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Enterovirus D68-Associated Acute Respiratory Illness — New Vaccine Surveillance Network, United States, July–November 2018–2020

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Enterovirus D68 (EV-D68) is associated with a broad spectrum of illnesses, including mild to severe acute respiratory illness (ARI) and acute flaccid myelitis (AFM). Enteroviruses, including EV-D68, are typically detected in the United States during late summer through fall, with year-to-year fluctuations. Before 2014, EV-D68 was infrequently reported to CDC (*1*). However, numbers of EV-D68 detection have increased in recent years, with a biennial pattern observed during 2014–2018 in the United States, after the expansion of surveillance and wider availability of molecular testing. In 2014, a national outbreak of EV-D68 was detected (*2*). EV-D68 was also reported in 2016 via local (*3*) and passive national (*4*) surveillance. EV-D68 detections were limited in 2017, but substantial circulation was observed in 2018 (*5*). To assess recent levels of circulation, EV-D68 detections in respiratory specimens collected from patients aged <18 years* with ARI evaluated in emergency departments (EDs) or admitted to one of seven U.S. medical centers† within the New Vaccine Surveillance Network (NVSN) were summarized. This report provides a provisional description of EV-D68 detections during July–November in 2018, 2019 and 2020, and describes the demographic and clinical characteristics of these patients. In 2018, a total of 382 EV-D68 detections in respiratory specimens obtained from patients aged <18 years with ARI were reported by NVSN; the number decreased to six detections in 2019 and 30 in 2020. Among patients aged <18 years with EV-D68 in 2020, 22 (73%) were non-Hispanic Black (Black) persons. EV-D68 detections in 2020 were lower than anticipated based on the biennial circulation pattern observed since 2014. The circulation of EV-D68 in 2020 might have been limited by widespread COVID-19 mitigation measures;

* Patients were aged <18 years; the youngest patient included in the analysis was aged 2 days.

† The seven sites were in Cincinnati, Ohio; Houston, Texas; Kansas City, Missouri; Nashville, Tennessee; Pittsburgh, Pennsylvania; Rochester, New York; and Seattle, Washington.

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how these changes in behavior might influence the timing and levels of circulation in future years is unknown. Ongoing monitoring of EV-D68 detections is warranted for preparedness for EV-D68-associated ARI and AFM.

Since 2017, active, population-based, prospective surveillance of EV-D68–associated ARI among patients aged <18 years has been conducted by seven medical institutions in NVSN.[§] Respiratory specimens are collected from pediatric patients experiencing ARI (including fever or respiratory symptoms) who are evaluated in EDs or inpatient settings within NVSN. For this study, specimens collected during July–November were tested for EV-D68 using a validated CDC-developed real-time reverse transcription–polymerase chain reaction assay (*5*). EV-D68 testing algorithms differed by site.[¶] Demographic and clinical data were collected from medical charts or enrollment interviews. This ARI surveillance platform was not designed to capture neurologic outcomes, such as AFM. Detections of EV-D68 in respiratory specimens during July–November in 2018, 2019, and 2020 were assessed by month, site, sex, race/ethnicity, age group, and comorbidities; characteristics were compared by year using univariable chi-square or Wilcoxon rank-sum tests. EV-D68 detections during July–October 2018 have been previously reported (*5*). For comparison with 2019 and 2020 data, 2018 data were reanalyzed to include July–November. Available EV-D68–positive specimens from 2020 were submitted to CDC for sequencing. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[**]

Provisional data from July–November indicated that 3,546 (2018), 3,769 (2019), and 2,189 (2020) patients with ARI were tested for EV-D68 across NVSN. Despite approximately 40% fewer patients aged <18 years being tested during 2020 than in 2018 and 2019, the percentage with a positive rhinovirus or enterovirus (RV/EV) test result remained similar (range = 37.0%–44.2%) (Table 1). Among all patients aged <18 years with ARI tested during July–November, EV-D68 was detected in 382 of 3,546 (10.8%) in 2018, but in only six of 3,769 (0.2%) in 2019 and 30 of 2,189 (1.4%) in 2020; among patients with positive RV/EV test results, EV-D68 was detected in 24.3%, 0.4%, and 3.6% in 2018, 2019, and 2020, respectively. EV-D68 was detected at all seven sites in 2018, at four sites in 2019 and at six sites in 2020 (Figure). During 2018, the highest number of EV-D68 detections occurred in September, and the timing of detections varied by site (Figure); in 2020, October had the highest number of

[§] https://www.cdc.gov/surveillance/nvsn/index.html

[¶] The sites in Nashville and Pittsburgh test all NVSN specimens with a pan-rhinovirus assay (which also detects some enteroviruses because of cross-reactivity) and an EV-D68 assay. The sites in Houston and Rochester conduct a pan-rhinovirus and a pan-enterovirus assay, and if either is positive, a specific EV-D68 assay is conducted. The other three sites (Cincinnati, Kansas City, and Seattle) use a combined rhinovirus/enterovirus assay and if positive, a specific EV-D68 assay is conducted.

[**] 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.

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TABLE 1. Cases of acute respiratory illness and detections of rhinovirus or enterovirus and enterovirus D68 in pediatric* respiratory specimens, by site† and year§ — New Vaccine Surveillance Network, United States, July–November 2018, 2019, and 2020

	2018			2019			2020		
NVSN site	Total ARI	RV/EV positive (% ARI)	EV-D68 positive (% RV/EV)	Total ARI	RV/EV positive (% ARI)	EV-D68 positive (% RV/EV)	Total ARI	RV/EV positive (% ARI)	EV-D68 positive (% RV/EV)
All sites	**3,546**	**1,569 (44.2)**	**382 (24.3)**	**3,769**	**1,393 (37.0)**	**6 (0.4)**	**2,189**	**841 (38.4)**	**30 (3.6)**
Cincinnati	489	169 (34.6)	56 (33.1)	552	99 (17.9)	0 (—)	468	132 (28.2)	3 (2.3)
Houston	525	156 (29.7)	28 (17.9)	527	183 (34.7)	2 (1.1)	324	81 (25.0)	3 (3.7)
Kansas City	565	306 (54.2)	54 (17.6)	631	282 (44.7)	1 (0.4)	478	244 (51.0)	16 (6.6)
Nashville	673	202 (30.0)	47 (23.3)	611	95 (15.5)	1 (1.1)	168	66 (39.3)	6 (9.1)
Pittsburgh	689	384 (55.7)	96 (25.0)	698	369 (52.9)	0 (—)	331	191 (57.7)	1 (0.5)
Rochester	308	173 (56.2)	63 (36.4)	471	233 (49.5)	0 (—)	181	62 (34.3)	1 (1.6)
Seattle	297	179 (60.3)	38 (21.2)	279	132 (47.3)	2 (1.5)	239	65 (27.2)	0 (—)

Abbreviations: ARI = acute respiratory illness; RV/EV = rhinovirus or enterovirus; EV-D68 = enterovirus D68.

* Patients were aged <18 years; the youngest patient included in the analysis was aged 2 days.

† The seven sites were in Cincinnati, Ohio; Houston, Texas; Kansas City, Missouri; Nashville, Tennessee; Pittsburgh, Pennsylvania; Rochester, New York; and Seattle, Washington. EV-D68 testing algorithms differed slightly across sites. Nashville and Pittsburgh sites test all ARI specimens directly for EV-D68; the other five sites (Cincinnati, Houston, Kansas City, Rochester, and Seattle) first test ARI specimens for RV/EV, and then test RV/EV-positive specimens for EV-D68. Because the Nashville and Pittsburgh sites test ARI specimens for RV and EV-D68 but no other EVs, the total number of RV/EV detections might be underestimated. For the Nashville and Pittsburgh sites, the total number of RV/EVs reported represents specimens positive for RV and/or EV-D68.

§ Updated data through November provided for direct comparison; preliminary data for July–October 2018 were previously reported. https://www.cdc.gov/mmwr/volumes/68/wr/mm6812a1.htm

detections. In 2020, 16 of 30 detections (53.3%) occurred in Kansas City, Missouri. Among 23 EV-D68–positive specimens sequenced from 2020, all were clade D.

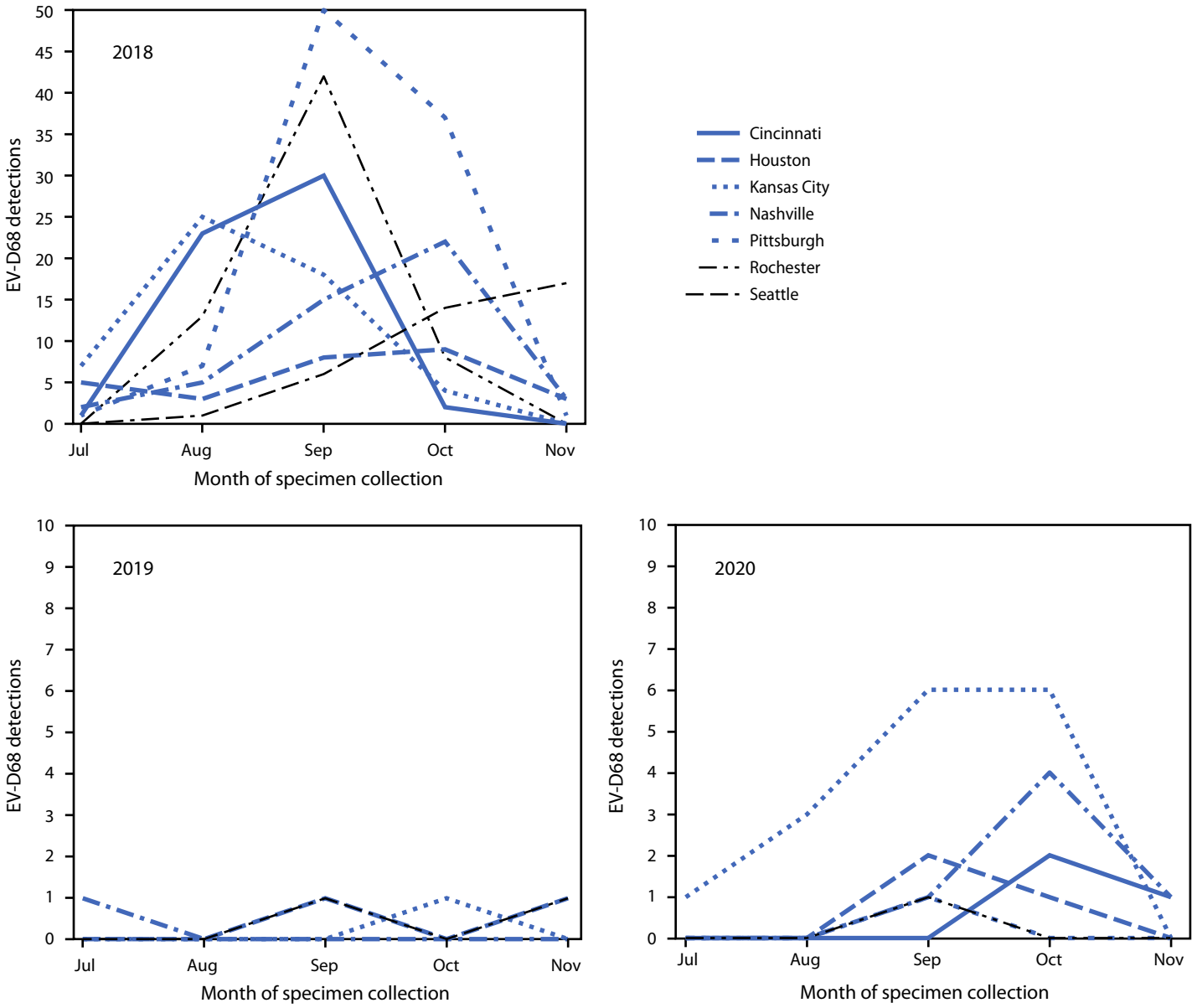
Among 30 patients aged <18 years with EV-D68 in 2020, the median age was 5.3 years, 19 (63.3%) were female, and 15 (50%) required inpatient care (one of whom required mechanical ventilation); none of the patients died (Table 2). Nasal congestion or rhinorrhea, cough, dyspnea, or wheezing were reported in >80% of patients. Asthma or reactive airway disease (RAD) were reported in nearly one half (14; 46.7%) of patients in whom EV-D68 was detected. Compared with the same time frame in 2018, when the median age was 2.9 years and 39.3% of patients with EV-D68–positive respiratory specimens were female, those in 2020 were older ($p = 0.04$) and more frequently female ($p = 0.01$).

Among 382 patients with EV-D68–positive specimens in 2018, 53 (13.9%) were Hispanic persons, 125 (32.7%) were non-Hispanic White (White) persons and 161 (42.1%) were Black persons. During the study period in 2019, among six patients with EV-D68–positive specimens, one person was Black and four were Hispanic persons. During the study period in 2020, among 30 patients with EV-D68–positive specimens, three (10.0%) persons were Hispanic, one (3.3%) was White, and 22 (73.3%) were Black. This race/ethnicity distribution was observed during the 2020 study period even after the site in Kansas City, Missouri was excluded, which accounted for approximately one half the cases. In contrast, the race/ethnicity distribution of all patients in NVSN sites with RV/EV was similar across all 3 years, with the proportion of Black persons ranging from 35.0% to 38.3%.

Discussion

Across all study sites, detection of EV-D68 in respiratory specimens collected from patients with ARI remained low during 2019 and 2020, accounting for 0.4% and 3.6% of RV/EV detections, respectively compared with 24.3% of RV/EV detections during 2018. Similar to 2019, EV-D68 represented only 0.3% RV/EV detections among NVSN sites during July–October 2017 (*5*). EV-D68 clade D was detected in 2020, whereas clade B3 was detected among NVSN sites in 2018 (*5*). Because the numbers of EV-D68 detections reported from local and national surveillance both within and outside NVSN during 2014, 2016, and 2018 were higher compared with 2015, 2017, and 2019, a biennial pattern of circulation had been postulated, and high circulation in 2020 was anticipated. Instead, EV-D68 circulation in NVSN in 2020 appeared only slightly higher than that in 2019 and 2017, but notably lower than that in 2018, with some variations in 2020 by site. As reported for other respiratory viruses (*6*), the lower EV-D68 circulation observed in 2020 might reflect interrupted transmission resulting from COVID-19 mitigation measures including wearing a mask, physical distancing, attention to hand hygiene, and school closures. However, the long-term stability of this biennial pattern of EV-D68 circulation was uncertain even before the COVID-19 pandemic (*7*), making the contribution of COVID-19 mitigation measures to low EV-D68 circulation in 2020 unclear. COVID-19 mitigation measures have been theorized to be less effective at reducing RV/EV circulation compared with that of other respiratory

FIGURE. Enterovirus D68 detections, by month and site of specimen collection — New Vaccine Surveillance Network,*,† United States, July–November 2018, 2019, and 2020



Abbreviation: EV-D68 = enterovirus D68.

* The seven sites were in Cincinnati, Ohio; Houston, Texas; Kansas City, Missouri; Nashville, Tennessee; Pittsburgh, Pennsylvania; Rochester, New York; and Seattle, Washington.

† Only sites with EV-D68 detections during that year are shown. During July–November 2019, there were no EV-D68 detections in Cincinnati, Pittsburgh, or Rochester. During July–November 2020, there were no EV-D68 detections in Seattle.

virus types because of differences in stability, transmission route, or rates of asymptomatic transmission (*6*). More information is needed to better understand which RV/EV species and types persisted in 2020, and why detections of EV-D68 were limited. Furthermore, the implications for future EV-D68 circulation are unknown, and continued monitoring is needed.

