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Long-Term Symptoms Among Adults Tested for SARS-CoV-2 — United States, January 2020–April 2021

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Long-term symptoms often associated with COVID-19 (post-COVID conditions or long COVID) are an emerging public health concern that is not well understood. Prevalence of post-COVID conditions has been reported among persons who have had COVID-19 (range = 5%–80%), with differences possibly related to different study populations, case definitions, and data sources (1). Few studies of post-COVID conditions have comparisons with the general population of adults with negative test results for SARS-CoV-2, the virus that causes COVID-19, limiting ability to assess background symptom prevalence (1). CDC used a nonprobability-based Internet panel established by Porter Novelli Public Services* to administer a survey to a nationwide sample of U.S. adults aged ≥18 years to compare the prevalence of long-term symptoms (those lasting >4 weeks since onset) among persons who self-reported ever receiving a positive SARS-CoV-2 test result with the prevalence of similar symptoms among persons who reported always receiving a negative test result. The weighted prevalence of ever testing positive for SARS-CoV-2 was 22.2% (95% confidence interval [CI] = 20.6%–23.8%). Approximately two thirds of respondents who had received a positive test result experienced longterm symptoms often associated with SARS-CoV-2 infection. Compared with respondents who received a negative test result, those who received a positive test result reported a significantly higher prevalence of any long-term symptom (65.9% versus 42.9%), fatigue (22.5% versus 12.0%), change in sense of smell or taste (17.3% versus 1.7%), shortness of breath (15.5% versus 5.2%), cough (14.5% versus 4.9%), headache (13.8% versus 9.9%), and persistence (>4 weeks) of at least one initially occurring symptom (76.2% versus 69.6%). Compared with respondents who received a negative test result, a larger proportion of

those who received a positive test result reported believing that receiving a COVID-19 vaccine made their long-term symptoms better (28.7% versus 15.7%). Efforts to address post-COVID conditions should include helping health care professionals recognize the most common post-COVID conditions and optimize care for patients with persisting symptoms, including messaging on potential benefits of COVID-19 vaccination.

During April 9–23, 2021, Porter Novelli Public Services and ENGINE Insights[†] conducted a nonprobability-based Internet

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^{*} https://styles.porternovelli.com/pn-view-panels/



[†] https://engine-insights.com/product/caravan/

panel survey among 6,021 noninstitutionalized U.S. adults aged ≥18 years via the Lucid platform. Quota sampling and statistical weighting were used to align the sample with U.S. population distributions by sex, age group, U.S. Census region, race and ethnicity, and education. Respondents self-reported ever having received a positive SARS-CoV-2 test result (698), always receiving a negative test result (2,437), or never having been tested for SARS-CoV-2 (2,750); only deidentified respondents who reported having received either a positive or a negative test result were included in this analysis. Respondents who received a negative test were selected to establish the prevalence of post-COVID symptoms in a population that did not receive a COVID-19 diagnosis. Assessment of initial symptoms, including symptoms that might have commenced before testing, was conducted by asking respondents who received a positive test result, "During the month of your first positive COVID-19 test, which, if any, of the following symptoms did you experience?" followed by a list of symptoms. Respondents who received a negative test result were asked, "Since January 2020, which, if any, of the following symptoms have you experienced?" Long-term symptoms were assessed by asking those who received a positive test result, "Which, if any, of your symptoms lasted longer than 4 weeks after your first positive COVID-19 test?"; those who received a negative test result were asked, "Which, if any, of your symptoms lasted longer than 4 weeks since you first experienced the symptoms?" Respondents were asked about health care use and receipt of ≥1 dose of a COVID-19 vaccine. Vaccine impact related to symptoms was assessed by asking respondents** how receiving a COVID-19 vaccination affected their long-term symptoms (those lasting ≥4 weeks).††

Point estimates and 95% CIs were calculated, overall and by demographic characteristics (age group, sex, marital status, highest educational attainment, employment, 2020 household income, race and ethnicity, U.S. Census region, and community type^{§§}).

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[§]https://luc.id/marketplace/

Change in mood; change in smell or taste; chest pain or pressure; cough; diarrhea; difficulty thinking clearly, concentrating, forgetfulness, memory loss, or "brain fog"; fatigue, tired, or weakness; fever or chills; hair loss; headache; joint or muscle pain; nausea or vomiting; palpitations (heart racing or pounding); postexertional malaise (worsening of symptoms after even minor physical, mental, or emotional exertion); problems sleeping; shortness of breath or breathlessness; sore throat; stomach pain; or other symptom.

^{**} Among those who experienced long-term symptoms and reported receiving ≥1 dose of a COVID-19 vaccine (100 respondents who received a positive test result and 285 respondents who received a negative test result).

^{††} Respondents were instructed, "Please select only one answer and do not count side effects (symptoms that you had in the first 7 days after getting a COVID-19 vaccine)." Responses included, "Made my symptoms a lot better," "Made my symptoms somewhat better," "Made my symptoms a little better," "Did not affect my symptoms at all," "Made my symptoms a little worse," "Made my symptoms somewhat worse," "Made my symptoms a lot worse," "Made some of my symptoms better and some worse," and "Not applicable: My symptoms were gone before I got the vaccine." Because of small cell sizes, those reporting that receiving a vaccine made their symptoms a lot, somewhat, or a little better were grouped under "Getting vaccine made symptoms a lot, somewhat, or a little worse were grouped under "Getting vaccine made symptoms a lot, somewhat, or a little worse were grouped under "Getting vaccine made symptoms worse."

^{§§} Úrban, suburban, or rural.

Comparisons of demographic characteristics and symptoms were performed using chi-square tests; p-values <0.05 were considered statistically significant. All analyses were conducted using SAS (version 9.4; SAS Institute) and were weighted by sex, age group, region, race and ethnicity, and education. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy. ¶¶

Among the 3,135 adults who reported having been tested for SARS-CoV-2 since January 2020, the weighted prevalence of ever receiving a positive test result was 22.2% (Table 1). Compared with respondents who received a negative test result (2,437), those who received a positive test result (698) were younger (median age = 39.3 years versus 45.3 years), and a higher proportion were working (70.5% versus 61.6%), had higher household income (50.8% versus 43.9% made ≥\$60,000), and lived in an urban community (43.8% versus 37.6%).

Overall, 603 (86.5%) respondents who received a positive test result and 1,526 (61.7%) of those who received a negative test result reported any initial symptoms. Among respondents who reported an initial symptom, more respondents who received a positive test result (76.2%) than those who received a negative test result (69.6%) reported persistence (>4 weeks) of at least one symptom (p = 0.005) (Supplementary Table, https://stacks.cdc.gov/view/cdc/108815). Hair loss (58.3%), cognitive dysfunction*** (55.5%), shortness of breath (52.8%), and postexertional malaise^{†††} (49.6%) persisted for ≥50% of those who received a positive test result and initially reported these symptoms; other symptoms, such as fatigue (48.4%), change in smell or taste (46.4%), cough (36.2%), and headache (31.1%) persisted for <50%.

A higher proportion of respondents who received a positive test result than those who received a negative test result reported any long-term symptoms (65.9% versus 42.9%; p<0.05) (Table 2). The most common symptoms were fatigue (22.5% versus 12.0%), change in smell or taste (17.3% versus 1.7%), shortness of breath (15.5% versus 5.2%), cough (14.5% versus 4.9%), and headache (13.8% versus 9.9%). Among only respondents who reported any long-term symptoms, the most common symptoms among those who received a positive test result compared with those who received a negative test result were fatigue (34.2% versus 28.0%), change in smell or taste (26.2% versus 3.9%), shortness of breath (23.6% versus 12.1%), cough (22.0% versus 11.5%), and headache (20.9% versus 23.0%) (all p<0.05 except for headache).

A larger proportion of respondents who received a positive test result than those who received a negative test result reported seeing a health care professional (54.1% versus 42.5%; p<0.001) or going to urgent or emergency care (19.5% versus 14.0%, p = 0.008) for symptoms when they first occurred; rates of hospitalization were similar (10.4% versus 9.3%) (Table 3). Among those reporting any long-term symptoms, fewer respondents who received a positive test result than those who received a negative test result reported seeing a health care professional for long-term symptoms at least once (24.7% versus 35.8%) or more than once (17.6% versus 27.9%).

Fewer respondents who received a positive test result than those who received a negative test result reported receiving ≥1 dose of a COVID-19 vaccine (28.3% versus 39.4%). Among those who ever experienced any long-term symptoms, more respondents who received a positive test result than those who received a negative test result reported that having longterm symptoms motivated them to receive or consider receiving a COVID-19 vaccine (11.0% versus 7.0%) and believed that receiving the vaccine made their long-term symptoms better (28.7% versus 15.7%; p = 0.023), or that their symptoms were gone before receiving the vaccine (28.4% versus 13.1%). A similar percentage of respondents who received a positive test result (16.1%) and those who received a negative test result (11.2%) reported that receiving the vaccine made their long-term symptoms worse (p = 0.271), whereas 26.4% of respondents who received a positive test result and 59.2% of those who received a negative test result believed that receiving a vaccine did not affect their symptoms (p<0.001).

Discussion

In this convenience sample of U.S. adults, the prevalence of long-term symptoms often associated with SARS-CoV-2 infection was higher among respondents who ever received a positive test result than among those who always received a negative test result, and symptoms in these persons tended to persist for >4 weeks. Previous studies have found that nonhospitalized persons with SARS-CoV-2 infection have higher prevalence of some long-term symptoms or conditions than nonhospitalized persons with negative SARS-CoV-2 test results (2–5). Similarly, in this investigation, more respondents who received a positive test result (65.9%) than those who received a negative test result (42.9%) experienced any long-term symptoms, and approximately one half of these symptoms were more likely to be reported among those who received a positive test result.

Early data on post-COVID conditions primarily came from hospitalized cohorts (1,6); more recent reports describe post-COVID conditions among nonhospitalized, asymptomatic, or mildly ill patients (1,7). The prevalence of the most common long-term symptoms among respondents who received

^{55 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.

^{***} Cognitive dysfunction refers to difficulty thinking clearly, concentrating, forgetfulness, memory loss, or "brain fog."

^{†††} Worsening of symptoms after even minor physical, mental, or emotional exertion.

TABLE 1. Demographic characteristics of respondents aged \geq 18 years who received at least one positive SARS-CoV-2 test result or only negative SARS-CoV-2 test results since January 2020 (N = 3,135), by selected characteristics — Porter Novelli Internet survey, United States, April 2021

	Testing status, weighted % (95% CI)			
Characteristic	At least one positive SARS-CoV-2 test result (n = 698)*	All negative SARS-CoV-2 test results (n = 2,437)*	p-value [†]	
Overall	22.2 (20.6–23.8)	77.8 (76.2–79.4)	_	
Age group, yrs				
18–29	26.3 (22.8–29.7)	23.2 (21.4–24.9)	< 0.001	
30–39	25.4 (22.0-28.8)	19.0 (17.4–20.6)	< 0.001	
10–49	18.6 (15.1–22.1)	16.4 (14.7–18.2)	< 0.001	
50–59	15.0 (11.8–18.2)	16.6 (14.8–18.4)	< 0.001	
60–69	10.3 (7.8–12.8)	16.4 (14.8–18.0)	< 0.001	
270	4.4 (2.8–6.0)	8.4 (7.2–9.5)	< 0.001	
ex				
Лale	51.5 (47.4–55.7)	48.5 (46.3–50.7)	0.204	
- Female	48.5 (44.3–52.6)	51.5 (49.3–53.7)	0.204	
Narital status				
Married	54.0 (49.9–58.1)	49.2 (47.0-51.4)	0.197	
iving with a partner	10.2 (7.7–12.6)	10.2 (8.8–11.6)	0.197	
single and never been married	22.2 (18.7–25.6)	24.4 (22.6–26.3)	0.197	
Other [§]	13.6 (10.6–16.6)	16.1 (14.5–17.8)	0.197	
lighest level of education completed				
some high school or less	4.7 (2.8-6.6)	5.2 (4.1–6.3)	0.545	
ligh school graduate/some college	50.7 (46.6-54.8)	49.2 (47.0-51.3)	0.545	
-year college/technical school	7.8 (5.7–10.0)	8.5 (7.3-9.8)	0.545	
-year college/some postgraduate education	19.6 (16.6–22.5)	21.7 (20.1–23.3)	0.545	
Postgraduate degree	17.2 (14.4–19.9)	15.4 (14.1–16.8)	0.545	
imployment status [¶]				
Employed	70.5 (66.6–74.3)	61.6 (59.5–63.8)	< 0.001	
Jnemployed	17.8 (14.5–21.1)	19.8 (17.9–21.6)	< 0.001	
Retired	11.7 (9.0–14.4)	18.6 (16.9–20.3)	< 0.001	
lousehold income in 2020, USD				
<25,000	14.5 (11.4–17.5)	20.4 (18.5-22.2)	0.016	
25,000–49,999	28.2 (24.4–32.0)	27.8 (25.8–29.9)	0.016	
0,000–74,999	17.2 (14.0–20.4)	17.3 (15.7–19.0)	0.016	
75,000–99,999	12.0 (9.5–14.5)	11.3 (9.9–12.6)	0.016	
00,000-149,999	16.3 (13.5–19.2)	14.4 (13.0–15.7)	0.016	
150,000	11.8 (9.2–14.3)	8.9 (7.8–10.0)	0.016	
Race/Ethnicity				
Vhite, non-Hispanic	59.8 (55.5-64.0)	62.0 (59.7-64.2)	0.190	
Black or African-American, non-Hispanic	12.4 (9.6–15.3)	12.3 (10.8–13.9)	0.190	
Other,** non-Hispanic	6.2 (4.1–8.4)	8.2 (6.9–9.5)	0.190	
lispanic	21.6 (17.6–25.5)	17.5 (15.6–19.4)	0.190	
J.S. Census region ^{††}				
Vortheast	21.5 (18.1–24.9)	19.0 (17.3–20.6)	0.156	
Midwest	21.1 (17.7–24.5)	19.5 (17.7–21.2)	0.156	
outh	38.1 (34.1–42.1)	38.4 (36.3–40.5)	0.156	
Vest	19.3 (16.1–22.5)	23.1 (21.3–25.0)	0.156	
Community type				
Jrban	43.8 (39.8–47.9)	37.6 (35.5–39.7)	0.028	
uburban	39.8 (35.7–43.9)	44.1 (41.9–46.3)	0.028	
Rural	16.4 (13.3–19.5)	18.3 (16.6–20.0)	0.028	

Abbreviations: CI = confidence interval; USD = U.S. dollars.

