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## Human Rabies — Utah, 2018

Dallin Peterson, MPH<sup>1</sup>; Bree Barbeau, MPH<sup>1</sup>; Keegan McCaffrey<sup>1</sup>; Randon Gruninger, MPH<sup>1</sup>; Jeffrey Eason, MPH<sup>1</sup>; Cindy Burnett, MPH<sup>1</sup>; Angela Dunn, MD<sup>1</sup>; Melissa Dimond, MPH<sup>1</sup>; Jesse Harbour, MS<sup>4</sup>; Alessandro Rossi, PhD<sup>1</sup>; Bert Lopansri, MD<sup>2</sup>; Kristin Dascomb, MD, PhD<sup>2</sup>; Tara Scribellito, MSN<sup>3</sup>; TaLeah Moosman<sup>4</sup>; Louise Saw, MPH<sup>4</sup>; Curtis Jones<sup>5</sup>; Michael Belenky, MD<sup>1</sup>; Lily Marsden, MD<sup>1</sup>; Michael Niezgoda, MS<sup>6</sup>; Crystal M. Gigante, PhD<sup>6,7</sup>; Rene Edgar Condori, MS<sup>6,7</sup>; James A. Ellison, PhD<sup>6</sup>; Lillian A. Orciari, MS<sup>6</sup>; Pamela Yager<sup>6</sup>; Jesse Bonwitt, BVSc<sup>6</sup>; Erin R. Whitehouse, PhD<sup>6,8</sup>; Ryan M Wallace, DVM<sup>6</sup>

On November 3, 2018, the Utah Department of Health (UDOH) was notified of a suspected human rabies case in a man aged 55 years. The patient's symptoms had begun 18 days earlier, and he was hospitalized for 15 days before rabies was suspected. As his symptoms worsened, he received supportive care, but he died on November 4. On November 7, a diagnosis of rabies was confirmed by CDC. This was the first documented rabies death in a Utah resident since 1944. This report summarizes the patient's clinical course and the subsequent public health investigation, which determined that the patient had handled several bats in the weeks preceding symptom onset. Public health agencies, in partnership with affected health care facilities, identified and assessed the risk to potentially exposed persons, facilitated receipt of postexposure prophylaxis (PEP), and provided education to health care providers and the community about the risk for rabies associated with bats. Human rabies is rare and almost always fatal. The findings from this investigation highlight the importance of early recognition of rabies, improved public awareness of rabies in bats, and the use of innovative tools after mass rabies exposure events to ensure rapid and recommended risk assessment and provision of PEP.

### Case Report

On October 17 and 18, 2018, a man aged 55 years who lived in Utah sought chiropractic treatment in Idaho for neck and arm pain thought to be caused by a recent work-related injury. On October 19, he was evaluated in the emergency department of hospital A for continued neck pain, nuchal muscle spasms, burning sensation in his right arm, and numbness in the palm of his right hand. He had no fever, chills, or other symptoms of infection. Dehydration was a concern because the patient reported he was unable to drink liquids because of severe pain

and muscle spasms. The patient received a prescription for a steroid for muscle spasms and decreased sensation in the right arm and was discharged home.

Two days later, on October 20, the patient developed shortness of breath, tachypnea, and lightheadedness and reported he had not been able to sleep for 4 days; he was transported by ambulance to hospital B. The patient continued to have right upper extremity pain and severe esophageal spasms, causing him to refuse oral fluids. Because of his worsening symptoms and acute delirium, he was transferred to hospital C.

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On October 21, the patient was intubated for airway protection. His symptoms worsened, with fever to 104.7°F (40.4°C), and he became comatose on October 25. Additional exposure history collected from family members included ownership of two healthy dogs and a healthy horse, and a recent grouse-hunting trip where the patient had dressed and cleaned the birds while wearing gloves. High-dose corticosteroid treatment was initiated for presumed autoimmune encephalitis. Because of refractory seizures beginning on October 26, he was transferred to hospital D on October 28, where steroids were continued. On November 3, an infectious disease physician was consulted at hospital D who noted that the patient's symptom of spasms when swallowing suggested a possible diagnosis of rabies. When specifically questioned about the patient's exposure to wild animals, family members reported extensive contact with bats that had occupied the patient's home in the weeks before illness onset. The physician notified UDOH, which recommended collecting clinical specimens, including skin, saliva, cerebral spinal fluid (CSF), and serum. Rabies PEP was not indicated because of the advanced state of disease (1). The patient continued to decline, supportive care was withdrawn, and he died on November 4, 19 days after symptom onset.

On November 7, antemortem specimens (serum, CSF, skin biopsy, and saliva) were sent to CDC for testing. CDC reported detection of rabies immunoglobulin M and immunoglobulin G in the CSF by indirect immunofluorescence assay. Rabies virus neutralizing antibodies were detected in

serum (titer = 1:5,400; 43.2 IU/ml) and in CSF (titer = 1:250; 2.0 IU/ml), by rapid fluorescent focus inhibition test. No rabies virus antigen was detected in skin biopsy by direct fluorescent antibody (DFA) test, and no viral RNA was detected in skin and saliva by real-time reverse transcription–polymerase chain reaction (RT-PCR) (2,3).

CDC confirmed the presence of rabies virus antigen and RNA in postmortem brain stem tissue and cerebellum specimens by DFA and real-time RT-PCR, respectively. Antigenic typing with monoclonal antibodies to the rabies virus nucleoprotein, and phylogenetic sequence analysis indicated that the virus identified in the patient's specimens was consistent with that of a rabies virus variant associated with Mexican free-tailed bats (*Tadarida brasiliensis*).

## Public Health Response

Once the rabies diagnosis was confirmed, UDOH established an Incident Command System structure to develop and coordinate response activities. The goals of the response were to 1) determine the source of the patient's infection; 2) identify possible exposure risk to hospital workers, community members, and family members during the patient's infectious period; 3) coordinate administration of PEP for exposed persons; and 4) educate health care providers and the public about the risk for rabies associated with contact with bats. Public health investigation and response partners included the Central Utah Public Health Department, Utah County

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**Summary****What is already known about this topic?**

Human rabies is preventable by early recognition of exposure and receipt of postexposure prophylaxis (PEP). Bats are the main source of rabies in the United States.

**What is added by this report?**

Delayed recognition of a human rabies case resulted in potential exposure of 279 health care workers and others in Utah. Exposures were evaluated through an online survey; 74 health care workers with likely rabies virus exposures and 30 family and community members who had contact with the patient's body fluids received PEP.

**What are the implications for public health practices?**

Educating the general public about the risk for rabies through bat exposure and advising health care providers to consider rabies in the differential diagnosis of unexplained neurologic symptoms could reduce exposures.

exposed health care workers, an online exposure assessment tool, modeled after a tool used in a mass bat exposure response in Virginia (4) was developed and distributed to the four affected health care facilities. Responses were collected at UDOH and provided to the health care facilities, which subsequently ensured that exposed employees received PEP according to Advisory Committee on Immunization Practices guidelines (5). The affected health care facilities identified and assessed 242 health care workers known to have had some contact with the patient, which included personnel at each hospital facility, emergency medical transport services, and laboratory workers. A total of 126 (52%) of the 242 exposed health care workers completed the online assessment within 72 hours, and 222 (90%) completed it within 12 days. Among the 242 assessed facility-based health care workers with some contact with the patient, 74 (31%) were determined to have been potentially exposed to infectious materials and received PEP; 63 (85%) of the 74 received PEP within 1 week of initial assessment. The chiropractic workers who initially evaluated the patient were surveyed separately using paper assessment forms; none of the workers were found to have been exposed.

In addition to the 242 potentially exposed facility-based health care workers, public health officials also assessed 37 family and community members who had contact with the patient (total persons assessed = 279); 30 (81%) of the 37 family and community members had contact with the patient's body fluids and received PEP. The PEP supply used during the response was coordinated and administered by health care facilities throughout Utah. All exposed health care workers completed the PEP regimen as scheduled with only one report of an adverse reaction to the rabies vaccine (gastrointestinal illness reported by one health care provider after receipt of the third vaccine dose).

In April 2019, CDC and UDOH conducted focus group discussions with local health departments involved in the response and with health care workers who cared for the patient. The discussions revealed knowledge gaps about human-to-human rabies transmission among health care workers, and rabies prevention among animal control workers and community members. In response, UDOH and CDC delivered a hospital presentation in hospital D, which was broadcast to hospitals A, B, and C and across the health care system to health care workers in urban and rural areas. Posters and fliers describing the risk for rabies associated with bats were distributed by local public health workers to animal health workers, health care facilities, public health offices, and other public locations.

**Discussion**

Human rabies deaths are rare in the United States, and early recognition of the disease can reduce the number of health

care-associated exposures and ensure timely receipt of PEP (3). Considerations for early recognition include providing education to medical providers (especially those in rural areas) regarding clinical symptoms, identifying patient exposures to wild animals such as bats, and emphasizing the importance of PEP if an exposure occurs. In Utah, humans and animals are most likely to be infected with rabies through exposure to bats, the only known rabies reservoir in Utah.\* The Mexican free-tailed bat is the most common host species detected in Utah through public health surveillance (42% of all bats) followed by the Big Brown (21%) and the Silver Haired (15%).

During the past 10 years, an average of 95 bats per year were submitted to the Utah Public Health Laboratory for testing, with 15–25 bats found to be rabid; however, this only accounts for bats tested through the state laboratory and does not count all bats in Utah. The delayed diagnosis of rabies in the patient in this report prevented him from receiving any early treatment for rabies and also resulted in potential rabies exposures for 279 persons in multiple settings during the patient's infectious period. Structured collaboration between public health partners and health care facilities, as well as the use of online exposure assessment, permitted rapid assessment of exposed persons across numerous settings, facilitating timely recommendation and administration of PEP.

\*<http://health.utah.gov/epi/diseases/rabies/surveillance/index.html>.

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Corresponding author: Dallin Peterson, ddpeterson@utah.gov, 801-538-6333.

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<sup>1</sup>Utah Department of Health, Salt Lake City; <sup>2</sup>Intermountain Healthcare, Salt Lake City, Utah; <sup>3</sup>Salt Lake County Health Department, Salt Lake City, Utah; <sup>4</sup>Central Utah Public Health Department, Nephi; <sup>5</sup>Utah County Health Department, Provo; <sup>6</sup>Division of High-Consequence Pathogens and Pathology, National Center for Emerging and Zoonotic Infectious Diseases, CDC; <sup>7</sup>Oak Ridge Institute for Science and Education, Oak Ridge, Tennessee; <sup>8</sup>Epidemic Intelligence Service, CDC.

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## Carfentanil Outbreak — Florida, 2016–2017

Chris Delcher, PhD<sup>1</sup>; Yanning Wang, MS<sup>2</sup>; Russell S. Vega, MD<sup>3</sup>; John Halpin, MD<sup>4</sup>; R. Matthew Gladden, PhD<sup>4</sup>; Julie K. O'Donnell, PhD<sup>4</sup>; Jessica A. Hvozdovich, MS<sup>5</sup>; Bruce A. Goldberger, PhD<sup>5</sup>

Increased prevalence of illicitly manufactured fentanyl and fentanyl analogs has contributed substantially to overdose deaths in the United States (1–3). On October 26, 2015, CDC issued a Health Advisory regarding rapid increases in deaths involving fentanyl. This CDC Health Advisory has been updated twice to address increases in fentanyl and fentanyl analog overdoses and their co-occurrence with nonopioids (4). Deaths involving carfentanil, an analog reportedly 10,000 times more potent than morphine and 100 times more potent than fentanyl, were first reported in Florida, Michigan, and Ohio in 2016 and described in an August 2016 CDC Health Advisory (1,5). Carfentanil is used to rapidly immobilize large animals in veterinary medicine and has no U.S. approved therapeutic use in humans. Carfentanil's street price per dose is likely lower than that of heroin. During 2016 and 2017, an outbreak of carfentanil-involved fatal overdoses in Florida emerged, and the Medical Examiner jurisdiction serving Sarasota, Manatee, and DeSoto counties (the Sarasota area) was the outbreak epicenter. This report describes toxicology profiles, sociodemographic information, and geographic distributions of carfentanil-involved fatal overdoses (carfentanil deaths) in the Sarasota area compared with those in the rest of Florida (i.e., all Florida counties excluding Sarasota area) from January 2016 to December 2017. The Sarasota area accounted for 19.0% of 1,181 statewide carfentanil deaths that occurred during this time and experienced a peak in carfentanil deaths preceding the larger Florida outbreak. The report of a single carfentanil death from August to December 2017 (compared with 73 reported deaths during the same period in 2016) appeared to mark the end of the outbreak in the area. The threat of such rapid, intense fatal overdose outbreaks highlights the need for accelerated reporting, reliable data sharing systems, and novel proactive surveillance to support targeted prevention and response efforts by public health and safety organizations (6).

