

Supplementary Online Content

Encinosa W, Moon K, Figueroa J, Elias Y. Complications, adverse drug events, high costs, and disparities in multisystem inflammatory syndrome in children vs COVID-19. *JAMA Netw Open*. 2023;6(1):e2244975. doi:10.1001/jamanetworkopen.2022.44975

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

eAppendix 1. Data Files.

We use the following AHRQ Healthcare Cost and Utilization Project's (HCUP) 2021 quarterly inpatient data files:

Q1: TX, VA, VT;

Q1-Q2: AZ, CA, FL, MD, ME, MI, MS, OH, SC, WI, WA;

Q1-Q3: CO, GA, IA, KY, NJ;

Q1-Q4: CT, HI, KS, MN, MO, MT, ND, OR, PA, RI, SD, WV.

Hospital characteristics are from the AHA annual survey and population rates are from 2021 US Census estimates.

COVID-19-related hospitalizations and in-hospital deaths, defined by the discharge disposition, are identified by any-listed ICD-10-CM code of U07.1 (2019 novel coronavirus disease) on the discharge record. Per coding guidelines, the use of U07.1 is based on documentation by the provider or documentation of a positive COVID-19 test result.

Source: HCUP State Inpatient Databases (SID). Healthcare Cost and Utilization Project (HCUP). 2005-2009. Agency for Healthcare Research and Quality, Rockville, MD.
<https://www.hcup-us.ahrq.gov/sidoverview.jsp> (accessed 1 Nov 2021).

eAppendix 2. Case Definition of MIS-C:

- An individual aged <21 years presenting with fever*, laboratory evidence of inflammation**, 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 exposure to a suspected or confirmed COVID-19 case within the 4 weeks prior to the onset of symptoms.

*Fever $\geq 38.0^{\circ}\text{C}$ for ≥ 24 hours, or report of subjective fever lasting ≥ 24 hours

**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.

Additional comments:

Some individuals may fulfill full or partial criteria for Kawasaki disease but should be reported if they meet the case definition for MIS-C.

Consider MIS-C in any pediatric death with evidence of SARS-CoV-2 infection.

Sources: Centers for Disease Control and Prevention. 2022. Information for Healthcare Providers about Multisystem Inflammatory Syndrome in Children (MIS-C). <https://www.cdc.gov/mis/mis-c/hcp/index.html> (accessed October 14, 2022). The May 2020 CDC Health Advisory on MIS-C: <https://emergency.cdc.gov/han/2020/han00432.asp> (accessed October 14, 2022).

