

Update: Influenza Activity — United States, September 30, 2018–February 2, 2019

Lenee Blanton, MPH¹; Vivien G. Dugan, PhD¹; Anwar Isa Abd Elal¹; Noreen Alabi, MPH¹; John Barnes, PhD¹; Lynnette Brammer, MPH¹; Alicia P. Budd, MPH¹; Erin Burns, MA¹; Charisse N. Cummings, MPH¹; Shikha Garg, MD¹; Rebecca Garten, PhD¹; Larisa Gubareva, PhD¹; Krista Kniss, MPH¹; Natalie Kramer¹; Alissa O'Halloran, MSPH¹; Carrie Reed, DSc¹; Melissa Rolfes, PhD¹; Wendy Sessions, MPH¹; Calli Taylor, MPH¹; Xiyun Xu, MD¹; Alicia M. Fry, MD¹; David E. Wentworth, PhD¹; Jacqueline Katz, PhD¹; Daniel Jernigan, MD¹

CDC collects, compiles, and analyzes data on influenza activity and viruses in the United States. During September 30, 2018–February 2, 2019,* influenza activity[†] in the United States was low during October and November, increased in late December, and remained elevated through early February. As of February 2, 2019, this has been a low-severity influenza season (1), with a lower percentage of outpatient visits for influenza-like illness (ILI), lower rates of hospitalization, and fewer deaths attributed to pneumonia and influenza, compared with recent seasons. Influenza-associated hospitalization rates among children are similar to those observed in influenza A(H1N1)pdm09 predominant seasons; 28 influenza-associated pediatric deaths occurring during the 2018–19 season have been reported to CDC. Whereas influenza A(H1N1)pdm09 viruses predominated in most areas of the country, influenza A(H3N2) viruses have predominated in the southeastern United States, and in recent weeks accounted for a growing proportion of influenza viruses detected in several other regions. Small numbers of influenza B viruses (<3% of all influenza-positive tests performed by public health laboratories) also were reported. The majority of the influenza viruses characterized antigenically are similar to the cell culture–propagated reference viruses representing the 2018–19 Northern Hemisphere influenza vaccine viruses.

* Data as of February 2, 2019.

[†] The CDC influenza surveillance system collects five categories of information from eight data sources: 1) virus surveillance (U.S. World Health Organization collaborating laboratories, the National Respiratory and Enteric Virus Surveillance System (NREVSS), and novel influenza A virus case reporting); 2) outpatient illness surveillance (U.S. Outpatient Influenza-Like Illness Surveillance Network [ILI-Net]); 3) mortality (the National Center for Health Statistics Mortality Surveillance System and influenza-associated pediatric mortality reports); 4) hospitalizations (FluSurv-NET, which includes the Emerging Infections Program and surveillance in three additional states); and 5) summary of the geographic spread of influenza (state and territorial epidemiologist reports). <https://www.cdc.gov/flu/weekly/fluactivitysurv.htm>.

Health care providers should continue to offer and encourage vaccination to all unvaccinated persons aged ≥ 6 months as long as influenza viruses are circulating. Finally, regardless of vaccination status, it is important that persons with confirmed or suspected influenza who have severe, complicated, or progressive illness; who require hospitalization; or who are at high risk for influenza complications be treated with antiviral medications.

INSIDE

- 135 Interim Estimates of 2018–19 Seasonal Influenza Vaccine Effectiveness — United States, February 2019
- 140 Days' Supply of Initial Opioid Analgesic Prescriptions and Additional Fills for Acute Pain Conditions Treated in the Primary Care Setting — United States, 2014
- 144 Increased Methamphetamine, Injection Drug, and Heroin Use Among Women and Heterosexual Men with Primary and Secondary Syphilis — United States, 2013–2017
- 149 Transmission Patterns in a Low HIV-Morbidity State — Wisconsin, 2014–2017
- 153 Recommendations of the Advisory Committee on Immunization Practices for Use of Hepatitis A Vaccine for Persons Experiencing Homelessness
- 157 Vital Signs: Tobacco Product Use Among Middle and High School Students — United States, 2011–2018
- 165 Notes from the Field: Assessment of State-Level Influenza Season Severity — Minnesota and Utah, 2017–18 Influenza Season
- 167 QuickStats

Continuing Education examination available at https://www.cdc.gov/mmwr/cme/conted_info.html#weekly.



Virus Surveillance

U.S. World Health Organization (WHO) and National Respiratory and Enteric Virus Surveillance System laboratories, which include both clinical and public health laboratories throughout the United States, contribute to virologic surveillance for influenza. During September 30, 2018–February 2, 2019, clinical laboratories tested 536,301 specimens for influenza virus; among these, 54,381 (10.1%) tested positive, including 52,028 (95.7%) for influenza A and 2,353 (4.3%) for influenza B (Figure 1). The percentage of specimens testing positive for influenza each week ranged from 1.7% to 21.6%.