Florida medical examiners report drug-related deaths to the Florida Department of Law Enforcement with details including cause and manner of death, demographic data, and toxicology findings. In Florida, fentanyl analog reporting (including carfentanil) began in January 2016.\* Deaths were determined by medical examiners as fentanyl analog–caused

deaths, and carfentanil was listed in the toxicology report. A substance was considered to be co-occurring if it was detected by toxicologic testing irrespective of whether the medical examiner determined that it contributed to the fatal overdose. Descriptive statistics, epidemic curves, and maps were used to describe the carfentanil outbreak and standard distribution tests (statistical significance defined as  $p < 0.05$ ) were used to compare characteristics of the Sarasota area outbreak with those of the outbreak in the rest of Florida. SAS (version 9.4; SAS Institute) was used to conduct all analyses.

Florida experienced 1,181 carfentanil-involved overdose deaths from 2016 (548) to 2017 (633). Among these, 224 (19.0%) occurred in the Sarasota area (Table), although according to the U.S. Census Bureau, this region accounts for only 4.0% of Florida's population.<sup>†</sup> The Sarasota area outbreak began with four carfentanil deaths in June 2016, and peaked at 37 deaths in July, accounting for 82.2% of the area's opioid overdose deaths that month (Figure 1) and 50% of all opioid overdose deaths in 2016. Carfentanil deaths in the Sarasota area declined substantially by the end of 2016 but increased again in January 2017 and remained elevated through July 2017 (110 deaths, 54% of all 2017 opioid overdose deaths). Only one death was reported during August–December 2017. The Sarasota area had the highest rate of carfentanil deaths for 2016 (13.8 per 100,000) and the second highest rate for 2017 (13.1 per 100,000), following the Palm Beach area (19.4 per 100,000) (Figure 2). In the rest of Florida, the number of carfentanil deaths peaked in October 2016, approximately 3 months after the initial Sarasota area spike, at 137 deaths (32.0% of Florida's October opioid overdose deaths). Carfentanil deaths accounted for 12% and 13% of opioid deaths in the rest of Florida during 2016 and 2017, respectively. Among Florida's 67 counties, 26 (39%) and 36 (54%) reported one or more carfentanil deaths in 2016 and 2017, respectively (Figure 2) (Supplementary Table, <https://stacks.cdc.gov/view/cdc/84586>), suggesting that the epidemic expanded from Florida's southern to northwestern counties. After the Sarasota outbreak subsided, carfentanil was still consistently present in approximately 8% of state opioid deaths from August to December 2017 (Figure 1).

<sup>\*</sup>Fentanyl-related overdoses in Florida before analog testing, during 2013–2015 available at <https://www.cdc.gov/mmwr/volumes/65/wr/mm6533a3.htm>.

<sup>†</sup>Annual estimates of the resident population, April 1, 2010 to July 1, 2018 available at <https://factfinder.census.gov>.

**TABLE.** Characteristics of carfentanil-involved overdose deaths — Sarasota area (Sarasota, Manatee, and DeSoto counties) and the rest of Florida, 2016 and 2017

Characteristic	2016 (N = 548)			2017 (N = 633)		
	Sarasota area n = 114	Rest of Florida n = 434	p-value*	Sarasota area n = 110	Rest of Florida n = 523	p-value*
<b>Age group (yrs)</b>						
<25	11 (9.7)	46 (10.6)	NS	9 (8.2)	64 (12.2)	NS
25–34	40 (35.1)	168 (38.7)		39 (35.4)	202 (38.6)	
35–44	33 (28.9)	107 (24.7)		31 (28.2)	123 (23.5)	
45–54	18 (15.8)	66 (15.2)		22 (20.0)	82 (15.7)	
≥55	12 (10.5)	47 (10.8)		9 (8.2)	52 (9.9)	
Median age (yrs)	35.5	35.0	—	36.0	34.0	—
<b>Sex</b>						
Female	22 (19.3)	94 (21.7)	NS	35 (31.8)	116 (22.2)	<0.05
Male	92 (80.7)	340 (78.3)		75 (68.2)	407 (77.8)	
<b>Race</b>						
White	105 (92.1)	391 (90.1)	NS	96 (87.3)	477 (91.2)	NS
Other	9 (7.9)	43 (9.9)		14 (12.7)	46 (8.8)	
<b>Co-occurring substance</b>						
<b>Opioid</b>						
Fentanyl	8 (7.0)	98 (22.6)	<0.001	23 (20.9)	124 (23.7)	NS
Heroin	9 (7.9)	102 (23.5)	<0.001	11 (10.0)	136 (26.0)	<0.001
Methadone	8 (7.0)	14 (3.2)	NS	8 (7.3)	12 (2.3)	<0.05
Morphine	18 (15.8)	162 (37.3)	<0.001	37 (33.6)	170 (32.5)	NS
Other fentanyl analog†	<5 (1.8)	112 (25.8)	<0.001	19 (17.3)	99 (18.9)	NS
Oxycodone	11 (9.6)	44 (10.1)	NS	<5 (3.6)	44 (8.4)	NS
<b>Other</b>						
Alcohol	37 (32.5)	104 (24.0)	NS	33 (30.0)	105 (20.1)	<0.05
Alprazolam	27 (23.7)	84 (19.4)	NS	18 (16.4)	128 (24.5)	NS
Cocaine	58 (50.9)	223 (51.4)	NS	59 (53.6)	218 (41.7)	<0.05
Methamphetamine	10 (8.8)	31 (7.1)	NS	16 (14.5)	37 (7.1)	<0.05

**Abbreviation:** NS = not significant.

\* By chi-squared test or Fisher's exact test when expected cell counts were <5.

† Beginning in January 2016, Florida tested for and reported the following analogs: acetyl fentanyl, beta-hydroxythiofentanyl, butyryl fentanyl/isobutyryl fentanyl, carfentanil, despropionyl fentanyl (4-ANPP), despropionyl fluorofentanyl, fluorobutyryl/fluoroisobutyryl fentanyl, fluorofentanyl, and furanyl fentanyl.

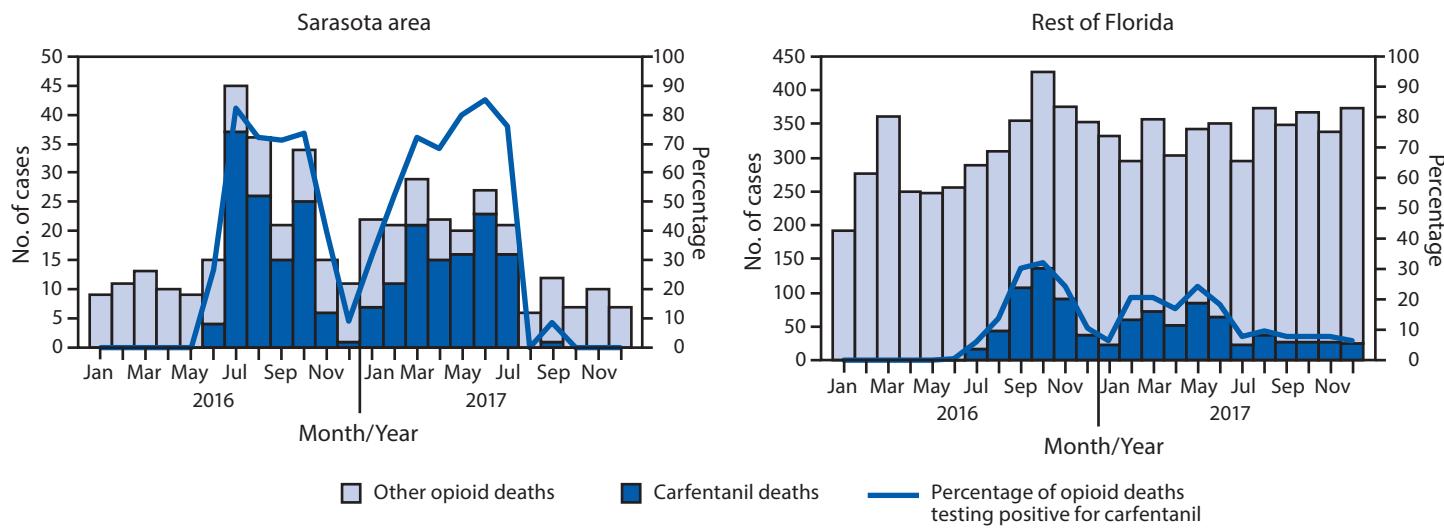
During 2016–2017, 35.3% of Sarasota area carfentanil-associated decedents were aged 25–34 years, and the majority were white (89.7%) and male (74.6%) (Table). In 2017, 32% of the carfentanil deaths in the Sarasota area occurred in women, whereas women accounted for 22% of carfentanil deaths in the rest of Florida. During 2016–2017, there was an approximate 59% increase in carfentanil deaths among women (22 versus 35) compared with an approximate 18% decrease among men (92 versus 75). Sarasota area decedents were significantly less likely to have heroin present compared with those in the rest of Florida in both 2016 and 2017, even when including positive morphine results as indicative of a possible heroin death. Carfentanil-involved decedents in the Sarasota area were significantly less likely to have fentanyl or a fentanyl analog other than carfentanil present than were those in the rest of Florida during 2016. In 2017, Sarasota carfentanil deaths became as likely to involve fentanyl or other fentanyl analogs as the rest of Florida (Table). Carfentanil deaths in the Sarasota area in 2017 were significantly more likely to test positive for cocaine (53.6%) and methamphetamine (14.5%) than were those in the rest of Florida

(41.7% and 7.1%, respectively); no difference was found for 2016. Differences in cocaine positivity in 2017 were driven by declines in cocaine co-occurrence in the rest of Florida in 2017, whereas differences in methamphetamine positivity were driven by increased co-occurrence in Sarasota area in 2017.

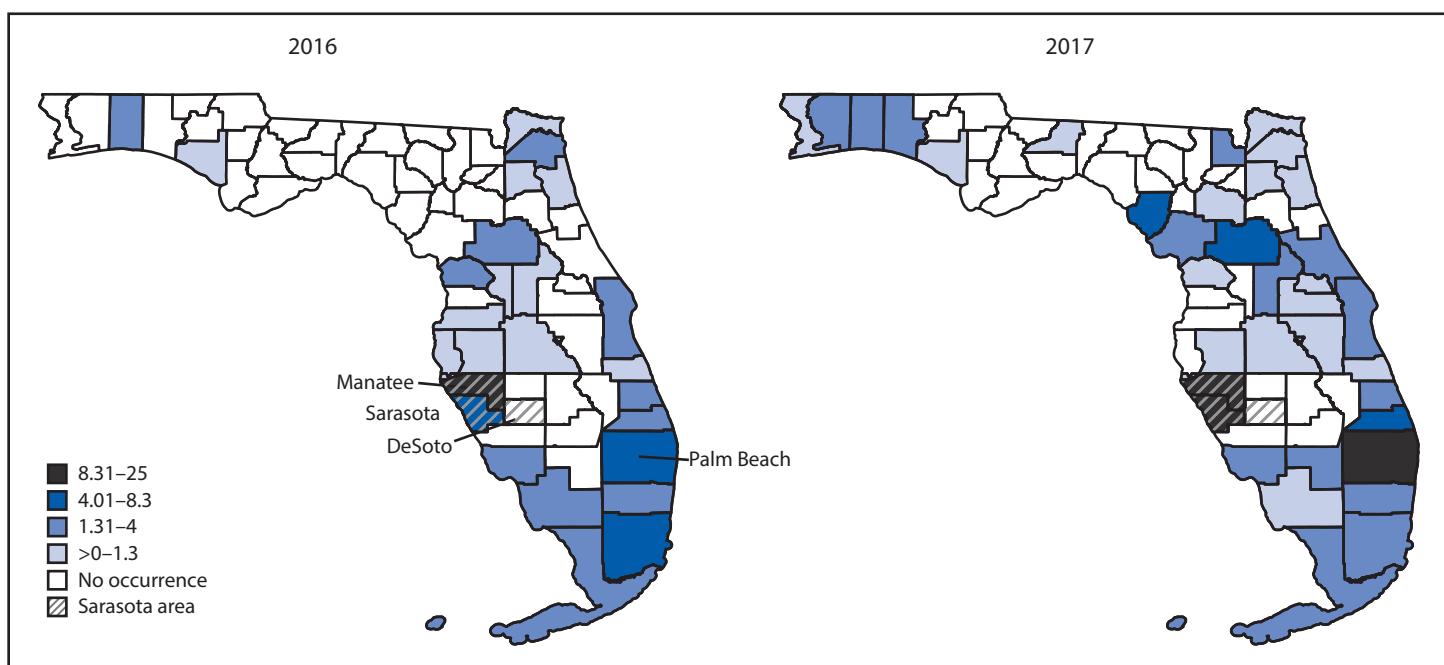
## Discussion

The carfentanil-involved fatal overdose outbreak in the Sarasota area epicenter began in June 2016, lasted for at least 12 months, and abruptly ended in August 2017. By the end of 2017, carfentanil had spread throughout the state and was still present in approximately one in 15 opioid-involved overdose deaths in Florida. Further evidence of carfentanil's ongoing presence in Florida's drug supply comes from Palm Beach County, Florida, where carfentanil became the second most frequently detected drug behind alcohol in impaired driving cases during this outbreak (7). These findings highlight the need for rapid implementation of geographically targeted and sustained multisector interventions to reduce the proliferation and impact of similar outbreaks as early as possible.

