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## Risk Factors for Severe COVID-19 in Children

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**Abbreviations:**

aRR	Adjusted risk ratio
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
COVID-19	Coronavirus Disease-2019
COVID-NET	Coronavirus Disease-2019-Associated Hospitalization Surveillance Network
HHS	Health and Human Services Department
ICU	Intensive Care Unit
MIS-C	Multisystem Inflammatory Syndrome in Children
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus-2
RR	Rate Ratio

**Article Summary:** This investigation presents population-based rates and identifies underlying medical conditions associated with increased risk of severe disease outcomes among hospitalized children with laboratory-confirmed SARS-CoV-2 infection.

### **What's Known on This Subject**

Children can experience severe disease outcomes due to COVID-19 illness, including intensive care unit admission, invasive mechanical ventilation, and death. However, more information is needed to identify the pediatric subgroups at greatest risk of severe disease to inform prevention efforts.

### **What This Study Adds**

Using data from 2,293 hospitalized children with laboratory-confirmed SARS-CoV-2 infection in 14 states during March 2020–May 2021, we found that specific underlying conditions were associated with increased risk of severe COVID-19, and these varied by age group.

### **Contributors' Statement Page**

*Rebecca Woodruff* conceptualized and designed the study; analyzed and interpreted the data; and drafted the manuscript.

*Angela Campbell, Christopher Taylor and Fiona Havers* conceptualized and designed the study; interpreted the data; drafted the manuscript; critically revised the manuscript for important intellectual content; and supervised the investigation.

*Shua Chai, Breanna Kawasaki, James Meek, Evan Anderson, Andy Weigel, Maya Monroe, Libby Reeg, Erica Bye, Daniel Sosin, Alison Muse, Nancy Bennett, Laurie Billing, Melissa Sutton, H. Keipp Talbot, and Keegan McCaffrey* participated in designing the study, interpreted the data and critically revised the manuscript for important intellectual content.

*Huong Pham, Kadam Patel, and Michael Whitaker* participated in designing the study, analyzed the data, and critically revised the manuscript for important intellectual content.

*Meredith McMorro* participated in designing the study, interpreted the data, and critically revised the manuscript for important intellectual content.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

## Abstract

**Objectives:** Describe population-based rates and risk factors for severe COVID-19 (i.e., intensive care unit admission, invasive mechanical ventilation, or death) among hospitalized children.

**Methods:** During March 2020–May 2021, the COVID-19-Associated Hospitalization Surveillance Network (COVID-NET) identified 3,106 children with laboratory-confirmed SARS-CoV-2 infection who were hospitalized in 14 states. Among a subset of 2,293 children primarily admitted for COVID-19, we used multivariable generalized estimating equations to generate adjusted risk ratios (aRRs) and 95% confidence intervals (CI) of the association between demographic and medical characteristics abstracted from patient electronic medical records and severe COVID-19. We calculated age-adjusted cumulative population-based rates of severe COVID-19 among all children.

**Results:** Approximately 30% of hospitalized children had severe COVID-19 and 0.5% died during hospitalization. Among hospitalized children aged <2 years, chronic lung disease (aRR=2.2, CI: 1.1–4.3), neurologic disorders (aRR=2.0, CI: 1.5–2.6), cardiovascular disease (aRR=1.7, CI: 1.2–2.3), prematurity (aRR=1.6, CI: 1.1–2.2) and airway abnormality (aRR=1.6, CI: 1.1–2.2) were associated with severe COVID-19. Among hospitalized children aged 2–17 years, feeding tube dependence (aRR=2.0, CI: 1.5–2.5), diabetes mellitus (aRR=1.9, CI: 1.6–2.3) and obesity (aRR=1.2, CI: 1.0–1.4) were associated with severe COVID-19. Severe COVID-19 occurred among 12.0 per 100,000 children aged <18 years, and was highest among infants, Hispanic children, and non-Hispanic Black children.

**Conclusions:** Results identify children at potentially higher risk of severe disease who may benefit from COVID-19 prevention efforts, including vaccination. Rates of severe COVID-19 establish a baseline for monitoring changes in pediatric illness severity following increased availability of COVID-19 vaccines and the emergence of new variants.

## Introduction

As of August 31, 2021, over four million cases of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection have been documented in US children aged <18 years.<sup>1</sup> Although children have lower rates of hospitalization for coronavirus disease 2019 (COVID-19) compared with adults,<sup>2, 3</sup> severe illness and death have occurred.<sup>4-8</sup> Children with SARS-CoV-2 infection may develop serious complications, including acute respiratory distress syndrome, myocarditis, acute renal failure, multisystem organ failure, and multisystem inflammatory syndrome in children (MIS-C).<sup>3-6, 8-14</sup> Among children hospitalized with COVID-19, approximately 28–40% were admitted to an intensive care unit (ICU), 6–18% required invasive mechanical ventilation, and up to 3% have died.<sup>3, 4, 6, 10-12</sup>

As of September 2021, the Food and Drug Administration has approved the Pfizer-BioNTech vaccine for use in children aged  $\geq 16$  years and has authorized two vaccines for emergency use in children aged 12–17 years.<sup>15-17</sup> Multiple clinical trials testing vaccine efficacy for preventing severe illness and death in the pediatric population are ongoing.<sup>18-22</sup> However, until these vaccines are authorized for use in younger age groups, children may continue to be at risk of severe illness. Information about the demographic and medical characteristics associated with severe COVID-19 in this population can be used to inform clinical decision-making, risk communication, and recommendations for vaccination and other preventive measures. Although several descriptive investigations have characterized the demographic and clinical characteristics of pediatric COVID-19-associated hospitalizations<sup>3, 10, 11</sup> and ICU admissions,<sup>5, 9</sup> most studies that have identified risk factors for severe COVID-19 among children have been conducted among geographically limited populations during the initial months of the pandemic.<sup>4, 6, 12, 23</sup>

Additionally, population-based rates of severe COVID-19 in children are needed to establish a baseline for monitoring trends as COVID-19 vaccines are approved for use in younger age groups, to compare with rates of severe adverse vaccine reactions, and as new SARS-CoV-2 variants emerge.

The objectives of this investigation were to identify demographic characteristics and underlying medical conditions associated with increased relative risk of severe COVID-19 among children hospitalized with SARS CoV-2 infection and to calculate population-based rates of severe COVID-19 among children during March 2020–May 2021.

## Methods

As described previously,<sup>2, 24</sup> the Coronavirus Disease 2019-Associated Hospitalizations Surveillance Network (COVID-NET) conducts population-based surveillance of laboratory-confirmed COVID-19-associated hospitalizations in 250 acute-care hospitals located in a defined catchment area that includes approximately 10% of the U.S. population. COVID-NET conducts surveillance in 99 counties across 14 states (California, Colorado, Connecticut, Georgia, Iowa, Maryland, Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah) located in each of the 10 Health and Human Services Department (HHS) regions.

Hospitalizations that meet the case definition of a COVID-19-associated hospitalization are included in surveillance if the patient resided in the catchment area and had a positive molecular or rapid antigen SARS-CoV-2 test during hospitalization or up to 14 days before admission. COVID-NET cases can include patients with acute COVID-19, MIS-C, or incidental SARS-

CoV-2 infections. Trained surveillance officers identify cases using notifiable disease and laboratory databases as well as hospital admission and infection control practitioner logs. Medical chart abstraction is completed for all COVID-19-associated hospitalizations among children aged <18 years using a standard case report form; hospitalizations are then reported to COVID-NET. This activity was reviewed by CDC and conducted consistent with applicable federal law and CDC policy.<sup>1</sup> Participating sites obtained approval from their respective state and local Institutional Review Boards, as required.

### Participants

During March 2020–May 2021, 3,106 children with COVID-19-associated hospitalization were identified by COVID-NET. To identify risk factors for severe COVID-19 among hospitalized children, we analyzed data from 2,293 (73.8%) hospitalizations. Hospitalizations were excluded if they had incomplete chart abstraction (n=81, 2.6%), were pregnant at the time of admission (n=127, 4.1%), or had unknown outcome data (n=15, 0.5%). Additionally, we excluded 718 children who had any of the following primary reasons for admission, which were not likely related to COVID-19: psychiatric admissions (n=270), obstetrics or gynecology (n=162), trauma (n=136), inpatient procedures (n=118), or other with no symptoms consistent with COVID-19 upon admission (n=32). Excluded children differed on demographic and medical characteristics compared with included children (eTable 1).

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<sup>1</sup> 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.



## Measures

*Severe COVID-19:* The dependent variable was severe COVID-19, defined as requiring ICU admission or invasive mechanical ventilation or in-hospital death.

*Demographic Characteristics:* Demographic variables included age group, sex, housing type, and race and/or Hispanic ethnicity group [Hispanic, non-Hispanic Black, non-Hispanic White, non-Hispanic Asian or Pacific Islander (PI), non-Hispanic other or unknown]. Children with unknown ethnicity (n=79, 3.5%) were presumed to be non-Hispanic.

*Clinical Characteristics:* COVID-NET collects information on 14 categories of underlying medical conditions (eTable 2); other medical conditions reported in free text were categorized after review by a pediatrician. The underlying conditions considered for each age group were determined based on clinical relevance and sample size. Among children aged <2 years, 7 underlying conditions were considered: airway abnormality, cardiovascular disease, chronic lung disease, feeding tube dependence, neurologic disorders, prematurity (gestational age <37 weeks), or other conditions (immunocompromised condition, gastrointestinal or liver disease, chronic metabolic disease, blood disorders, renal disease or other condition). Among children aged 2–17 years, 13 underlying conditions were considered: airway abnormality, asthma, blood disorders, cardiovascular disease, developmental delay, diabetes mellitus (type I or 2), feeding tube dependence, immunocompromised conditions, obesity (body mass index  $\text{kg/m}^2 \geq 95^{\text{th}}$  percentile for age and sex based on CDC growth charts, ICD-10 codes for obesity, or obesity selected on the case report form), non-asthma chronic lung disease, non-diabetes chronic metabolic disease,

non-developmental delay neurologic disorders, or other conditions (gastrointestinal or liver disease; renal disease; or rheumatologic, autoimmune, or inflammatory disease).

