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# Multistate Outbreak of *Salmonella* Infections Linked to Raw Turkey Products — United States, 2017–2019

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During 2018–2019, CDC, local and state public health partners, the U.S. Department of Agriculture (USDA), and the Food and Drug Administration (FDA) investigated a multistate outbreak of 356 *Salmonella* Reading infections from 42 states and the District of Columbia (DC) linked to turkey. The outbreak strain was isolated from raw turkey products, raw turkey pet food, and live turkeys. In July 2018, CDC and USDA's Food Safety and Inspection Service (FSIS) shared outbreak investigation results with representatives from the U.S. turkey industry, engaging with an industry group rather than a specific company for the first time during an outbreak, and CDC issued a public investigation notice. During the investigation, four recalls of turkey products were issued. Evidence suggested that the outbreak strain of *Salmonella* was widespread in the turkey industry, and therefore, interventions should target all parts of the supply chain, including slaughter and processing facilities and upstream farm sources.

## Epidemiologic Investigation

In January 2018, through routine state surveillance, Minnesota Department of Health investigators identified four *Salmonella* Reading infections with an indistinguishable pulsed-field gel electrophoresis (PFGE) pattern, suggesting they likely shared a common source. One patient had consumed ground turkey, and two lived in the same household where pets in the home ate raw turkey pet food. Minnesota investigators also identified this same strain in one sample of retail ground turkey. This PFGE pattern is the most common subtype of *Salmonella* Reading; however, the Reading serotype is uncommon, not ranking in the 20 most common types of human *Salmonella* infections reported in the United States (*1*). In response to Minnesota's investigation, PulseNet,* the national laboratory network for foodborne disease surveillance, was queried for additional *Salmonella* infections with this PFGE pattern. CDC began a multistate cluster investigation,

* https://www.cdc.gov/pulsenet.

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collecting information on patient exposures from local and state health departments and information on food and pet food products from FDA and FSIS.

CDC defined a case as an infection with *Salmonella* Reading with the outbreak PFGE pattern with illness onset from during November 20, 2017–March 31, 2019. Patients were interviewed to collect information on consumption of turkey and other poultry foods, exposure to raw poultry pet food, and contact with live poultry.

Investigators from DC Health and the Iowa Department of Health identified two illness subclusters of cases in which attendees ate at a common event before becoming ill. The two events occurred in November 2018 and February 2019, and 152 persons became ill, including 51 whose clinical isolates matched the outbreak strain and 101 who had clinically compatible illness without culture confirmation of *Salmonella* infection. Investigators identified whole turkey and boneless roast turkey as the food items significantly associated with illness at these two events and found that turkey was not handled or prepared in accordance with FSIS guidelines and was not held at proper temperatures to prevent bacterial growth (*2*).

Overall, 356 outbreak cases from 42 states and DC were identified (Figure 1) (Figure 2). Patients ranged in age from <1 to 101 years (median = 42 years), and 175 (52%) of 336 patients for whom information on sex was available were male. Among 300 patients with available information, 132 (44%) were hospitalized, and one died. Among 198 interviewed patients, 132 (67%) reported direct or indirect contact with turkey in the week before illness; 123 reported preparing or eating turkey products that were purchased raw (including whole turkey, turkey pieces, and ground turkey), four became sick after pets in their home ate raw ground turkey pet food, and five worked in a facility that raises or processes turkeys or lived with someone who worked in such a facility. No common type, brand, or source of turkey was identified.

## Product Testing and Laboratory Investigation

During the investigation, the outbreak strain was identified in 178 samples of raw turkey products from 24 slaughter and 14 processing establishments in 21 states that were collected by FSIS as part of routine testing and in 120 retail turkey samples collected as part of the National Antimicrobial Resistance Monitoring System retail meat sampling program (*3*,*4*). These samples represented several brands and types of raw turkey products. The outbreak strain was also identified in 10 samples from live turkeys in several states.

Investigators from the Arizona State Public Health Laboratory and the Michigan Department of Agriculture and Rural Development identified the outbreak strain in two of three unopened ground turkey samples collected from two patient homes. These were the same brand of ground turkey but were produced in different facilities. Investigators from the Minnesota Department of Agriculture identified the outbreak strain in samples of two brands of raw turkey pet food that were served to pets in patients' homes. No commercial connections

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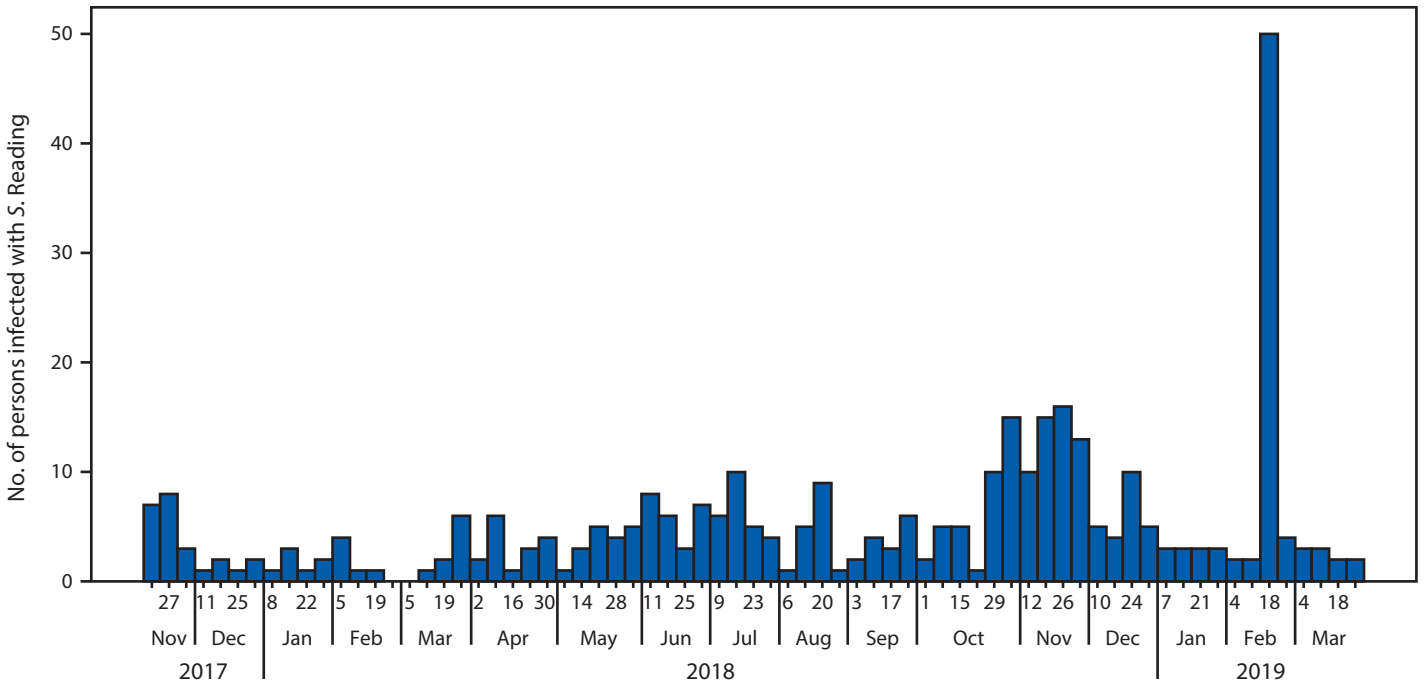
**FIGURE 1. Number of persons (N = 356) infected with the outbreak strain of *Salmonella* Reading by date of illness onset* — United States, November 20, 2017–March 31, 2019**




* Approximately 20% of illness onset dates were estimated from other reported information.

or common source materials were identified among any of these facilities.

## Public Health Response

In July 2018, CDC and FSIS shared investigation results with the National Turkey Federation, an industry group that represents turkey farmers and processors, and asked about steps they could take to reduce *Salmonella* contamination in their products. This was the first time that CDC and FSIS engaged an industry group rather than a specific company during an outbreak, a step taken because no single product or common supplier was identified. Upon learning of the outbreak, the National Turkey Federation compiled *Salmonella* control programs to share industry-wide, conducted studies about *Salmonella* in processing plants, sought research on interventions, and began bolstering consumer food safety education (*5*).

On July 19, 2018, CDC issued an initial investigation notice describing the outbreak. Because no single, common supplier of turkey products was identified, CDC reminded consumers to always follow appropriate food handling techniques to prevent *Salmonella* infection (*6*).

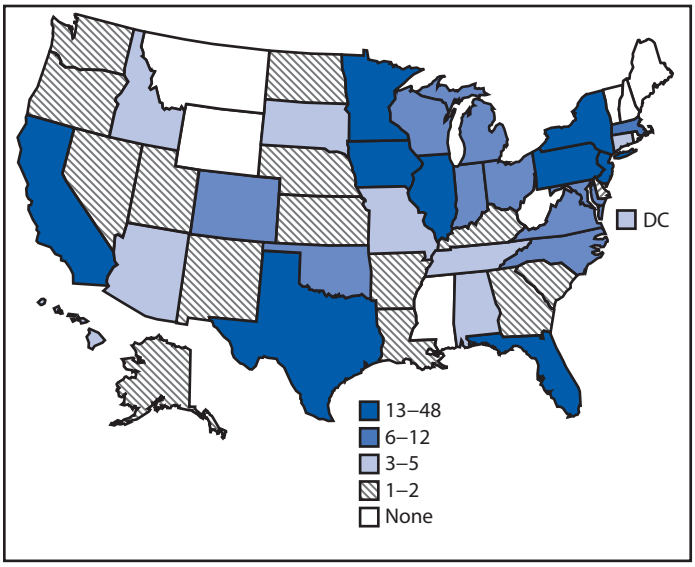
Four recalls of turkey products were issued during this investigation after investigators identified the outbreak strain in ground turkey and raw turkey pet food associated with illnesses in Arizona, Michigan, and Minnesota. In February 2018 and January 2019, approximately 4,000 pounds of raw turkey pet food were recalled by two separate pet food companies based in Minnesota. In addition, in November and December 2018, approximately 300,000 pounds of ground turkey products were recalled by two turkey establishments of the same company.

## Discussion

From 2018 to 2019, public health officials investigated a large and protracted multistate outbreak of *Salmonella* infections linked to raw turkey products. Evidence demonstrated that the outbreak strain was present throughout the turkey industry in live turkeys and in raw turkey products meant for human and animal consumption. This was one of the first times CDC used a new communication tool, an investigation notice, to provide information and recommendations to consumers when no specific product source was identified during an outbreak investigation (*6*). This tool allows for timely and pertinent communication with partners, which is important to identifying the cause of outbreaks and stopping them more quickly.

Although previous multistate outbreaks of *Salmonella* Heidelberg (associated with ground turkey) (*7*) and *Salmonella* Hadar infections (associated with turkey burgers) (*8*) have occurred, a noteworthy aspect of this outbreak was that no single common source or supplier was identified as the cause of illnesses. For this investigation, it was necessary to determine whether illnesses were part of an outbreak or sporadic infections

**FIGURE 2. Number of persons (N = 356) infected with the outbreak strain of *Salmonella* Reading, by state — United States, November 2017–March 2019**




**Abbreviation:** DC = District of Columbia.

with a common strain of *Salmonella*. The evidence suggested that an outbreak occurred and that turkey products were the source for two reasons. First, there was a strong epidemiologic association between illness and exposure to turkey. Second, laboratory evidence indicated that the outbreak strain was present in turkey facilities around the country and in live turkeys. The outbreak strain might have been introduced into the turkey supply chain and subsequently spread to many establishments and products throughout the industry before isolates from the Minnesota investigation were identified and the number of isolates were enough to initiate a multistate investigation.

Because contamination was widespread, interventions needed to target all parts of the supply chain, including slaughter and processing facilities as well as upstream farm sources. Although elimination of *Salmonella* from poultry flocks and products is challenging, the responsibility to develop effective strategies for *Salmonella* reduction along the production chain begins with industry. This investigation ended in April 2019 because new cases of illness decreased; however, cases continue to be identified. Evidence suggests that this outbreak strain has become widespread within the turkey production industry, warranting continued preventive actions to reduce contamination.

The two illness subclusters in this outbreak indicate improper handling and cooking of raw turkey products and highlight the need to reinforce consumer education. A 2017 study found

**Summary**

What is already known about this topic?

*Salmonella* Reading is a serotype that is uncommonly associated with human illness. *Salmonella* outbreaks have previously been associated with ground turkey and turkey burgers.

What is added by this report?

During November 2017–March 2019, a multistate outbreak of *S.* Reading involving 356 cases in 42 states occurred. Patients reported exposure to various turkey products, suggesting industry-wide contamination, a novel type of outbreak in which contamination is not isolated to a single food or facility.

What are the implications for public health practice?

Interventions should target all parts of the supply chain, including slaughter and processing facilities and upstream farm sources. Public health agencies and industry can take steps to provide more consumer education about food safety.

that adherence to food safety practices among persons preparing turkey burgers was low but did improve after watching a USDA video on proper thermometer use (*9*). This same study also found very low adherence to CDC's recommended steps for handwashing during food preparation and noted that approximately half of the participants contaminated other kitchen items, such as spice containers, by touching them while preparing turkey (*9*). These findings underscore the impact that food safety messaging can have on consumer behavior and the importance of proper food safety throughout the food preparation process. Consumers should always thaw turkeys safely (in the refrigerator in a container, in a leak-proof plastic bag in a sink of cold water, or in a microwave oven following the manufacturer's instructions), avoid the spread of bacteria from raw turkey by keeping it separate from other foods and keeping food surfaces clean, and cook turkey to 165°F (74°C), measured on a food thermometer inserted into the thickest portions of the breast, thigh, and wing joint.[†] In addition to emphasizing the importance of food safety messaging, this outbreak reinforced the need for awareness of the recommendations against feeding pets a raw meat diet, which can lead to both human and animal illnesses (*10*). Finally, industries can take steps to provide consumer education through their marketing programs and on product packages. Consumers, public health agencies, and industry officials all play important roles in promoting and implementing *Salmonella* prevention and control strategies to prevent future illnesses.

[†] https://www.cdc.gov/foodsafety/communication/holiday-turkey.html.

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# Traumatic Brain Injury–Related Deaths by Race/Ethnicity, Sex, Intent, and Mechanism of Injury — United States, 2000–2017

Jill Daugherty, PhD[1]; Dana Waltzman, PhD[1]; Kelly Sarmiento, MPH[1]; Likang Xu, MD[1]

Traumatic brain injury (TBI) affects the lives of millions of Americans each year (*1*). To describe the trends in TBI-related deaths among different racial/ethnic groups and by sex, CDC analyzed death data from the National Vital Statistics System (NVSS) over an 18-year period (2000–2017). Injuries were also categorized by intent, and unintentional injuries were further categorized by mechanism of injury. In 2017, TBI contributed to 61,131 deaths in the United States, representing 2.2% of approximately 2.8 million deaths that year. From 2015 to 2017, 44% of TBI-related deaths were categorized as intentional injuries (i.e., homicides or suicides). The leading category of TBI-related death varied over time and by race/ethnicity. For example, during the last 10 years of the study period, suicide surpassed unintentional motor vehicle crashes as the leading category of TBI-related death. This shift was in part driven by a 32% increase in TBI-related suicide deaths among non-Hispanic whites. Firearm injury was the underlying mechanism of injury in nearly all (97%) TBI-related suicides among all groups. An analysis of TBI-related death rates by sex and race/ethnicity found that TBI-related deaths were significantly higher among males and persons who were American Indians/Alaska Natives (AI/ANs) than among all other groups across all years. Other leading categories of TBI-related deaths included unintentional motor vehicle crashes, unintentional falls, and homicide. Understanding the leading contributors to TBI-related death and identifying groups at increased risk is important in preventing this injury. Broader implementation of evidence-based TBI prevention efforts for the leading categories of injury, such as those aimed at stemming the significant increase in TBI-related deaths from suicide, are warranted.

Data from CDC's NVSS multiple-cause-of-death files were analyzed for 2000–2017. NVSS collects data for all deaths among U.S. residents. TBI-related deaths were classified using codes from the *International Classification of Diseases, Tenth Revision* (ICD-10) using an established surveillance definition (*2*). Deaths were classified as TBI-related if any multiple codes for causes of deaths listed in the death record indicated a TBI-related diagnosis, and the single underlying cause of death was listed as an injury. This methodology represents a change in the calculation of estimates from previous CDC reports (*1*,*2*), which did not require that an injury be listed as an underlying cause of death.† Data on TBI-related deaths were stratified by year, race/ethnicity, sex, and principal mechanism of injury. Racial/ethnic groups included non-Hispanic white (white), non-Hispanic black (black), non-Hispanic American Indian/Alaska Native (AI/AN), non-Hispanic Asian/Pacific Islander (Asian/PI), Hispanic, and other. Injuries were categorized first by intent (intentional, unintentional, and undetermined intent). Intentional injuries were further categorized as suicide or homicide. Unintentional injuries were further categorized by mechanism of injury (motor vehicle crashes, falls, being struck by or against an object, or unspecified). Principal mechanism of injury was categorized based on the CDC-recommended external cause of injury mortality matrix for ICD-10 (*3*) and are presented as the pooled average of 3-year groupings.

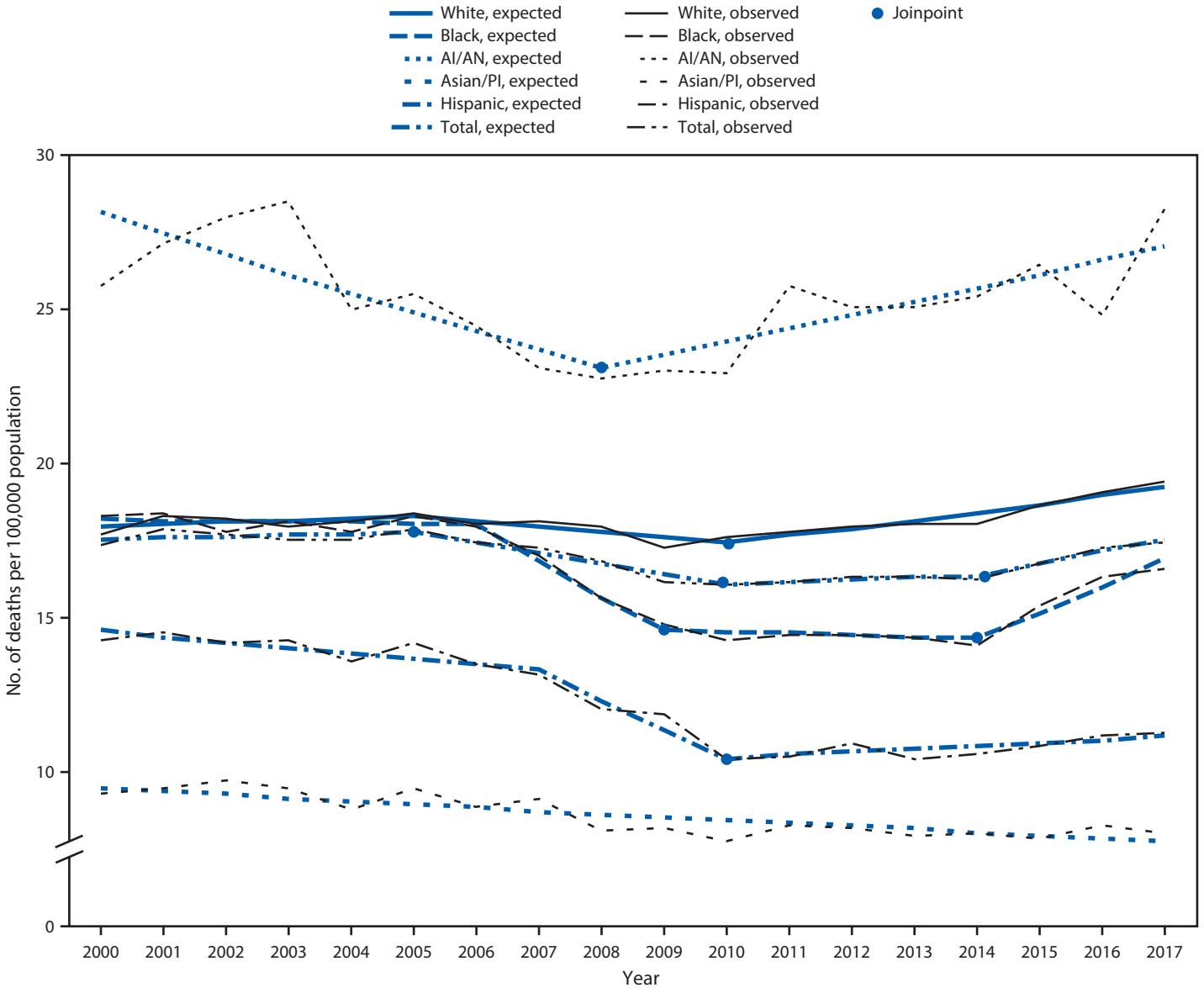
Each rate and its corresponding 95% confidence interval were based on U.S. bridged-race population estimates of the resident population (*4*). U.S. census population estimates for the year 2000 were used as the standard for age-adjusted rates by direct method (*5*). T-tests were used to analyze between-group differences for rates of TBI-related deaths. Only selected comparisons were tested for statistical significance. Differences with p-values <0.05 were considered statistically significant. JoinPoint regression software (version 4.7.0.0; National Cancer Institute) was used to calculate the average annual percent changes of TBI-related death rates from 2000 to 2017 for each race and Hispanic origin group to illustrate trends over time. Average annual percent changes were considered significantly different from zero for p-values <0.05. SAS (version 9.4; SAS Institute, Inc.) was used for all statistical analyses.

The overall rate of TBI-related deaths remained constant from 2000 to 2005, followed by a statistically significant decrease in the overall rate from 2005 to 2010 and then a flattening out from 2010 to 2014. From 2014 to 2017, a small but statistically significant increase in the overall rate of TBI-related deaths occurred (Figure). TBI-related death rates were significantly higher among males of all races than among females throughout the study period (p<0.001) (Table 1), and age-adjusted rates were significantly higher among AI/AN persons than among other racial/ethnic groups (p<0.001). From

* https://www.cdc.gov/nchs/products/databriefs/db328.htm.

† Previous estimates of TBI-related deaths included all cases in which a TBI-related ICD-10 code was listed in the NVSS mortality record, regardless of whether an injury code was listed as the underlying cause of death. The current methodology only includes deaths for which an injury was more directly related to the cause of death.

**FIGURE. Age-adjusted rates* of traumatic brain injury–related deaths, by year and race/ethnicity† — United States, 2000–2017**




**Abbreviations:** AI/AN = American Indian/Alaska Native; A/PI = Asian/Pacific Islander.
* Per 100,000 population.
† Persons who were white, black, AI/AN, and A/PI were non-Hispanic; Hispanic persons could be of any race.

2001 to 2006, the death rates of whites and blacks were similar (p>0.05), but since 2007, the rate of TBI-related deaths has been significantly higher among whites (p<0.001).

Unintentional TBIs combined across mechanism of injury were responsible for a higher number and rate of deaths than were suicide and homicide across all study years (p<0.001) (Table 2). Unintentional motor vehicle crashes led to the highest number and rate of all TBI-related deaths from 2000–2002 to 2006–2008 (p<0.05). Beginning in 2009–2011 and continuing through 2015–2017, suicide was responsible for the most TBI-related deaths (p<0.001). Across all data years, firearm-related injuries were responsible for approximately 97% of all TBI-related suicides. The leading category of TBI-related injury death varied by race/ethnicity and changed for some groups during the study period. For example, from 2000–2002 to 2003–2005, unintentional motor vehicle crashes accounted for the highest rate of TBI-related deaths for whites (p<0.001). Beginning in 2006–2008 and continuing through 2015–2017, suicide accounted for the highest rate of TBI-related deaths for this group (p<0.002). Among blacks, homicide was responsible for the highest rate of TBI-related deaths from 2000–2002 to 2015–2017 (p<0.001).