Public health laboratories tested 30,344 specimens during September 30, 2018–February 2, 2019; 12,200 were positive for influenza viruses, including 11,863 (97.2%) positive for influenza A and 337 (2.8%) for influenza B (Figure 2). Among the 11,284 influenza A viruses subtyped, 9,023 (80.0%) were influenza A(H1N1)pdm09, and 2,261 (20.0%) were influenza A(H3N2). Influenza B lineage information was available for 249 (73.9%) influenza B viruses; 143 (57.4%) were B/Yamagata lineage, and 106 (42.6%) were B/Victoria lineage. Influenza A(H1N1)pdm09 viruses accounted for the majority of circulating viruses; however, in the southeastern United States, influenza A(H3N2) viruses have predominated (accounting for 29.8% of all influenza A(H3N2) viruses reported in the United States). From late December 2018 to early February 2019, influenza A(H3N2) viruses have accounted for a growing proportion of influenza viruses detected in several other regions.

Among 10,766 (88.2%) patients with positive test results for seasonal influenza virus by public health laboratories and for whom age data were available, 1,627 (15.1%) were aged 0–4 years; 3,493 (32.4%) were aged 5–24 years; 3,991 (37.1%) were aged 25–64 years; and 1,654 (15.4%) were aged ≥65 years. Influenza A(H1N1)pdm09 viruses predominated among all age groups, ranging from 64.4% among persons aged ≥65 years to 79.4% among persons aged 25–64 years. The percentage of influenza A(H3N2) viruses ranged from 30.1% among persons aged ≥65 years to 13.5% in persons aged 25–64 years. From late December 2018 to early February 2019, the proportion of influenza A(H3N2) viruses among persons aged 5–24 years has increased from 24.4% to 46.2%. Among all age groups, influenza B viruses have accounted for ≤5% of positive influenza test results.

Antigenic and Genetic Characterization of Influenza Viruses

In the United States, public health laboratories participating in influenza surveillance as WHO collaborating laboratories are asked to submit a subset of influenza-positive respiratory specimens to CDC for virus characterization according to specific guidelines.[§] Data obtained from antigenic characterization are

[§] Association of Public Health Laboratories. Influenza Virologic Surveillance Right Size Roadmap. https://www.aphl.org/AboutAPHL/publications/Documents/ID_July2013_Influenza-Virologic-Surveillance-Right-Size-Roadmap.pdf.

The *MMWR* series of publications is published by the Center for Surveillance, Epidemiology, and Laboratory Services, Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services, Atlanta, GA 30329-4027.

Suggested citation: [Author names; first three, then et al., if more than six.] [Report title]. *MMWR Morb Mortal Wkly Rep* 2019;68:[inclusive page numbers].

Centers for Disease Control and Prevention

Robert R. Redfield, MD, *Director*
 Anne Schuchat, MD, *Principal Deputy Director*
 Leslie Dauphin, PhD, *Acting Associate Director for Science*
 Barbara Ellis, PhD, MS, *Acting Director, Office of Science Quality*
 Chesley L. Richards, MD, MPH, *Deputy Director for Public Health Scientific Services*
 Michael F. Iademarco, MD, MPH, *Director, Center for Surveillance, Epidemiology, and Laboratory Services*

MMWR Editorial and Production Staff (Weekly)

Charlotte K. Kent, PhD, MPH, *Editor in Chief*
 Jacqueline Gindler, MD, *Editor*
 Mary Dott, MD, MPH, *Online Editor*
 Teresa F. Rutledge, *Managing Editor*
 Douglas W. Weatherwax, *Lead Technical Writer-Editor*
 Glenn Damon, Soumya Dunworth, PhD, Teresa M. Hood, MS,
Technical Writer-Editors

Martha F. Boyd, *Lead Visual Information Specialist*
 Maureen A. Leahy, Julia C. Martinroe,
 Stephen R. Spriggs, Tong Yang,
Visual Information Specialists
 Quang M. Doan, MBA, Phyllis H. King,
 Terraye M. Starr, Moua Yang,
Information Technology Specialists

