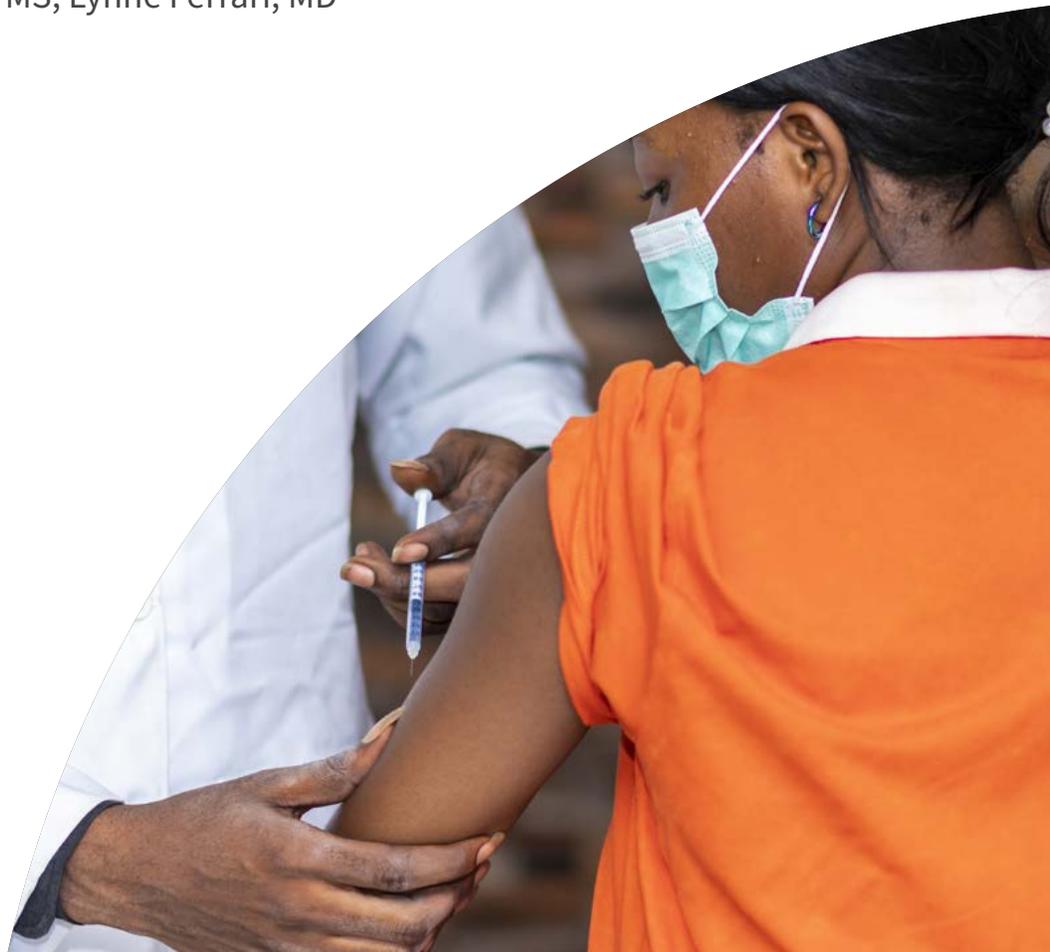


# Prevalence of Risk Factors for Severe COVID-19 Disease

## Implications for Children and Youth with Special Health Care Needs

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### **AUTHORSHIP CRITERIA AND CONTRIBUTIONS**

Dr. Berry takes responsibility for the integrity of the work as a whole, from inception to the published report.

Dr. Berry, Dr. Ferrari, Ms. Teves, Ms. Desmarais, Mr. Rodean, and Mr. Yang all made substantial contributions to conception or design of the work; interpreted the data for the work; drafted the work and revised it critically for important intellectual content; gave final approval of the version to be published; and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Mr. Yang and Mr. Rodean had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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## Introduction

March 2021 marked the one-year anniversary of the outbreak of Coronavirus 2019 (COVID-19) in the U.S. To date, there have been over 29 million COVID-19 cases, 1.8 million hospitalizations, and 527,000 deaths confirmed in the U.S.<sup>1</sup> Adults have experienced the majority of the COVID-19 illness burden; severe acute respiratory syndrome coronavirus <sup>2</sup> (SARS-CoV-2) has been substantially less prevalent in children and youth. Nevertheless, many children and youth with special health care needs (CYSHCN) are at risk for severe COVID-19 illness.<sup>2</sup> Herein, we report on the at-risk health conditions in these children, including how the conditions are being used to prioritize vaccine distribution, how to identify the conditions using health care claims, and how estimating the prevalence of these conditions can help ensure that children and youth receive the care they need during the pandemic.