**TABLE 1. Estimated number* and age-adjusted rates† of traumatic brain injury–related deaths,§ by year, sex, and race/ethnicity¶ — United States, 2000–2017****

| Year/ Sex | Race/Ethnicity | | | | | | | | | | | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | White | | Black | | American Indian/Alaska Native | | Asian/Pacific Islander | | Hispanic | | Other | | | |
| | No. | Rate (95% CI) | No. | Rate (95% CI) | No. | Rate (95% CI) | No. | Rate (95% CI) | No. | Rate (95% CI) | No. | | No. | Rate (95% CI) |
| **2000** | | | | | | | | | | | | | | |
| Male | 26,497 | 27.6 (27.3–28.0) | 4,832 | 30.5 (29.6–31.4) | 412 | 38.5 (34.3–42.6) | 599 | 13.0 (11.9–14.2) | 3,593 | 22.5 (21.6–23.4) | 164 | | **36,097** | **27.3 (27.0–27.6)** |
| Female | 9,982 | 9.0 (8.8–9.2) | 1,436 | 8.0 (7.5–8.4) | 169 | 14.4 (12.2–16.7) | 291 | 6.0 (5.3–6.7) | 912 | 6.3 (5.8–6.8) | 40 | | **12,830** | **8.5 (8.4–8.7)** |
| **Total** | **36,479** | **17.7 (17.5–17.9)** | **6,268** | **18.3 (17.8–18.8)** | **581** | **25.8 (23.6–28.1)** | **890** | **9.3 (8.6–9.9)** | **4,505** | **14.3 (13.8–14.8)** | **204** | | 48,927 | 17.4 (17.2–17.5) |
| **2001** | | | | | | | | | | | | | | |
| Male | 27,747 | 28.6 (28.3–29.0) | 4,915 | 30.8 (29.9–31.7) | 429 | 39.4 (35.2–43.6) | 648 | 13.8 (12.6–15.0) | 3,865 | 22.7 (21.8–23.6) | 166 | | **37,770** | **28.2 (28.0–28.5)** |
| Female | 10,307 | 9.1 (8.9–9.3) | 1,410 | 7.9 (7.4–8.3) | 184 | 16.0 (13.5–18.4) | 306 | 5.9 (5.2–6.6) | 961 | 6.4 (6.0–6.9) | 43 | | **13,211** | **8.7 (8.5–8.8)** |
| **Total** | **38,054** | **18.3 (18.1–18.5)** | **6,325** | **18.4 (17.9–18.8)** | **613** | **27.2 (24.9–29.5)** | **954** | **9.5 (8.8–10.1)** | **4,826** | **14.5 (14.0–15.0)** | **209** | | 50,981 | 17.9 (17.7–18.0) |
| **2002** | | | | | | | | | | | | | | |
| Male | 27,771 | 28.4 (28.1–28.7) | 4,811 | 30.0 (29.1–30.9) | 480 | 42.2 (38.1–46.4) | 652 | 13.6 (12.4–14.7) | 3,908 | 22.5 (21.6–23.4) | 186 | | **37,808** | **27.9 (27.6–28.2)** |
| Female | 10,400 | 9.1 (9.0–9.3) | 1,402 | 7.6 (7.2–8.0) | 171 | 14.7 (12.4–17.0) | 334 | 6.4 (5.7–7.2) | 973 | 6.1 (5.7–6.5) | 31 | | **13,311** | **8.6 (8.5–8.8)** |
| **Total** | **38,171** | **18.2 (18.0–18.4)** | **6,213** | **17.8 (17.3–18.2)** | **651** | **28.0 (25.7–30.3)** | **986** | **9.7 (9.1–10.4)** | **4,881** | **14.2 (13.7–14.6)** | **217** | | 51,119 | 17.7 (17.6–17.9) |
| **2003** | | | | | | | | | | | | | | |
| Male | 27,631 | 28.0 (27.7–28.4) | 4,923 | 30.0 (29.1–30.9) | 491 | 44.1 (39.8–48.4) | 671 | 13.3 (12.2–14.4) | 3,977 | 22.1 (21.3–23.0) | 119 | | **37,812** | **27.6 (27.3–27.9)** |
| Female | 10,439 | 9.0 (8.8–9.2) | 1,472 | 8.0 (7.6–8.4) | 162 | 14.2 (11.9–16.5) | 338 | 6.1 (5.4–6.8) | 1,038 | 6.4 (6.0–6.9) | 40 | | **13,489** | **8.6 (8.5–8.8)** |
| **Total** | **38,070** | **18.0 (17.8–18.2)** | **6,395** | **18.1 (17.7–18.6)** | **653** | **28.6 (26.2–30.9)** | **1,009** | **9.4 (8.8–10.0)** | **5,015** | **14.2 (13.8–14.7)** | **159** | | 51,301 | 17.6 (17.4–17.7) |
| **2004** | | | | | | | | | | | | | | |
| Male | 27,799 | 27.9 (27.6–28.3) | 4,842 | 29.7 (28.8–30.6) | 435 | 37.9 (34.0–41.8) | 604 | 11.7 (10.7–12.7) | 3,938 | 20.9 (20.1–21.7) | 117 | | **37,735** | **27.2 (26.9–27.5)** |
| Female | 10,921 | 9.4 (9.2–9.6) | 1,466 | 7.9 (7.5–8.3) | 163 | 13.2 (11.1–15.3) | 366 | 6.2 (5.6–6.9) | 1,012 | 6.1 (5.7–6.5) | 40 | | **13,968** | **8.8 (8.7–9.0)** |
| **Total** | **38,720** | **18.1 (18.0–18.3)** | **6,308** | **17.8 (17.4–18.3)** | **598** | **25.0 (22.9–27.1)** | **970** | **8.7 (8.1–9.3)** | **4,950** | **13.5 (13.1–14.0)** | **157** | | 51,703 | 17.5 (17.3–17.6) |
| **2005** | | | | | | | | | | | | | | |
| Male | 28,771 | 28.6 (28.3–29.0) | 5,126 | 30.5 (29.6–31.4) | 471 | 39.0 (35.2–42.7) | 741 | 13.9 (12.9–15.0) | 4,261 | 22.4 (21.5–23.2) | 122 | | **39,492** | **28.0 (27.8–28.3)** |
| Female | 10,852 | 9.2 (9.0–9.4) | 1,462 | 7.9 (7.5–8.3) | 157 | 12.9 (10.8–15.0) | 352 | 5.8 (5.2–6.4) | 1,068 | 6.1 (5.7–6.5) | 25 | | **13,916** | **8.6 (8.5–8.8)** |
| **Total** | **39,623** | **18.4 (18.2–18.6)** | **6,588** | **18.3 (17.9–18.8)** | **628** | **25.6 (23.5–27.6)** | **1,093** | **9.5 (8.9–10.1)** | **5,329** | **14.2 (13.8–14.6)** | **147** | | 53,408 | 17.8 (17.7–18.0) |
| **2006** | | | | | | | | | | | | | | |
| Male | 28,336 | 27.9 (27.5–28.2) | 5,205 | 30.4 (29.5–31.3) | 453 | 37.8 (34.1–41.5) | 703 | 12.6 (11.7–13.6) | 4,254 | 21.3 (20.5–22.1) | 105 | | **39,056** | **27.3 (27.0–27.6)** |
| Female | 10,905 | 9.2 (9.0–9.3) | 1,401 | 7.4 (7.0–7.7) | 152 | 12.1 (10.1–14.0) | 355 | 5.7 (5.1–6.3) | 1,025 | 5.7 (5.3–6.1) | 29 | | **13,867** | **8.5 (8.4–8.6)** |
| **Total** | **39,241** | **18.0 (17.9–18.2)** | **6,606** | **18.0 (17.5–18.4)** | **605** | **24.5 (22.4–26.5)** | **1,058** | **8.9 (8.3–9.4)** | **5,279** | **13.5 (13.1–13.9)** | **134** | | 52,923 | 17.4 (17.3–17.6) |
| **2007** | | | | | | | | | | | | | | |
| Male | 28,849 | 28.1 (27.8–28.4) | 4,980 | 28.2 (27.4–29.0) | 422 | 35.6 (31.9–39.2) | 752 | 12.9 (11.9–13.9) | 4,141 | 20.6 (19.9–21.4) | 104 | | **39,248** | **27.1 (26.8–27.4)** |
| Female | 11,003 | 9.1 (8.9–9.2) | 1,395 | 7.2 (6.8–7.6) | 141 | 11.4 (9.4–13.3) | 373 | 5.8 (5.2–6.4) | 1,056 | 5.7 (5.3–6.1) | 29 | | **13,997** | **8.4 (8.3–8.6)** |
| **Total** | **39,852** | **18.1 (17.9–18.3)** | **6,375** | **17.0 (16.6–17.4)** | **563** | **23.1 (21.1–25.1)** | **1,125** | **9.1 (8.5–9.6)** | **5,197** | **13.1 (12.7–13.5)** | **133** | | 53,245 | 17.3 (17.2–17.5) |
| **2008** | | | | | | | | | | | | | | |
| Male | 29,211 | 28.1 (27.8–28.5) | 4,670 | 26.4 (25.6–27.2) | 430 | 35.2 (31.7–38.8) | 703 | 11.9 (11.0–12.8) | 3,810 | 19.0 (18.3–19.7) | 84 | | **38,908** | **26.5 (26.3–26.8)** |
| Female | 10,807 | 8.7 (8.6–8.9) | 1,253 | 6.4 (6.0–6.7) | 139 | 11.1 (9.2–13.0) | 327 | 4.8 (4.3–5.4) | 968 | 5.2 (4.8–5.6) | 32 | | **13,526** | **8.0 (7.8–8.1)** |
| **Total** | **40,018** | **18.0 (17.8–18.2)** | **5,923** | **15.7 (15.3–16.1)** | **569** | **22.7 (20.8–24.7)** | **1,030** | **8.1 (7.6–8.6)** | **4,778** | **12.0 (11.6–12.4)** | **116** | | 52,434 | 16.8 (16.7–17.0) |
| **2009** | | | | | | | | | | | | | | |
| Male | 28,236 | 26.9 (26.6–27.2) | 4,346 | 24.5 (23.7–25.3) | 411 | 33.2 (29.8–36.5) | 711 | 11.6 (10.7–12.5) | 3,789 | 18.3 (17.6–18.9) | 154 | | **37,647** | **25.4 (25.1–25.6)** |
| Female | 10,610 | 8.5 (8.3–8.6) | 1,298 | 6.5 (6.1–6.9) | 169 | 13.2 (11.2–15.3) | 362 | 5.2 (4.7–5.7) | 1,034 | 5.4 (5.1–5.8) | 43 | | **13,516** | **7.9 (7.7–8.0)** |
| **Total** | **38,846** | **17.2 (17.1–17.4)** | **5,644** | **14.8 (14.4–15.2)** | **580** | **23.0 (21.1–25.0)** | **1,073** | **8.1 (7.6–8.6)** | **4,823** | **11.8 (11.4–12.2)** | **197** | | 51,163 | 16.2 (16.0–16.3) |
| **2010** | | | | | | | | | | | | | | |
| Male | 28,678 | 27.5 (27.2–27.8) | 4,303 | 24.0 (23.2–24.7) | 401 | 34.4 (30.8–38.1) | 749 | 11.8 (10.9–12.7) | 3,381 | 16.3 (15.6–16.9) | 144 | | **37,656** | **25.3 (25.0–25.5)** |
| Female | 10,948 | 8.7 (8.5–8.8) | 1,168 | 5.8 (5.5–6.2) | 150 | 12.5 (10.4–14.5) | 327 | 4.4 (3.9–4.9) | 975 | 4.9 (4.5–5.2) | 40 | | **13,608** | **7.8 (7.6–7.9)** |
| **Total** | **39,626** | **17.6 (17.4–17.8)** | **5,471** | **14.2 (13.9–14.6)** | **551** | **22.9 (20.9–24.9)** | **1,076** | **7.7 (7.2–8.2)** | **4,356** | **10.4 (10.0–10.7)** | **184** | | 51,264 | 16.0 (15.9–16.2) |
| 2011 | | | | | | | | | | | | | | |
| Male | 29,067 | 27.6 (27.3–27.9) | 4,420 | 24.3 (23.5–25.0) | 462 | 39.3 (35.4–43.1) | 798 | 12.4 (11.4–13.3) | 3,581 | 16.8 (16.1–17.4) | 114 | | **38,442** | **25.4 (25.2–25.7)** |
| Female | 11,086 | 8.8 (8.6–8.9) | 1,237 | 6.0 (5.7–6.4) | 166 | 13.3 (11.2–15.4) | 384 | 5.1 (4.5–5.6) | 937 | 4.6 (4.3–4.9) | 36 | | **13,846** | **7.8 (7.7–7.9)** |
| **Total** | **40,153** | **17.8 (17.6–17.9)** | **5,657** | **14.4 (14.1–14.8)** | **628** | **25.7 (23.6–27.9)** | **1,182** | **8.3 (7.8–8.8)** | **4,518** | **10.5 (10.1–10.8)** | **150** | | 52,288 | 16.2 (16.0–16.3) |
| **2012** | | | | | | | | | | | | | | |
| Male | 29,678 | 27.9 (27.6–28.2) | 4,549 | 24.5 (23.7–25.2) | 495 | 40.3 (36.5–44.0) | 797 | 11.7 (10.8–12.5) | 3,700 | 17.3 (16.6–17.9) | 137 | | **39,356** | **25.7 (25.4–25.9)** |
| Female | 11,402 | 8.9 (8.8–9.1) | 1,187 | 5.7 (5.4–6.0) | 144 | 11.1 (9.2–12.9) | 422 | 5.3 (4.8–5.8) | 1,045 | 5.0 (4.7–5.3) | 38 | | **14,238** | **7.9 (7.8–8.1)** |
| **Total** | **41,080** | **18.0 (17.8–18.2)** | **5,736** | **14.4 (14.0–14.8)** | **639** | **25.1 (23.1–27.1)** | **1,219** | **8.1 (7.6–8.6)** | **4,745** | **10.9 (10.5–11.2)** | **175** | | 53,594 | 16.3 (16.2–16.5) |
| **2013** | | | | | | | | | | | | | | |
| Male | 30,118 | 28.0 (27.7–28.4) | 4,525 | 24.0 (23.3–24.8) | 461 | 38.7 (34.9–42.4) | 841 | 11.5 (10.7–12.3) | 3,605 | 16.4 (15.8–17.0) | 120 | | **39,670** | **25.5 (25.3–25.8)** |
| Female | 11,588 | 9.0 (8.8–9.1) | 1,257 | 5.9 (5.6–6.3) | 160 | 12.7 (10.6–14.7) | 424 | 5.0 (4.5–5.5) | 1,044 | 4.8 (4.5–5.1) | 35 | | **14,508** | **7.9 (7.8–8.1)** |
| **Total** | **41,706** | **18.1 (17.9–18.3)** | **5,782** | **14.4 (14.0–14.7)** | **621** | **25.1 (23.1–27.2)** | **1,265** | **7.9 (7.5–8.4)** | **4,649** | **10.4 (10.0–10.7)** | **155** | | 54,178 | 16.3 (16.1–16.4) |

See table footnotes on next page.

**TABLE 1. (*Continued*) Estimated number* and age-adjusted rates† of traumatic brain injury–related deaths,§ by year, sex, and race/ethnicity¶ — United States, 2000–2017****

| Year/ Sex | Race/Ethnicity | | | | | | | | | | | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | White | | Black | | American Indian/Alaska Native | | Asian/Pacific Islander | | Hispanic | | Other | | | |
| | No. | Rate (95% CI) | No. | Rate (95% CI) | No. | Rate (95% CI) | No. | Rate (95% CI) | No. | Rate (95% CI) | No. | | No. | Rate (95% CI) |
| **2014** | | | | | | | | | | | | | | |
| Male | 30,432 | 28.0 (27.6–28.3) | 4,501 | 23.6 (22.8–24.3) | 486 | 39.6 (35.9–43.4) | 888 | 11.6 (10.8–12.4) | 3,738 | 16.5 (15.9–17.1) | 152 | | **40,197** | **25.5 (25.2–25.7)** |
| Female | 11,714 | 9.0 (8.8–9.2) | 1,242 | 5.9 (5.6–6.2) | 158 | 12.4 (10.4–14.4) | 442 | 4.9 (4.5–5.4) | 1,139 | 5.1 (4.8–5.4) | 49 | | **14,744** | **8.0 (7.8–8.1)** |
| **Total** | **42,146** | **18.0 (17.9–18.2)** | **5,743** | **14.1 (13.7–14.5)** | **644** | **25.4 (23.4–27.5)** | **1,330** | **8.0 (7.5–8.4)** | **4,877** | **10.6 (10.3–10.9)** | **201** | | **54,941** | **16.3 (16.1–16.4)** |
| **2015** | | | | | | | | | | | | | | |
| Male | 31,353 | 28.8 (28.5–29.1) | 5,007 | 25.8 (25.1–26.6) | 490 | 39.2 (35.5–42.8) | 902 | 11.2 (10.4–11.9) | 3,970 | 16.8 (16.2–17.4) | 166 | | **41,888** | **26.3 (26.0–26.5)** |
| Female | 12,070 | 9.2 (9.1–9.4) | 1,359 | 6.3 (6.0–6.6) | 195 | 14.8 (12.7–16.9) | 478 | 5.0 (4.6–5.5) | 1,203 | 5.2 (4.9–5.5) | 53 | | **15,358** | **8.2 (8.1–8.3)** |
| Total | 43,423 | 18.6 (18.4–18.8) | 6,366 | 15.4 (15.0–15.8) | 685 | 26.5 (24.5–28.5) | 1,380 | 7.8 (7.4–8.2) | 5,173 | 10.8 (10.5–11.1) | 219 | | **57,246** | **16.8 (16.6–16.9)** |
| **2016** | | | | | | | | | | | | | | |
| Male | 32,241 | 29.4 (29.1–29.8) | 5,359 | 27.3 (26.5–28.0) | 486 | 38.2 (34.7–41.8) | 988 | 11.6 (10.9–12.3) | 4,310 | 17.5 (16.9–18.1) | 141 | | **43,525** | **26.9 (26.6–27.2)** |
| Female | 12,501 | 9.5 (9.4–9.7) | 1,498 | 6.8 (6.5–7.2) | 166 | 12.4 (10.4–14.3) | 540 | 5.3 (4.9–5.8) | 1,275 | 5.2 (4.9–5.5) | 29 | | **16,009** | **8.5 (8.3–8.6)** |
| **Total** | **44,742** | **19.1 (18.9–19.3)** | **6,857** | **16.4 (16.0–16.8)** | **652** | **24.8 (22.9–26.8)** | **1,528** | **8.2 (7.8–8.6)** | **5,585** | **11.2 (10.9–11.5)** | **170** | | **59,534** | **17.3 (17.1–17.4)** |
| **2017** | | | | | | | | | | | | | | |
| Male | 33,209 | 30.0 (29.6–30.3) | 5,577 | 27.8 (27.0–28.5) | 542 | 42.2 (38.5–45.9) | 1,041 | 11.9 (11.1–12.6) | 4,463 | 17.9 (17.3–18.4) | 129 | | **44,961** | **27.4 (27.2–27.7)** |
| Female | 12,688 | 9.6 (9.4–9.8) | 1,473 | 6.6 (6.3–7.0) | 210 | 15.5 (13.3–17.6) | 512 | 4.8 (4.4–5.3) | 1,254 | 5.1 (4.8–5.4) | 33 | | **16,170** | **8.4 (8.3–8.6)** |
| **Total** | **45,897** | **19.4 (19.2–19.6)** | **7,050** | **16.6 (16.2–17.0)** | **752** | **28.3 (26.2–30.4)** | **1,553** | **8.0 (7.6–8.4)** | **5,717** | **11.3 (10.9–11.6)** | **162** | | **61,131** | **17.5 (17.3–17.6)** |

**Abbreviation:** CI = confidence interval.

* Death estimates obtained from CDC's National Vital Statistics System. Visits with missing age or sex were excluded; numbers subject to rounding error.

† Per 100,000 population, age-adjusted to the 2000 U.S. standard population, using 12 age groups: 0–4, 5–9, 10–14, 15–19, 20–24, 25–34, 35–44, 45–54, 55–64, 65–74, 74–84, and ≥85 years.

§ Record-axis condition codes were used (usually included both part I and part II of entity-axis condition codes). https://www.cdc.gov/nchs/data/datalinkage/underlying_and_multiple_causes_of_death557_2011.pdf.

¶ Persons who were white, black, American Indian/Alaska Native, Asian/ Pacific Islander, or Other were non-Hispanic; Hispanics could be of any race.

** Differences in any two rates were considered statistically significant if their CIs were not overlapping.

Across the study period, the highest rate of TBI-related deaths among AI/AN was attributed to unintentional motor vehicle crashes ($p<0.05$). Among Hispanics, unintentional motor vehicle crashes were the most common cause of TBI-related deaths from 2000–2002 to 2006–2008 ($p<0.001$). During 2009–2011, the rates of TBI-related death from unintentional motor vehicle crashes and unintentional falls were similar ($p = 0.16$) in Hispanics; beginning in 2012–2014 and through 2015–2017, unintentional falls were the most common cause of TBI-related deaths among Hispanics ($p<0.001$).

## Discussion

Over the 18-year study period, approximately 960,000 TBI-related deaths occurred in the United States; however, the patterns differed over time and among racial/ethnic groups. Whereas the rates of TBI-related deaths among whites and blacks were similar from 2001 to 2006, the rates among whites subsequently exceeded those among blacks, presumably related to a 32% increase in TBI-related suicide deaths among whites, from 5.9 per 100,000 during 2006–2008 to 7.8 during 2015–2017. Previous data have documented an increasing prevalence of suicide among whites and AI/ANs (*6*). These findings suggest that tailored prevention efforts might be needed to help reduce the prevalence of TBI among different groups at risk for injury.

This analysis corroborated findings in a 2017 study of TBI-related emergency department visits, hospitalizations, and deaths (*1*) that identified a shift in the leading category of TBI-related deaths in the United States during the last 10 years from unintentional motor vehicle crashes to suicide. That shift was driven by a significant increase in TBI-related suicide deaths as well as an overall decrease in motor vehicle crash deaths during the last decade (*7*). CDC supports suicide prevention efforts by encouraging the use of strategies that reflect the best available evidence, including strengthening access and delivery of suicide care, creating protective environments, teaching coping and problem-solving skills, and identifying and supporting persons at risk (*8*). Firearm injury was the underlying mechanism of injury in nearly all TBI-related suicides among all groups. Reducing access to lethal means among persons at risk for suicide is an important approach to creating protective environments (*8*).