eTable 1: ICD-10-CM Codes for the Complications

<i>Complications</i>	<i>ICD-10-CM dx and ICD-10-PCS procedure codes (all-listed diagnoses and procedures)</i>
Cardiovascular Complication	AMI I21, I22, I23 Heart failure I50, I73.9 Heart valve I34, I35, I36, I08 Arrest I46.9 Myocarditis I40, I41, I63, I51.4, I09.0, I01.2, A38.1, J11.82, J10.82 Arrhythmia I49, I47, I45.9, P29.1, P03.81 Cardiomyopathy I42, I25.5, I43, B33.24 Pericarditis/peri effusion I32, I30, M32.12, I313
	Coronary-artery aneurysm I25.41, I25.42, I72, I25.3, I28.1 Cardio Shock/SIRS R57.0, R652.1, R65.1
Respiratory Complication	Respiratory failure J80, J96, R09.2 Hemorrhage R04, P26 Bronchospasm J95.851 Lower respiratory infection, J98.01, J20, J21, J22, J93, J40 A01.03, A02.22, A20.2, A21.2, A22.1, A31.0, A37.01, A37.11, A37.81, A37.91, A43.0, A48.1, A50.04, A52.72, A54.84, B01.2, B05.2, B06.81, B25.0, B37.1, B38.0, B38.1, B39.0, B39.1, B39.2, B58.3, B59, B77.81, J09.X1, J10.00, J10.01, J10.08, J11.00, J11.08, J12.0, J12.1, J12.2, J12.3, J12.81, J12.89, J12.9, J13, J14, J15.0, J15.1, J15.20, J15.211, J15.212, J15.3, J15.4, J15.5, J15.6, J15.7, J15.8, J15.9, J16.0, J16.8, J17, J18.0, J18.1, J18.8, J18.9, J85.1
	ARDS J80
	Mechanical ventilation 5A1935, 5A1945, 5A1955, 5A0935, 5A0945, 5A0955
	Pleural effusion J90, J91
Neurological Complication	Hemiplegia G81, Encephalitis G04, G05 Cerebral infarction I63, I67 Convulsion R56 Critical illness polyneuropathy G62.81, G72.81 Encephalopathy G93.40, G93.49, G93.41 Iritis/ uveitis H20.0, H44.13 Coma P91.5, R40.2, Intracranial hemorrhage I61, Demyelinating disorder G36, G37, Acute disseminated encephalomyelitis G04.0
Hematological Complication	Embolism/thrombosis I82, I76, I26, I74 Defibrination syndrome D65, P60 Anemia D64 Lymphopenia D72.81 Thrombocytopenia D69.3, D69.4, D69.5, D69.6
Renal Failure	N17, N99.0 Dialysis Z99.2, Z91.15, Z49.01, Z49.02, Z49.31, Z49.32 5A1D00Z, 5A1D60Z, 3E1M39Z
Gastrointestinal Complications	Dehydration (E860), nausea, vomiting, and abdominal pain (R10, R11), diarrhea/gastroenteritis (R19.7, P78.3, K59.1, K58.0, K52.9), Liver Failure K72 Pancreatitis K85 Hepatitis/Hepatomegaly B15, B16, B17, B19, R16.2 Gallbladder Hydrops K82.1 Ascites R18
Musculoskeletal Complication	Arthritis or arthralgia M08, M13, M25.5, M26.62, M08.2 Myositis or myalgia M60, G72.41, M79.1

eTable 1. Continued: ICD-10 codes for the complications

<i>Complications</i>	<i>ICD-10-CM dx and ICD-10-PCS procedure codes (all-listed diagnoses and procedures)</i>
Mucocutaneous Complication	Conjunctivitis H10 Erythema L51-L54 Local edema R60.0 Desquamation R23.4 Rash R21
Adverse Medication Event	Glucocorticoids T38.0X5 Immunoglobulin T50.Z15 Anti-infective T37.1X5-T37.9X5 Diuretics T50.1X5-T50.2X5 Antibiotics T36.0X5-T36.9X5- T37.0X5 Unspecified T50.9X5 Aspirin T39.015 Antihypertensive, anticoagulant, antithrombotic, fibrinolysis, thrombolytic T46.5X5, T45.515, T45.7X5, T45.525, T45.605, T45.695, T45.615

eTable 2. 2021 Q1 Reporting of MIS-C Cases: Surveillance Data vs Hospital Billing Data

States with public Q1 reports	State Department of Health MIS-C Cases Reported to CDC	All Hospital Billed MIS-C Cases in HCUP
Washington	20	28
Minnesota	26	37
Michigan	36	64
Florida	37	190
Wisconsin	40	48
Georgia	170	225
California	370	581
CDC, National (50 States/ DC)	1,924	
HCUP, 31 States (77% of US)		2,715

Our HCUP data's 2,715 MIS-C hospitalizations in Q1 is a rate of 1.48 per 100,000 children per month. In eFigure 2, the CDC data records 1,924 MIS-C cases for the country in Q1, a rate of .75 per 100,000 children per month. The two rates differ at significance level $p=.001$.

Sources:

HCUP (authors' calculations). Centers for Disease Control and Prevention. 2022. Health Department-Reported Cases of Multisystem Inflammatory Syndrome in Children (MIS-C) in the United States <https://covid.cdc.gov/covid-data-tracker/#mis-national-surveillance> (accessed 13 Oct 2022).

Florida Department of Health. COVID-19: characteristics of cases in pediatric Florida residents <18 years old. http://www11.doh.state.fl.us/comm/_partners/covid19_report_archive/pediatric-reports/pediatric_report_latest.pdf (accessed 13 Oct 2022).

Multisystem Inflammatory Syndrome in Children Associated with COVID-19 in Washington. Oct 11, 2022. <https://doh.wa.gov/sites/default/files/2022-02/MultisystemInflammatorySyndromeChildrenCOVID19WA2020.pdf>

MIS-C Statistics. Sept, 2022 (accessed 15 Oct, 2022).