Although overall detections of EV-D68 were low, severe respiratory illness was observed in infected patients aged <18 years during 2019 and 2020, with one half of patients requiring inpatient admission. Approximately one half of the patients aged <18 years with EV-D68–positive respiratory specimens in 2020 had underlying asthma/RAD, which has been previously associated with EV-D68 (*2*). EV-D68–associated severe respiratory illness continues to be a significant medical concern warranting monitoring and preparedness. In addition, EV-D68 is associated with AFM, a rare but debilitating

TABLE 2. Demographic and clinical characteristics of patients* evaluated for acute respiratory illness who had positive enterovirus D68 test results — New Vaccine Surveillance Network,† United States, July–November 2018, 2019, and 2020

Characteristic	No. (%)		
	2018	2019	2020
Total	**382 (100)**	**6 (100)**	**30 (100)**
Age group, yrs			
Median (IQR)	2.9 (1.4–5.1)	7.3 (1.5–12.2)	5.3 (1.7–9.0)
<5	284 (74.3)	3 (50.0)	14 (46.7)
5–17	98 (25.7)	3 (50.0)	16 (53.3)
Sex			
Female	150 (39.3)	2 (33.3)	19 (63.3)
Male	232 (60.7)	4 (66.7)	11 (36.7)
Race/Ethnicity			
Hispanic	53 (13.9)	4 (66.7)	3 (10.0)
Black, non-Hispanic	161 (42.1)	1 (16.7)	22 (73.3)
White, non-Hispanic	125 (32.7)	0 (—)	1 (3.3)
Other, non-Hispanic	42 (11.0)	1 (16.7)	4 (13.3)
Unknown	1 (0.3)	0 (—)	0 (—)
Comorbidities			
Asthma or reactive airway disease	139 (36.4)	2 (33.3)	14 (46.7)
Atopy/Allergic condition (excluding asthma)	75 (19.6)	1 (16.7)	10 (33.3)
Signs/Symptoms			
Cough	372 (97.4)	6 (100.0)	27 (90.0)
Nasal congestion/Rhinorrhea	324 (84.8)	5 (83.3)	29 (96.7)
Wheezing	317 (83.0)	6 (100.0)	23 (76.7)
Dyspnea	342 (89.5)	6 (100.0)	25 (83.3)
Hospital status			
Treated in ED, not admitted	125 (32.7)	1 (16.7)	15 (50.0)
Admitted	257 (67.3)	5 (83.3)	15 (50.0)

Abbreviation: ED = emergency department.
* Patients were aged <18 years; the youngest patient included in the analysis was aged 2 days.
† The seven sites were in Cincinnati, Ohio; Houston, Texas; Kansas City, Missouri; Nashville, Tennessee; Pittsburgh, Pennsylvania; Rochester, New York; and Seattle, Washington.

neurologic condition characterized by flaccid limb weakness or paralysis which has been increasingly recognized in recent years.†† Similar to the low number of EV-D68–associated ARI cases in 2020 described in this report, national reports of AFM were also low during 2020 (*8*).

Among 36 patients aged <18 years with EV-D68 detected in respiratory specimens in 2019 and 2020, most were Black persons or Hispanic persons. Health disparities by race and ethnicity have been reported previously for multiple respiratory viruses (*9*), and possibly EV-D68 (*10*). Additional years of NVSN data are needed to better understand potential health disparities related to EV-D68 infection. Disparities might arise from multiple factors including differences by race in asthma prevalence,§§ differences in access to health care and preventive measures, or higher risk of EV-D68 exposure or severe disease.

The findings in this report are subject to at least four limitations. First, the results are not representative of the entire year and might underestimate EV-D68 detections. However, this report describes EV-D68 testing during July–November when enterovirus detections are highest in the United States. Second, although NVSN surveillance sites are located across the United States, they might not be representative of all regions nationwide. Third, the inclusion of data for only 3 years as well as the small number of EV-D68 detections in 2020 limited multivariable analyses. Finally, NVSN enrollment was lower in 2020, compared with previous years, and health care–seeking behaviors might have been different because of the COVID-19 pandemic.

Circulation of EV-D68 in 2020 might have been limited by widespread COVID-19 mitigation measures, and changing mitigation measures might influence future EV-D68 circulation patterns. Continued monitoring of EV-D68 circulation is critical to guiding clinical and public health preparedness for both EV-D68–associated ARI and AFM.

†† https://www.cdc.gov/acute-flaccid-myelitis/index.html
§§ https://www.cdc.gov/asthma/most_recent_national_asthma_data.htm (Accessed November 19, 2021).

Summary

What is already known about this topic?

Enterovirus D68 (EV-D68) is associated with acute respiratory illness (ARI) and acute flaccid myelitis. Annual U.S. detections of EV-D68 in respiratory specimens vary; biennial circulation was observed during 2014–2018.

What is added by this report?

During July–November 2019 and 2020, six and 30 EV-D68 detections, respectively, were identified in children with ARI enrolled in the seven New Vaccine Surveillance Network sites, representing 0.2% and 1.4% of children with ARI; most patients with EV-D68 were Hispanic or Black persons.

What are the implications for public health practice?

EV-D68 is an important pediatric pathogen causing respiratory disease. Circulation in 2020 was lower than anticipated; implications for future circulation are unknown. Continued monitoring and characterization of EV-D68 are critical.

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Forced Sexual Initiation and Early Sexual Debut and Associated Risk Factors and Health Problems Among Adolescent Girls and Young Women — Violence Against Children and Youth Surveys, Nine PEPFAR Countries, 2007–2018

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Adolescent girls and young women aged 13–24 years are disproportionately affected by HIV in sub-Saharan Africa (*1*), resulting from biologic, behavioral, and structural* factors, including violence. Girls in sub-Saharan Africa also experience sexual violence at higher rates than do boys (*2*), and women who experience intimate partner violence have 1.3–2.0 times the odds of acquiring HIV infection, compared with those who do not (*3*). Violence Against Children and Youth Survey (VACS) data during 2007–2018 from nine countries funded by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) were analyzed to estimate prevalence and assess factors associated with early sexual debut and forced sexual initiation.† Among adolescent girls and young women aged 13–24 years who ever had sex, the prevalence of lifetime sexual violence ranged from 12.5% to 49.3%, and forced sexual initiation ranged from 14.7% to 38.9%; early sexual debut among adolescent girls and young women aged 16–24 years ranged from 14.4% to 40.1%. In multiple logistic regression models, forced sexual initiation was associated with being unmarried, violence victimization, risky sexual behaviors, sexually transmitted infections (STIs), and poor mental health. Early sexual debut was associated with lower education, marriage, ever witnessing parental intimate partner violence during childhood, risky sexual behaviors, poor mental health, and less HIV testing. Comprehensive violence and HIV prevention programming is needed to delay sexual debut and protect adolescent girls and young women from forced sex.

VACS are nationally representative, multistage cluster household surveys of persons aged 13–24 years. All study protocols included oral informed consent, parental consent for minors, safeguards to protect privacy and confidentiality of participants, and referrals to postviolence care as needed.§ CDC and in-country Institutional Review Boards approved study protocols.¶ This report examines lifetime experiences of sexual violence, early sexual debut, and forced sexual initiation among adolescent girls and young women aged 13–24 years in Eswatini,** Haiti, Kenya, Malawi, Nigeria, Tanzania, Uganda, Zambia, and Zimbabwe, using 2007–2018 data from VACS.†† Lifetime sexual violence included ever experiencing 1) unwanted sexual touching, 2) unwanted attempted sex, 3) pressured or coerced sex, or 4) physically forced sex. Early sexual debut was defined as first sexual intercourse at or before age 15 years among adolescent girls and young women aged 16–24 years who had ever had sex with or without violence. Forced sexual initiation was defined as pressured, coerced, or physically forced first sex among adolescent girls or young women aged 13–24 years who had ever had sex. Orphan status was defined as having one or both parents deceased before the 18th birthday. Weighted prevalences of lifetime sexual violence, early sexual debut, and forced sexual initiation were estimated for each country using SAS (version 9.4; SAS Institute); prevalences were weighted to the most recent census or population projections to account for the multistage cluster design and nonresponse. Multiple logistic regression models were fit to the data combined across all countries to examine the odds of forced sexual initiation and early sexual debut by demographic characteristics and childhood experiences and health problems and behaviors. These models included a fixed

* Structural factors include gender-based violence, child sexual abuse, orphanhood, low education level, spousal separation, harmful gender and societal norms, gender inequity, and unequal power.

† Detailed information about individual country survey partners, methodology, sampling design, samples, and response rates is available in VACS country reports. https://www.cdc.gov/violenceprevention/childabuseandneglect/vacs/reports.html

§ https://www.cdc.gov/violenceprevention/pdf/vacs/VACS-trainingwhitepaper.pdf

¶ This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy (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.). Detailed information about institutional review boards is available in VACS country reports. https://www.cdc.gov/violenceprevention/childabuseandneglect/vacs/reports.html

** Formerly Swaziland.

†† Eswatini: 2007, Tanzania: 2009, Haiti: 2013, Malawi: 2013, Nigeria: 2014, Zambia: 2014, Uganda: 2015, Zimbabwe: 2017, and Kenya: 2018.

effect for country and accounted for survey design, including stratification and clustering, and were adjusted to control for age and marital status.

Prevalence of lifetime sexual violence among adolescent girls and young women varied across countries, ranging from 12.5% (Zimbabwe) to 49.3% (Eswatini) (Table 1). Among those who had ever had sex, the prevalence of forced sexual initiation ranged from 14.7% (Zimbabwe) to 38.9% (Malawi) and early sexual debut ranged from 14.4% (Zimbabwe) to 40.1% (Nigeria). Among adolescent girls and young women who had ever had sex, the odds of having experienced forced sexual initiation were elevated among those aged 13–15 years (adjusted odds ratio [aOR] = 1.77), those who experienced nonpenetrative sexual violence during childhood (aOR = 2.38) and who experienced emotional violence during childhood (aOR = 1.44) (Table 2). Odds were lower among those who were ever married or cohabitating (aOR = 0.47) and those who never attended school (aOR = 0.56). The odds of early sexual debut were higher among adolescent girls and young women aged 16–19 years (aOR = 3.29), those who had no education (aOR = 5.16) or less than primary education (aOR = 2.19), were ever married or cohabitating (aOR = 3.03), or who had witnessed parental intimate partner violence before age 18 years (aOR = 1.31). The odds of forced sexual initiation or early sexual debut did not differ by orphan status, childhood physical violence, or witnessing violence in the community during childhood.

Compared with adolescent girls and young women who did not experience forced sexual initiation, those who did had elevated odds of engaging in transactional sex[§§] during the past 12 months (aOR = 1.6), infrequent condom use during the past 12 months (among those who were never married) (aOR = 1.7), ever having had an STI (aOR = 1.6), experiencing one or more (aOR = 2.8) and two or more (aOR = 2.6) types of violence during the past 12 months, having recent moderate or severe mental distress (aOR = 1.6), and ever having suicidal thoughts (aOR = 2.1) (Table 3). Compared with those who did not experience early sexual debut, those who did had increased odds of having multiple sexual partners during the past 12 months (aOR = 1.7), infrequent condom use among those who were ever married (aOR = 2.1) or never married (aOR = 1.9), having recent moderate or severe mental distress (aOR = 1.5), and ever having attempted suicide (among those who ever thought of suicide) (aOR = 2.1). The odds were lower for ever having been tested for HIV (aOR = 0.4) and having been tested during the past year (aOR = 0.5). The odds of alcohol abuse did not differ among those who did and did not experience forced sexual initiation or early sexual debut.

[§§] Sex in exchange for money, favors, or material support.

Discussion

Sexual violence, forced sexual initiation, and early sexual debut were common among adolescent girls and young women in the nine countries examined. Increased odds of risky sexual behaviors among adolescent girls and young women who experienced forced sexual initiation and early sexual debut suggest that those with negative early sexual experiences are at increased risk for HIV acquisition. Forced sexual initiation was associated with having experienced violence during childhood and multiple types of recent violence, highlighting the complex interplay between early sexual experiences and violence. Association of forced sexual initiation and early sexual debut with recent mental distress, as well as with lifetime suicidal ideation and attempted suicide, indicate the deep and lasting impact of early or forced first sex on mental health.

These findings are consistent with previous studies showing that sexual violence, early sexual debut, and forced sexual initiation are associated with HIV acquisition and risky sexual behaviors (*4*,*5*). These findings also corroborate previous work relating recent violence with infrequent condom use and poor mental health (*6*) and underscore the need to provide post-violence care and mental health services for adolescent girls and young women to lower HIV risk (*7*). In these analyses, adolescent girls and young women who experienced early sexual debut had lower HIV testing rates despite higher HIV risk behaviors, indicating a need to reach girls who have early sexual debut for HIV testing services. These findings reinforce the importance of primary prevention of sexual violence and delayed sexual initiation as essential elements of HIV prevention and control (*8*).

The high prevalence of forced sexual initiation among the youngest members of this population who ever had sex demonstrates a need for sexual violence prevention programs to include girls aged <13 years. The following subgroups should be targeted for sexual violence prevention: in-school and never-married adolescent girls and young women, those who experienced sexual violence or emotional violence in childhood or forced sex, and families of adolescent girls and young women and their communities. In addition to encouraging girls to stay in school, programs might target adolescent girls and young women with primary education or less and those out of school, at risk for early marriage, and who witnessed parental intimate partner violence in childhood with programs to delay early sexual debut. Programs can adopt approaches from INSPIRE's seven strategies for ending violence against

TABLE 1. Prevalence of sexual violence, forced sexual initiation, and early sexual debut among adolescent girls and young women aged 13–24 years — Violence Against Children and Youth Surveys, nine countries, 2007–2018

Country (survey yr)	Lifetime sexual violence*		Forced sexual initiation†		Early sexual debut§	
	No.	Weighted prevalence,¶ % (95% CI)	No.	Weighted prevalence,¶ % (95% CI)	No.	Weighted prevalence,¶ % (95% CI)
Eswatini** (2007)	1,232	49.3 (45.0–53.6)	646	19.5 (15.1–23.9)	620	16.8 (13.2–20.4)
Haiti (2013)	1,438	40.3 (36.7–43.8)	733	23.5 (19.9–27.0)	682	32.6 (28.4–36.8)
Kenya (2018)	1,335	25.5(22.5–28.5)	520	23.1 (18.6–27.6)	471	18.3 (14.0–22.6)
Malawi (2013)	1,028	33.6 (28.8–38.4)	595	38.9 (32.2–45.7)	557	32.4 (26.9–38.0)
Nigeria (2014)	1,737	35.6 (32.4–38.8)	882	25.0 (21.0–29.0)	807	40.1 (34.7–45.5)
Tanzania (2009)	1,947	35.3 (30.5–40.0)	261	33.4 (25.4–41.5)	219	21.9 (12.8–31.0)
Uganda (2015)	3,143	44.3 (40.8–47.9)	1,867	18.8 (15.4–22.2)	1,784	25.0 (20.4–29.5)
Zambia (2014)	880	31.7 (28.2–35.2)	515	27.6 (23.0–32.1)	469	27.6 (22.5–32.7)
Zimbabwe (2017)	7,893	12.5 (11.6–13.3)	3,462	14.7 (13.4–16.0)	3,434	14.4 (13.1–15.7)

Abbreviation: VACS = Violence Against Children and Youth Surveys.

* Lifetime sexual violence is defined as unwanted touching, unwanted attempted sex, pressured or coerced sex, or physically forced sex. For this analysis, lifetime sexual violence was examined for adolescent girls and young women aged ≤24 years.

† Forced sexual initiation defined as first sexual intercourse was physically forced, pressured, or coerced, among adolescent girls and young women aged 13–24 years who had ever had sex. Definitions of pressured sex varied among countries.

§ Early sexual debut defined as first sex at aged ≤15 years among adolescent girls and young women aged 16–24 years who had ever had sex.