Also consistent with previous research, AI/ANs consistently had the highest age-adjusted rates of TBI-related deaths across the study period, and unintentional motor vehicle crashes contributed the highest number and accounted for the highest rate of these TBI-related deaths in all years (*9*). Lower rates of seat belt use and higher rates of alcohol-related motor vehicle crash deaths among AI/ANs compared with other groups might be contributing factors (*9*). Expansion of evidence-based strategies

**TABLE 2. Estimated average annual number* and age-adjusted rates† per 100,000 population of traumatic brain injury (TBI)–related deaths§ by year, intent, mechanism of injury, and race/ethnicity¶ — United States, 2007–2017****

| 3-year interval/ mechanism of injury | Race/Ethnicity | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | White | | Black | | American Indian/Alaska Native | | Asian/Pacific Islander | | Hispanic | | Other | Total | | |
| | No. | Rate (95% CI) | No. | Rate (95% CI) | No. | Rate (95% CI) | No. | Rate (95% CI) | No. | Rate (95% CI) | No. | No. | Rate (95% CI) | |
| **2000–2002** | | | | | | | | | | | | | | |
| **Total unintentional TBI-related deaths** | **22,908** | **11.0 (10.9–11.1)** | **2,914** | **8.9 (8.7–9.1)** | **414** | **18.5 (17.4–19.6)** | **622** | **6.8 (6.5–7.2)** | **2,940** | **9.3 (9.1–9.6)** | **103** | **29,902** | **10.5 (10.4–10.6)** | |
| Unintentional motor vehicle crashes | 12,416 | 6.3 (6.2–6.4) | 1,919 | 5.4 (5.2–5.5) | 311 | 12.8 (12.0–13.7) | 343 | 3.0 (2.8–3.2) | 2,014 | 5.3 (5.1–5.4) | 52 | **17,055** | **6.0 (5.9–6.0)** | |
| Unintentional falls†† | 6,496 | 2.8 (2.8–2.8) | 477 | 1.8 (1.7–1.9) | 53 | 3.4 (2.8–4.0) | 194 | 2.8 (2.6–3.1) | 484 | 2.5 (2.4–2.7) | 30 | **7,734** | **2.7 (2.7–2.8)** | |
| Unintentionally struck by/ against an object | 304 | 0.1 (0.1–0.2) | 34 | 0.1 (0.1–0.1) | 2§§ | 0.1(0.0–0.2) | 5§§ | 0.0 (0.0–0.1)§§ | 46 | 0.1 (0.1–0.2) | 2§§ | **393** | **0.1 (0.1–0.1)** | |
| Other unintentional injury, mechanism unspecified¶¶ | 3,692 | 1.7 (1.7–1.8) | 484 | 1.6 (1.5–1.7) | 48 | 2.2 (1.8–2.6) | 81 | 0.9 (0.8–1.1) | 396 | 1.4 (1.3–1.5) | 19§§ | **4,719** | **1.7 (1.6–1.7)** | |
| **Total intentional TBI-related deaths** | **14,312** | **6.9 (6.9–7.0)** | **3,258** | **9.0 (8.8–9.1)** | **188** | **7.9 (7.3–8.6)** | **307** | **2.6 (2.4–2.7)** | **1,718** | **4.8 (4.6–4.9)** | **98** | **19,882** | **7.0 (6.9–7.0)** | |
| Suicide | 11,909 | 5.7 (5.7–5.8) | 883 | 2.5 (2.4–2.6) | 102 | 4.4 (3.9–4.9) | 164 | 1.4 (1.2–1.5) | 728 | 2.3 (2.2–2.4) | 46 | **13,833** | **4.8 (4.8–4.9)** | |
| Homicide | 2,403 | 1.2 (1.2–1.2) | 2,375 | 6.4 (6.3–6.6) | 86 | 3.6 (3.1–4.0) | 143 | 1.2 (1.1–1.3) | 990 | 2.5 (2.4–2.6) | 51 | **6,049** | **2.1 (2.1–2.1)** | |
| Other (no intent or mechanism specified)*** | 348 | 0.2 (0.2–0.2) | 96 | 0.3 (0.3–0.3) | 13§§ | 0.6 (0.4–0.8)§§ | 14§§ | 0.1 (0.1–0.2)§§ | 79 | 0.2 (0.2–0.3) | 9§§ | **559** | **0.2 (0.2–0.2)** | |
| **Total** | **37,568** | **18.1 (18.0–18.2)** | **6,269** | **18.2 (17.9–18.4)** | **615** | **27.0 (25.7–28.3)** | **943** | **9.5 (9.1–9.9)** | **4,737** | **14.3 (14.1–14.6)** | **210** | **50,342** | **17.6 (17.6–17.7)** | |
| **2003–2005** | | | | | | | | | | | | | | |
| **Total unintentional TBI-related deaths** | **23,940** | **11.1 (11.0–11.2)** | **3,009** | **9.0 (8.8–9.2)** | **406** | **17.5 (16.4–18.5)** | **709** | **6.9 (6.6–7.2)** | **3,181** | **9.3 (9.0–9.5)** | **81** | **31,326** | **10.6 (10.5–10.7)** | |
| Unintentional motor vehicle crashes | 11,827 | 5.9 (5.9–6.0) | 1,873 | 5.1 (5.0–5.3) | 276 | 10.8 (10.0–11.5) | 349 | 2.8 (2.6–2.9) | 2,146 | 5.1 (5.0–5.2) | 46 | **16,516** | **5.6 (5.6–5.7)** | |
| Unintentional falls†† | 8,325 | 3.4 (3.4–3.5) | 570 | 2.1 (2.0–2.2) | 65 | 3.8 (3.2–4.4) | 272 | 3.3 (3.0–3.5) | 609 | 3.0 (2.8–3.1) | 22 | **9,863** | **3.3 (3.3–3.4)** | |
| Unintentionally struck by/ against an object | 286 | 0.1 (0.1–0.1) | 33 | 0.1 (0.1–0.1) | 5§§ | 0.2(0.1–0.4)§§ | 7 | 0.1 (0.0–0.1)§§ | 50 | 0.1 (0.1–0.2) | 1§§ | **381** | **0.1 (0.1–0.1)** | |
| Other unintentional injury, mechanism unspecified¶¶ | 3,502 | 1.6 (1.6–1.7) | 534 | 1.7 (1.6–1.8) | 61 | 2.7 (2.3–3.1) | 82 | 0.8 (0.7–0.9) | 376 | 1.1 (1.0–1.1) | 13§§ | **4,566** | **1.5 (1.5–1.6)** | |
| **Total intentional TBI-related deaths** | **14,482** | **6.9 (6.8–6.9)** | **3,286** | **8.7 (8.5–8.9)** | **205** | **8.2 (7.6–8.9)** | **302** | **2.2 (2.1–2.4)** | **1,823** | **4.5 (4.3–4.6)** | **69** | **20,168** | **6.8 (6.8–6.9)** | |
| Suicide | 12,305 | 5.8 (5.7–5.8) | 851 | 2.4 (2.3–2.4) | 112 | 4.6 (4.1–5.1) | 168 | 1.3 (1.1–1.4) | 754 | 2.1 (2.0–2.1) | 36 | **14,225** | **4.8 (4.8–4.8)** | |
| Homicide | 2,177 | 1.1 (1.1–1.1) | 2,436 | 6.3 (6.2–6.5) | 93 | 3.6 (3.2–4.1) | 135 | 1.0 (0.9–1.1) | 1,069 | 2.4 (2.3–2.5) | 34 | **5,943** | **2.0 (2.0–2.0)** | |
| Other (no intent or mechanism specified)*** | 382 | 0.2 (0.2–0.2) | 135 | 0.4 (0.3–0.4) | 15§§ | 0.6 (0.5–0.9)§§ | 12 | 0.1 (0.1–0.1)§§ | 95 | 0.2 (0.2–0.3) | 4§§ | **643** | **0.2 (0.2–0.2)** | |
| **Total** | **38,804** | **18.2 (18.1–18.3)** | **6,430** | **18.1 (17.8–18.3)** | **626** | **26.3 (25.1–27.6)** | **1,024** | **9.2 (8.9–9.6)** | **5,098** | **14.0 (13.7–14.2)** | **154** | **52,137** | **17.6 (17.5–17.7)** | |
| **2006–2008** | | | | | | | | | | | | | | |
| **Total unintentional TBI-related deaths** | **24,156** | **10.8 (10.7–10.9)** | **2,829** | **8.1 (7.9–8.2)** | **372** | **15.4 (14.4–16.3)** | **750** | **6.4 (6.2–6.7)** | **3,133** | **8.4 (8.2–8.6)** | **68** | **31,308** | **10.1 (10.1–10.2)** | |
| Unintentional motor vehicle crashes | 10,662 | 5.3 (5.2–5.3) | 1,724 | 4.5 (4.4–4.6) | 243 | 9.2 (8.5–9.9) | 329 | 2.4 (2.3–2.6) | 1,952 | 4.2 (4.1–4.3) | 33 | **14,943** | **4.9 (4.9–5.0)** | |
| Unintentional falls†† | 9,920 | 3.9 (3.9–3.9) | 591 | 2.1 (2.0–2.2) | 74 | 4.0 (3.4–4.5) | 345 | 3.4 (3.2–3.6) | 741 | 3.1 (2.9–3.2) | 23 | **11,694** | **3.7 (3.7–3.8)** | |
| Unintentionally struck by/ against an object | 283 | 0.1 (0.1–0.1) | 33 | 0.1 (0.1–0.1) | 3§§ | 0.1 (0.1–0.2)§§ | 7 | 0.1 (0.0–0.1)§§ | 55 | 0.1 (0.1–0.1) | 0§§ | **381** | **0.1 (0.1–0.1)** | |
| Other unintentional injury, mechanism unspecified¶¶ | 3,291 | 1.5 (1.5–1.5) | 481 | 1.4 (1.3–1.5) | 52 | 2.1 (1.8–2.5) | 70 | 0.6 (0.5–0.7) | 385 | 1.0 (0.9–1.1) | 12§§ | **4,290** | **1.4 (1.4–1.4)** | |
| **Total intentional TBI-related deaths** | **15,125** | **7.0 (7.0–7.1)** | **3,339** | **8.4 (8.3–8.6)** | **189** | **7.3 (6.7–7.9)** | **301** | **2.1 (1.9–2.2)** | **1,844** | **4.2 (4.0–4.3)** | **55** | **20,854** | **6.8 (6.8–6.9)** | |
| Suicide | 12,913 | 5.9 (5.9–6.0) | 876 | 2.3 (2.2–2.4) | 107 | 4.2 (3.7–4.6) | 176 | 1.2 (1.1–1.3) | 795 | 2.0 (1.9–2.1) | 36 | **14,903** | **4.8 (4.8–4.9)** | |
| Homicide | 2,212 | 1.1 (1.1–1.1) | 2,463 | 6.1 (6.0–6.3) | 82 | 3.1 (2.7–3.5) | 125 | 0.9 (0.8–1.0) | 1,049 | 2.2 (2.1–2.2) | 20§§ | **5,950** | **2.0 (1.9–2.0)** | |
| Other (no intent or mechanism specified)*** | 422 | 0.2 (0.2–0.2) | 134 | 0.4 (0.3–0.4) | 18§§ | 0.8 (0.6–1.0)§§ | 20 | 0.1 (0.1–0.2)§§ | 108 | 0.3 (0.2–0.3) | 4§§ | **706** | **0.2 (0.2–0.2)** | |
| **Total** | **39,704** | **18.0 (17.9–18.2)** | **6,301** | **16.9 (16.6–17.1)** | **579** | **23.4 (22.3–24.6)** | **1,071** | **8.7 (8.4–9.0)** | **5,085** | **12.9 (12.6–13.1)** | **128** | **52,867** | **17.2 (17.1–17.3)** | |

See table footnotes on next page.

for reducing the likelihood of injury once a motor vehicle crash has occurred, for example enactment of universal motorcycle helmet laws and enforcement of existing seat belt and child restraint/booster laws, might be beneficial.§

TBI-related homicides disproportionately affected blacks compared with all other groups. CDC's National Center for Injury Prevention and Control has created technical packages that outline the best available evidence-based strategies for preventing violence¶; the strategies are intended to work together and to be used in combination in a multilevel, multisector effort to prevent violence. Implementation might help stop violence before it starts and decrease the rates of TBI-related homicides.

§ https://www.cdc.gov/motorvehiclesafety/index.html.

¶ https://www.cdc.gov/violenceprevention/pub/technical-packages.html.

**TABLE 2. (*Continued*) Estimated Average Annual number* and age-adjusted rates† per 100,000 population of traumatic brain injury (TBI)–related deaths§ by year, intent, mechanism of injury, and race/ethnicity¶ — United States, 2007–2017****

| 3-year interval/ mechanism of injury | Race/Ethnicity | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | White | | Black | | American Indian/Alaska Native | | Asian/Pacific Islander | | Hispanic | | Other | Total | | |
| | No. | Rate (95% CI) | No. | Rate (95% CI) | No. | Rate (95% CI) | No. | Rate (95% CI) | No. | Rate (95% CI) | No. | No. | Rate (95% CI) | |
| **2009–2011** | | | | | | | | | | | | | | |
| **Total unintentional TBI-related deaths** | **22,629** | **9.7 (9.6–9.8)** | **2,444** | **6.7 (6.6–6.9)** | **347** | **14.7 (13.7–15.6)** | **773** | **6.0 (5.7–6.2)** | **2,695** | **7.0 (6.8–7.1)** | **81** | **28,969** | **9.0 (8.9–9.1)** | |
| Unintentional motor vehicle crashes | 8,112 | 4.0 (3.9–4.0) | 1,365 | 3.4 (3.3–3.5) | 202 | 7.6 (7.0–8.2) | 270 | 1.7 (1.6–1.9) | 1,498 | 3.0 (2.9–3.1) | 35 | **11,482** | **3.7 (3.6–3.7)** | |
| Unintentional falls†† | 11,281 | 4.3 (4.2–4.3) | 675 | 2.2 (2.1–2.3) | 87 | 4.7 (4.1–5.3) | 415 | 3.6 (3.4–3.8) | 810 | 3.1 (3.0–3.2) | 32 | **13,301** | **4.0 (4.0–4.0)** | |
| Unintentionally struck by/ against an object | 276 | 0.1 (0.1–0.1) | 31 | 0.1 (0.1–0.1) | 2§§ | 0.1 (0.0–0.2)§§ | 8 | 0.1 (0.0–0.1)§§ | 43 | 0.1 (0.1–0.1) | 0§§ | **360** | **0.1 (0.1–0.1)** | |
| Other unintentional injury, mechanism unspecified¶¶ | 2,960 | 1.3 (1.3–1.4) | 373 | 1.0 (1.0–1.1) | 56 | 2.2 (1.9–2.6) | 80 | 0.6 (0.5–0.6) | 343 | 0.8 (0.8–0.9) | 14§§ | **3,826** | **1.2 (1.2–1.2)** | |
| **Total intentional TBI-related deaths** | **16,465** | **7.6 (7.5–7.7)** | **3,016** | **7.4 (7.3–7.6)** | **216** | **8.3 (7.6–8.9)** | **321** | **2.0 (1.8–2.1)** | **1,768** | **3.7 (3.6–3.8)** | **90** | **21,877** | **6.9 (6.9–7.0)** | |
| Suicide | 14,416 | 6.6 (6.5–6.7) | 908 | 2.3 (2.2–2.4) | 130 | 5.0 (4.5–5.5) | 204 | 1.2 (1.1–1.3) | 867 | 2.0 (1.9–2.0) | 55 | **16,580** | **5.2 (5.1–5.2)** | |
| Homicide | 2,049 | 1.0 (1.0–1.0) | 2,109 | 5.1 (5.0–5.2) | 86 | 3.3 (2.9–3.7) | 117 | 0.7 (0.6–0.8) | 901 | 1.7 (1.6–1.8) | 35 | **5,297** | **1.7 (1.7–1.7)** | |
| Other (no intent or mechanism specified)*** | 448 | 0.2 (0.2–0.2) | 130 | 0.3 (0.3–0.4) | 23 | 0.9 (0.7–1.1) | 16§§ | 0.1 (0.1–0.1)§§ | 103 | 0.2 (0.2–0.3) | 6§§ | **726** | **0.2 (0.2–0.2)** | |
| **Total** | **39,542** | **17.5 (17.4–17.6)** | **5,591** | **14.5 (14.3–14.7)** | **586** | **23.9 (22.7–25.0)** | **1,110** | **8.0 (7.7–8.3)** | **4,566** | **10.9 (10.7–11.1)** | **177** | **51,572** | **16.1 (16.0–16.2)** | |
| **2012–2014** | | | | | | | | | | | | | | |
| **Total unintentional TBI-related deaths** | **23,486** | **9.7 (9.6–9.8)** | **2,530** | **6.6 (6.5–6.8)** | **373** | **15.2 (14.2–16.1)** | **888** | **5.9 (5.7–6.2)** | **2,895** | **7.0 (6.9–7.2)** | **87** | **30,260** | **9.0 (8.9–9.0)** | |
| Unintentional motor vehicle crashes | 7,566 | 3.7 (3.7–3.8) | 1,370 | 3.3 (3.2–3.4) | 212 | 7.8 (7.2–8.4) | 257 | 1.5 (1.4–1.6) | 1,482 | 2.8 (2.7–2.8) | 29 | **10,916** | **3.4 (3.4–3.4)** | |
| Unintentional falls†† | 12,677 | 4.6 (4.5–4.6) | 746 | 2.2 (2.1–2.3) | 104 | 5.1 (4.5–5.7) | 527 | 3.8 (3.6–4.0) | 1,006 | 3.4 (3.2–3.5) | 46 | **15,107** | **4.3 (4.2–4.3)** | |
| Unintentionally struck by/ against an object | 276 | 0.1 (0.1–0.1) | 28 | 0.1 (0.1–0.1) | 4§§ | 0.2 (0.1–0.3)§§ | 10 | 0.1 (0.0–0.1)§§ | 48 | 0.1 (0.1–0.1) | 0§§ | **367** | **0.1 (0.1–0.1)** | |
| Other unintentional injury, mechanism unspecified¶¶ | 2,967 | 1.3 (1.3–1.3) | 386 | 1.0 (0.9–1.1) | 53 | 2.1 (1.8–2.4) | 94 | 0.6 (0.5–0.6) | 359 | 0.8 (0.7–0.8) | 11§§ | **3,870** | **1.2 (1.1–1.2)** | |
| **Total intentional TBI-related deaths** | **17,692** | **8.1 (8.0–8.2)** | **3,100** | **7.4 (7.2–7.5)** | **239** | **9.2 (8.5–9.9)** | **363** | **2.0 (1.8–2.1)** | **1,750** | **3.4 (3.3–3.5)** | **83** | **23,227** | **7.1 (7.1–7.2)** | |
| Suicide | 15,755 | 7.1 (7.1–7.2) | 966 | 2.4 (2.3–2.5) | 155 | 6.0 (5.4–6.5) | 242 | 1.3 (1.2–1.4) | 959 | 1.9 (1.9–2.0) | 60 | **18,138** | **5.5 (5.4–5.5)** | |
| Homicide | 1,937 | 1.0 (0.9–1.0) | 2,134 | 5.0 (4.9–5.1) | 84 | 3.2 (2.8–3.6) | 121 | 0.7 (0.6–0.7) | 791 | 1.4 (1.4–1.5) | 23 | **5,089** | **1.6 (1.6–1.6)** | |
| Other (no intent or mechanism specified)*** | 465 | 0.2 (0.2–0.2) | 123 | 0.3 (0.3–0.3) | 23 | 0.9 (0.7–1.1) | 20 | 0.1 (0.1–0.1) | 112 | 0.2 (0.2–0.3) | 7§§ | **751** | **0.2 (0.2–0.2)** | |
| **Total** | **41,644** | **18.0 (17.9–18.1)** | **5,754** | **14.3 (14.1–14.5)** | **635** | **25.2 (24.0–26.4)** | **1,271** | **8.0 (7.7–8.3)** | **4,757** | **10.6 (10.4–10.8)** | **177** | **54,238** | **16.3 (16.2–16.4)** | |
| **2015–2017** | | | | | | | | | | | | | | |
| **Total unintentional TBI-related deaths** | **24,843** | **9.9 (9.8–10.0)** | **2,919** | **7.3 (7.1–7.4)** | **391** | **15.3 (14.4–16.2)** | **1,018** | **5.7 (5.5–5.9)** | **3,273** | **7.2 (7.0–7.3)** | **102** | **32,547** | **9.2 (9.1–9.2)** | |
| Unintentional motor vehicle crashes | 7,508 | 3.7 (3.6–3.7) | 1,579 | 3.7 (3.6–3.8) | 211 | 7.7 (7.1–8.3) | 279 | 1.4 (1.3–1.5) | 1,627 | 2.8 (2.8–2.9) | 32 | **11,236** | **3.4 (3.4–3.5)** | |
| Unintentional falls†† | 13,977 | 4.8 (4.8–4.9) | 859 | 2.4 (2.3–2.5) | 109 | 4.8 (4.3–5.3) | 626 | 3.7 (3.6–3.9) | 1,203 | 3.4 (3.3–3.6) | 54 | **16,828** | **4.5 (4.4–4.5)** | |
| Unintentionally struck by/ against an object | 257 | 0.1 (0.1–0.1) | 24 | 0.1 (0.0–0.1) | 4§§ | 0.1 (0.1–0.2)§§ | 6 | 0.0 (0.0–0.0)§§ | 47 | 0.1 (0.1–0.1) | 1§§ | **339** | **0.1 (0.1–0.1)** | |
| Other unintentional injury, mechanism unspecified¶¶ | 3,100 | 1.3 (1.3–1.3) | 457 | 1.1 (1.1–1.2) | 67 | 2.6 (2.2–3.0) | 108 | 0.6 (0.5–0.6) | 396 | 0.8 (0.8–0.9) | 16§§ | **4,144** | **1.2 (1.2–1.2)** | |
| **Total intentional TBI-related deaths** | **19,367** | **8.9 (8.8–9.0)** | **3,701** | **8.5 (8.4–8.7)** | **275** | **10.1 (9.4–10.9)** | **445** | **2.2 (2.0–2.3)** | **2,101** | **3.7 (3.6–3.8)** | **75** | **25,965** | **7.8 (7.7–7.8)** | |
| Suicide | 17,236 | 7.8 (7.7–7.9) | 1,187 | 2.8 (2.7–2.9) | 184 | 6.9 (6.3–7.5) | 323 | 1.6 (1.5–1.7) | 1,200 | 2.2 (2.1–2.3) | 55 | **20,186** | **5.9 (5.9–6.0)** | |
| Homicide | 2,131 | 1.1 (1.0–1.1) | 2,514 | 5.7 (5.6–5.9) | 90 | 3.3 (2.9–3.7) | 122 | 0.6 (0.5–0.7) | 901 | 1.5 (1.5–1.6) | 20 | **5,779** | **1.8 (1.8–1.8)** | |
| Other (no intent or mechanism specified)*** | 477 | 0.2 (0.2–0.2) | 137 | 0.3 (0.3–0.4) | 31 | 1.2 (0.9–1.4) | 23 | 0.1 (0.1–0.1) | 118 | 0.2 (0.2–0.2) | 6§§ | **792** | **0.2 (0.2–0.2)** | |

**Abbreviation:** CI = confidence interval.

* Death estimates obtained from CDC's National Vital Statistics System. Visits with missing age were excluded; numbers subject to rounding error.

† Per 100,000 population, age-adjusted to the 2000 U.S. standard population, using 12 age groups: 0–4, 5–9, 10–14, 15–19, 20–24, 25–34, 35–44, 45–54, 55–64, 65–74, 74–84, and ≥85 years.

§ Record-axis condition codes were used (usually included both part I and part II of entity-axis condition codes). https://www.cdc.gov/nchs/data/datalinkage/underlying_and_multiple_causes_of_death557_2011.pdf.

¶ Persons who were white, black, American Indian/Alaska Native, Asian/ Pacific Islander, or Other were non-Hispanic; Hispanics could be of any race.

** Differences in any two rates were considered statistically significant if their CIs were not overlapping.

†† Includes falls of undetermined intent to maintain consistency with past data releases.

§§ Rates based on ≤20 deaths might be unstable and should be interpreted with caution.

¶¶ External cause of injury codes specify that the injury was unintentional but do not specify the actual mechanism of injury.

*** Includes TBIs for which the intent was not determined as well as those caused by legal intervention or war. Includes TBIs in which no mechanism was specified in the record. Does not include falls of undetermined intent.

**Summary**

What is already known about this topic?

Traumatic brain injuries (TBIs) contribute to a substantial number of deaths each year.

What is added by this report?

In 2017, approximately 61,000 TBI-related deaths occurred in the United States. Suicide surpassed motor vehicle crashes as the leading category of TBI-related deaths during 2009–2011 and through 2015–2017. Males and American Indians/Alaska Natives experienced the highest rates of TBI-related death.

What are the implications for public health practice?

Broader implementation of evidence-based prevention strategies for the leading categories of TBI-related death, particularly those aimed at stemming the significant increase in suicide, are warranted. Health care providers can play an important role in assessing patients at increased risk for suicide and providing appropriate interventions.

Falls are the second-leading cause of TBI-related deaths and have been increasing in number and rate, particularly among older adults (*1*). Health care providers can play an important role in in the prevention of older adult falls. CDC's STEADI** (Stopping Elderly Accidents Deaths and Injuries) initiative can help providers address patient fall risk through the identification of modifiable risk factors and implementation of effective interventions (e.g., strength and balance exercises and medication management).

The findings in this report are subject to at least two limitations. First, misclassification of race and Hispanic origin is a common problem on death certificates, especially for AI/AN, Asian/PI, and Hispanic populations (*10*). Therefore, for these groups, mortality estimates are most likely underestimates. Second, incomplete reporting or misclassification of cause of death on death certificates might bias estimates of TBI-related deaths.

Understanding the leading contributors to TBI-related death and identifying groups at increased risk is important in preventing this injury. Health care providers can play an important role in assessing patients at increased risk, such as those at risk for suicide, unintentional motor vehicle crashes, or unintentional falls, and provide referrals or tailored interventions.