### Statistical Analysis

Age-adjusted cumulative population-based rates of severe COVID-19 during March 2020–May 2021 were calculated using the number of catchment area residents aged <18 years hospitalized with severe COVID-19 as the numerator and 2019 bridged-race postcensal population estimates from the National Center for Health Statistics as the denominator.<sup>25</sup> Rates and rate ratios (RR) by age group, sex, and race/ethnicity groups are presented. Hospitalizations with complete data on age group, sex, and race/ethnicity were included; no additional exclusion criteria were applied to the numerator data. Rates with relative standard errors  $\geq 30\%$  were suppressed.

To identify risk factors for severe COVID-19, we specified bivariate and multivariable log-linked Poisson generalized estimating equations in SAS (version 9.4; SAS Institute) using robust variance estimators to account for clustering of hospitalizations within 10 HHS regions. We present unadjusted and adjusted risk ratios (aRR), 95% confidence intervals (CI), and *p* values using a Type I error rate of 5%. Multivariable models identifying demographic characteristics associated with severe COVID-19 included all children aged <18 years and were adjusted for the presence of  $\geq 1$  underlying medical conditions. Multivariable models identifying underlying medical conditions associated with severe COVID-19 were adjusted for demographic characteristics and specified separately for children aged <2 years and 2–17 years, as some underlying medical conditions (e.g., prematurity, obesity) are only clinically relevant for specific pediatric subgroups. In supplementary analyses, we stratified models by additional age groups

(i.e., <6 months, 6–23 months, 2–4 years, 5–11 years, 12–17 years) and by race/ethnicity group among children aged 2–17 years. We also conducted sensitivity analyses excluding patients with a discharge diagnosis of MIS-C.<sup>8</sup>

## Results

Of 2,293 pediatric hospitalizations, 745 (32.5%) were infants and children aged <2 years; 1,548 (67.5%) were children aged 2–17 years (Table 1). Half (53.4%) were male, and the median age was 7 years (IQR: 1–14). Most were Hispanic (33.7%) or non-Hispanic Black (32.1%), followed by non-Hispanic White (22.9%) or non-Hispanic Asian/PI (5.2%). Over half (55.0%) had  $\geq 1$  underlying medical conditions, though the prevalence varied by age group (28.7% among infants and children <2 years, 67.7% among children 2–17 years). The most common underlying conditions were obesity, chronic lung disease, neurologic disorders, cardiovascular disease, and blood disorders. Within the latter categories, asthma, developmental delay, congenital heart disease, and sickle cell disease were the most common conditions respectively.

### Demographic Characteristics Associated with Severe COVID-19

Among hospitalized children aged <18 years, 30.1% had severe COVID-19 (Table 1). In multivariable analyses, the risk of severe COVID-19 among hospitalized children was higher among children with  $\geq 1$  underlying medical condition (aRR=1.5, 95% CI: 1.2–1.9,  $p=.001$ ; Figure 1). Severe disease was significantly less likely in infants aged <6 months (aRR=0.7, 95% CI: 0.5–0.9,  $p=.004$ ). Race/ethnicity group were not statistically significantly associated with severe COVID-19. In sensitivity analyses excluding children with MIS-C, children living in a congregate, other, or unknown residence type also had a higher risk of severe disease (aRR=1.5,

95% CI: 1.0–2.2,  $p=0.3$ ) and children aged 5–11 years had a lower risk of severe COVID-19 relative to children aged 12–17 years (aRR=0.9, 95% CI: 0.8–1.0,  $p=0.3$ ; eTable 3).

#### Underlying Medical Conditions Associated with Severe COVID-19

Among hospitalized children aged <2 years, 22.0% had severe COVID-19 (Table 1). In multivariable analyses, the risk of severe COVID-19 was higher among children with chronic lung disease (aRR=2.2, 95% CI: 1.1–4.3,  $p=.03$ ), neurologic disorders (aRR=2.0, 95% CI: 1.5–2.6,  $p<.0001$ ), cardiovascular disease (aRR=1.7, 95% CI: 1.2–2.3,  $p=.004$ ), prematurity (aRR=1.6, 95% CI: 1.3–2.1,  $p<.0001$ ) or airway abnormality (aRR=1.6, 95% CI: 1.1–2.2,  $p=.02$ ; Figure 2A). Other conditions were not significantly associated with increased risk of severe COVID-19. Results from sensitivity analyses excluding children with MIS-C were similar (eTable 4).

Among hospitalized children aged 2–17 years, 34.0% had severe COVID-19 (Table 1). In multivariable analyses, the risk of severe COVID-19 was higher among children with feeding tube dependence (aRR=2.0, 95% CI: 1.5–2.5,  $p<.0001$ ), diabetes mellitus (aRR=1.9, 95% CI: 1.6–2.3,  $p<.0001$ ) and obesity (aRR=1.2, 95% CI: 1.0–1.4,  $p=.0003$ ; Figure 2B). Other conditions were not significantly associated with increased risk of severe COVID-19. In sensitivity analyses excluding children with MIS-C, developmental delay was also a risk factor for severe COVID-19 (aRR=1.3, 95% CI: 1.1–1.6,  $p=.004$ ; eTable 4).

### Sensitivity Analyses

In sensitivity analyses among additional age groups, the categories of underlying medical conditions associated with increased risk of severe disease varied by age groups (eTable 5).

Among children aged 6–23 months, chronic lung disease (aRR=2.4, 95% CI: 1.3–4.3), neurologic disorders (aRR=2.3, 95% CI: 1.8–2.9), and cardiovascular disease (aRR=1.4, 95% CI: 1.2–1.5) were associated with increased risk of severe COVID-19. Among children aged 2–4 years, feeding tube dependence (aRR=2.1, 95% CI: 1.1–3.9) and chronic metabolic disease (aRR=1.3, 95% CI: 1.1–1.5) were associated with increased risk of severe COVID-19. Among children ages 5–11 years, obesity (aRR=1.4, 95% CI: 1.2–1.6) was associated with increased risk of severe COVID-19. Among children 12–17 years, feeding tube dependence (aRR=3.0, 95% CI: 2.6–3.5), chronic metabolic disease (aRR=1.7, 95% CI: 1.5–1.9), and obesity (aRR=1.3, 95% CI: 1.0–1.6) were associated with increased risk of severe COVID-19. Other conditions were not significantly associated with increased risk of severe COVID-19.

In sensitivity analyses among children aged 2–17 years hospitalized with COVID-19, the categories of underlying medical conditions associated with increased risk of severe disease varied by race/ethnicity group (eTable 6). Among Hispanic children 2–17 years, chronic metabolic disease (aRR=1.6, 95% CI: 1.1–2.5,  $p=.03$ ) and obesity (aRR=1.4, 95% CI: 1.0–1.8,  $p=.03$ ) were associated with increased risk of severe COVID-19. Among non-Hispanic Black children aged 2–17 years, obesity (aRR=1.2, 95% CI: 1.0–1.4,  $p=.01$ ) and cardiovascular disease (aRR=1.1, 95% CI: 1.1–1.1,  $p<.0001$ ) were associated with increased risk of severe COVID-19. Among non-Hispanic White children 2–17 years, chronic metabolic disease (aRR=1.6, 95% CI: 1.1–2.3,  $p=.01$ ), obesity (aRR=1.5, 95% CI: 1.0–2.2,  $p=.04$ ), and feeding tube dependence

(aRR=2.1, 95% CI: 1.3–3.3,  $p=.002$ ) were associated with increased risk of severe COVID-19. Other underlying medical conditions were not significantly associated with increased risk of severe COVID-19 among race/ethnicity groups.

### In-Hospital Deaths

Among children <18 years hospitalized with COVID-19, 12 (0.5%) died during hospitalization (Table 2). The median age was 7 years (IQR: 0–14), and most were male ( $n=7$ , 58%), Hispanic ( $n=6$ , 50%) or non-Hispanic Black ( $n=4$ , 33%). The majority ( $n=10$ , 83%) had  $\geq 1$  underlying medical conditions; neurologic disorders ( $n=7$ , 58%) was the most common underlying condition.

### Population-Based Rates of Severe COVID-19 among Children <18 Years

During March 2020–May 2021, the overall cumulative population-based rate of hospitalization was 43.2 per 100,000 children aged <18 years and the rate of severe COVID-19 was 12.0 per 100,000 children aged <18 years (Table 3). Hospitalization rates were highest among infants <12 months (177.5 per 100,000; RR: 3.2 vs. children aged 2–17 years), Hispanic children (71.2 per 100,000; RR: 3.3 vs. non-Hispanic White children), and non-Hispanic Black children (63.0 per 100,000; RR: 2.9 vs. non-Hispanic White children). Rates of severe disease were highest among infants <12 months (36.8 per 100,000; RR: 2.4 vs. children 2–17 years), Hispanic children (17.6 per 100,000; RR: 3.3 vs. non-Hispanic White children) and non-Hispanic Black children (21.1 per 100,000; RR: 3.9 vs. non-Hispanic White children).

## Discussion

Almost one-third of hospitalized children with SARS-CoV-2 infection required ICU admission or invasive mechanical ventilation and children with specific underlying medical conditions were at greater risk of severe COVID-19. A strength of this investigation was the large, geographically diverse sample of children hospitalized with SARS-CoV-2 infection, which enabled the identification of demographic and medical characteristics associated with severe COVID-19 among pediatric subgroups, including by age and race/ethnicity. These results provide needed descriptive information about COVID-19 severity in children prior to widespread availability of pediatric COVID-19 vaccination and can serve as a baseline to assess changes in trends as COVID-19 vaccines are approved for use in younger age groups, to compare with severe adverse vaccine reactions, and as new SARS-CoV-2 variants emerge. Additionally, information about pediatric risk factors for severe COVID-19 can inform clinical decision making by identifying children who may benefit from closer monitoring following hospitalization. These results may also guide other prevention measures, including health education and risk communication campaigns and recommendations for vaccination<sup>26-28</sup> once COVID-19 vaccines are approved for use among younger children.

