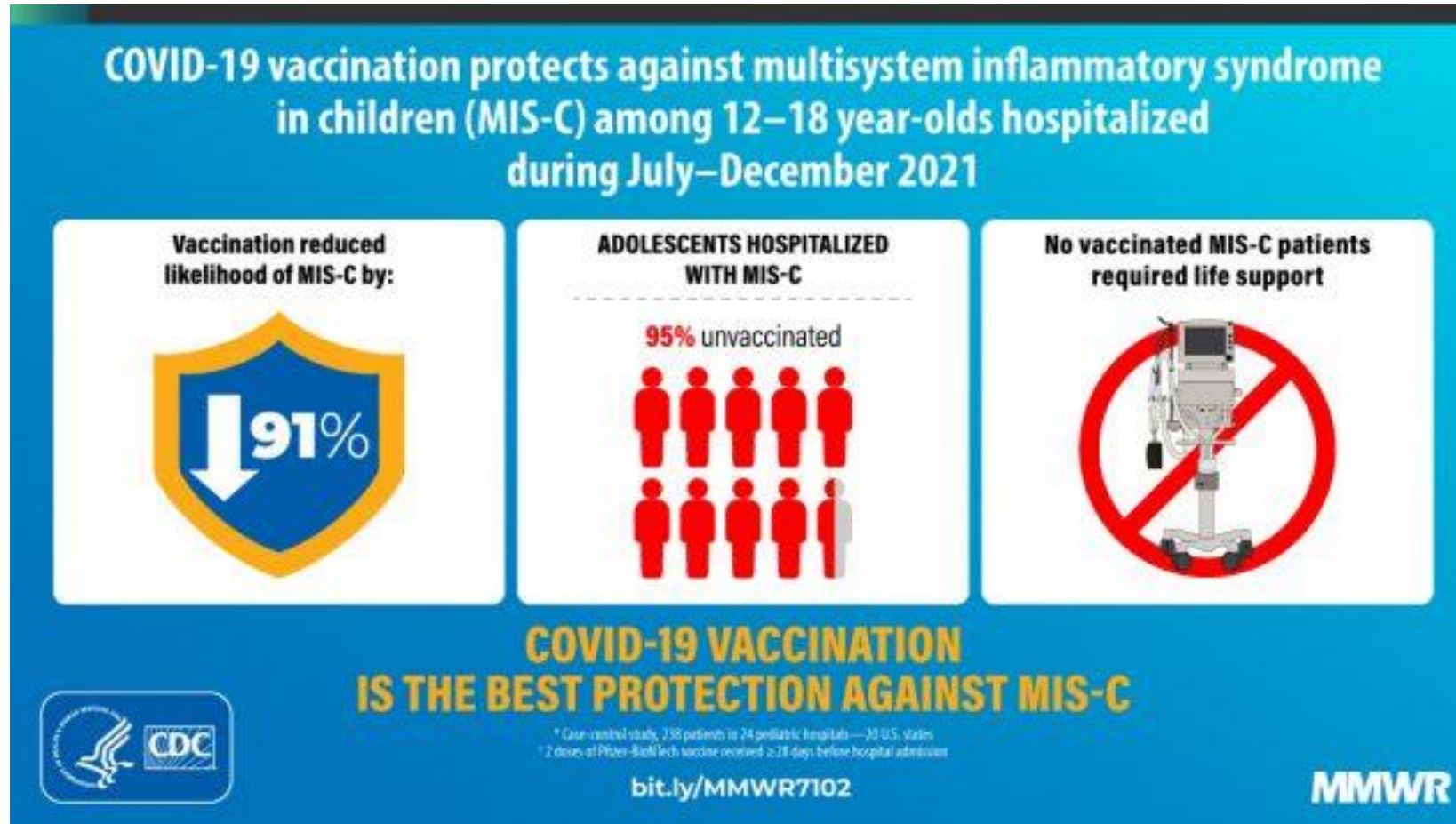


MIS-C Follow up

- 1-2 weeks after hospital discharge ekg, echo, and laboratory evaluation
- 4-6 weeks after the first hospital discharge ekg and echo
- 3-6 months after diagnosis if there is ventricular dysfunction with an exercise stress test and stress echo
- 1 year after illness with ekg and echo

COVID Vaccines for MIS-C

- Can be given after 3 months of the MIS-C episodes



Conclusions

- MIS-C patients are distinct from Kawasaki Disease patients
- Echocardiography evaluation is important in taking care of these patients as institution of early therapy can make a difference in patient care
- All patients with Exercise Stress Tests at 3-6 months are normal
- All patients with coronary artery dilation/aneurysms have resolved but one
- All patients back to normal activity with no complications
- CHCO is the top 3 enrollment site (85 patients) for the national Long-Term Outcomes after the Multisystem Inflammatory Syndrome in Children (MUSIC) study

Thank you!

Kawasaki Disease / MIS-C Team

Research Team



Echo lab sonographers

Medical MAs and Nurses in Clinic