**FIGURE 1. Carfentanil- and opioid-involved deaths and percentage of opioid-involved deaths testing positive for carfentanil — Sarasota area\* and the rest of Florida,† 2016 and 2017**



**FIGURE 2. Carfentanil-involved deaths per 100,000 population,\* by county where death occurred — Florida, 2016 and 2017†**



There was significant in-state variation regarding the presence of fentanyl and fentanyl analogs in carfentanil deaths. Earlier in the outbreak, fentanyl and fentanyl analogs were infrequently detected in carfentanil deaths in the Sarasota area, in contrast to those in the rest of Florida. In addition,

heroin was coinvolved in nearly 9% of carfentanil deaths in the Sarasota area, compared with approximately 25% of carfentanil deaths in the rest of Florida. This suggests that a substantial percentage of the early carfentanil deaths in Sarasota involved drug products in which the only illicit opioid present was

**Summary****What is already known about this topic?**

Deaths involving fentanyl analogs, such as carfentanil, have increased the severity of the opioid overdose epidemic in Florida.

**What is added by this report?**

During January 2016–December 2017, 224 of Florida's 1,181 carfentanil-involved fatal overdoses occurred in the Sarasota area, preceding a larger statewide outbreak in the rest of the state. The outbreak ended in the Sarasota area in August 2017, but carfentanil continued to be detected in overdose deaths in other areas of Florida through the end of 2017.

**What are the implications for public health practice?**

Accelerated reporting, better communication and data sharing across agencies, and increased surveillance for novel substances are needed to mitigate harm associated with introduction of illicitly manufactured fentanyl analogs into drug markets.

partially explain the substantial decline in carfentanil deaths in Florida during late 2017. Closer analyses of law enforcement laboratory submissions and overdose deaths during that period are needed to study this hypothesis.

The findings in this report are subject to at least three limitations. First, medical examiners' cause of death determinations involve subjective clinical evaluation of incomplete information and different laboratory testing protocols, and thus, might vary across districts in Florida. Second, reports are based on the county where death occurred, which might be different from those where the drug was used, acquired, or where a decedent resided, which might have resulted in misclassification of location. Finally, misclassification of heroin-associated deaths might have occurred: in 55 Sarasota area carfentanil deaths, morphine was detected, but 6-acetylmorphine was absent. Only the presence of 6-acetylmorphine can confirm heroin use; therefore, heroin-involved cases might be undercounted (9). Sensitivity analyses was performed by reclassifying these cases as heroin-involved, but the findings did not change.

New data platforms and sharing of disparate data sources (e.g., forensic laboratory samples, dark web advertising, drug-focused social media, emergency medical services transports, and nonfatal overdose mapping) across local agencies might help identify and respond to emergent drug trends more rapidly (6,10). Routine testing for fentanyl analogs and identifying novel substances in biologic specimens remains a significant national challenge because of the cost and time needed for method validation.<sup>\*\*††</sup> CDC's Enhanced State Opioid Overdose Surveillance Program provides funding to 32 states (including Florida) and the District of Columbia, to support comprehensive toxicology testing of opioid overdose decedents, along with rapid overdose surveillance using emergency department data that might help identify emerging threats such as fentanyl analogs.<sup>§§</sup> In 2019, CDC's new Overdose Data to Action funding expanded to 49 health departments and included all drug overdose decedents.<sup>¶¶</sup> With improved testing and surveillance providing actionable intelligence, laboratories, medical examiners, and coroners will be able to alert public health and safety agencies more quickly of suspected overdose outbreaks. This will enable more efficient responses and the deployment of necessary resources to prevent future overdose deaths.

<sup>\*\*</sup> Review of fentanyl and fentanyl analogs chemistry available at <https://doi.org/10.1016/j.neuropharm.2017.10.016>.

<sup>††</sup> In 2019, Traceable Opioid Material Kits (TOM Kits) containing traceable opioid reference material were developed by the National Center for Environmental Health at CDC to improve and support laboratory detection of emerging opioids. [https://www.cdc.gov/nceh/dls/pdf/Opiod\\_Factsheet-508.pdf](https://www.cdc.gov/nceh/dls/pdf/Opiod_Factsheet-508.pdf).

<sup>§§</sup> <https://www.cdc.gov/drugoverdose/foa/state-opioid-mm.html>.

<sup>¶¶</sup> <https://www.cdc.gov/drugoverdose/od2a/index.html>.

carfentanil. However, as the Sarasota area outbreak spread, fentanyl and other fentanyl analogs were more frequently detected, as was heroin, to a lesser extent. These findings from later in the outbreak are consistent with the pattern of new drug products being mixed with more diverse adulterants over time as they are exchanged by persons involved in the illicit drug market (5). Whether decedents were aware of the presence of carfentanil in drug products is unknown.

This is one of the first examinations of a large number of carfentanil fatalities (>1,000 deaths) showing the disproportionate spatiotemporal intensity associated with an outbreak. This outbreak event started at a specific point in time and space, which provided an opportunity to examine changes in drug markets that might have led to these deaths. Law enforcement and the media provided early signals in Florida before mortality data became available, highlighting the need to communicate and share local data across multiple agencies to inform a timely, data-driven response. These findings, along with those from a concurrent carfentanil outbreak in Wayne County, Michigan (8), and the timing of carfentanil-positive international drug seizures, suggest that Florida's outbreak was one of multiple global events leading to the rapid introduction and reduction of carfentanil availability in the illicit drug supply.<sup>§</sup> In the first half of 2018, the national illicit supply of carfentanil appeared to drop sharply, indicated by an 83% reduction in carfentanil-positive laboratory submissions to the National Forensic Laboratory Information System.<sup>¶</sup> A similar supply reduction might have occurred in Florida and would

<sup>§</sup> [https://www.who.int/medicines/access/controlled-substances/Critical\\_Review\\_Carfentanil.pdf](https://www.who.int/medicines/access/controlled-substances/Critical_Review_Carfentanil.pdf).

<sup>¶</sup> <https://www.nflis.deadiversion.usdoj.gov/Resources/NFLISPublicResourceLibrary.aspx>.

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Jungjun Bae; Michelle Duong.

<sup>1</sup>Department of Pharmacy Practice and Science, University of Kentucky, Lexington; <sup>2</sup>Department of Health Outcomes and Biomedical Informatics, University of Florida, Gainesville; <sup>3</sup>District Twelve Medical Examiner's Office, Sarasota, Florida; <sup>4</sup>Division of Unintentional Injury Prevention, National Center for Injury Prevention and Control, CDC; <sup>5</sup>Forensic Medicine Division, Department of Pathology, Immunology and Laboratory Medicine, College of Medicine, University of Florida, Gainesville.

Corresponding author: Chris Delcher, chris.delcher@uky.edu, 859-562-2175.

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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# Advisory Committee on Immunization Practices Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger — United States, 2020

Candice L. Robinson, MD<sup>1</sup>; Henry Bernstein, MD<sup>2</sup>; Katherine Poehling, MD<sup>3</sup>; José R. Romero, MD<sup>4</sup>; Peter Szilagyi, MD<sup>5</sup>

At its October 2019 meeting, the Advisory Committee on Immunization Practices (ACIP)\* approved the 2020 Recommended Child and Adolescent Immunization Schedule for Ages 18 Years or Younger. The 2020 child and adolescent immunization schedule summarizes ACIP recommendations, including several changes from the 2019 immunization schedule<sup>†</sup> on the cover page, three tables, and notes found on the CDC immunization schedule website (<https://www.cdc.gov/vaccines/schedules/index.html>). Health care providers are advised to use the tables and the notes together. This immunization schedule is recommended by ACIP (<https://www.cdc.gov/vaccines/acip/index.html>) and approved by the CDC Director, the American Academy of Pediatrics, the American Academy of Family Physicians, the American College of Obstetricians and Gynecologists, and, for the first time, the American College of Nurse-Midwives.

ACIP's recommendations on use of each vaccine are developed after in-depth reviews of vaccine-related data, including the epidemiology and burden of the vaccine-preventable disease, vaccine efficacy and effectiveness, vaccine safety, quality of evidence, feasibility of program implementation, and economic analyses of immunization policy (1). The child and adolescent immunization schedule is published annually to consolidate and summarize updates to ACIP recommendations on vaccination of children and adolescents and to assist health care providers in implementing current ACIP recommendations. The use of vaccine trade names in this report and in the child and adolescent immunization schedule is for identification purposes only and does not imply endorsement by ACIP or CDC.

For further guidance on the use of each vaccine, including contraindications and precautions, health care providers are referred to the respective ACIP vaccine recommendations at <https://www.cdc.gov/vaccines/hcp/acip-recommendations/index.html>. Providers should be aware that changes in recommendations for specific vaccines can occur between annual updates to the child and adolescent immunization schedule. If errors or omissions are discovered within the child and adolescent schedule, CDC posts revised versions on the CDC immunization schedule website.<sup>§</sup> Printable versions of the 2020 child and adolescent immunization schedule and ordering instructions are available on the immunization schedule website at <https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html>.

## Changes in the 2020 Child and Adolescent Immunization Schedule

Changes in the 2020 child and adolescent immunization schedule for persons aged 18 years or younger include new or updated ACIP recommendations for hepatitis A vaccine (HepA) (2); influenza vaccine (3); meningococcal B vaccine (MenB) (2); and tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (Tdap) (4). Changes also include clarification of the recommendations for diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP), *Haemophilus influenzae* type b vaccine (Hib), hepatitis B vaccine (HepB), meningococcal ACWY vaccine (MenACWY), and poliovirus vaccine. Following are the changes to the cover page, Tables 1–3, and the Vaccine Notes.

### Cover page

- The American College of Nurse-Midwives has been added to the list of organizations that approve the child and adolescent immunization schedule.

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<sup>§</sup>CDC encourages organizations to use syndication as a more reliable method for displaying the most current and accurate immunization schedules on an organization's website rather than copying these schedules to their websites. Use of content syndication requires a one-time step that ensures an organization's website displays current schedules as soon as they are published or revised; instructions for the syndication code are available on CDC's website (<https://www.cdc.gov/vaccines/schedules/syndicate.html>). CDC also offers technical assistance for implementing this form of content syndication (e-mail request to [ncirdwebteam@cdc.gov](mailto:ncirdwebteam@cdc.gov)). Information on changes in ACIP recommendations in the child and adolescent immunization schedule before the next scheduled annual update, if any, is available at <https://www.cdc.gov/vaccines/schedules/hcp/schedule-changes.html#child>.

- Trademark symbols (°) were added to all vaccine trade names.

**Table 1**

- HepA row:** The bar for persons aged 2–18 years has been changed to solid green to denote the recommendation for routine catch-up immunization for all persons in this age group.
- HPV row:** An asterisk has been added to the blue bar that appears for children aged 9–10 years to indicate that for this group, the HPV vaccine series can be started at the clinician’s discretion. The text that defines the blue box in the table’s legend has been edited and now reads “Recommended based on shared clinical decision-making or \*can be used in this age group.”
- Legend:** The text that defines the gray box has been edited and now reads “No recommendation/not applicable.”

**Table 2**

- Meningococcal rows:** The letters “ACWY” were added to clarify that these catch-up intervals apply only to MenACWY and not to MenB.