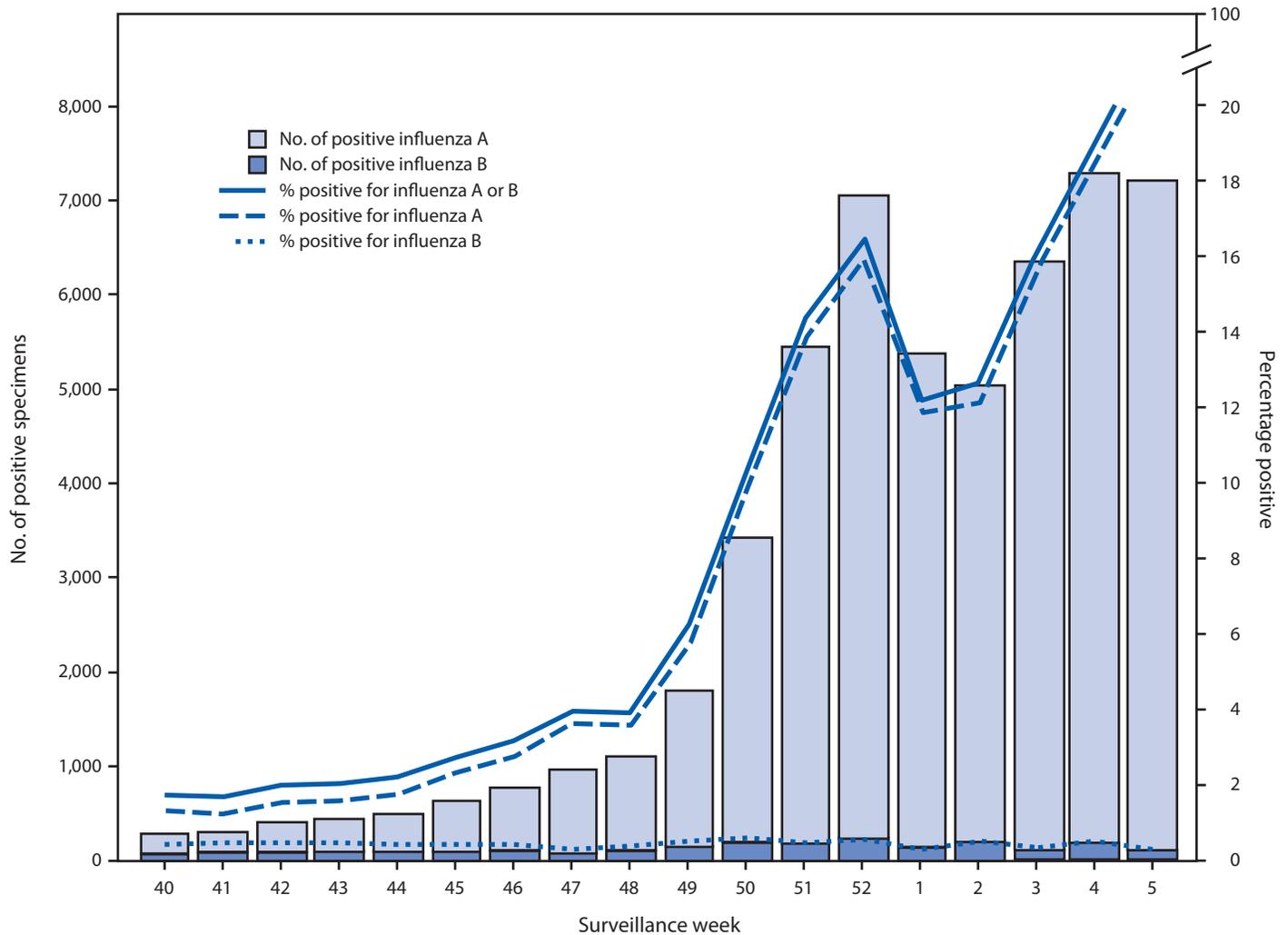
MMWR Editorial Board

Timothy F. Jones, MD, *Chairman*
 Robin Ikeda, MD, MPH
 Phyllis Meadows, PhD, MSN, RN
 Jewel Mullen, MD, MPH, MPA
 Jeff Niederdeppe, PhD
 Patricia Quinlisk, MD, MPH

Matthew L. Boulton, MD, MPH
 Virginia A. Caine, MD
 Katherine Lyon Daniel, PhD
 Jonathan E. Fielding, MD, MPH, MBA
 David W. Fleming, MD
 William E. Halperin, MD, DrPH, MPH

Stephen C. Redd, MD
 Patrick L. Remington, MD, MPH
 Carlos Roig, MS, MA
 William Schaffner, MD
 Morgan Bobb Swanson, BS

FIGURE 1. Number* and percentage of respiratory specimens testing positive for influenza reported by clinical laboratories, by influenza virus type and surveillance week – United States, September 30, 2018–February 2, 2019†



* Results for 54,381 (10.1%) of 536,301 specimens tested were positive during September 30, 2018–February 2, 2019.