^{*} Unweighted number of persons who received positive or negative SARS-CoV-2 test results.

[†] p-value for weighted Wald chi-square test; all p-values <0.05 indicate significant differences.

[§] Other marital status includes separated, divorced, and widowed.

[¶] Employed includes full-time or part-time work and self-employment; unemployed includes students, homemakers, and those who were not employed currently or were unable to work.

^{**} Other race/ethnicity includes Native American or Alaskan Native, Asian, and other (unspecified).

^{††} Northeast: Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont; Midwest: Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin; South: Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia; West: Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming.

TABLE 2. Prevalence of symptoms lasting >4 weeks among respondents aged ≥18 years who received at least one positive SARS-CoV-2 test result or only negative SARS-CoV-2 test results since January 2020 — Porter Novelli Internet survey, United States, April 2021

	SARS-CoV-2 test result, weighted % (95% CI)				
		prevalence s receiving testing	Symptom prevalence among persons receiving testing who reported a symptom lasting >4 weeks since onset		
Symptom	Respondents who received a positive test result (n = 698)*	Respondents who received a negative test result (n = 2,437)*	Respondents who received a positive test result (n = 465)*	Respondents who received a negative test result (n = 1,058)*	
Any symptom	65.9 [†] (61.9–69.8)	42.9 (40.8–45.1)	<u> </u>	_	
1 symptom only	27.2 [†] (23.7–30.8)	18.7 (17.0-20.4)	41.4 (36.5-46.3)	43.6 (40.3-46.9)	
2 symptoms	14.0 [†] (11.1–16.8)	9.5 (8.2-10.7)	21.2 (17.1–25.3)	22.1 (19.3-24.8)	
≥3 symptoms	24.7 [†] (21.0–28.3)	14.7 (13.2–16.3)	37.4 (32.5-42.4)	34.3 (31.1-37.5)	
Fatigue/Tired/Weakness	22.5 [†] (19.0–26.1)	12.0 (10.6-13.4)	34.2 [†] (29.3–39.1)	28.0 (25.0-31.0)	
Change in smell or taste	17.3 [†] (14.1–20.4)	1.7 (1.1–2.3)	26.2 [†] (21.8–30.7)	3.9 (2.6-5.3)	
Shortness of breath or breathlessness	15.5 [†] (12.4–18.7)	5.2 (4.2-6.2)	23.6 [†] (19.1–28.1)	12.1 (9.9–14.2)	
Cough	14.5 [†] (11.6–17.4)	4.9 (4.0-5.9)	22.0 [†] (17.8–26.2)	11.5 (9.4–13.6)	
Headache	13.8 [†] (10.9–16.7)	9.9 (8.6-11.2)	20.9 (16.7-25.1)	23.0 (20.2-25.8)	
Problems sleeping	12.0 [†] (9.3–14.7)	16.5 (14.8–18.1)	18.1 [†] (14.2–22.1)	38.3 (35.1-41.6)	
Joint or muscle pain	11.1 (8.4–13.9)	12.4 (10.9–13.9)	16.9 [†] (12.9–20.9)	28.9 (25.8-32.0)	
Cognitive dysfunction [§]	10.2 [†] (7.7–12.8)	7.3 (6.1–8.4)	15.5 (11.8–19.3)	16.9 (14.4–19.4)	
Chest pain or pressure	7.3 [†] (5.2–9.4)	2.3 (1.6-2.9)	11.0 [†] (7.9–14.2)	5.3 (3.7-6.8)	
Change in mood	6.6 (4.6-8.7)	8.8 (7.6-10.0)	10.1 [†] (7.1–13.1)	20.6 (17.9-23.2)	
Postexertional malaise [¶]	6.1 [†] (4.1–8.0)	2.4 (1.7-3.0)	9.2 [†] (6.3–12.2)	5.5 (3.9–7.0)	
Stomach pain	5.8 (3.9-7.7)	5.1 (4.1-6.1)	8.9 (6.0-11.7)	11.9 (9.7–14.1)	
Hair loss	5.6 (3.7–7.5)	4.1 (3.3-5.0)	8.5 (5.6–11.3)	9.7 (7.6–11.7)	
Diarrhea	5.3 (3.3-7.2)	3.3 (2.6-4.1)	8.0 (5.0-10.9)	7.8 (6.0–9.5)	
Sore throat	4.9 [†] (3.1–6.8)	1.7 (1.1–2.2)	7.5 [†] (4.7–10.3)	3.9 (2.7-5.1)	
Fever or chills	4.9 [†] (3.0–6.8)	1.9 (1.4–2.5)	7.5 (4.7–10.3)	4.5 (3.2–5.8)	
Palpitations (heart racing or pounding)	4.5 (2.7-6.3)	2.5 (1.9-3.2)	6.8 (4.1–9.5)	5.9 (4.3-7.5)	
Nausea/Vomiting	4.1 [†] (2.5–5.8)	1.9 (1.3-2.4)	6.3 (3.8-8.8)	4.3 (3.0-5.7)	
Other symptom	1.3 (0.3-2.2)**	1.0 (0.6–1.5)	2.0 (0.5-3.4)**	2.4 (1.4-3.4)	

Abbreviation: CI = confidence interval.

a positive test result in this investigation was similar to that in earlier studies (1,8). Many studies on post-COVID conditions lack comparisons with the general population of adults with negative test results for SARS-CoV-2; however, this investigation included a comparison group, allowing for assessment of background symptom frequencies. Estimating population-level frequency of specific long-term symptoms among the general population and patients infected with SARS-CoV-2 could help health care professionals better understand the types and prevalences of symptoms their patients might experience and could help guide health systems in preparing care management strategies for patients with post-COVID conditions.

Among respondents who initially reported symptoms during the month of their first positive test results, >75% reported persistence of any symptoms >4 weeks, with hair loss, cognitive dysfunction, shortness of breath, and postexertional malaise persisting in approximately one half of respondents. This finding is consistent with findings from other studies reported in a systematic review (1) and provides patient-level perspective on long-term symptoms

associated with COVID-19; taken together, these studies highlight the importance of continued monitoring and clinical care for long-term symptoms among patients who have these symptoms early in the course of their illness.

With the increasing availability of COVID-19 vaccines, how vaccination affects post-COVID conditions remains unclear. Compared with respondents who received a negative test result, a higher proportion of those who received a positive test result believed that receiving a COVID-19 vaccine made their long-term symptoms better, and no difference was found in reported beliefs that receiving a vaccine made long-term symptoms worse. Early findings indicate that vaccination is not associated with worsening of post-COVID conditions \$\frac{\sqrt{\sqrt{\geq}}}{\sqrt{\geq}}\$ (9). However, because no data were collected on the trajectory of long-term symptoms in persons who had not been vaccinated, whether any of the observed changes in symptoms are attributable to vaccination is uncertain. More data are needed to fully

^{*} Unweighted number of persons who received at least one positive or only negative SARS-CoV-2 test results.

[†] p-value for weighted Wald chi-square test < 0.05, indicating significant differences between those receiving a positive test result and those receiving a negative SARS-CoV-2 test result

[§] Difficulty thinking clearly, concentrating, forgetfulness, memory loss, or "brain fog."

[¶] Worsening of symptoms after even minor physical, mental, or emotional exertion.

^{**} Estimate is unstable; relative standard error is >30%.

^{§§§} https://www.medrxiv.org/content/10.1101/2021.03.11.21253225v2

TABLE 3. Frequency of health care use, vaccination, and reported vaccine effects on symptoms lasting >4 weeks among respondents aged ≥18 years who received at least one positive SARS-CoV-2 test result or only negative SARS-CoV-2 test results since January 2020 — Porter Novelli Internet survey, United States, April 2021

	Weighted		
ltem	At least one positive SARS-CoV-2 test result	All negative SARS-CoV-2 test results	p-value*
Health care utilization among those with any initial symptom Saw health care professional for symptoms Went to urgent or emergency care for symptoms Hospitalized for symptoms	603 [†]	1,526 [†]	N/A
	54.1 (49.7–58.6)	42.5 (39.8–45.2)	<0.001
	19.5 (16.0–23.0)	14.0 (12.1–15.9)	0.008
	10.4 (7.8–13.0)	9.3 (7.6–11.0)	0.492
Health care utilization among those with symptoms lasting >4 wks (long-term symptoms) Saw health care professional for long-term symptoms Saw health care professional more than once for long-term symptoms	465 [†]	1,058 [†]	N/A
	24.7 (20.5–28.9)	35.8 (32.6–39.0)	<0.001
	17.6 (13.7–21.5)	27.9 (24.8–30.9)	<0.001
COVID-19 vaccination status Received at least 1 dose of vaccine [§] Having long-term symptoms was a motivator to receive or consider receiving vaccine	698 [†]	2,437 [†]	N/A
	28.3 (24.5–32.0)	39.4 (37.3–41.5)	<0.001
	11.0 (8.0–14.0)	7.0 (5.3–8.7)	0.023
Reported vaccination effects on long-term symptoms [¶] Vaccine made symptoms better** Vaccine did not affect symptoms at all Vaccine made symptoms worse ^{††} Symptoms were gone before receiving vaccine	100 [†] 28.7 (18.6–38.7) 26.4 (16.7–36.0) 16.1 (8.4–23.7) 28.4 (18.4–38.5)	285 [†] 15.7 (11.3–20.0) 59.2 (53.1–65.4) 11.2 (6.9–15.4) 13.1 (8.9–17.3)	N/A 0.023 <0.001 0.271 0.007

Abbreviations: CI = confidence interval; N/A = not applicable.

- * p-value for weighted Wald chi-square test; all p-values < 0.05 indicate significant differences.
- [†] Unweighted number of persons who received positive or negative SARS-CoV-2 test results.
- ⁵ 189 of 698 respondents who received a positive test result and 961 of 2,437 respondents who received a negative test result reported receiving 1 dose of vaccine.
- ¶ Respondents who ever experienced a long-term symptom and received at least 1 vaccine dose.
- ** Includes those reporting receiving a vaccine made symptoms a lot better, somewhat better, or a little better.

understand the effects of COVID-19 vaccines on persons with post-COVID conditions.

The findings in this report are subject to at least six limitations. First, the study used a nonprobability-based sample, which limits its generalizability. Second, responses were selfreported and thus subject to recall bias. Third, new symptoms occurring after the month when the first positive COVID-19 test result was received among those who received a positive test result were not assessed, and the reported symptoms could not be linked directly to SARS-CoV-2. Fourth, because the survey did not ask about symptom duration or severity, differences in duration or severity of long-term symptoms in respondents who received a positive rather than a negative test result could not be assessed. Fifth, respondents who always received a negative test result generally had a longer period in which to report symptoms, potentially inflating prevalence of their health care use and long-term symptoms. Finally, this study could not assess validity of SARS-CoV-2 tests, and some false-positive or false-negative test results might have resulted in misclassification of some respondents.

These findings can help guide public health preparedness efforts, resource needs for care and management of persons with post-COVID conditions, and communication about experiences with vaccination. The findings can also aid efforts to address post-COVID conditions, including helping health

Summary

What is already known about this topic?

Long-term symptoms associated with COVID-19 represent an emerging public health concern.

What is added by this report?

In a nonprobability-based sample of U.S. adults tested for SARS-CoV-2, symptoms often associated with SARS-CoV-2 infection were common; 65.9% of respondents whose SARS-CoV-2 test results were positive reported symptoms lasting >4 weeks compared with 42.9% of those whose test results were negative. More persons who received positive test results (76.2%) reported persistence (>4 weeks) of at least one initially occurring symptom compared with those whose test results were negative (69.6%).

What are the implications for public health practice?

These findings can aid efforts to address post-COVID conditions and messaging on potential benefits of vaccination.

care professionals recognize the most common symptoms and optimize care for patients whose symptoms persist. Future research to assess long-term symptoms and risk factors, including disease severity, disease duration, and sociodemographic characteristics, will be important to help guide current and future health care services.

^{††} Includes those reporting receiving a vaccine made symptoms a little worse, somewhat worse, or a lot worse.

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References

- Cabrera Martimbianco AL, Pacheco RL, Bagattini ÂM, Riera R. Frequency, signs and symptoms, and criteria adopted for long COVID-19: a systematic review. Int J Clin Pract 2021;e14357. Epub May 11, 2021. PMID:33977626
- Office for National Statistics. Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK: 1 April 2021. London, UK: Office for National Statistics; 2021. https://www. ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/ conditionsanddiseases/bulletins/fongoingsymptomsfollowingcoronavir uscovid19infectionintheuk/1april2021
- Chevinsky JR, Tao G, Lavery AM, et al. Late conditions diagnosed 1–4 months following an initial COVID-19 encounter: a matched cohort study using inpatient and outpatient administrative data—United States, March 1–June 30, 2020. Clin Infect Dis 202173(Suppl 1):S5–16. https:// doi.org/10.1093/cid/ciab338

- Lund LC, Hallas J, Nielsen H, et al. Post-acute effects of SARS-CoV-2 infection in individuals not requiring hospital admission: a Danish population-based cohort study. Lancet Infect Dis 2021:S14. Epub May 10, 2021. PMID:33984263
- 5. Al-Aly Z, Xie Y, Bowe B. High-dimensional characterization of post-acute sequelae of COVID-19. Nature 2021;594:259–64. PMID:33887749 https://doi.org/10.1038/s41586-021-03553-9
- Jacobs LG, Gourna Paleoudis E, Lesky-Di Bari D, et al. Persistence of symptoms and quality of life at 35 days after hospitalization for COVID-19 infection. PLoS One 2020;15:e0243882. PMID:33306721 https://doi.org/10.1371/journal.pone.0243882
- Havervall S, Rosell A, Phillipson M, et al. Symptoms and functional impairment assessed 8 months after mild COVID-19 among health care workers. JAMA 2021;325:2015–6. PMID:33825846 https://doi. org/10.1001/jama.2021.5612
- Hernandez-Romieu AC, Leung S, Mbanya A, et al. Health care utilization and clinical characteristics of nonhospitalized adults in an integrated health care system 28–180 days after COVID-19 diagnosis—Georgia, May 2020–March 2021. MMWR Morb Mortal Wkly Rep 2021;70:644–50 PMID:33914727 https://doi.org/10.15585/mmwr.mm7017e3
- Arnold DT, Milne A, Samms E, Stadon L, Maskell NA, Hamilton FW. Symptoms after COVID-19 vaccination in patients with persistent symptoms after acute infection: a case series. Ann Intern Med 2021. Epub May 25, 2021. PMID:34029484 https://doi.org/10.7326/M21-1976

Using Wastewater Surveillance Data to Support the COVID-19 Response — United States, 2020–2021

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Wastewater surveillance, the measurement of pathogen levels in wastewater, is used to evaluate community-level infection trends, augment traditional surveillance that leverages clinical tests and services (e.g., case reporting), and monitor public health interventions (1). Approximately 40% of persons infected with SARS-CoV-2, the virus that causes COVID-19, shed virus RNA in their stool (2); therefore, community-level trends in SARS-CoV-2 infections, both symptomatic and asymptomatic (2) can be tracked through wastewater testing (3–6). CDC launched the National Wastewater Surveillance System (NWSS) in September 2020 to coordinate wastewater surveillance programs implemented by state, tribal, local, and territorial health departments to support the COVID-19 pandemic response. In the United States, wastewater surveillance was not previously implemented at the national level. As of August 2021, NWSS includes 37 states, four cities, and two territories. This report summarizes NWSS activities and describes innovative applications of wastewater surveillance data by two states, which have included generating alerts to local jurisdictions, allocating mobile testing resources, evaluating irregularities in traditional surveillance, refining health messaging, and forecasting clinical resource needs. NWSS complements traditional surveillance and enables health departments to intervene earlier with focused support in communities experiencing increasing concentrations of SARS-CoV-2 in wastewater. The ability to conduct wastewater surveillance is not affected by access to health care or the clinical testing capacity in the community. Robust, sustainable implementation of wastewater surveillance requires public health capacity for wastewater testing, analysis, and interpretation. Partnerships between wastewater utilities and public health departments are needed to leverage wastewater surveillance data for the COVID-19 response for rapid assessment of emerging threats and preparedness for future pandemics.