** https://www.cdc.gov/steadi/index.html.

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# State-Specific Prevalence of Obesity Among Children Aged 2–4 Years Enrolled in the Special Supplemental Nutrition Program for Women, Infants, and Children — United States, 2010–2016

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Obesity negatively affects children's health because of its associations with cardiovascular disease risk factors, type 2 diabetes, asthma, fatty liver disease, victimization stemming from social stigma and bullying, and poor mental health (e.g., anxiety and depression) (*1*). Children who have overweight or obesity in early childhood are approximately four times as likely to have overweight or obesity in young adulthood as their normal weight peers (*2*). Obesity prevalence is especially high among children from low-income families (*3*). In 2010, the overall upward trend in obesity prevalence turned downward among children aged 2–4 years enrolled in the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC), a program of the U.S. Department of Agriculture (USDA); prevalence decreased significantly in all racial/ethnic groups and in 34 of the 56 WIC state or territory agencies during 2010–2014 (*4*). A more recent study among young children enrolled in WIC reported that the overall obesity prevalence decreased from 15.9% in 2010 to 13.9% in 2016 and statistically significant decreases were observed in all age, sex, and racial/ethnic subgroups (*3*). However, this study did not provide obesity trends at the state level. In collaboration with USDA, CDC used data from the WIC Participant and Program Characteristics (WIC PC) to update state-specific trends through 2016. During 2010–2016, modest but statistically significant decreases in obesity prevalence among children aged 2–4 years enrolled in WIC occurred in 41 (73%) of 56 WIC state or territory agencies. Comprehensive approaches that create positive changes to promote healthy eating and physical activity for young children from all income levels,* strengthen nutrition education and breastfeeding support among young children enrolled in WIC, and encourage redemptions of healthy foods in WIC food packages could help maintain or accelerate these declining trends.

As a federal grant program, WIC is administered by states, territories, and Indian Tribal Organizations to provide supplemental nutritious foods, breastfeeding support, health care referrals, and nutrition education for low-income children aged <5 years and pregnant, postpartum, or breastfeeding women. WIC PC is a biennial census in even years of all participants certified to receive WIC benefits. WIC state and territory agencies extract WIC PC data in April of the reporting year. To be eligible for WIC, participants must live in the states in which they apply, have gross household income ≤185% of the federal poverty guidelines or be eligible for other programs (e.g., Supplemental Nutrition Assistance Program, Medicaid, and Temporary Assistance for Needy Families), and be at nutrition risk.† Children's weight and height are measured by WIC staff members during certification and recertification clinical visits.§

Obesity was defined as a body mass index ≥95th percentile for age and sex on the 2000 CDC growth charts.¶ To estimate relative change in obesity prevalence during 2010–2016, a log binomial regression analysis was performed for each WIC state or territory agency to obtain the prevalence ratio from 2010 to 2016 adjusted for age, sex, and race/ethnicity, using SAS software (version 9.4; SAS Institute). An obesity trend was considered statistically significant if the two-sided p-value was <0.05 in state-level log binomial regression model including all years of data. For absolute change in obesity prevalence, marginal effect was obtained from state-level logistic regression using the Margins package in R software (version 3.6; R Foundation for Statistical Computing) to show the adjusted prevalence difference from 2010 to 2016.

The final analytic sample included 12,403,629 children aged 2–4 years enrolled in the program from WIC agencies in 50 states, the District of Columbia, and five U.S. territories in 2010, 2012, 2014, and 2016. Among approximately 12.6 million original enrollees, a total of 171,272 (1.4%) children whose age, sex, weight, height, or body mass index were missing and 44,578 (0.4%) children whose anthropometric data were biologically implausible were excluded; biologically implausible z scores were defined as height for age <−5.0 or >4.0, weight for age <−5.0 or >8.0, and body mass index for age <−4.0 or >8.0.**

In 2010, crude obesity prevalence ranged from 9.6% (95% confidence interval [CI] = 9.3%–9.8%) in Colorado to 21.5% (95% CI = 21.2%–21.9%) in Virginia (Table). Obesity

* https://www.nap.edu/read/13275/chapter/1.

† https://www.fns.usda.gov/wic/wic-eligibility-requirements.

§ https://wicworks.fns.usda.gov/wicworks/Sharing_Center/PA/Anthro/lib/pdf/Anthropometric_Training_Manual.pdf.

¶ https://www.cdc.gov/growthcharts/cdc_charts.htm.

** https://www.cdc.gov/nccdphp/dnpao/growthcharts/resources/sas.htm.

**TABLE. Prevalence of obesity among children aged 2–4 years enrolled in the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC), by WIC state or territory agency — United States, 2010–2016**

| State | 2010 | | 2016 | | 2016 versus 2010 | |
|---|---|---|---|---|---|---|
| | No. | Crude prevalence % (95% CI) | No. | Crude prevalence % (95% CI) | Adjusted prevalence ratio*(95% CI) | Adjusted prevalence difference† % (95% CI) |
| Alabama§,¶ | 45,743 | 15.8 (15.5 to 16.2) | 42,671 | 16.3 (15.9 to 16.6) | 1.03 (1.00 to 1.06) | 0.5 (0.0 to 1.0) |
| Alaska** | 10,108 | 21.2 (20.4 to 22.0) | 5,983 | 19.8 (18.8 to 20.8) | 0.92 (0.86 to 0.97) | −1.6 (−2.8 to −0.3) |
| Arizona** | 72,933 | 15.0 (14.8 to 15.3) | 58,054 | 12.1 (11.8 to 12.3) | 0.81 (0.79 to 0.84) | −2.7 (−3.1 to −2.4) |
| Arkansas** | 31,245 | 14.8 (14.4 to 15.2) | 23,647 | 13.3 (12.8 to 13.7) | 0.90 (0.87 to 0.94) | −1.4 (−2.0 to −0.8) |
| California** | 583,008 | 18.4 (18.3 to 18.5) | 495,095 | 15.5 (15.4 to 15.6) | 0.86 (0.86 to 0.87) | −2.5 (−2.6 to −2.3) |
| Colorado** | 39,612 | 9.6 (9.3 to 9.8) | 31,307 | 8.1 (7.8 to 8.4) | 0.85 (0.81 to 0.90) | −1.4 (−1.8 to −1.0) |
| Connecticut** | 22,988 | 17.1 (16.6 to 17.6) | 18,748 | 14.4 (13.9 to 14.9) | 0.87 (0.83 to 0.91) | −2.2 (−2.9 to −1.5) |
| Delaware | 7,650 | 18.4 (17.5 to 19.2) | 6,906 | 16.2 (15.3 to 17.0) | 0.93 (0.87 to 1.00) | −1.1 (−2.3 to 0.2) |
| District of Columbia** | 5,182 | 14.4 (13.5 to 15.4) | 5,181 | 11.4 (10.5 to 12.3) | 0.83 (0.75 to 0.91) | −2.4 (−3.7 to −1.1) |
| Florida** | 194,924 | 14.6 (14.4 to 14.7) | 193,749 | 12.7 (12.6 to 12.9) | 0.87 (0.86 to 0.89) | −1.8 (−2.0 to −1.6) |
| Georgia** | 104,959 | 14.4 (14.2 to 14.6) | 78,023 | 12.5 (12.3 to 12.8) | 0.88 (0.86 to 0.90) | −1.8 (−2.1 to −1.4) |
| Hawaii | 14,504 | 9.7 (9.3 to 10.2) | 11,589 | 9.6 (9.1 to 10.1) | 0.98 (0.91 to 1.06) | −0.2 (−0.9 to 0.6) |
| Idaho** | 18,704 | 11.9 (11.5 to 12.4) | 14,521 | 11.3 (10.8 to 11.8) | 0.95 (0.89 to 1.00) | −0.6 (−1.3 to 0.1) |
| Illinois** | 108,762 | 15.7 (15.5 to 15.9) | 79,949 | 14.8 (14.6 to 15.0) | 0.98 (0.96 to 1.00) | −0.3 (−0.6 to 0.1) |
| Indiana** | 63,220 | 15.1 (14.8 to 15.4) | 55,955 | 13.0 (12.7 to 13.2) | 0.91 (0.88 to 0.93) | −1.4 (−1.8 to −1.0) |
| Iowa | 29,481 | 15.6 (15.2 to 16.0) | 24,427 | 15.2 (14.8 to 15.7) | 1.00 (0.96 to 1.04) | 0.0 (−0.6 to 0.6) |
| Kansas** | 30,458 | 13.7 (13.4 to 14.1) | 24,306 | 12.5 (12.1 to 12.9) | 0.91 (0.87 to 0.95) | −1.3 (−1.8 to−0.7) |
| Kentucky** | 45,761 | 18.2 (17.9 to 18.6) | 38,361 | 15.9 (15.6 to 16.3) | 0.88 (0.85 to 0.91) | −2.2 (−2.7 to −1.7) |
| Louisiana** | 48,145 | 13.8 (13.5 to 14.1) | 37,527 | 13.2 (12.9 to 13.6) | 0.94 (0.91 to 0.98) | −0.8 (−1.2 to −0.3) |
| Maine** | 10,410 | 15.2 (14.6 to 15.9) | 8,233 | 13.9 (13.2 to 14.7) | 0.92 (0.85 to 0.98) | −1.3 (−2.3 to −0.2) |
| Maryland** | 51,280 | 17.1 (16.8 to 17.4) | 50,469 | 15.6 (15.3 to 16.0) | 0.92 (0.90 to 0.95) | −1.3 (−1.8 to −0.9) |
| Massachusetts** | 49,178 | 17.1 (16.8 to 17.5) | 41,740 | 16.4 (16.0 to 16.7) | 0.94 (0.91 to 0.96) | −1.0 (−1.5 to −0.6) |
| Michigan** | 85,293 | 14.4 (14.2 to 14.6) | 84,387 | 13.3 (13.1 to 13.5) | 0.95 (0.93 to 0.97) | −0.7 (−1.0 to −0.3) |
| Minnesota** | 57,529 | 12.7 (12.4 to 13.0) | 47,219 | 12.2 (11.9 to 12.5) | 0.95 (0.92 to 0.98) | −0.6 (−1.0 to −0.2) |
| Mississippi** | 36,519 | 14.9 (14.6 to 15.3) | 28,493 | 14.4 (14.0 to 14.8) | 0.96 (0.92 to 0.99) | −0.6 (−1.2 to −0.1) |
| Missouri** | 50,575 | 14.4 (14.1 to 14.8) | 43,404 | 12.3 (12.0 to 12.6) | 0.86 (0.83 to 0.88) | −2.1 (−2.5 to −1.6) |
| Montana | 7,194 | 13.4 (12.6 to 14.2) | 6,647 | 12.1 (11.3 to 12.8) | 0.89 (0.82 to 0.97) | −1.5 (−2.6 to −0.4) |
| Nebraska | 15,622 | 14.4 (13.8 to 14.9) | 13,807 | 15.2 (14.6 to 15.7) | 1.05 (1.00 to 1.11) | 0.8 (0.0 to 1.6) |
| Nevada** | 25,855 | 15.0 (14.6 to 15.5) | 24,493 | 11.6 (11.2 to 12.0) | 0.80 (0.77 to 0.84) | −2.9 (−3.5 to −2.3) |
| New Hampshire | 7,263 | 15.0 (14.1 to 15.8) | 6,042 | 15.8 (14.9 to 16.7) | 1.05 (0.97 to 1.14) | 0.8 (−0.5 to 2.0) |
| New Jersey** | 59,000 | 18.9 (18.6 to 19.2) | 53,917 | 15.0 (14.7 to 15.3) | 0.80 (0.78 to 0.82) | −3.9 (−4.3 to −3.4) |
| New Mexico** | 21,968 | 15.7 (15.2 to 16.1) | 18,619 | 12.1 (11.6 to 12.5) | 0.77 (0.73 to 0.81) | −3.7 (−4.4 to −3.0) |
| New York** | 186,760 | 16.1 (16.0 to 16.3) | 182,401 | 13.7 (13.6 to 13.9) | 0.88 (0.87 to 0.89) | −1.9 (−2.1 to −1.7) |
| North Carolina§,¶ | 89,798 | 13.9 (13.6 to 14.1) | 97,286 | 14.2 (14.0 to 14.5) | 1.04 (1.02 to 1.06) | 0.6 (0.3 to 0.9) |
| North Dakota | 5,484 | 14.5 (13.5 to 15.4) | 4,723 | 14.3 (13.3 to 15.3) | 0.99 (0.90 to 1.09) | −0.1 (−1.4 to 1.3) |
| Ohio | 102,803 | 12.6 (12.4 to 12.8) | 74,753 | 12.4 (12.2 to 12.6) | 0.98 (0.96 to 1.01) | −0.2 (−0.5 to 0.1) |
| Oklahoma** | 37,849 | 15.4 (15.1 to 15.8) | 34,486 | 13.1 (12.8 to 13.5) | 0.85 (0.82 to 0.88) | −2.4 (−2.9 to −1.8) |
| Oregon** | 43,209 | 15.8 (15.5 to 16.2) | 34,485 | 14.7 (14.4 to 15.1) | 0.94 (0.91 to 0.97) | −1.0 (−1.5 to −0.5) |
| Pennsylvania** | 96,762 | 12.8 (12.6 to 13.1) | 80,202 | 12.2 (12.0 to 12.4) | 0.96 (0.94 to 0.98) | −0.5 (−0.8 to −0.2) |
| Rhode Island** | 10,783 | 16.4 (15.7 to 17.1) | 6,984 | 15.4 (14.5 to 16.2) | 0.93 (0.86 to 0.99) | −1.2 (−2.3 to −0.1) |
| South Carolina** | 39,785 | 13.3 (13.0 to 13.7) | 32,399 | 11.4 (11.1 to 11.8) | 0.89 (0.85 to 0.92) | −1.5 (−2.0 to −1.0) |
| South Dakota | 7,884 | 17.3 (16.5 to 18.1) | 6,771 | 17.1 (16.2 to 18.0) | 0.95 (0.88 to 1.02) | −0.8 (−2.1 to 0.4) |
| Tennessee** | 57,153 | 16.0 (15.7 to 16.3) | 51,157 | 14.6 (14.3 to 14.9) | 0.92 (0.89 to 0.94) | −1.3 (−1.8 to −0.9) |
| Texas** | 361,823 | 16.9 (16.8 to 17.0) | 268,787 | 14.6 (14.4 to 14.7) | 0.89 (0.88 to 0.90) | −1.9 (−2.0 to −1.7) |
| Utah** | 26,045 | 12.5 (12.1 to 12.9) | 21,599 | 7.9 (7.6 to 8.3) | 0.64 (0.60 to 0.67) | −4.6 (−5.1 to −4.0) |
| Vermont | 6,964 | 13.8 (13.0 to 14.7) | 5,254 | 14.5 (13.5 to 15.4) | 1.04 (0.95 to 1.13) | 0.6 (−0.7 to 1.8) |
| Virginia¶,** | 48,920 | 21.5 (21.2 to 21.9) | 47,376 | 15.3 (14.9 to 15.6) | 0.73 (0.71 to 0.75) | −5.8 (−6.3 to −5.3) |
| Washington** | 78,336 | 14.9 (14.6 to 15.1) | 69,870 | 13.3 (13.0 to 13.5) | 0.89 (0.87 to 0.91) | −1.6 (−2.0 to −1.3) |
| West Virginia§,¶ | 17,669 | 14.4 (13.9 to 14.9) | 14,222 | 16.6 (16.0 to 17.2) | 1.15 (1.09 to 1.21) | 2.2 (1.4 to 3.0) |
| Wisconsin** | 48,511 | 15.2 (14.9 to 15.5) | 37,116 | 14.3 (14.0 to 14.7) | 0.94 (0.91 to 0.97) | −0.9 (−1.4 to −0.4) |
| Wyoming** | 4,413 | 11.8 (10.9 to 12.8) | 3,458 | 9.1 (8.1 to 10.1) | 0.76 (0.67 to 0.87) | −2.8 (−4.2 to −1.5) |
| **Territory** | | | | | | |
| American Samoa | 3,221 | 14.6 (13.4 to 15.8) | 2,824 | 13.7 (12.4 to 15.0) | 0.94 (0.83 to 1.06) | −0.9 (−2.7 to 0.9) |
| Guam** | 3,248 | 11.4 (10.3 to 12.5) | 2,710 | 8.3 (7.3 to 9.4) | 0.73 (0.62 to 0.85) | −3.1 (−4.6 to −1.6) |
| Northern Mariana Islands** | 2,157 | 14.1 (12.6 to 15.6) | 1,418 | 7.8 (6.4 to 9.2) | 0.55 (0.45 to 0.68) | −6.4 (−8.4 to −4.4) |
| Puerto Rico** | 70,699 | 20.3 (20.0 to 20.6) | 63,251 | 12.0 (11.8 to 12.3) | 0.60 (0.58 to 0.61) | −8.2 (−8.6 to −7.8) |
| U.S. Virgin Islands | 2,093 | 12.4 (11.0 to 13.8) | 1,593 | 13.1 (11.5 to 14.8) | 1.07 (0.90 to 1.26) | 0.8 (−1.4 to 3.0) |

**Abbreviation:** CI = confidence interval.

* Obtained from log binomial regression model adjusted for age in month, sex, and race/ethnicity.

† Calculated as 100 times the average marginal effect of year (2010 versus 2016) from logistic regression controlling for age, sex, and race. A negative value indicates that the prevalence decreased.

§ Statistically significant increase in obesity prevalence during 2010–2016 determined by trend test using log binomial regression model adjusted for age, sex, and race/ethnicity with all years of data included.

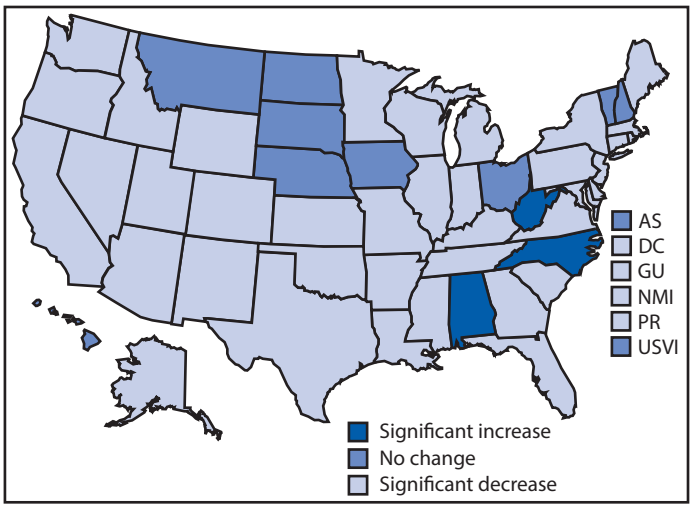
¶ Change in the data reporting system in 2016 might affect obesity prevalence.

** Statistically significant decrease in obesity prevalence during 2010–2016 determined by trend test using log binomial regression model adjusted for age, sex, and race/ethnicity with all years of data included.

prevalence was ≥20% among children aged 2–4 years in three state or territory agencies (Alaska, Puerto Rico, and Virginia) and was <10% in only two WIC state agencies (Colorado and Hawaii). In 2016, crude obesity prevalences ranged from 7.8% (95% CI = 6.4%–9.2%) in the Northern Mariana Islands to 19.8% (95% CI = 18.8%–19.8%) in Alaska. Crude obesity prevalence among children aged 2–4 years was <20% in any state or territory and was <10% in six WIC state or territory agencies (Colorado, Guam, Hawaii, Northern Mariana Islands, Utah, and Wyoming).

During 2010–2016, statistically significant decreases in obesity prevalence occurred in 41 of 56 WIC state or territory agencies ($p<0.05$ for trend test) across all years (Table) (Figure). Adjusted obesity prevalences decreased by >3 percentage points in seven WIC state or territory agencies (Guam, New Jersey, New Mexico, Northern Mariana Islands, Puerto Rico, Utah, and Virginia); the largest significant decrease was in Puerto Rico, where adjusted obesity prevalence among WIC beneficiaries aged 2–4 years decreased by 8.2 percentage points from 2010 to 2016. Only three WIC state agencies reported significant increases in obesity prevalence across all years; adjusted obesity prevalence increased by 0.5 percentage points in Alabama, 0.6 percentage points in North Carolina, and 2.2 percentage points in West Virginia (Table).

**FIGURE. Changes* in obesity prevalence among children aged 2–4 years enrolled in the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC), by WIC state or territory agency — United States, 2010–2016**




**Abbreviations:** AS = American Samoa; DC = District of Columbia; GU = Guam; NMI = Northern Mariana Islands; PR = Puerto Rico; USVI = U.S. Virgin Islands.
* Statistically significant changes were determined by trend tests using log binomial regression models adjusted for age, sex, and race/ethnicity with all years of data included.

## Discussion

These findings indicate statistically significant decreases in obesity prevalence during 2010–2016 among children aged 2–4 years enrolled in WIC in 41 (73%) of 56 WIC state or territory agencies. A previous study using these data reported that children aged 2–4 years in 34 (61%) of 56 WIC state or territory agencies experienced decreases in obesity prevalence during 2010–2014 (*4*). The present study found that obesity prevalence among children in this age group continued to decrease through 2016 in 33 of the 34 WIC state or territory agencies, with previous significant decreases and identified decreases during 2010–2016 in eight additional WIC agencies having no significant changes during 2010–2014. Although decreases in obesity prevalence in the present study were small, the trends in obesity prevalence among young WIC beneficiaries overall (*3*) and in the majority of states and territories were in contrast to the national trend, which was that obesity prevalence decreased for children aged 2–5 years from all income levels from 10.1% in 2007–2008 to 8.4% in 2011–2012 and then increased to 13.9% in 2015–2016 (*5*). Thus, even these small decreases indicate progress for this vulnerable WIC population.

The WIC program reaches low-income infants and children during the critical period of child growth. One factor that might have contributed to the observed decreases in obesity prevalence in WIC enrollees is the 2009 revisions to the WIC food packages (*6*), which was carried out to better align with nutrition research, the 2005 Dietary Guidelines for Americans (*7*), and the infant food and feeding practice guidelines of the American Academy of Pediatrics.[††] The revised food packages include a broader range of healthy food options; promote fruit, vegetable, and whole wheat product purchases; support breastfeeding; and give WIC state and territory agencies more flexibility to accommodate cultural food preferences (*6*). The WIC package revisions had plausible impact on improving diet quality measured by the Healthy Eating Index–2010 scores among WIC children aged 2–4 years (*8*). In addition, the availability of healthier foods and beverages in authorized WIC stores has increased. Children enrolled in WIC consumed more fruits, vegetables, and whole grain products and less juice, white bread, and whole milk after the revisions (*9*) than they did before.

Additional contributors to these decreases in obesity prevalence might include other local, state, and national efforts and programs that affect changes in systems outside of WIC to improve diet quality and physical activity for young children from all income levels, including children enrolled in WIC. For example, CDC distributes funding on a competitive basis to state and local grantees to enable implementation of

[††] https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/HALF-Implementation-Guide/Age-Specific-Content/Pages/Infant-Food-and-Feeding.aspx/.

**Summary**

What is already known about this topic?

Among children aged 2–4 years enrolled in the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC), obesity prevalence decreased from 15.9% in 2010 to 13.9% in 2016 and during 2010–2014, decreased in 34 of the 56 WIC state or territory agencies.

What is added by this report?

During 2010–2016, statistically significant decreases in obesity prevalence among WIC beneficiaries aged 2–4 years occurred in 41 of 56 WIC state or territory agencies; obesity prevalence ranged from 7.8% to 19.8%.

What are the implications for public health practice?

To accelerate these trends, expanded positive changes in multiple settings to promote healthy eating and physical activity for young children are needed.

childhood obesity prevention strategies through increasing involvement of health care providers, community leaders, and early care and education providers (*10*). Many of the funding recipients focus on both population-level strategies such as state-level standards that can potentially benefit all children and more directed interventions for populations at the highest risk (*10*). In addition, CDC provides technical support for states to promote maternity care policies and practices to support breastfeeding in birthing facilities and workplaces.[§§] CDC also provides support for states and communities to implement nutrition, breastfeeding support, physical activity, and screen time standards in early care and education systems and setting.[¶¶]

The findings in this report are subject to at least four limitations. First, approximately 15% fewer children were enrolled in WIC in 2016, compared with 2010 (*3*), and characteristics of those enrolled in WIC might have changed over time. Although the trend analyses adjusted for age, sex, and race/ethnicity, other unmeasured factors might have contributed to the declining trends in obesity. Second, the findings might not apply to all low-income children because children enrolled in WIC might be systematically different from others who are eligible but not enrolled. Third, the study findings cannot be applied to U.S. children from families with other income levels. Finally, certain states changed their data reporting systems in recent years, which might have affected obesity trends. Strengths of this study include the use of a large sample of children enrolled in WIC as derived from census data, allowing for stratification by state or territory and the use of measured weight and height data.