¶ Weights accounted for the multistage cluster sampling design (e.g., enumeration area, household, and household member), nonresponse, and calibration to a known population (i.e., the most recent census for Eswatini, Kenya, Tanzania, Uganda, and Zimbabwe; for the remaining countries, the country's population projections for the year of VACS data used).

** Formerly Swaziland.

children: implementation and enforcement of laws, norms and values, safe environments, parent and caregiver support, income and economic strengthening, response and support services, and education and life skills (*9*).

The findings in this report are subject to at least four limitations. First, data were self-reported, and are subject to recall bias. Second, slight variations in questions could contribute to differences in estimates across countries. Third, older data might not reflect recent changes in policies or programs. Finally, VACS only includes adolescent girls and young women living in households, so findings are not generalizable to those living in institutions or dormitories or to street youth.

Prevention of sexual violence and early sexual debut are key components of the comprehensive efforts of PEPFAR to control the HIV epidemic. In countries examined in this report, PEPFAR's Determined, Resilient, AIDS-free, Mentored, and Safe (DREAMS) partnership provides a core package of interventions to help prevent sexual violence and HIV acquisition among adolescent girls and young women. These interventions include community mobilization and norms change, school-based interventions, caregiver programs, social protection, social asset building, economic strengthening, sexual and reproductive health care including postviolence care, and access to preexposure prophylaxis (*10*). HIV prevention among girls aged 9–14 years includes evidence-based programs to prevent violence and risky sexual behaviors and strengthen family and community support (*10*). Although some reductions in new HIV infections among adolescent girls and young women have been achieved, HIV incidence among this population remains high compared with that in young men (*1*) and calls for increased efforts to protect this vulnerable population with multiple evidence-based approaches to HIV and violence prevention.

Summary

What is already known about this topic?

Early sexual debut (first intercourse at or before age 15 years) and forced sexual initiation are associated with increased risk behaviors for HIV acquisition, including transactional sex and multiple sexual partners, but studies are limited.

What is added by this report?

During 2007–2018, in nine countries funded by the U.S. President's Emergency Plan for AIDS Relief, 14.4% to 40.1% of adolescent girls and young women had early sexual debut. Among those with early sexual debut, the odds of having been tested for HIV was 40% lower and the odds of increased risky sexual behaviors were elevated.

What are the implications for public health practice?

Comprehensive violence and HIV prevention programs for adolescent girls and young women are needed to prevent early sexual debut and reduce the risk for HIV infection.

TABLE 2. Prevalence of and odds ratios for forced sexual initiation and early sexual debut among adolescent girls and young women aged 13–24 years who had ever had sex,* (N = 20,770), by characteristics — Violence Against Children and Youth Surveys, nine countries, 2007–2018

Characteristic/Health risk behavior	Forced or sexual initiation†		Early sexual debut§	
	Weighted average prevalence¶ (95% CI)	aOR (95% CI)	Weighted average prevalence¶ (95% CI)	aOR (95% CI)
Age group at time of survey, yrs				
13–15	38.1 (30.6–46.2)	1.8** (1.3–2.5)	—§	—§
16–19	27.4 (24.2–30.9)	1.2 (0.9–1.5)	36.3 (32.7–40.0)	3.3** (2.6–4.2)
20–24	21.5 (19.4–23.7)	Referent	18.4 (16.5–20.5)	Referent
Education				
None	13.0 (9.3–17.9)	0.6** (0.4–0.8)	59.4 (51.1–67.2)	5.2** (3.6–7.4)
Less than primary	29.2 (22.8–36.6)	1.1 (0.7–1.8)	36.7 (29.3–44.6)	2.2** (1.5–3.2)
Primary or higher	24.5 (22.5–26.6)	Referent	19.5 (17.6–21.6)	Referent
Orphan status††				
No	24.1 (22.1–26.1)	Referent	24.0 (21.9–26.2)	Referent
One parent	26.1 (22.1–30.5)	1.1 (0.8–1.5)	24.6 (21.1–28.4)	1.0 (0.8–1.3)
Both parents	18.8 (13.0–26.2)	0.8 (0.5–1.3)	27.8 (20.4–36.7)	1.4 (0.9–2.1)
Ever married or lived as married				
Yes	18.6 (16.5–20.9)	0.5** (0.4–0.6)	29.5 (27.1–32.1)	3.0¶ (2.3–3.9)
No	34.4 (30.8–38.2)	Referent	15.9 (13.3–19)	Referent
Any nonpenetrative sexual violence during childhood§§				
Yes	40.6 (36.1–45.3)	2.4** (1.8–3.1)	27.2 (22.8–32.1)	1.3 (1.0–1.6)
No	19.6 (17.8–21.6)	Referent	24.5 (22.4–26.6)	Referent
Any childhood physical violence¶¶				
Yes	27.2 (24.7–29.9)	1.2 (0.9–1.5)	22.9 (20–26)	0.8 (0.6–1.1)
No	21.7 (19.1–24.5)	Referent	27.0 (24.2–30.1)	Referent
Any emotional violence during childhood* **				
Yes	31.1 (27.5–35.1)	1.4** (1.1–1.8)	28.7 (24.4–33.4)	1.3 (1.0–1.7)
No	22.3 (20.4–24.3)	Referent	23.6 (21.6–25.8)	Referent
Ever witnessed parental intimate partner violence during childhood†††				
Yes	29.0 (25.2–33.1)	1.3 (1.0–1.6)	32.8 (28.9–36.9)	1.3** (1.0–1.7)
No	24.7 (22.1–27.5)	Referent	25.0 (22.1–28.2)	Referent
Witnessed violence in the community during childhood§§§				
Yes	29.1 (25.9–32.6)	1.3 (1.0–1.6)	28.1 (24.5–31.9)	1.2 (0.9–1.5)
No	23.6 (20.6–26.9)	Referent	27.7 (24.7–31)	Referent

Abbreviation: aOR = adjusted odds ratio.

* Sex was defined as ever experiencing vaginal, oral, or anal sex (Kenya, Malawi, Nigeria, Uganda, Zambia, and Zimbabwe); vaginal or anal intercourse (Haiti); or sexual intercourse (Eswatini and Tanzania).

† Forced sexual initiation was defined as having sexual intercourse at first sexual encounter through physical force, pressure, or coercion, among adolescent girls and young women aged 13–24 years who had ever had sex. Definitions of pressured sex varied among countries.

§ Early sexual debut was defined as first sex at age ≤15 years among adolescent girls and young women aged 16–24 years who had ever had sex. Participants aged 13–15 years were excluded from this analysis because they are still in the period during which early sexual debut could occur.

¶ Prevalence is weighted to the population of each of the nine included countries (except where fewer countries are included, as noted).

** Statistically significant ($p<0.05$).

†† Orphan status was defined as having one or both parents deceased before the 18th birthday.

§§ Nonpenetrative sexual violence was defined as unwanted sexual touching or unwanted attempted sex.

¶¶ Physical violence included being "punched, kicked, whipped, or beat with an object," "choked, smothered, drowned, or burned," or "threatened with a weapon" by an intimate/romantic partner, peer, family member or caregiver, or adult in community before age 18 years.

*** Emotional violence included having a parent, caregiver, or other adult telling child they were not loved, do not deserve to be loved, that they wished the child was dead or never born, or if they ever ridiculed or put down the child before age 18 years.

††† Ever witnessed parental intimate partner violence included seeing or hearing a parent punched, kicked, or beaten by their partner. Data from Eswatini, Haiti, Tanzania, and Zimbabwe were not included.

§§§ Ever witnessed violence in the community included seeing anyone get attacked outside of home or family environment. Data from Eswatini, Haiti, Tanzania, and Zimbabwe were not included.

TABLE 3. Prevalence of health outcomes and behaviors among adolescent girls and young women aged 13–24 years who had ever had sex,* and their association with forced sexual initiation and early sexual debut (N = 20,770) — Violence Against Children and Youth Surveys, nine countries, 2007–2018

	Forced sexual initiation†			Early sexual debut§		
	Weighted average prevalence¶		aOR	Weighted average prevalence¶		aOR
Health outcome and behavior	Yes, % (95% CI)	No, % (95% CI)	(95% CI)	Yes, % (95% CI)	No, % (95% CI)	(95% CI)
Risky sexual behavior (past 12 mos)**						
Transactional sex	8.7 (6.6–11.4)	5.2 (4.1–6.5)	1.6†† (1.0–2.3)	6.6 (4.9–8.8)	5.3 (4.2–6.6)	1.3 (0.8–2.0)
Multiple sex partners	9.1 (6.2–13.3)	6.0 (4.7–7.5)	1.4 (0.9–2.3)	7.9 (5.6–11.1)	6.1 (4.6–8.1)	1.7†† (1.1–2.8)
Infrequent condom use (past 12 mos)						
Ever married or cohabiting females	95.9 (92.5–97.7)	96.6 (95.6–97.4)	0.8 (0.4–1.5)	97.8 (96.3–98.6)	95.3 (93.7–96.4)	2.1†† (1.1–3.7)
Never married females	71.9 (63.4–79.0)	59.0 (53.1–64.7)	1.7†† (1.2–2.6)	74.4 (66.7–80.8)	57.4 (51.4–63.2)	1.9†† (1.2–3.0)
STI (lifetime)§§	21.7 (17.5–26.6)	15.1 (13.4–17.0)	1.6†† (1.1–2.2)	14.7 (12.0–17.9)	17.4 (15.5–19.5)	1.0 (0.7–1.4)
Recent violence (past 12 mos)¶¶						
One or more types of violence	58.0 (52.6–63.2)	30.2 (28.0–32.4)	2.8†† (2.1–3.6)	36.3 (31.8–41.0)	36.1 (33.9–38.4)	1.1 (0.9–1.4)
Two or more types of violence	22.6 (19.4–26.2)	8.5 (7.3–9.7)	2.6†† (1.9–3.4)	11.5 (9.0–14.6)	11.1 (9.8–12.5)	1.1 (0.8–1.5)
Mental health problems***						
Moderate or severe mental distress in the past 30 days	58.9 (53.9–63.7)	46.4 (44.0–48.9)	1.6†† (1.3–2.1)	55.6 (50.7–60.3)	47.5 (44.9–50.1)	1.5†† (1.2–2.0)
Ever thought of suicide	24.8 (20.6–29.5)	12.7 (11.1–14.5)	2.1†† (1.6–3.0)	16.3 (12.7–20.6)	15.7 (13.9–17.7)	1.1 (0.8–1.5)
Ever attempted suicide among those who ever thought of suicide	32.9 (24.6–42.4)	23.6 (17.9–30.4)	1.7 (1.0–2.8)	39.5 (29.4–50.7)	21.9 (16.9–28.0)	2.1†† (1.2–3.7)
Alcohol abuse in the past 30 days†††	7.6 (5.7–10.2)	9.3 (8.1–10.8)	0.8 (0.5–1.1)	6.8 (5.2–8.9)	9.2 (8.0–10.5)	0.8 (0.6–1.1)
HIV testing						
Ever tested for HIV	73.4 (68.3–77.9)	73.0 (70.5–75.3)	1.2 (0.9–1.7)	61.3 (56.0–66.3)	80.7 (78.4–82.8)	0.4†† (0.3–0.6)
HIV test in last 12 months	44.3 (38.7–50.0)	43.2 (40.4–46.0)	1.2 (0.9–1.5)	32.0 (27.9–36.5)	49.2 (46.6–51.9)	0.5†† (0.4–0.7)

Abbreviations: aOR = adjusted odds ratio; STI = sexually transmitted infection.

* Sex was defined as ever experiencing vaginal, oral, or anal sex (Kenya, Malawi, Nigeria, Uganda, Zambia, and Zimbabwe); vaginal or anal intercourse (Haiti); or sexual intercourse (Eswatini and Tanzania).

† Forced sexual initiation was defined as having sexual intercourse at first sexual encounter through physical force, pressure, or coercion, among women and girls aged 13–24 years who had ever had sex. Definitions of pressured sex varied among countries.

§ Early sexual debut was defined as first sex at age ≤15 years among adolescent girls and young women aged 16–24 years who had ever had sex.

¶ Prevalence is weighted to the population of each of the nine included countries (except where fewer countries are included, as noted).

** Among adolescent girls and young women who had sex in the past 12 months. Data for Eswatini (risky sexual behavior) and Tanzania (multiple sex partners) were not included. Models for transactional sex and infrequent condom use did not include a fixed effect for country as it made the model unstable.

†† Statistically significant ($p<0.05$).

§§ STI was defined as ever having symptoms or a diagnosis of an STI. Data for Tanzania were not included. Model does not include a fixed effect for country because it made the model unstable.

¶¶ Data for Eswatini were not included.

*** Mental distress was defined as a score of five or higher on the Kessler 6 scale (https://onlinelibrary.wiley.com/doi/10.1002/mpr.310). Data for Eswatini and Tanzania were not included.

††† Data for Eswatini and Tanzania were not included.

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Racial, Ethnic, and Gender Disparities in Awareness of Preexposure Prophylaxis Among HIV-Negative Heterosexually Active Adults at Increased Risk for HIV Infection — 23 Urban Areas, United States, 2019

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In 2019, heterosexual sex accounted for 23% of new HIV diagnoses in the United States and six dependent areas (*1*). Although preexposure prophylaxis (PrEP) can safely reduce the risk for HIV infection among heterosexual persons, this group is underrepresented in PrEP research (*2*). CDC analyzed National HIV Behavioral Surveillance (NHBS) data to describe PrEP awareness among heterosexually active adults in cities with high HIV prevalence. Overall, although 32.3% of heterosexually active adults who were eligible were aware of PrEP, <1% used PrEP. Racial, ethnic, and gender disparities were identified, with the lowest awareness of PrEP among residents of Puerto Rico (5.8%) and Hispanic or Latino (Hispanic) men (19.5%) and women (17.6%). Previous studies have found that heterosexual adults are interested in taking PrEP when they are aware of it (*3*); tailoring PrEP messaging, including Spanish-language messaging, to heterosexual adults, might increase PrEP awareness and mitigate disparities in use.

The 2019 NHBS cycle included face-to-face interviews and HIV testing among eligible* heterosexually active adults in 23 urban areas with high HIV prevalence. Detailed information about the 2019 NHBS cycle, including sampling methods, have been described in the CDC's HIV Surveillance Special Report 26 (*4*). This analysis was limited to participants who received a negative HIV test result and reported low income†; NHBS uses low income as a proxy for increased risk for acquiring HIV through heterosexual sex (*4*). PrEP awareness was defined as having ever heard of PrEP. Not all participants might be candidates for PrEP use; however, PrEP awareness might be beneficial to persons regardless of their own PrEP eligibility.§ Demographic and social determinants of health¶ differences in PrEP awareness were assessed using log-linked Poisson regression models** with generalized estimating equations to calculate adjusted prevalence ratios (aPRs) and 95% CIs. PrEP use could not be analyzed or stratified because use prevalence was <1%. 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.††

Among 9,359 total participants, 3,026 (32.3%) were aware of PrEP, including 1,221 (29.2%) men and 1,805 (34.8%) women (Table). Overall, 19.5% of Hispanic, 24.2% of White, and 31.9% of Black heterosexually active men were aware of PrEP (Figure). Overall, 17.6% of Hispanic, 32.7% of White, and 40.3% of Black heterosexually active women were aware of PrEP. Awareness of PrEP was lower among Hispanic

* Eligibility to participate in the study included never having had male-to-male sexual contact, aged 18–60 years, no previous participation in NHBS during 2019, residence in a participating urban area, ability to complete the survey in English or Spanish, report of vaginal or anal sex with an opposite-sex partner in the past 12 months, and never having injected drugs.

† Low income is defined as income at or below 150% of the federal poverty level, adjusted for geographic cost of living differences.