Similar to previous investigations,<sup>29, 30</sup> we found that the presence of one or more underlying medical conditions was associated with increased risk of severe COVID-19 and identified the specific underlying conditions associated with severe COVID-19 within pediatric subgroups. Results underscore the importance of obesity and diabetes, which have previously been documented as risk factors for severe COVID-19 among both adults and children,<sup>4, 12, 24, 30-33</sup> and identify additional risk factors, including neurologic and cardiovascular disease, feeding tube

dependence, airway abnormality, and prematurity among specific pediatric subgroups. These results highlight the potential importance of neurologic disorders (including developmental delay), which were reported in over half of the 12 in-hospital pediatric deaths and were associated with increased risk of severe COVID-19 across several pediatric population subgroups, including children 2–17 years of age without a discharge diagnosis of MIS-C and infants and children <2 years. Neurologic disorders have been shown to increase risk of severe illness in other respiratory diseases, potentially through decreased muscle tone and strength, impaired mobility, or structural conditions that diminish pulmonary function.<sup>34–36</sup> Consistent with findings from influenza-associated hospitalizations,<sup>37</sup> we found that some underlying medical conditions, including immunocompromised conditions and blood disorders, were not associated with increased risk of severe COVID-19, which may be explained by lower thresholds for hospital admission among children with conditions, such as sickle cell disease.

When we examine population-based rates, which have not been calculated in most other studies, infants <12 months had the highest rates of hospitalization and severe COVID-19 compared to all other pediatric age groups, an important finding when assessing infant risk from COVID-19 disease.<sup>3</sup> However, similar to other studies,<sup>4, 12, 29</sup> we found that once hospitalized with SARS-CoV-2 infection, infants were not at significantly increased risk of severe COVID-19 relative to older children. Young infants may have a lower threshold for admission compared with older children and therefore some hospitalized infants may not be as seriously ill from SARS-CoV-2 disease as hospitalized older children, potentially obscuring the true risk to infants compared with older children. More research is needed to evaluate the risk of severe COVID-19 among infants relative to older children.



Consistent with other studies,<sup>2, 3</sup> Hispanic and non-Hispanic Black children had higher population-based rates of hospitalization and severe disease relative to non-Hispanic White children. However, as reported elsewhere,<sup>6, 12, 23, 29</sup> once hospitalized with SARS-CoV-2 infection, Hispanic and Black children aged 2–17 years were not at increased risk of severe COVID-19 relative to White children after controlling for the presence of  $\geq 1$  underlying medical conditions. These results may suggest that Hispanic and non-Hispanic Black children may be at greater risk of SARS-CoV-2 infection, COVID-19 illness, and associated hospitalization, but are not necessarily at greater risk of severe disease outcomes after accounting for variation in the prevalence of underlying medical conditions. Hispanic and non-Hispanic Black children may be at greater risk of SARS-CoV-2 infection relative to non-Hispanic White children by, for example, increased risk of infection with SARS-CoV-2 among household members who may be disproportionately represented among essential occupations, structural barriers to accessing health care, or other mechanisms.<sup>38-40</sup>

Limitations of this investigation include geographic and temporal variability in testing availability, capacity, and performance across contributing sites. Additionally, this investigation may have had limited statistical power to detect differences in severe COVID-19, particularly by less prevalent underlying medical conditions or among pediatric subgroups. In addition, ICU admission and invasive mechanical ventilation may not be proxies for disease severity for all children, particularly if the threshold for admission to the ICU for monitoring varied by pediatric subgroup. Also, children could have been misclassified if underlying conditions were not noted on their electronic medical records or case report form. Finally, these results are from a network

of acute care hospitals in 14 states and may not generalize to all hospitalized children with SARS-CoV-2 infection in the US.

## Conclusion

Children experience severe COVID-19 and, in hospitalized children, the presence of specific underlying medical conditions may be associated with greater risk of severe COVID-19 outcomes. Results provide baseline information about disease severity among children prior to widespread pediatric COVID-19 vaccination and can be used to inform clinical decision-making, monitor population-based trends over time, and improve risk communication.

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**Table 1. Demographic characteristics and underlying medical conditions among hospitalized children aged <18 years identified through the COVID-19-Associated Hospitalization Surveillance Network, March 2020–May 2021**

Characteristic	Total		Infants and Children aged <2 years		Children aged 2–17 years	
	No. 2,293		No. 745		No. 1,548	
	No.	(%)	No.	(%)	No.	(%)
Age – median (IQR) <sup>a</sup>	7	(1–14)	2	(1–11)	12	(7–16)
Age Group						
<6 months	450	(19.6)	450	(60.4)	-	-
6–23 months	295	(12.9)	295	(39.6)	-	-
2–4 years	249	(10.9)	-	-	249	(16.1)
5–11 years	470	(20.5)	-	-	470	(30.4)
12–17 years	829	(36.2)	-	-	829	(53.6)
Sex						
Male	1,224	(53.4)	409	(54.9)	815	(52.7)
Female	1,069	(46.6)	336	(45.1)	733	(47.4)
Race/Ethnicity						
Hispanic	773	(33.7)	267	(35.8)	506	(32.7)
NH Black	737	(32.1)	192	(25.8)	545	(35.2)
NH White	525	(22.9)	181	(24.3)	344	(22.2)
NH Asian/Pacific Islander	118	(5.2)	53	(7.1)	65	(4.2)
NH Other <sup>b</sup>	140	(6.1)	52	(7.0)	88	(5.7)
Residential type						
Private residence <sup>c</sup>	2,240	(97.7)	717	(96.2)	1,523	(98.4)
Congregate setting, other or unknown <sup>d</sup>	53	(2.3)	28	(3.8)	25	(1.6)
Hospitalized since birth	25	(1.1)	25	(3.4)	0	(0.0)
<b>Underlying medical conditions</b>						
≥1 underlying medical conditions	1,262	(55.0)	214	(28.7)	1,048	(67.7)
Obesity <sup>e</sup>	478	(20.9)	-	-	478	(30.9)
Chronic lung disease	468	(20.4)	38	(5.1)	430	(27.8)
Asthma	373	(16.3)	13	(1.7)	360	(23.3)
Neurologic disorder	348	(15.2)	49	(6.6)	299	(19.3)
Developmental delay	218	(9.5)	30	(4.0)	188	(12.1)
Cardiovascular disease	146	(6.4)	57	(7.7)	89	(5.8)
Congenital heart disease	94	(4.1)	44	(5.9)	50	(3.2)
Blood disorder	142	(6.2)	21	(2.8)	121	(7.8)
Sickle cell	102	(4.5)	16	(2.2)	86	(5.6)
Chronic metabolic disease	136	(5.9)	8	(1.1)	128	(8.3)
Diabetes mellitus (type I or II)	89	(3.9)	1	(0.1)	88	(5.7)
Immunocompromised condition	129	(5.6)	7	(0.9)	122	(7.9)
Feeding tube dependent	114	(5.0)	33	(4.4)	81	(5.2)
Premature <sup>f</sup>	100	(4.4)	100	(13.4)	-	-
Airway abnormality	58	(2.5)	24	(3.2)	34	(2.2)

<b>Characteristic</b>	<b>Total</b>		<b>Infants and Children aged &lt;2 years</b>		<b>Children aged 2–17 years</b>	
	<b>No. 2,293</b>		<b>No. 745</b>		<b>No. 1,548</b>	
	<b>No.</b>	<b>(%)</b>	<b>No.</b>	<b>(%)</b>	<b>No.</b>	<b>(%)</b>
Renal disease	46	(2.0)	9	(1.2)	37	(2.4)
Liver disease	41	(1.8)	6	(0.8)	35	(2.3)
Rheumatologic, autoimmune, inflammatory condition	14	(0.6)	0	(0.0)	14	(0.9)
Other	133	(5.8)	36	(4.8)	97	(6.3)
Discharge diagnosis of MIS-C	198	(8.6)	15	(2.0)	183	(11.8)
<b>Outcomes</b>						
ICU Admission or Invasive Mechanical Ventilation	691	(30.1)	164	(22.0)	527	(34.0)
Invasive Mechanical Ventilation	122	(5.3)	34	(4.6)	88	(5.7)
In-hospital deaths	12	(0.5)	4	(0.5)	8	(0.5)

Abbreviations: COVID-19=Coronavirus Disease-2019; NH=non-Hispanic

<sup>a</sup> Reported in months for children aged <2 years and in years for all other age groups

<sup>b</sup> Includes NH American Indian/Alaska Native (n=20, 0.9%), NH multiple races (n=25, 1.1%), or unknown (n=95, 4.1%)

<sup>c</sup> Includes private residence or home with services

<sup>d</sup> Includes hospitalized since birth, group home/retirement, homeless shelter, psychiatric facility, facility, long-term acute care hospital, corrections facility, other, and unknown

<sup>e</sup> Children aged 2–17 years were classified as having obesity if they had body mass index (kg/m<sup>2</sup>) ≥95<sup>th</sup> percentile for age and sex based on CDC growth charts, ICD-10 codes for obesity in the electronic medical record, or obesity selected on the case report form.