In nearly 80% of U.S. households, fecal waste is transported from homes to wastewater treatment plants within hours (7). Wastewater represents a pooled community stool sample that can provide information on infection trends in the community served by the sewer network (sewershed), which can range in size from fewer than 2,000 to >3 million persons. Wastewater surveillance data provide information about symptomatic and asymptomatic SARS-CoV-2 infections. The accuracy of this

surveillance approach is not influenced by health care access or clinical testing capacity. In addition, SARS-CoV-2 infection trends in a community can be detected in wastewater before other COVID-19 surveillance metrics, such as case reports and hospital admissions (3–6). To build sustainable national wastewater surveillance capacity, CDC focused NWSS development in four areas: 1) offering technical assistance to implementing jurisdictions; 2) creating a data portal for centralized data submission and standardized data analysis and visualization; 3) coordinating communities of practice* to share best practices among health departments, public health laboratories, and utilities; and 4) building epidemiology and laboratory capacity for wastewater surveillance at health departments.

In the NWSS framework, health departments coordinate sample collection and laboratory testing, upload data to a CDC platform for analysis, and use findings to guide public health actions. To facilitate robust analysis, data comparability, and appropriate interpretation, the NWSS data platform receives SARS-CoV-2 RNA measurements and quality control data, performs automated data quality checks, adjusts SARS-CoV-2 concentrations for wastewater composition and method performance,† and performs regression analyses from serial measurements to classify SARS-CoV-2 wastewater trends. A dashboard available to public health departments provides data visualization (Supplementary Figure, https://stacks.cdc.gov/view/cdc/109216). NWSS activities were reviewed by CDC and were conducted consistent with applicable federal law and CDC policy.§

Initial SARS-CoV-2 wastewater surveillance efforts in the United States were led by academic researchers, commercial laboratories, and wastewater utilities, with limited public health engagement. Laboratories used diverse testing methods with different performance characteristics, which complicated data analysis and interpretation for public health action. SARS-CoV-2 wastewater sampling strategies need to balance public health objectives with available resources. The objective is to detect the presence of SARS-CoV-2 within a population

^{*}https://www.cdc.gov/phcommunities/index.html

[†] https://www.cdc.gov/healthywater/surveillance/wastewater-surveillance/data-reporting-analytics.html#data-analytics

^{§ 45} C.F.R. part 46.102(l)(2), 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.

or to monitor infection trends using changes in the concentration of SARS-CoV-2 RNA in wastewater. Sewersheds can be selected to achieve coverage for a specific proportion of the population, to provide data on communities at higher risk for COVID-19, or to provide data where clinical testing is limited. Laboratories prepare samples, concentrate and extract RNA, and measure SARS-CoV-2 RNA concentrations using methods optimized for wastewater (8), emphasizing the need to build environmental microbiology capacity and expertise at public health laboratories (9). Data need to be available within 5–7 days of sample collection to ensure timely application for response decisions. The following descriptions of states using wastewater surveillance data to track community trends of SARS-CoV-2 infection provide examples of public health action taken in Ohio and Utah.

The Ohio Wastewater Monitoring Network, a statewide network launched in June 2020, was designed to provide early warning of increasing SARS-CoV-2 infection in communities and continues to support and guide local and state public health actions to mitigate COVID-19. The network, managed by the Ohio Department of Health (ODH), is a collaboration between local, state, and federal agencies and academic institutions. Twice weekly, 24-hour composite wastewater samples are collected at the influents of 65 wastewater treatment plants, which serve nearly half the state's population and represent communities ranging in size from 3,300 to 655,000 persons. Samples are tested by six participating universities and one commercial laboratory. The wastewater is analyzed within 3–4 days of collection, and results are uploaded daily for display on the state's web-based coronavirus dashboard. §

Before joining NWSS, ODH established criteria for notifying local health districts (LHDs), utilities, and community leaders of substantial increases of SARS-CoV-2 levels in wastewater (reported as gene copies per day). A notification is emailed if ODH observes a tenfold increase in SARS-CoV-2 levels over those detected in the past two samples. These local groups use this early warning information, alongside wastewater dashboard data, to guide actions to limit further disease spread. Wastewater increase notifications are also shared with state testing and contact tracing teams that offer assistance to LHDs; since June 2020, approximately 500 notifications have been generated. A toolkit** of social media and press resources and answers to frequently asked questions is provided to LHDs to assist in communicating information to the public.

Utah began piloting SARS-CoV-2 wastewater surveillance in March 2020 as a collaboration between the Utah Department

of Environmental Quality, the Utah Department of Health (UDOH), and several academic laboratories. Sampling was extended to wastewater facilities across the state in July 2020. Samples are currently collected twice a week from 42 facilities that serve approximately 80% of the state's population. Utah developed a public dashboard^{††} and currently disseminates a summary of new data at least twice weekly to local health departments, UDOH leadership, and other pandemic response personnel. Utah's wastewater surveillance data have been used to help direct clinical testing resources to areas experiencing increased SARS-CoV-2 RNA levels in wastewater. Beginning in 2021, wastewater data are one of the main components of a ranking system to determine where to send mobile testing teams. Wastewater data have also been used when interpreting clinical case surveillance data. As an example, declining clinical case rates occurred in some regions in July 2020. However, the number of persons being tested was also decreasing in some of these areas, raising the possibility that the case rate decreases were a result of declining clinical testing volume. Consistently decreasing SARS-CoV-2 RNA levels in wastewater indicated that the declining case rates were accurate.

Discussion

Wastewater surveillance is a valuable tool to guide health departments' COVID-19 response efforts. State health departments have used wastewater data to allocate testing resources, evaluate possible irregularities in traditional surveillance, refine health messaging, and forecast clinical resource needs at the community level. CDC developed NWSS to coordinate and build capacity for wastewater surveillance and transform independent local implementation efforts into a robust, sustainable national surveillance system.

The findings in this report are subject to at least four limitations. First, wastewater surveillance cannot provide data in communities and facilities that are not served by municipal sewer systems. Second, interpretation of the results is limited in communities with highly transient populations, such as industrial or tourist regions. Third, the limit of detection for wastewater surveillance (e.g., the fewest infections in a community that can be reliably detected in wastewater) is not well established. Thus, wastewater surveillance cannot be used to determine whether a community is free from SARS-CoV-2 infections. Finally, wastewater system design and operations, such as pretreatment of incoming wastewater, can affect test results. Communication with wastewater utility partners is important in identifying system characteristics that might affect testing.

https://coronavirus.ohio.gov/wps/portal/gov/covid-19/dashboards/other-resources/wastewater

^{**} https://coronavirus.ohio.gov/wps/portal/gov/covid-19/healthcare-providersand-local-health-districts/for-local-health-districts-and-governments

^{††} https://deq.utah.gov/water-quality/sars-cov-2-sewage-monitoring

NWSS participation is expected to grow as health departments and public health laboratories develop wastewater surveillance coordination, epidemiology, and laboratory capacity. As of August 2021, 43 public health departments are using CDC funds to support wastewater surveillance activities, 32 state and local health departments are participating in the public health community of practice and nine states are reporting data to NWSS. NWSS provides a robust, highly adaptable platform for community-level disease surveillance that can be expanded to collect data on multiple pathogens, such as antibiotic resistant bacteria and enteric pathogens, and leveraged for rapid assessment of emerging threats and preparedness for pandemics.

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References

- Lickness JS, Gardner T, Diop OM, et al. Surveillance to track progress toward polio eradication—worldwide, 2018–2019. MMWR Morb Mortal Wkly Rep 2020;69:623–9. PMID:32437342 https://doi.org/10.15585/ mmwr.mm6920a3
- 2. Parasa S, Desai M, Thoguluva Chandrasekar V, et al. Prevalence of gastrointestinal symptoms and fecal viral shedding in patients with coronavirus disease 2019: a systematic review and meta-analysis. JAMA Netw Open 2020;3:e2011335. PMID:32525549 https://doi.org/10.1001/jamanetworkopen.2020.11335
- Peccia J, Zulli A, Brackney DE, et al. Measurement of SARS-CoV-2 RNA in wastewater tracks community infection dynamics. Nat Biotechnol 2020;38:1164-7. PMID:32948856 https://doi.org/10.1038/ s41587-020-0684-z

Summary

What is already known about this topic?

Wastewater surveillance measures community infection trends. The accuracy of this surveillance approach is independent of health care–seeking behavior, health care access, or testing capacity. The National Wastewater Surveillance System (NWSS) is a 43-jurisdiction, CDC-coordinated system for SARS-CoV-2 wastewater surveillance.

What is added by this report?

Wastewater surveillance data have been used to deploy clinical testing resources, investigate possible irregularities in traditional surveillance, refine health messaging, and forecast clinical resource needs.

What are the implications for public health practice?

NWSS provides community-level surveillance data that complement traditional surveillance and facilitate earlier, focused health department intervention and support in communities experiencing increasing trends in wastewater SARS-CoV-2 concentrations. Community-level wastewater surveillance data can be leveraged for rapid assessment of emerging threats and preparedness for future pandemics.

- D'Aoust PM, Graber TE, Mercier E, et al. Catching a resurgence: increase in SARS-CoV-2 viral RNA identified in wastewater 48 h before COVID-19 clinical tests and 96 h before hospitalizations. Sci Total Environ 2021;770:145319. PMID:33508669 https://doi.org/10.1016/j.scitotenv.2021.145319
- Medema G, Heijnen L, Elsinga G, Italiaander R, Brouwer A. Presence of SARS-coronavirus-2 RNA in sewage and correlation with reported COVID-19 prevalence in the early stage of the epidemic in The Netherlands. Environ Sci Technol Lett 2020;7:511–6. https://doi. org/10.1021/acs.estlett.0c00357
- Saguti F, Magnil E, Enache L, et al. Surveillance of wastewater revealed peaks of SARS-CoV-2 preceding those of hospitalized patients with COVID-19. Water Res 2021;189:116620. PMID:33212338 https://doi. org/10.1016/j.watres.2020.116620
- Kapo KE, Paschka M, Vamshi R, Sebasky M, McDonough K. Estimation of U.S. sewer residence time distributions for national-scale risk assessment of down-the-drain chemicals. Sci Total Environ 2017;603-604:445–52. PMID:28641184 https://doi.org/10.1016/j.scitotenv.2017.06.075
- Pecson BM, Darby E, Haas CN, et al.; SARS-CoV-2 Interlaboratory Consortium. Reproducibility and sensitivity of 36 methods to quantify the SARS-CoV-2 genetic signal in raw wastewater: findings from an interlaboratory methods evaluation in the U.S. Environ Sci (Camb) 2021;7:504–20. PMID:34017594 https://doi.org/10.1039/D0EW00946F
- McClary-Gutierrez JS, Mattioli MC, Marcenac P, et al. SARS-CoV-2 wastewater surveillance for public health action. Emerg Inf Dis 2021;27:1–8. PMID:34424162 https://doi.org/10.3201/eid2709.210753

SARS-CoV-2 Transmission to Masked and Unmasked Close Contacts of University Students with COVID-19 — St. Louis, Missouri, January–May 2021

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Universities open for in-person instruction during the 2020–21 academic year implemented a range of prevention strategies to limit the transmission of SARS-CoV-2, the virus that causes COVID-19, including physical distancing, mask use, vaccination, contact tracing, case investigation, and quarantine protocols (1). However, in some academic programs, such as health-related programs, aviation, and kindergarten through grade 12 (K-12) education, maintaining physical distance while still providing instruction is difficult; for universities with such programs, a single confirmed case of COVID-19 could result in a large number of students, staff members, and instructors being designated close contacts and requiring quarantine if they are not fully vaccinated, even if masks were worn when contact occurred. In January 2021, the St. Louis City Health Department allowed Saint Louis University (SLU) to implement a modified quarantine protocol that considered mask use when determining which close contacts required quarantine.* To assess the impact of the protocol, SLU assessed positive SARS-CoV-2 test result rates by masking status of the persons with COVID-19 and their close contacts. During January-May 2021, 265 students received a positive SARS-CoV-2 test result; these students named 378 close contacts. Compared with close contacts whose exposure only occurred when both persons were masked (7.7%), close contacts with any unmasked exposure (32.4%) had higher adjusted odds ratios (aORs) of receiving a positive SARS-CoV-2 test result (aOR = 4.9; 95% confidence interval [CI] = 1.4–31.1). Any additional exposures were associated with a 40.0% increase in odds of a positive test result (aOR = 1.4; 95% CI = 1.2-1.6). These findings reinforce that universal masking and having fewer encounters in close contact with persons with COVID-19 prevents the spread of SARS-CoV-2 in a university setting. Universities opening for in-person instruction could consider taking mask use into account when determining which unvaccinated close contacts require quarantine if enforced testing protocols are in place. However, this study was conducted before the B.1.617.2 (Delta) variant became the dominant strain of SARS-CoV-2

in the United States, which could have affected these findings given that the Delta variant has been found to be associated with increased transmissibility compared to previous variants.