[§§] https://www.cdc.gov/nccdphp/dnpao/state-local-programs/breastfeeding.html.
[¶¶] https://www.cdc.gov/obesity/strategies/childcareece.html.

Despite these recent decreases in obesity among children enrolled in WIC, obesity prevalence remained high in most states in 2016. Multiple approaches are needed to address and eliminate childhood obesity. The National Academy of Medicine and other groups have recommended a comprehensive and integrated approach that calls for positive changes in physical activity and food and beverage environments in multiple settings including home, early care and education (e.g., nutrition standards for food served), and community (e.g., neighborhood designs that encourage walking and biking) to promote healthy eating and physical activity for young children. Further implementation of these positive changes across the United States could further the decreases in childhood obesity.

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

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# Guidance for Using Tafenoquine for Prevention and Antirelapse Therapy for Malaria — United States, 2019

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An estimated 219 million cases of malaria occurred worldwide in 2017, causing approximately 435,000 deaths (*1*). Malaria is caused by intraerythrocytic protozoa of the genus *Plasmodium* transmitted to humans through the bite of an infective *Anopheles* mosquito. Five *Plasmodium* species that regularly cause illness in humans are *P. falciparum*, *P. vivax, P. ovale*, *P. malariae,* and *P. knowlesi* (*2*). The parasite first develops in the liver before infecting red blood cells. Travelers to areas with endemic malaria can prevent malaria by taking chemoprophylaxis. However, most antimalarials do not kill the liver stages of the parasite, including hypnozoites that cause relapses of disease caused by *P. vivax* or *P. ovale*. Therefore, patients with these relapsing species must be treated with two medications: one for the acute infection, and another to treat the hypnozoites (antirelapse therapy). Until recently, primaquine was the only drug available worldwide to kill hypnozoites. Tafenoquine, a long-acting 8-aminoquinoline drug related to primaquine, was approved by the Food and Drug Administration (FDA) on July 20, 2018, for antirelapse therapy (Krintafel) and August 8, 2018, for chemoprophylaxis (Arakoda) (*3*,*4*). This report reviews evidence for the efficacy and safety of tafenoquine and provides CDC guidance for clinicians who prescribe chemoprophylaxis for travelers to areas with endemic malaria and treat malaria.

## Background

In 2016, a total of 2,078 imported malaria cases were reported in the United States; of the 1,853 (89.2%) cases with known species, 76.6% were caused by *P. falciparum*, 18.8% by *P. vivax* or *P. ovale,* and 4.5% by *P. malariae* or mixed infections (*5*). Plasmodium first develops in the liver before emerging up to 1 month later to infect red blood cells. Almost all antimalarials target only the blood stage of the parasite. Therefore, most chemoprophylaxis drugs are taken for 1 month after leaving the malaria area to allow the parasite to reach the targeted blood stage. However, *P. vivax* and *P. ovale* develop hypnozoites, a dormant stage of the parasite in the liver that can emerge months later to cause disease relapses. Treatment of these species requires antirelapse therapy (also known as radical treatment or radical cure). For travelers with intense or prolonged exposure to relapsing species of malaria, presumptive antirelapse therapy (PART) is recommended to kill hypnozoites (*6*). Until recently, only primaquine was used for this indication.

Tafenoquine, an 8-aminoquinoline drug related to primaquine, is only the second drug of its class to receive FDA approval. Tafenoquine kills both the liver and blood stages of the parasite, broadening its applicability for chemoprophylaxis to all species of malaria. FDA approved tafenoquine for prophylaxis of malaria in adults aged ≥18 years (Arakoda, 100 mg tablets) in August 2018 and antirelapse therapy of *P. vivax* malaria in persons aged ≥16 years (Krintafel, 150 mg tablets) in July 2018 (*7*,*8*). Like primaquine, tafenoquine can cause severe hemolysis in persons with glucose-6-phosphate dehydrogenase (G6PD) deficiency and quantitative G6PD testing is required before prescribing. Tafenoquine use is contraindicated in persons with G6PD deficiency (*9*).

This report summarizes the published efficacy and safety evidence for the recommended doses for both indications and provides guidance for the use of tafenoquine in the United States. A more comprehensive review of the literature on tafenoquine along with the biologic rationale for its use has been published elsewhere (*10*).

## Methods

CDC conducted a search of English-language articles available in PubMed, Ovid Medline, Scopus, and Global Health (CABDirect) on January 17, 2019, using keywords "tafenoquine or WR238605" and "prevent, prevention, prophylaxis, treatment, radical, or cure." A total of 269 articles were collated and underwent title, abstract, and full text reviews by two physicians: an infectious disease specialist and a malaria subject matter expert. The references from review articles and meta-analyses, and the FDA labeling for both Krintafel and Arakoda were also reviewed to identify any additional studies. Randomized, double-blind, controlled trials performed in human subjects using the labeled recommended dosing regimens were preferentially included in the final review. Data on dosing regimen, outcome, and adverse events were abstracted. Based on the results of the review, CDC subject matter experts developed guidance for the use of tafenoquine.

## Rationale and Evidence

A total of 269 articles were identified. After excluding 232 during title review and 29 during abstract review, the eight remaining articles were reviewed fully and included in the analysis: five articles related to prophylaxis (*11*–*15*) and

three to antirelapse (*16*–*18*); among these eight articles, seven included additional information for safety (*11*–*13*,*15*–*18*). All five studies cited by the FDA label were captured. An additional four peer-reviewed articles addressing the in vivo activity of hypnozoites of *P. ovale* and use of primaquine for *P. ovale* were reviewed (*6*,*19*–*21*); however, because they did not assess tafenoquine use, they were not included in the tafenoquine review.

**Prophylaxis.** Three of the five articles included were randomized controlled trials (RCTs), one was a reanalysis of data from an RCT, and one was a randomized human challenge study (*11*–*15*) (Table 1). Two RCTs compared tafenoquine (200 mg for 3 days, then weekly thereafter for up to 6 months) to placebo; both found a protective efficacy of 86% (95% confidence intervals [CIs] = 73–93 and 76–92) (*11*,*12*). Although not powered to detect statistical differences in efficacy, one of these RCTs described the efficacy between tafenoquine (protective efficacy = 86%, 95% CI = 76–92) and mefloquine (protective efficacy = 86%, 95% CI = 72–93) (*12*). The third RCT compared tafenoquine to mefloquine and observed no cases of malaria in either arm (*13*). The data from this study were reanalyzed in a separate study, using an estimation of attack rate, and found protective efficacy to be 100% (95% CI = 93–100) (*14*). These studies suggest comparable efficacy between tafenoquine and mefloquine, the current standard of care. Finally, the randomized human challenge study demonstrated 100% efficacy (95% CI = 40–100) of tafenoquine against the blood stage of *P. falciparum* in healthy volunteers compared with placebo (*15*).

**Antirelapse therapy.** One phase 2b randomized dose-selection trial and two phase 3 RCTs examined the efficacy of tafenoquine in the prevention of relapse in patients with confirmed *P. vivax* malaria at the labeled recommended regimen (Table 1) (*16*–*18*). Among these studies, tafenoquine was found to prevent relapse in 62%–89% of cases with a single 300 mg dose. In the large phase 2 dose-response study, efficacy of 300 mg and 600 mg were similar, and significantly higher than that of chloroquine alone (300 mg dose: 89.2%, 95% CI = 77–95, log-rank test p-value <0.001; 600 mg dose: 91.9%, 95% CI = 80–97, p<0.001; chloroquine: 36.5%, 95% CI = 23–52) (*16*).

***P. ovale* efficacy.** Tafenoquine is not labeled for use in *P. ovale*. Because *P. ovale* is relatively rare, accounting for fewer than 5% of malaria cases globally (*19*), it was not evaluated in the tafenoquine studies. Based on the biologic similarity of the hypnozoites of ovale and vivax, a CDC expert committee previously recommended the use of primaquine off-label for antirelapse therapy of *P. ovale* (*6*). With similar in vivo response of *P. ovale* to primaquine to that of *P. vivax* (*20*,*21*), CDC subject matter experts are extrapolating the use of tafenoquine to *P. ovale*.

**Safety.** Seven of the eight reviewed studies provided safety outcomes; four reported safety outcomes at the prophylaxis dose and three at the antirelapse therapy dose (Table 2) (*11*–*13*,*15*–*18*). Common adverse events included abdominal pain, constipation, diarrhea, vertigo, dizziness, sleep disturbances, and headache. Two studies described a nonsignificant increase in methemoglobin (*11*,*13*). Another reported asymptomatic decreases in hemoglobin, which resolved without intervention (*18*). One study described vortex keratopathy (a condition characterized by changes in the corneal epithelium resulting in a whorl pattern) in approximately 90% of patients receiving tafenoquine prophylaxis; the condition did not affect visual acuity and resolved within 1 year following drug discontinuation (*13*). Of note, persons with G6PD deficiency were excluded because 8-aminoquinolines can cause hemolytic anemia in these persons.

## Recommendations

Tafenoquine is an additional FDA-approved antimalarial option for malaria prophylaxis in adults aged ≥18 years, and for antirelapse therapy in persons aged ≥16 years (Box).

**Dosage and indication.** In adults traveling to areas with malaria, tafenoquine (Arakoda, 100 mg tablets) can be used for chemoprophylaxis for all species of malaria. The prophylactic dose is 200 mg daily for the 3 days preceding the trip, 200 mg weekly during the trip, and a single 200 mg dose during the week after returning. In persons aged ≥16 years, tafenoquine (Krintafel, 150 mg tablets) can be used for presumptive antirelapse therapy or PART for *P. vivax* and off-label for *P. ovale*. The single 300 mg antirelapse or PART dose should ideally overlap with blood-stage treatment or the last dose of prophylaxis. If this is not feasible, tafenoquine may be taken as soon as possible afterwards. PART is not necessary if primaquine or tafenoquine is taken for primary prophylaxis. Tafenoquine should be administered with food.

**Contraindications and warnings.** Like primaquine, tafenoquine is contraindicated in persons with G6PD deficiency because it might cause hemolytic anemia. If G6PD status is unknown, quantitative G6PD testing must be performed to confirm normal activity before administration of tafenoquine. Qualitative G6PD testing might miss persons with intermediate deficiency and is inadequate to guide tafenoquine administration. Tafenoquine is contraindicated in pregnancy because of the unknown G6PD status of the fetus and should not be used in breastfeeding women if the infant has G6PD deficiency or if the infant's G6PD status is unknown. Because psychiatric adverse reactions were observed in persons with a previous history of psychiatric conditions, tafenoquine should not be used in these

**TABLE 1. Findings from seven blinded, randomized trials of tafenoquine for prophylaxis and antirelapse treatment of malaria at recommended doses**

| Indication | Year published | Country (*Plasmodium* species) | Study population characteristics | Study length | Drug regimen | Sample size | Treatment | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Outcome | % with outcome (95% CI) |
| Prophylaxis | 2001* | Kenya (*P. falciparum* primarily) | Semi-immune | 13 wks intervention, follow-up | TQ 200 mg x 3 days, then weekly | 53 | Protective efficacy | 86 (73–93) |
| | | | | | Placebo | 59 | | Reference |
| | 2003† | Ghana (*P. falciparum* primarily) | Semi-immune | 12 wks intervention, 4 wks additional follow-up (double-blind) | TQ 200 mg x 3 days, then weekly | 91 | Protective efficacy | 86 (76–92)§ |
| | | | | | MQ 250 mg/wk | 46 | | 86 (72–93)§ |
| | | | | | Placebo | 94 | | Reference |
| | 2010¶ | Timor-Leste (*P. falciparum* and *P. vivax*) | Nonimmune | 6 mos intervention, follow-up 20 weeks | TQ 200 mg x 3 days, then weekly | 492 | No. of cases (protective efficacy)** | During intervention: 0 cases; During follow-up: 4 cases [100% (93–100)]†† |
| | | | | | MQ 250 mg/wk | 162 | | During intervention: 0; during follow-up: 1 case [100% (79–100)] |
| | 2018§§ | Australia (*P. falciparum* challenge) | Healthy, nonimmune | 34 days | TQ 200 mg x 3 days, and 200 mg on day 10 | 12 | Rescue treatment needed | 0 (0–27)¶¶ |
| | | | | | Placebo | 4 | | 100 (40–100) |
| Antirelapse therapy | 2014*** | Peru, India, Thailand, Brazil | ≥16 yrs; microscopically confirmed *P. vivax* monoinfection | 180 days from chloroquine initiation | CQ x 3 days + TQ 300 mg x 1 | 57 | Relapse-free efficacy (ITT population) | 89 (77–95)††† |
| | | | | | CQ x 3 days + PQ 15 mg x 14 days | 50 | | 77 (63–87)††† |
| | | | | | CQ x 3 days only | 54 | | 38 (23–52) |
| | 2019§§§ | Peru, Brazil, Colombia, Vietnam, Thailand | ≥16 yrs; Hospitalized with microscopically confirmed *P. vivax* infection | 180 days | CQ x 3 days + TQ 300 mg x 1 | 166 | Recurrence-free efficacy (ITT population) | 73 (65–79) |
| | | | | | CQ x 3 days + PQ 15 mg/day x 14 days | 85 | | 75 (64–83) |
| | 2019¶¶¶ | Peru, Brazil, Ethiopia, Cambodia, Thailand, Philippines | ≥16 yrs (≥18 in Ethiopia); microscopically confirmed *P. vivax* infection | 180 days | CQ x 3 days + TQ 300 mg x 1 | 260 | Recurrence-free efficacy (ITT population) | 62 (55–69)**** |
| | | | | | CQ x 3 days + PQ 15 mg/day x 14 days | 133 | | 70 (60–77) |
| | | | | | Placebo | 129 | | 28 (20–36) |

**Abbreviations:** CI = confidence interval; CQ = chloroquine; ITT = intention to treat; MQ = mefloquine; PQ = primaquine; TQ = tafenoquine.

* Shanks GD, Oloo AJ, Aleman GM, et al. A new primaquine analog, tafenoquine (WR 238605), for prophylaxis against *Plasmodium falciparum* malaria. Clin Infect Dis 2001;33:968–74.

† Hale BR, Owusu-Agyei S, Fryauff DJ, et al. A randomized, double-blind, placebo-controlled, dose-ranging trial of tafenoquine for weekly prophylaxis against *Plasmodium falciparum*. Clin Infect Dis 2003;36:541–9.

§ Chi squared test (p<0.05).

¶ Nasveld PE, Edstein MD, Reid M, et al. Randomized, double-blind study of the safety, tolerability, and efficacy of tafenoquine versus mefloquine for malaria prophylaxis in nonimmune subjects. Antimicrob Agents Chemother 2010;54:792–8.

** Dow GS, McCarthy WF, Reid M, Smith B, Tang D, Shanks GD. A retrospective analysis of the protective efficacy of tafenoquine and mefloquine as prophylactic anti-malarials in non-immune individuals during deployment to an area with endemic malaria area. Malar J 2014;13:49.

†† Fisher exact TQ versus MQ p = 1.0.

§§ McCarthy JS, Smith B, Reid M, et al. Blood schizonticidal activity and safety of tafenoquine when administered as chemoprophylaxis to healthy, non-immune participants followed by blood stage *Plasmodium falciparum* challenge: a randomized, double-blinded, placebo-controlled Phase 1b study. Clin Infect Dis 2019;69:480–6.

¶¶ Fisher exact p<0.005.

*** Llanos-Cuentas A, Lacerda MV, Rueangweerayut R, et al. Tafenoquine plus chloroquine for the treatment and relapse prevention of *Plasmodium vivax* malaria (DETECTIVE Phase IIb): a multicentre, double-blind, randomized, phase 2b dose-selection study. Lancet 2014;383:1049–58.

††† Log-rank TQ versus placebo p<0.0001; PQ versus placebo p = 0.0004.

§§§ Llanos-Cuentas A, Lacerda MVG, Hien TT, et al. Tafenoquine versus primaquine to prevent relapse of *Plasmodium vivax* malaria (GATHER). N Engl J Med 2019;380:229–41.

¶¶¶ Lacerda MVG, Llanos-Cuentas A, Krudsood S, et al. Single-dose tafenoquine to prevent relapse of *Plasmodium vivax* malaria (DETECTIVE Phase III). N Engl J Med 2019;380:215–28.

**** TQ hazard ratio (HR) 0.3; PQ HR 0.26, p<0.001.

persons (*3*,*4*), and other antimalarials could be considered for prophylaxis, or primaquine can be considered as an alternative for antirelapse therapy. Tafenoquine is contraindicated in persons with known hypersensitivity to 8-aminoquinolines.

**Adverse events and reporting.** Adverse events might be delayed in onset or duration because of tafenoquine's long half-life. Common adverse reactions include dizziness, nausea, vomiting, and headache. When used for prophylaxis, elevated liver enzyme levels, insomnia, depression, abnormal dreams, and anxiety were also observed. Suspected adverse reactions can be reported to FDA via MedWatch at https://www.fda.gov/safety/medwatch.

## Discussion

This guidance regarding use of tafenoquine for both prophylaxis of all species of malaria and antirelapse therapy for *P. vivax* is consistent with FDA labeling. Recommendations for PART and antirelapse therapy of *P. ovale* are off-label. It is not feasible to conduct adequately powered clinical trials for *P. ovale* malaria because of its relatively low incidence. Therefore, evidence for efficacy against *P. vivax* was extrapolated to *P. ovale*.

For persons with contraindications to tafenoquine, other antimalarial options for malaria chemoprophylaxis and radical cure can be considered. There are several other options for chemoprophylaxis, each with its own contraindications and

**TABLE 2. Summary of key adverse events observed in persons receiving tafenoquine at recommended doses versus placebo or mefloquine**

| Year published | Study length | Drug regimen | Sample Size | Adverse event type reported, no. (%) | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Gastrointestinal | Dermatologic | Neurologic | Ophthalmologic | Cardiac | Hematologic |
| **Prophylaxis dose** | | | | | | | | | |
| 2001* | 13 weeks intervention, follow up 4 wks | TQ 200 mg x 3 days, then weekly | 55 | Gastrointestinal 16 (29)<br>-Abdominal pain 2 (4)<br>-Constipation 4 (7)<br>-Diarrhea 4 (7<br>-Gastritis 2(4)<br>-Gastroenteritis 3(6) | Any dermatologic 12 (22)<br>-Skin disorder 6 (11)<br>-Rash 2 (4) | Neurologic 14 (26)<br>-Headache 13 (24) | — | — | Methemoglobinemia, mean plateau concentrations 2.5%±1.6% |
| | | TQ 200 mg x 3 days | 60 | Gastrointestinal 20 (33)<br>-Abdominal pain 1 (2)<br>-Constipation 7 (12)<br>-Diarrhea 4 (7)<br>-Gastritis 4 (7)<br>-Gastroenteritis 7 (12) | Any dermatologic 12 (20)<br>-Skin disorder 5 (8)<br>-Rash 1 (2) | Neurologic 11 (18)<br>-Headache 10 (17) | — | — | — |
| | | Placebo | 61 | Gastrointestinal 17 (28)<br>-Abdominal pain 2 (3)<br>-Constipation 3 (5)<br>-Diarrhea 2 (3)<br>-Gastritis 4 (7)<br>-Gastroenteritis 5 (8) | Any dermatologic 6 (8)<br>-Skin disorder 4 (7)<br>-Rash 1 (2) | Neurologic 11 (18)<br>-Headache 11 (18) | — | — | — |
| 2003† | 12 weeks intervention, 4 wks additional follow-up | TQ 200 mg x 3 days, then weekly | 91 | Elevated ALT 6 (6)§<br>Gastritis 5 (5) | — | — | — | — | — |
| | | MQ 250 mg/ week | 46 | Elevated ALT 0<br>Gastritis 1 (3) | — | — | — | — | — |
| | | Placebo | 94 | Elevated ALT 2 (2)<br>Gastritis 2 (2) | — | — | — | — | — |
| 2010¶ | 6 mos intervention, follow-up 20 wks | TQ 200 mg x 3 days, then weekly | 492 | Severe gastrointestinal 8 (1) ** | — | Neuropsychiatric 64 (13)†† | Vortex keratopathy 69/74 (93) §§ | — | Methemoglobinemia, mean increase 1.8% |
| | | MQ 250 mg/ week | 162 | Severe gastrointestinal 0 (0) | — | Neuropsychiatric 23 (14) | Vortex keratopathy 0 (0) | — | Methemoglobinemia, mean increase 0.1% |
| 2018¶¶ | 34 days after initiation of TQ (challenge study) | TQ 200mg x 3 days and then 200 mg on day 10 | 12 | Abdominal discomfort 1 (8)<br>Abdominal pain 1 (8)<br>Diarrhea 0 (0)<br>Dry mouth 1 (8)<br>Nausea 1 (8)<br>Vomiting 1 (8) | — | Headache 4 (33)<br>Hypoesthesia 0 (0)<br>Lethargy 0 (0) | — | — | Hemoglobin decreased 2 (17) |
| | | Placebo | 4 | Abdominal discomfort 1 (25)<br>Abdominal pain 0 (0)<br>Diarrhea 1 (25)<br>Dry mouth 0 (0)<br>Nausea 3 (75)<br>Vomiting 2 (50) | — | Headache 4 (100)<br>Hypoesthesia 1 (25)<br>Lethargy 1 (25) | — | — | Hemoglobin decreased 0 (0) |

See table footnotes on next page.

warnings, which can be used depending on the patient and drug-resistance in the areas of travel. These include atovaquone-proguanil, chloroquine, doxycycline, and mefloquine. For antirelapse therapy, the only alternative is primaquine. For nonpregnant persons with borderline or intermediate G6PD deficiency requiring antirelapse treatment, an alternative dosing regimen of primaquine could be considered at 45 mg (base) once weekly for 8 weeks, with close monitoring and consultation with an infectious disease expert. Persons with severe G6PD deficiency will require antimalarials at prophylaxis doses for 1 year instead of an 8-aminoquinoline (i.e., primaquine or tafenoquine). Pregnant women with normal G6PD levels, requiring antirelapse therapy could be given chloroquine at chemoprophylaxis doses (500 mg salt once weekly) until after delivery, and then an 8-aminoquinoline, depending on whether the woman is breastfeeding and the G6PD status of the infant.

The approval of tafenoquine marks a notable advancement for the prevention of malaria and treatment of *P. vivax* and *P. ovale*. Its long half-life of 15 days allows for weekly prophylactic dosing during travel and a single dose for antirelapse

**TABLE 2. (*Continued*) Summary of key adverse events observed in persons receiving tafenoquine at recommended doses versus placebo or mefloquine**

| Year published | Study length | Drug regimen | Sample Size | Adverse event type reported, no. (%) | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Gastrointestinal | Dermatologic | Neurologic | Ophthalmologic | Cardiac | Hematologic |
| **Antirelapse therapy dose** | | | | | | | | | |
| 2014*** | Follow up to 180 days posttreatment | TQ 300 mg plus CQ | 57 | Upper abdominal pain 6 (11)<br>Nausea 5 (9) | Pruritus 8 (14) | Asthenia 5 (9)<br>Insomnia 5 (9) | — | QT prolongation 3 (5) | Anemia 1 (2) |
| | | PQ 15 mg plus CQ | 50 | Upper abdominal pain 7 (14)<br>Nausea 4 (8) | Pruritus 3 (6) | Asthenia 0 (0)<br>Insomnia 3 (6) | — | QT prolongation 5 (10) | Anemia 0 (0) |
| | | CQ only | 54 | Upper abdominal pain 5 (9)<br>Nausea 3 (6) | Pruritus 7 (13) | Asthenia 0 (0)<br>Insomnia 1 (2) | — | QT prolongation 4 (7) | Anemia 0 (0) |
| 2019††† | Follow up to 180 days posttreatment | TQ 300 mg plus CQ | 166 | Nausea 16 (10)<br>Vomiting 11 (7) | Pruritus 20 (12) | Dizziness 27 (16)<br>Headache 19 (11) | Vortex keratopathy 1 (1)<br>Retinal hypo-pigmentation 1 (1)<br>Retinal hyper-pigmentation 1 (1) | — | — |
| | | PQ 15 mg plus CQ | 85 | Nausea 6 (7)<br>Vomiting 5 (6) | Pruritus 19 (22) | Dizziness 13 (15)<br>Headache 10 (12) | Retinal hypo-pigmentation 1 (2) | — | — |
| 2019 §§§ | Follow up to 180 days posttreatment | TQ 300 mg plus CQ | 260 | Nausea 16 (6)<br>Vomiting 15 (6)<br>Diarrhea 10 (4)<br>Upper abdominal pain 8 (3)<br>Elevated ALT 6 (2) | Pruritus 127 (49) | Dizziness 22 (9)<br>Headache 12 (5) | Unilateral keratopathy 1<br>Unilateral retinal change 2 | — | Hemoglobin decreased >3g/dL 14 (5) |
| | | PQ 15 mg plus CQ | 129 | Nausea 7 (5)<br>Vomiting 9 (7)<br>Diarrhea 2 (2)<br>Upper abdominal pain 6 (5)<br>Elevated ALT 3 (2) | Pruritus 14 (11) | Dizziness 8 (6)<br>Headache 5 (4) | Retinal hypo-pigmentation 1 | — | Hemoglobin decreased >3g/dL 2 (2) |
| | | CQ only | 133 | Nausea 9 (7)<br>Vomiting 7 (5)<br>Diarrhea 4 (3)<br>Upper abdominal pain 9 (7)<br>Elevated ALT 6 (5) | Pruritus 17 (13) | Dizziness 4 (3)<br>Headache 9 (7) | — | — | Hemoglobin decreased >3g/dL 2 (2) |

**Abbreviations:** ALT = alanine aminotransferase; CQ = chloroquine; MQ = mefloquine; PQ = primaquine; TQ = tafenoquine.

* Shanks GD, Oloo AJ, Aleman GM, et al. A new primaquine analog, tafenoquine (WR 238605), for prophylaxis against *Plasmodium falciparum* malaria. Clin Infect Dis 2001;33:1968–74.