<sup>f</sup> Gestational age <37 weeks at birth among children aged <2 years



**Table 2. Demographic characteristics and underlying medical conditions among children aged <18 years who died while hospitalized with COVID-19—COVID-19-Associated Hospitalization Surveillance Network, March 2020–May 2021**

<b>Characteristic</b>	<b>Children aged &lt;18 years (N=12)</b>	
	<b>No.</b>	<b>(%)</b>
Age (yrs) – mean (range)	7	(0–14)
Age Group		
<6 mos	1	(8.3)
6–23 mos	3	(25.0)
2–4 yrs	2	(16.7)
5–11 years	2	(16.7)
12–17 years	4	(33.3)
Sex		
Male	7	(58.3)
Female	5	(41.7)
Race/Ethnicity		
Hispanic	6	(50.0)
NH Black	4	(33.3)
NH White	0	(0.0)
Unknown	2	(14.3)
Residential Type <sup>a</sup>		
Private Residence	12	(100)
Congregate setting, other or unknown	0	(0)
<b>Underlying medical conditions</b>		
≥1 underlying medical conditions	10	(83.3)
Neurologic disorder	7	(58.3)
Chronic lung disease	2	(16.7)
Immunocompromised condition	2	(16.7)
Feeding tube dependence	2	(16.7)
<b>Outcomes</b>		
Intensive care unit admission	12	(100)
Invasive mechanical ventilation	10	(83.3)

Abbreviations: NH=non-Hispanic

<sup>a</sup> Private residence includes home with services. Congregate setting includes hospitalized since birth, group home/retirement, homeless shelter, psychiatric facility, facility, long-term acute care hospital, corrections facility, other, and unknown.

**Table 3. Age-adjusted cumulative population-based rates of hospitalization and severe COVID-19 per 100,000 children aged <18 Years by age group, sex, and race and Hispanic ethnicity identified through the COVID-19-Associated Hospitalization Surveillance Network, March 2020–May 2021**

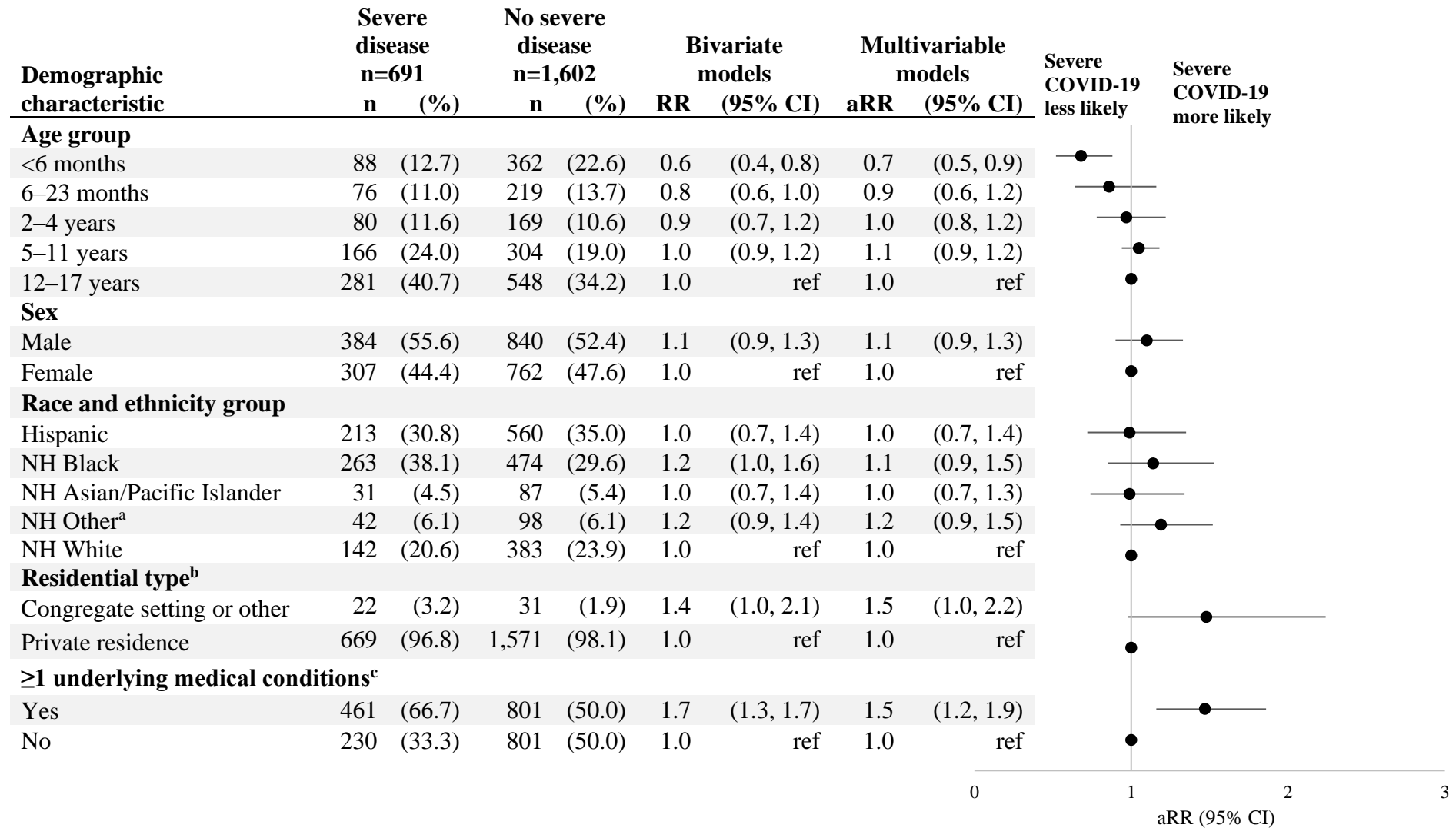
Group	Hospitalization			Severe COVID-19		
	No.	Rate	RR	No.	Rate	RR
Overall	3,106	43.2	–	860	12.0	–
Age Group						
<2 years	862	113.7	–	199	26.3	–
<12 months	671	177.5	3.2	139	36.8	2.4
12–23 months	191	50.3	0.9	60	15.8	1.03
2–17 years	2,244	34.9	–	661	10.3	–
2–5 years	375	23.8	0.4	123	7.8	0.5
6–11 years	493	20.5	0.4	159	6.6	0.4
12–17 years	1,376	56.1	ref	379	15.5	ref
Sex						
Male	1,556	42.5	0.97	476	13.0	1.2
Female	1,550	44.0	ref	384	10.9	ref
Race and Hispanic Ethnicity Group <sup>a</sup>						
Hispanic	1,051	71.2	3.3	259	17.6	3.3
NH Black	936	63.0	2.9	314	21.1	3.9
NH Asian or Pacific Islander	149	25.3	1.2	36	6.0	1.1
NH White	767	21.4	ref	193	5.4	ref

Abbreviations: COVID-19=Coronavirus Disease-2019, NH=non-Hispanic, RR=Rate Ratio

Note. Age-adjusted cumulative rates reflect the number of intensive care unit admissions or invasive mechanical ventilations among children aged <18 years divided by the 2019 bridged-race postcensal population estimates from the National Center for Health Statistics

<sup>a</sup> Rates not presented for the following race and ethnicity groups due to insufficient sample size: NH American Indian or Alaska Native, NH multiple races, NH other or unknown

**Figure 1. Demographic characteristics associated with severe COVID-19**



**Legend:** Demographic characteristics and ≥1 underlying conditions associated with intensive care unit admission, invasive mechanical ventilation, or death among children <18 years hospitalized with COVID-19—14 states, March 2020–May 2021

## Prepublication Release

Abbreviations: aRR=Adjusted Risk Ratio, CI=Confidence Interval, RR=risk ratio, NH=non-Hispanic

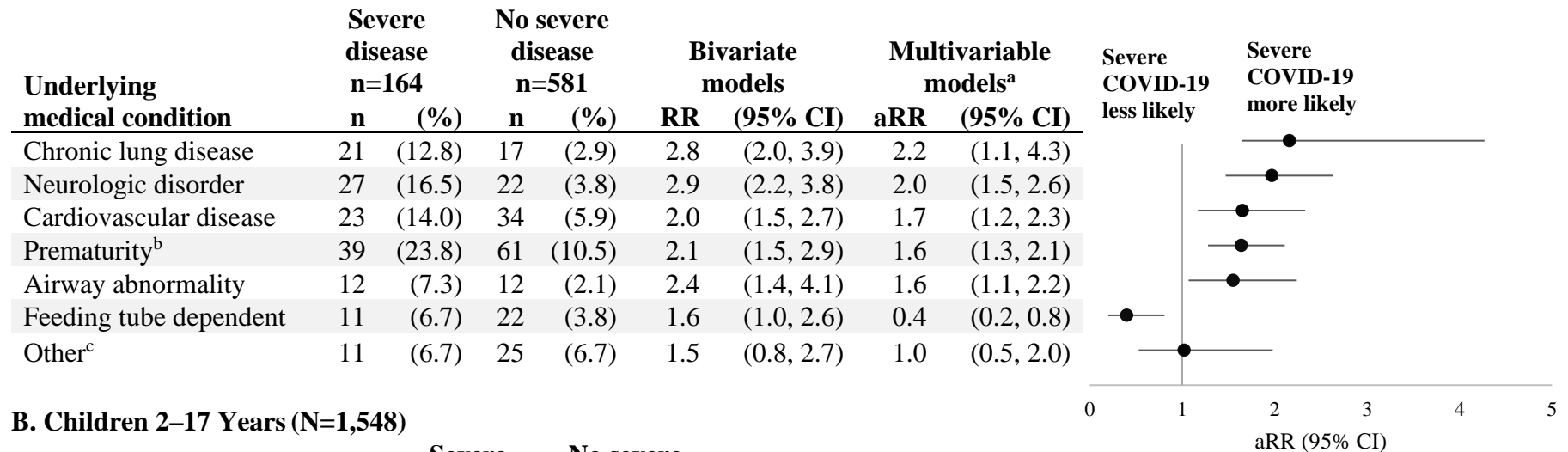
<sup>a</sup> Includes non-Hispanic American Indian or Alaska Native, non-Hispanic multiple races, or unknown

<sup>b</sup> Private residence includes home with services. Congregate setting includes hospitalized since birth, group home/retirement, homeless shelter, psychiatric facility, facility, long-term acute care hospital, corrections facility, other, and unknown