**Table 3**

- HepA row:** All boxes now appear yellow to denote the recommendation for routine vaccination for all persons aged 18 years or younger, including those with the medical indications outlined in the table.
- MenACWY row:** The pregnancy box is now yellow, because the meningococcal vaccine may be administered to pregnant women, if indicated.
- Legend:** The text that defines the red box has been edited and now reads “Not recommended/contraindicated—vaccine should not be administered.” The text that defines the gray box has been edited and now reads “No recommendation/not applicable.”

**Vaccine Notes**

- DTaP:** To clarify the recommendations for catch-up vaccination, the note has been updated to indicate that dose 5 is not necessary if dose 4 was administered at age 4 years or older AND at least 6 months after dose 3.
- Hib:** A bullet has been added to note that catch-up vaccination is not recommended for previously unvaccinated children aged 5 years (60 months) or older who are not at high risk.
- HepA:** The note was revised to include the recommendation that all children and adolescents aged 2 through 18 years who have not previously received Hep A should receive catch-up vaccination and complete a 2-dose series.
- HepB:** A “Special situations” section has been added which contains information regarding populations for whom revaccination might be recommended. The ACIP HepB

recommendations are referenced for detailed revaccination recommendations.

- Influenza vaccine:** The note has been updated to reflect the recommendations for the 2019–20 influenza season. The “Routine vaccination” section was reformatted to more clearly outline circumstances under which 1 or 2 doses of influenza vaccine are recommended. In addition, the bullet that outlines circumstances under which live attenuated influenza vaccine (LAIV) should not be used was reformatted into a bulleted list.
- MenACWY:** Guidance regarding adolescent vaccination for children who received MenACWY before age 10 years has been added to the note.
- MenB:** Booster doses are now recommended for persons aged ≥10 years with complement deficiency, those who use complement inhibitors, persons with asplenia, persons who are microbiologists, and persons determined by public health officials to be at increased risk during an outbreak. The MenB note has been updated to include a link to the detailed recommendations.
- Poliovirus vaccination:** Detailed information has been added regarding which oral poliovirus vaccine (OPV) doses may be counted toward the U.S. vaccination requirements.
- Tdap:** The note has been updated to allow either Td or Tdap, as an option for decennial tetanus booster doses and catch-up series doses in persons who have previously received Tdap. In addition, the note has been edited to reflect recent updates to the clinical guidance for children aged 7 through 18 years who received doses of Tdap or DTaP at age 7 through 10 years. A dose of Tdap or DTaP administered at age 10 years may now be counted as the adolescent Tdap booster. A dose of Tdap or DTaP administered at age 7 through 9 years should not be counted as the adolescent dose, and Tdap should be administered at age 11–12 years.

**Additional Information**

The Recommended Child and Adolescent Immunization Schedule, United States, 2020 is available at <https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html>. The full ACIP recommendations for each vaccine are also available at <https://www.cdc.gov/vaccines/hcp/acip-recs/index.html>. All vaccines identified in Tables 1, 2, and 3 (except DTaP, rotavirus, and poliovirus vaccines) also appear in the Recommended Adult Immunization Schedule for Ages 19 Years or Older, United States, 2020.<sup>¶</sup> The notes for vaccines that appear in both the adult immunization schedule and the child and

<sup>¶</sup><https://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html>.

adolescent immunization schedule have been harmonized to the greatest extent possible.

### Acknowledgments

Rosters of current and past members of the Advisory Committee on Immunization Practices (ACIP) are available at <https://www.cdc.gov/vaccines/acip/committee/members-archive.html>.

### ACIP Child/Adolescent Immunization Work Group

Chair: Henry Bernstein. Members: Sarah Coles, Katherine Debiec, Susan Lett, Sarah McQueen, Amy B. Middleman, Sean O'Leary, Diane Peterson, Katherine Poehling, José Romero, Patricia Stinchfield, Peter Szilagyi, Thomas Weiser. CDC Lead: Candice Robinson; CDC Contributors: Mark Freedman, Holly Hill, Suzanne Johnson-DeLeon, David Kim, Andrew Kroger, Elissa Meites, Tina Objio, Ginger Redmon, Raymond Strikas, Akiko Wilson, Charles Wolfe, JoEllen Wolicki.

Corresponding author: Candice L. Robinson, [crobinson4@cdc.gov](mailto:crobinson4@cdc.gov), 404-718-1400.

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<sup>1</sup>Immunization Services Division, National Center for Immunization and Respiratory Diseases, CDC; <sup>2</sup>Zucker School of Medicine at Hofstra/Northwell and Cohen Children's Medical Center, New Hyde Park, New York; <sup>3</sup>Wake Forest School of Medicine/Wake Forest Baptist Health and Brenner Children's Hospital, Winston-Salem, North Carolina; <sup>4</sup>University of Arkansas for Medical Sciences and Arkansas Children's Hospital, Little Rock, Arkansas; <sup>5</sup>Department of Pediatrics, University of California Los Angeles, Los Angeles, California.

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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# Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older — United States, 2020

Mark S. Freedman, DVM<sup>1</sup>; Paul Hunter, MD<sup>2,3</sup>; Kevin Ault, MD<sup>4</sup>; Andrew Kroger, MD<sup>1</sup>

At its October 2019 meeting, the Advisory Committee on Immunization Practices (ACIP)\* voted to recommend approval of the 2020 Recommended U.S. Adult Immunization Schedule for Persons Aged 19 Years and Older. The 2020 adult immunization schedule, available at <https://www.cdc.gov/vaccines/schedules/index.html>,† summarizes ACIP recommendations in two tables and accompanying notes. This 2020 adult immunization schedule has been approved by the CDC Director, the American College of Physicians, the American Academy of Family Physicians, the American College of Obstetricians and Gynecologists, and the American College of Nurse-Midwives. Health care providers are advised to use the tables and the notes together.

ACIP's recommendations on use of each vaccine are developed after in-depth reviews of vaccine-related data, including the epidemiology and burden of the vaccine-preventable disease, vaccine efficacy and effectiveness, vaccine safety, quality of evidence, feasibility of program implementation, and economic analyses of immunization policy (1). The adult immunization schedule is published annually to consolidate and summarize updates to ACIP recommendations on vaccination of adults and to assist health care providers in implementing current ACIP recommendations. The use of vaccine trade names in this report and in the adult immunization schedule is for identification purposes only and does not imply endorsement by ACIP or CDC.

For further guidance on the use of each vaccine, including contraindications and precautions, health care providers are referred to the respective ACIP vaccine recommendations at <https://www.cdc.gov/vaccines/hcp/acip-recs/index.html>. Changes in recommended use of vaccines can occur between annual updates to the adult immunization schedule.

\*Recommendations for routine use of vaccines in adults are developed by Advisory Committee on Immunization Practices (ACIP), a federal advisory committee chartered to provide expert external advice and guidance to the CDC Director on use of vaccines and related agents for the control of vaccine-preventable diseases in the civilian population of the United States. Recommendations for routine use of vaccines in adults are harmonized to the greatest extent possible with recommendations made by the American Academy of Family Physicians (AAP) and the American College of Obstetricians and Gynecologists (ACOG). ACIP recommendations approved by the CDC Director become agency guidelines on the date published in the *Morbidity and Mortality Weekly Report (MMWR)*. Additional information about ACIP is available at <https://www.cdc.gov/vaccines/acip>.

† Past immunization schedules are available at <https://www.cdc.gov/vaccines/schedules/past.html>.

Information on these changes, if made, is available at <https://www.cdc.gov/vaccines/acip/recommendations.html>.§ Printable versions of the 2020 adult immunization schedule and ordering instructions are available at <https://www.cdc.gov/vaccines/schedules/hcp/adult.html#note>.

## Changes in the 2020 Adult Immunization Schedule

Changes in the 2020 adult immunization schedule for persons aged ≥19 years include new or revised recommendations for hepatitis A vaccine (HepA) (2); human papillomavirus vaccine (HPV) (3); influenza vaccine (4); serogroup B meningococcal vaccine (MenB); pneumococcal vaccine (5); and tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (Tdap) (6). Following are the changes to the cover page, Table 1, Table 2, and Notes.

### Cover page

- Trademark symbols (\*) were added to all vaccine trade names.
- PedvaxHIB was added to the table of trade names for *Haemophilus influenzae* type b vaccine.
- The footnote on the cover page has been edited and now reads “Do not restart or add doses to vaccine series if there are extended intervals between doses.”

### Table 1

- **Age ranges:** The columns for age groups 19–21 years and 22–26 years have been combined, thereby reducing the number of columns for age ranges from five to four. This change was made because of the change in recommendation for catch-up HPV vaccination for all adults aged ≤26 years.
- **Tetanus, diphtheria, pertussis row:** This row has been edited to state that tetanus and diphtheria toxoids (Td) or Tdap may be used for the decennial tetanus booster.

§CDC encourages organizations to use syndication as a more reliable method for displaying the most current and accurate immunization schedules on an organization's website rather than copying these schedules to their websites. Use of content syndication requires a one-time step that ensures an organization's website displays current schedules as soon as they are published or revised; instructions for the syndication code are available on CDC's website (<https://www.cdc.gov/vaccines/schedules/syndicate.html>). CDC also offers technical assistance for implementing this form of content syndication (e-mail request to [ncirdwebteam@cdc.gov](mailto:ncirdwebteam@cdc.gov)). Information on changes in ACIP recommendations in the adult immunization schedule before the next scheduled annual update, if any, is available at <https://www.cdc.gov/vaccines/schedules/hcp/schedule-changes.html#adult>.

- **Human papillomavirus (HPV) row:** The rows for males and females have been combined, reflecting that catch-up vaccination is now recommended for all adults aged ≤26 years. In addition, a blue box has been added for persons aged 27–45 years to indicate that shared clinical decision-making regarding vaccination is now recommended for this group.
- **Pneumococcal conjugate (PCV13) row:** The box for persons aged ≥65 years who do not have an additional risk factor or another indication has been changed to blue to indicate that shared clinical decision-making regarding vaccination is now recommended for this group.
- **Meningococcal B (MenB) row:** A blue box has been added for persons aged 19–23 years who are not at increased risk for meningococcal disease, indicating that shared clinical decision-making regarding vaccination is now recommended for this group.
- **Legend:** A blue box has been added to indicate that shared clinical decision-making is recommended regarding vaccination. The text defining the gray box has been edited and now reads “No recommendation/not applicable.”

**Table 2**

- **Tdap or Td row:** This row has been revised to read that Td or Tdap may be used for the decennial tetanus booster.
- **Human Papillomavirus (HPV) row:** This row has been combined into a single row including both males and females, reflecting that HPV vaccine is now recommended for all adults aged ≤26 years.
- **Hepatitis A (HepA) row:** The box for persons living with human immunodeficiency virus (HIV) infection (regardless of CD4 count) is now yellow, reflecting the new recommendation that previously unvaccinated persons in this group should be vaccinated.
- **Legend and bar text:** The gray box in the Legend has been edited and now reads “No recommendation/not applicable.” The red box has been edited and now reads “Not recommended/contraindicated — vaccine should not be administered.” The text appearing in the red bars has been changed from “Contraindicated” to “Not Recommended.”

**Notes**

- Edits have been made throughout the Notes section to harmonize language between the child/adolescent immunization schedule and the adult immunization schedule, where possible.
- A new subsection entitled “Shared Clinical Decision-Making” was added for each vaccine that includes this new ACIP recommendation (e.g., for HPV, PCV13, and MenB).
- **Hepatitis A:** The note was revised to include minor changes to the chronic liver disease definition, minor

changes for the pregnancy indication, addition of the recommendation for vaccination in settings of exposure, and removal of clotting factor disorders as an indication for vaccination.

- **Hepatitis B:** The note was revised to include minor changes to the chronic liver disease definition and minor changes for the pregnancy indication.
- **Human papillomavirus:** The note was revised to indicate that HPV vaccination is recommended for all persons aged ≤26 years. A shared clinical decision-making subsection was added for persons aged 27–45 years.
- **Influenza:** The note was updated to include a bulleted list indicating when live attenuated influenza vaccine (LAIV) should not be used and minor edits to the guidance for persons with a history of Guillain-Barré syndrome.
- **Measles, mumps, and rubella:** The note was revised to clarify recommendations for health care personnel, with a separate bullet for personnel born in 1957 or later with no evidence of immunity and for health care personnel born before 1957 with no evidence of immunity.
- **Meningococcal:** The note was revised to include the use of the complement inhibitor ravulizumab as an indication for MenB administration in these patients. A shared clinical decision-making subsection was added that includes a bullet for adolescents and young adults aged 16–23 years who are not at increased risk for meningococcal disease. Under the “Special situations” section, the recommendation to administer a booster dose of MenB 1 year after the primary series and to revaccinate every 2–3 years if the risk remains was added.
- **Pneumococcal:** The note has been updated to reflect the updated recommendations for vaccination of immunocompetent (defined as adults without an immunocompromising condition, cerebrospinal fluid leak, or cochlear implants) adults aged ≥65 years. One dose of 23-valent pneumococcal polysaccharide vaccine (PPSV23) is still recommended. Shared clinical decision-making is recommended regarding administration of PCV13 to immunocompetent persons aged ≥65 years.
- **Tetanus, diphtheria, and pertussis:** The note has been updated to indicate that Td or Tdap may be used in situations where only Td vaccine was indicated for the decennial tetanus, diphtheria, and pertussis booster vaccination, tetanus prophylaxis for wound management, and catch-up vaccination.
- **Varicella:** The note has been updated to indicate that vaccination may be considered for persons with HIV infection without evidence of varicella immunity who have CD4 counts ≥200 cells/µL.