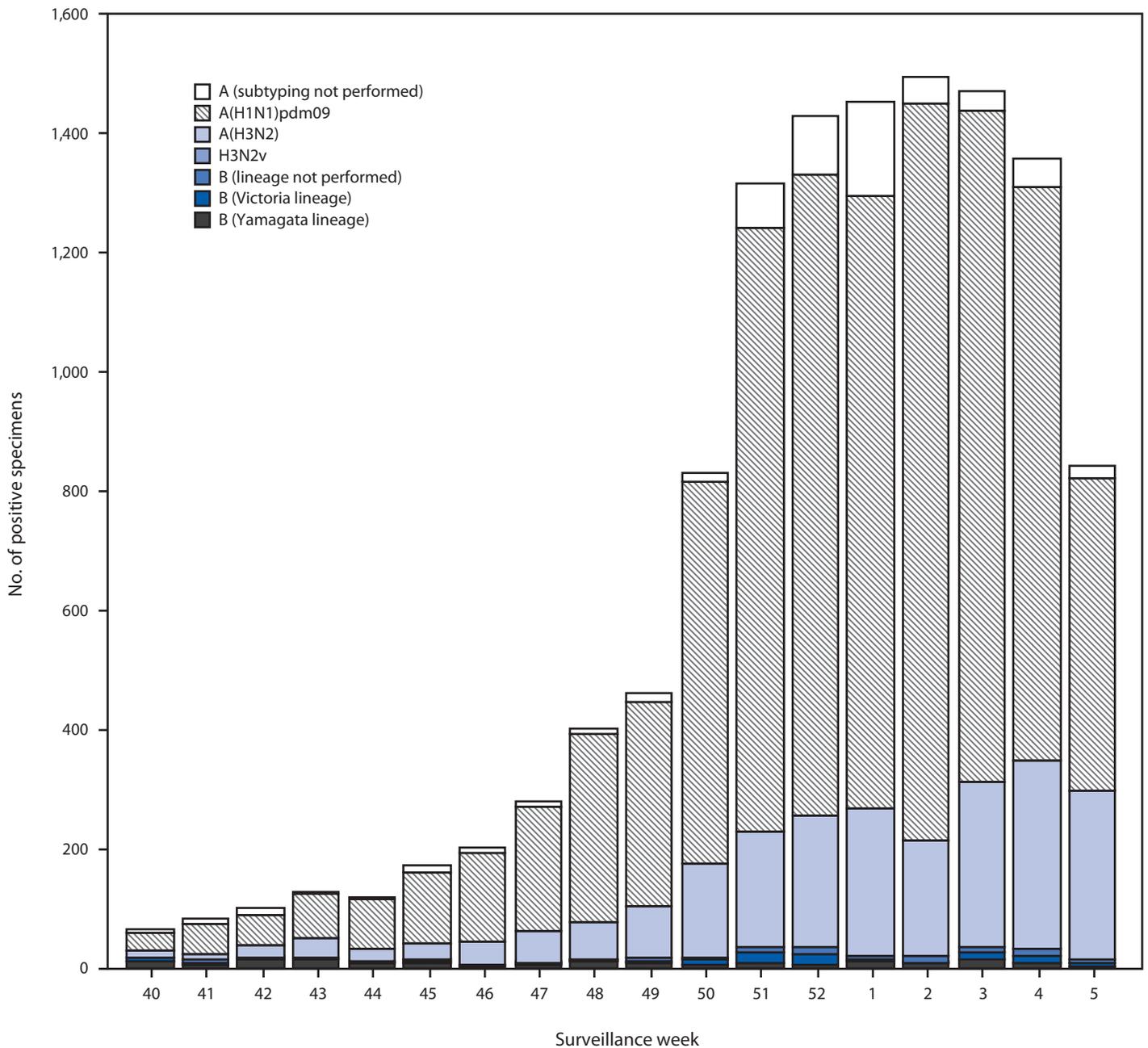
† As of February 2, 2019.

important in the assessment of the similarity between reference vaccine viruses and circulating viruses. In vitro antigenic characterization data acquired through hemagglutination inhibition assays or virus neutralization–based focus reduction assays evaluate whether genetic changes in circulating viruses affect antigenicity; substantial differences could affect vaccine effectiveness. Nearly all influenza viruses received by CDC are genomically characterized using next generation sequencing, and the genomic data are analyzed and submitted to public databases (GenBank: <https://www.ncbi.nlm.nih.gov/genbank> or EpiFlu: <https://www.gisaid.org/>). CDC has genetically characterized 769 influenza viruses collected and submitted by U.S. laboratories since September 30, 2018, including 450 influenza A(H1N1)pdm09 viruses, 239 influenza A(H3N2)

viruses, and 80 influenza B viruses. A subset of these viruses were also antigenically characterized.

Phylogenetic analysis of the hemagglutinin (HA) gene segments from the 450 characterized A(H1N1)pdm09 viruses determined that all belonged to clade 6B.1. Considerable genetic diversity within clade 6B.1 has emerged; further evolution in the HA gene has occurred, resulting in the circulation of multiple clades. Among 194 A(H1N1)pdm09 viruses antigenically characterized, 191 (98.5%) were antigenically similar (analyzed using hemagglutination inhibition with ferret antisera) to A/Michigan/45/2015 (6B.1), a cell culture–propagated A/Michigan/45/2015-like reference virus representing the A(H1N1)pdm09 component for the 2018–19 Northern Hemisphere influenza vaccines.

FIGURE 2. Number* of respiratory specimens testing positive for influenza reported by public health laboratories, by influenza virus type, subtype/lineage, and surveillance week — United States, September 30, 2018–February 2, 2019†



* N = 12,200.

† As of February 2, 2019.

A total of 239 influenza A(H3N2) viruses were sequenced, and phylogenetic analysis of the HA gene segments illustrated that multiple clades/subclades were cocirculating. Circulating viruses possessed HA gene segments that belonged to clade 3C.2a (55; 23.0%), subclade 3C.2a1 (98; 41.0%), or clade 3C.3a (86; 36.0%). The frequency of 3C.3a viruses has increased, from 16% of the A(H3N2) viruses sequenced and

collected in November 2018 to 51% of those sequenced and collected in December 2018. The geographic distribution of 3C.3a viruses also has increased, from the southeastern United States in November 2018 to throughout the continental United States by the end of December 2018. Among the 145 representative A(H3N2) viruses that were antigenically characterized by focus reduction assay with ferret antisera, 102 (70.3%) were

well-inhibited (reacting at titers that were within fourfold of the homologous virus titer) by ferret antisera raised against A/Singapore/INFIMH-16-0019/2016 (3C.2a1), a cell culture-propagated reference virus representing the A(H3N2) component of 2018–19 Northern Hemisphere influenza vaccines. Forty-three (29.7%) viruses reacted poorly (at titers that were reduced eightfold or more when compared with the homologous virus A/Singapore/INFIMH-16-0019/2016) and, of the 43 viruses, 42 (97.7%) belonged to clade 3C.3a. However, only 28 of the 145 viruses tested were well-inhibited by antiserum raised against egg-propagated A/Singapore/INFIMH-16-0019/2016 reference virus representing the A(H3N2) vaccine component, likely because of egg-adaptive amino acid changes in the HA of the egg-propagated virus.