§ https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf

¶ Race and Hispanic ethnicity were presented separately, consistent with U.S. Department of Health and Human Services (HHS) and Office of Management and Budget standards for race/ethnicity categorization. All racial groups are mutually exclusive (https://aspe.hhs.gov/reports/hhs-implementation-guidance-data-collection-standards-race-ethnicity-sex-primary-language-disability-0). Poverty was defined as income at or below the 2018 HHS poverty guidelines (https://aspe.hhs.gov/topics/poverty-economic-mobility/poverty-guidelines/prior-hhs-poverty-guidelines-federal-register-references/2018-poverty-guidelines). Place of birth was defined as country or territory of birth. Participants born in Puerto Rico were presented separately from participants born in the 50 U.S. states and the District of Columbia. Frequently reported countries or territories were reported individually; other countries were grouped by global region. Years of U.S. residence was defined as the number of years the participant had resided in the United States. Participants residing in Puerto Rico were excluded from analysis of years of U.S. residency because of the design of the survey instrument. The South U.S. Census Region was selected as the referent Census region because CDC's Division of HIV Prevention's Strategic Plan prioritized the South (https://www.cdc.gov/hiv/pdf/dhap/cdc-hiv-dhap-external-strategic-plan.pdf). Participants were asked to self-rate their English proficiency based on the HHS data standard for primary language (https://aspe.hhs.gov/reports/hhs-implementation-guidance-data-collection-standards-race-ethnicity-sex-primary-language-disability-0). All U.S.-born participants were proficient in English; non–U.S.-born participants were analyzed by English proficiency level. Participants residing in Puerto Rico were excluded from analysis of English proficiency because Spanish is the predominant language in Puerto Rico. Usual source of care was defined as having a usual source for health care other than a hospital emergency department.

** Models were adjusted for urban area and network size and clustered on recruitment chain.

†† 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.

TABLE. Preexposure prophylaxis awareness among HIV-negative* heterosexually active men and women who are at increased risk for HIV infection (N = 9,359) — National HIV Behavioral Surveillance, 23 urban areas, United States, 2019

Characteristic	Awareness of PrEP no. (%)†	Adjusted prevalence ratio (95% CI)§
Overall	**3,026 (32.3)**	**NA**
Sex		
Men	1,221 (29.2)	0.79 (0.74–0.85)
Women	1,805 (34.8)	Ref
Race/Ethnicity¶		
AI/AN	23 (39.7)	1.10 (0.81–1.48)
Asian	8 (47.1)	1.39 (0.94–2.05)
Black	2,322 (36.4)	Ref
Hispanic	382 (18.4)	0.69 (0.60–0.79)
NH/OPI	11 (33.3)	1.02 (0.65–1.61)
White	122 (29.5)	0.87 (0.73–1.03)
Multiple races	147 (40.6)	1.14 (1.02–1.28)
Age group, yrs		
18–29	968 (30.3)	1.10 (1.02–1.19)
30–39	826 (36.4)	1.31 (1.21–1.42)
40–49	600 (34.2)	1.19 (1.08–1.31)
50–60	632 (29.5)	Ref
Federal poverty level**		
At or below federal poverty level	2,391 (31.4)	0.86 (0.80–0.92)
Above federal poverty level	635 (36.4)	Ref
Education		
Less than high school	707 (29.3)	0.66 (0.56–0.76)
High school diploma or equivalent	1,414 (30.2)	0.68 (0.59–0.79)
Some college or technical degree	803 (39.6)	0.92 (0.79–1.06)
College degree or more	101 (42.6)	Ref
Currently have health insurance		
Yes	2,427 (34.2)	Ref
No	586 (26.4)	0.76 (0.70–0.83)
Have a usual source of health care		
Yes	2,002 (34.3)	Ref
No	1,001 (29.1)	0.82 (0.78–0.87)
Place of birth††		
50 U.S. states or District of Columbia	2,896 (35.1)	Ref
Puerto Rico	42 (8.2)	0.57 (0.47–0.69)
Mexico	22 (12.6)	0.57 (0.42–0.77)
Central America (other)	8 (5.8)	0.21 (0.10–0.45)
Cuba	9 (15.5)	0.39 (0.18–0.84)
Caribbean (other)	20 (23.0)	0.67 (0.43–1.06)
South America	3 (6.8)	0.26 (0.12–0.56)
Europe	5 (20.0)	0.67 (0.27–1.64)
Asia	10 (45.5)	1.30 (0.78–2.15)
Africa	8 (26.7)	0.83 (0.45–1.51)
Years lived in United States§§		
U.S.-born	2,895 (35.2)	Ref
Non–U.S.-born, >5 yrs	94 (17.4)	0.58 (0.48–0.71)
Non–U.S.-born, ≤5 yrs	9 (8.4)	0.33 (0.22–0.50)
Proficiency in English§§		
U.S.-born	2,895 (35.2)	Ref
Non–U.S.-born, speaks English well	86 (22.3)	0.69 (0.57–0.84)
Non–U.S.-born, does not speak English well	17 (6.5)	0.26 (0.19–0.37)
U.S. Census region of current residence¶¶		
Northeast	717 (33.2)	0.97 (0.82–1.15)
Midwest	310 (37.6)	1.21 (1.02–1.43)
South	1,364 (36.0)	Ref
West	607 (28.8)	0.73 (0.62–0.88)
Puerto Rico	28 (5.8)	0.14 (0.11–0.17)

Abbreviations: AI/AN = American Indian/Alaska Native; HHS = U.S. Department of Health and Human Services; NA = not applicable; NHBS = National HIV Behavioral Surveillance; NH/OPI = Native Hawaiian/Other Pacific Islander; Ref = referent group.

* Participants with a valid negative NHBS HIV test result.

† Row percentages of persons who had ever heard of PrEP: "Preexposure prophylaxis, or PrEP, is an antiretroviral medicine, such as Truvada, taken for months or years by a person who is HIV-negative to reduce the risk for acquiring HIV. Before today, have you ever heard of PrEP?"

§ Log-linked Poisson regression models were adjusted for urban area and network size and clustered on recruitment chain.

¶ Hispanic persons could be of any race; all racial and ethnic groups are mutually exclusive.

** Poverty level was defined by the 2018 HHS Poverty Guidelines. https://aspe.hhs.gov/2018-poverty-guidelines

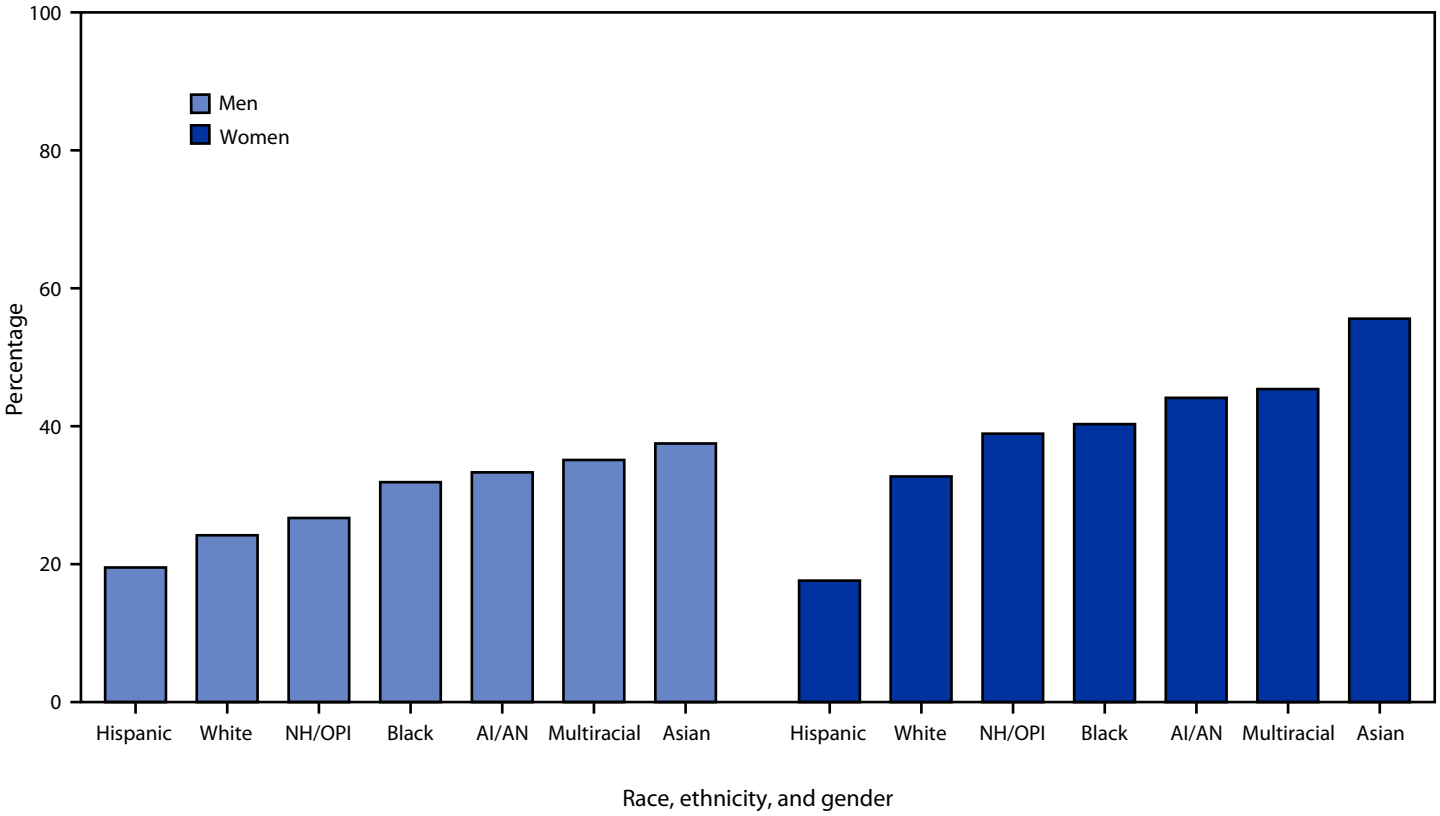
†† Frequently reported countries or territories were reported separately; other countries were grouped by geographic region.

§§ Participants residing in San Juan, Puerto Rico were excluded. English language proficiency was measured using HHS data collection standards. https://aspe.hhs.gov/reports/hhs-implementation-guidance-data-collection-standards-race-ethnicity-sex-primary-language-disability-0

¶¶ *Northeast:* Boston, Massachusetts; Nassau and Suffolk counties, New York; New York City, New York; Newark, New Jersey; and Philadelphia, Pennsylvania. *Midwest:* Chicago, Illinois and Detroit, Michigan. *South*: Atlanta, Georgia; Baltimore, Maryland; Dallas, Texas; Houston, Texas; Miami, Florida; New Orleans, Louisiana; and Washington, DC. *West:* Denver, Colorado; Los Angeles, California; San Diego, California; San Francisco, California; and Seattle, Washington. *Puerto Rico:* San Juan, Puerto Rico.

women than among both Hispanic men and other racial/ethnic groups of women. Lower PrEP awareness was found among uninsured participants (26.4%) than among insured participants (34.2%) (aPR = 0.76) and among participants without a usual source of care (29.1%) than among those with a usual source of care (34.3%) (aPR = 0.82) (Table). PrEP awareness was lower among participants born in Puerto Rico (8.2%; aPR = 0.57) or Mexico (12.6%; aPR = 0.57) than among participants born in the 50 United States and the District of Columbia (35.1%). Non–U.S.-born participants who did not speak English well reported lower PrEP awareness than did U.S.-born participants (6.5% versus 35.2%; aPR = 0.26); higher PrEP awareness was reported with increasing English proficiency. Participants residing in Puerto Rico reported lower PrEP awareness than did participants residing in the South U.S. Census Region (5.8% versus 36.0%; aPR = 0.14).

FIGURE. Percentage of HIV-negative heterosexually active men and women who had heard of preexposure prophylaxis (N = 9,359), by race, ethnicity,* and gender — National HIV Behavioral Surveillance, 23 urban areas, United States, 2019



Abbreviations: AI/AN = American Indian/Alaska Native; NH/OPI = Native Hawaiian/Other Pacific Islander.
* Hispanic persons could be of any race; other race groups were non-Hispanic. NH/OPI, AI/AN, and Asian men and women included ≤15 persons per group.

Discussion

In 2019, PrEP use among eligible heterosexually active adults was negligible (<1%), and approximately one in three heterosexually active adults was aware of PrEP. Overall, men reported lower PrEP awareness than did women. Awareness of PrEP was particularly low among Hispanic persons, with approximately one in six Hispanic women and approximately one in five Hispanic men having heard of PrEP. Awareness of PrEP was also low among persons who were not born in the United States, did not speak English well, or who resided in Puerto Rico. Given the high prevalence of HIV infection among Black persons, it is notable that their PrEP awareness was relatively higher than that among White or Hispanic persons. This might be attributable to HIV prevention campaigns tailored toward Black persons.

Awareness of PrEP and its potential to prevent sexually transmitted HIV infection is needed to end the HIV epidemic in the United States. PrEP use has the potential to reduce persistent racial, ethnic, and gender disparities in HIV infection observed among heterosexually active adults. In 2019, Black and Hispanic women accounted for 60.0% and 18.6% of new HIV diagnoses among women, respectively. Black and Hispanic men accounted for 61.2% and 20.3% of new HIV diagnoses attributed to heterosexual sex among men, respectively (*1*).

PrEP awareness might be low for multiple reasons, including limited tailored communications and infrequent patient-provider discussions about PrEP. In addition, few PrEP campaigns focus on heterosexual adults, particularly Hispanic persons. Although some prevention resources for heterosexual adults are inclusive of PrEP,[§§] most PrEP campaigns focus on men who have sex with men (MSM), which can reinforce stereotypes that PrEP is only intended for MSM (*5*). Because of stigma and gender norms, these stereotypes might interfere with marketing HIV prevention to some heterosexual Hispanic adults (*6*). Previous studies have indicated that heterosexual adults might not perceive themselves as being at risk for HIV infection or as candidates for PrEP (*7*).

[§§] https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/prep-program

Campaigns and interventions providing PrEP information and resources designed for heterosexual adults are limited. In 2021, CDC launched #ShesWell,[¶¶] which promotes PrEP among women; however, there are currently no national PrEP campaigns focused on all heterosexual adults at increased risk for HIV acquisition or heterosexual Hispanic men or women. Existing HIV interventions, such as Sister to Sister,[***] which is geared toward Black women aged 18–45 years and implemented in primary care provider settings, could be expanded and tailored to other groups.

Although some PrEP resources are available in Spanish,[†††] few PrEP materials are designed for specific groups of heterosexually active adults, including Hispanic persons, women, persons born outside the United States, and persons residing in Puerto Rico. Studies have also found that persons at high risk for HIV infection need messaging specifically customized for their population (*8*). Culturally competent PrEP materials and media campaigns geared toward heterosexual adults, including products tailored for heterosexual Hispanic persons, communicated through channels that might better reach Hispanic audiences, and which are available in Spanish, could increase PrEP awareness and use in this group (*6*). In addition, personalized PrEP campaign messaging might help heterosexual adults envision how PrEP could benefit them (*9*).

PrEP awareness might also be low because, despite CDC guidance, health care providers often do not discuss PrEP with heterosexual patients at increased risk for acquiring HIV (*10*). Primary care physicians and obstetricians and gynecologists can use routine visits and HIV and sexually transmitted infection testing encounters to educate their heterosexual patients about PrEP and screen for PrEP eligibility (*5*). Providers can assess barriers to PrEP use at multiple levels, including individual (e.g., side effects), interpersonal (e.g., judgment from others), community (e.g., caregiving duties), and structural (e.g., insurance and unstable housing) (*10*). Alternative PrEP options are emerging that allow ease of use, convenience, and confidentiality (e.g., vaginal rings and long-acting injectables) (*10*). Alternative modalities might broaden the appeal of PrEP among women (*2*) and encourage patient-provider discussions as part of sexual health assessments.