† Hale BR, Owusu-Agyei S, Fryauff DJ, et al. A randomized, double-blind, placebo-controlled, dose-ranging trial of tafenoquine for weekly prophylaxis against *Plasmodium falciparum*. Clin Infect Dis 2003;36:541–9.

§ For all six, ALT exceeded a predetermined threshold and returned to normal levels when drug was discontinued. No clinical significance.

¶ Nasveld PE, Edstein MD, Reid M, et al. Randomized, double-blind study of the safety, tolerability, and efficacy of tafenoquine versus mefloquine for malaria prophylaxis in nonimmune subjects. Antimicrob Agents Chemother 2010;54:792–8.

** Most common gastrointestinal events: abdominal pain, constipation, and diarrhea. No difference between tafenoquine and mefloquine gastrointestinal events.

†† No difference between tafenoquine and mefloquine, and no severe neuropsychiatric events observed. Most common events were vertigo, dizziness, and sleep disorders. One tafenoquine subject withdrew because of depression (moderate), and one for hyperesthesia (moderate).

§§ Subset analysis for vortex keratopathy. Not associated with visual disturbances and resolved by 1 year.

¶¶ McCarthy JS, Smith B, Reid M, et al. Blood schizonticidal activity and safety of tafenoquine when administered as chemoprophylaxis to healthy, non-immune participants followed by blood stage *Plasmodium falciparum* challenge: a randomized, double-blinded, placebo-controlled Phase 1b study. Clin Infect Dis 2019;69:480–6.

*** Llanos-Cuentas A, Lacerda MV, Rueangweerayut R, Krudsood S, Gupta SK, Kochar SK, et al. Tafenoquine plus chloroquine for the treatment and relapse prevention of *Plasmodium vivax* malaria (DETECTIVE): a multicentre, double-blind, randomized, phase 2b dose-selection study. Lancet. 2014;383:1049–58.

††† Llanos-Cuentas A, Lacerda MVG, Hien TT, et al. Tafenoquine versus primaquine to prevent relapse of *Plasmodium vivax* malaria (GATHER). N Engl J Med 2019;380:229–41.

§§§ Lacerda MVG, Llanos-Cuentas A, Krudsood S, et al. Single-dose tafenoquine to prevent relapse of *Plasmodium vivax* malaria (DETECTIVE Phase III). N Engl J Med 2019;380:215–28.

therapy, which has the potential to increase adherence for both indications (*7*,*8*). With two strengths of tafenoquine tablets available, it is important that clinicians ensure that the appropriate dose is used for each specific indication.

Malaria is a notifiable disease in the United States. CDC's National Malaria Surveillance System collects information about cases of malaria occurring in the United States, providing an opportunity to assess the use and clinical outcomes of tafenoquine. Postmarketing surveillance is being conducted to monitor the occurrence of adverse events. Adverse events related to tafenoquine should be reported voluntarily to FDA's MedWatch adverse event reporting system, and as part of routine reporting to CDC.

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**Summary**

What is already known about this topic?

Malaria can be prevented by taking antimalarials when traveling to an area with malaria. Treatment of malaria caused by *Plasmodium vivax* and *Plasmodium ovale* requires antirelapse therapy to kill the dormant liver-stage parasite.

What is added by this report?

Adults aged ≥18 years can take tafenoquine (Arakoda 100 mg tablets) to prevent malaria. Persons aged ≥16 years requiring antirelapse therapy for *P. vivax* or *P. ovale* can take tafenoquine (Krintafel 150 mg tablets). Before using tafenoquine, quantitative testing to rule out glucose-6-phosphate dehydrogenase deficiency is required.

What are the implications for public health practice?

Tafenoquine is another option for malaria chemoprophylaxis and for antirelapse therapy. The simplified dosing regimen has the potential to improve adherence.

**BOX. Guidance for the use of tafenoquine by indication***

**Prophylaxis†**

- Loading regimen
  - 200 mg daily by mouth x 3 days before departure
- Maintenance regimen
  - 200 mg once weekly by mouth beginning 7 days after last loading dose
  - Continue for entire duration of travel plus one additional dose after returning
  - Take on the same day of the week each week

**Antirelapse therapy§**

- Single 300 mg dose by mouth, ideally on the first or second day of blood-stage treatment
- If not feasible to overlap with blood-stage treatment, may be taken as soon as possible afterwards

**Presumptive antirelapse therapy§**

- Single 300 mg dose by mouth, ideally on the same day as the last dose of prophylaxis
- If not feasible to overlap with last dose of prophylaxis, may be taken as soon as possible afterwards
- Antirelapse dose not needed if primaquine or tafenoquine is used for prophylaxis

* Contraindications: glucose-6-phosphate dehydrogenase (G6PD) deficiency, pregnancy, breastfeeding (if infant has G6PD deficiency or if G6PD status is unknown), known hypersensitivity to 8-aminoquinolines, history of psychiatric disorder.
† Persons aged ≥18 years.
§ Persons aged ≥16 years.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. Kathrine Tan reports that she is a coinvestigator for postmarketing surveillance for adverse events associated with tafenoquine use; she receives no compensation for this work. No other potential conflicts of interest were disclosed.

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# Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine Among Adults Aged ≥65 Years: Updated Recommendations of the Advisory Committee on Immunization Practices

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## Introduction

Two pneumococcal vaccines are currently licensed for use in adults in the United States: a 13-valent pneumococcal conjugate vaccine (PCV13 [Prevnar 13, Pfizer, Inc.]) and a 23-valent pneumococcal polysaccharide vaccine (PPSV23 [Pneumovax 23, Merck and Co., Inc.]). In 2014, the Advisory Committee on Immunization Practices (ACIP)* recommended routine use of PCV13 in series with PPSV23 for all adults aged ≥65 years based on demonstrated PCV13 safety and efficacy against PCV13-type pneumonia among adults aged ≥65 years (*1*). At that time, ACIP recognized that there would be a need to reevaluate this recommendation because it was anticipated that PCV13 use in children would continue to reduce disease burden among adults through reduced carriage and transmission of vaccine serotypes from vaccinated children (i.e., PCV13 indirect effects). On June 26, 2019, after having reviewed the evidence accrued during the preceding 3 years (https://www.cdc.gov/vaccines/acip/recs/grade/PCV13.html), ACIP voted to remove the recommendation for routine PCV13 use among adults aged ≥65 years and to recommend administration of PCV13 based on shared clinical decision-making for adults aged ≥65 years who do not have an immunocompromising condition,† cerebrospinal fluid (CSF) leak, or cochlear implant, and who have not previously received PCV13. ACIP recognized that some adults aged ≥65 years are potentially at increased risk for exposure to PCV13 serotypes, such as persons residing in nursing homes or other long-term care facilities and persons residing in settings with low pediatric PCV13 uptake or traveling to settings with no pediatric PCV13 program, and might attain higher than average benefit from PCV13 vaccination. When patients and vaccine providers§ engage in shared clinical decision-making for PCV13 use to determine whether PCV13 is right for a particular person, considerations might include both the person's risk for exposure to PCV13 serotypes and their risk for developing pneumococcal disease as a result of underlying medical conditions. All adults aged ≥65 years should continue to receive 1 dose of PPSV23. If the decision is made to administer PCV13, it should be given at least 1 year before PPSV23. ACIP continues to recommend PCV13 in series with PPSV23 for adults aged ≥19 years with an immunocompromising condition, CSF leak, or cochlear implant (*2*).

## Background

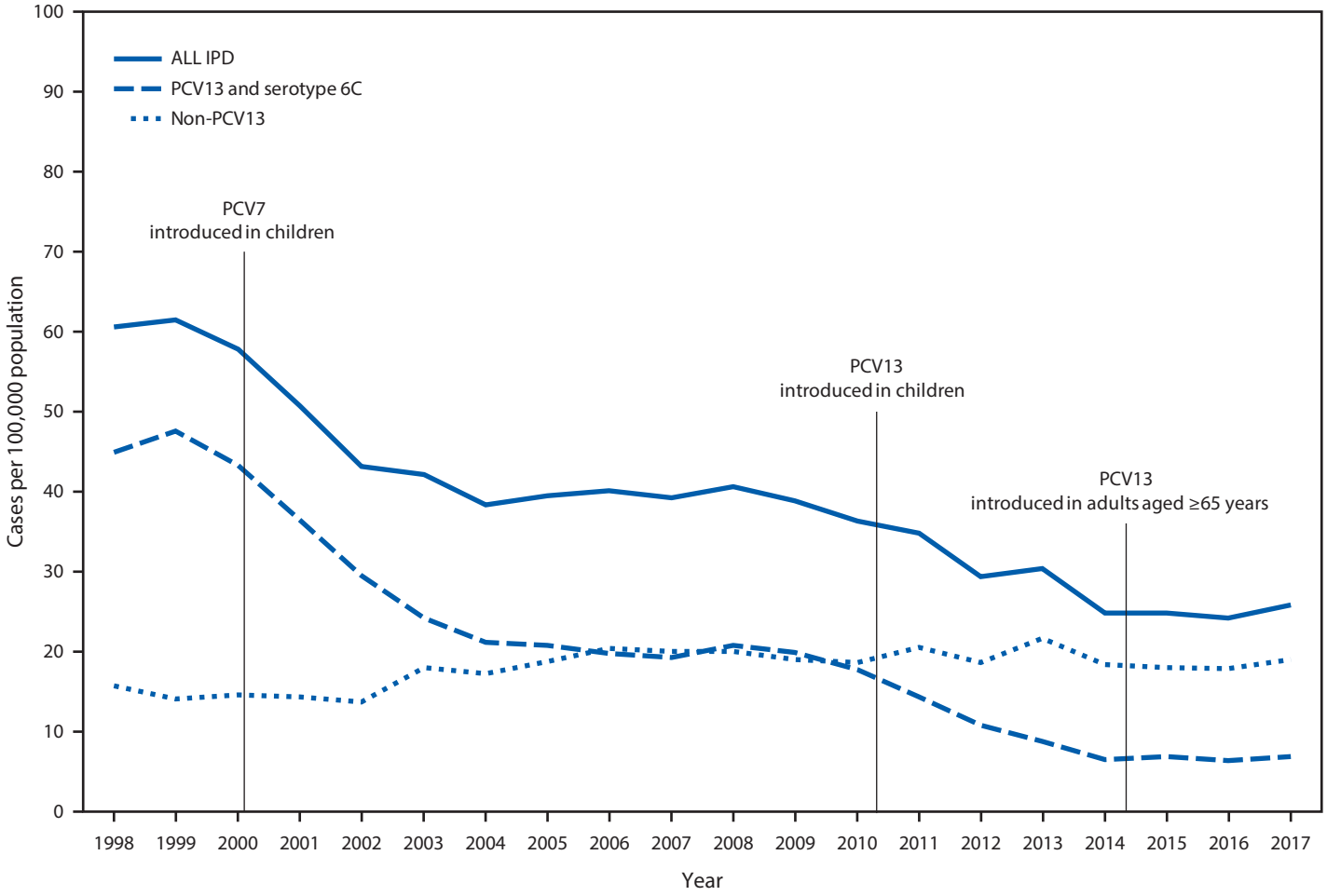
*Streptococcus pneumoniae* (pneumococcus) can cause serious illness, including sepsis, meningitis, and pneumonia with bacteremia (invasive) or without bacteremia (noninvasive). Since the early 1980s, PPSV23 has been recommended for persons aged ≥2 years with certain underlying medical conditions, and all adults aged ≥65 years (*3*). 7-valent pneumococcal conjugate vaccine (PCV7) was introduced into the routine pediatric immunization schedule in 2000 and was replaced by PCV13 in 2010 (*4*). In 2012, PCV13 was recommended in series with PPSV23 for adults aged ≥19 years with immunocompromising conditions, CSF leaks, or cochlear implants (*2*). In 2014, PCV13 was recommended for all adults aged ≥65 years (*1*,*5*). Widespread use of PCV7 and PCV13 in children has led to sharp declines in pneumococcal disease among unvaccinated children and adults by preventing carriage, and thereby transmission, of vaccine-type strains (Figure). In 2014, ACIP recognized that, while in the short-term, routine PCV13 use among adults aged ≥65 years was warranted, in the long-term, continued indirect effects from PCV13 use in children might limit the utility of this recommendation. In addition, models predicted limited public health benefits in the long-term, given the relatively low remaining PCV13-type disease burden (*1*). Therefore, ACIP proposed that the recommendation for routine PCV13 use among adults aged ≥65 years be evaluated 4 years after implementation of the 2014 recommendation.

* Recommendations for 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 the Director of the CDC on use of vaccines and related agents for the control of vaccine-preventable diseases in the civilian population of the United States. Recommendations for 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. Recommendations for use of vaccines in adults are harmonized with recommendations of AAFP, ACOG, and the American College of Physicians (ACP). ACIP recommendations approved by the CDC Director become agency guidelines on the date published in the *Morbidity and Mortality Weekly Report*. Additional information is available at https://www.cdc.gov/vaccines/acip.

† Immunocompromising conditions include: chronic renal failure, nephrotic syndrome, immunodeficiency, iatrogenic immunosuppression, generalized malignancy, human immunodeficiency virus, Hodgkin disease, leukemia, lymphoma, multiple myeloma, solid organ transplants, congenital or acquired asplenia, sickle cell disease, or other hemoglobinopathies.

§ Vaccine providers include anyone who provides or administers vaccines: primary care physicians, specialists, physician assistants, nurse practitioners, registered nurses, and pharmacists.

**FIGURE. Invasive pneumococcal disease (IPD) incidence among adults aged ≥65 years, by pneumococcal serotype* — United States, 1998–2017**




**Source:** Active Bacterial Core Surveillance, unpublished data, 2019.
**Abbreviations:** PCV = pneumococcal conjugate vaccine; PCV7 = 7-valent PCV (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F); PCV13 = 13 valent PCV (PCV7 serotypes plus 1, 3, 5, 6A, 19A and 7F).
* Serotype 6C showed cross-protection from 6A antigen in PCV13 and was grouped with PCV13 serotypes for IPD.

## Methods

During 2016–2019, using the Evidence to Recommendations Framework, (https://www.cdc.gov/vaccines/acip/recs/grade/PCV13-etr.html) the ACIP Pneumococcal Vaccines Work Group reviewed relevant scientific evidence regarding the benefits and harms of PCV13 use among adults aged ≥65 years without an immunocompromising condition, CSF leak, or cochlear implant, in the context of >5 years of pediatric PCV13 use. The Work Group evaluated the quality of evidence for PCV13 efficacy, effectiveness, safety, and population-level impact on pneumococcal-related disease using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (https://www.cdc.gov/vaccines/acip/recs/grade/PCV13.html).

A systematic review of scientific literature published from January 1, 2014, to July 3, 2018, was conducted to identify studies evaluating direct and indirect effects of vaccination with PCV13 on invasive pneumococcal disease (IPD), pneumonia (PCV13-type,[¶] all pneumococcal, and all-cause), and mortality (pneumococcal or all-cause). In addition, PCV13 safety was evaluated by looking for severe adverse events, including death, occurring after receipt of PCV13 in adults aged ≥65 years. Title and abstract screening yielded 364 studies for in-depth review. Of these, 344 did not use PCV13 or did not include an outcome or population of interest. Observational studies with <20% adult PCV13 coverage and studies conducted in settings with low pediatric PCV13 coverage were excluded, as were studies evaluating PCV13 safety if PCV13 was administered with another vaccine, because severe adverse events could not be attributed to PCV13. The remaining 20 studies were included in the GRADE tables. The policy question considered

[¶] Serotype 6C showed cross-protection from 6A antigen in PCV13 and was grouped with PCV13 serotypes for IPD.

was whether PCV13 should be administered routinely to all immunocompetent** adults aged ≥65 years in the context of indirect effects from pediatric PCV use experienced to date.

## Summary of Evidence

**PCV13 effectiveness and safety (individual-level benefits and harms).** Before the 2014 recommendation, a randomized placebo-controlled Community-Acquired Pneumonia Immunization Trial in Adults (CAPiTA) conducted in the Netherlands demonstrated 75% (95% confidence interval [CI] = 41%–91%) efficacy against PCV13-type IPD and 45% (CI = 14%–65%) efficacy against noninvasive PCV13-type pneumonia among adults aged ≥65 years (*6*). Postlicensure studies included in the GRADE tables in 2019 (https://www.cdc.gov/vaccines/acip/recs/grade/PCV13.html) demonstrated PCV13 effectiveness against PCV13-type IPD (47%–59%) (*7*,*8*), noninvasive PCV13-type pneumonia (38%–70%) (*9*,*10*), and all-cause pneumonia (6%–11%) (*11*,*12*). PCV13 efficacy was not demonstrated against PCV13-type or all-cause mortality (*6*); no studies evaluating PCV13 effectiveness against mortality were identified. Three randomized controlled trials (*6*,*13*,*14*) and six observational studies (*15*–*20*) that assessed harms were evaluated (https://www.cdc.gov/vaccines/acip/recs/grade/PCV13.html). The rates of severe adverse events were similar among participants vaccinated with PCV13 versus placebo or PPSV23 (https://www.cdc.gov/vaccines/acip/recs/grade/PCV13.html). Common reported PCV13-associated adverse reactions included pain, redness, and swelling at the injection site, limitation of movement of the arm in which the injection was given, fatigue, headache, chills, decreased appetite, generalized muscle pain, and joint pain (*21*). Overall, PCV13 was assessed to be safe and effective in preventing PCV13-type IPD and noninvasive pneumonia.

**PCV13 population-level impact (indirect and direct effects) on disease among adults aged ≥65 years.** The U.S. pediatric PCV program has been successful in preventing disease among young children through direct protection of vaccinated children as well as in unvaccinated populations through indirect effects (Figure). The incidence of PCV13-type IPD among adults aged ≥65 years declined ninefold during 2000–2014, before the adult PCV13 program was implemented (*22*). During the same period, indirect effects of similar magnitude were observed among adults aged ≥65 years at increased risk for IPD because of either older age (≥85 years) (*22*,*23*) or presence of underlying chronic medical conditions (*24*). Indirect effects on PCV13-type and all-cause pneumonia among adults have also been demonstrated since 2000 (*25*–*27*). In 2014, additional reductions in disease incidence among adults aged ≥65 years were expected to occur as a result of ongoing indirect effects of the pediatric PCV13 program, as well as through direct effects of PCV13 use among adults. PCV13 uptake among adults aged ≥65 years increased rapidly, with coverage in 2018 estimated at 47%; coverage with any pneumococcal vaccine was 62%, with PPSV23 was 45%, and with both PCV13 and PPSV23 was 30% (*23*). However, from 2014–2017, no further reduction in PCV13-type IPD incidence was observed among adults aged ≥65 years, with the incidence stable at five of 100,000 population (20% of all IPD) (*22*). Similarly, since 2014, no impact on PCV13-type IPD incidence has been observed among adults aged 19–64 years, a population only experiencing indirect PCV13 effects during this period. During 2014–2016, no reduction in the incidence of noninvasive pneumococcal pneumonia (all serotypes combined) was observed among adults (*28*). One recent unpublished cohort study found a 31.5% reduction in PCV13-type pneumonia and a 13.8% reduction in all-cause pneumonia between 2014–2015 and 2015–2016 (*29*). In this study, PCV13-types contributed to 4% of all-cause pneumonia among adults aged ≥65 years during 2015–2016 (*29*) compared with the estimated 10% in 2014 (*1*). Overall, since the 2014 recommendation for PCV13 use among adults, minimal changes in the incidence of pneumococcal disease among adults at the population-level were observed, through

**Summary**

What is already known about this topic?

In 2014, the Advisory Committee on Immunization Practices (ACIP) recommended 13-valent pneumococcal conjugate vaccine (PCV13) in series with 23-valent polysaccharide vaccine (PPSV23) for all adults aged ≥65 years.

What is added by this report?

PCV13 use in children has led to sharp declines in pneumococcal disease among adults and children. Based on a review of accrued evidence ACIP changed the recommendation for PCV13 use in adults.

What are the implications for public health practice?

ACIP recommends a routine single dose of PPSV23 for adults aged ≥65 years. Shared clinical decision-making is recommended regarding administration of PCV13 to persons aged ≥65 years who do not have an immunocompromising condition, cerebrospinal fluid leak, or cochlear implant and who have not previously received PCV13. If a decision to administer PCV13 is made, PCV13 should be administered first, followed by PPSV23 at least 1 year later.

** Immunocompetent defined in discussion as adults without an immunocompromising condition (chronic renal failure, nephrotic syndrome, immunodeficiency, iatrogenic immunosuppression, generalized malignancy, human immunodeficiency virus, Hodgkin disease, leukemia, lymphoma, multiple myeloma, solid organ transplants, congenital or acquired asplenia, sickle cell disease, or other hemoglobinopathies), CSF leak, or cochlear implant.

both direct PCV13 effects from vaccinating older adults and continued indirect effects from PCV13 use in children.

**Economic analyses.** Two independent economic models evaluated the expected public health impact and cost effectiveness of continued PCV13 use in series with PPSV23 versus use of PPSV23 alone. These models estimated that, over the lifetime of a single cohort of 2.7 million adults aged 65 years, an expected 76–175 cases of PCV13-type IPD and 4,000–11,000 cases of PCV13-type pneumonia would be averted through continued PCV13 use in series with PPSV23, compared with PPSV23 alone (*30*). Applying the total costs to quality adjusted life years (QALY), the estimated cost effectiveness ratios were $200,000 to $560,000 per QALY. In 2014, the estimated cost per QALY for PCV13 use in series with PPSV23 was $65,000 (*31*). Considering the range of values for sensitivity analyses for key inputs in these models, the results of the economic analyses were less favorable toward continued PCV13 use for all adults aged ≥65 years compared with PPSV23 alone.

## Rationale

Incidence of PCV13-type disease has been reduced to historically low levels among adults aged ≥65 years through indirect effects from pediatric PCV13 use. Implementation of a PCV13 recommendation for all adults aged ≥65 years in 2014 has had minimal impact on PCV13-type disease at the population level in this age group. However, PCV13 is a safe and effective vaccine that can reduce the risk for PCV13-type IPD and noninvasive pneumonia among persons aged ≥65 years. Balancing this evidence and considering acceptability and feasibility concerns, in June 2019 ACIP voted to no longer routinely recommend PCV13 for all adults aged ≥65 years and instead, to recommend PCV13 based on shared clinical decision-making for adults aged ≥65 years who do not have an immunocompromising condition, CSF leak, or cochlear implant (Table 1) (Table 2).