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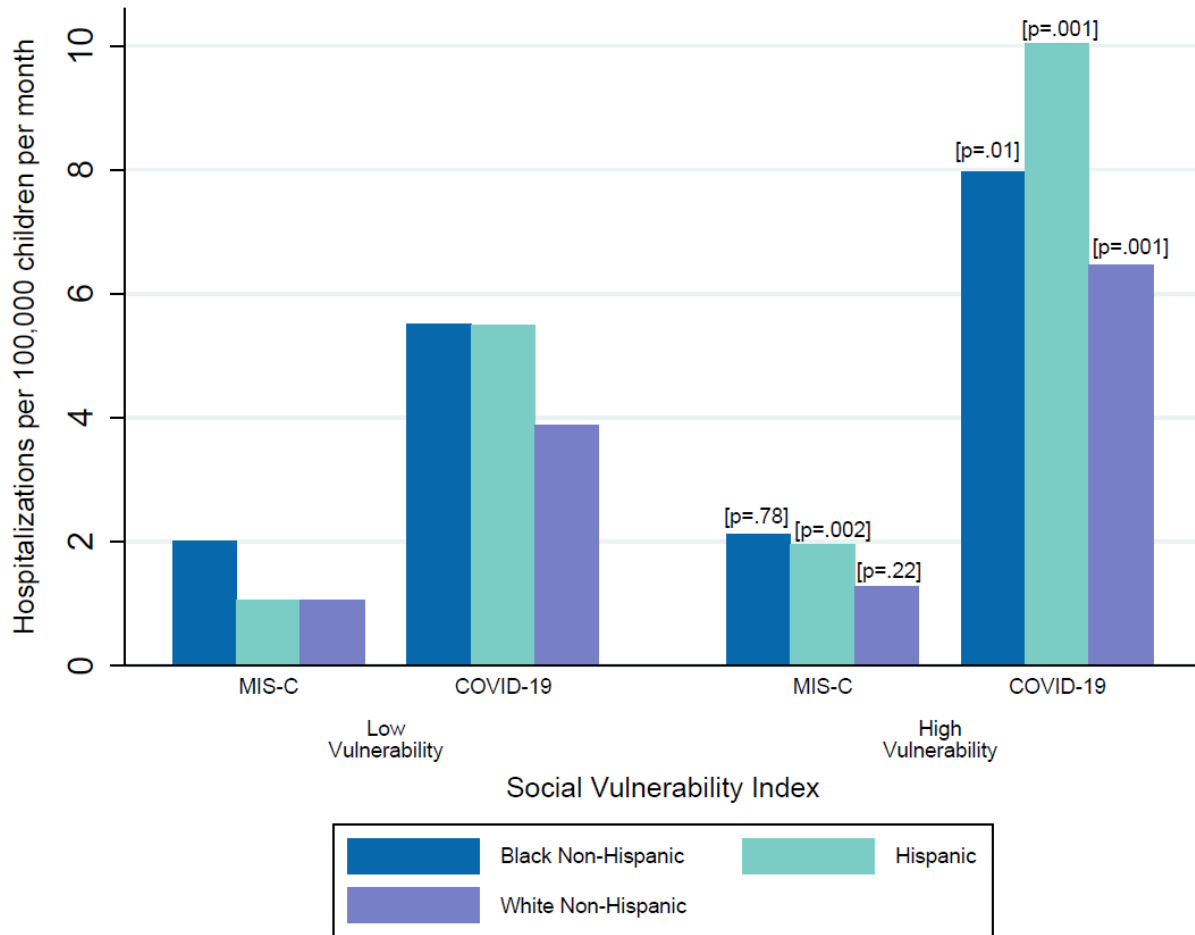
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Wisconsin Department of Health Services. <https://www.dhs.wisconsin.gov/disease/mis-c-data.htm> . Multisystem Inflammatory Syndrome in Children (MIS-C) Data. Sept, 2022 (accessed 15 Oct, 2022)..

California Dept of Public Health. <https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/COVID-19/MIS-C-Data.aspx> . Multi-system Inflammatory Syndrome in Children- Associated with COVID 19 (MIS-C). June 28, 2022 (accessed 15 Oct, 2022).