## Additional Information

The Recommended Adult Immunization Schedule, United States, 2020 is available at <https://www.cdc.gov/vaccines/schedules/hcp/adult.html> and in the Annals of Internal Medicine (7). The full ACIP recommendations for each vaccine are also available at <https://www.cdc.gov/vaccines/hcp/acip-recommendations/index.html>. All vaccines identified in Tables 1 and 2 (except zoster vaccines) also appear in the Recommended Child and Adolescent Immunization Schedule for Ages 18 Years or Younger, United States, 2020.<sup>¶</sup> The notes for vaccines that appear in both the adult immunization schedule and the child and adolescent immunization schedule have been harmonized to the greatest extent possible.

<sup>¶</sup><https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html>.

## Acknowledgments

Rosters of current and past members of the Advisory Committee on Immunization Practices (ACIP) are available at <https://www.cdc.gov/vaccines/acip/committee/members-archive.html>.

## ACIP Adult Immunization Work Group

Chair: Paul Hunter. Contributors: Kevin Ault, John Epling, Sandra Fryhofer, Kathleen Harriman, Robert Hopkins, Molly Howell, Maria Lanzi, Marie-Michelle Leger, Susan Lett, Diane Peterson, Laura Pinkston Koenings, Chad Rittle, Ken Schmader, William Shaffner, Rhoda Sperling, Litjen Tan, David Weaver. CDC Lead: Mark Freedman. CDC contributors: Melissa Arvay, Carolyn Bridges, Kathy Byrd, Amanda Cohn, Mitesh Desai, Kathleen Dooling, Lisa Grohskopf, Fiona Havers, Ram Koppaka, Andrew Kroger, Jennifer Liang, Jessica MacNeil, Sarah Mbaeyi, Lauri Markowitz, Mona Marin, Almea Matanock, Amy Parker Fiebelkorn, Manisha Patel, Priti Patel, Tamara Pilishvili, Ginger Redmon, Candice Robinson, Sarah Schillie, Ray Strikas, Cindy Weinbaum, Walter Williams, LaDora Woods.

Corresponding author: Mark S. Freedman, fll0@cdc.gov, 404-639-6356.

<sup>1</sup>Immunization Services Division, National Center for Immunization and Respiratory Diseases, CDC; <sup>2</sup>University of Wisconsin, School of Medicine and Public Health, Madison, Wisconsin; <sup>3</sup>City of Milwaukee Health Department, Milwaukee, Wisconsin; <sup>4</sup>University of Kansas Medical Center, Kansas City, Kansas.

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# Licensure of a Diphtheria and Tetanus Toxoids and Acellular Pertussis, Inactivated Poliovirus, *Haemophilus influenzae* Type b Conjugate, and Hepatitis B Vaccine, and Guidance for Use in Infants

Sara E. Oliver MD<sup>1</sup>; Kelly L. Moore, MD<sup>2</sup>

On December 21, 2018 the Food and Drug Administration (FDA) licensed a hexavalent combined diphtheria and tetanus toxoids and acellular pertussis (DTaP) adsorbed, inactivated poliovirus (IPV), *Haemophilus influenzae* type b (Hib) conjugate (meningococcal protein conjugate) and hepatitis B (HepB) (recombinant) vaccine, DTaP-IPV-Hib-HepB (Vaxelis; MCM Vaccine Company),\* for use as a 3-dose series in infants at ages 2, 4, and 6 months (1). On June 26, 2019, after reviewing data on safety and immunogenicity, the Advisory Committee on Immunization Practices (ACIP)<sup>†</sup> voted to include DTaP-IPV-Hib-HepB in the federal Vaccines for Children (VFC) program.<sup>§</sup> This report summarizes the indications for DTaP-IPV-Hib-HepB and provides guidance for its use.

## Introduction

Combination vaccines merge equivalent component vaccines into a single product to prevent more than one disease. The use of combination vaccines can reduce the number of injections patients receive and improve vaccine coverage rates (2,3). ACIP has previously stated that the use of a combination vaccine generally is preferred over separate injections of the equivalent component vaccines; considerations can include provider assessment, patient preference, and the potential for adverse events (4). Until 2018, there were two pentavalent combination vaccines licensed for use in the infant vaccine series: DTaP-HepB-IPV (Pediarix; GlaxoSmithKline) and DTaP-IPV/Hib (Pentacel; Sanofi Pasteur). In late 2018, a

new hexavalent combination vaccine (DTaP-IPV-Hib-HepB) from the MCM Vaccine Company, a joint venture between Merck and Sanofi Pasteur, received FDA approval. Each dose of DTaP-IPV-Hib-HepB contains the same amount of diphtheria and tetanus toxoids and pertussis antigens (inactivated pertussis toxin [PT], filamentous hemagglutinin [FHA], pertactin, and fimbriae types 2 and 3) as does Pentacel. The poliovirus component of DTaP-IPV-Hib-HepB contains the same strains of inactivated poliovirus types 1, 2, and 3 as the poliovirus vaccine IPOL (Sanofi Pasteur), but in decreased amounts. The Hib component (Hib capsular polysaccharide polyribosyl-ribitol-phosphate [PRP] coupled to the outer membrane protein complex [OMP] of *Neisseria meningitidis*) is the same as that in PedvaxHIB (Merck), but in a decreased amount. The HepB component is the same as the pediatric formulation of Recombivax HB (Merck), but in an increased amount. The DTaP-IPV-Hib-HepB vaccine is a fully liquid formulation and requires no reconstitution.

## Methods

During December 2018–June 2019, the ACIP Combination Vaccines Work Group held monthly conference calls to review and discuss relevant scientific evidence regarding the inclusion of DTaP-IPV-Hib-HepB in the federal VFC program. The work group evaluated the relevant evidence related to the potential benefits and harms of DTaP-IPV-Hib-HepB. The new combination vaccine will not alter the established vaccination schedule, and no changes to current policy were discussed. At the June 2019 ACIP meeting, after discussion by ACIP members and a period for public comment, the ACIP members voted unanimously to include DTaP-IPV-Hib-HepB in the federal VFC program.

## Summary of Key Findings

Six Phase III studies evaluated the safety and immunogenicity of DTaP-IPV-Hib-HepB (5–10), including two non-inferiority studies enrolling >4,200 children using the U.S. infant immunization schedule of 2, 4, and 6 months (5,6). The immunologic responses were assessed after the third dose of DTaP-IPV-Hib-HepB. Overall, the measured antibodies were noninferior to licensed comparator vaccines, with one exception: noninferiority was not met for the geometric

\*The manufacturer has stated that vaccine will not be commercially available in the United States before 2021.

<sup>†</sup>Recommendations for routine use of vaccines in children, adolescents, and adults are developed by the Advisory Committee on Immunization Practices (ACIP). ACIP is chartered as a federal advisory committee to provide expert external advice and guidance to CDC Director on use of vaccines and related agents for the control of vaccine-preventable diseases in the civilian population of the United States. Recommendations for routine use of vaccines in children and adolescents are harmonized to the greatest extent possible with recommendations made by the American Academy of Pediatrics (AAP), the American Academy of Family Physicians (AAFP), the American College of Obstetricians and Gynecologists (ACOG), and the American College of Nurse-Midwives (ACNM). Recommendations for routine use of vaccines in adults are harmonized with recommendations of AAFP, ACOG, the American College of Physicians (ACP), and ACNM. ACIP recommendations approved by the CDC Director become agency guidelines on the date published in the *Morbidity and Mortality Weekly Report (MMWR)*. Additional information is available at <https://www.cdc.gov/vaccines/acip>.

<sup>§</sup><https://www.cdc.gov/vaccines/programs/vfc/index.html>.

mean concentration against one of five pertussis antigens (FHA) 1 month after completion of the 3-dose infant series. However, all pertussis antigens met noninferiority criteria for a second measured endpoint (the percentage that met a prespecified vaccine response). The DTaP-IPV-Hib-HepB vaccine had a safety profile consistent with that of the licensed component vaccines. A higher rate of fever was detected among DTaP-IPV-Hib-HepB recipients when compared with that among pentavalent vaccine (DTaP-IPV/Hib) recipients (47.1%–47.4% versus 33.2%–34.4%) (5,6). However, the rates of fever-related medical events, such as hospital visits or febrile seizures, were similar in the two groups.

Simultaneous administration of DTaP-IPV-Hib-HepB was tested with rotavirus and pneumococcal conjugate vaccines. Concomitant administration did not affect immunogenicity at measured endpoints for rotavirus (5). One of 13 pneumococcal serotypes, 6B, missed the prespecified noninferiority endpoint after the third dose (6). Pneumococcal serotype-specific correlates of protection are unknown, and it is unclear whether this would be clinically relevant. However, since the introduction of pneumococcal conjugate vaccines, pneumococcal serotype 6B is rarely detected in nasopharyngeal carriage or as a cause of invasive disease among U.S. children (11).

## Indications and Guidance for Use

DTaP-IPV-Hib-HepB is licensed for use in children aged 6 weeks through 4 years (before the fifth birthday) (Table) (1). DTaP-IPV-Hib-HepB is only indicated for use in infants at ages 2, 4, and 6 months.

For the prevention of diphtheria, tetanus and pertussis, children are recommended to receive a 3-dose primary series of DTaP, at ages 2, 4, and 6 months, and booster doses at ages 15–18 months and 4–6 years (12). DTaP-IPV-Hib-HepB can be used for the first 3 doses of the recommended DTaP series but should not be used for the fourth or fifth dose. However, if DTaP-IPV-Hib-HepB is inadvertently given for either booster dose, the dose does not need to be repeated with another DTaP-containing vaccine when the proper spacing of previous doses is maintained. Circumstances might warrant an accelerated schedule to provide early protection against pertussis, starting as soon as the infant is aged 6 weeks, with the second and third DTaP doses administered no earlier than 4 weeks after each preceding dose. The recommended minimum age for the third dose of the DTaP-IPV-Hib-HepB vaccine is 24 weeks, the minimum age for completion of the HepB vaccine series. Therefore, this combination vaccine is not recommended for use for the third dose of the primary series on an accelerated schedule at 4-week intervals for the prevention of pertussis.

For prevention of poliomyelitis, children are recommended to receive 4 doses of IPV, at ages 2, 4, 6–18 months, and

**TABLE. Recommended minimum ages for administration of DTaP-IPV-Hib-HepB vaccine and intervals between doses — United States, 2020\***

Parameter	Age/Interval
Minimum age for any dose	6 weeks
Minimum interval between doses 1 and 2	4 weeks
Minimum age for dose 2	10 weeks
Minimum interval between doses 2 and 3	4 weeks
Minimum age for dose 3	24 weeks <sup>†</sup>
Maximum age for any dose	4 years, 364 days (do not administer on or after the fifth birthday)

**Abbreviations:** DTaP = diphtheria and tetanus toxoids and acellular pertussis; Hib = *Haemophilus influenzae* type b; HepB = hepatitis B; IPV = inactivated poliovirus.

\* The DTaP-IPV-Hib-HepB vaccine (Vaxelis; MCM Vaccine Company) was licensed in December 2018 and will not be commercially available in the United States before 2021.

<sup>†</sup> If the third dose of DTaP-IPV-Hib-HepB is given before age 24 weeks, an additional dose of hepatitis B vaccine should be given at age ≥24 weeks to complete the hepatitis B series.

4–6 years (13). DTaP-IPV-Hib-HepB may be used for the first 3 doses of the IPV series but is not indicated for the fourth dose; however, if DTaP-IPV-Hib-HepB is inadvertently given for the booster dose, the dose does not need to be repeated with another IPV-containing vaccine, when the proper spacing of previous doses is maintained.