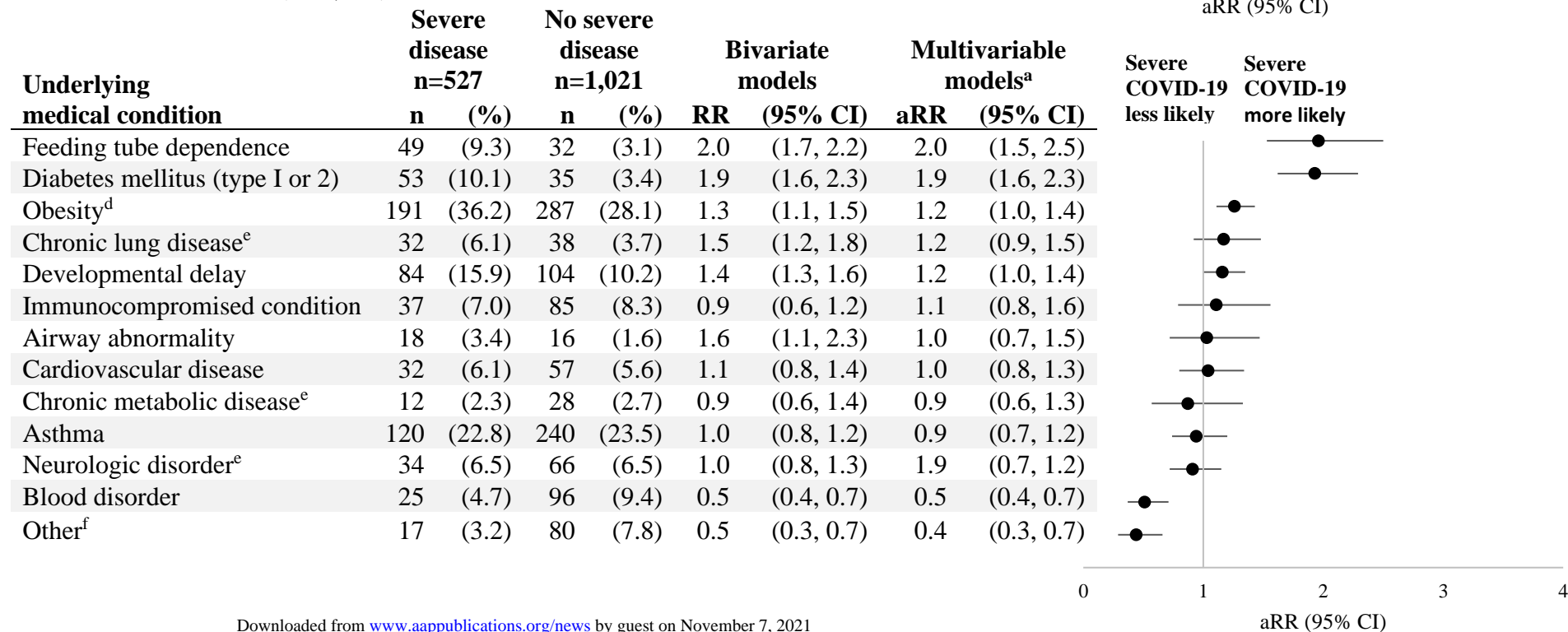
<sup>c</sup> Includes obesity (among aged 2–17 years); prematurity (among aged <2 years); chronic lung disease; airway abnormality; neurologic disorders; immunocompromised conditions; feeding tube dependence; cardiovascular disease; chronic metabolic disease; blood disorders; gastrointestinal/liver disease; renal disease; rheumatologic, autoimmune, or inflammatory conditions; or other conditions.

Figure 2, A–B. Underlying conditions associated with severe COVID-19 by age group

## A. Children &lt;2 Years (N=745)



## B. Children 2–17 Years (N=1,548)



# Prepublication Release

**Legend:** Underlying conditions associated with intensive care unit admission, invasive mechanical ventilation, or death among children (A.) aged <2 years and (B.) aged 2–17 years hospitalized with COVID-19—14 states, March 2020–May 2021

Abbreviations: aRR=adjusted risk ratio, CI=confidence interval, RR=risk ratio

<sup>a</sup> Multivariable models are adjusted for age group, sex, race/ethnicity group, and housing type.

<sup>b</sup> Born <37 weeks gestational age

<sup>c</sup> Includes immunocompromised conditions, liver disease, chronic metabolic disease, blood disorders, renal disease, and other disease specified on the case report form

<sup>d</sup> Children aged 2–17 years were classified as having obesity if they had body mass index ( $\text{kg/m}^2$ )  $\geq 95^{\text{th}}$  percentile for age and sex based on CDC growth charts, ICD-10 codes for obesity in the electronic medical record, or obesity selected on the COVID-NET case report form.

<sup>e</sup> Chronic lung disease excludes asthma, chronic metabolic disease excludes type 1 or 2 diabetes mellitus, and neurologic disorder excludes developmental delay.

<sup>f</sup> Includes liver disease; renal disease; rheumatologic, autoimmune, and inflammatory conditions; and other conditions specified on the case report form

## SUPPLEMENTAL TABLES AND FIGURES

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eTable 1. Demographic characteristics of children ages <18 years hospitalized with SARS-CoV-2 infection included vs. excluded from the analysis—COVID-19-Associated Hospitalization Surveillance Network, March 2020–May 2021

	Pediatric Hospitalizations Excluded from Analysis N=813		Pediatric Hospitalizations Included In Analysis N=2,293	
	n	(%)	n	(%)
<b>Reason for Exclusion</b>				
Incomplete chart abstraction	81	(10.0)	0	(0.0)
Currently pregnant upon admission	127	(15.9)	0	(0.0)
Unknown outcome	15	(0.5)	0	(0.0)
Primary reason for admission not likely related to COVID-19	718	(23.1)	0	(0.0)
OB/Labor & Delivery	162	(19.9)	0	(0.0)
Inpatient surgery/procedure	118	(14.5)	0	(0.0)
Psychiatric admissions	270	(33.2)	0	(0.0)
Trauma	136	(16.7)	0	(0.0)
Other, missing or unknown	92	(11.3)	0	(0.0)
<b>Demographic characteristics</b>				
Age in year – median (IQR)	14	(9–16)	7	(1–14)
Age group				
<6 months	84	(10.3)	450	(19.6)
6–23 months	33	(4.1)	295	(12.9)
2–4 years	52	(6.4)	249	(10.9)
5–11 years	97	(11.9)	470	(20.5)
12–17 years	547	(67.3)	829	(36.2)
Sex				
Male	332	(40.8)	1,224	(53.4)
Female	481	(59.2)	1,069	(46.6)
Race and Ethnicity Group				
Hispanic	278	(34.2)	773	(33.7)
NH White	242	(29.8)	525	(22.9)
NH Black	199	(24.5)	737	(32.1)
NH Asian or Pacific Islander	31	(3.8)	118	(5.2)
NH Other <sup>a</sup>	63	(7.8)	140	(6.1)
Housing type				
Private residence <sup>b</sup>	699	(86.0)	2,240	(28.0)
Congregate setting, other, or unknown <sup>c</sup>	114	(14.0)	53	(2.3)
<b>Underlying medical conditions</b>				
≥1 underlying medical conditions	299	(36.8)	1,262	(55.0)
Obesity <sup>d</sup>	119	(14.6)	478	(20.9)
Chronic lung disease	87	(10.7)	468	(20.4)
Asthma	78	(9.6)	373	(16.3)
Neurologic disorder	70	(8.6)	348	(15.2)
Developmental delay	46	(5.7)	218	(9.5)
Cardiovascular disease	24	(3.0)	146	(6.4)



	Pediatric Hospitalizations Excluded from Analysis N=813		Pediatric Hospitalizations Included In Analysis N=2,293	
	n	(%)	n	(%)
Congenital heart disease	14	(1.7)	94	(4.1)
Blood disorder	10	(1.2)	142	(6.2)
Sickle cell disease	6	(0.7)	102	(4.5)
Chronic metabolic disease	35	(4.3)	136	(5.9)
Diabetes mellitus (type I or II)	13	(1.6)	89	(3.9)
Immunocompromised condition	25	(3.1)	129	(5.6)
Feeding tube dependent	6	(0.7)	114	(5.0)
Premature <sup>e</sup>	19	(2.3)	100	(4.4)
Airway abnormality	3	(0.4)	58	(2.5)
Other	21	(2.6)	133	(5.8)
Renal disease	7	(0.9)	46	(2.0)
Liver disease	6	(0.7)	41	(1.8)
Rheumatologic, autoimmune, inflammatory condition	2	(0.3)	14	(0.6)
Discharge diagnosis of MIS-C	4	(0.5)	198	(8.6)
<b>Outcomes</b>				
ICU admission or invasive mechanical ventilation	170	(20.9)	691	(30.1)
Invasive mechanical ventilation	67	(8.2)	122	(5.3)
In-hospital deaths	10	(1.2)	12	(0.5)

Note. Chi-square tests or Fisher's exact tests generated *p*-values assessing the uniformity of the prevalence distributions by primary reason for admission.

Abbreviations: NH=non-Hispanic

<sup>a</sup> Includes NH American Indian/Alaska Native (n=21, 1.1%); NH multiple races (n=20, 1.0%); or unknown (n=77, 3.9%)

<sup>b</sup> Includes private residence or home with services

<sup>c</sup> Includes hospitalized since birth, group home/retirement, homeless shelter, psychiatric facility, facility, long-term acute care hospital, corrections facility, other, and unknown

<sup>d</sup> Children 2–17 years were classified as having obesity if they had body mass index (kg/m<sup>2</sup>) ≥95<sup>th</sup> percentile for age and sex based on CDC growth charts, ICD-10 codes for obesity in the electronic medical record, or obesity selected on the case report form.