The findings in this report are subject to at least five limitations. First, data are not representative of all heterosexual men and women because the sample consists of low-income persons residing in 23 urban areas. Second, self-reported data are subject to recall and social desirability biases. Third, although awareness of PrEP is low, it is unknown whether participants had been exposed to existing PrEP campaigns. Fourth, PrEP awareness does not necessarily imply accurate knowledge or positive attitudes about PrEP. Persons might have heard of PrEP but might not be aware of their own eligibility. Finally, NHBS data are cross-sectional and do not support causal inference.

Summary

What is already known about this topic?

Heterosexual sex accounts for 23% of new HIV diagnoses annually. Heterosexual adults are underrepresented in preexposure prophylaxis (PrEP) research and campaigns. Increasing PrEP awareness and use in this population is needed to prevent HIV transmission and end the HIV epidemic in the United States.

What is added by this report?

PrEP awareness (32.3%) and use (<1%) among heterosexually active adults in high-prevalence cities is low, especially among Hispanic or Latino men and women (19.5% and 17.6%, respectively) and persons residing in Puerto Rico (5.8%).

What are the implications for public health practice?

Tailored PrEP campaigns and routine screening can increase PrEP awareness and use among heterosexual adults, particularly among Hispanic persons.

PrEP awareness among heterosexually active adults in the United States is low, especially among Hispanic men and women and persons residing in Puerto Rico. Although PrEP is not recommended for everyone, increasing awareness of PrEP in the general population could shape public attitudes and reduce stigma associated with PrEP and HIV (*8*,*9*). In addition to tailored, culturally appropriate campaigns for heterosexually active adults at risk for HIV infection, there are opportunities to increase awareness and use of PrEP through increased screening and patient-provider communication. Along with other preventive measures, increasing PrEP use among heterosexual persons is needed to end the HIV epidemic in the United States.

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[¶¶] https://www.cdc.gov/stophivtogether/sheiswell/index.html
[***] https://www.cdc.gov/hiv/effective-interventions/prevent/sister-to-sister
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Risk for Stillbirth Among Women With and Without COVID-19 at Delivery Hospitalization — United States, March 2020–September 2021

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Pregnant women are at increased risk for severe COVID-19–related illness, and COVID-19 is associated with an increased risk for adverse pregnancy outcomes and maternal and neonatal complications (*1*–*3*). To date, studies assessing whether COVID-19 during pregnancy is associated with increased risk for stillbirth have yielded mixed results (*2*–*4*). Since the B.1.617.2 (Delta) variant of SARS-CoV-2 (the virus that causes COVID-19) became the predominant circulating variant,* there have been anecdotal reports of increasing rates of stillbirths in women with COVID-19.† CDC used the Premier Healthcare Database Special COVID-19 Release (PHD-SR), a large hospital-based administrative database,§ to assess whether a maternal COVID-19 diagnosis documented at delivery hospitalization was associated with stillbirth during March 2020–September 2021 as well as before and during the period of Delta variant predominance in the United States (March 2020–June 2021 and July–September 2021, respectively). Among 1,249,634 deliveries during March 2020–September 2021, stillbirths were rare (8,154; 0.65%): 273 (1.26%) occurred among 21,653 deliveries to women with COVID-19 documented at the delivery hospitalization, and 7,881 (0.64%) occurred among 1,227,981 deliveries without COVID-19. The adjusted risk for stillbirth was higher in deliveries with COVID-19 compared with deliveries without COVID-19 during March 2020–September 2021 (adjusted relative risk [aRR] = 1.90; 95% CI = 1.69–2.15), including during the pre-Delta (aRR = 1.47; 95% CI = 1.27–1.71) and Delta periods (aRR = 4.04; 95% CI = 3.28–4.97). COVID-19 documented at delivery was associated with increased risk for stillbirth, with a stronger association during the period of Delta variant predominance. Implementing evidence-based COVID-19 prevention strategies, including vaccination before or during pregnancy, is critical to reducing the impact of COVID-19 on stillbirths.

Delivery hospitalizations were identified from PHD-SR using *International Classification of Diseases, Tenth Revision, Clinical Modification* (ICD-10-CM) diagnostic and procedure codes pertaining to obstetric delivery and diagnosis-related group delivery codes.¶ Deliveries with discharge dates during March 2020–September 2021 were included. Stillbirths, defined as fetal deaths at ≥20 weeks' gestation, were identified using maternal ICD-10-CM diagnosis codes.** Hospitalizations without ICD-10-CM codes indicating gestational age or with ICD-10-CM codes indicating gestational age <20 weeks were excluded to reduce misclassification of fetal deaths at <20 weeks' gestation as stillbirths (1.5% of the overall sample).

Maternal demographic variables assessed included age, race/ethnicity (i.e., Hispanic, non-Hispanic Black, non-Hispanic White, non-Hispanic Asian, and non-Hispanic other), and primary payor (i.e., Medicaid, private insurance, self-pay, and other). Assessed hospital characteristics included urban or rural location and U.S. Census division. COVID-19†† and selected underlying medical conditions (i.e., obesity, smoking,§§ any diabetes,¶¶ any hypertension,*** and multiple-gestation

* https://covid.cdc.gov/covid-data-tracker/#datatracker-home

† https://msdh.ms.gov/msdhsite/_static/23,23645,341.html

§ PHD-SR, formerly known as the PHD COVID-19 Database, is a large U.S. hospital-based, service-level, all-payor database that includes inpatient and hospital-based outpatient (e.g., emergency department or clinic) health care encounters from >900 geographically diverse nonprofit, nongovernmental, community, and teaching hospitals and health systems from rural and urban areas. PHD-SR represents approximately 20% of inpatient admissions in the United States. Data for this study represent a subset of 736 hospitals with delivery hospitalizations that contributed inpatient encounters to the PHD-SR during March 2020–September 2021. Updated PHD-SR data are released every 2 weeks; release date November 9, 2021, access date November 12, 2021. https://offers.premierinc.com/rs/381-NBB-525/images/PHD_COVID-19_White_Paper.pdf

¶ ICD-10-CM diagnostic and procedure codes pertaining to obstetric delivery: Z37.0, Z37.1, Z37.2, Z37.3, Z37.4, Z37.50, Z37.51, Z37.52, Z37.53, Z37.54, Z37.59, Z37.60, Z37.61, Z37.62, Z37.63, Z37.64, Z37.69, Z37.7, Z37.9, O75.82, O80, O82, 10D00Z0, 10D00Z1, 10D00Z2, 10D07Z3, 10D07Z4, 10D07Z5, 10D07Z6, 10D07Z7, 10D07Z8, 10E0XZZ; Diagnosis-related group delivery codes: 765, 766, 767, 768, 774, 775, 783, 784, 785, 786, 787, 788, 796, 797, 798, 805, 806, 807; Excluded codes for ectopic or molar pregnancies and pregnancies with abortive outcomes: O00, O01, O02, O03, O04, O07, O08, Z33.2, 10A0. Deliveries with the O82 code were excluded if they did not cooccur with another delivery code. Females aged 12–55 years were included. Multiple delivery events per woman during March 2020–September 2021 were included if the deliveries were >6 months apart.

** ICD-10-CM maternal diagnostic codes indicating a stillbirth: Z37.1, Z37.3, Z37.4, Z37.60, Z37.61, Z37.62, Z37.63, Z37.64, Z37.69, Z37.7. In multiple-gestation pregnancies, if a woman experienced multiple stillbirths, she was counted once as experiencing a stillbirth. If she experienced both a live birth and a stillbirth during one delivery hospitalization, she was also counted once as experiencing a stillbirth.

†† COVID-19 was identified using ICD-10-CM code U07.1 (COVID-19, virus identified) during April 2020–September 2021 or B97.29 (Other coronavirus as the cause of disease classified elsewhere) during March–April 2020.

§§ Includes smoking (tobacco) complicating pregnancy, childbirth, or the puerperium.

¶¶ Includes prepregnancy diabetes and gestational diabetes.

*** Includes chronic hypertension; gestational hypertension; chronic hypertension with superimposed preeclampsia; preeclampsia; hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome; and eclampsia

pregnancy) were included if the relevant ICD-10-CM diagnosis code was documented during the delivery hospitalization (*3*). In addition, among deliveries with documented COVID-19, indicators of severe illness (i.e., adverse cardiac event/outcome,[†††] placental abruption, sepsis, shock, acute respiratory distress syndrome, mechanical ventilation, and intensive care unit [ICU] admission) were considered present if the relevant ICD-10-CM diagnosis code was documented during the delivery hospitalization (*3*). Vaccination status was unable to be assessed in this analysis.

Poisson regression models with robust standard errors were used to calculate overall unadjusted and adjusted[§§§] relative risks for stillbirth among deliveries with COVID-19 versus deliveries without COVID-19, accounting for within-hospital and within-woman correlation. To better understand the potential biologic mechanism for stillbirth among women with COVID-19 at delivery, Poisson regression models with robust SEs were used to calculate unadjusted and adjusted[¶¶¶] prevalence ratios for stillbirth for each underlying medical condition and indicator of severe illness among deliveries with documented COVID-19. Relative risks and prevalence ratios were calculated overall as well as during the pre-Delta and Delta periods. Effect modification by period was assessed using adjusted models with interaction terms. For all models, p-values <0.05 were considered statistically significant. All analyses were performed using SAS software (version 9.4; SAS Institute). This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[****]

Among 1,249,634 deliveries at 736 hospitals during March 2020–September 2021, 53.7% of women were non-Hispanic White, and 50.6% had private insurance as the primary payor (Table 1). Overall, 15.4% had obesity, 11.2% had diabetes, 17.2% had a hypertensive disorder, 1.8% had a multiple-gestation pregnancy, and 4.9% had smoking (tobacco) documented on the delivery hospitalization record. Overall, 21,653 (1.73%) delivery hospitalizations had COVID-19 documented.

During March 2020–September 2021, a total of 8,154 stillbirths were documented, affecting 0.64% and 1.26% of deliveries without COVID-19 and with COVID-19, respectively (aRR = 1.90; 95% CI = 1.69–2.15) (Figure). During the pre-Delta period (March 2020–June 2021), 6,983 stillbirths were documented, involving 0.98% of deliveries with COVID-19 compared with 0.64% of deliveries without COVID-19 (aRR = 1.47; 95% CI = 1.27–1.71). During the Delta period (July–September 2021), 1,171 stillbirths were documented, involving 2.70% of deliveries with COVID-19 compared with 0.63% of deliveries without COVID-19 (aRR = 4.04; 95% CI = 3.28–4.97).[††††] Effect modification was present in the model; the risk for stillbirth was significantly higher during the period of Delta predominance than during the pre-Delta period (p<0.001).

Among deliveries with COVID-19, chronic hypertension, multiple-gestation pregnancy, adverse cardiac event/outcome, placental abruption, sepsis, shock, acute respiratory distress syndrome, mechanical ventilation, and ICU admission were associated with a higher prevalence of stillbirth (Table 2). The associations for adverse cardiac event/outcome and ICU admission varied significantly between the periods before and during Delta predominance (p = 0.03 and p = 0.003, respectively); for each of these, the associations were stronger during the period of Delta predominance.

Discussion

Although stillbirth was a rare outcome overall, a COVID-19 diagnosis documented during the delivery hospitalization was associated with an increased risk for stillbirth in the United States, with a stronger association during the period of Delta variant predominance. A previous study of pregnancies complicated by SARS-CoV-2 infection identified placental histopathologic abnormalities, suggesting that placental hypoperfusion and inflammation might occur with maternal COVID-19 infection (*5*); these findings might, in part, explain the association between COVID-19 and stillbirth. Among deliveries with COVID-19 documented during the delivery hospitalization, certain underlying medical conditions and markers of maternal morbidity, including the need for intensive care, were associated with stillbirth. Additional studies are warranted to investigate the role of maternal complications from COVID-19 on the risk for stillbirth. Further, given the differences observed before and during the period of Delta variant predominance, comparisons of placental findings might improve understanding of biologic reasons for the observed differences.

[†††] Includes acute myocardial infarction, cardiomyopathy, heart failure/arrest during surgery or procedure, cardiac arrest/ventricular fibrillation, conversion of cardiac rhythm, incident ventricular tachycardia, ischemia, pulmonary edema/acute heart failure, and atrial fibrillation/atrial flutter/supraventricular tachycardia.

[§§§] Models accounted for within-facility and within-woman correlation, and were adjusted for maternal age, race/ethnicity (Hispanic, non-Hispanic Black, non-Hispanic White, and non-Hispanic other), primary payor (Medicaid, private insurance, and other), obesity, smoking, any diabetes, any hypertension, and multiple-gestation pregnancy.

[¶¶¶] Models accounted for within-facility and within-woman correlation, and were adjusted for maternal age, race/ethnicity (Hispanic, non-Hispanic Black, non-Hispanic White, and non-Hispanic other), and primary payor (Medicaid, private insurance, and other).

[****] 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. Sect. 3501 et seq.

[††††] Sensitivity analyses were conducted to check for possible seasonality of stillbirths. In models using calendar year quarters, traditional seasons based on temperature patterns, and waves of SARS-CoV-2 variants, the results did not substantively change.

TABLE 1. Maternal demographic and health characteristics and hospital characteristics among delivery hospitalizations with and without a documented COVID-19 diagnosis — Premier Healthcare Database Special COVID-19 Release, United States, March 2020–September 2021