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## COVID-19 Vaccine

Optimism about overcoming the COVID-19 pandemic has increased as state governments, public health departments, hospitals, and other entities continue to distribute coronavirus 2019 (COVID-19) vaccines to the U.S. populace.<sup>3</sup> Phases of distribution for COVID-19 vaccination using target groups have been designed to first protect the most vulnerable individuals and to maintain capacity of health care system personnel and other essential workers.<sup>4</sup> Although most vaccine distribution plans across the U.S. have focused on elderly individuals and other at-risk adult populations, deliberations continue on the value, safety, and approach for vaccination programs in children and youth.<sup>5</sup> As of March 2021, the Pfizer/BioNTech COVID-19 vaccine is approved for individuals ages 16 years and older.<sup>6</sup> Moderna and Johnson and Johnson vaccines are approved for individuals age 18 years and older. Pfizer and BioNTech recently requested that the Food and Drug Administration expand emergency use authorization for their vaccine to children ages 12-to-15 years.<sup>7-10</sup>

## Risk Factors for Severe COVID-19 Illness

The World Health Organization and Centers for Disease Control and Prevention (CDC) encourage priority of vaccination to individuals who have a high risk for severe COVID-19 illness due to underlying medical conditions.<sup>4,11</sup> The CDC stewards lists of health conditions that associate with severe COVID-19 illness, resulting in hospitalization, admission to the intensive care unit, intubation and mechanical ventilation, or death.<sup>12,13</sup> These lists, derived from comprehensive reviews of published research studies, include condition-specific underlying diseases (e.g., sickle cell anemia), broad categories of disease (e.g., neurologic conditions), and behaviors (e.g., cigarette smoking). Although most of the supporting evidence on these conditions arises from research on adult patients, many of the CDC conditions that are associated with severe COVID-19 illness originate in childhood. And, most of the conditions apply to CYSHCN.

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## Risk Factors for Severe COVID-19 Illness and Vaccine Distribution

Many U.S. states include the CDC conditions in plans for COVID-19 vaccine distribution, highlighting the conditions that are supported by the strongest evidence of risk for severe COVID-19 illness.<sup>14-16</sup> The CDC categorizes conditions associated with severe COVID-19 illness in tiers of evidence defined by types of study designs: (1) meta-analysis/systematic review, (2) cohort, case-control, or cross-sectional studies, (3) case series, case reports or, if other study design, the sample size is small (and no systematic review or meta-analysis were available to review), and (4) mixed evidence.<sup>12</sup>

The evidence on risk factors for severe COVID-19 illness in children and youth is especially limited because of (1) the short amount of time that scientists have had to understand the relationship between COVID-19 and pediatric chronic conditions; (2) the heterogeneity and low prevalence of pediatric chronic conditions; and (3) the small number of children and youth who have experienced severe COVID-19 illness. In this context, the absence of a specific condition on a CDC list may indicate that the condition has not been evaluated for severe COVID-19 illness, even though an actual association may exist. The CDC aggregates many childhood chronic conditions into a pediatric category. This category includes conditions that are distinguished as risk factors in other, higher-grade evidence categories on the CDC lists (e.g., asthma) as well as conditions that are not listed elsewhere (e.g., congenital heart disease and use of feeding tube).<sup>17-32</sup>

There has been variation across U.S. states (and counties) in the conditions that are given higher priority for COVID-19 vaccination. For example, some areas prioritize Down syndrome, cystic fibrosis, and type I diabetes, whereas other areas do not.<sup>32</sup> Moreover, some states prioritize vaccination to individuals with two or more CDC conditions, since there is stronger evidence to suggest that these patients will experience a more severe case of COVID-19 disease.<sup>34</sup> This variation has contributed to the challenges and confusion experienced by individuals with risk factors for severe COVID-19 illness in their attempt to receive the vaccine.