**TABLE 1. Recommendations for 13-valent pneumococcal conjugate vaccine (PCV13) and 23-valent pneumococcal polysaccharide vaccine (PPSV23) among adults aged ≥19 years**

| Medical indication group | Specific underlying medical condition | PCV13 for persons aged ≥19 years | PPSV23* for persons aged 19–64 years | PCV13 for persons aged ≥65 years | PPSV23 for persons aged ≥65 years |
|---|---|---|---|---|---|
| None | None of the below | No recommendation | No recommendation | Based on shared clinical decision-making† | 1 dose; if PCV13 has been given, then give PPSV23 ≥1 year after PCV13 |
| Immunocompetent persons | Alcoholism<br>Chronic heart disease§<br>Chronic liver disease<br>Chronic lung disease¶<br>Cigarette smoking<br>Diabetes mellitus | No recommendation | 1 dose | Based on shared clinical decision-making† | 1 dose; if PCV13 has been given, then give PPSV23 ≥1 year after PCV13 and ≥5 years after any PPSV23 at age <65 years |
| | Cochlear implant<br>CSF leak | 1 dose | 1 dose ≥8 weeks after PCV13 | 1 dose if no previous PCV13 vaccination | 1 dose ≥8 weeks after PCV13 and ≥5 years after any PPSV23 at <65 years |
| Immunocompromised persons | Congenital or acquired asplenia<br>Sickle cell disease/other hemoglobinopathies<br>Chronic renal failure<br>Congenital or acquired immunodeficiencies**<br>Generalized malignancy<br>HIV infection<br>Hodgkin disease<br>Iatrogenic immunosuppression††<br>Leukemia<br>Lymphoma<br>Multiple myeloma<br>Nephrotic syndrome<br>Solid organ transplant | 1 dose | 2 doses, 1st dose ≥8 weeks after PCV13 and 2nd dose ≥5 years after first PPSV23 dose | 1 dose if no previous PCV13 vaccination | 1 dose ≥8 weeks after PCV13 and ≥5 years after any PPSV23 at <65 years |

**Abbreviations:** CSF = cerebrospinal fluid; HIV = human immunodeficiency virus.

* Only refers to adults aged 19–64 years. All adults aged ≥65 years should receive 1 dose of PPSV23 ≥5 years after any previous PPSV23 dose, regardless of previous history of vaccination with pneumococcal vaccine. No additional doses of PPSV23 should be administered following the dose administered at age ≥65 years.

† Recommendations that changed in 2019.

§ Includes congestive heart failure and cardiomyopathies.

¶ Includes chronic obstructive pulmonary disease, emphysema, and asthma.

** Includes B- (humoral) or T-lymphocyte deficiency, complement deficiencies (particularly C1, C2, C3, and C4 deficiencies), and phagocytic disorders (excluding chronic granulomatous disease).

†† Diseases requiring treatment with immunosuppressive drugs, including long-term systemic corticosteroids and radiation therapy.

## New Pneumococcal Vaccine Recommendations for Adults Aged ≥65 Years Old

**PCV13.** PCV13 vaccination is no longer routinely recommended for all adults aged ≥65 years. Instead, shared clinical decision-making for PCV13 use is recommended for persons aged ≥65 years who do not have an immunocompromising condition, CSF leak, or cochlear implant and who have not previously received PCV13 (Table 1).

**CDC guidance for shared clinical decision-making.** When patients and vaccine providers engage in shared clinical decision-making for PCV13 use to determine whether PCV13 is right for the specific individual aged ≥65 years, considerations may include the individual patient's risk for exposure to PCV13 serotypes and the risk for pneumococcal disease for that person as a result of underlying medical conditions (Box).

If a decision to administer PCV13 is made, it should be administered before PPSV23 (*5*). The recommended intervals between pneumococcal vaccines remain unchanged for adults without an immunocompromising condition, CSF leak, or cochlear implant (≥1 year between pneumococcal vaccines, regardless of the order in which they were received) (*5*). PCV13 and PPSV23 should not be coadministered.

ACIP continues to recommend PCV13 in series with PPSV23 for adults aged ≥19 years (including those aged ≥65 years) with immunocompromising conditions, CSF leaks, or cochlear implants (Table 1) (*2*).

**PPSV23 for adults aged ≥65 years**. ACIP continues to recommend that all adults aged ≥65 years receive 1 dose of PPSV23. A single dose of PPSV23 is recommended for routine use among all adults aged ≥65 years (*1*). PPSV23 contains 12 serotypes in common with PCV13 and an additional 11 serotypes for which there are no indirect effects from PCV13 use in children. The additional 11 serotypes account for 32%–37% of IPD among adults aged ≥65 years (*22*). Adults aged ≥65 years who received ≥1 dose of PPSV23 before age 65 years should receive 1 additional dose of PPSV23 at age ≥65 years (2), at least 5 years after the previous PPSV23 dose (Table 1) (*5*).

## Future Research and Monitoring Priorities

CDC will continue to assess the safety, implementation and the impact of shared clinical decision-making regarding administration of PCV13 to adults aged ≥65 years; the indirect effect of pediatric PCV13 vaccination on disease burden among older adults; and the emergence of nonvaccine serotypes, to inform

**TABLE 2. Policy options* for use of pneumococcal vaccines in adults aged ≥65 years presented for a vote and considerations by the Advisory Committee on Immunization Practices (ACIP), June 2019**

| Proposed policy | Considerations raised at the June 2019 ACIP meeting | | Outcome (votes in favor: against) |
|---|---|---|---|
| | In favor | Against | |
| ACIP recommends PCV13 for all adults aged ≥65 years who have not previously received PCV13. PCV13 should be given first, followed by a dose of PPSV23 | PCV13 is effective against invasive pneumococcal disease and pneumonia<br>Changing the recommendation could negatively impact the perceived importance of adult pneumococcal vaccine recommendations<br>Universal recommendations are easier for clinicians to understand and implement than the recommendation based on shared clinical decision-making | Low burden of PCV13-type disease remaining<br>Population-level impact from PCV13 use among older adults observed to date has been minimal<br>Universal PCV13 recommendation for older adults are not a judicious use of resources | Rejected (6:8) |
| ACIP no longer recommends PCV13 for adults aged ≥65 years who do not have an immunocompromising condition,† CSF leak, or cochlear implant. All adults aged ≥65 years should receive a dose of PPSV23 | Largest public health benefit for older adults is gained through indirect effects from pediatric PCV13 use | PCV13 is effective against PCV13-type invasive pneumococcal disease and pneumonia | Rejected (1:13) |
| ACIP recommends PCV13 based on shared clinical decision-making for adults aged ≥65 years who do not have an immunocompromising condition,† CSF leak, or cochlear implant and who have not previously received PCV13.All adults aged ≥65 years should receive a dose of PPSV23 | Balances the minimal population-level impact of a routine recommendation with the potential for individual-level protection<br>PCV13 would remain available to patients who want this added protection | —§ | Affirmed (13:1) |

**Abbreviations:** CSF = cerebrospinal fluid; PCV13 = 13-valent pneumococcal conjugate vaccine; PPSV23 = 23-valent pneumococcal polysaccharide vaccine.
* Policy options listed in the order they were presented to ACIP for a vote.
† Includes adults with chronic renal failure, nephrotic syndrome, immunodeficiency, iatrogenic immunosuppression, generalized malignancy, human immunodeficiency virus, Hodgkin disease, leukemia, lymphoma, multiple myeloma, solid organ transplants, congenital or acquired asplenia, sickle cell disease, or other hemoglobinopathies.
§ No content for this cell.

**BOX. Considerations for shared clinical decision-making regarding use of 13-valent pneumococcal conjugate vaccine (PCV13) in adults aged ≥65 years**

- PCV13 is a safe and effective vaccine for older adults. The risk for PCV13-type disease among adults aged ≥65 years is much lower than it was before the pediatric program was implemented, as a result of indirect PCV13 effects (by preventing carriage and, thereby, transmission of PCV13-type strains). The remaining risk is a function of each individual patient's risk for exposure to PCV13 serotypes and the influence of underlying medical conditions on the patient's risk for developing pneumococcal disease if exposure occurs.
- The following adults aged ≥65 years are potentially at increased risk for exposure to PCV13 serotypes and might attain higher than average benefit from PCV13 vaccination, and providers/practices caring for many patients in these groups may consider regularly offering PCV13 to their patients aged ≥65 years who have not previously received PCV13:
  - Persons residing in nursing homes or other long-term care facilities
  - Persons residing in settings with low pediatric PCV13 uptake
  - Persons traveling to settings with no pediatric PCV13 program
- Incidence of PCV13-type invasive pneumococcal disease and pneumonia increases with increasing age and is higher among persons with chronic heart, lung, or liver disease, diabetes, or alcoholism, and those who smoke cigarettes or who have more than one chronic medical condition.* Although indirect effects from pediatric PCV13 use were documented for these groups of adults and were comparable to those observed among healthy adults, the residual PCV13-type disease burden remains higher in these groups. Providers/practices caring for patients with these medical conditions may consider offering PCV13 to such patients who are aged ≥65 years and who have not previously received PCV13.

*Ahmed SS, Pondo T, Xing W, et al. Early impact of 13-valent pneumococcal conjugate vaccine use on invasive pneumococcal disease among adults with and without underlying medical conditions—United States. Clin Infect Dis 2019. Epub August 12, 2019.

policy decisions for higher valency conjugate vaccines currently in development. ACIP will continue to review relevant data as they become available and update pneumococcal vaccination policy as appropriate.

Before administering PCV13 or PPSV23, health care providers should consult the relevant package inserts (*21*,*32*) regarding precautions, warnings, and contraindications. Adverse events occurring after administration of any vaccine should be reported to the Vaccine Adverse Event Reporting System (VAERS). Reports can be submitted to VAERS online, by facsimile, or by mail. More information about VAERS is available at https://vaers.hhs.gov/.

## Acknowledgments

Members of the Advisory Committee on Immunization Practices (member roster for June 2019 is available at https://www.cdc.gov/vaccines/acip/members/index.html).

## ACIP Pneumococcal Vaccines Work Group

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# Characteristics of Hospitalized and Nonhospitalized Patients in a Nationwide Outbreak of E-cigarette, or Vaping, Product Use–Associated Lung Injury — United States, November 2019

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CDC, the Food and Drug Administration (FDA), state and local health departments, and public health and clinical stakeholders are investigating a nationwide outbreak of e-cigarette, or vaping, product use–associated lung injury (EVALI) (*1*). As of November 13, 2019, 49 states, the District of Columbia, and two U.S. territories (Puerto Rico and U.S. Virgin Islands) have reported 2,172 EVALI cases to CDC, including 42 (1.9%) EVALI-associated deaths. To inform EVALI surveillance, including during the 2019–20 influenza season, case report information supplied by states for hospitalized and nonhospitalized patients with EVALI were analyzed using data collected as of November 5, 2019. Among 2,016 EVALI patients with available data on hospitalization status, 1,906 (95%) were hospitalized, and 110 (5%) were not hospitalized. Demographic characteristics of hospitalized and nonhospitalized patients were similar; most were male (68% of hospitalized versus 65% of nonhospitalized patients), and most were aged <35 years (78% of hospitalized versus 74% of nonhospitalized patients). These patients also reported similar use of tetrahydrocannabinol (THC)-containing products (83% of hospitalized versus 84% of nonhospitalized patients). Given the similarity between hospitalized and nonhospitalized EVALI patients, the potential for large numbers of respiratory infections during the emerging 2019–20 influenza season, and the potential difficulty in distinguishing EVALI from respiratory infections, CDC will no longer collect national data on nonhospitalized EVALI patients. Further collection of data on nonhospitalized patients will be at the discretion of individual state, local, and territorial health departments. Candidates for outpatient management of EVALI should have normal oxygen saturation (≥95% while breathing room air), no respiratory distress, no comorbidities that might compromise pulmonary reserve, reliable access to care, strong social support systems, and should be able to ensure follow-up within 24–48 hours of initial evaluation and to seek medical care promptly if respiratory symptoms worsen. Health care providers should emphasize the importance of annual influenza vaccination for all persons aged ≥6 months, including persons who use e-cigarette, or vaping, products (*2*,*3*).

State health departments, the Council of State and Territorial Epidemiologists Vaping Associated Pulmonary Injury Epidemiology Task Force, and CDC developed and disseminated surveillance case definitions and data collection tools (i.e., patient interview and medical record abstraction forms) to monitor and track cases beginning in August 2019.* Some states are using these tools, whereas others elected to use state-specific tools. States and jurisdictions routinely report the number of confirmed and probable EVALI cases to CDC on a voluntary basis and, when available, include data from patient interviews and medical record abstractions. Some states have restricted case finding to hospitalized patients. Proxies (e.g., spouses or parents) were interviewed if patients were too ill or if they had died. Most states and jurisdictions report the number of cases to CDC as case status is determined; however, completing and submitting information from interviews and medical record abstraction can take up to several weeks.

This report provides updated data on patient demographic characteristics and substances used in e-cigarette, or vaping, products among hospitalized and nonhospitalized patients, as well as clinical characteristics observed among nonhospitalized patients, according to cases reported to CDC with available interview data, medical record abstraction data, or both as of November 5, 2019. Nonhospitalized EVALI patients were defined as those receiving care in an outpatient clinic, urgent care, or emergency department without report of hospitalization. Demographic and product use characteristics were compared across groups using the chi-square test, and the median ages of patients were compared using the Wilcoxon rank-sum test. SAS statistical software (version 9.4; SAS Institute) was used for the analysis.

Among 2,016 EVALI patients with available data on hospitalization status, 1,906 (95%) were hospitalized, and 110 (5%) were not hospitalized (Table 1). The nonhospitalized patients were reported from 27 states. Demographic characteristics of hospitalized and nonhospitalized patients were similar; most were male (68%; [1,228 of 1,797] of hospitalized versus 65%

* https://www.cdc.gov/tobacco/basic_information/e-cigarettes/assets/2019-Lung-Injury-Surveillance-Case-Definition-508.pdf.

[70 of 108] of nonhospitalized patients; p = 0.4) and non-Hispanic white (79% [830 of 1,048] of hospitalized versus 82% [46 of 56] of nonhospitalized patients; p = 0.5). A similar age distribution was observed: 78% (1,395 of 1,800) of hospitalized and 74% (78 of 106) of nonhospitalized patients were aged <35 years (p = 0.3), and median age was 24 years for both hospitalized and nonhospitalized patients (p = 0.9). A higher percentage of hospitalized (55%; 1,039 of 1,896) patients compared with nonhospitalized (12%; 13 of 110) were classified with confirmed cases rather than probable cases (p<0.01). Hospitalized and nonhospitalized patients reported similar use of THC-containing products (83% [932 of 1,122] versus 84% [52 of 62], respectively; p = 0.9) and nicotine-containing products (60% [678 of 1,122] versus 73% [45 of 62], respectively; p = 0.06).

According to medical chart abstraction data reported to CDC on nonhospitalized EVALI patients' initial outpatient medical visit, 85% (47 of 55) experienced respiratory symptoms (e.g., cough, chest pain, and shortness of breath), 57% (27 of 47) had gastrointestinal symptoms (e.g., abdominal pain, nausea, vomiting, and diarrhea), and 76% (41 of 54) had constitutional symptoms (e.g., fever, chills, and weight loss) (Table 2). Very few patients reported only one symptom type (e.g., 9% [four of 47] reported having only respiratory symptoms). Initial oxygen saturation <95% (while breathing room air) was reported among 30% (eight of 27) of patients

**TABLE 1. Demographic and e-cigarette, or vaping, product use characteristics among patients with e-cigarette, or vaping, product use–associated lung injury (EVALI) reported to CDC, by hospitalization status — United States, August–November 2019***

| Characteristic | No./Total no. (%)† | Hospitalized no./Total no. (%)† | Nonhospitalized no./Total no. (%)† | P-value§ |
|---|---|---|---|---|
| **Sex** | | | | |
| Male | 1,298/1,905 (68) | 1,228/1,797 (68) | 70/108 (65) | 0.4 |
| Female | 607/1,905 (32) | 569/1,797 (32) | 38/108 (35) | |
| **Median age, yrs (range)** | 24 (13–78) | 24 (13–78) | 24 (15–71) | 0.9 |
| **Age group (yrs)** | | | | |
| 13–17 | 293/1,906 (15) | 275/1,800 (15) | 18/106 (17) | 0.3 |
| 18–24 | 721/1,906 (38) | 685/1,800 (38) | 36/106 (34) | |
| 25–34 | 459/1,906 (24) | 435/1,800 (24) | 24/106 (23) | |
| 35–44 | 256/1,906 (13) | 242/1,800 (13) | 14/106 (13) | |
| 45–64 | 141/1,906 (7) | 132/1,800 (7) | 9/106 (8) | |
| ≥65 | 36/1,906 (2) | 31/1,800 (2) | 5/106 (5) | |
| **Race/Ethnicity¶** | | | | |
| White | 876/1,104 (79) | 830/1,048 (79) | 46/56 (82) | 0.5 |
| Black or African American | 45/1,104 (4) | 43/1,048 (4) | 2/56 (4) | |
| American Indian or Alaska Native | 5/1,104 (0) | 4/1,048 (0) | 1/56 (2) | |
| Asian, Native Hawaiian, or other Pacific Islander | 19/1,104 (2) | 19/1,048 (2) | 0/56 (0) | |
| Other | 26/1,104 (2) | 24/1,048 (2) | 2/56 (4) | |
| Hispanic | 133/1,104 (12) | 128/1,048 (12) | 5/56 (9) | |
| **Case status** | | | | |
| Confirmed | 1,052/2,006 (52) | 1,039/1,896 (55) | 13/110 (12) | <0.001 |
| Probable | 954/2,006 (48) | 857/1,896 (45) | 97/110 (88) | |
| **Substances used in e-cigarette, or vaping, products**,†† | | | | |
| THC-containing product (any use) | 984/1,184 (83) | 932/1,122 (83) | 52/62 (84) | 0.9 |
| Nicotine-containing product (any use) | 723/1,184 (61) | 678/1,122 (60) | 45/62 (73) | 0.06 |
| Both THC- and nicotine-containing product use | 573/1,184 (48) | 538/1,122 (48) | 35/62 (56) | |
| THC-containing product use only | 411/1,184 (35) | 394/1,122 (35) | 17/62 (27) | 0.2§§ |
| Nicotine-containing product use only | 150/1,184 (13) | 140/1,122 (12) | 10/62 (16) | |
| No THC- or nicotine-containing product use reported | 50/1,184 (4) | 50/1,122 (4) | 0/62 (0) | |

**Abbreviation:** THC = tetrahydrocannabinol.

* For cases reported as of November 5, 2019.

† Percentages might not sum to 100% because of rounding.

§ To assess for statistically significant differences between the hospitalized and nonhospitalized patients, a chi-square test was performed for comparing categorical data and Wilcoxon rank-sum test for the comparison of the median ages.

¶ Whites, blacks or African Americans, American Indians or Alaska Natives, Asians, Native Hawaiians or other Pacific Islanders, and Others were non-Hispanic. Hispanic persons could be of any race.

** Data on both THC- and nicotine-containing product use required to be included.

†† In the 3 months preceding symptom onset.

§§ Comparison of the mutually exclusive categories of "Both THC- and nicotine-containing product use," "THC-containing product use only," "Nicotine-containing product use only," and "No THC- or nicotine-containing product use reported."

and tachycardia among 40% (10 of 25); no patients had tachypnea. Twenty-one (81%) of 26 patients with available data were reportedly prescribed corticosteroids. Among 34 patients with results reported for initial chest radiographs (CXR), 28 (82%) had abnormal findings, and 76% (19 of 25) had bilateral findings; three cases had missing information and were excluded. All 28 patients with results reported for chest computed tomography (CT) scans had abnormal findings, including 27 (96%) with bilateral findings. Six of 16 (38%) patients with information on both a CXR and chest CT had an initial normal CXR but abnormal chest CT; 10 (63%) had both an abnormal CXR and chest CT.

**TABLE 2. Clinical characteristics among nonhospitalized patients with e-cigarette, or vaping, product use–associated lung injury (EVALI) reported to CDC — United States, August–November 2019***

| Characteristic | No./Total no. (%)† |
|---|---|
| **Symptoms reported** | |
| Any respiratory | 47/55 (85) |
| Any gastrointestinal | 27/47 (57) |
| Any constitutional | 41/54 (76) |
| **Among cases with complete symptom information** | |
| Respiratory symptoms only§ | 4/47 (9) |
| Gastrointestinal symptoms only¶ | 0/47 (0) |
| Constitutional symptoms only** | 1/47 (2) |
| **Vital signs on initial presentation** | |
| Oxygen saturation <95% while breathing room air | 8/27 (30) |
| Tachycardia (heart rate >100 beats/min) | 10/25 (40) |
| Tachypnea (respiratory rate >20 breaths/min) | 0/10 (0) |
| **Corticosteroids prescribed** | 21/26 (81) |
| **Initial radiographic findings** | |
| Abnormal chest radiograph | 28/34 (82) |
| Bilateral findings†† | 19/25 (76) |
| Abnormal chest CT | 28/28 (100) |
| Bilateral findings | 27/28 (96) |
| **Among cases with both chest radiograph and chest CT findings reported§§** | |
| Chest radiograph normal but chest CT abnormal | 6/16 (38) |
| Chest radiograph abnormal but chest CT normal | 0/16 (0) |
| Both abnormal | 10/16 (63) |

**Abbreviation:** CT = computed tomography.
* For cases reported as of November 5, 2019.
† Percentages might not sum to 100% because of rounding.
§ Self-reported symptoms (e.g., cough, chest pain, and shortness of breath).
¶ Self-reported symptoms (e.g., abdominal pain, nausea, vomiting, and diarrhea).
** Self-reported symptoms (e.g., fever, chills, and weight loss).
†† Three cases had missing chest radiograph information on unilateral versus bilateral findings and were excluded from this calculation.
§§ Dates of chest radiographs and CT scans were not consistently reported, so it is unknown whether they were performed on the same or subsequent days, which could explain, in part, why the findings for the imaging tests were inconsistent among some patients.

## Discussion

Available data suggest that nonhospitalized EVALI patients have similar demographic and product use characteristics as do hospitalized EVALI patients. In anticipation of increasing incidence of influenza and other respiratory infections during the winter, CDC engaged with state health departments and clinical partners to assess the value of continuing to report EVALI patients who are not hospitalized. EVALI is a diagnosis of exclusion because, at present, no specific test or marker exists for its diagnosis, and evaluation should be guided by clinical judgment. Because patients with EVALI can have symptoms similar to those associated with influenza or other respiratory infections (e.g., fever, cough, headache, myalgias, or fatigue), it might be difficult to differentiate EVALI from influenza or community-acquired pneumonia on initial assessment, and EVALI might co-occur with respiratory infections. Further, continued case finding and case reporting of patients with EVALI who are treated in the outpatient setting will likely impose a significant burden on health systems and health departments during the emerging 2019–20 influenza season. Given this burden, the demographic and clinical findings from this report suggest that data from these outpatient EVALI patients likely will not provide sufficient additional evidence to the continuing investigation. Thus, CDC is no longer requesting national data on outpatient EVALI patients. Further collection of data on nonhospitalized patients will be at the discretion of individual state, local, and territorial health departments.

The findings in this report are subject to at least four limitations. First, data on substances used in e-cigarette, or vaping, products were self-reported or reported by proxies and might be subject to recall bias or social desirability bias. Therefore, underreporting might have occurred. Second, these data might be subject to misclassification of substance use for multiple reasons. Patients might not know the content of the e-cigarette, or vaping, products they used, and methods used to collect data regarding substance use varied across state. Third, data on some variables were missing for many patients, including where nonhospitalized patients received care (e.g., outpatient clinic, urgent care, or emergency department), and conclusions derived from these data might not be generalizable to the entire patient population. Finally, some states have restricted case finding to hospitalized patients, thus these data likely underestimate the actual number of nonhospitalized EVALI patients.

Candidates for outpatient management of EVALI should have normal oxygen saturation (≥95% while breathing room air), no respiratory distress, no comorbidities that might compromise pulmonary reserve, reliable access to care, strong social support systems and should be able to ensure follow-up within 24–48 hours of initial evaluation and to seek medical care promptly if respiratory symptoms worsen; in some cases, patients who initially had mild symptoms experienced a rapid worsening of symptoms within 48 hours (*2*,*3*). Health care providers should consider obtaining a chest CT scan if patients have an initial normal CXR but have symptoms and an exposure history suggestive of EVALI. Further, health care providers should consider use of antimicrobials, including

antivirals, in accordance with established guidelines. Use of corticosteroids for the treatment of EVALI in the outpatient setting should be considered with caution because it might worsen respiratory infections. Health care providers should emphasize the importance of annual influenza vaccination for all persons aged ≥6 months, including persons who use e-cigarette, or vaping, products (*2*,*3*).