Among influenza B viruses, phylogenetic analysis of 50 influenza B/Yamagata lineage viruses determined that the HA gene segments belonged to clade Y3. Thirty-three B/Yamagata lineage viruses were antigenically characterized, and all were antigenically similar to cell culture-propagated B/Phuket/3073/2013, the reference virus representing the B/Yamagata lineage component of quadrivalent vaccines for the 2018–19 Northern Hemisphere influenza season.

Among the 30 influenza B/Victoria lineage viruses sequenced and phylogenetically analyzed, the HA gene segment of all viruses belonged to genetic clade V1A (10; 33.3%), subclade V1A.1 (18; 60.0%), or subclade V1A-3Del (2; 7%). Viruses with a two-amino acid-deletion (162–163) in the HA protein belong to subclade V1A.1, and viruses with a three-amino acid-deletion (162–164) in the HA protein belong to subclade V1A-3Del. Twenty-one B/Victoria lineage viruses were antigenically characterized and 15 (71.4%) were antigenically similar to cell culture-propagated B/Colorado/06/2017-like V1A.1 reference virus. Six (28.6%) reacted poorly (at titers that were eightfold or greater reduced compared with the homologous virus titer) but were antigenically related to the previous vaccine virus B/Brisbane/60/2008 and belonged to clade V1A.

Antiviral Susceptibility of Influenza Viruses

Testing of influenza A(H1N1)pdm09, influenza A(H3N2), and influenza B viruses for resistance to the neuraminidase inhibitors oseltamivir, zanamivir, and peramivir is performed at CDC using next generation sequencing analysis, a functional assay, or both. Neuraminidase sequences of viruses are examined for the presence of amino acid substitutions, previously associated with reduced or highly reduced inhibition by any of the three neuraminidase inhibitors.[¶] The amino acid

[¶] https://www.who.int/influenza/gisrs_laboratory/antiviral_susceptibility/NAI_Reduced_Susceptibility_Marker_Table_WHO.pdf;ua = 1.

substitution H275Y is considered clinically relevant, because of the frequency of occurrence and the availability of clinical data to demonstrate a reduced treatment efficacy; however, the other amino acid substitutions have been observed less frequently and caused reduced susceptibility in vitro but with clinical significance being less clear (2).

A total of 823 influenza virus specimens (481 influenza A(H1N1)pdm09, 254 influenza A(H3N2), 34 influenza B/Victoria, and 54 influenza B/Yamagata viruses) collected in the United States during October 1, 2018–February 2, 2019, were tested for resistance to oseltamivir, zanamivir, and peramivir. Two (0.4%) influenza A(H1N1)pdm09 viruses displayed highly reduced inhibition by oseltamivir and peramivir. An additional two (0.4%) influenza A(H1N1)pdm09 viruses displayed reduced inhibition by oseltamivir. All influenza viruses tested were found to be sensitive to zanamivir. Reporting of baloxavir susceptibility testing for the 2018–19 influenza season will begin later this season. High levels of resistance to the adamantanes (amantadine and rimantadine) persist among influenza A(H1N1)pdm09 and influenza A(H3N2) viruses (the adamantanes are not effective against influenza B viruses).