In January 2021, the St. Louis City Health Department allowed SLU to implement a modified quarantine protocol that considered mask use when determining who would be considered a close contact requiring quarantine. SLU is a midsized private university with approximately 12,000 students and 6,000 employees, approximately 80% of whom lived, worked, or studied on its urban campus during the spring 2021 semester (January-May 2021), when the modified policy was implemented. Mask use was enforced on campus for all students, staff members, and visitors, including outside and in all classrooms and laboratory spaces. Faculty and staff members asked those who were unmasked or improperly wearing a mask to comply. Noncompliant students received sanctions, including being unable to attend classes in-person. While actively eating or drinking, persons were allowed to be unmasked in dining halls. COVID-19 cases among students were identified through SLU's symptomatic and surveillance testing protocols.[†]

After a case in a student was identified, the SLU Contact Tracing team conducted contact tracing. Staff member exposures and cases were tracked differently and were excluded from this study. Students with COVID-19 were asked to identify their number of exposure incidents with each close contact, defined as each single encounter in which the two persons were within 6 feet of each other for ≥15 minutes during a 24-hour period, regardless of location of the exposure. The number of exposures was then calculated for each close contact. Close contacts could have had a single exposure to one infected student or multiple exposures to one or more

^{*}Quarantine is required for all unvaccinated close contacts who had any unmasked exposure. A close contact was defined as any unvaccinated person who spent a total of ≥15 minutes during a 24-hour period within 6 ft of a person with confirmed COVID-19 while that person was contagious, regardless of whether a mask was worn. The modified protocol allowed those with only masked exposure to forego quarantine.

[†] All symptomatic employees and students were offered COVID-19 testing through the Office of Employee Health or Student Health. Surveillance testing consisted of mandatory testing of all students living in on-campus housing before move-in for fall 2020 (August 2020) and spring 2021 (January 2021). Surveillance testing was optional for all students who lived off campus during fall and spring move-in. Throughout the fall 2020 and spring 2021 semesters, surveillance testing was conducted on a random sample of approximately 10% of students who lived in on-campus housing. In addition, student athletes and athletic staff members received surveillance testing per the National Collegiate Athletic Association (NCAA) guidelines: https://www.ncaa.org/sport-science-institute/covid-19-coronavirus

infected persons. Mask use for persons with COVID-19 and close contacts was recorded for each exposure incident. If either person (patient or contact) was unmasked, the incident was considered an unmasked exposure. All close contacts underwent saliva-based molecular reverse transcription—polymerase chain reaction (RT-PCR) testing 5–7 days after exposure. Only unvaccinated close contacts with unmasked exposures were required to quarantine; however, close contacts with only masked exposures were informed of their exposure to persons with COVID-19 and counseled to conduct daily health screenings and to immediately report any symptoms.

The percentages of positive SARS-CoV-2 test results among close contacts were assessed by demographic characteristics and exposure variables; differences were tested using chi-square tests or Fisher's exact test for small cell counts for categorical variables and using t-tests for continuous variables; p-values < 0.05 were considered statistically significant. Assessed demographic characteristics included sex, age, on-versus off-campus residence, vaccination status, enrollment as an undergraduate student versus graduate student, participation in school athletics, and membership in a student fraternity or sorority, Reserve Officers' Training Corps, or a health major with clinical responsibilities. Full vaccination was defined as having received either a single dose of Janssen (Johnson & Johnson) vaccine or the second dose of Moderna or Pfizer-BioNTech COVID-19 vaccine ≥14 days before exposure. Partial vaccination was defined as receipt of a single dose of Janssen or the second dose of Moderna or Pfizer-BioNTech <14 days before the exposure, or receipt of 1 dose of Moderna or Pfizer-BioNTech COVID-19 vaccine. Students who had received no vaccine doses were considered unvaccinated. Close contacts were categorized as those who had only masked exposure or those with unmasked exposure to a COVID-19-infected person. Logistic regression was used to calculate adjusted odds ratios and 95% CIs pertaining to the odds of a close contact receiving a positive test result following masked versus unmasked exposure to a person with COVID-19, adjusting only for the number of exposure incidents⁹; vaccination status was not included in the model because of small sample sizes. Most students were not eligible for vaccination during the spring semester. Statistical analyses were conducted using R software (version 4.1.1; R Foundation). The SLU Institutional Review Board approved this study.

A total of 9,335 student SARS-CoV-2 tests were performed during January-May 2021, including 1,009 (10.8%) diagnostic tests and 8,326 (89.2%) surveillance tests; students might have been tested more than once. Of all tests conducted, 265 (2.8%) yielded a positive SARS-CoV-2 result; no student received two positive test results. Among students with a positive SARS-CoV-2 test result, 378 close contacts were named (mean = 1.4 close contacts per case), 26 (6.9%) of whom reported only masked exposure; 352 (93.1%) reported any unmasked exposure. Close contacts had a median of one exposure incident (range = one-16). Reported exposures occurred between roommates, significant others, or in offcampus social gatherings. Among the 378 close contacts, 116 (30.7%) received a positive test result. Percentages of positive test result rates were substantially higher among contacts with any unmasked exposure (114 of 352; 32.4%) than among those who had masked exposure only (two of 26; 7.7%) (aOR = 5.4, 95% CI = 1.5–36.5; p = 0.008) and for those who were unvaccinated (33.0%) or partially vaccinated (20.8%) compared with those who were fully vaccinated (none) (p = 0.007) (Table).

In multivariate analyses, close contacts with unmasked exposure had higher adjusted odds of receiving a positive test result than did those with only masked exposure (aOR = 4.9; 95% CI = 1.4–31.1). Any additional exposure was associated with a 40.0% increase in adjusted odds of a positive test result (aOR = 1.4; 95% CI = 1.2–1.6); the median number of exposures was 2.0 for close contacts with positive test results and 1.0 for close contacts with negative test results. The two persons with only masked exposures who received positive test results were moved immediately to isolation upon receipt of test results. Neither of these two persons was linked to any additional COVID-19 cases, despite having nine close contacts between them and not having been placed into quarantine.

Discussion

Close contacts with any unmasked exposure to persons with COVID-19 had significantly higher odds of receiving a positive SARS-CoV-2 test result compared with those who had only masked exposure. In addition, close contacts who had multiple exposures, whether masked or unmasked, had higher odds of a positive test result than did those with only a single exposure. The percentage of positive test results among close contacts in this study (30.7%) was similar to that observed in previous studies (approximately 31%) (2,3). Consistent with findings

[§] COVID-19 testing was conducted using Abbott BinaxNOW rapid antigen test and LabCorp molecular RT-PCR for all symptomatic persons collected via self-administered anterior nasal swab, or Clinical Reference Laboratory salivabased molecular RT-PCR for all asymptomatic persons. Each symptomatic person was only counted once in the analyses, even though both an antigen and RT-PCR test were conducted.

I Logistic regression included masked status (any unmasked exposure versus only masked exposure) and number of exposure incidents (modeled as a continuous variable) with the persons with COVID-19 as predictors. These variables were chosen because of the strength of bivariate association with having a positive test result. The small number of close contacts with only masked exposures precluded more complex modeling; therefore, no demographic or other variables were included in the model. Linearity assumption was assessed by visual comparison of percentage of positive results by number of incidents. The model produced a Nagelkerke R-squared of 0.103 and a c-statistic of 0.654.

TABLE. Demographic characteristics, mask use, and number of exposure incidents of close contacts* of SARS-CoV-2-infected students, by SARS-CoV-2 test results — Saint Louis University, United States January–May 2021

	SARS-CoV-2 test results, no. (%)			
Characteristic	All (n = 378)	Negative (n = 262)	Positive (n = 116)	– p value [†]
Sex				
Female	268 (70.9)	175 (66.8)	93 (80.2)	0.012
Male	110 (29.1)	87 (33.2)	23 (19.8)	
Housing status				
Off-campus	115 (30.4)	84 (32.1)	31 (26.7)	0.358
On-campus	263 (69.6)	178 (67.9)	85 (73.3)	
Student level				
Graduate	33 (8.7)	23 (8.8)	10 (8.6)	1.000
Undergraduate	345 (91.3)	239 (91.2)	106 (91.4)	
Vaccination status§				
Fully vaccinated	18 (4.8)	18 (6.9)	0 (—)	0.007
Partially vaccinated	24 (6.3)	19 (7.3)	5 (4.3)	
Unvaccinated	336 (88.9)	225 (85.9)	111 (95.7)	
Student athlete				
No	330 (87.3)	228 (87.0)	102 (87.9)	0.939
Yes	48 (12.7)	34 (13.0)	14 (12.1)	
Reserve Officers' Training Corps member				
No .	376 (99.5)	261 (99.6)	115 (99.1)	1.000
Yes	2 (0.5)	1 (0.4)	1 (0.9)	
Member of student fraternity or sorority				
No	239 (63.2)	168 (64.1)	71 (61.2)	0.670
Yes	139 (36.8)	94 (35.9)	45 (38.8)	
Health major with clinical responsibilities				
No	294 (77.8)	201 (76.7)	93 (80.2)	0.541
Yes	84 (22.2)	61 (23.3)	23 (19.8)	
Mask use				
Masked exposure only	26 (6.9)	24 (9.2)	2 (1.7)	0.016
Any unmasked exposure	352 (93.1)	238 (90.8)	114 (98.3)	
No. of exposure incidents, median (IQR)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	2.0 (1.0, 3.0)	< 0.001

Abbreviation: IQR = interquartile range.

 † Determined by chi-square test for all comparisons except for number of exposure incidents (continuous variable), which was assessed using a t test.

from studies in nonuniversity settings (4,5), the findings from this study reinforce that universal masking and having fewer encounters in close contact with persons with COVID-19 helps prevent further transmission in in-person university settings.

Two close contacts, who had only masked exposure and were permitted to forego quarantine because of the university's modified protocol, received positive SARS-CoV-2 test results. Neither was linked to any additional COVID-19 cases (i.e., secondary transmission). For universities considering a similar approach, if masked unvaccinated close contacts are not required to quarantine, testing 5–7 days after exposure will be important because of the small risk for infection that could lead to secondary transmission if isolation is not implemented rapidly, especially in populations with low vaccination coverage. Modified quarantine, such as that implemented by this

university, might be feasible on other university campuses or in other settings that have an internal contact tracing team and enforced testing protocols. For example, studies in K–12 school settings have found reduced SARS-CoV-2 transmission when masking is enforced even when 6 feet of physical distance cannot be maintained (6). Such modifications to quarantine policies might also have the potential to reduce the number of missed days from critical academic activities (e.g., clinical hours, flight hours) because of quarantine, which are days that are needed for degree completion and program accreditation. Modified quarantine, similar to that implemented by SLU, might also help minimize the negative psychosocial effects associated with quarantine (7). As of September 7, 2021, 1,014 universities have a COVID-19 vaccine requirement policy for students and employees (8).

^{*} A close contact was defined as any unvaccinated person who spent a cumulative total of ≥15 minutes in one 24-hour period within 6 feet of a confirmed case of COVID-19 while that person was contagious, regardless of whether a mask was worn.

[§] Full vaccination was defined as having received either a single dose of Janssen (Johnson & Johnson) vaccine or the second dose of Moderna or Pfizer-BioNTech COVID-19 vaccine ≥14 days before the exposure. Partial vaccination was defined as receipt of a single dose of Janssen or the second dose of Moderna or Pfizer-BioNTech <14 days before the exposure, or receipt of 1 dose of Moderna or Pfizer-BioNTech COVID-19 vaccine. Being unvaccinated was defined as not having received a dose of any COVID-19 vaccine.

[¶] Exposure incidents were defined as each single encounter in which a contact was within 6 feet of a student with COVID-19 for ≥15 minutes during a 24-hour period, regardless of location of the exposure.

Summary

What is already known about this topic?

During January–May 2021, Saint Louis University implemented a modified quarantine protocol that considered mask use when determining which close contacts required quarantine among an almost entirely unvaccinated student population.

What is added by the report?

Compared with only masked exposure, close contacts with any unmasked exposure had higher adjusted odds of a positive test result. Each additional exposure was associated with a 40% increase in odds of a positive test.

What are the implications for public health practice?

Universal masking and fewer encounters in close proximity to persons with COVID-19 can limit the spread of SARS-CoV-2 in university settings.

The findings in this report are subject to at least five limitations. First, contact tracing data were self-reported, which could introduce social desirability or recall bias or inaccurate data regarding mask use. Second, the two students who received positive SARS-CoV-2 test results and reported only masked exposure might have had unmasked exposure to COVID-19 cases other than those under investigation, which could lead to underestimating the association between mask use and the percentage of positive test results. Third, most students were not vaccine-eligible until late spring, so this analysis included very few fully vaccinated students; therefore, vaccination status could not be included in the regression analysis because of low cell counts. Fourth, indoor versus outdoor exposure information and exposure time were collected but could not be included in the analysis because of a large amount of missing data. Finally, this study was conducted before the Delta variant became the dominant strain of SARS-CoV-2 in the United States, which could have an impact on these findings given that the Delta variant has increased transmissibility compared to previous variants.**

Wearing masks and having fewer encounters with persons with COVID-19 reduced the odds of transmission in a university setting. In addition, there was no evidence of secondary transmission from either of the two students with only masked exposure who received positive SARS-CoV-2 test results, and who, because of the modified protocol in place, were allowed to forego quarantine. Universities opening for in-person instruction could consider taking mask use into account when determining which unvaccinated close contacts require quarantine if enforced testing protocols are in place. CDC recommends that universal masking be adopted in indoor spaces for vaccinated

and unvaccinated persons in areas with substantial or high transmission rates and that masks should be worn in indoor spaces in areas without substantial or high transmission rates if you are not fully vaccinated (9). In addition, CDC recommends COVID-19 vaccination for individuals aged ≥12 years.