Georgia Dept of Health. <https://dph.georgia.gov/document/document/mis-c-june-2022-data-report/download> (accessed 15 Oct, 2022).

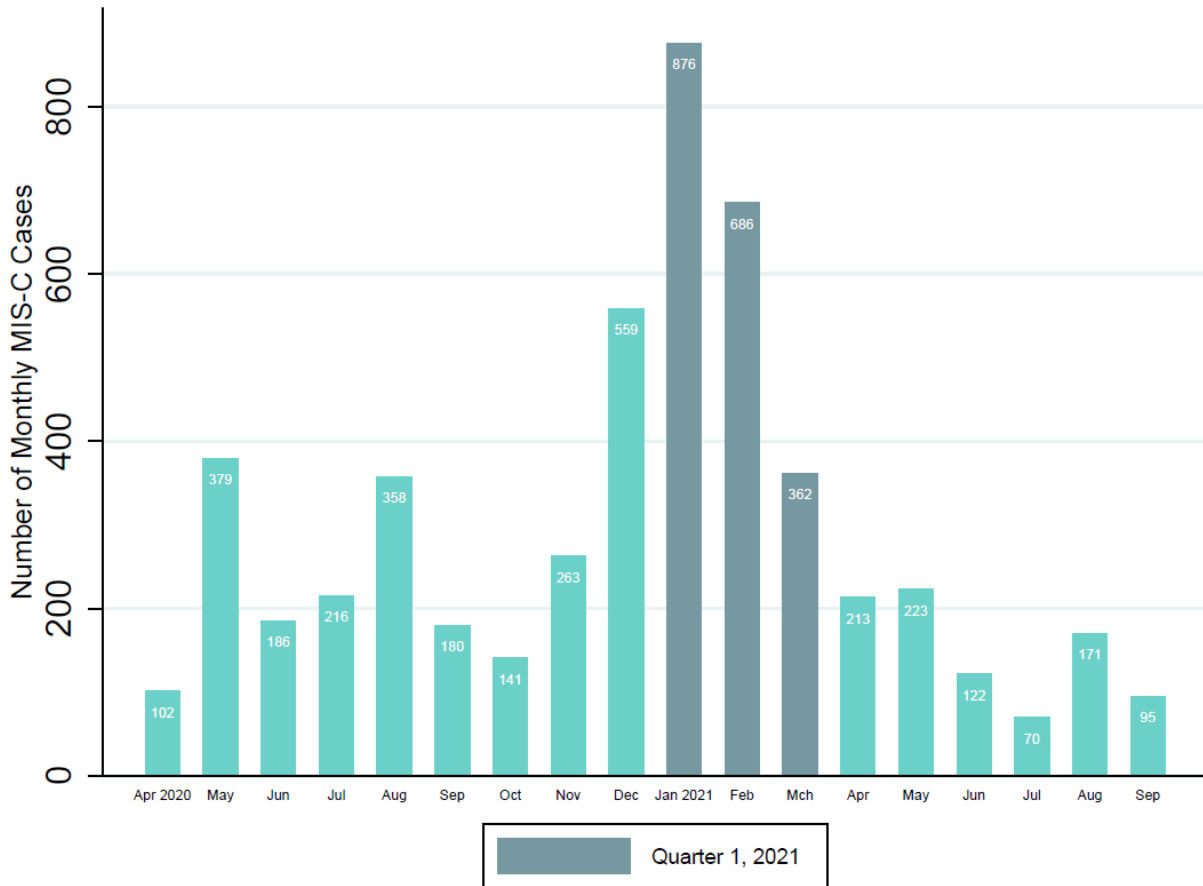
eFigure 1: Socioeconomic and Racial and Ethnic Disparities in Incidence of MIS-C and COVID-19



eFigure 2: 2021 CDC MIS-C Surveillance Data

Source: Centers for Disease Control and Prevention. 2022. Health Department-Reported Cases of Multisystem Inflammatory Syndrome in Children (MIS-C) in the United States

<https://covid.cdc.gov/covid-data-tracker/#mis-national-surveillance> (accessed 13 Oct 2022).



Notes: Monthly Multisystem Inflammatory Syndrome for Children (MIS-C) infection cases (age<21). Source: Authors' calculations using the CDC COVID Data Tracker, based on CDC surveillance data.