For prevention of invasive *H. influenzae* type b disease, children are recommended to receive a primary series (2 or 3 doses, depending on the vaccine used) of a Hib conjugate vaccine and a booster dose of vaccine at age 12–15 months (14). Although monovalent PRP-OMP Hib vaccines are licensed as a 2-dose primary series at ages 2 and 4 months, DTaP-IPV-Hib-HepB is licensed as a 3-dose primary series. Therefore, 3 doses of a Hib conjugate-containing vaccine are needed to complete the primary series if DTaP-IPV-Hib-HepB is used for any doses. DTaP-IPV-Hib-HepB should not be used for the booster dose (after completion of the 3-dose primary series). Any Hib conjugate vaccine licensed for a booster dose can be used. If DTaP-IPV-Hib-HepB is inadvertently given for the booster dose, the dose does not need to be repeated with another Hib-containing vaccine, when the proper spacing of previous doses is maintained.

For prevention of hepatitis B, children are recommended to receive 3 doses of a HepB vaccine at ages 0, 1–2, and 6–18 months, with variations depending on the maternal hepatitis B infection status, infant birthweight, and vaccine manufacturer (15). Universal HepB vaccination of all infants beginning at birth provides a critical safeguard and prevents infection among infants born to hepatitis B surface antigen (HBsAg)-positive mothers not identified prenatally. DTaP-IPV-Hib-HepB is not licensed for the birth dose but can be used for doses given at age ≥6 weeks to infants of

## Summary

### What is already known about this topic?

Combination vaccines merge equivalent component vaccines into a single product to prevent multiple diseases, which can reduce the number of injections administered and improve vaccination coverage.

### What is added by this report?

A new hexavalent vaccine was approved by the Food and Drug Administration to prevent diphtheria, tetanus, pertussis, polio, *Haemophilus influenzae* type b, and hepatitis B (DTaP-IPV-Hib-HepB). At a recent Advisory Committee on Immunization Practices meeting, members voted unanimously to include this vaccine in the federal Vaccines for Children program.

### What are the implications for public health practice?

The vaccine is licensed for use in children aged 6 weeks through 4 years and is indicated for the primary vaccination series in infants at ages 2, 4 and 6 months.

of DTaP-IPV-Hib-HepB in AI/AN infants are not currently available; therefore, DTaP-IPV-Hib-HepB does not have a preferential recommendation for AI/AN infants at this time. If data on antibody response after the first dose of DTaP-IPV-Hib-HepB become available, ACIP will re-evaluate the preferential language for the Hib component for AI/AN infants.

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Corresponding author: Sara E. Oliver, seoliver@cdc.gov, 404-639-1204.

<sup>1</sup>Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, CDC; <sup>2</sup>Department of Health Policy, Vanderbilt School of Medicine, Nashville, Tennessee.

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## ACIP Combination Vaccines Work Group

Chair: Kelly L. Moore; Members: Jillian Doss-Walker, Phil Griffin, Jennifer L. Hamilton, Veronica McNally, Sarah McQueen, Sean T. O'Leary, Elizabeth Rausch-Phung, Ann Schwartz, Patsy Stinchfield, Thomas Weiser; CDC Contributors: Anna Acosta, Mike Bruce, Fiona P. Havers, Andrew Kroger, Pedro Moro, Janell A. Routh, Sarah Schillie, Rosalyn Singleton, Cindy Weinbaum, JoEllen Wolicki.

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## Special Considerations

Before the routine use of Hib vaccines, incidence of *H. influenzae* meningitis among American Indian/Alaska Native (AI/AN) infants peaked at a younger age (4–6 months) than it did among other U.S. infant populations (6–7 months). Vaccination with a primary series of a Hib vaccine that contains PRP-OMP is preferred for AI/AN infants to provide early protection because these vaccines can provide a protective antibody response after the first dose (13). Data on antibody response after the first dose

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## Initial Public Health Response and Interim Clinical Guidance for the 2019 Novel Coronavirus Outbreak — United States, December 31, 2019–February 4, 2020

Anita Patel, PharmD<sup>1</sup>; Daniel B. Jernigan, MD<sup>1</sup>; 2019-nCoV CDC Response Team

*On February 5, 2020, this report was posted as an MMWR Early Release on the MMWR website (<https://www.cdc.gov/mmwr>).*

On December 31, 2019, Chinese health officials reported a cluster of cases of acute respiratory illness in persons associated with the Hunan seafood and animal market in the city of Wuhan, Hubei Province, in central China. On January 7, 2020, Chinese health officials confirmed that a novel coronavirus (2019-nCoV) was associated with this initial cluster (1). As of February 4, 2020, a total of 20,471 confirmed cases, including 2,788 (13.6%) with severe illness,\* and 425 deaths (2.1%) had been reported by the National Health Commission of China (2). Cases have also been reported in 26 locations outside of mainland China, including documentation of some person-to-person transmission and one death (2). As of February 4, 11 cases had been reported in the United States. On January 30, the World Health Organization (WHO) Director-General declared that the 2019-nCoV outbreak constitutes a Public Health Emergency of International Concern.<sup>†</sup> On January 31, the U.S. Department of Health and Human Services (HHS) Secretary declared a U.S. public health emergency to respond to 2019-nCoV.<sup>§</sup> Also on January 31, the president of the United States signed a “Proclamation on Suspension of Entry as Immigrants and Nonimmigrants of Persons who Pose a Risk of Transmitting 2019 Novel Coronavirus,” which limits entry into the United States of persons who traveled to mainland China to U.S. citizens and lawful permanent residents and their families (3). CDC, multiple other federal agencies, state and local health departments, and other partners are implementing aggressive measures to slow transmission of 2019-nCoV in the United States (4,5). These measures require the identification of cases and their contacts in the United States and the appropriate assessment and care of travelers arriving from mainland China to the United States. These measures are being implemented in anticipation of additional 2019-nCoV

cases in the United States. Although these measures might not prevent the eventual establishment of ongoing, widespread transmission of the virus in the United States, they are being implemented to 1) slow the spread of illness; 2) provide time to better prepare health care systems and the general public to be ready if widespread transmission with substantial associated illness occurs; and 3) better characterize 2019-nCoV infection to guide public health recommendations and the development of medical countermeasures including diagnostics, therapeutics, and vaccines. Public health authorities are monitoring the situation closely. As more is learned about this novel virus and this outbreak, CDC will rapidly incorporate new knowledge into guidance for action by CDC and state and local health departments.

Some coronaviruses, such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS), are the result of human-animal interactions. Preliminary investigation of 2019-nCoV also suggests a zoonotic origin (6), but the exact origin has not yet been determined. Person-to-person spread is evident (7); however, how easily the virus is transmitted between persons is currently unclear. 2019-nCoV is similar to coronaviruses that cause MERS and SARS, which are transmitted mainly by respiratory droplets. Signs and symptoms of patients with confirmed 2019-nCoV infection include fever, cough, and shortness of breath (8). Based on the incubation period of illness from MERS and SARS coronaviruses, CDC believes that symptoms of 2019-nCoV infection occur within 2 to 14 days following infection. Preliminary information suggests that older adults and persons with underlying health conditions or compromised immune systems might be at higher risk for severe illness from this virus (9); however, many characteristics of this novel coronavirus and how it might affect individual persons and potentially vulnerable population subgroups, such as the elderly or those with chronic health conditions, remain unclear.

### Epidemiology of First U.S. Cases

On January 21, 2020, the first person in the United States with diagnosed 2019-nCoV infection was reported. As of February 4, a total of 293 persons from 36 states, the District of Columbia, and the U.S. Virgin Islands were under investigation based on current patient under investigation

\*Includes any of the following: dyspnea, respiratory rate >30 breaths per minute, hypoxemia, or chest x-ray with multilobular infiltrates or >50% progression of pulmonary infiltration within 24–48 hours per WHO. <https://www.who.int/docs/default-source/coronavirus/situation-reports/20200123-sitrep-3-2019-ncov.pdf>.

†[https://www.who.int/news-room/detail/30-01-2020-statement-on-the-second-meeting-of-the-international-health-regulations-\(2005\)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-\(2019-ncov\)](https://www.who.int/news-room/detail/30-01-2020-statement-on-the-second-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-(2019-ncov)).

§<https://www.phe.gov/emergency/news/healthactions/phe/Pages/2019-nCoV.aspx>.

(PUI) definitions,<sup>¶</sup> and also included those being evaluated because they are close contacts. Of these PUIs, 11 patients have confirmed 2019-nCoV infection using a real-time reverse transcription–polymerase chain reaction (RT-PCR) assay developed by CDC. These 11 cases were diagnosed in the following states: Arizona (one), California (six), Illinois (two), Massachusetts (one), and Washington (one) (Table). Nine cases were in travelers from Wuhan. Eight of these nine cases were identified as a result of patients seeking clinical care for symptoms and clinicians connecting with the appropriate public health systems. Two cases (one each in California and Illinois) occurred in close contacts of two confirmed cases and were diagnosed as part of routine monitoring of case contacts. All patients are being monitored closely for progressing illness. No deaths have been reported in the United States.

## Public Health Response

CDC established a 2019-nCoV Incident Management Structure on January 7, 2020. On January 21, CDC activated its Emergency Operations Center to optimize coordination for domestic and international 2019-nCoV response efforts. To date, CDC has deployed teams to the U.S. jurisdictions with cases to assist with epidemiologic investigation and to work closely with state and local partners to identify and monitor close contacts and better understand the spectrum of illness, transmission, and virulence associated with this novel virus. Information learned from these investigations will help inform response actions. CDC has closely monitored the global impact of this virus with staff members positioned in CDC offices around the world, including mainland China, and in coordination with other countries and WHO. This coordination has included deploying CDC staff members to work with WHO and providing active support to CDC offices in affected countries. In addition, CDC in response to the escalating risks of travel from China has issued a series of Travelers' Health Notices for both Wuhan and the rest of China regarding the 2019-nCoV outbreak. On January 27, CDC issued a Level 3 travel notice for travelers to avoid all nonessential travel to mainland China.<sup>\*\*</sup>

<sup>¶</sup> Criteria to guide evaluation and testing of patients under investigation for 2019-nCoV include 1) fever or signs or symptoms of lower respiratory tract illness (e.g., cough or shortness of breath) in any person, including a health care worker, who has had close contact with a patient with laboratory-confirmed 2019-nCoV infection within 14 days of symptom onset; 2) fever and signs or symptoms of lower respiratory tract illness (e.g., cough or shortness of breath) in any person with a history of travel from Hubei Province, China, within 14 days of symptom onset; or 3) fever and signs or symptoms of lower respiratory tract illness (e.g., cough or shortness of breath) requiring hospitalization in any person with a history of travel from mainland China within 14 days of symptom onset. More information is available at <https://emergency.cdc.gov/han/han00427.asp> and <https://emergency.cdc.gov/han/han00426.asp>.

<sup>\*\*</sup><https://wwwnc.cdc.gov/travel/notices/warning/novel-coronavirus-china>.

## Summary

### What is already known about this topic?

In December 2019, an outbreak of acute respiratory illness caused by a novel coronavirus (2019-nCoV) was detected in mainland China. Cases have been reported in 26 additional locations, including the United States.

### What is added by this report?

Nine of the first 11 U.S. 2019-nCoV patients were exposed in Wuhan, China. CDC expects more U.S. cases.

### What are the implications for public health practice?

CDC, multiple other federal agencies, state and local health departments, and other partners are implementing aggressive measures to substantially slow U.S. transmission of 2019-nCoV, including identification of U.S. cases and contacts and managing travelers arriving from mainland China to the United States. Interim guidance is available at <https://www.cdc.gov/coronavirus/index.html> and will be updated as more information becomes available.

U.S. quarantine stations, located at 18 major U.S. ports of entry, are part of a comprehensive regulatory system authorized under section 361 of the Public Health Service Act (42 U.S. Code Section 264), that limits the introduction of infectious diseases into the United States to prevent their spread. On January 17, consistent with existing communicable disease response protocols, CDC Quarantine staff members instituted enhanced entry screening of travelers on direct and connecting flights from Wuhan, China, arriving at three major U.S. airports: Los Angeles (LAX), New York City (JFK), and San Francisco (SFO),<sup>††</sup> which then expanded to include travelers arriving in Atlanta (ATL) and Chicago (ORD). These five airports together receive approximately 85% of all air travelers from Wuhan, China, to the United States. U.S. Customs and Border Protection officers identified travelers arriving from Wuhan and referred them to CDC for health screening.<sup>§§</sup> Any traveler from Wuhan with signs or symptoms of illness (e.g., fever, cough, or difficulty breathing) received a more comprehensive public health assessment performed by CDC public health and medical officers.<sup>¶¶</sup> All travelers from Wuhan were also provided CDC's Travel Health Alert Notice (T-HAN)<sup>\*\*\*</sup>

<sup>††</sup><https://www.cdc.gov/media/releases/2020/p0117-coronavirus-screening.html>.