	No. (%)						
	Overall N = 1,249,634			Pre-Delta* (Mar 2020–Jun 2021) n = 1,076,745		Delta* (Jul–Sep 2021) n = 172,889	
Characteristic	Total N = 1,249,634	No COVID-19 n = 1,227,981	COVID-19 n = 21,653	No COVID-19 n = 1,058,651	COVID-19 n = 18,094	No COVID-19 n = 169,330	COVID-19 n = 3,559
Maternal age, median (SD)	**29.0 (5.8)**	29.0 (5.8)	28.0 (6.0)	29.0 (5.8)	28.0 (6.0)	29.0 (5.7)	28.0 (5.8)
Maternal race/ethnicity							
White, non-Hispanic	**671,392 (53.7)**	663,136 (54.0)	8,256 (38.1)	574,368 (54.3)	6,660 (36.8)	88,768 (52.4)	1,596 (44.8)
Hispanic	**230,836 (18.5)**	223,784 (18.2)	7,052 (32.6)	188,114 (17.8)	6,164 (34.1)	35,670 (21.1)	888 (25.0)
Black, non-Hispanic	**181,143 (14.5)**	177,508 (14.5)	3,635 (16.8)	153,408 (14.5)	2,947 (16.3)	24,100 (14.2)	688 (19.3)
Asian	**57,535 (4.6)**	56,855 (4.6)	680 (3.1)	49,583 (4.7)	604 (3.3)	7,272 (4.3)	76 (2.1)
Other/Unknown, non-Hispanic	**108,728 (8.7)**	106,698 (8.7)	2,030 (9.4)	93,178 (8.8)	1,719 (9.5)	13,520 (8.0)	311 (8.7)
Primary payor							
Private	**631,894 (50.6)**	624,069 (50.8)	7,825 (36.1)	537,957 (50.8)	6,367 (35.2)	86,112 (50.9)	1,458 (41.0)
Medicaid	**534,139 (42.7)**	521,739 (42.5)	12,400 (57.3)	450,813 (42.6)	10,548 (58.3)	70,926 (41.9)	1,852 (52.0)
Self-pay	**21,022 (1.7)**	20,557 (1.7)	465 (2.1)	17,351 (1.6)	386 (2.1)	3,206 (1.9)	79 (2.2)
Other	**62,579 (5.0)**	61,616 (5.0)	963 (4.4)	52,530 (5.0)	793 (4.4)	9,086 (5.4)	170 (4.8)
Hospital location							
Rural	**159,634 (12.8)**	157,006 (12.8)	2,628 (12.1)	134,615 (12.7)	2,014 (11.1)	22,391 (13.2)	614 (17.3)
Urban	**1,090,000 (87.2)**	1,070,975 (87.2)	19,025 (87.9)	924,036 (87.3)	16,080 (88.9)	146,939 (86.8)	2,945 (82.7)
U.S. Census division							
East North Central	**200,701 (16.1)**	198,061 (16.1)	2,640 (12.2)	169,631 (16.0)	2,259 (12.5)	28,430 (16.8)	381 (10.7)
East South Central	**94,224 (7.5)**	92,902 (7.6)	1,322 (6.1)	80,335 (7.6)	1,018 (5.6)	12,567 (7.4)	304 (8.5)
Middle Atlantic	**147,774 (11.8)**	144,423 (11.8)	3,351 (15.5)	124,755 (11.8)	3,123 (17.3)	19,668 (11.6)	228 (6.4)
Mountain	**91,554 (7.3)**	90,458 (7.4)	1,096 (5.1)	77,393 (7.3)	939 (5.2)	13,065 (7.7)	157 (4.4)
New England	**25,158 (2.0)**	24,892 (2.0)	266 (1.2)	21,463 (2.0)	246 (1.4)	3,429 (2.0)	20 (0.6)
Pacific	**126,615 (10.1)**	124,277 (10.1)	2,338 (10.8)	107,760 (10.2)	1,890 (10.4)	16,517 (9.8)	448 (12.6)
South Atlantic	**332,317 (26.6)**	326,419 (26.6)	5,898 (27.2)	283,595 (26.8)	4,683 (25.9)	42,824 (25.3)	1,215 (34.1)
West North Central	**80,263 (6.4)**	78,710 (6.4)	1,553 (7.2)	66,326 (6.3)	1,310 (7.2)	12,384 (7.3)	243 (6.8)
West South Central	**151,028 (12.1)**	147,839 (12.0)	3,189 (14.7)	127,393 (12.0)	2,626 (14.5)	20,446 (12.1)	563 (15.8)
Obesity							
No	**1,057,646 (84.6)**	1,039,849 (84.7)	17,797 (82.2)	897,069 (84.7)	14,881 (82.2)	142,780 (84.3)	2,916 (81.9)
Yes	**191,988 (15.4)**	188,132 (15.3)	3,856 (17.8)	161,582 (15.3)	3,213 (17.8)	26,550 (15.7)	643 (18.1)
Diabetes (any)†							
No	**1,109,053 (88.8)**	1,090,087 (88.8)	18,966 (87.6)	940,575 (88.8)	15,803 (87.3)	149,512 (88.3)	3,163 (88.9)
Yes	**140,581 (11.2)**	137,894 (11.2)	2,687 (12.4)	118,076 (11.2)	2,291 (12.7)	19,818 (11.7)	396 (11.1)
Hypertensive disorders of pregnancy (any)§							
No	**1,034,519 (82.8)**	1,016,918 (82.8)	17,601 (81.3)	877,063 (82.8)	14,678 (81.1)	139,855 (82.6)	2,923 (82.1)
Yes	**215,115 (17.2)**	211,063 (17.2)	4,052 (18.7)	181,588 (17.2)	3,416 (18.9)	29,475 (17.4)	636 (17.9)
Multiple-gestation pregnancy							
No	**1,226,534 (98.2)**	1,205,299 (98.2)	21,235 (98.1)	1,039,095 (98.2)	17,751 (98.1)	166,204 (98.2)	3,484 (97.9)
Yes	**23,100 (1.8)**	22,682 (1.8)	418 (1.9)	19,556 (1.8)	343 (1.9)	3,126 (1.8)	75 (2.1)
Smoking¶							
No	**1,187,831 (95.1)**	1,166,855 (95.0)	20,976 (96.9)	1,005,234 (95.0)	17,598 (97.3)	161,621 (95.4)	3,378 (94.9)
Yes	**61,803 (4.9)**	61,126 (5.0)	677 (3.1)	53,417 (5.0)	496 (2.7)	7,709 (4.6)	181 (5.1)
Stillbirth							
No	**1,241,480 (99.3)**	1,220,100 (99.4)	21,380 (98.7)	1,051,845 (99.4)	17,917 (99.0)	168,255 (99.4)	3,463 (97.3)
Yes	**8,154 (0.7)**	7,881 (0.6)	273 (1.3)	6,806 (0.6)	177 (1.0)	1,075 (0.6)	96 (2.7)
Timing of stillbirth, wks (trimester)**							
20–27 (2nd)	**3,607 (44.2)**	3,498 (44.4)	109 (39.9)	3,058 (44.9)	77 (43.5)	440 (40.9)	32 (33.3)
28–42 (3rd)	**4,547 (55.8)**	4,383 (55.6)	164 (60.1)	3,748 (55.1)	100 (56.5)	635 (59.1)	64 (66.7)
Gestational age at stillbirth, wks, median (SD)	**29.0 (6.8)**	**29.0 (6.8)**	**29.0 (6.2)**	**29.0 (6.8)**	**29.0 (6.5)**	**30.0 (6.7)**	**30.0 (5.7)**

Abbreviation: HELLP = hemolysis, elevated liver enzymes, low platelet count.

* Deliveries with discharge dates during March 2020–June 2021 were considered to have occurred during the pre-Delta period, whereas deliveries with discharge dates during July–September 2021 were considered to have occurred during the period of Delta predominance.

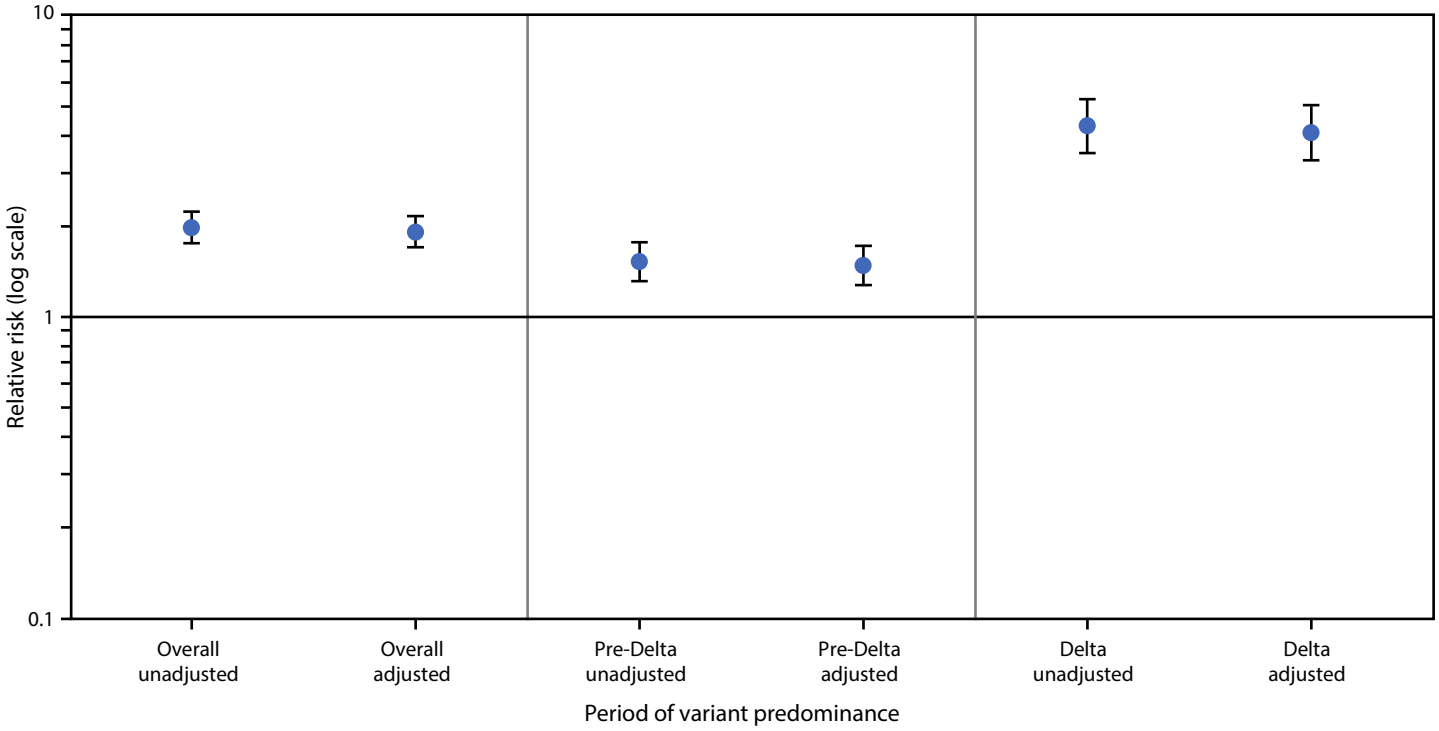
† Includes prepregnancy diabetes and gestational diabetes.

§ Includes chronic hypertension, gestational hypertension, chronic hypertension with superimposed preeclampsia, preeclampsia, HELLP syndrome, and eclampsia.

¶ Includes smoking (tobacco) complicating pregnancy, childbirth, or the puerperium.

** Only among deliveries with a stillbirth.

FIGURE. Relative risk for stillbirth among women with COVID-19 at delivery hospitalization compared with those without COVID-19 at delivery hospitalization — Premier Healthcare Database Special COVID-19 Release, United States, March 2020–September 2021[*,†,§]



Abbreviation: RR = relative risk.

* Deliveries with discharge dates during March 2020–June 2021 were considered to have occurred during the period preceding SARS-CoV-2 B.1.617.2 (Delta) variant predominance, whereas those with discharge dates during July–September 2021 were considered to have occurred during the period of Delta predominance.

† Overall: unadjusted RR = 1.96 (95% CI = 1.74–2.21); adjusted RR = 1.90 (95% CI = 1.69–2.15); pre-Delta: unadjusted RR = 1.52 (95% CI = 1.31–1.77); adjusted RR = 1.47 (95% CI = 1.27–1.71); Delta: unadjusted RR = 4.25 (95% CI = 3.46–5.22); adjusted RR = 4.04 (95% CI = 3.28–4.97); p-value for effect modification by period (pre-Delta period versus period of Delta predominance): <0.001.

§ Models accounted for within-facility and within-woman correlation, and were adjusted for maternal age, race/ethnicity (Hispanic, non-Hispanic Black, non-Hispanic White, and non-Hispanic other), primary payor (Medicaid, private insurance, and other), obesity, smoking, any diabetes, any hypertension, and multiple-gestation pregnancy.

The rates of stillbirth in women without COVID-19 at delivery in this analysis (0.64% overall) were similar to the known prepandemic stillbirth rate of 0.59% (*6*). However, 0.98% of COVID-19–affected deliveries pre-Delta and 2.70% during the Delta period resulted in stillbirth. Data on the association between COVID-19 in pregnancy and stillbirth are emerging. Two metaanalyses found an association between COVID-19 during pregnancy and stillbirth but were unable to adjust for potential confounders (*2*,*4*). In a previous analysis of the PHD-SR data, comparing women with and without COVID-19 documented at the delivery hospitalization during March–September 2020, the risk for stillbirth was not significantly increased after adjusting for confounders (*3*). The current analysis includes an additional year of data, adding to the growing evidence that COVID-19 is associated with an increased risk for stillbirth.

Delta became the predominant variant of SARS-CoV-2 in the United States in July 2021.[§§§§] The Delta variant is more infectious and is associated with increased risk for hospitalization compared with previous variants (*7*,*8*); however, nonpregnant patients are not more likely to have severe outcomes during hospitalization (*9*). In this analysis, the association between COVID-19 and stillbirth was stronger during the period of Delta predominance. Further studies that examine the effect of SARS-CoV-2 infection, including with the Delta variant, on fetal well-being are warranted.

The findings in this report are subject to at least seven limitations. First, the analysis relied on administrative data from hospital discharge ICD-10-CM codes; thus, identification of COVID-19 status, underlying medical conditions, gestational age, and stillbirths might be misclassified. Second, gestational age at SARS-CoV-2 infection was not available, and it is unknown whether COVID-19 diagnoses documented during the delivery hospitalization represented current or past infection. Third, many hospitals implemented universal SARS-CoV-2 testing among pregnant women assessed in labor and delivery units during spring 2020 (*10*), which would increase the detection of asymptomatic COVID-19. Laboratory information was unavailable for most hospitals in

[§§§§] https://www.reuters.com/world/us/delta-variant-already-dominant-us-cdc-estimates-show-2021-07-07/

TABLE 2. Risk for stillbirth by maternal health characteristics and indicators of severe illness among delivery hospitalizations with a documented COVID-19 diagnosis — Premier Healthcare Database Special COVID-19 Release, United States, March 2020–September 2021

	Overall N = 21,653				Pre-Delta* (Mar 2020–Jun 2021) n = 18,094				Delta* (Jul–Sep 2021) n = 3,559				
	Outcome No. (%)		RR (95% CI)		Outcome No. (%)		RR (95% CI)		Outcome No. (%)		RR (95% CI)		
Characteristic	No stillbirth	Stillbirth	Unadjusted	Adjusted†	No stillbirth	Stillbirth	Unadjusted	Adjusted†	No stillbirth	Stillbirth	Unadjusted	Adjusted†	p-value§
Hypertensive disorders of pregnancy (any)¶	3,995 (18.7)	57 (20.9)	1.15 (0.86–1.53)	1.08 (0.81–1.44)	3,379 (18.9)	37 (20.9)	1.14 (0.79–1.63)	1.05 (0.73–1.50)	616 (17.8)	20 (20.8)	1.21 (0.74–1.96)	1.19 (0.74–1.92)	<0.001
Chronic hypertension	515 (2.4)	13 (4.8)	2.00 (1.15–3.47)	1.79 (1.03–3.11)	418 (2.3)	7 (4.0)	1.71 (0.81–3.62)	1.49 (0.70–3.19)	97 (2.8)	6 (6.3)	2.24 (1.00–4.99)	2.11 (0.94–4.74)	0.02
Pregnancy-associated hypertension**	3,480 (16.3)	44 (16.1)	0.99 (0.72–1.36)	0.94 (0.68–1.29)	2,961 (16.5)	30 (16.9)	1.03 (0.70–1.52)	0.97 (0.66–1.43)	519 (15.0)	14 (14.6)	0.97 (0.66–1.43)	0.96 (0.55–1.69)	0.005
Obesity	3,810 (17.8)	46 (16.8)	0.94 (0.68–1.28)	0.90 (0.66–1.23)	3,181 (17.8)	32 (18.1)	1.02 (0.70–1.50)	0.97 (0.66–1.42)	629 (18.2)	14 (14.6)	0.77 (0.44–1.36)	0.78 (0.44–1.37)	0.02
Diabetes (any)††	2,659 (12.4)	28 (10.3)	0.81 (0.55–1.19)	0.80 (0.53–1.18)	2,273 (12.7)	18 (10.2)	0.78 (0.48–1.27)	0.78 (0.47–1.30)	386 (11.1)	10 (10.4)	0.93 (0.49–1.77)	0.88 (0.46–1.67)	0.005
Smoking§§	663 (3.1)	14 (5.1)	1.67 (0.98–2.85)	1.56 (0.91–2.68)	488 (2.7)	8 (4.5)	1.68 (0.83–3.39)	1.60 (0.79–3.27)	175 (5.1)	6 (6.3)	1.24 (0.55–2.80)	1.09 (0.47–2.52)	0.18
Multiple-gestation pregnancy	399 (1.9)	19 (7.0)	3.80 (2.41–6.00)	3.54 (2.24–5.59)	330 (1.8)	13 (7.3)	4.10 (2.36–7.14)	3.76 (2.16–6.57)	69 (2.0)	6 (6.3)	3.10 (1.40–6.85)	3.04 (1.35–6.82)	0.11
Adverse cardiac event/ outcome¶¶	160 (0.7)	10 (3.7)	4.81 (2.60–8.87)	4.44 (2.38–8.29)	120 (0.7)	4 (2.3)	3.35 (1.26–8.89)	3.09 (1.15–8.34)	40 (1.2)	6 (6.3)	5.09 (2.35–11.03)	5.18 (2.34–11.48)	0.03
Placental abruption	273 (1.3)	36 (13.2)	10.49 (7.53–14.63)	10.12 (7.28–14.08)	206 (1.1)	22 (12.4)	11.12 (7.26–17.05)	10.63 (6.96–16.22)	67 (1.9)	14 (14.6)	7.33 (4.35–12.36)	7.53 (4.47–12.66)	0.07
Sepsis	306 (1.4)	10 (3.7)	2.57 (1.38–4.78)	2.55 (1.37–4.76)	211 (1.2)	6 (3.4)	2.89 (1.30–6.45)	2.83 (1.27–6.31)	95 (2.7)	4 (4.2)	1.52 (0.57–4.05)	1.58 (0.59–4.21)	0.56
Shock	121 (0.6)	15 (5.5)	9.20 (5.62–15.05)	9.31 (5.65–15.35)	91 (0.5)	8 (4.5)	8.60 (4.35–17.00)	8.70 (4.35–17.39)	30 (0.9)	7 (7.3)	7.49 (3.73–15.04)	7.95 (3.95–16.00)	0.07
Acute respiratory distress syndrome	915 (4.3)	25 (9.2)	2.22 (1.48–3.33)	2.16 (1.44–3.23)	601 (3.4)	12 (6.8)	2.07 (1.16–3.71)	2.01 (1.13–3.59)	314 (9.1)	13 (13.5)	1.55 (0.87–2.75)	1.53 (0.87–2.70)	0.09
Mechanical ventilation	379 (1.8)	20 (7.3)	4.21 (2.70–6.57)	4.12 (2.62–6.48)	257 (1.4)	12 (6.8)	4.82 (2.72–8.55)	4.79 (2.67–8.61)	122 (3.5)	8 (8.3)	2.40 (1.19–4.84)	2.41 (1.17–4.95)	0.57
ICU admission	1,074 (5.0)	36 (13.2)	2.81 (1.99–3.97)	2.74 (1.93–3.89)	800 (4.5)	18 (10.2)	2.39 (1.48–3.87)	2.31 (1.42–3.76)	274 (7.9)	18 (18.8)	2.58 (1.57–4.25)	2.57 (1.54–4.28)	0.003