Outpatient Illness Surveillance

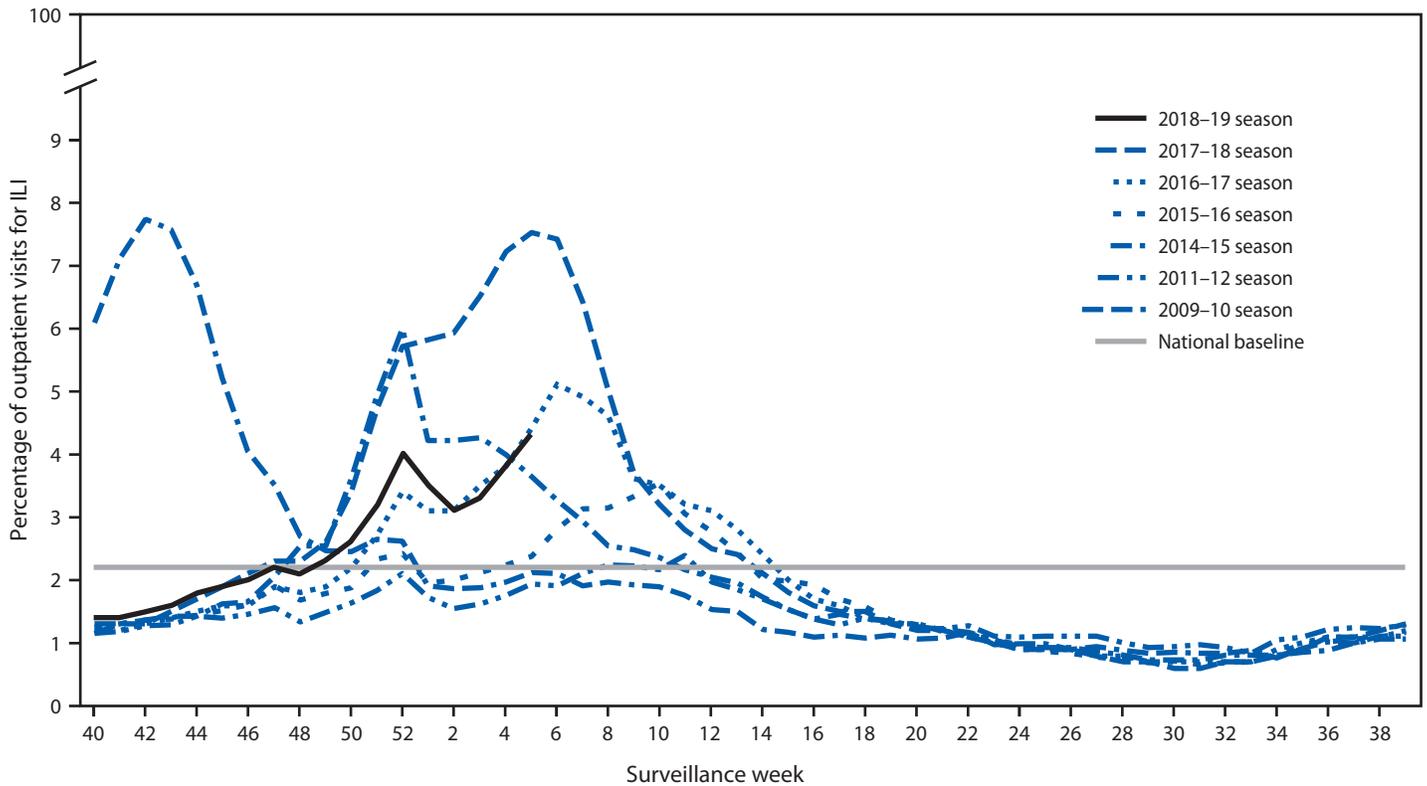
Nationally, during September 30, 2018–February 2, 2019, the weekly percentage of outpatient visits for ILI** to health care providers participating in the United States Outpatient Influenza-like Illness Surveillance Network (ILINet) has been at or above the national baseline^{††} level of 2.2% for 9 consecutive weeks (weeks 49–5) (Figure 3). For the week ending February 2, 2019 (week 5), the percentage of outpatient visits for ILI was 4.3%, and all 10 U.S. Department of Health and Human Services regions^{§§}

** Defined as a fever (temperature $\geq 100^{\circ}\text{F}$ [$\geq 37.8^{\circ}\text{C}$], oral or equivalent) and cough or sore throat, without a known cause other than influenza.

†† The national and regional baselines are the mean percentages of visits for ILI during noninfluenza weeks for the previous three seasons plus two standard deviations. Noninfluenza weeks are defined as periods of ≥ 2 consecutive weeks during which each week accounted for $< 2\%$ of the season's total number of specimens that tested positive for influenza. National and regional percentages of patient visits for ILI are weighted based on state population. Use of the national baseline for regional data are not appropriate.

§§ The 10 U.S. Department of Health and Human Services regions include the following jurisdictions: *Region 1:* Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont; *Region 2:* New Jersey, New York, Puerto Rico, and the U.S. Virgin Islands; *Region 3:* Delaware, District of Columbia, Maryland, Pennsylvania, Virginia, and West Virginia; *Region 4:* Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, and Tennessee; *Region 5:* Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin; *Region 6:* Arkansas, Louisiana, New Mexico, Oklahoma, and Texas; *Region 7:* Iowa, Kansas, Missouri, and Nebraska; *Region 8:* Colorado, Montana, North Dakota, South Dakota, Utah, and Wyoming; *Region 9:* Arizona, California, Hawaii, Nevada, American Samoa, Commonwealth of the Northern Mariana Islands, Federated States of Micronesia, Guam, Marshall Islands, and Republic of Palau; *Region 10:* Alaska, Idaho, Oregon, and Washington.

FIGURE 3. Percentage of outpatient visits for influenza-like illness (ILI)* reported to CDC, by surveillance week — U.S. Outpatient Influenza-Like Illness Surveillance Network, 2018–19 influenza season and selected previous influenza seasons†



* Defined as fever (temperature of $\geq 100^{\circ}\text{F}$ [$\geq 37.8^{\circ}\text{C}$], oral or equivalent) and cough or sore throat, without a known cause other than influenza.

† As of February 2, 2019.

reported ILI activity at or above region-specific baseline levels. During the past five influenza seasons, the peak percentage of visits for ILI has ranged from 3.6% (2015–16) to 7.5% (2017–18) and remained at or above baseline levels for an average of 16 weeks (range = 11–20 weeks).