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References

- Losina E, Leifer V, Millham L, et al. College campuses and COVID-19 mitigation: clinical and economic value. Ann Intern Med 2021;174:472–83. PMID:33347322 https://doi.org/10.7326/M20-6558
- Denny TN, Andrews L, Bonsignori M, et al. Implementation of a pooled surveillance testing program for asymptomatic SARS-CoV-2 infections on a college campus—Duke University, Durham, North Carolina, August 2—October 11, 2020. MMWR Morb Mortal Wkly Rep 2020;69:1743–7. PMID:33211678 https://doi.org/10.15585/mmwr. mm6946e1
- 3. Jones A, Fialkowski V, Prinzing L, Trites J, Kelso P, Levine M. Assessment of day-7 postexposure testing of asymptomatic contacts of COVID-19 patients to evaluate early release from quarantine—Vermont, May-November 2020. MMWR Morb Mortal Wkly Rep 2021;70:12–3. PMID:33411700 https://doi.org/10.15585/mmwr.mm7001a3
- Cheng VC, Wong SC, Chuang VW, et al. The role of community-wide wearing of face mask for control of coronavirus disease 2019 (COVID-19) epidemic due to SARS-CoV-2. J Infect 2020;81:107–14. PMID:32335167 https://doi.org/10.1016/j.jinf.2020.04.024
- Pringle JC, Leikauskas J, Ransom-Kelley S, et al. COVID-19 in a correctional facility employee following multiple brief exposures to persons with COVID-19—Vermont, July–August 2020. MMWR Morb Mortal Wkly Rep 2020;69:1569–70. PMID:33119564 https://doi.org/10.15585/ mmwr.mm6943e1
- 6. Dawson P, Worrell MC, Malone S, et al.; CDC COVID-19 Surge Laboratory Group. Pilot investigation of SARS-CoV-2 secondary transmission in kindergarten through grade 12 schools implementing mitigation strategies—St. Louis County and City of Springfield, Missouri, December 2020. MMWR Morb Mortal Wkly Rep 2021;70:449–55. PMID:33764961 https://doi.org/10.15585/mmwr.mm7012e4
- Kaparounaki CK, Patsali ME, Mousa DV, Papadopoulou EVK, Papadopoulou KKK, Fountoulakis KN. University students' mental health amidst the COVID-19 quarantine in Greece. Psych Res 2020 290:113111. PMID:32450416 https://doi.org/10.1016/j.psychres.2020.113111
- 8. Thomason A, O'Leary B. Here's a list of colleges that require students or employees to be vaccinated against COVID-19. Washington, DC: Chronicles of Higher Education; 2021. Accessed September 7, 2021. https://www.chronicle.com/blogs/live-coronavirus-updates/heres-a-list-of-colleges-that-will-require-students-to-be-vaccinated-against-covid-19
- 9. Brown CM, Vostok J, Johnson H, et al. Outbreak of SARS-CoV-2 infections, including COVID-19 vaccine breakthrough infections, associated with large public gatherings—Barnstable County, Massachusetts, July 2021. MMWR Morb Mortal Wkly Rep 2021;70:1059–62. PMID:34351882 https://doi.org/10.15585/mmwr.mm7031e2

^{**} https://www.medrxiv.org/content/10.1101/2021.06.03.21258293v1

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Morbidity and Mortality Weekly Report

Trends in COVID-19 Cases, Emergency Department Visits, and Hospital Admissions Among Children and Adolescents Aged 0–17 Years — United States, August 2020–August 2021

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Although COVID-19 generally results in milder disease in children and adolescents than in adults, severe illness from COVID-19 can occur in children and adolescents and might require hospitalization and intensive care unit (ICU) support (1–3). It is not known whether the B.1.617.2 (Delta) variant,* which has been the predominant variant of SARS-CoV-2 (the virus that causes COVID-19) in the United States since late June 2021,† causes different clinical outcomes in children and adolescents compared with variants that circulated earlier. To assess trends among children and adolescents, CDC analyzed new COVID-19 cases, emergency department (ED) visits with a COVID-19 diagnosis code, and hospital admissions of patients with confirmed COVID-19 among persons aged 0-17 years during August 1, 2020-August 27, 2021. Since July 2021, after Delta had become the predominant circulating variant, the rate of new COVID-19 cases and COVID-19related ED visits increased for persons aged 0-4, 5-11, and 12-17 years, and hospital admissions of patients with confirmed COVID-19 increased for persons aged 0-17 years. Among persons aged 0–17 years during the most recent 2-week period (August 14-27, 2021), COVID-19-related ED visits and hospital admissions in the states with the lowest vaccination coverage were 3.4 and 3.7 times that in the states with the highest vaccination coverage, respectively. At selected hospitals, the proportion of COVID-19 patients aged 0-17 years who were admitted to an ICU ranged from 10% to 25% during August 2020-June 2021 and was 20% and 18% during July and August 2021, respectively. Broad, community-wide vaccination of all eligible persons is a critical component of mitigation strategies to protect pediatric populations from SARS-CoV-2 infection and severe COVID-19 illness.

CDC analyzed COVID-19 cases, ED visits with a COVID-19 diagnosis code, and hospital admissions of patients

with laboratory-confirmed COVID-19 among persons aged 0–17 years during August 1, 2020–August 27, 2021. Daily COVID-19 case data were obtained from CDC's case-based surveillance system. Daily ED visits were obtained from the National Syndromic Surveillance Program and were stratified into three age groups: 0–4, 5–11, and 12–17 years. Daily hospital admission data were obtained from the U.S. Department of Health and Human Services (HHS) Unified Hospital Data Surveillance System.** The number of daily cases, ED

The National Syndromic Surveillance Program collects electronic health data, including ED visits with COVID-19 diagnoses, from a subset of hospitals in 49 states and the District of Columbia (71% of nonfederal EDs in the United States). ED visits for COVID-19 are defined as ED visits with any of the following: *International Classification of Diseases, Tenth Revision* codes U07.1 or J12.82 or Systematized Nomenclature of Medicine codes 840539006, 840544004, or 840533007. https://www.cdc.gov/nssp/overview.html

^{*}https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-info.html#Concern

[†] https://covid.cdc.gov/covid-data-tracker/#variant-proportions

SCDC official counts of COVID-19 cases and deaths, released daily (https://covid.cdc.gov/covid-data-tracker), are aggregate counts from reporting jurisdictions. Some jurisdictions electronically submit standardized information for individual cases of COVID-19 to CDC via a case report form developed for the CDC COVID-19 response (https://www.cdc.gov/coronavirus/2019-ncov/php/reporting-pui.html) or via the CDC National Notifiable Diseases Surveillance System (https://www.cdc.gov/nndss/action/covid-19-response.html). Individual-level case report data were available for approximately 80% of the aggregate number of reported cases. A COVID-19 case is defined by detection of SARS-CoV-2 RNA or antigen in a respiratory specimen collected from a person (confirmed or probable case) according to the Council of State and Territorial Epidemiologists' Update to the standardized surveillance case definition and national notification for COVID-19 (21-ID-01): https://cdn.ymaws.com/www.cste.org/resource/resmgr/ps/ps/2021/21-ID-01_COVID-19.pdf.

^{**} The HHS Unified Hospital Data Surveillance System includes data from all U.S. hospitals registered with the Centers for Medicare & Medicaid Services (CMS) as of June 1, 2020, and from hospitals not CMS-registered but reporting COVID-19 data through this system since July 1, 2020. Data, including counts of new hospital admissions of patients with confirmed COVID-19 by age group, are reported to HHS either directly from facilities or via a state health department submission; on August 27, 2021, 97% of hospitals reported data. This analysis includes children's, short-term acute care, long-term acute care, critical access, Veterans Administration, Defense Health Agency, and Indian Health Services hospitals and excludes psychiatric, rehabilitation, and religious nonmedical hospitals. Reporting guidelines are published in the HHS COVID-19 Guidance for Hospital Reporting and FAQs document (https://www.hhs.gov/sites/default/files/covid-19-faqshospitals-hospital-laboratory-acute-care-facility-data-reporting.pdf). The hospital admissions rate in the lowest vaccination coverage quartile states excludes data from Georgia because of a data quality issue.

visits, and hospital admissions were averaged over a 7-day period to obtain a 7-day average. The state-specific percentage of the population aged ≥12 years who had completed the COVID-19 vaccination series as of July 31, 2021, was used to group states into vaccination coverage quartiles. †† Results were also examined by HHS Region. U.S. Census Bureau midyear 2019 population estimates were used to calculate vaccination coverage and cases and hospital admissions per 100,000 persons. COVID-19-associated ED visits were assessed as a percentage of all ED visits. To assess differences in COVID-19 outcomes by vaccination coverage quartile, ratios for ED visits and rate ratios for hospital admissions during the 2-week period August 14-27, 2021, along with corresponding 95% confidence intervals (CIs), were calculated. R (Version 4.1.0; R Foundation) was used for calculations.

The BD Insights Research Database was used to describe indicators of severe disease among pediatric patients hospitalized with laboratory-confirmed COVID-19. §§ CDC analyzed the monthly percentage of hospitalizations resulting in ICU admission and in invasive mechanical ventilation, and median length of hospital stay during August 1, 2020-August 21, 2021. These analyses were conducted using SAS (version 9.4; SAS Institute).*** This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.†††

COVID-19 incidence among persons aged 0-4, 5-11, and 12-17 years during August 2020-August 2021 peaked in January 2021 at 21.2, 30.1, and 51.7 cases per 100,000 persons, respectively (Figure 1). Incidence declined in June 2021 to a low of 1.7, 1.9, and 2.9, respectively, across the three

†† Obtained from COVID-19 Data Tracker (https://covid.cdc.gov/covid-datatracker/#vaccinations_vacc-total-admin-rate-total). Persons aged 12-17 years became eligible for vaccination on May 10, 2021. Age 12 years is the current lowest age of eligibility for COVID-19 vaccination. https://www.fda.gov/ news-events/press-announcements/coronavirus-covid-19-update-fdaauthorizes-pfizer-biontech-covid-19-vaccine-emergency-use

§§ Population estimates as of July 1, 2020. https://www.census.gov/data/tables/ time-series/demo/popest/2010s-national-detail.html

*** Statistical testing and CIs were not used for the BD Research Insights Database because of its small size and design (i.e., census of patient data from select hospitals); the convenience sample does not allow for the use of weights to adjust for complex sampling.

††† 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.

age groups; however, incidence in August 2021 among the three age groups reached 16.2, 28.5, and 32.7 per 100,000 persons, respectively.

Overall, COVID-19 ED visits and hospital admissions increased since June 2021 among states in all vaccination coverage quartiles (Supplementary Figure, https://stacks.cdc. gov/view/cdc/109403). The percent of COVID-19 ED visits in August 2021 in the quartile of states with the lowest vaccination coverage was 3.4 times that in the quartile of states with the highest vaccination coverage (Table). The rate (per 100,000 persons) of COVID-19 admissions in August 2021 in the quartile of states with the lowest vaccination coverage was 3.7 times that in the quartile of states with the highest vaccination coverage.

The lowest vaccination coverage among persons aged ≥12 years (49.9%), highest percentage of COVID-19associated ED visits (8.32), and highest COVID-19 hospital admission rates (0.84) were observed in HHS Region 4. §§§ In contrast, the highest vaccination coverage (72.2%), lowest COVID-19 incidence (13.3), and lowest rate of hospital admission (0.12) among persons aged 0–17 years were observed in HHS Region 1 (Supplementary Table, https://stacks.cdc. gov/view/cdc/109402).

In the BD Insights Research Database, 1,790 COVID-19 hospitalizations occurred among persons aged 0-17 years during August 1, 2020-August 21, 2021. Median length of stay ranged from 2 to 3 days during the entire period. The percentage of hospitalizations resulting in an ICU admission ranged from 10% to 25% during August 2020-June 2021; percentages were 20% and 18% in July and August 2021, respectively (Figure 2). The percentage of hospitalizations resulting in invasive mechanical ventilation ranged from 0% to 3% and was highest in October 2020; percentages in July and August 2021 were 2% and <1%, respectively. A total of eight in-hospital COVID-19-related deaths in persons aged 0-17 years occurred during August 2020-August 2021 (0.4% of hospitalized patients). Among 63 patients aged 0–17 years admitted to an ICU in July and August 2021, 17 (27%) were aged 0-4 years, 17 (27%) were 5-11 years, and 29 (46%) were 12-17 years.

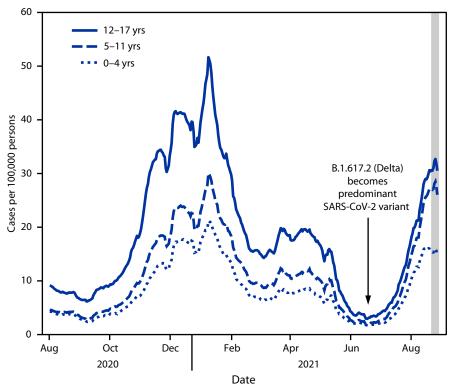
Discussion

Among U.S. children and adolescents aged 0-17 years, COVID-19 cases and associated ED visits and hospital admissions increased during June 2021-August 2021. During a 2-week period in August 2021, COVID-19-associated ED

[¶] BD Insights Research Database is a large U.S. hospital-based database that includes inpatient data from approximately 260 hospitals in rural and urban areas. Of these, 140 hospitals had COVID-19 hospitalizations among patients aged 0–17 years during the study period; by U.S. Census Region, most hospitals were in the South (52%), followed by the Midwest (18%), West (16%), and Northeast (14%). COVID-19 hospitalizations were identified by positive results on SARS-CoV-2 reverse transcription-polymerase chain reaction or antigen testing. Data are updated weekly; release date August 25, 2021, access date August 25, 2021. The database includes three children's hospitals; the remainder of patients were mostly admitted to community hospitals.

[💖] HHS Region 4 includes Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, and Tennessee. Hospital admissions data in this report do not include Georgia.

FIGURE 1. Average daily COVID-19 case incidence* among persons aged 0–17 years, by age group — United States, August 1, 2020–August 27, 2021



Source: CDC's case-based COVID-19 surveillance system, accessed August 30, 2021. https://www.cdc.gov/nndss/action/covid-19-response.html

visits and hospital admissions for children and adolescents with confirmed COVID-19 were highest in states with lowest vaccination coverage, particularly states in the South, whereas in the states with the highest coverage, COVID-19 ED visits and the rate of hospital admissions among children and adolescents were lowest. These findings underscore the importance of community vaccination, in coordination with testing strategies and other prevention measures, to protect children from SARS-CoV-2 infection and severe COVID-19.

Children and adolescents can experience severe acute COVID-19, which might require mechanical ventilation, or result in other complications, such as multisystem inflammatory syndrome in children (MIS-C) (2) \$55 and persistent symptoms from COVID-19 (4). Pediatric patients who have underlying medical conditions might be at risk for more severe

Increases in COVID-19 ED visits and hospital admissions were observed in all four state COVID-19 vaccination coverage quartiles during June-August 2021. Although some data suggest that persons infected with the Delta SARS-CoV-2 variant might be at higher risk for hospitalization (6), it is not clear whether the Delta variant causes more severe illness in adult or pediatric populations. Although it is possible that increases in COVID-19-related ED visits and hospital admissions for pediatric patients with confirmed COVID-19 could be related to increased severity of disease for the Delta variant compared with severity for earlier circulating variants, increases in ED visits and hospitalizations could be related to other factors such as increased transmission (6).****

Pediatric ED visits and hospital admissions were higher in August 2021 in states with the lowest vaccination coverage among persons aged ≥12 years. Although the SARS-CoV-2 Delta variant is highly transmissible, only a modest decrease in vaccine effectiveness against infection with the Delta variant has been reported (7); therefore, transmission might

be a major factor driving increases in ED visits and hospital admissions. However, beyond community vaccination coverage, other factors driving regional variation might include differences in implementation of other prevention measures, including masking, physical distancing, and kindergarten through grade 12 (K–12) school opening policies (8).