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**“ Estimating the prevalence of these risk factors in adolescents and young adults will (1) assist states, public health departments, Medicaid programs, health plans, hospitals, and other health care entities with vaccine allocation and administration; and (2) help ensure that the most vulnerable adolescents and young adults receive the health care services and supports needed to optimize their health and well-being throughout the pandemic. ”**

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## Importance of Population Assessment of Risk Factors for Severe COVID-19 Illness in Children and Youth

Identifying CYSHCN with risk factors for severe COVID-19 illness is paramount to assist strategic planning efforts for vaccine distribution. Estimating the prevalence of these risk factors in adolescents and young adults will (1) assist states, public health departments, Medicaid programs, health plans, hospitals, and other health care entities with vaccine allocation and administration; and (2) help ensure that the most vulnerable adolescents and young adults receive the health care services and supports needed to optimize their health and well-being throughout the pandemic.

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## Health Care Claims and Risk Factors for Severe COVID-19 Illness

Health care claims are positioned to help identify health conditions that have been distinguished as risk factors for severe COVID-19 illness. A health care claim is the charge that health care providers and entities submit to payers for payment of health services delivered to a patient. These claims can include International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes. The diagnosis codes contain valuable information on acute and chronic health conditions that patients experience. Most CDC conditions that are associated with severe COVID-19 illness can be distinguished with ICD-10-CM diagnosis codes.

## Development and Testing of an Approach to Assess Risk Factors for Severe COVID-19 Illness Using Health Care Claims

We applied the Agency for Healthcare Research and Quality's open-source Chronic Condition Indicator (CCI) and Clinical Classification System (CCS) to match ICD-10-CM diagnosis codes with the CDC risk factors for severe COVID-19 illness (ICD diagnosis codes available upon request to the study team). CCI distinguishes chronic from non-chronic health conditions and CCS categorizes the conditions into a distinct diagnosis and affected body system.<sup>34,35</sup> Some CDC conditions are a single diagnosis (e.g., type 1 diabetes mellitus) whereas others encompass an entire organ system (e.g., neurologic chronic conditions).

We tested this system with two analytical cohorts of adolescents and young adults age 12-to-21 years. Cohort one included 1,820,176 enrollees in 12 U.S. state Medicaid programs from January 1 to December 31, 2018, that contributed data to the IBM Watson Market-scan Medicaid Database. Cohort two included 103,906 patients who received outpatient, inpatient, or emergency department care between January 1 and December 31, 2018, in a tertiary, freestanding U.S. children's hospital. We arrayed claims across patients' health care encounters (e.g., inpatient, outpatient, emergency department) to identify those with a CDC condition. The conditions were categorized by CDC tiers of evidence based on study designs as well as by the number of conditions.

## Prevalence of Risk Factors for Severe COVID-19 Illness in Adolescents and Young Adults

The prevalence of CDC conditions associated with severe COVID-19 illness was 21.3% and 31.8% in the Medicaid and children's hospital cohorts, respectively ([Table 1](#)). Prevalence was slightly higher in individuals age 16 years and older vs. 12-to-15 years [24.8% vs. 17.6% (Medicaid); 33.5% vs. 29.9% (children's hospital)]. Of individuals with a condition, most had only one of them (72.4% Medicaid; 67.9% children's hospital). The prevalence of conditions with the strongest evidence of severe COVID-19 illness was 7.8% (Medicaid) and 7.2% (children's hospital). Across both cohorts, the most common conditions were asthma (8.7%, Medicaid; 8.1% children's hospital) and neurologic condition (2.6%, Medicaid; 9.4% children's hospital) ([Table 2](#)). Epilepsy and cerebral palsy were among the most common neurologic conditions in both cohorts.