<sup>§§</sup> CDC's initial health screening includes a measurement of each traveler's temperature with a handheld noncontact thermometer, observation of these travelers for visible signs of respiratory illness (e.g., cough or difficulty breathing), and review of symptoms through a self-administered questionnaire.

<sup>¶¶</sup> The more comprehensive public health assessment determines, based on the traveler's illness and exposure, whether the traveler should be taken to a hospital for further medical evaluation and care, which might include testing for 2019-nCoV.

<sup>\*\*\*</sup><https://www.cdc.gov/coronavirus/2019-ncov/travelers/communication-resources.html>.

**TABLE. Characteristics of initial 2019 novel coronavirus cases (N = 11) — United States, January 21–February 4, 2020**

Case	State	Approximate age (yrs)	Sex	Place of exposure	Date laboratory confirmation announced
1	Washington	30s	M	Wuhan	1/21/2020
2	Illinois	60s	F	Wuhan	1/24/2020
3	Arizona	20s	M	Wuhan	1/26/2020
4	California	30s	M	Wuhan	1/27/2020
5	California	50s	M	Wuhan	1/27/2020
6	Illinois	60s	M	Household Illinois	1/30/2020
7	California	40s	M	Wuhan	1/31/2020
8	Massachusetts	20s	M	Wuhan	2/01/2020
9	California	50s	F	Wuhan	2/02/2020
10	California	50s	M	Wuhan	2/02/2020
11	California	50s	F	Household California	2/02/2020

Abbreviations: F = female; M = male.

that advised them to monitor their health for 14 days and described recommended actions to take if relevant symptoms develop. As of February 1, 2020, a total of 3,099 persons on 437 flights were screened; five symptomatic travelers were referred by CDC to local health care providers for further medical evaluation, and one of these persons tested positive for 2019-nCoV.

On January 24, 2020, travel bans began to be instituted by the Chinese government, resulting in restricted travel in and out of Hubei Province, including the city of Wuhan, and fewer travelers undergoing entry screening in the United States. In response to the escalating risks associated with travel from mainland China, on January 31, 2020, the Presidential Proclamation further refined the border health strategy to temporarily suspend entry, undergo additional screening, or possible quarantine for individuals that have visited China (excluding Hong Kong, Macau, and Taiwan) in the past 14 days. These enhanced entry screening efforts are taking place at 11 airports at which all air travelers from China are being directed.

## Laboratory and Diagnostic Support

Chinese health officials posted the full 2019-nCoV genome sequence on January 10, 2020, to inform the development of specific diagnostic tests for this emergent coronavirus (1). Within a week, CDC developed a Clinical Laboratory Improvement Amendments-approved real-time RT-PCR test that can diagnose 2019-nCoV respiratory samples from clinical specimens. On January 24, CDC publicly posted the assay protocol for this test (<https://www.cdc.gov/coronavirus/2019-nCoV/lab/index.html>). On January 4, 2020, the Food and Drug Administration issued an Emergency Use Authorization to enable emergency use of CDC's 2019-nCoV Real-Time RT-PCR Diagnostic Panel. To date, this test has been limited to use at CDC laboratories. This authorization allows the use

of the test at any CDC-qualified lab across the country. CDC is working closely with FDA and public health partners, including the American Public Health Laboratories, to rapidly share these tests domestically and internationally through CDC's International Reagent Resource (<https://www.internationalreagentresource.org/>). In addition, CDC uploaded the genome of the virus from the first reported cases in the United States to GenBank, the National Institutes of Health genetic sequence database of publicly available DNA sequences (<https://www.ncbi.nlm.nih.gov/genbank/>). CDC also is growing the virus in cell culture, which is necessary for further studies, including for additional genetic characterization. Once isolated, the virus will be made available through BEI Resources (<https://www.beiresources.org/>) to assist research efforts.

## Clinical and Infection Control Guidance

Additional information about 2019-nCoV is needed to better understand transmission, disease severity, and risk to the general population. Although CDC and partners are actively learning about 2019-nCoV, initial CDC guidance is based on guidance for management and prevention of respiratory illnesses including influenza, MERS, and SARS. No vaccine or specific treatment for 2019-nCoV infection is currently available. At present, medical care for patients with 2019-nCoV is supportive.

On January 31, CDC published its third Health Advisory with interim guidance for clinicians and public health practitioners.<sup>†††</sup> In addition, CDC issued a Clinical Action Alert through its Clinician Outreach and Communication Activity network on January 31.<sup>§§§</sup> Interim guidance for health care professionals is available at <https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html>.

<sup>†††</sup> <https://emergency.cdc.gov/han/han00427.asp>.

<sup>§§§</sup> [https://emergency.cdc.gov/coca/calls/2020/callinfo\\_013120.asp](https://emergency.cdc.gov/coca/calls/2020/callinfo_013120.asp).

Health care providers should identify patients who might have been exposed and who have signs or symptoms related to 2019-nCoV infection, isolate these patients, and inform public health departments. This includes obtaining a detailed travel history for patients being evaluated with fever and lower respiratory tract illness. Criteria to guide evaluation and testing of PUIs for 2019-nCoV include 1) fever or signs or symptoms of lower respiratory tract illness (e.g., cough or shortness of breath) in any person, including health care workers, who has had close contact<sup>\*\*\*</sup> with a patient with laboratory-confirmed 2019-nCoV infection within 14 days of symptom onset; 2) fever and signs or symptoms of lower respiratory tract illness (e.g., cough or shortness of breath) in any person with a history of travel from Hubei Province, China, within 14 days of symptom onset; or 3) fever and signs or symptoms of lower respiratory tract illness (e.g., cough or shortness of breath) requiring hospitalization in any person with a history of travel from mainland China within 14 days of symptom onset. Additional nonhospitalized PUIs may be tested based on consultation with state and local public health officials. Clinicians should evaluate PUIs for other possible causes of illness (e.g., influenza and respiratory syncytial virus) as clinically indicated.

CDC currently recommends a cautious approach to the examination of PUIs. These patients should be asked to wear a surgical mask as soon as they are identified, and directed to a separate area, if possible, separated by at least 6 ft (2 m) from other persons. Patients should be evaluated in a private room with the door closed, ideally an airborne infection isolation room, if available. Health care personnel entering the room should use standard precautions, contact precautions, airborne precautions, and eye protection (e.g., goggles or a face shield).

Clinicians should immediately notify the health care facility's infection control personnel and local health department. The health department will determine whether the patient needs to be considered a PUI for 2019-nCoV and be tested for infection. If directed by the health department, to increase the likelihood of detecting 2019-nCoV infection, CDC recommends collecting and testing both upper and lower respiratory tract specimens.<sup>\*\*\*\*</sup> Additional specimen types (e.g., stool or urine)

<sup>\*\*\*</sup> Close contact is defined as 1) being within approximately 6 ft (2 m) of a 2019-nCoV patient for a prolonged period while not wearing recommended personal protective equipment (PPE) (e.g., gowns, gloves, National Institute for Occupational Safety and Health–certified disposable N95 respirator, and eye protection); close contact can occur while caring for, living with, visiting, or sharing a health care waiting area or room with a 2019-nCoV patient; or 2) having direct contact with infectious secretions of a 2019-nCoV patient (e.g., being coughed on) while not wearing recommended PPE.

<sup>\*\*\*\*</sup> <https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html>.

may be collected and stored. Specimens should be collected as soon as possible once a PUI is identified regardless of time since symptom onset.

For persons who might have 2019-nCoV infection and their close contacts, information and guidance on how to reduce the risk for transmitting and acquiring infection is available at <https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-prevent-spread.html>. Close contacts should immediately call their health care providers if they develop symptoms. In addition, CDC is working closely with state and local health partners to develop and disseminate information to the public on general prevention of respiratory illness, including the 2019-nCoV. This includes everyday preventive actions such as washing your hands, covering your cough, and staying home when you are ill. Additional information and resources for this outbreak are available on the CDC website (<https://www.cdc.gov/coronavirus/2019-ncov/index.html>).

## Discussion

The 2019-nCoV has impacted multiple countries, caused severe illness, and sustained person-to-person transmission making it a concerning and serious public health threat. It is unclear how this virus will impact the U.S. over time. For the general population, who are unlikely to be exposed to this virus at the current time, the immediate health risk from 2019-nCoV is considered low. CDC, multiple other federal agencies, state and local health departments, and other partners are implementing aggressive measures to slow U.S. transmission of 2019-nCoV (4,5). These measures require the identification of cases and contacts in the United States and the effective management of the estimated 14,000 travelers arriving from mainland China to the United States each day (3). These measures are being implemented based on the assumption that there will be more U.S. 2019-nCoV cases occurring with potential chains of transmission, with the understanding that these measures might not prevent the eventual establishment of ongoing, widespread transmission of the virus in the United States.

It is important for public health agencies, health care providers, and the public to be aware of this new 2019-nCoV so that coordinated, timely, and effective actions can help prevent additional cases or poor health outcomes. The critical role that the U.S. health care system plays in halting or significantly slowing U.S. transmission of 2019-nCoV is already evident: eight of the first 11 U.S. cases were detected by clinicians collaborating with public health to test persons at risk. The early recognition of cases in the United States reduces transmission risk and increases understanding of the virus, including its transmission and severity, to inform national and global response actions.

2019-nCoV symptoms are similar to those of influenza (e.g., fever, cough, or sore throat), and the outbreak is occurring during a time of year when respiratory illnesses from influenza, respiratory syncytial virus, and other respiratory viruses are highly prevalent. To prevent influenza, all persons aged ≥6 months should receive an annual influenza vaccine, and vaccination is still available and effective in helping to prevent influenza (10). Reducing the number of persons in the United States with seasonal influenza will reduce possible confusion with 2019-nCoV infection and possible additional risk to patients with seasonal influenza. Public health authorities are monitoring the situation closely. As more is learned about this novel virus and this outbreak, CDC will rapidly incorporate new knowledge into guidance for action.

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### 2019-nCoV CDC Response Team

Fatuma Abdirizak, National Center for Immunization and Respiratory Diseases, CDC; Glen Abedi, National Center for Immunization and Respiratory Diseases, CDC; Sharad Aggarwal, National Center for Immunization and Respiratory Diseases, CDC; Denise Albina, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Elizabeth Allen, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Lauren Andersen, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Jade Anderson, Center for Preparedness and Response, CDC; Megan Anderson, Center for Preparedness and Response, CDC; Tara Anderson, Center for State, Tribal, Local and Territorial Support, CDC; Kayla Anderson, National Center on Birth Defects and Developmental Disabilities, CDC; Ana Cecilia Bardossy, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Vaughn Barry, National Center for Injury Prevention and Control, CDC; Karlyn Beer, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Michael Bell, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Sherri Berger, Office of the Director, CDC; Joseph Bertulfo, Office of the Director, CDC; Holly Biggs, National Center for Immunization and Respiratory Diseases, CDC; Jennifer Bornemann, Office of the Director, CDC; Josh Bornstein, Office of the Director, CDC; Willie Bower, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Joseph Bresee, National Center for Immunization and Respiratory Diseases, CDC; Clive Brown, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Alicia Budd,