This analysis found that the percentage of COVID-19 hospitalizations resulting in ICU admission has remained near 20% since Delta became the predominant SARS-CoV-2 variant. A study of children and adolescents hospitalized for COVID-19 during March 2020–July 2021 found that the proportion of those patients admitted to an ICU during the pre-Delta period (March 1, 2020–June 19, 2021) and the Delta-predominant period (June 20–July 31, 2021) did not differ (26.5% and 23.2%, respectively) (9). This same study

^{*}Incidence calculated as daily cases averaged over a 7-day period to obtain a 7-day moving daily average per 100,000 persons using 2019 U.S. Census population as denominators (three age groups: 0-4, 5-11, and 12-17 years). Delta became the predominant SARS-CoV-2 variant in the United States in late June 2021, accounting for 63% of new COVID-19 cases the week ending June 26, 2021 (https://covid.cdc.gov/covid-data-tracker/#variant-proportions). Because of potential reporting delays, data reported in the most recent 7 days (as represented by the shaded bar) should be interpreted with caution.

disease (3). The increases in COVID-19 hospital admissions found in this study occurred for all assessed pediatric age groups during July–August 2021, with most admissions among patients aged ≤4 or 12–17 years. This bimodal age distribution is consistent with other published data (5).

^{¶¶¶} Accessed September 1, 2021. https://www.cdc.gov/mis/index.html

^{****} Accessed September 1, 2021. https://www.cdc.gov/coronavirus/2019-ncov/variants/delta-variant.html

TABLE. Ratio of percentage of COVID-19-associated emergency department visits among all emergency department visits and rate ratio of COVID-19 hospital admissions* (compared with highest vaccination coverage quartile states) among persons aged 0–17 years, by quartile of states grouped by vaccination coverage and age group — United States, August 14, 2021–August 27, 2021[†]

		Ratio (95% CI)				
State vaccination		ED visits				
coverage quartile§	0–17 yrs	0-4 yrs	5–11 yrs	12-17 yrs	0–17 yrs	
Highest [¶]	Ref	Ref	Ref	Ref	Ref	
Second highest**	0.99 (0.94-1.05)	1.02 (0.93-1.12)	0.99 (0.90-1.10)	0.96 (0.89-1.05)	1.40 (0.87-2.25)	
Second lowest ^{††}	2.65 (2.55-2.76)	2.31 (2.15-2.47)	2.64 (2.44-2.84)	2.84 (2.67-3.03)	3.46 (2.26-5.28)	
Lowest ^{§§}	3.38 (3.24–3.52)	2.61 (2.42-2.82)	3.34 (3.08–3.61)	3.76 (3.52-4.02)	3.70 (2.32-5.90)	

Sources: COVID-19 Vaccination Trends in the United States (https://data.cdc.gov/Vaccinations/COVID-19-Vaccination-Trends-in-the-United-States-N/rh2h-3yt2) and National Syndromic Surveillance Program, U.S. Department of Health and Human Services Unified Hospital Data Surveillance System, accessed August 30, 2021. **Abbreviations:** ED = emergency department; Ref = referent group.

- * The hospital admission incidence rates that were used to calculate the rate ratios are 14-day average daily confirmed COVID-19 pediatric admissions per 100,000 persons aged 0–17 years. Rate in the lowest vaccination coverage quartile excludes data from Georgia because of a data quality issue.
- † ED visit data are from the National Syndromic Surveillance Program (NSSP). Data are limited to ED visits with a discharge diagnosis. Data from Hawaii and Ohio are not included. Fewer than 50% of facilities in California, Iowa, Minnesota, South Dakota, and Wyoming report to NSSP. In HHS Region 7, fewer than 50% of all ED visits have a discharge diagnosis.
- § Vaccine coverage data are for the population aged ≥12 years who completed COVID-19 vaccination series as of July 31, 2021. Idaho provides vaccine data only for vaccine recipients who are aged ≥18 years.
- Highest vaccination states: Connecticut, Maine, Maryland, Massachusetts, New Hampshire, New Jersey, New Mexico, New York, Oregon, Rhode Island, Vermont, Virginia, and Washington (>63.45%).
- ** Second highest vaccination states: California, Colorado, District of Columbia, Delaware, Hawaii, Illinois, Iowa, Michigan, Minnesota, Nebraska, Pennsylvania, and Wisconsin (>56.30% and ≤63.45%).
- †† Second Iowest vaccination states: Alaska, Arizona, Florida, Indiana, Kansas, Kentucky, Montana, Nevada, North Carolina, Ohio, South Dakota, Texas, and Utah (>49.75% and ≤56.30%).
- §§ Lowest vaccination states: Alabama, Arkansas, Georgia, Idaho, Louisiana, Mississippi, Missouri, North Dakota, Oklahoma, South Carolina, Tennessee, West Virginia, and Wyoming (≤49.75%).

found a median length of stay of 3 days during the pre-Delta period and 2 days during the Delta-predominant period among hospitalized patients aged 0–17 years with COVID-19 (9).

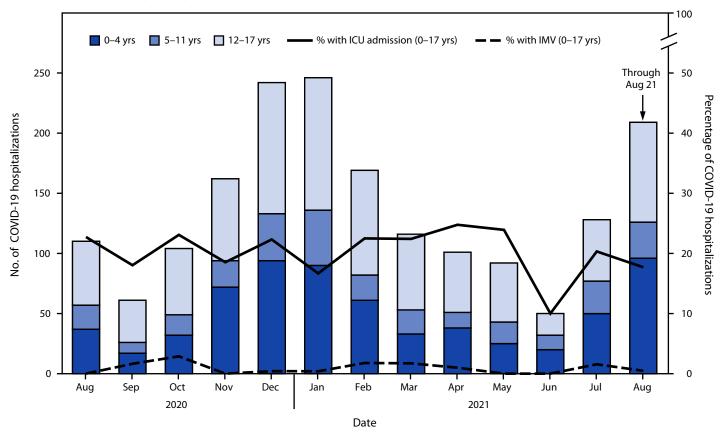
The findings in this report are subject to at least seven limitations. First, data sets used to quantify COVID-19 cases, ED visits, and hospital admissions are subject to reporting inconsistencies. Second, testing rates for SARS-CoV-2 infection in persons aged 0-17 years are lower than they are in older age groups^{††††}; therefore, pediatric case rates are likely underreported. Third, ED visits and hospital admissions were not characterized by reason for visit or admission and might include cases of MIS-C or asymptomatic SARS-CoV-2 infection. Fourth, admissions in the Unified Hospital Data Surveillance System could not be stratified by age and were only counted if the patient was "admitted to a pediatric bed." Fifth, because the BD Insights Research Database represents three children's hospitals and the remainder of patients were mostly from community hospitals, patients with severe COVID-19 might be under- or overrepresented, which might account for some differences compared with past studies. Sixth, patients are added to this database on hospital discharge; therefore, recent data do not include patients currently admitted. Finally, geographic representativeness varies across data sources.

Continued assessment of trends in ED visits and admissions, including evaluation of reason for seeking medical care, could help guide public health practice, including planning for any decreases in pediatric care capacity. Evaluating more specific measures of severity (e.g., hypoxia and duration of mechanical ventilation), potential co-infection (e.g., respiratory syncytial virus), vaccination status, and underlying medical conditions might help determine whether children and adolescents infected with the Delta variant have more severe disease than do those infected with other variants. As schools resume inperson activities, CDC recommends multiple prevention measures in early child care and education programs and K-12 schools, "" such as masking for students and staff members and maintaining adequate ventilation to reduce transmission of SARS-CoV-2. Vaccination of eligible persons against COVID-19, especially those in close contact with children aged <12 years who are not yet eligible for vaccination, is anticipated to protect students, teachers, staff members, visitors, and other household members. Community vaccination, in coordination with testing strategies and other prevention measures, are critical to protecting pediatric populations from SARS-CoV-2 infection and severe COVID-19.

^{††††} COVID-19 electronic laboratory reporting data set, accessed August 29, 2021. \$\$\$\$ https://www.hhs.gov/sites/default/files/covid-19-faqs-hospitals-hospital-laboratory-acute-care-facility-data-reporting.pdf

⁵⁵⁵⁵ https://www.cdc.gov/coronavirus/2019-ncov/community/schools-childcare/k-12-guidance.html

FIGURE 2. Number and percentage of COVID-19 hospitalizations resulting in intensive care unit admission or invasive mechanical ventilation among persons aged 0–17 years, by age group — United States, August 1, 2020–August 21, 2021



Source: BD Insights Research Database.

Abbreviations: ICU = intensive care unit; IMV = invasive mechanical ventilation.

Summary

What is already know about this topic?

Severe illness from COVID-19 can and does occur in children and adolescents.

What is added by this report?

COVID-19 cases, emergency department visits, and hospital admissions increased from June to August 2021 among persons aged 0-17 years. Emergency department visits and hospital admissions in a 2-week period in August 2021 were higher in states with lower population vaccination coverage and lower in states with higher vaccination coverage.

What are the implications for public health?

Community vaccination, in coordination with testing strategies and other prevention measures, is critical to protecting pediatric populations from SARS-CoV-2 infection and severe COVID-19.

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References

- Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. Acta Paediatr 2020;109:1088–95. PMID:32202343 https://doi.org/10.1111/apa.15270
- Fernandes DM, Oliveira CR, Guerguis S, et al.; Tri-State Pediatric COVID-19 Research Consortium. Severe acute respiratory syndrome coronavirus 2 clinical syndromes and predictors of disease severity in hospitalized children and youth. J Pediatr 2021;230:23–31.e10. PMID:33197493 https://doi.org/10.1016/j.jpeds.2020.11.016

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- 3. Kompaniyets L, Agathis NT, Nelson JM, et al. Underlying medical conditions associated with severe COVID-19 illness among children. JAMA Netw Open 2021;4:e2111182. PMID:34097050 https://doi.org/10.1001/jamanetworkopen.2021.11182
- Ashkenazi-Hoffnung L, Shmueli E, Ehrlich S, et al. Long COVID in children: observations from a designated pediatric clinic. Pediatr Infect Dis J 2021; Epub August 5, 2021. PMID:34371507 https://doi. org/10.1097/INE.000000000003285
- Kainth MK, Goenka PK, Williamson KA, et al.; Northwell Health COVID-19 Research Consortium. Early experience of COVID-19 in a US children's hospital. Pediatrics 2020;146:e2020003186. PMID:32680880 https://doi.org/10.1542/peds.2020-003186
- Sheikh A, McMenamin J, Taylor B, Robertson C; Public Health Scotland and the EAVE II Collaborators. SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness. Lancet 2021;397:2461–2. PMID:34139198 https://doi.org/10.1016/ S0140-6736(21)01358-1

- 7. Lopez Bernal J, Andrews N, Gower C, et al. Effectiveness of Covid-19 vaccines against the B.1.617.2 (Delta) variant. N Engl J Med 2021;385:585–94. PMID:34289274 https://doi.org/10.1056/NEJMoa2108891
- Fisher KA, Barile JP, Guerin RJ, et al. Factors associated with cloth face covering use among adults during the COVID-19 pandemic—United States, April and May 2020. MMWR Morb Mortal Wkly Rep 2020;69:933–7. PMID:32673303 https://doi.org/10.15585/mmwr. mm6928e3
- 9. Delahoy MJ, Ujamaa D, Whitaker M, et al.; COVID-NET Surveillance Team. Hospitalizations associated with COVID-19 among children and adolescents—COVID-NET, 14 states, March 1, 2020–August 14, 2021. MMWR Morb Mortal Wkly Rep 2021;70. Epub September 3, 2021.

Hospitalizations Associated with COVID-19 Among Children and Adolescents — COVID-NET, 14 States, March 1, 2020–August 14, 2021

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Although COVID-19-associated hospitalizations and deaths have occurred more frequently in adults,† COVID-19 can also lead to severe outcomes in children and adolescents (1,2). Schools are opening for in-person learning, and many prekindergarten children are returning to early care and education programs during a time when the number of COVID-19 cases caused by the highly transmissible B.1.617.2 (Delta) variant of SARS-CoV-2, the virus that causes COVID-19, is increasing.§ Therefore, it is important to monitor indicators of severe COVID-19 among children and adolescents. This analysis uses Coronavirus Disease 2019-Associated Hospitalization Surveillance Network (COVID-NET) data to describe COVID-19-associated hospitalizations among U.S. children and adolescents aged 0-17 years. During March 1, 2020–August 14, 2021, the cumulative incidence of COVID-19-associated hospitalizations was 49.7 per 100,000 children and adolescents. The weekly COVID-19-associated hospitalization rate per 100,000 children and adolescents during the week ending August 14, 2021 (1.4) was nearly five times the rate during the week ending June 26, 2021 (0.3); among children aged 0-4 years, the weekly hospitalization rate during the week ending August 14, 2021, was nearly 10 times that during the week ending June 26, 2021.** During June 20-July 31, 2021, the hospitalization rate among unvaccinated adolescents (aged 12-17 years) was 10.1 times higher than that among fully vaccinated adolescents. Among all hospitalized children and adolescents with COVID-19, the proportions

with indicators of severe disease (such as intensive care unit [ICU] admission) after the Delta variant became predominant (June 20–July 31, 2021) were similar to those earlier in the pandemic (March 1, 2020–June 19, 2021). Implementation of preventive measures to reduce transmission and severe outcomes in children is critical, including vaccination of eligible persons, universal mask wearing in schools, recommended mask wearing by persons aged ≥2 years in other indoor public spaces and child care centers,^{††} and quarantining as recommended after exposure to persons with COVID-19.^{§§}

COVID-NET conducts population-based surveillance for laboratory-confirmed COVID-19-associated hospitalizations in 99 counties across 14 states § (1). Residents of the surveillance catchment area who received positive molecular or rapid antigen detection test results for SARS-CoV-2 during hospitalization or within 14 days before admission were classified as having COVID-19-associated hospitalizations. Unadjusted age-specific cumulative and weekly COVID-19associated hospitalization rates (hospitalizations per 100,000 children and adolescents residing in the catchment area) during March 1, 2020-August 14, 2021, were calculated by dividing the total number of hospitalized patients by the National Center for Health Statistics' population estimates within each age group for the counties included in the surveillance catchment area.*** Among adolescents, who are currently eligible for vaccination^{†††} (3), age-specific hospitalization rates during June 20-July 31, 2021, were calculated by COVID-19

^{*} These authors contributed equally to this report.