<sup>e</sup> Gestational age <37 weeks at birth among children <2 years

eTable 2. Underlying medical conditions among children <18 years hospitalized with SARS-CoV-2 infection identified through the Coronavirus Disease-2019-Associated Hospitalization Surveillance Network, March 2020–January 2021

Underlying Medical Conditions	Population	Included conditions
Airway abnormality	Children <18 years	<ul style="list-style-type: none"> <li>Abnormality of airway (e.g., tracheostomy and abnormalities of mouth or throat that affect ability to handle secretions—laryngomalacia, tracheomalacia, laryngotracheomalacia, subglottic stenosis, subglottic cyst, glottic web, subglottic hemangioma, vascular ring of trachea, congenital stridor, or vocal cord paralysis)</li> </ul>
Blood disorders /hemoglobinopathy underlying conditions	Children <18 years	<ul style="list-style-type: none"> <li>Alpha thalassemia</li> <li>Aplastic anemia</li> <li>Beta thalassemia</li> <li>Coagulopathy</li> <li>Hemoglobin S-beta thalassemia</li> <li>Leukopenia</li> <li>Myelodysplastic syndrome</li> <li>Neutropenia</li> <li>Pancytopenia</li> <li>Sickle cell disease</li> <li>Splenectomy/Asplenia</li> <li>Thrombocytopenia</li> </ul>
Cardiovascular disease	Children <18 years	<ul style="list-style-type: none"> <li>Aortic/Mitral/Tricuspid/Pulmonic valve replacement</li> <li>Aortic stenosis</li> <li>Atrioventricular blocks</li> <li>Automated implantable devices (AID/AICD)/Pacemaker</li> <li>Bundle branch block (BBB, LBBB, RBBB)</li> <li>Cardiomyopathy</li> <li>Cerebral vascular accident/incident/Stroke, history of</li> <li>Congenital heart disease</li> <li>Coronary artery disease</li> <li>Deep vein thrombosis, history of</li> <li>Heart failure/congestive heart failure</li> <li>Myocardial infarction</li> <li>Mitral stenosis</li> <li>Pulmonary embolism</li> <li>Pulmonary hypertension, history of</li> <li>Pulmonary regurgitation</li> <li>Tricuspid regurgitation</li> <li>Ventricular fibrillation</li> <li>Ventricular tachycardia</li> <li>Other cardiovascular disease categorized based on free-text review</li> </ul>
Chronic lung disease	Children <18 years	<ul style="list-style-type: none"> <li>Active tuberculosis</li> <li>Asthma</li> <li>Bronchiectasis</li> <li>Bronchiolitis obliterans</li> </ul>

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Underlying Medical Conditions	Population	Included conditions
		<ul style="list-style-type: none"> <li>• Chronic respiratory failure</li> <li>• Cystic fibrosis</li> <li>• Emphysema/Chronic Obstructive Pulmonary Disease</li> <li>• Interstitial lung disease</li> <li>• Obstructive sleep apnea</li> <li>• Oxygen dependent</li> <li>• Pulmonary fibrosis</li> <li>• Restrictive lung disease</li> <li>• Chronic lung disease of prematurity/Bronchopulmonary dysplasia</li> <li>• Other chronic lung disease categorized based on free-text review</li> </ul>
Chronic metabolic disease	Children <18 years	<ul style="list-style-type: none"> <li>• Adrenal Disorders</li> <li>• Diabetes mellitus (type I or II)</li> <li>• Hyper/hypo-function of pituitary gland</li> <li>• Inborn errors of metabolism</li> <li>• Metabolic Syndrome</li> <li>• Parathyroid dysfunction</li> <li>• Thyroid Dysfunction</li> <li>• Other chronic metabolic disease categorized based on free-text review</li> </ul>
Feeding tube dependent	Children <18 years	<ul style="list-style-type: none"> <li>• Feeding tube dependent</li> </ul>
Gastrointestinal/liver disease	Children <18 years	<ul style="list-style-type: none"> <li>• Autoimmune hepatitis</li> <li>• Chronic pancreatitis</li> <li>• Cirrhosis/End stage liver disease</li> <li>• Crohn's Disease</li> <li>• Esophageal varices</li> <li>• Hepatitis B, chronic</li> <li>• Non-alcoholic fatty liver disease</li> <li>• Ulcerative colitis</li> </ul>
Immunocompromised condition	Children <18 years	<ul style="list-style-type: none"> <li>• Complement deficiency</li> <li>• Immunoglobulin deficiency/Immunodeficiency</li> <li>• Immunosuppressive therapy (within the last 12 months prior to admission)</li> <li>• Leukemia<sup>a</sup></li> <li>• Lymphoma/Hodgkin's/Non-Hodgkin's<sup>a</sup></li> <li>• Metastatic cancer<sup>a</sup></li> <li>• Solid organ malignancy<sup>a</sup></li> <li>• Steroid therapy (within 2 weeks of admission)</li> <li>• Transplant, hematopoietic stem cell (Bone marrow transplant, peripheral stem cell transplant), history of</li> <li>• Transplant, solid organ, history of</li> <li>• Other immunocompromised condition categorized based on free-text review</li> </ul>
Neurologic disorder	Children <18 years	<ul style="list-style-type: none"> <li>• Cerebral palsy</li> </ul>

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Underlying Medical Conditions	Population	Included conditions
		<ul style="list-style-type: none"> <li>• Cognitive dysfunction</li> <li>• Developmental delay</li> <li>• Down syndrome/Trisomy 21</li> <li>• Epilepsy/seizure/seizure disorder</li> <li>• Mitochondrial disorder</li> <li>• Muscular dystrophy</li> <li>• Neural tube defects/Spina bifida</li> <li>• Neuropathy</li> <li>• Plegias/Paralysis/Quadriplegia</li> <li>• Scoliosis/Kyphoscoliosis</li> <li>• Traumatic brain injury, history of</li> <li>• Other neurologic disorder categorized based on free-text review</li> </ul>
Obesity	Children 2–17 years	<ul style="list-style-type: none"> <li>• Body mass index (kg/m<sup>2</sup>) ≥95<sup>th</sup> percentile for age and sex based on CDC growth charts, ICD-10 codes for obesity in the electronic medical chart, or obesity selected on COVID-NET the case report form</li> </ul>
Other underlying conditions	Children <18 years	<ul style="list-style-type: none"> <li>• Other free text underlying medical conditions not categorized into a previous category after review by pediatrician</li> </ul>
Prematurity	Children <2 years	<ul style="list-style-type: none"> <li>• Gestational age &lt;37 weeks at birth among children &lt;2 years.</li> </ul>
		<ul style="list-style-type: none"> <li>•</li> </ul>
Renal disease	Children <18 years	<ul style="list-style-type: none"> <li>• Chronic kidney disease/chronic renal insufficiency</li> <li>• Dialysis</li> <li>• End stage renal disease</li> <li>• Glomerulonephritis</li> <li>• Nephrotic syndrome</li> </ul>
Rheumatologic/autoimmune/inflammatory condition	Children <18 years	<ul style="list-style-type: none"> <li>• Juvenile idiopathic arthritis</li> <li>• Kawasaki disease</li> <li>• Systemic Lupus Erythematosus, Lupus</li> <li>• Vasculitis, other</li> <li>• Other rheumatologic, autoimmune, or inflammatory disorders</li> </ul>

<sup>a</sup>Currently in treatment or diagnosed in previous 12 months

eTable 3. Demographic characteristics associated with severe disease among children hospitalized with COVID-19 who did not have a discharge diagnosis of MIS-C

	Severe Disease (N=567)		No severe Disease (N=1,528)		Bivariate models			Multivariable model		
	n	(%)	n	(%)	RR	95% CI	p	aRR	95% CI	p
Age group										
<6 months	86	(15.2)	361	(23.6)	0.6	(0.5, 0.8)	.0004	0.8	(0.6, 1.1)	.21
6–23 months	70	(12.4)	213	(13.9)	0.8	(0.6, 1.1)	.16	1.0	(0.7, 1.4)	.84
2–4 years	63	(11.1)	150	(9.8)	0.9	(0.8, 1.1)	.44	1.0	(0.8, 1.2)	.89
5–11 years	105	(18.5)	272	(17.8)	0.9	(0.8, 1.0)	.07	0.9	(0.8, 1.0)	.03
12–17 years	243	(42.9)	532	(34.8)	ref			ref		
Sex										
Male	313	(55.2)	788	(51.6)	1.1	(0.9, 1.4)	.27	1.1	(0.9, 1.4)	.35
Female	254	(44.8)	740	(48.4)	ref			ref		
Race and Ethnicity Group										
Hispanic	175	(30.9)	538	(35.2)	1.0	(0.7, 1.4)	.77	0.9	(0.7, 1.3)	.75
NH Black	204	(36.0)	447	(29.3)	1.2	(0.8, 1.6)	.37	1.0	(0.7, 1.5)	.87
NH Asian or Pacific Islander	26	(4.6)	84	(5.5)	0.9	(0.6, 1.3)	.66	1.0	(0.7, 1.3)	.75
NH Other <sup>a</sup>	37	(6.5)	95	(6.2)	1.2	(0.9, 1.5)	.21	1.2	(0.9, 1.6)	.15
NH White	125	(22.1)	364	(23.8)	Ref			ref		
Residential type <sup>b</sup>										
Congregate setting, other or unknown	21	(3.7)	31	(2.0)	1.5	(1.1, 2.3)	.02	1.5	(1.0, 2.2)	.03
Private residence	546	(96.3)	1,497	(98.0)	ref			ref		
≥1 underlying medical conditions <sup>c</sup>										
Yes	409	(72.1)	777	(50.9)	2.0	(1.6, 2.6)	<.0001	1.9	(1.5, 2.6)	<.0001
No	158	(27.9)	751	(49.2)	ref			ref		

Note. Multivariable generalized estimating equations modeling demographic characteristics and ≥1 underlying medical conditions associated with intensive care unit admission or invasive mechanical ventilation among children ages <18 years hospitalized with SARS-CoV-2 infection who did not have a discharge diagnosis of MIS-C identified through the Coronavirus Disease-2019 Hospitalization Surveillance Network (COVID-NET), March 2020–May 2021.