National Center for Immunization and Respiratory Diseases, CDC; Jennifer Buigut, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Stephen Burke, National Center for Immunization and Respiratory Diseases, CDC; Rachel Burke, National Center for Immunization and Respiratory Diseases, CDC; Erin Burns, National Center for Immunization and Respiratory Diseases, CDC; Jay Butler, Office of the Deputy Director of Infectious Disease, CDC; Russell Cantrell, Center for State, Tribal, Local and Territorial Support, CDC; Cristina Cardemil, National Center for Immunization and Respiratory Diseases, CDC; Jordan Cates, National Center for Immunization and Respiratory Diseases, CDC; Marty Cetron, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Kevin Chatham-Stephens, National Center on Birth Defects and Developmental Disabilities, CDC; Kevin Chatham-Stevens, National Center on Birth Defects and Developmental Disabilities, CDC; Nora Chea, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Bryan Christensen, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Victoria Chu, National Center for Immunization and Respiratory Diseases, CDC; Kevin Clarke, Center for Global Health, CDC; Angela Cleveland, National Center for Immunization and Respiratory Diseases, CDC; Nicole Cohen, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Max Cohen, Center for State, Tribal, Local and Territorial Support, CDC; Amanda Cohn, National Center for Immunization and Respiratory Diseases, CDC; Jennifer Collins, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Erin Conners, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Aaron Curns, National Center for Immunization and Respiratory Diseases, CDC; Rebecca Dahl, National Center for Immunization and Respiratory Diseases, CDC; Walter Daley, Center for Preparedness and Response, CDC; Vishal Dasari, Center for State, Tribal, Local and Territorial Support, CDC; Elizabeth Davlantes, Center for State, Tribal, Local and Territorial Support, CDC; Patrick Dawson, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Lisa Delaney, National Institute for Occupational Safety and Health, CDC; Matthew Donahue, Center for State, Tribal, Local and Territorial Support, CDC; Chad Dowell, National Institute for Occupational Safety and Health, CDC; Jonathan Dyal, National Center for Immunization and Respiratory Diseases, CDC; William Edens, National Center for Immunization and Respiratory Diseases, CDC; Rachel Eidex, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Lauren Epstein, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Mary Evans, National Center for Injury Prevention and Control, CDC; Ryan Fagan, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Kevin Farris, National Center for Immunization and Respiratory Diseases, CDC; Leora Feldstein, National Center for Immunization and Respiratory Diseases, CDC; LeAnne Fox, National Center for Immunization and Respiratory Diseases, CDC; Mark Frank, Center for Preparedness and Response, CDC; Brandi Freeman, National Center for Immunization and Respiratory Diseases, CDC; Alicia Fry, National Center for Immunization and Respiratory Diseases, CDC; James Fuller, Center for Global Health, CDC; Romeo Galang,

National Center for Chronic Disease Prevention and Promotion, CDC; Sue Gerber, National Center for Immunization and Respiratory Diseases, CDC; Runa Gokhale, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Sue Goldstein, National Center for Immunization and Respiratory Diseases, CDC; Sue Gorman, Center for Preparedness and Response, CDC; William Gregg, National Center for Immunization and Respiratory Diseases, CDC; William Greim, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Steven Grube, Office of the Director, CDC; Aron Hall, National Center for Immunization and Respiratory Diseases, CDC; Amber Haynes, National Center for Immunization and Respiratory Diseases, CDC; Sherrasa Hill, National Center for Immunization and Respiratory Diseases, CDC; Jennifer Hornsby-Myers, National Institute for Occupational Safety and Health, CDC; Jennifer Hunter, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Christopher Ionta, National Center for Immunization and Respiratory Diseases, CDC; Cheryl Isenhour, National Center for Immunization and Respiratory Diseases, CDC; Max Jacobs, Center for State, Tribal, Local and Territorial Support, CDC; Kara Jacobs Slifka, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Daniel Jernigan, National Center for Immunization and Respiratory Diseases, CDC; Michael Jhung, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Jamie Jones-Wormley, Center for Preparedness and Response, CDC; Anita Kambhampati, National Center for Immunization and Respiratory Diseases, CDC; Shifaq Kamili, National Center for Immunization and Respiratory Diseases, CDC; Pamela Kennedy, National Center for Immunization and Respiratory Diseases, CDC; Charlotte Kent, Center for Surveillance, Epidemiology and Laboratory Services, CDC; Marie Killerby, National Center for Immunization and Respiratory Diseases, CDC; Lindsay Kim, National Center for Immunization and Respiratory Diseases, CDC; Hannah Kirking, National Center for Immunization and Respiratory Diseases, CDC; Lisa Koonin, National Center for Immunization and Respiratory Diseases, CDC; Ram Koppaka, National Center for Immunization and Respiratory Diseases, CDC; Christine Kosmos, Center for Preparedness and Response, CDC; David Kuhar, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Wendi Kuhnert-Tallman, Deputy Director for Infectious Diseases, CDC; Stephanie Kujawski, National Center for Immunization and Respiratory Diseases, CDC; Archana Kumar, National Center for Immunization and Respiratory Diseases, CDC; Alexander Landon, Office of the Director, CDC; Leslie Lee, National Center for Immunization and Respiratory Diseases, CDC; Jessica Leung, National Center for Immunization and Respiratory Diseases, CDC; Stephen Lindstrom, National Center for Immunization and Respiratory Diseases, CDC; Ruth Link-Gelles, National Center for Immunization and Respiratory Diseases, CDC; Joana Lively, National Center for Immunization and Respiratory Diseases, CDC; Xiaoyan Lu, National Center for Immunization and Respiratory Diseases, CDC; Brian Lynch, National Center for Immunization and Respiratory Diseases, CDC; Lakshmi Malapati, National Center for Immunization and Respiratory Diseases, CDC; Samantha Mandel, National Center for Immunization and Respiratory Diseases, CDC; Brian Manns, National Center for Immunization and Respiratory Diseases, CDC; Nina Marano, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Mariel Marlow, National Center for Immunization and Respiratory Diseases, CDC; Barbara Marston, Center for Global Health, CDC; Nancy McClung, National Center for Immunization and Respiratory Diseases, CDC; Liz McClure, Center for Global Health, CDC; Emily McDonald, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Oliva McGovern, National Center for Immunization and Respiratory Diseases, CDC; Nancy Messonnier, National Center for Immunization and Respiratory Diseases, CDC; Claire Midgley, National Center for Immunization and Respiratory Diseases, CDC; Danielle Moulia, National Center for Immunization and Respiratory Diseases, CDC; Janna Murray, National Center for Immunization and Respiratory Diseases, CDC; Kate Noelte, Center for Preparedness and Response, CDC; Michelle Noonan-Smith, Office of the Director, CDC; Kristen Nordlund, National Center for Immunization and Respiratory Diseases, CDC; Emily Norton, National Institute for Occupational Safety and Health, CDC; Sara Oliver, National Center for Immunization and Respiratory Diseases, CDC; Mark Pallansch, National Center for Immunization and Respiratory Diseases, CDC; Umesh Parashar, National Center for Immunization and Respiratory Diseases, CDC; Anita Patel, National Center for Immunization and Respiratory Diseases, CDC; Manisha Patel, National Center for Immunization and Respiratory Diseases, CDC; Kristen Petrone, National Center for Health Statistics, CDC; Taran Pierce, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Harald Pietz, Center for Preparedness and Response, CDC; Satish Pillai, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Lewis Radonovich, National Institute for Occupational Safety and Health, CDC; Sarah Reagan-Steiner, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Amy Reel, National Center for Immunization and Respiratory Diseases, CDC; Heather Reese, National Center for Immunization and Respiratory Diseases, CDC; Brian Rha, National Center for Immunization and Respiratory Diseases, CDC; Philip Ricks, Center for Global Health, CDC; Melissa Rolfs, National Center for Immunization and Respiratory Diseases, CDC; Shahrokh Roohi, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Lauren Roper, National Center for Immunization and Respiratory Diseases, CDC; Lisa Rotz, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Janell Routh, National Center for Immunization and Respiratory Diseases, CDC; Senthil Kumar Sakthivel, National Center for Immunization and Respiratory Diseases, CDC; Luisa Sarmiento, National Institute for Occupational Safety and Health, CDC; Jessica Schindelar, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Eileen Schneider, National Center for Immunization and Respiratory Diseases, CDC; Anne Schuchat, Office of the Director, CDC; Sarah Scott, Center for State, Tribal, Local and Territorial Support, CDC; Varun Shetty, Center for State, Tribal, Local and Territorial Support, CDC; Caitlin Shockley, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Jill Shugart, National Institute for Occupational Safety and Health, CDC; Mark Stenger, National Center for HIV/AIDS, Viral

Hepatitis, STD, and TB Prevention, CDC; Matthew Stuckey, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Brittany Sunshine, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Tamara Sykes, Office of the Director, CDC; Jonathan Trapp, Office of the Director, CDC; Timothy Uyeki, National Center for Immunization and Respiratory Diseases, CDC; Grace Vahey, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Amy Valderrama, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Julie Villanueva, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Tunicia Walker, Center for Preparedness and Response, CDC; Megan Wallace, National Center for Immunization and Respiratory Diseases, CDC; Lijuan Wang, National Center for Immunization and Respiratory Diseases, CDC; John Watson, National Center for Immunization and Respiratory Diseases, CDC; Angie Weber, National Institute for Occupational Safety and Health, CDC; Cindy Weinbaum, National Center for Immunization and Respiratory Diseases, CDC; William Weldon, National Center for Immunization and Respiratory Diseases, CDC; Michael Whitaker, National Center for Immunization and Respiratory Diseases, CDC; Alcia Williams, Office of the Director, CDC; Holly Williams, Office of the Director, CDC; Ian Williams, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Karen Wong, Center for Surveillance, Epidemiology and Laboratory Services, CDC; Amy Xie, Center for State, Tribal, Local and Territorial Support, CDC; Anna Yousef, National Center for Immunization and Respiratory Diseases, CDC.

Corresponding author: Anita Patel, APatel7@cdc.gov, 770-488-7100.

<sup>1</sup>Incident Manager, 2019-nCoV CDC Response, CDC.

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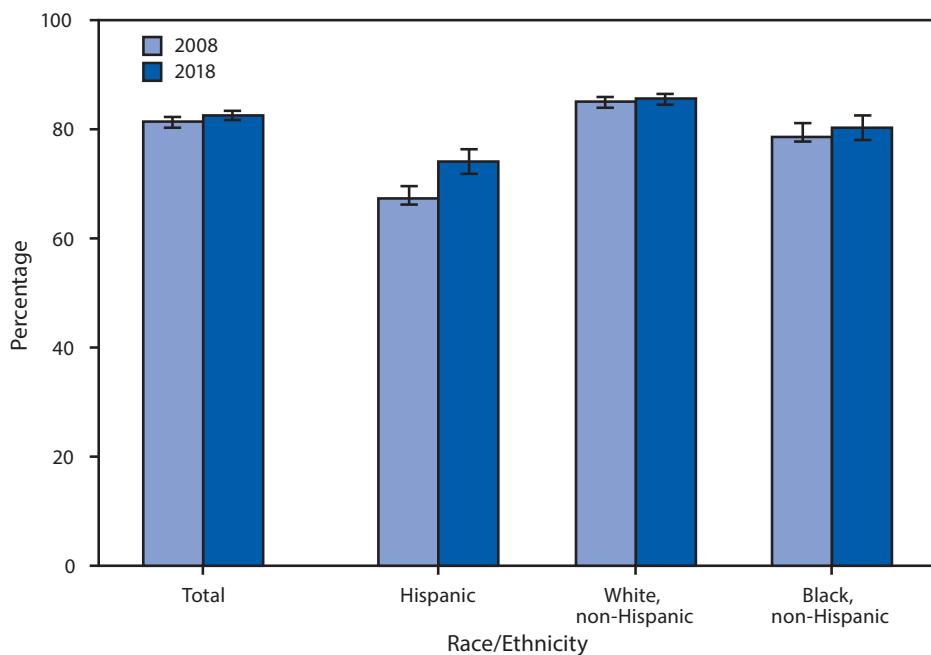
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**QuickStats**

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

**Percentage\* of Adults Aged 18–64 Years with a Usual Place for Health Care,<sup>†</sup>  
by Race/Ethnicity<sup>§</sup> — National Health Interview Survey,  
United States, 2008 and 2018**



\* With 95% confidence intervals indicated by error bars.

<sup>†</sup> Household interviews of a sample of the civilian, noninstitutionalized U.S. population were conducted using the National Health Interview Survey Sample Adult component. Estimates were derived from answers to the question “Is there a place that you usually go to when you are sick or need advice about your health?” Adults who indicated that the emergency room was their usual place for care were considered not to have a usual place of health care.

<sup>§</sup> Categories of race shown are for non-Hispanic respondents who selected one racial group; respondents had the option to select one or more racial groups. Hispanic origin refers to persons who are of Hispanic ethnicity and might be of any race or combination of races. Only selected individual groups are shown in graph. Total bar is based on all adults aged 18–64 years.

Although the percentage of Hispanic adults aged 18–64 years who had a usual place to go for medical care was higher in 2018 (74.1%) than in 2008 (67.3%), Hispanic adults remained the least likely to have a usual place to go for medical care. Non-Hispanic white adults were the most likely to have a usual place for medical care in both 2008 (85.0%) and 2018 (85.5%). In 2008, 78.7% of non-Hispanic black adults had a usual place for health care compared with 80.4% in 2018.

Source: National Health Interview Survey, 2008 and 2018 data. <https://www.cdc.gov/nchs/nhis.htm>.

Reported by: Michael E. Martinez, MPH, MHSA, bmd7@cdc.gov, 301-458-4758; Tainya C. Clarke, PhD.

## Morbidity and Mortality Weekly Report

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