[†] https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-age.html

https://www.cdc.gov/coronavirus/2019-ncov/variants/index.html

https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covid-net/purpose-methods.html

^{**} COVID-NET hospitalization data are preliminary and subject to change as more data become available. In particular, case counts and rates for recent hospital admissions are subject to lag.

^{††} https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/about-face-coverings.html

^{§§} https://www.cdc.gov/coronavirus/2019-ncov/your-health/quarantine-isolation.html

⁵⁵ California, Colorado, Connecticut, Georgia, Iowa, Maryland, Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah. The included counties have been listed previously. https://www.cdc.gov/mmwr/volumes/69/wr/mm6932e3.htm

^{***} Rates are calculated using the National Center for Health Statistics' vintage 2019 bridged-race postcensal population estimates for the counties included in surveillance (https://www.cdc.gov/nchs/nvss/bridged_race.htm).

^{†††} https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/adolescents.html

vaccination status, which was determined for both hospitalized patients and the catchment area population using state immunization information systems data. §§§ Because the number of fully vaccinated persons in the underlying population changed weekly, incidence (cases per 100,000 person-weeks) was calculated by dividing the total number of vaccinated hospitalized adolescents by the sum of vaccinated adolescents in the underlying population each week; the same method was used to calculate incidence among unvaccinated adolescents. 555 Rate ratios and 95% confidence intervals (CIs) were calculated. Trained surveillance staff members conducted medical chart abstractions for all pediatric COVID-NET patients using a standardized case report form. Data on the following measures of severe disease were collected: median hospital length of stay, ICU admission, highest level of respiratory support received (i.e., invasive mechanical ventilation [IMV], bilevel positive airway pressure or continuous positive airway pressure, or high-flow nasal cannula), vasopressor use, and inhospital death. Deaths occurring after hospital discharge were not included in this analysis. To assess COVID-19 severity among hospitalized children and adolescents in the setting of widespread Delta variant circulation, the proportions with measures of severe disease were compared between the periods before (March 1, 2020-June 19, 2021) and after (June 20-July 31, 2021) the Delta variant became the predominant strain circulating in the United States**** (4). A Wilcoxon rank sum test was used to compare medians; chi square or Fisher's exact tests were used to compare proportions. Data were analyzed using SAS (version 9.4; SAS Institute); statistical significance

was defined as p<0.05. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy. $\dagger^{\dagger\dagger\dagger\dagger}$

During March 1, 2020-August 14, 2021, COVID-NET identified 49.7 cumulative COVID-19-associated hospitalizations per 100,000 children and adolescents (Figure 1); rates were highest among children aged 0-4 years (69.2) and adolescents aged 12-17 years (63.7) and lowest among children aged 5-11 years (24.0). Weekly hospitalization rates were at their lowest in 2021 during the weeks ending June 12-July 3 (0.3 per 100,000 children and adolescents each week) (Figure 2). During a subsequent 6-week period after the Delta variant became predominant, rates rose each week to 1.4 during the week ending August 14, 2021, which was 4.7 times the rate during the week ending June 26, 2021 and approached the peak hospitalization rate of 1.5 observed during the week ending January 9, 2021. Weekly rates increased among all age groups; the sharpest increase occurred among children aged 0-4 years, for whom the rate during the week ending August 14, 2021 (1.9) was nearly 10 times that during the week ending June 26, 2021 (0.2). During June 20-July 31, 2021, among 68 adolescents hospitalized with COVID-19 whose vaccination status had been ascertained, 59 were unvaccinated, five were partially vaccinated, and four were fully vaccinated; the hospitalization rate among unvaccinated adolescents was 0.8 per 100,000 person-weeks (95% CI = 0.6-0.9), comparedwith 0.1 (95% CI = 0.0-0.1) in fully vaccinated adolescents (rate ratio = 10.1; 95% CI = 3.7-27.9).

Among 3,116 hospitalized children and adolescents with COVID-19 during March 1, 2020–June 19, 2021, for whom complete clinical data were available, \$555 827 (26.5%) were admitted to an ICU, 190 (6.1%) required IMV, and 21 (0.7%) died. Among 164 hospitalized children and adolescents with COVID-19 during June 20–July 31, 2021, for whom complete clinical data were available, ***** 38 (23.2%) were admitted to

SSS The Food and Drug Administration granted emergency use authorization for the Pfizer-BioNTech COVID-19 vaccine for adolescents aged 12–15 years on May 10, 2021. The earliest date that adolescents in this age group could have met the definition for being a fully vaccinated patient hospitalized with COVID-19 was June 14, 2021. Because vaccination data are subject to lag, rates by vaccination status were only calculated through July 31, 2021.

Fully vaccinated adolescents with COVID-19-associated hospitalizations were defined as those who had received a second vaccine dose ≥14 days before a positive SARS-CoV-2 test result associated with their hospitalization. Adolescents whose positive SARS-CoV-2 test date was ≥14 days after a single dose through <14 days after a second dose were considered partially vaccinated and were not included in rates; adolescents who had received a single dose of vaccine <14 days before the positive SARS-CoV-2 test result were also not included in rates If the SARS-CoV-2 test date was not available, hospital admission date was used. Adolescents whose vaccination status had not yet been verified using the immunization information system data were considered to having missing vaccination status and were excluded. Adolescents whose vaccination status was checked against the immunization information system and who did not have documented receipt of any vaccine dose before the test date were considered unvaccinated. Additional COVID-NET methods for determining vaccination status have been described previously. https://medrxiv.org/cgi/ content/short/2021.08.27.21262356v1

^{****} https://covid.cdc.gov/covid-data-tracker/#variant-proportions

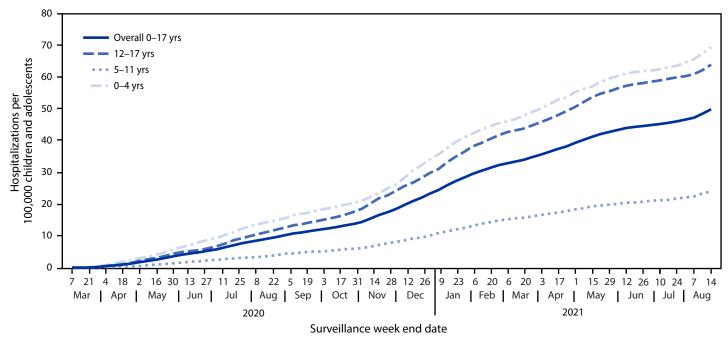
^{†††† 45} C.F.R. part 46.102(l)(2); 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

SSSS Smoothed 3-week running averages are used for visualization purposes in Figure 2; however, raw (nonaveraged) age-specific weekly rates are used in the text of the report. The smoothed 3-week running average rate of COVID-19-associated hospitalizations during the week ending January 9, 2021 (displayed in Figure 2) is 1.3 hospitalizations per 100,000 children and adolescents.

⁵⁵⁵⁵ Among the 3,194 children and adolescents with COVID-19—associated hospitalizations during March 1, 2020—June 19, 2021, a total of 3,116 (97.6%) had data available on hospital length of stay, ICU admission, receipt of IMV or other respiratory support, vasopressor use, and inhospital death at the time of reporting.

^{*****} Among the 191 children and adolescents with COVID-19–associated hospitalizations during June 20, 2020–July 31, 2021, a total of 164 (85.9%) had data available on hospital length of stay, ICU admission, receipt of IMV or other respiratory support, vasopressor use, and inhospital death at the time of reporting.

FIGURE 1. COVID-19–associated cumulative hospitalizations per 100,000 children and adolescents,* by age group — COVID-NET, 14 states,† March 1, 2020–August 14, 2021



* Rates are subject to change as additional data are reported.

an ICU, 16 (9.8%) required IMV, and three (1.8%) died. The differences in these indicators of severe disease between the two periods were not statistically significant (Table).

Discussion

Weekly COVID-19-associated hospitalization rates rose rapidly during late June to mid-August 2021 among U.S. children and adolescents aged 0-17 years; by mid-August, the rate among children aged 0-4 years was nearly 10 times the rate 7 weeks earlier. This increase coincides with widespread circulation of the highly transmissible Delta variant. COVID-NET data indicate that vaccination was highly effective in preventing COVID-19-associated hospitalizations in adolescents during late June to late July 2021. Since March 2020, approximately one in four hospitalized children and adolescents with COVID-19 has required intensive care, although the proportions with indicators of severe disease during the period when the Delta variant predominated were generally similar compared with those earlier in the pandemic. The observed indicators of severe COVID-19 among children and adolescents, as well as the potential for serious longer-term sequelae (e.g., multisystem inflammatory syndrome in children) documented elsewhere (5,6), underscore the importance of implementing multipronged preventive measures to reduce severe COVID-19 disease, including nonpharmaceutical interventions and vaccination among eligible age groups. †††††

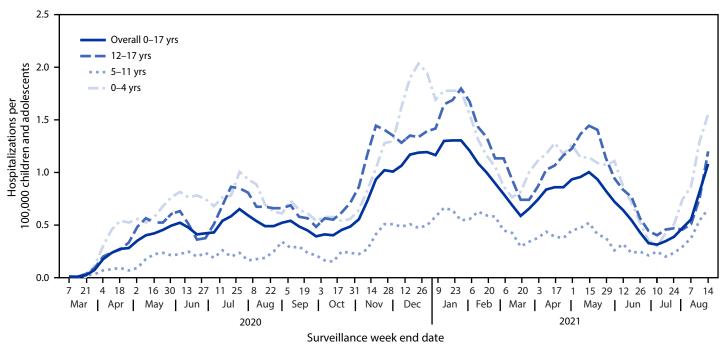
Among adolescents aged 12–17 years, the only pediatric age group for whom a COVID-19 vaccine is currently approved, hospitalization rates were approximately 10 times higher in unvaccinated compared with fully vaccinated adolescents, indicating that vaccines were highly effective at preventing serious COVID-19 illness in this age group during a period when the Delta variant predominated. As of July 31, 2021, 32% of U.S. adolescents had completed a COVID-19 vaccination series (7); increasing vaccination coverage among adolescents, as well as expanding eligibility for COVID-19 vaccination to younger age groups if approved and recommended, is expected to reduce severe COVID-19—associated outcomes among children and adolescents.

Similar to another recent analysis, COVID-NET data suggest that indicators of severe disease among hospitalized children during an early period when the Delta variant predominated were generally similar to those observed earlier in the pandemic (8). Trends in outcomes will need to be monitored closely as more data become available. For example, whereas

[†] Select counties in California, Colorado, Connecticut, Georgia, Iowa, Maryland, Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah.

^{††††††} https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html

FIGURE 2. COVID-19-associated weekly hospitalizations per 100,000 children and adolescents,* by age group — COVID-NET, 14 states,† March 1, 2020-August 14, 2021 (3-week smoothed running averages)§



* Rates are subject to change as additional data are reported.

the point estimate of the proportion of hospitalized children who required IMV during the period of Delta predominance (9.8%) was higher than that earlier in the pandemic (6.1%), the comparison of these proportions was based on a relatively small number of children (16) requiring IMV during the period of Delta predominance, and the difference was not statistically significant (p = 0.06). Further, surveillance data limited to hospitalized persons cannot be used to assess whether increases in COVID-19—associated hospitalization rates among children and adolescents are due to increased community SARS-CoV-2 transmission or increased disease severity caused by the Delta variant.

The findings in this report are subject to at least five limitations. First, children and adolescents meeting COVID-NET criteria with a positive SARS-CoV-2 test result might have been hospitalized primarily for reasons other than COVID-19 (2), resulting in potential overestimations of hospitalization rates. Second, COVID-19—associated hospitalizations might have been missed because of testing practices and test availability. Third, the number of hospitalized children with severe outcomes was small during June 20–July 31, 2021, limiting comparisons between periods before and during Delta variant predominance. Fourth, the number of fully vaccinated hospitalized adolescents remained low at the time of reporting, and

hospitalization rates stratified by vaccination status are subject to error if misclassification of vaccination status occurred. Finally, the COVID-NET catchment areas include approximately 10% of the U.S. population; thus, findings might not be nationally generalizable.

Rates of COVID-19—associated hospitalization among children and adolescents increased rapidly from late June to mid-August 2021, coinciding with predominance of the Delta variant. With more activities resuming, including in-person school attendance and a return of younger children to congregate child care settings, preventive measures to reduce the incidence of severe COVID-19 are critical. Universal indoor masking is recommended for all teachers, staff members, students, and visitors in kindergarten through grade 12 schools, regardless of vaccination status. SSSSS CDC recommends that persons aged ≥2 years who are unvaccinated, as well as vaccinated persons in areas of substantial or high transmission, wear masks in all indoor public spaces. SSSSS CDC also recommends that child care centers serving children too young to be vaccinated consider implementing

[†] Select counties in California, Colorado, Connecticut, Georgia, Iowa, Maryland, Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah.

[§] Smoothed running averages are used for visualization purposes only.

^{\$\$\$\$\$} https://www.cdc.gov/coronavirus/2019-ncov/community/schools-childcare/k-12-guidance.html

⁵⁵⁵⁵⁵ https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated. html

TABLE. Clinical interventions and outcomes among children and adolescents aged 0-17 years during COVID-19-associated hospitalizations—COVID-NET, 14 states,* March 1, 2020–June 19, 2021 and June 20–July 31, 2021

	Children and adole No.				
Interventions and outcomes	March 1, 2020– June 19, 2021 (N = 3,116) [†]	June 20– July 31, 2021 (N = 164)†	p-value [§]		
Hospital length of stay, median (interquartile range)	3 (2–5)	2 (1–4)	0.01		
Outcome					
Died during hospitalization	21 (0.7)	3 (1.8)	0.12		
ICU admission	827 (26.5)	38 (23.2)	0.34		
Vasopressor support	233 (7.5)	13 (7.9)	0.83		
Highest level of respiratory support¶					
High flow nasal cannula	162 (5.2)	13 (7.9)	0.13		
BiPAP/CPAP	131 (4.2)	6 (3.7)	0.73		
Invasive mechanical ventilation	190 (6.1)	16 (9.8)	0.06		

Abbreviations: BiPAP = bilevel positive airway pressure; CPAP = continuous positive airway pressure; ICU = intensive care unit.