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**“ Among pediatric adolescents and young adults, one in five in the Medicaid cohort and one in three in the children’s hospital cohort had an underlying CDC condition associated with severe COVID-19 illness. ”**

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## Interpretation and Implications of Results

Among pediatric adolescents and young adults, one in five in the Medicaid cohort and one in three in the children’s hospital cohort had an underlying CDC condition associated with severe COVID-19 illness. Compared with existing literature, the most common types of risk factors were different in adolescents and young adults (i.e., asthma and neurologic conditions) than in older adults (i.e., hypertension and obesity).<sup>37</sup> And, older adults have a higher prevalence of multiple risk factors.<sup>3</sup>

The current work has several limitations to consider. Health conditions reported by patients and also abstracted from health records are more accurate than conditions identified with health care claims. There is variation in sensitivity and specificity across ICD-10-CM diagnosis codes. Some of the codes (e.g., smoking and obesity) may be underused more than others, therefore generating lower estimates of prevalence. The National Health and Nutrition Examination Survey reports that the prevalence of obesity and severe obesity in children are 19% and 6%, respectively, which are much higher than our estimates using ICD-10-CM diagnosis codes.<sup>38</sup> We did not measure the COVID-19 risk factor for chronic use of a corticosteroid or immunosuppressive medication. There is collinearity of this use with multiple other COVID-19 risk factors, including cancer, digestive, immunologic, and respiratory conditions. New evidence is emerging on risk factors for severe COVID-19 illness, which could necessitate revision of the CDC condition lists and therefore lead to new findings on prevalence. New findings on vaccine safety and effectiveness in younger children may warrant replication of the current work in additional pediatric populations.

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**“ Medicaid programs may use the prevalence findings to advocate for vaccination in vulnerable patient populations, especially CYSHCN with economic and/or disability challenges. ”**

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## Conclusions

Although the impact of COVID-19 illness has been less in children and youth than adults, most risk factors for severe COVID-19 illness apply to CYSHCN. The prevalence of these risk factors is high in adolescents and young adults who are enrolled in Medicaid and who use children’s hospitals. Although review of individuals’ health histories, as well as health records, is warranted for verification, use of health care claims should be considered with screening efforts to identify children and youth across populations with underlying conditions associated with severe COVID-19 illness.

The findings from the current work can be used by U.S. states, hospitals, and other health care entities for preparation of vaccination in younger individuals. Medicaid programs may use the prevalence findings to advocate for vaccination in vulnerable patient populations, especially CYSHCN with economic and/or disability challenges. In their role as regional referral centers that span large geographic catchment areas children’s hospitals may be positioned to enable vaccination uptake in adolescents and young adults with risk factors.

**Table 1.**

## Prevalence of Risk Factors for Severe COVID-19 Illness in Adolescents and Young Adults.

Attribute	Medicaid Cohort			Children's Hospital Cohort		
	All (N=1,820,176)	12-to-15 years (N=891,720)	16 years and older (N=928,456)	All (N=103,472)	12-to-15 years (N=48,205)	16 years and older (N=55,267)
<b>COVID-19 Risk Factor</b>						
Any	387,331 (21.3%)	157,238 (17.6%)	230,093 (24.8%)	33,072 (31.8%)	14,394 (29.9%)	18,678 (33.5%)
One	280,436 (15.4%)	127,921 (14.3%)	152,515 (16.4%)	22,444 (21.6%)	10,084 (21.0%)	12,360 (22.2%)
Two or more	106,895 (5.9%)	29,317 (3.3%)	77,578 (8.4%)	10,628 (10.2%)	4,310 (9.0%)	6,318 (11.3%)
<b>Evidence Category<sup>1</sup></b>						
Meta-analysis/ Systematic Review	141,379 (7.8%)	31,502 (3.5%)	109,877 (11.8%)	7,435 (7.2%)	2,679 (5.6%)	4,756 (8.5%)
Cohort, Case- Control, or Cross-Sectional Studies	160,237 (8.8%)	56,484 (6.3%)	103,753 (11.2%)	23,339 (22.5%)	10,136 (21.1%)	13,203 (23.7%)
Case Series, Case Reports or, if Other Study Design, Sample Size is Small	1,352 (0.1%)	565 (0.1%)	787 (0.1%)	375 (0.4%)	139 (0.3%)	236 (0.4%)
Mixed Evidence	182,443 (10.0%)	94,499 (10.6%)	87,944 (9.5%)	11,541 (11.1%)	5,160 (10.7%)	6,381 (11.4%)