ILINet data are used to produce a weekly jurisdiction-level measure of ILI activity,^{¶¶} ranging from minimal to high. For the weeks ending October 6, 2018–February 2, 2019, fewer than half of the 53 jurisdictions reporting to ILINet (50 states, New York City, the District of Columbia, and Puerto Rico) experienced high ILI activity each week, with the highest number (25; 47%) during the week ending February 2, 2019 (week 5). During the past five seasons, the largest number of jurisdictions experiencing

high ILI activity in a single week ranged from 16 (30%) during the 2015–16 season to 46 (87%) during the 2017–18 season.

Geographic Spread of Influenza Activity

State and territorial epidemiologists report the geographic distribution of influenza in their jurisdictions (50 states, District of Columbia, Guam, Puerto Rico, and U.S. Virgin Islands) through a weekly influenza activity code.^{***} During September 30, 2018–February 2, 2019, the peak number of jurisdictions reporting widespread activity in a single week was 48 (89%); this occurred during

*** Levels of activity are 1) no activity; 2) sporadic: isolated laboratory-confirmed influenza cases or a laboratory-confirmed outbreak in one institution, with no increase in activity; 3) local: increased ILI, or two or more institutional outbreaks (ILI or laboratory-confirmed influenza) in one region of the state, with recent laboratory evidence of influenza in that region; virus activity no greater than sporadic in other regions; 4) regional: increased ILI activity or institutional outbreaks (ILI or laboratory-confirmed influenza) in two or more outbreaks, but with fewer than half of the regions in the state with recent laboratory evidence of influenza in those regions; and 5) widespread: increased ILI activity or institutional outbreaks (ILI or laboratory-confirmed influenza) in at least half of the regions in the state, with recent laboratory evidence of influenza in the state.

¶¶ Activity levels are based on the percentage of outpatient visits in a jurisdiction attributed to ILI and are compared with the average percentage of ILI visits that occur during weeks with little or no influenza virus circulation. Activity levels range from minimal (corresponding to ILI activity from outpatient clinics at or below the average) to high (corresponding to ILI activity from outpatient clinics much higher than the average). Because the clinical definition of ILI is nonspecific, not all ILI is caused by influenza; however, when combined with laboratory data, the information on ILI activity provides a clearer picture of influenza activity in the United States.

week 5 (the week ending February 2, 2019). During the previous five influenza seasons, the peak number of jurisdictions reporting widespread activity in a single week during each season has ranged from 41 (76%) (2015–16 season) to 50 (93%) (2017–18 season).

Influenza-Associated Hospitalizations

CDC monitors hospitalizations associated with laboratory-confirmed influenza infections through the Influenza Hospitalization Surveillance Network (FluSurv-NET),^{†††} which covers approximately 27 million persons (9% of the U.S. population). In addition, FluSurv-NET data are being used to generate preliminary national estimates of the cumulative in-season numbers of symptomatic illnesses, medical visits, hospitalizations, and deaths in the United States.

During October 1, 2018–February 2, 2019, a total of 5,791 laboratory-confirmed influenza-related hospitalizations were reported (cumulative incidence for all age groups = 20.1 per 100,000 population). By age group, the cumulative hospitalization rate was 33.5 per 100,000 population among children aged 0–4 years, 7.6 among children and adolescents aged 5–17 years, 9.6 among adults aged 18–49 years, 27.2 among adults aged 50–64 years, and 53.0 among adults aged ≥65 years. Among 5,791 hospitalizations, 5,434 (93.8%) were associated with influenza A virus, 299 (5.2%) with influenza B virus, 28 (0.5%) with influenza A virus and influenza B virus coinfection, and 30 (0.5%) with an influenza virus for which the type was not determined. Among hospitalizations associated with influenza A for which subtype information was known, 975 (76.8%) were A(H1N1)pdm09 virus, and 294 (23.2%) were A(H3N2).

Complete medical chart abstraction data in FluSurv-NET will not be finalized until later in 2019; however, as of February 2,

^{†††} FluSurv-NET conducts population-based surveillance for laboratory-confirmed, influenza-associated hospitalizations in children and adolescents aged <18 years (since the 2003–04 influenza season) and adults aged ≥18 years (since the 2005–06 influenza season). FluSurv-NET covers approximately 70 counties in the 10 states in the Emerging Infections Program (California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee) and additional Influenza Hospitalization Surveillance Project (IHSP) states. IHSP began during the 2009–10 season to enhance surveillance during the 2009 H1N1 pandemic. IHSP sites included Idaho, Iowa, Michigan, Oklahoma, and South Dakota during the 2009–10 season; Idaho, Michigan, Ohio, Oklahoma, Rhode Island, and Utah during the 2010–11 season; Michigan, Ohio, Rhode Island, and Utah during the 2011–12 season; Iowa, Michigan, Ohio, Rhode Island, and Utah during the 2012–13 season; and Michigan, Ohio, and Utah during the 2013–14, 2014–15, 2015–16, 2016–17, 2017–18, and 2018–19 seasons. Cumulative unadjusted incidence rates are calculated using CDC's National Center for Health Statistics population estimates for the counties included in the surveillance catchment area. Laboratory confirmation is dependent on clinician-ordered influenza testing and testing for influenza often is underutilized because of the poor reliability of rapid test results and greater reliance on clinical diagnosis for influenza. Therefore, cases identified as part of influenza hospitalization surveillance likely are an underestimation of the actual number of persons hospitalized with influenza.