Recent CDC laboratory testing has detected vitamin E acetate in bronchoalveolar lavage fluid samples from a convenience sample of 29 patients with EVALI (*4*). These findings provide direct evidence of vitamin E acetate at the primary site of injury within the lungs. However, evidence is not yet sufficient to rule out other chemicals of potential concern contributing to EVALI. Many different substances and product sources are still under investigation, and there might be more than one cause of this outbreak. Therefore, since the specific cause or causes of EVALI are not yet known, the only way for persons to assure that they are not at risk is to consider refraining from use of all e-cigarette, or vaping, products while this investigation continues. In particular, because most patients with EVALI report using THC-containing products before the onset of symptoms, CDC recommends that persons not use e-cigarette, or vaping, products that contain THC, especially those acquired from informal sources like friends, family members, or in-person or online dealers. Persons should not modify or add any substances to e-cigarette, or vaping, products that are not intended by the manufacturer; these include but are not limited to vitamin E acetate and other cutting agents and additives obtained from informal sources or purchased through retail establishments. Irrespective of the ongoing investigation, e-cigarette, or vaping, products should never be used by youths, young adults, or women who are pregnant. Moreover, persons who do not currently use tobacco products should not start using e-cigarette, or vaping, products (*2*). Adults using e-cigarette, or vaping, products to quit smoking should not return to smoking cigarettes; they should weigh all risks and benefits and consider using FDA-approved cessation medications.[†] Adults who continue to use e-cigarette, or vaping, products should carefully monitor themselves for symptoms and see a health care provider immediately if they develop symptoms like those reported in this outbreak.

[†] https://www.cdc.gov/tobacco/campaign/tips/quit-smoking/index.html?s_cid.

**Summary**

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

A total of 2,172 e-cigarette, or vaping, product use–associated lung injury (EVALI) cases have been reported in the nationwide outbreak as of November 13, 2019; most patients reported using tetrahydrocannabinol-containing products in the 3 months before symptom onset.

**What is added by this report?**

As of November 5, 2019, 5% of EVALI patients were not hospitalized. Hospitalized and nonhospitalized patients had similar demographic and product use characteristics.

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

CDC will no longer collect national data on nonhospitalized EVALI cases. Further collection of data on nonhospitalized patients will be at the discretion of individual health departments. Clinical criteria are available to identify candidates for outpatient management of EVALI. Influenza vaccination should be considered for all persons who use e-cigarette, or vaping, products.

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# Update: Interim Guidance for Health Care Providers for Managing Patients with Suspected E-cigarette, or Vaping, Product Use–Associated Lung Injury — United States, November 2019

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CDC, the Food and Drug Administration (FDA), state and local health departments, and public health and clinical stakeholders are investigating a nationwide outbreak of e-cigarette, or vaping, product use–associated lung injury (EVALI) (*1*). CDC has published recommendations for health care providers regarding EVALI (*2–4*). Recently, researchers from Utah and New York published proposed diagnosis and treatment algorithms for EVALI (*5,6*). EVALI remains a diagnosis of exclusion because, at present, no specific test or marker exists for its diagnosis, and evaluation should be guided by clinical judgment. Because patients with EVALI can experience symptoms similar to those associated with influenza or other respiratory infections (e.g., fever, cough, headache, myalgias, or fatigue), it might be difficult to differentiate EVALI from influenza or community-acquired pneumonia on initial assessment; EVALI might also co-occur with respiratory infections. This report summarizes recommendations for health care providers managing patients with suspected or known EVALI when respiratory infections such as influenza are more prevalent in the community than they have been in recent months (*7*). Recommendations include 1) asking patients with respiratory, gastrointestinal, or constitutional symptoms about the use of e-cigarette, or vaping, products; 2) evaluating those suspected to have EVALI with pulse oximetry and obtaining chest imaging, as clinically indicated; 3) considering outpatient management for clinically stable EVALI patients who meet certain criteria; 4) testing patients for influenza, particularly during influenza season, and administering antimicrobials, including antivirals, in accordance with established guidelines; 5) using caution when considering prescribing corticosteroids for outpatients, because this treatment modality has not been well studied among outpatients, and corticosteroids could worsen respiratory infections; 6) recommending evidence-based treatment strategies, including behavioral counseling to help patients discontinue using e-cigarette, or vaping, products; and 7) emphasizing the importance of annual influenza vaccination for all persons aged ≥6 months, including patients who use e-cigarette, or vaping products.

As of November 13, 2019, 49 states, the District of Columbia, and two U.S. territories (Puerto Rico and U.S. Virgin Islands) have reported 2,172 EVALI cases to CDC, including 42 (1.9%) EVALI-associated deaths. Based on established definitions,* patients with EVALI require reported use of e-cigarette, or vaping, products within 3 months of symptom onset, positive imaging findings, and an evaluation to rule out infectious causes.

In anticipation of increasing incidence of influenza and other respiratory infections during the winter, CDC, the Council of State and Territorial Epidemiologists, state health departments, and clinical partners assessed the need for additional clinical guidance. CDC obtained individual clinical perspectives on the management of patients with suspected EVALI from nine national experts (Lung Injury Response Clinical Working Group) involved in previously published clinical guidance for EVALI patients (*4*).

## Clinical Guidance

**Patient interview.** Health care providers should ask about the use of e-cigarette, or vaping, products in a confidential and nonjudgmental manner when evaluating patients with respiratory symptoms (e.g., cough, chest pain, and shortness of breath), gastrointestinal symptoms (e.g., abdominal pain, nausea, vomiting, and diarrhea), or constitutional symptoms (e.g., fever, chills, and weight loss) (Figure). Confidentiality is essential when assessing sensitive information, including all forms of substance use, especially among adolescents and young adults.† Empathetic, nonjudgmental, and private questioning of patients should be employed to encourage truthful

* https://www.cdc.gov/tobacco/basic_information/e-cigarettes/assets/2019-Lung-Injury-Surveillance-Case-Definition-508.pdf.
† https://depts.washington.edu/dbpeds/Screening%20Tools/HEADSS.pdf.

disclosure (*8*). The most critical step in assessing EVALI is to ask patients about recent use of e-cigarette, or vaping, products. If confirmed, the types of substances used (e.g., [tetrahydrocannabinol] THC and nicotine) and where they were obtained should be ascertained. Evidence to date implicates products containing THC, particularly those obtained from informal sources like friends, family members, or in-person or online dealers (*1*,*9*). Therefore, clinicians might seek additional information to inform the ongoing investigation (Box).

**Physical examination**. The physical exam should include assessment of vital signs and pulse oximetry; tachycardia, tachypnea, and hypoxemia have been commonly reported among cases (*4*,*9*,*10*).

**Laboratory testing and imaging studies**. Laboratory testing should be guided by clinical findings to evaluate multiple etiologies, including the possibility of EVALI and concomitant infection (*4*–*6*). A chest radiograph (CXR) should be considered for patients with a recent history of e-cigarette, or vaping, product use, who have respiratory or gastrointestinal symptoms, particularly when chest pain, dyspnea, or decreased oxygen saturation (<95% while breathing room air) are present. Measured oxygen saturation should be interpreted with consideration of factors such as altitude. A chest computed tomography scan might be considered if EVALI is in the differential diagnosis and the CXR is normal. Radiographic findings have varied and abnormalities are not present in all patients upon initial assessment (*11*). Health care providers should evaluate for causes of community-acquired pneumonia according to established guidelines as indicated by imaging findings (*12*,*13*).

**Consideration of outpatient management**. Some patients with recent history of e-cigarette, or vaping, product use who are evaluated for respiratory, gastrointestinal, or constitutional symptoms might be candidates for outpatient management. Hospital admission should be strongly considered for patients with concurrent illness such as influenza and suspected EVALI, especially if respiratory distress, comorbidities that compromise pulmonary reserve, or decreased oxygen saturation (<95% while breathing room air) are present. Candidates for outpatient management should have normal oxygen saturation (≥95%), no respiratory distress, no comorbidities that might compromise pulmonary reserve, reliable access to care, strong social support systems, and should be able to ensure follow up within 24–48 hours of initial evaluation and to seek medical care promptly if respiratory symptoms worsen; in some cases, patients who initially had mild symptoms experienced a rapid worsening of symptoms within 48 hours (*4*,*10*). Additional follow-up might be indicated, based on clinical findings.

**Influenza testing and empiric antimicrobial treatment**. Influenza testing should be strongly considered, particularly during influenza season.[§] It might be difficult to differentiate EVALI, a diagnosis of exclusion, from influenza or community-acquired pneumonia on initial assessment, and EVALI might co-occur with respiratory infections. Treatment with empiric antimicrobials, including antivirals, should be considered in accordance with established guidelines and local microbiology and resistance patterns for bacterial pneumonia (*12*–*14*). Persons with suspected influenza who are at high risk for influenza complications, those with severe or progressive illness, and hospitalized patients are recommended for prompt administration of antiviral treatment. Antiviral treatment also can be considered for any previously healthy, symptomatic outpatient not at high risk for influenza complications, who is diagnosed with confirmed or suspected influenza, on the basis of clinical judgment, if treatment can be initiated within 48 hours of illness onset (*14*).

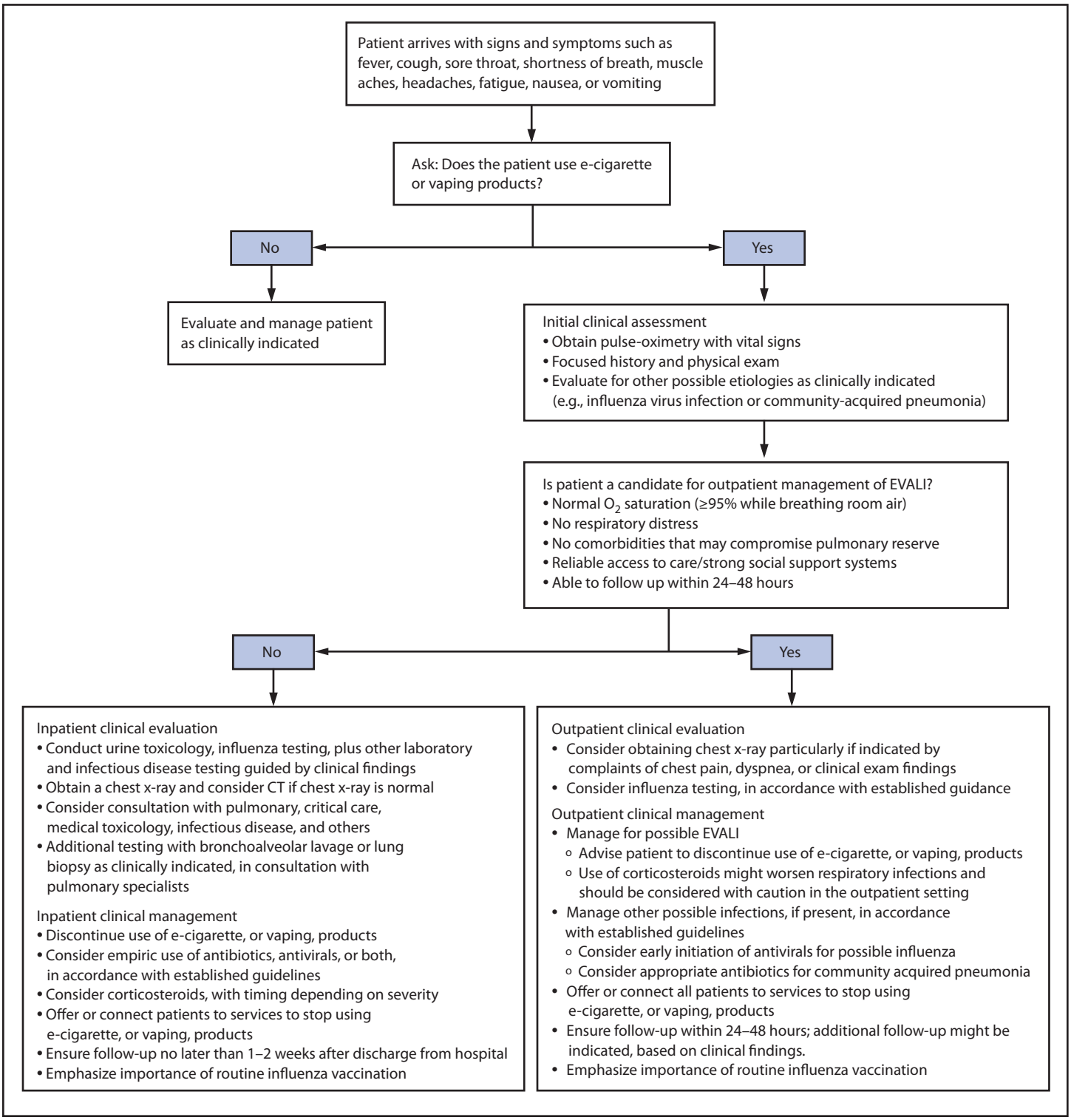
**Corticosteroids and treatment of EVALI**. Corticosteroids might be helpful in treating EVALI (*4*). In published reports primarily including hospitalized patients, most patients with EVALI who received corticosteroids had rapid improvement; dosages have been previously described (*4*–*6*,*10*,*15*). In some circumstances, it would be advisable to withhold corticosteroids while evaluating patients for infectious etiologies that might worsen with corticosteroid treatment. Use of corticosteroids for the treatment of EVALI in the outpatient setting has not been well studied and should be considered with caution. Corticosteroids might worsen respiratory infections commonly seen in the outpatient setting (*13*,*14*). Some patients who have not received corticosteroids have also had clinical improvement with cessation of e-cigarette, or vaping, products (*4*–*6*,*10*,*15*), and comparative studies have not been conducted. Consultation with pulmonary, infectious disease, psychology, psychiatry, and addiction medicine specialists should be considered, as indicated, to optimize patient management.

Special consideration should be given to patients who might be at increased risk for severe outcomes with EVALI, including those who are older or have a history of cardiac or lung disease, or those who are pregnant. Among reported cases, those who were older or had past cardiac disease had more severe EVALI-associated outcomes (e.g., higher percentage requiring endotracheal intubation and mechanical ventilation and longer duration of hospitalization) (*4*).

**Discontinuation of e-cigarette, or vaping, product use**. Advising patients to discontinue use of e-cigarette, or vaping, products should be integral to the care approach. Health care providers should offer or connect patients to services to stop

[§] https://www.cdc.gov/flu/professionals/diagnosis/index.htm.

**FIGURE. Algorithm for management of patients*,†,§,¶ with respiratory, gastrointestinal, or constitutional symptoms and e-cigarette, or vaping, product use**




**Abbreviations:** CT = computed tomography; EVALI = e-cigarette, or vaping, product use–associated lung injury.
* https://www.cdc.gov/flu/professionals/diagnosis/consider-influenza-testing.htm.
† https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm.
§ https://www.atsjournals.org/doi/full/10.1164/rccm.201908-1581ST#readcube-epdf.
¶ https://academic.oup.com/cid/article/68/6/e1/5251935.

**BOX. Assessment of recent history of use of e-cigarette, or vaping products**

The most critical step in assessing e-cigarette, or vaping, product use–associated lung injury (EVALI) is to ask patients about recent use of e-cigarette, or vaping, products. Health care providers evaluating patients with respiratory symptoms (e.g., cough, chest pain, or shortness of breath), gastrointestinal symptoms (e.g., abdominal pain, nausea, vomiting, or diarrhea), or constitutional symptoms (e.g., fever, chills, or weight loss) should ask about the use of e-cigarette, or vaping, products.

- Confidentiality is essential when assessing sensitive information, including all forms of substance use, especially for young adults and adolescents.
- Empathetic, nonjudgmental, and private questioning of patients to encourage truthful disclosure should be employed.*,†
- Repeat questioning might elicit additional information about exposures, as trust is established.

The strongest evidence to date implicates products containing tetrahydrocannabinol (THC), particularly those obtained from informal sources like friends, family members, or in-person or online dealers. Therefore, it is important to ascertain the following information:

- What types of substances were used (see details below for examples)
- Where they were obtained

To assist with the ongoing investigation, the following details might provide additional necessary information:

- Types of substances used
  - THC or cannabis [specify if oil or dabs]
  - Nicotine
  - Modified products or the addition of substances (e.g., addition of vitamin E acetate)
- Product source
- Product brand and name
- Duration and frequency of use
- Time of last use
- Product delivery system
- Method of use (aerosolization, dabbing, or dripping)

*https://www.aafp.org/afp/2017/0101/p29.pdf.
†https://depts.washington.edu/dbpeds/Screening%20Tools/HEADSS.pdf.

using e-cigarette, or vaping, products. Resuming use of these products has the potential to cause slowed recovery, recurrence of symptoms, or further lung injury (*5*). Adult patients who are using e-cigarette, or vaping, products for smoking cessation should be advised not to return to smoking cigarettes. They should be provided with evidence-based interventions, including behavioral counseling and FDA-approved cessation medications.¶ Adolescents and young adults might benefit from specialized services, such as addiction treatment services and providers who have experience with counseling and behavioral health follow-up. Persons with ongoing marijuana use that causes significant impairment or distress might have a cannabis use disorder. Persons with cannabis use disorder should receive evidence-based interventions such as cognitive-behavioral therapy, contingency management, motivational enhancement therapy, and multidimensional family therapy. Consultation with addiction medicine services should be considered (*16*–*18*).

**Influenza vaccination**. Health care providers should emphasize the importance of annual influenza vaccination for all persons aged ≥6 months, including their patients who use e-cigarette, or vaping products. It is not known whether patients with EVALI are at higher risk for severe complications of influenza or other respiratory infections. In addition, administration

¶https://www.cdc.gov/tobacco/campaign/tips/quit-smoking/index.html.

of pneumococcal vaccine should be considered for patients with a history of EVALI, according to current guidelines.**

**Postdischarge follow-up**. Patients discharged from the hospital after inpatient treatment for EVALI should have a follow-up visit within 1–2 weeks. The follow-up evaluation should include pulse-oximetry and consideration of a repeat CXR. Additional follow-up testing 1–2 months after discharge might include spirometry, diffusion capacity for carbon monoxide, and CXR.

Long-term effects and the risk for recurrence of EVALI are not known. Whereas many patients' symptoms resolved, clinicians report that some patients have relapsed during corticosteroid tapers or with resumption of e-cigarette, or vaping, product use after hospitalization, underscoring the need for cessation and close follow-up (personal communication, Lung Injury Response Clinical Working Group, October 2019). Some patients have had persistent hypoxemia requiring home oxygen at discharge and might require ongoing pulmonary follow-up. Patients treated with high-dose corticosteroids might require care from an endocrinologist to monitor adrenal function.

Health care providers should also advise patients with a history of EVALI to return as soon as possible if they develop new or worsening respiratory symptoms, with or without fever, for early evaluation with influenza testing and early initiation of antiviral (*14*)†† or antibiotic treatment (*12,13*), as indicated.

## Public Health Recommendations

Recent testing has detected vitamin E acetate in bronchoalveolar lavage fluid samples from a convenience sample of 29 patients with EVALI (*19*); however, evidence is not yet sufficient to rule out contributions of other chemicals of potential concern contributing to EVALI. Many different substances and product sources are still under investigation, and it might be that there is more than one cause of this outbreak. Because most patients with EVALI report using THC-containing products before the onset of symptoms, CDC recommends that persons not use e-cigarette, or vaping, products that contain THC. Persons should not buy any type of e-cigarette, or vaping products, particularly those containing THC, from informal sources, like friends, family members, or in-person or online dealers.§§ Persons should not modify or add any substances to e-cigarette, or vaping, products that are not intended by the manufacturer; these include but are not limited to vitamin E acetate and other cutting agents and additives obtained from informal sources or purchased through retail establishments.

**Summary**

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

A total of 2,172 U.S. e-cigarette, or vaping, product use-associated lung injury (EVALI) cases have been reported to CDC. Vitamin E acetate and tetrahydrocannabinol appear to be associated with the outbreak; however, no single causative agent has been identified.

**What is added by this report?**

As rates of influenza increase, providers evaluating patients with respiratory illnesses should ask them about e-cigarette, or vaping, product use; evaluate whether patients require hospital admission; and consider empiric use of antimicrobials, including antivirals, as well as possible corticosteroids.

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

EVALI is a diagnosis of exclusion; rapid recognition of EVALI patients by health care providers is critical to reduce severe outcomes.

Because the specific cause or causes of EVALI are not yet known, the only way for persons to assure that they are not at risk is to consider refraining from use of all e-cigarette, or vaping, products while the investigation continues. Irrespective of the investigation, e-cigarette, or vaping, products should never be used by youths, young adults, or pregnant women (*20*). Moreover, persons who do not currently use tobacco products should not start using e-cigarette, or vaping products. Adults using e-cigarette, or vaping, products to aid with smoking cessation should not return to smoking cigarettes; they should weigh all risks and benefits and consider using FDA-approved cessation medications¶¶. Adults who continue to use e-cigarette, or vaping, products should carefully monitor themselves for symptoms and see a health care provider immediately if they develop symptoms like those reported in this outbreak.

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** https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/pneumo.html.
†† https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm.
§§ https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html#latest-outbreak-information.
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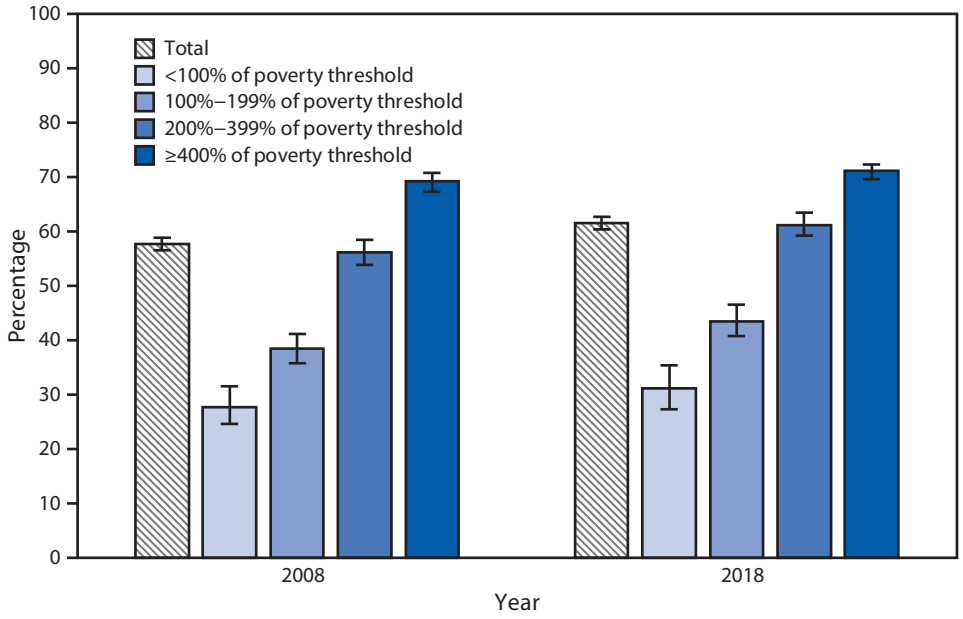
# QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

## Percentage* of Currently Employed Adults Aged 18–64 Years Who Have Paid Sick Leave,† by Poverty Status§ — National Health Interview Survey,¶ United States, 2008 and 2018




* With 95% confidence intervals indicated with error bars.
† Based on a positive response to the question "Do you have paid sick leave on this main job or business?"
§ Poverty status was based on family income and family size using the U.S. Census Bureau poverty thresholds. Family income was imputed when missing.
¶ Estimates are based on household interviews of a sample of the civilian, noninstitutionalized U.S. population and are derived from the National Health Interview Survey Sample Adult component.

The percentage of currently employed adults aged 18–64 years who have paid sick leave increased from 57.8% in 2008 to 61.7% in 2018. For both 2008 and 2018, the percentage of employees with paid sick leave increased with family income. In 2018, the percentage with paid sick leave was 31.5% for those with incomes <100% of the poverty threshold, increasing to 71.4% for those with incomes ≥400% of the poverty threshold. The percentage of employees with paid sick leave increased from 2008 to 2018 in all poverty groups, although the increase was not significant for those with incomes <100% of the poverty threshold or for those with incomes ≥400% of the poverty threshold.

**Source:** National Health Interview Survey, 2008 and 2018. https://www.cdc.gov/nchs/nhis/index.htm.

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