Abbreviations: aRR= adjusted risk ratio, CI=Confidence Interval, COVID-NET=Coronavirus Disease-2019, MIS-C=Multisystem Inflammatory Syndrome in Children, NH=non-Hispanic

<sup>a</sup> Includes non-Hispanic American Indian or Alaska Native, non-Hispanic multiple races, or unknown

<sup>b</sup> Private residence includes home with services. Congregate setting includes hospitalized since birth, group home/retirement, homeless shelter, psychiatric facility, facility, long-term acute care hospital, corrections facility, other, and unknown

<sup>c</sup> Includes obesity (among ages 2–17 years); prematurity (among ages <2 years); chronic lung disease; airway abnormality; neurologic disorders; immunocompromised conditions; feeding tube dependence; cardiovascular disease; chronic metabolic disease; blood disorders; gastrointestinal/liver disease; renal disease; rheumatologic, autoimmune, or inflammatory conditions; or other conditions.

eTable 4. Underlying medical conditions associated with severe disease among children ages &lt;18 years hospitalized with COVID-19 who did not have a discharge diagnosis of MIS-C

	Severe disease		No severe disease		RR	Bivariate models		p	Multivariable models		p
	n	(%)	n	(%)		95% CI	aRR		95% CI		
<b>Infants and children &lt;2 years without MIS-C</b>	156	(21.4)	574	(78.6)							
Chronic lung disease	21	(13.5)	17	(3.0)	2.9	(2.1, 4.0)	<.0001	2.2	(1.1, 4.3)		.02
Neurologic disorder	27	(17.3)	22	(3.8)	3.0	(2.3, 3.9)	<.0001	2.1	(1.5, 2.9)		<.0001
Cardiovascular disease	22	(14.1)	34	(5.9)	2.0	(1.5, 2.7)	<.0001	1.6	(1.1, 2.3)		.007
Airway abnormality	12	(7.7)	12	(2.1)	2.5	(1.4, 4.3)	.001	1.6	(1.1, 2.3)		.02
Prematurity <sup>a</sup>	38	(24.4)	61	(10.6)	2.1	(1.5, 3.0)	<.0001	1.6	(1.3, 2.1)		<.0001
Feeding tube dependent	11	(7.1)	22	(3.8)	1.6	(1.0, 2.7)	.04	0.4	(0.2, 0.8)		.02
Other <sup>b</sup>	11	(7.1)	25	(4.4)	1.5	(0.8, 2.7)	.19	1.1	(0.6, 2.0)		.89
<b>Children 2–17 years without MIS-C</b>	411	(30.1)	954	(69.9)							
Diabetes mellitus (type I or II)	52	(12.7)	35	(3.6)	2.2	(1.9, 2.6)	<.0001	2.4	(2.0, 2.8)		<.0001
Feeding tube dependent	49	(11.9)	30	(3.1)	2.3	(2.0, 2.7)	<.0001	2.2	(1.7, 2.9)		<.0001
Chronic lung disease <sup>d</sup>	32	(7.8)	38	(4.0)	1.7	(1.3, 2.2)	.0001	1.2	(0.9, 1.6)		.14
Obesity <sup>c</sup>	154	(37.5)	276	(28.9)	1.3	(1.1, 1.6)	.002	1.3	(1.1, 1.5)		.002
Developmental delay	80	(19.5)	103	(10.8)	1.6	(1.5, 1.8)	<.0001	1.3	(1.1, 1.6)		.004
Chronic metabolic disease <sup>d</sup>	12	(2.9)	28	(2.9)	1.0	(0.6, 1.7)	.91	0.9	(0.6, 1.4)		.61
Asthma	105	(25.6)	231	(24.2)	1.1	(0.8, 1.4)	.66	1.1	(0.8, 1.4)		.70
Airway abnormality	18	(4.4)	16	(1.7)	1.8	(1.3, 2.7)	.002	1.0	(0.7, 1.5)		.99
Immunocompromised condition	37	(9.0)	85	(8.9)	1.0	(0.7, 1.4)	.98	1.3	(0.9, 1.9)		.17
Cardiovascular disease	30	(7.3)	53	(5.6)	1.3	(0.9, 1.8)	.19	1.1	(0.8, 1.5)		.46
Neurologic disorder <sup>d</sup>	33	(8.0)	63	(6.6)	1.2	(0.9, 1.6)	.28	1.1	(0.8, 1.4)		.59
Blood disorder	24	(5.8)	95	(10.0)	0.6	(0.4, 0.7)	<.0001	0.6	(0.4, 0.8)		.002
Other <sup>e</sup>	14	(3.4)	76	(8.0)	0.5	(0.3, 0.7)	<.0001	0.4	(0.3, 0.6)		<.0001

Note: Multivariable generalized estimating equations modeling underlying medical conditions associated with intensive care unit admission or invasive mechanical ventilation among children ages <18 years hospitalized with COVID-19 who

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did not have a discharge diagnosis of MIS-C identified through the Coronavirus Disease-2019 Hospitalization Surveillance Network (COVID-NET), March 2020–May 2021. Estimates are adjusted for age group, sex, race/ethnicity group, and housing type.

Abbreviations: CI=confidence interval, MIS-C=Multisystem Inflammatory Syndrome in Children, RR=risk ratio

<sup>a</sup> Born <37 weeks gestational age

<sup>b</sup> Includes immunocompromised conditions, liver disease, chronic metabolic disease, blood disorders, renal disease, and other disease specified on the case report form

<sup>c</sup> Children ages 2–17 years were classified as having obesity if they had body mass index ( $\text{kg}/\text{m}^2$ )  $\geq 95^{\text{th}}$  percentile for age and sex based on CDC growth charts, ICD-10 codes for obesity in the electronic medical record, or obesity selected on the COVID-NET case report form.

<sup>d</sup> Chronic lung disease excludes asthma, chronic metabolic disease excludes type 1 or 2 diabetes mellitus, and neurologic disorder excludes developmental delay.

<sup>e</sup> Includes liver disease; renal disease; rheumatologic, autoimmune, and inflammatory conditions; and other conditions specified on the case report form



eTable 5. Underlying conditions associated with severe COVID-19 by additional age groups

	Severe disease		No severe disease		Bivariate Models			Multivariable Model			
	n	(%)	n	(%)	RR	95% CI	<i>p</i>	aRR	95% CI	<i>p</i>	
<b>&lt;6 months</b>	88	(19.6)	362	(80.4)							
Prematurity <sup>a</sup>	25	(28.4)	34	(9.4)	2.6	(1.8, 3.8)	<.0001	2.4	(1.7, 3.5)	<.0001	
Cardiovascular disease	8	(9.1)	10	(2.8)	2.4	(1.5, 3.9)	.0004	2.4	(1.3, 4.3)	.005	
Other <sup>b</sup>	10	(11.4)	22	(6.1)	1.7	(1.2, 2.3)	.002	1.2	(1.0, 1.4)	.03	
<b>6–23 months</b>	76	(25.8)	219	(74.2)							
Chronic lung disease <sup>d</sup>	17	(22.4)	13	(5.9)	2.7	(1.7, 4.2)	<.0001	2.4	(1.3, 4.2)	.004	
Neurologic disorders <sup>d</sup>	25	(32.9)	20	(9.1)	2.7	(2.4, 3.2)	<.0001	2.3	(1.8, 2.9)	<.0001	
Abnormality of airway	9	(11.8)	8	(3.7)	2.2	(1.2, 4.2)	.02	1.5	(0.8, 2.9)	.22	
Cardiovascular disease	15	(19.7)	24	(11.0)	1.6	(1.4, 2.0)	<.0001	1.4	(1.2, 1.5)	<.0001	
Prematurity <sup>a</sup>	14	(18.4)	27	(12.3)	1.4	(0.6, 3.2)	.41	1.0	(0.5, 1.8)	.91	
Feeding tube dependence	9	(11.8)	17	(7.8)	1.4	(1.0, 2.0)	.04	0.5	(0.1, 1.6)	.23	
Other <sup>b</sup>	10	(13.2)	29	(13.2)	1.0	(0.5, 2.0)	.08	0.9	(0.4, 2.0)	.80	
<b>2–4 years</b>	80	(32.1)	169	(67.9)							
Feeding tube dependence	18	(22.5)	8	(4.7)	2.5	(1.1, 5.7)	.02	2.1	(1.1, 3.9)	.02	
Obesity <sup>c</sup>	16	(20.0)	23	(13.6)	1.4	(0.8, 2.5)	.19	1.4	(0.9, 2.0)	.13	
Neurologic disorder <sup>d</sup>	30	(37.5)	37	(21.9)	1.8	(1.1, 2.9)	.02	1.4	(1.0, 1.9)	.06	
Chronic lung disease <sup>d</sup>	19	(23.8)	22	(13.0)	1.7	(0.9, 3.1)	.08	1.3	(0.9, 1.7)	.18	
Chronic metabolic disease <sup>d</sup>	10	(12.5)	8	(4.7)	1.9	(1.7, 2.0)	<.0001	1.3	(1.1, 1.5)	.006	
Cardiovascular disease	7	(8.8)	11	(6.5)	1.5	(0.9, 2.5)	.14	0.8	(0.6, 1.1)	.13	
Other <sup>b</sup>	13	(16.3)	33	(19.5)	0.7	(0.7, 0.8)	<.0001	0.6	(0.5, 0.7)	<.0001	
<b>5–11 years</b>	166	(35.3)	304	(64.7)							
Chronic metabolic disease <sup>d</sup>	10	(6.0)	14	(4.6)	1.3	(1.0, 1.8)	.10	1.4	(0.9, 2.1)	.10	
Obesity <sup>c</sup>	52	(31.3)	71	(23.4)	1.3	(1.2, 1.5)	<.0001	1.4	(1.2, 1.6)	<.0001	
Feeding tube dependence	10	(6.0)	17	(6.0)	1.1	(0.8, 1.5)	.48	1.3	(1.0, 1.7)	.06	
Neurologic disorder <sup>d</sup>	37	(22.3)	64	(21.1)	1.1	(0.9, 1.3)	.27	1.1	(0.9, 1.3)	.41	