<sup>1</sup>Informed by the Centers for Disease Control and Prevention (CDC) study design categories for existing evidence:

- **Meta-analysis/systematic review:** Defined as having a significant association in at least one meta-analysis or systematic review.
- **Cohort, case-control, or cross-sectional studies:** Defined as having an association in cohort, case-control or cross-sectional studies; may include systematic review or meta-analysis that represents one condition in a larger group of conditions (for example, kidney transplant under the category of solid organ or blood stem cell transplantation).
- **Case series, case reports or, if other study design, the sample size is small (and no systematic review or meta-analysis were available to review):** Defined as having an association in one or more case series studies. If there are cohort or case-control studies, sample sizes were small. Conditions included may be rare.
- **Mixed evidence:** Defined as having an association in at least one meta-analysis or systematic review and additional studies or reviews that reached different conclusions about risk associated with a condition.

**Table 2.**

## Types of Risk Factors for Severe COVID-19 Illness in Adolescents and Young Adults.

Risk Factor <sup>1</sup>	Medicaid Cohort			Children's Hospital Cohort		
	All	12-to-15 years	16 years and older	All	12-to-15 years	16 years and older
<b>Mixed Evidence</b>						
Asthma	159,141 (8.7%)	87,622 (9.8%)	71,519 (7.7%)	8400 (8.1%)	4033 (8.4%)	4367 (7.8%)
Immune Deficiencies	4,325 (0.2%)	1,741 (0.2%)	2,584 (0.3%)	2,083 (2.0%)	884 (1.8%)	1,199 (2.2%)
Hypertension	21,170 (1.2%)	5,722 (0.6%)	15,448 (1.7%)	1,510 (1.5%)	452 (0.9%)	1,058 (1.9%)
Liver Disease	5,860 (0.3%)	2,013 (0.2%)	3,847 (0.4%)	727 (0.7%)	257 (0.5%)	470 (0.8%)
<b>Case Series, Case Reports or, if Other Study Design, Sample Size is Small</b>						
Cystic Fibrosis	651 (0.0%)	290 (0.0%)	361 (0.0%)	232 (0.2%)	77 (0.2%)	155 (0.3%)
Thalassemia	701 (0.0%)	275 (0.0%)	426 (0.0%)	143 (0.1%)	62 (0.1%)	81 (0.2%)
<b>Cohort, Case-Control, or Cross-Sectional Studies</b>						
Children with Certain Underlying Conditions <sup>2</sup>	40,932 (2.2%)	16,476 (1.8%)	24,456 (2.6%)	10,808 (10.4%)	4,514 (9.4%)	6,294 (11.3%)
Congenital heart	10,943 (0.6%)	5,248 (0.6%)	5,695 (0.6%)	7,571 (7.3%)	3,162 (6.6%)	4,409 (7.9%)
Hematologic	23,918 (1.3%)	8,549 (1.0%)	15,369 (1.7%)	2,288 (2.2%)	848 (1.8%)	1,440 (2.6%)
Genetic/ chromosomal	3,292 (0.2%)	1,662 (0.2%)	1,630 (0.2%)	1,687 (1.6%)	832 (1.7%)	855 (1.5%)
Feeding tube	3,248 (0.2%)	1,477 (0.2%)	1,771 (0.2%)	811 (0.8%)	367 (0.8%)	444 (0.8%)
Congenital anomaly	2,270 (0.1%)	779 (0.1%)	1,491 (0.2%)	718 (0.7%)	346 (0.7%)	372 (0.7%)
Prematurity	146 (0.0%)	57 (0.0%)	89 (0.0%)	107 (0.1%)	58 (0.1%)	49 (0.1%)
Neurologic Conditions	47,980 (2.6%)	19,879 (2.2%)	28,101 (3.0%)	9,790 (9.4%)	4,378 (9.1%)	5,412 (9.7%)
Other Lung Diseases <sup>3</sup>	25,660 (1.4%)	12,785 (1.4%)	12,875 (1.4%)	3,238 (3.1%)	1,651 (3.4%)	1,587 (2.9%)
Overweight <sup>4</sup>	31,432 (1.7%)	16,588 (1.9%)	14,844 (1.6%)	2,620 (2.5%)	1,171 (2.4%)	1,449 (2.6%)