Abbreviations: HELLP = hemolysis, elevated liver enzymes, low platelet count; ICU = intensive care unit; RR = relative risk.

* Deliveries with discharge dates during March 2020–June 2021 were considered to occur during the pre-Delta period, whereas deliveries with discharges dates during July–September 2021 were considered to occur during the period of Delta predominance.

† Models accounted for within-facility and within-woman correlation, and were adjusted for maternal age, race/ethnicity (Hispanic, non-Hispanic Black, non-Hispanic White, and non-Hispanic other), and primary payor (Medicaid, private insurance, and other).

§ Assessing for effect modification by period (pre-Delta versus period of Delta predominance), based on interaction term added to adjusted model.

¶ Includes chronic hypertension, gestational hypertension, chronic hypertension with superimposed preeclampsia, preeclampsia, HELLP syndrome, and eclampsia.

** Includes gestational hypertension, chronic hypertension with superimposed preeclampsia, preeclampsia, HELLP syndrome, and eclampsia.

†† Includes prepregnancy diabetes and gestational diabetes.

§§ Includes smoking (tobacco) complicating pregnancy, childbirth, or the puerperium.

¶¶ Includes acute myocardial infarction, cardiomyopathy, heart failure/arrest during surgery or procedure, cardiac arrest/ventricular fibrillation, conversion of cardiac rhythm, incident ventricular tachycardia, ischemia, pulmonary edema/acute heart failure, and atrial fibrillation/atrial flutter/supraventricular tachycardia.

PHD-SR and therefore not used in this analysis; if participating hospitals had different screening practices, some patients with SARS-CoV-2 infection might have been missed or misclassified. In hospitals not conducting universal SARS-CoV-2 testing, women experiencing adverse outcomes during the delivery hospitalization, including stillbirth, might have been more likely to be tested for SARS-CoV-2 infection. Fourth, because outpatient records were not universally available, and linkage across different hospital systems was not possible, the analysis was restricted to codes included during the delivery hospitalization and did not examine COVID-19 diagnoses or underlying medical conditions recorded before the delivery hospitalization (i.e., during a prenatal visit). Fifth, whole genome sequencing data were not available to confirm the variant of SARS-CoV-2 for this analysis, and period was used as a proxy; however, the Delta variant accounted for >90% of U.S. COVID-19 cases during July–September 2021.¶¶¶¶ Sixth, it was not

¶¶¶¶ https://covid.cdc.gov/covid-data-tracker/#variant-proportions

Summary

What is already known about this topic?

Pregnant women are at increased risk for severe disease from COVID-19, and COVID-19 is associated with an increased risk for adverse perinatal outcomes.

What is added by this report?

Among 1,249,634 delivery hospitalizations during March 2020–September 2021, U.S. women with COVID-19 were at increased risk for stillbirth compared with women without COVID-19 (adjusted relative risk [aRR] = 1.90; 95% CI = 1.69–2.15). The magnitude of association was higher during the period of SARS-CoV-2 B.1.617.2 (Delta) variant predominance than during the pre-Delta period.

What are the implications for public health practice?

Implementing evidence-based COVID-19 prevention strategies, including vaccination before or during pregnancy, is critical to reduce the impact of COVID-19 on stillbirths.

possible to assess vaccination status in this analysis. However, because COVID-19 vaccines are highly effective,***** and COVID-19 vaccination coverage among pregnant women was approximately 30% as of July 2021,††††† most women with COVID-19 at delivery were likely unvaccinated. Finally, although the PHD-SR included a large population across U.S. Census divisions, it represents delivery hospitalizations from a convenience sample of reporting hospitals, limiting generalizability of results to the U.S. population.

This analysis adds to growing evidence of an association between COVID-19 in pregnancy and stillbirth, highlights that the risk for stillbirth associated with COVID-19 is affected by maternal morbidity, and demonstrates that the risk has increased during the Delta period. Further investigation from prospective studies is warranted to confirm these findings, identify the biologic mechanism for the observed increased risk for stillbirth with maternal COVID-19, and assess differences in risks relative to the timing and severity of infection and the contribution of maternal risk factors. In addition, further investigation of vaccine effectiveness during pregnancy, including prevention of stillbirth, is warranted. Most importantly, these findings underscore the importance of COVID-19 prevention strategies, including vaccination before or during pregnancy.

***** https://covid.cdc.gov/covid-data-tracker/#vaccine-effectiveness

††††† https://www.cdc.gov/vaccines/imz-managers/coverage/covidvaxview/interactive.html

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All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

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COVID-19–Associated Deaths After SARS-CoV-2 Infection During Pregnancy — Mississippi, March 1, 2020–October 6, 2021

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On November 19, 2021, this report was posted as an MMWR *Early Release on the* MMWR *website (https://www.cdc.gov/mmwr).*

Pregnant and recently pregnant women are at increased risk for severe illness and death from COVID-19 compared with women who are not pregnant or were not recently pregnant (*1*,*2*). CDC recommends COVID-19 vaccination for women who are pregnant, recently pregnant, trying to become pregnant, or might become pregnant in the future.*,† This report describes 15 COVID-19–associated deaths after infection with SARS-CoV-2 (the virus that causes COVID-19) during pregnancy in Mississippi during March 1, 2020–October 6, 2021.

The Mississippi State Department of Health (MSDH) identifies COVID-19 cases and deaths through required health care provider and hospital reporting§ and death certificate reviews. A COVID-19–associated death after SARS-CoV-2 infection during pregnancy was defined as the death of a woman with confirmed or probable SARS-CoV-2 infection during pregnancy who subsequently died during pregnancy or within 90 days after the pregnancy ended.¶ This study assessed characteristics of the decedents and timing of infection, for the periods before the highly transmissible SARS-CoV-2 B.1.617.2 (Delta) variant became predominant (March 2020–June 2021) and during Delta variant predominance (July 2021–October 2021).** For each period, the ratio of the number of COVID-19–associated deaths per 1,000 SARS-CoV-2 infections during pregnancy was assessed.†† Poisson 95% CIs were calculated using CDC's National Center for Health Statistics methods for computing confidence limits for a death rate based on a Poisson variable of 1–99 deaths.§§ This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.¶¶

During March 1, 2020–October 6, 2021, a total of 1,637 SARS-CoV-2 infections during pregnancy were reported, and 15 COVID-19–associated deaths occurred (nine deaths per 1,000 SARS-CoV-2 infections). During the pre-Delta period, six COVID-19–associated deaths occurred (five deaths per 1,000 SARS-CoV-2 infections during pregnancy; 95% CI = 1.7–10.3); during the period of Delta predominance, nine COVID-19–associated deaths occurred (25 deaths per 1,000 SARS-CoV-2 infections during pregnancy; 95% CI = 11.3–46.8) (Table).

The median age of the 15 decedents was 30 years (range = 23–40 years). Nine were non-Hispanic Black women, three were non-Hispanic White women, and three were Hispanic women. The median interval from symptom onset to death before and during Delta predominance was 18 days (pre-Delta range = 1–87 days; Delta range = 9–45 days). All decedents had been admitted to an intensive care unit, and 14 required invasive mechanical ventilation. Seven underwent emergency cesarean delivery (including two at the bedside). Three died during pregnancy, resulting in one spontaneous abortion at 9 weeks and two stillbirths at 22 and 23 weeks' gestation, and 12 died after a live birth (median = 5 days postpartum, range = 1–87 days). Underlying

* https://emergency.cdc.gov/han/2021/han00453.asp

† https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/pregnancy.html#anchor_1628692562866

§ COVID-19 infection, including COVID-19–associated death, was added to the Mississippi List of Reportable Diseases and Conditions on March 10, 2020. Reported deaths are reviewed alongside surveillance data to ascertain the presence of a case report or a positive laboratory test result and to determine whether the death resulted from an acute SARS-CoV-2 infection. A review of each death established clinical characteristics and pregnancy status at time of infection.

¶ For COVID-19–associated deaths, pregnancy status at time of SARS-CoV-2 infection was determined based on direct communications from health care providers or hospitals, COVID-19 case report forms, or death certificates. For COVID-19–associated deaths after SARS-CoV-2 infection during pregnancy identified through this process, pregnancy status at time of SARS-CoV-2 infection was confirmed through review of medical records.

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

†† The total number of SARS-CoV-2 infections during pregnancy by period was obtained from MSDH COVID-19 case surveillance data. Pregnancy status for SARS-CoV-2 infections is ascertained by a pregnancy field on the case report form. The proportion of cases with known pregnancy status among females aged 10–49 years in Mississippi was higher at the beginning of the pandemic (March 2020–June 2020) when case counts were lower and decreased as case counts increased (July 2020–October 2021). However, the proportion of cases with known pregnancy status has remained relatively stable (approximately 17%) since July 2020.

§§ https://www.cdc.gov/nchs/data/statab/techap99.pdf

¶¶ 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.

TABLE. Characteristics of women who died after SARS-CoV-2 infection during pregnancy before or during the period of SARS-CoV-2 B.1.617.2 (Delta) variant predominance — Mississippi, March 1, 2020–October 6, 2021

Characteristic	Total (Mar 1, 2020–Oct 6, 2021)	Before Delta predominance (Mar 2020–Jun 2021)	During Delta predominance (Jul–Oct 2021)
No. of COVID-19–associated deaths (deaths per 1,000 SARS-CoV-2 infections in pregnant women)*	**15 (9)**	6 (5)	9 (25)
Age, median (range), yrs	**30 (23–40)**	27 (23–38)	35 (23–40)
Race/Ethnicity, no. (%)			
Black, non-Hispanic	**9 (60)**	4 (67)	5 (56)
White, non-Hispanic	**3 (20)**	1 (17)	2 (22)
Hispanic	**3 (20)**	1 (17)	2 (22)
Gestational age at symptom onset, median (range), wks	**26 (8–37)**	34 (8–37)	24 (22–37)
Gestational age at end of pregnancy or death, median (range), wks	**28 (9–37)**	35 (9–37)	24 (22–37)
Interval from symptom onset to death, median (range), days	**18 (1–87)**	18 (1–87)	18 (9–45)
Disease course/complications, no. (%)			
Admitted to ICU	**15 (100)**	6 (100)	9 (100)
Invasive mechanical ventilation	**14 (93)**	5 (83)	9 (100)
Emergency cesarean delivery	**7 (47)**	1 (17)	6 (67)
Died during pregnancy	**3[†] (20)**	1 (17)	2 (22)
Died after live birth	**12[§] (80)**	5 (83)	7 (78)
Underlying medical conditions, no. (%)	**14 (93)**	6 (100)	8 (89)
Obesity	**10 (67)**	4 (67)	6 (67)
Hypertension[¶]	**8 (53)**	4 (67)	4 (44)
Diabetes (preexisting or gestational)	**4 (27)**	1 (17)	3 (33)
Cancer	**2 (13)**	0 (—)	2 (22)
HIV with pneumocystis pneumonia	**1 (7)**	1 (17)	0 (—)
COVID-19 vaccination status, no. (%)			
Fully vaccinated	**0 (—)**	0 (—)	0 (—)
Partially vaccinated	**1 (7)**	1 (17)	0 (—)
Unvaccinated**	**14 (93)**	5 (83)	9 (100)

Abbreviation: ICU = intensive care unit.

* The total number of SARS-CoV-2 infections in pregnant women was 1,637. The number of SARS-CoV-2 infections in pregnant women before and during Delta variant predominance was 1,272 and 365, respectively.

† Three deaths during pregnancy resulted in one spontaneous abortion (9 weeks' gestation) before Delta predominance and two stillbirths (22 and 23 weeks' gestation) during Delta predominance.

§ Median = 5 days postpartum; range = 1–87 days.

¶ Before and during pregnancy.

** Five (83%) deaths in the period before Delta predominance occurred before vaccines were available.

medical conditions were present in 14 decedents. Receipt of monoclonal antibodies was not documented for any of the decedents. None of the 15 decedents had been fully vaccinated against COVID-19: five deaths occurred before COVID-19 vaccinations became available in December 2020; one decedent had been partially vaccinated; and nine were unvaccinated.

The findings in this report are subject to at least six limitations. First, there are limitations to identifying history of pregnancy from death certificates and through COVID-19 case reporting systems (*3*,*4*), which likely result in underascertainment of COVID-19 cases during pregnancy in Mississippi. Second, reported ratios of deaths per 1,000 SARS-CoV-2 infections during pregnancy might be overestimated if the total numbers of SARS-CoV-2 infections during pregnancy were undercounted. Third, because of the small number of deaths, the statistical significance of the difference in the ratios between periods was not assessed. Fourth, genomic sequencing was not performed on decedents' viral samples for the deaths that occurred during July 2021–October 2021; however, the Delta variant accounted for nearly 100% of sequenced SARS-CoV-2 specimens in Mississippi during that period. Fifth, deaths among patients with more recent COVID-19 cases might be undercounted because less time has elapsed for the death to occur. Finally, an in-depth review of whether death was pregnancy-related (from any cause related to or aggravated by pregnancy) was not performed, so these data cannot be compared with pregnancy-related mortality ratios.*** Maternal mortality review committees (MMRCs)[†††,§§§] identify all pregnancy-associated deaths as those occurring during

*** Pregnancy-related mortality ratio = number of pregnancy-related deaths per 100,000 live births.

††† https://www.cdc.gov/reproductivehealth/maternal-mortality/erase-mm/index.html

§§§ https://msdh.ms.gov/msdhsite/_static/31,0,299,359.html

pregnancy and ≤1 year after the end of pregnancy using linked death and birth certificate data.