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	Severe disease		No severe disease		Bivariate Models		p	Multivariable Model		
	n	(%)	n	(%)	RR	95% CI		aRR	95% CI	p
Chronic lung disease <sup>d</sup>	42	(25.3)	95	(31.3)	0.8	(0.7, 0.9)	.0001	0.8	(0.7, 1.0)	.09
Cardiovascular disease	7	(4.2)	22	(7.2)	0.7	(0.4, 1.1)	.13	0.8	(0.4, 1.3)	.32
Immunocompromised condition	7	(4.2)	32	(10.5)	0.5	(0.3, 0.7)	.0002	0.5	(0.4, 0.8)	.003
Blood disorder	9	(5.4)	32	(10.5)	0.5	(0.4, 0.8)	.001	0.6	(0.3, 1.0)	.05
Other <sup>b</sup>	6	(3.6)	25	(8.2)	0.6	(0.4, 0.8)	.0006	0.6	(0.4, 0.7)	<.0001
<b>12–17 years</b>	281	(33.9)	548	(66.1)						
Feeding tube dependence	21	(7.5)	7	(1.3)	2.4	(2.1, 2.8)	<.0001	3.0	(2.6, 3.5)	<.0001
Chronic metabolic disease <sup>d</sup>	45	(16.0)	41	(7.5)	1.7	(1.5, 1.9)	<.0001	1.7	(1.5, 1.9)	<.0001
Immunocompromised conditions	26	(9.3)	38	(6.9)	1.2	(0.9, 1.7)	.18	1.4	(1.0, 2.1)	.05
Obesity <sup>c</sup>	123	(43.8)	193	(35.2)	1.3	(1.0, 1.6)	.03	1.3	(1.0, 1.6)	.04
Cardiovascular disease	18	(6.4)	24	(4.4)	1.3	(0.7, 2.5)	.40	1.2	(0.6, 2.4)	.63
Chronic lung disease <sup>d</sup>	91	(32.4)	161	(29.4)	1.1	(0.9, 1.3)	.20	1.0	(0.9, 1.2)	.61
Neurologic disorder <sup>d</sup>	56	(19.9)	75	(13.7)	1.4	(1.2, 1.6)	<.0001	1.0	(0.9, 1.0)	.33
Blood disorder	11	(3.9)	50	(9.1)	0.4	(0.4, 0.6)	<.0001	0.4	(0.3, 0.6)	<.0001
Other <sup>b</sup>	21	(7.5)	53	(9.7)	0.8	(0.6, 1.2)	.29	0.6	(0.4, 0.8)	.001

Note: Multivariable generalized estimating equations modeling underlying medical conditions associated with intensive care unit admission or invasive mechanical ventilation by additional age groups among children ages <18 years hospitalized with COVID-19 identified through the COVID-19-Associated Hospitalization Surveillance Network (COVID-NET), March 2020–May 2021. Estimates are adjusted for sex and race/ethnicity group.

Abbreviations: CI=confidence interval, RR=risk ratio

<sup>a</sup> Born <37 weeks gestational age

<sup>b</sup> Includes liver disease; renal disease; and rheumatologic, autoimmune, and inflammatory conditions; and other conditions specified on the case report form. Additionally, among children aged <6 months, chronic metabolic disease, immunocompromised conditions, chronic lung disease, neurologic disorders, airway abnormalities, feeding tube dependence, and blood disorders are included.

Among children aged 6–23 months, chronic metabolic disease, immunocompromised conditions, and blood disorders are included.

Among children aged 2–4 years, blood disorders, immunocompromised conditions, and airway abnormalities are included. Among children aged 5–11 years and 12–17 years, airway abnormalities are included.

<sup>c</sup> Children ages 2–17 years were classified as having obesity if they had body mass index (kg/m<sup>2</sup>) ≥95<sup>th</sup> percentile for age and sex based on CDC growth charts, ICD-10 codes for obesity in the electronic medical record, or obesity selected on the COVID-NET case report form.

<sup>d</sup> Chronic lung disease includes asthma, neurologic disorders include developmental delay, and chronic metabolic disease includes type I or II diabetes mellitus.

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eTable 6. Underlying conditions associated with severe disease among children ages 2–17 years hospitalized with COVID-19 by race/ethnicity group

Underlying medical condition	Severe disease		No severe disease		Bivariate models		p	Multivariable models <sup>a</sup>		p
	n	(%)	n	(%)	RR	(95% CI)		aRR	(95% CI)	
<b>Hispanic children ages 2–17 years</b>	162	(32.0)	344	(68.0)						
Chronic metabolic disease <sup>b</sup>	19	(11.7)	19	(5.5)	1.7	(1.2, 2.2)	.0014	1.6	(1.1, 2.5)	.03
Neurologic disorder <sup>b</sup>	37	(22.8)	54	(15.7)	1.3	(1.0, 1.8)	.04	1.3	(1.0, 1.8)	.05
Obesity <sup>c</sup>	73	(45.1)	119	(34.6)	1.4	(1.1, 1.8)	.01	1.4	(1.0, 1.8)	.03
Chronic lung disease <sup>b</sup>	43	(26.5)	79	(23.0)	1.1	(0.8, 1.5)	.71	1.0	(0.8, 1.3)	.85
Cardiovascular disease	11	(6.8)	22	(6.4)	1.0	(0.7, 1.6)	.90	0.9	(0.7, 1.2)	.47
Immunocompromised condition	12	(7.4)	35	(10.2)	0.9	(0.8, 1.0)	.02	0.9	(0.7, 1.0)	.13
Other <sup>d</sup>	24	(14.8)	49	(14.2)	1.0	(0.8, 1.2)	.90	1.0	(0.8, 1.2)	.90
<b>Non-Hispanic Black children ages 2–17 years</b>	216	(39.6)	329	(60.4)						
Feeding tube dependence	17	(7.9)	13	(4.0)	1.5	(1.3, 1.9)	<.0001	1.5	(1.0, 2.3)	.06
Obesity <sup>c</sup>	75	(32.7)	87	(26.4)	1.3	(1.1, 1.5)	.003	1.2	(1.0, 1.4)	.01
Cardiovascular disease	14	(6.5)	17	(5.2)	1.2	(0.9, 1.6)	.34	1.1	(1.1, 1.1)	<.0001
Neurologic disorder <sup>b</sup>	47	(21.8)	57	(17.3)	1.2	(1.0, 1.5)	.12	1.0	(0.6, 1.7)	.93
Chronic lung disease <sup>b</sup>	67	(31.0)	118	(35.9)	0.9	(0.7, 1.1)	.23	0.9	(0.7, 1.1)	.21
Immunocompromised condition	10	(4.6)	25	(7.6)	0.7	(0.4, 1.4)	.31	0.9	(0.5, 1.5)	.60
Chronic metabolic disease <sup>b</sup>	25	(11.6)	21	(6.4)	1.5	(1.3, 1.7)	<.0001	0.8	(0.5, 1.2)	.24
Blood disorder	17	(7.9)	69	(21.0)	0.4	(0.3, 0.5)	<.0001	0.5	(0.3, 0.6)	<.0001
Other <sup>d</sup>	19	(8.8)	31	(9.4)	0.9	(0.6, 1.4)	.76	0.8	(0.5, 1.2)	.24
<b>Non-Hispanic White children ages 2–17 years</b>	97	(28.2)	247	(71.8)						
Chronic metabolic disease <sup>b</sup>	11	(11.3)	18	(7.3)	1.5	(1.3, 1.8)	<.0001	1.6	(1.1, 2.3)	.01
Obesity <sup>c</sup>	27	(27.8)	50	(29.2)	1.5	(1.0, 2.3)	.06	1.5	(1.0, 2.2)	.04
Feeding tube dependence	10	(10.3)	10	(4.1)	1.8	(1.6, 2.0)	<.0001	2.1	(1.3, 3.3)	.002
Chronic lung disease <sup>b</sup>	29	(29.9)	53	(21.5)	1.4	(1.2, 1.7)	.0002	1.2	(0.9, 1.5)	.23

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Underlying medical condition	Severe disease		No severe disease		Bivariate models		Multivariable models <sup>a</sup>			
	n	(%)	n	(%)	RR	(95% CI)	p	aRR	(95% CI)	p
Neurologic disorder <sup>b</sup>	23	(23.7)	46	(18.6)	1.3	(1.0, 1.7)	.08	1.1	(0.6, 2.0)	.79
Immunocompromised condition	9	(9.3)	20	(8.1)	1.2	(0.7, 2.0)	.49	1.2	(0.7, 2.2)	.52
Other <sup>d</sup>	10	(10.3)	37	(15.0)	0.8	(0.6, 1.0)	.02	0.6	(0.5, 0.7)	<.0001

Note: Multivariable generalized estimating equations modeling underlying medical conditions associated with intensive care unit admission or invasive mechanical ventilation by race/ethnicity group among children ages <18 years hospitalized with COVID-19 identified through the Coronavirus Disease-2019 Hospitalization Surveillance Network (COVID-NET), March 2020–May 2021. Estimates are adjusted for age group and sex.

Abbreviations: aRR=adjusted risk ratio, CI=confidence interval, RR=risk ratio

<sup>a</sup> Multivariable models are adjusted for age group, sex, race and/or Hispanic ethnicity group, and housing type.

<sup>b</sup> Chronic lung disease includes asthma, neurologic disorders include developmental delay, and chronic metabolic disease includes type I or II diabetes mellitus.

<sup>c</sup> Children 2–17 years were classified as having obesity if they had body mass index (kg/m<sup>2</sup>) ≥95<sup>th</sup> percentile for age and sex based on CDC growth charts, ICD-10 codes for obesity in the electronic medical record, or obesity selected on the COVID-NET case report form.

<sup>d</sup> Includes airway abnormalities, liver disease; renal disease; rheumatologic, autoimmune, and inflammatory conditions; and other conditions specified on the case report form. Feeding tube dependence and blood disorders are also included for Hispanic children and cardiovascular disease and blood disorders are also included for non-Hispanic White children.

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