(Table 2. Continued on next page)

Risk Factor <sup>1</sup>	Medicaid Cohort			Children's Hospital Cohort		
	All	12-to-15 years	16 years and older	All	12-to-15 years	16 years and older
<b>Cohort, Case-Control, or Cross-Sectional Studies (Continued)</b>						
Substance Use Disorders	59,596 (3.3%)	11,543 (1.3%)	48,053 (5.2%)	1,182 (1.1%)	243 (0.5%)	939 (1.7%)
Solid organ or Blood Stem Cell Transplantation	1,475 (0.1%)	571 (0.1%)	904 (0.1%)	578 (0.6%)	234 (0.5%)	344 (0.6%)
Down Syndrome	3,178 (0.2%)	1,417 (0.2%)	1,761 (0.2%)	551 (0.5%)	268 (0.6%)	283 (0.5%)
Sickle Cell Disease	4,494 (0.2%)	1,751 (0.2%)	2,743 (0.3%)	227 (0.2%)	104 (0.2%)	123 (0.2%)
HIV	824 (0.0%)	154 (0.0%)	670 (0.1%)	36 (0.0%)	8 (0.0%)	28 (0.1%)
<b>Meta-analysis/Systematic Review</b>						
Diabetes Mellitus Type 1	8,547 (0.5%)	3,438 (0.4%)	5,109 (0.6%)	1,712 (1.7%)	613 (1.3%)	1,099 (2.0%)
Chronic Kidney Disease	5,787 (0.3%)	2,187 (0.2%)	3,600 (0.4%)	1,708 (1.6%)	781 (1.6%)	927 (1.7%)
Cancer	3,873 (0.2%)	1,561 (0.2%)	2,312 (0.2%)	1,512 (1.5%)	593 (1.2%)	919 (1.7%)
Heart Conditions <sup>5</sup>	2,328 (0.1%)	740 (0.1%)	1,588 (0.2%)	1,220 (1.2%)	434 (0.9%)	786 (1.4%)
Obesity <sup>4</sup>	13,235 (0.7%)	908 (0.1%)	12,327 (1.3%)	630 (0.6%)	33 (0.1%)	597 (1.1%)
Diabetes Mellitus Type 2	11,018 (0.6%)	3,253 (0.4%)	7,765 (0.8%)	512 (0.5%)	151 (0.3%)	361 (0.7%)
Chronic Obstructive Pulmonary Disease	1,340 (0.1%)	523 (0.1%)	817 (0.1%)	303 (0.3%)	111 (0.2%)	192 (0.3%)
Cerebrovascular Disease	2,344 (0.1%)	1,378 (0.2%)	966 (0.1%)	257 (0.3%)	112 (0.2%)	145 (0.3%)
Smoking, current or former	65,786 (3.6%)	18,859 (2.1%)	46,927 (5.1%)	255 (0.3%)	93 (0.2%)	162 (0.3%)
Pregnancy	52,586 (2.9%)	1,281 (0.1%)	51,305 (5.5%)	204 (0.2%)	30 (0.1%)	174 (0.3%)

<sup>1</sup>Risk factors were derived from sources reported by the Centers for Disease Control and Prevention (CDC):

- (1) <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html>; and  
(2) <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/evidence-table.html>

<sup>2</sup>To avoid double counting of individuals, the conditions reported in this Pediatrics category are limited to those that have not been distinguished in other areas of the CDC lists. For example, the CDC includes asthma in both the Pediatrics category and also in a stand-alone category for asthma (under mixed evidence). All adolescents and young adults in the analytical cohort are represented in the stand-alone category for asthma.

<sup>3</sup>Other lung diseases include interstitial lung disease, pulmonary fibrosis, and pulmonary hypertension.

<sup>4</sup>The CDC defines weight categories as the following: overweight (BMI >25 kg/m<sup>2</sup> but <30 kg/m<sup>2</sup>) and obesity (BMI ≥30 kg/m<sup>2</sup>).

<sup>5</sup>Heart conditions consist of heart failure, coronary artery disease, cardiomyopathies, pulmonary hypertension.

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