This study found 15 COVID-19–associated deaths after SARS-CoV-2 infection during pregnancy (nine deaths per 1,000 SARS-CoV-2 infections); during the same period, 413 COVID-19–associated deaths were reported among females of reproductive age (2.5 deaths per 1,000 SARS-CoV-2 infections).¶¶¶ In addition, this study found an apparent increase in the ratio of COVID-19–associated deaths per 1,000 cases among pregnant women as the Delta variant became predominant (pre-Delta period: five deaths per 1,000 SARS-CoV-2 infections during pregnancy; Delta predominance period: 25 deaths per 1,000 SARS-CoV-2 infections during pregnancy). A similar increase in the ratio of deaths per 1,000 cases was observed for females of reproductive age in Mississippi, although the magnitude of the ratios was lower overall and by period (pre-Delta period: 2.1 deaths per 1,000 SARS-CoV-2 infections among females of reproductive age; Delta predominance period: 3.3 deaths per 1,000 SARS-CoV-2 infections among females of reproductive age). Twelve of the 15 decedents were Black women or Hispanic women. In comparison, during March 2020–October 2021 in Mississippi, an estimated 43% of births were among Black women and an estimated 5% of births were among Hispanic women. The Mississippi MMRC will conduct a comprehensive, multidisciplinary review of all pregnancy-associated deaths among Mississippi residents, including those attributable to COVID-19, to determine relatedness to pregnancy and contributing factors, including inequities in social determinants of health, and to develop recommendations for the prevention of future deaths. CDC recommends COVID-19 vaccination for pregnant women to prevent serious illness, death, and adverse pregnancy outcomes from COVID-19. Given existing disparities in vaccination rates among pregnant women,****,†††† partnerships to address vaccine access, hesitancy, or other concerns about vaccination can enhance fair and just access to COVID-19 vaccination, including among Black persons and Hispanic persons.

¶¶¶ In Mississippi, during March 1, 2020–October 6, 2021, a total of 163,975 SARS-CoV-2 infections among females aged 10–49 years were reported, and 413 COVID-19–associated deaths occurred (2.5 deaths per 1,000 SARS-CoV-2 infections). During the pre-Delta period, 219 COVID-19–associated deaths occurred (2.1 deaths per 1,000 SARS-CoV-2 infections among females aged 10–49 years; 95% CI = 1.8–2.3); during the period of Delta predominance, 194 COVID-19–associated deaths occurred (3.3 deaths per 1,000 SARS-CoV-2 infections among females aged 10–49 years; 95% CI = 2.9–3.8).

**** https://covid.cdc.gov/covid-data-tracker/#vaccinations-pregnant-women (Accessed November 15, 2021).

†††† https://www.cdc.gov/vaccines/imz-managers/coverage/covidvaxview/interactive.html (Accessed November 15, 2021).

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Testing for Nonprescribed Fentanyl and Percentage of Positive Test Results Among Patients with Opioid Use Disorder — United States, 2019–2020

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Overdose deaths involving synthetic opioids excluding methadone (primarily illicitly manufactured fentanyl) have increased approximately tenfold since 2013 (*1*) and have accelerated during the COVID-19 pandemic, with provisional estimates indicating that synthetic opioid–involved deaths increased 49.4% for the 12-month period ending April 2021.* During the pandemic, persons requiring medication for opioid use disorder (MOUD) might face additional challenges to accessing treatment (e.g., due to closure of providers' offices) (*2*). Early in the pandemic, urine drug testing results indicated increases in nonprescribed fentanyl use (*3*,*4*). To determine trends in testing for fentanyl and the percentage of positive test results before and during the pandemic, clinical drug monitoring of urine specimens from patients residing in all U.S. states and the District of Columbia were tested for fentanyl by using definitive mass spectrometry at Quest Diagnostics during 2019–2020. A positive test result for nonprescribed fentanyl was defined as detection of norfentanyl (major fentanyl metabolite) or fentanyl not listed as prescribed.† Patients receiving MOUD were identified as those having an *International Classification of Diseases, Tenth Revision, Clinical Modification* (ICD-10-CM) F11 code (opioid-related disorders)§ and a positive test result for buprenorphine or methadone listed as prescribed. Among 427,915 specimens, 53,969 (12.6%) from patients whose opioid use disorder medication status was inconclusive were excluded from the analyses.¶ Among the 373,946 included specimens, 57,749 (15.4%) were from patients receiving MOUD. SAS Studio (version 3.6; SAS Institute) was used to conduct all analyses. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.**

The numbers of specimens tested among patients receiving and not receiving MOUD declined 65% and 72%, respectively, during March 29–April 11, 2020 (weeks 14–15), compared with the same weeks in 2019. During September–December 2020 (weeks 35–52), the numbers of specimens tested among patients receiving and not receiving MOUD were 43% and 13% lower, respectively, compared with the same period in 2019.

In the first 2 full weeks of January 2019, before the beginning of the COVID-19 pandemic, 9.6% of specimens from patients receiving MOUD tested positive for nonprescribed fentanyl; the percentage testing positive approximately doubled by the end of 2019 (weeks 51–52) to 26.7% (Figure). During 2020, positive test result rates were highest during March 29–April 11 (weeks 13–14) when the percentage of positive test results peaked at 40.5%. Despite the decline in volume during this period, the overall demographic proportions of patients receiving drug testing remained similar (*3*), suggesting that substantial shifts in the patient demographics were not driving the increase. During April 26–May 9, 2020 (weeks 17–18), the percentage of positive test results declined to 24.3% and continued to decline during September–December 2020 (weeks 35–52; range = 11.9%–18.5% positive per week), levels considerably lower than the corresponding period during 2019 (range = 18.5%–26.7% per week). Among patients not receiving MOUD, the prevalence of positive nonprescribed fentanyl test results did not increase significantly during the early pandemic months compared with that in 2019 (Figure). A limited but significant increase during the second half of 2020 (weeks 27–52; range = 1.4%–1.8%) was observed, compared with the corresponding period during 2019 (range = 1.1%–1.7%).

A decline in drug monitoring disproportionately affected patients receiving MOUD during March–May 2020 (*3*) and continued through the end of 2020, raising concerns regarding potential treatment disruptions or patients forgoing monitoring tests during the pandemic. Naloxone prescriptions also disproportionately declined compared with all other medications during the pandemic and have remained at lower levels (*5*). These observations highlight the urgency of continuing

* https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm (Accessed July 15, 2021).

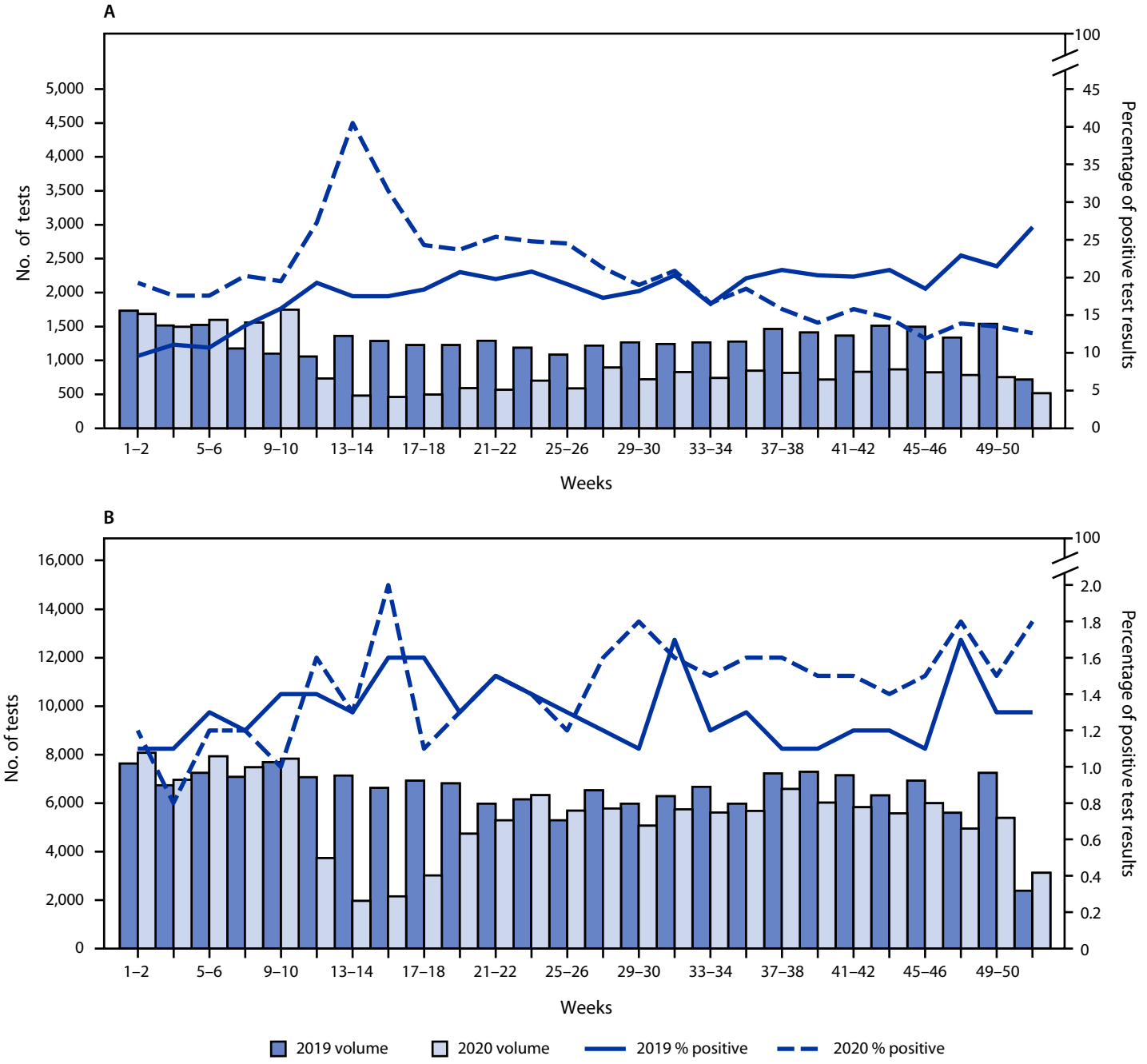
† Quest Diagnostics medMATCH uses clinician-provided prescribed medications (frequently assessed by using state prescription drug monitoring programs) to assess nonprescribed positivity. https://www.questdrugmonitoring.com/medmatch-reports

§ The ICD-10-CM F11 codes are administrative codes used to indicate a diagnosis from a physician and for billing purposes related to opioid abuse (F11.1), dependence (F11.2), or use (F11.9).

¶ Inconclusive MOUD status was assigned for positive test results for buprenorphine or methadone without an ICD-10-CM F11 code, ICD-10-CM F11 codes without buprenorphine or methadone positivity, or buprenorphine or methadone positivity not listed as prescribed.

** 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.

FIGURE. Biweekly nonprescribed fentanyl specimens tested and percentage of positive test results* among patients receiving (A)† and not receiving (B)§ medication for opioid use disorder — United States, 2019–2020



Abbreviation: ICD-10-CM = *International Classification of Diseases, Tenth Revision, Clinical Modification*.

* Primary and secondary y-axis scales are different between panels.

† Patients receiving medication for opioid use disorder were defined as those with an ICD-10-CM code F11 (opioid related disorders) and a positive urine drug test result for buprenorphine or methadone indicated as prescribed.

§ Patients not receiving medication for opioid use disorder had no ICD-10-CM F11 code and a negative urine drug test result for buprenorphine and methadone.

and expanding access to MOUD and other treatment and harm reduction services, including, when indicated,[††] resuming drug monitoring. In the context of predicted increases in opioid-involved and synthetic opioid–involved overdoses throughout 2020 (*6*), the continued lower test volume and lower percentage of positive test results for nonprescribed fentanyl during September–December 2020 among patients receiving MOUD should be investigated to ensure that patients at highest risk for health harms are receiving health care and are retained in care. Reported reductions in specimen submissions from New England and the Midwest (areas with higher nonprescribed fentanyl positivity rates) might also partially explain the lower percentage of positive nonprescribed fentanyl test results (*3*). With continued increases in the percentage of positive nonprescribed fentanyl test results among persons not receiving MOUD, intensified prevention of nonprescribed fentanyl use and overdose is urgently needed (e.g., fentanyl test strip dissemination, enhanced linkage to care, and expanded use of MOUD).[§§,¶¶]

[††] https://www.asam.org/docs/default-source/quality-science/the-asam-appropriate-use-of-drug-testing-in-clinical-addiction-medicine-full-document.pdf?Status%20=%20Temp&sfvrsn%20=%20700a7bc2_2
[§§] https://www.samhsa.gov/newsroom/press-announcements/202104070200
[¶¶] https://emergency.cdc.gov/han/2020/han00438.asp

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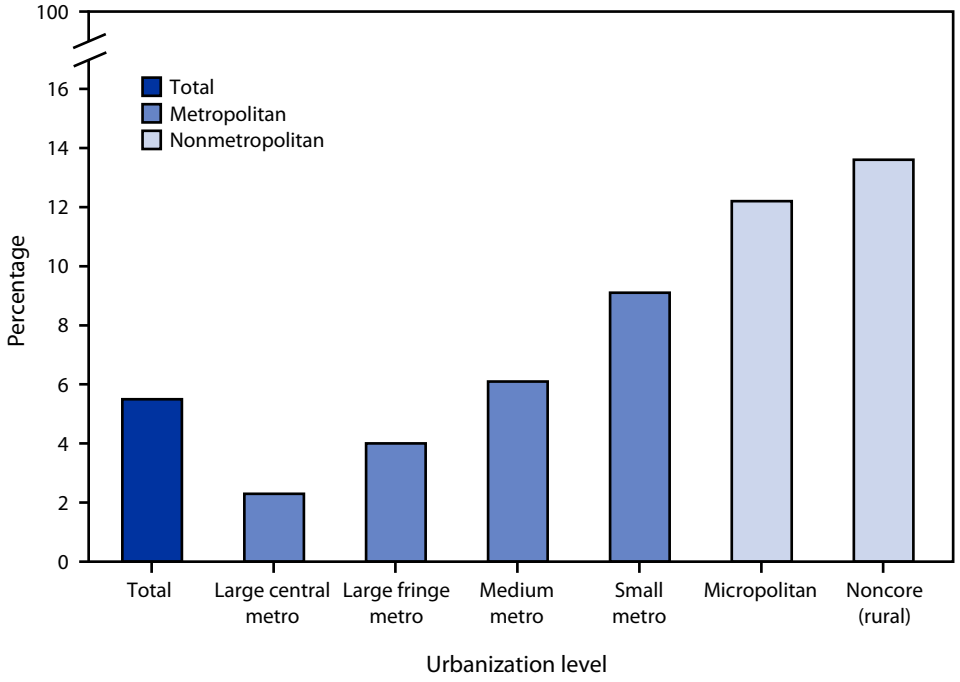
QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage of Births to Mothers Who Reported Smoking Cigarettes at Any Time During Pregnancy, by Urbanization Level* of County of Residence — United States, 2020



* Urbanization level is based on county of residence using the National Center for Health Statistics Urban-Rural Classification Scheme for Counties. http://www.cdc.gov/nchs/data/series/sr_02/sr02_166.pdf

In 2020, 5.5% of all births were to women who reported smoking cigarettes at any time during pregnancy. This percentage was lowest in large central metropolitan areas (2.3%) and increased as the county of residence became less urbanized, reaching a high of 13.6% in the most rural (noncore) counties.

Source: National Vital Statistics System, natality file. https://wonder.cdc.gov/natality-expanded-current.html

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