- * Select counties in California, Colorado, Connecticut, Georgia, Iowa, Maryland, Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah.
- [†] Includes those with complete clinical data on hospital length of stay, ICU admission, highest level of respiratory support (invasive mechanical ventilation, BiPAP/CPAP, or high flow nasal cannula), vasopressor support, and disposition discharge (i.e., discharged alive or died in-hospital).
- § Medians were compared using a Wilcoxon rank sum test. Proportions were compared using chi square tests. The proportions who died during hospitalization were compared using Fisher's exact test.
- Highest level of respiratory support for each patient that needed respiratory support.

universal indoor masking for persons aged ≥2 years.****** All persons who are eligible should receive COVID-19 vaccines to reduce the risk for severe disease for themselves and others with whom they come into contact, including children who are currently too young to be vaccinated.

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Summary

What is already known about this topic?

COVID-19 can cause severe illness in children and adolescents.

What is added by this report?

Weekly COVID-19—associated hospitalization rates among children and adolescents rose nearly five-fold during late June—mid-August 2021, coinciding with increased circulation of the highly transmissible SARS-CoV-2 Delta variant. The proportions of hospitalized children and adolescents with severe disease were similar before and during the period of Delta predominance. Hospitalization rates were 10 times higher among unvaccinated than among fully vaccinated adolescents.

What are the implications for public health practice?

Preventive measures to reduce transmission and severe outcomes in children and adolescents are critical, including vaccination, universal masking in schools, and masking by persons aged ≥2 years in other indoor public spaces and child care centers.

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^{******} https://www.cdc.gov/coronavirus/2019-ncov/community/schoolschildcare/child-care-guidance.html

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References

- Kim L, Whitaker M, O'Halloran A, et al.; COVID-NET Surveillance Team. Hospitalization rates and characteristics of children aged <18 years hospitalized with laboratory-confirmed COVID-19—COVID-NET, 14 states, March 1–July 25, 2020. MMWR Morb Mortal Wkly Rep 2020;69:1081–8. PMID:32790664 https://doi.org/10.15585/mmwr. mm6932e3
- Havers FP, Whitaker M, Self JL, et al.; COVID-NET Surveillance Team. Hospitalization of adolescents aged 12–17 years with laboratory-confirmed COVID-19—COVID-NET, 14 states, March 1, 2020–April 24, 2021. MMWR Morb Mortal Wkly Rep 2021;70:851–7. PMID:34111061 https://doi.org/10.15585/mmwr.mm7023e1
- Wallace M, Woodworth KR, Gargano JW, et al. The Advisory Committee on Immunization Practices' interim recommendation for use of Pfizer-BioNTech COVID-19 vaccine in adolescents aged 12–15 years—United States, May 2021. MMWR Morb Mortal Wkly Rep 2021;70:749–52. PMID:34014913 https://doi.org/10.15585/mmwr.mm7020e1
- 4. Nanduri S, Pilishvili T, Derado G, et al. Effectiveness of Pfizer-BioNTech and Moderna vaccines in preventing SARS-CoV-2 infection among nursing home residents before and during widespread circulation of the SARS-CoV-2 B.1.617.2 (Delta) variant—National Healthcare Safety Network, March 1–August 1, 2021. MMWR Morb Mortal Wkly Rep 2021;70:1163–6. PMID:34437519 https://doi.org/10.15585/mmwr.mm7034e3
- Buonsenso D, Munblit D, De Rose C, et al. Preliminary evidence on long COVID in children. Acta Paediatr 2021;110:2208–11. PMID:33835507 https://doi.org/10.1111/apa.15870
- Feldstein LR, Rose EB, Horwitz SM, et al.; Overcoming COVID-19 Investigators; CDC COVID-19 Response Team. Multisystem inflammatory syndrome in U.S. children and adolescents. N Engl J Med 2020;383:334–46. PMID:32598831 https://doi.org/10.1056/ NEJMoa2021680
- 7. Murthy BP, Zell E, Saelee R, et al. COVID-19 vaccination coverage among adolescents aged 12–17 years—United States, December 14, 2020–July 31, 2021. MMWR Morb Mortal Wkly Rep 2021;70:1206–13.
- Siegel DA, Reses HE, Cool AJ, et al. Trends in COVID-19 cases, emergency department visits, and hospital admissions among children and adolescents aged 0–17 years—United States, August 2020– August 2021. MMWR Morb Mortal Wkly Rep 2021. Epub September 3, 2021.

Notes from the Field

Tuberculosis Outbreak Linked to a Contaminated Bone Graft Product Used in Spinal Surgery — Delaware, March–June 2021

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On May 25, 2021, a Delaware acute care hospital notified the Delaware Division of Public Health (DPH) of seven patients who developed tuberculosis after spinal surgery during March–April 2021. Hospital staff members identified a single common exposure: implantation of bone allograft material (product A) from a single product lot. DPH notified CDC, requested a field investigation, and issued a nationwide call for cases. In collaboration with the Food and Drug Administration, a CDC team was deployed to Delaware on June 2 to investigate the epidemiology of cases and opportunities for transmission and to provide prevention and treatment recommendations. On the same day, another state health department notified CDC about a person who developed tuberculosis after surgery involving the same product A lot, and the manufacturer issued a voluntary nationwide recall (1).

Investigators abstracted clinical, laboratory, and imaging data from medical records and interviewed patients. They also assessed potential exposures to *Mycobacterium tuberculosis* related to product A storage, handling, and use during surgery; reprocessing of surgical instruments; and patient care. This investigation was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[†]

Twenty-three patients at the hospital underwent surgery that involved the recalled product lot. The median patient age was 66 years (range = 37–80 years). No patient had an immunocompromising condition. § One patient had a history of latent tuberculosis infection and completed treatment in 2003. Nineteen (83%) patients reported new symptoms beginning 2–66 days (median = 19 days) after product implantation (Figure). Fifteen (65%) patients reported constitutional signs

*These authors contributed equally to this report.

and symptoms, including fever, chills, night sweats, weight loss, fatigue, and loss of appetite; 16 (70%) had redness, pain, or drainage at the surgical site; four (17%) experienced neurologic symptoms, including paresthesia and dysphagia; and seven (30%) experienced pulmonary symptoms, including cough and shortness of breath. Four (17%) patients were asymptomatic. Sixteen (70%) required hospital readmission 23–84 days after product implantation (median = 52 days). Twelve (52%) underwent additional surgical procedures to manage complications of infection. One patient died at home 3 weeks after product implantation, which was 2 months before the product recall.

As of June 25, 19 (83%) of the 23 patients had laboratory or imaging evidence of tuberculosis in the spine or chest. Among 19 patients who had received microbiologic testing of a vertebral, paraspinal soft tissue, or sputum specimen, 15 (79%) had a positive acid-fast bacilli smear, M. tuberculosis nucleic acid amplification test, or culture. Among 21 patients who had received spinal imaging, 19 (90%) had findings consistent with infection, including abscesses (17, 81%) and osteomyelitis or discitis (eight, 38%). Among 21 patients with sputum testing or chest imaging, six (28%) demonstrated evidence of pulmonary tuberculosis, suggesting bloodborne dissemination of *M. tuberculosis*. Isolates cultured from specimens from three patient specimens were susceptible to all first-line medications and shared a genotype not previously identified in the United States; drug-susceptibility testing and genotyping of subsequent isolates were pending. All 22 living patients began standard four-drug treatment for drug-susceptible tuberculosis 41–91 days after product implantation (median = 69 days).

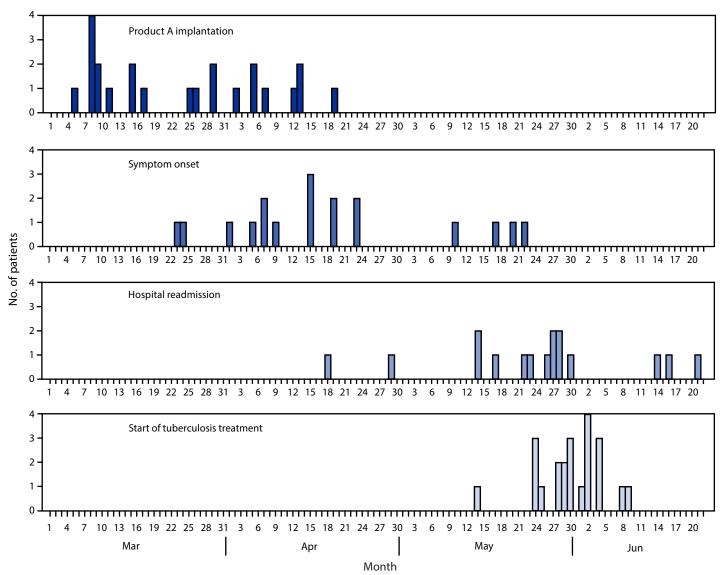
Product A was shipped frozen and was opened inside the operating room. Health care personnel could have been exposed to *M. tuberculosis* during product A implantation and subsequent procedures involving suctioning, drilling, wound irrigation, and decontamination of cannulated instruments. In addition, health care personnel and patients could have been exposed to *M. tuberculosis* from patients who had received implantations with product A and subsequently developed draining tuberculous lesions or pulmonary tuberculosis (2–4). As of June 24, the hospital had identified 152 health care personnel and seven patients who were exposed to recipients of product A who had tuberculous abscesses or pulmonary tuberculosis; investigations are ongoing to identify additional exposures.

This investigation found high attack rates of spinal and disseminated tuberculosis after surgical implantation of product A and multiple opportunities for *M. tuberculosis* exposure related to surgery and patient care. On June 4, CDC recommended

[†] 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.

[§] Eight patients had diabetes mellitus and two patients had chronic kidney disease, stage 2–3.

FIGURE. Time line of product implantation, symptom onset,* hospital readmission,† and start of tuberculosis treatment§ in patients exposed to product A^{\P} (N = 23) — Delaware, March–June 2021



^{*} Excludes one patient with insidious onset of weight loss.

that all patients nationwide who had undergone surgery involving the affected product A lot be immediately assessed and begin the four-drug treatment for tuberculosis disease, even if they were asymptomatic. On June 8, CDC recommended evaluation of contacts in health care settings, including risk assessment, symptom screening, and an interferon-gamma release assay or tuberculin skin test (3,4).

M. tuberculosis transmission via bone graft was last described in 1953 (5). The hospital's rapid detection of this unusual

cluster triggered a multistate investigation resulting in sequestration of all unused units of the contaminated product, identification of all patients who underwent surgical procedures with the contaminated product lot, and initiation of tuberculosis treatment by all living patients. Public health authorities and health care facilities should continue efforts to identify and evaluate all exposed contacts and identify opportunities to prevent *M. tuberculosis* exposures from contaminated tissues or other products.

[†] One patient was readmitted 4 days after product implantation with a surgical site infection caused by nonmycobacterial species; this readmission was excluded from the figure. The patient subsequently developed worsening lumbar back pain and was readmitted with a tuberculous abscess; this subsequent symptom onset and readmission were included in the figure.

[§] All 22 living patients have started tuberculosis treatment. One patient died 3 weeks after product implantation, before the tuberculosis outbreak was recognized.

Numbers of patients in each category are as follows: product A implantation = 23 patients; symptom onset = 18; readmission = 16; start of tuberculosis treatment = 22.

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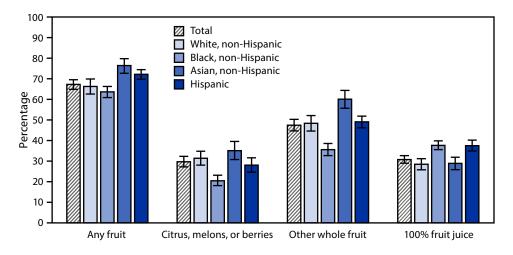
References

- Food and Drug Administration. Urgent voluntary notification: FiberCel Fiber Viable Bone Matrix ("FiberCel")—lot number: NMDS210011. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2021. https://www.fda.gov/vaccines-blood-biologics/recalls-biologics/urgent-voluntary-notification-fibercel-fiber-viable-bone-matrix-fibercel-lot-number-nmds210011
- Hutton MD, Stead WW, Cauthen GM, Bloch AB, Ewing WM. Nosocomial transmission of tuberculosis associated with a draining abscess. J Infect Dis 1990;161:286–95 PMID:2105362https://doi. org/10.1093/infdis/161.2.286.
- Siegel JD, Rhinehart E, Jackson M, Chiarello L; Healthcare Infection Control Practices Advisory Committee. 2007 Guideline for isolation precautions: preventing transmission of infectious agents in healthcare settings. Atlanta, GA: US Department of Health and Human Services, CDC; 2019. https://www.cdc.gov/infectioncontrol/pdf/guidelines/ isolation-guidelines-H.pdf
- National Tuberculosis Controllers Association. CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis. Recommendations from the National Tuberculosis Controllers Association and CDC. MMWR Recomm Rep 2005;54(No. RR-15).
- James JI. Tuberculosis transmitted by banked bone. J Bone Joint Surg Br 1953;35-B:578 PMID:13108919https://doi.org/10.1302/0301-620X.35B4.578.

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FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage*,[†] of Adults Aged ≥20 Years Who Consumed Fruit on a Given Day, by Race and Hispanic Origin§ — United States, 2015–2018



^{*} Percentages are based on fruit reported during the 24-hour dietary recall, day 1. Fruits were defined using U.S. Department of Agriculture's Food Patterns Equivalents Database food groups. https://www.ars.usda.gov/ARSUserFiles/80400530/pdf/fped/FPED_1718.pdf

During 2015–2018, on a given day, 67.3% of adults aged ≥20 years consumed any fruit; 29.7% consumed citrus, melons, or berries; 47.5% consumed other whole fruits; and 30.8% consumed 100% fruit juice. Non-Hispanic Asian (76.5%) and Hispanic adults (72.2%) were more likely to consume any fruit on a given day than non-Hispanic White (66.3%) and non-Hispanic Black adults (63.7%). Non-Hispanic Black adults were least likely to consume citrus, melons, or berries (20.5%) and other whole fruit (35.6%), and non-Hispanic Asian adults were most likely to consume other whole fruits (60.1%). A higher percentage of non-Hispanic Black (37.7%) and Hispanic (37.5%) adults consumed 100% fruit juice compared with non-Hispanic White (28.5%) and non-Hispanic Asian (28.9%) adults.

Source: NCHS Data Brief, no. 397, National Center for Health Statistics. https://www.cdc.gov/nchs/data/databriefs/db397-H.pdf **Reported by:** Nicholas Ansai, MPH, qjk0@cdc.gov, 301-458-4385; Edwina Wambogo, PhD; Ana Terry, MS.

[†] 95% confidence intervals indicated with error bars.

[§] Estimates for persons reporting more than one race are not shown separately but are included in the total.

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