2019, data were available for 905 (15.6%) hospitalized adults and children with laboratory-confirmed influenza. Among 755 hospitalized adults with information on underlying medical conditions,^{§§§} 681 (90.2%) had at least one reported underlying medical condition; those most commonly reported were cardiovascular disease (40.6% of 681), obesity (40.1%), and metabolic disorder (39.3%). Among 150 hospitalized children with information on underlying medical conditions, 62 (41.3%) had at least one underlying medical condition; the most commonly reported being asthma (19.7% of 150) and obesity (11.0%). Among 131 hospitalized women aged 15–44 years with information on pregnancy status, 20 (15.3%) were pregnant.

Pneumonia and Influenza-Associated Mortality

CDC tracks pneumonia and influenza (P&I)-attributed deaths through CDC's National Center for Health Statistics (NCHS) Mortality Reporting System. To allow for collection of sufficient data to produce stable P&I percentages, NCHS surveillance data are released 2 weeks after the week of death. During September 30, 2018–January 26, 2019, based on data from NCHS, the weekly percentage of deaths attributed to P&I ranged from 5.5% to 7.4%. P&I has been at or above the epidemic threshold^{¶¶¶} for 3 consecutive weeks (the weeks ending January 5–January 19, 2019).

Influenza-Associated Pediatric Mortality

CDC monitors influenza-associated deaths among children aged <18 years through the Influenza-Associated Pediatric Mortality Surveillance System. As of February 2, 2019, a total of 28 laboratory-confirmed influenza-associated pediatric deaths during the 2018–19 season had been reported to CDC from New York City and 21 states. One death occurred in a non-U.S. resident. Fifteen (54%) of these deaths were

^{§§§} Persons at higher risk include 1) children aged <2 years; 2) adults aged ≥65 years; 3) persons with chronic pulmonary conditions (including asthma), cardiovascular disease (except hypertension alone), renal, hepatic, hematologic (including sickle cell) disease, metabolic disorders (including diabetes mellitus), or neurologic and neurodevelopmental conditions (including disorders of the brain, spinal cord, peripheral nerves, and muscles, such as cerebral palsy, epilepsy [seizure disorders], stroke, intellectual disability [mental retardation], moderate to severe developmental delay, muscular dystrophy, or spinal cord injury); 4) persons with immunosuppression, including that caused by medications or by human immunodeficiency virus infection; 5) women who are pregnant or postpartum (within 2 weeks after delivery); 6) persons aged ≤18 years who are receiving long-term aspirin therapy; 7) American Indians/Alaska Natives; 8) persons with extreme obesity (i.e., body mass index ≥40); and 9) residents of nursing homes and other chronic care facilities.

^{¶¶¶} The seasonal baseline proportion of P&I deaths is projected using a robust regression procedure, in which a periodic regression model is applied to the observed percentage of deaths from P&I that were reported by the National Center for Health Statistics Mortality Surveillance System during the preceding 5 years. The epidemic threshold is set at 1.645 standard deviations above the seasonal baseline.

associated with an infection with an influenza A(H1N1)pdm09 virus, two (7%) with an influenza A(H3N2) virus, 10 (36%) with an influenza A virus for which no subtyping was performed, and one (4%) with an influenza B virus. The mean age of the pediatric deaths reported this season was 6.5 years (range = 8 months–15 years); 15 (54%) children died after admission to the hospital. Among the 26 children who died with a known medical history, 12 (46%) had at least one underlying medical condition recognized by the Advisory Committee on Immunization Practices (ACIP) as placing them at high risk for influenza-related complications (3). Among the 22 children who were eligible for influenza vaccination and for whom vaccination status was known, six had received at least 1 dose of influenza vaccine before illness onset (three were fully vaccinated according to 2018 ACIP recommendations, and three had received 1 of 2 recommended doses). Since influenza-associated pediatric mortality became a nationally notifiable condition in 2004, the total number of influenza-associated pediatric deaths each season has ranged from 37 during the 2011–12 season to 185 during the 2017–18 season. These numbers are likely an underestimate of the actual number of influenza-associated pediatric deaths.

Preliminary Prevalence Estimates of Influenza

CDC estimates the cumulative prevalence of influenza using the cumulative rates of influenza-associated hospitalizations reported through FluSurv-NET and a mathematical model.^{****} From October 1, 2018 to February 2, 2019, CDC estimates that influenza virus infection has caused 13,200,000–15,200,000 symptomatic illnesses, 6,170,000–7,220,000 medical visits, 155,000–186,000 hospitalizations, and 9,600–15,900 deaths.

Discussion

In the United States, influenza activity remained elevated through early February. Influenza A(H1N1)pdm09 viruses have predominated nationwide, but influenza A(H3N2) viruses have predominated in the southeastern United States. Influenza A(H3N2) viruses have accounted for an increasing proportion of reported influenza viruses in several regions. The number of influenza B viruses reported has been low; influenza B/Yamagata viruses were more commonly reported from September through late December, and influenza B/Victoria viruses have been reported more frequently since late December. ILI activity and the percentage of respiratory specimens testing positive for influenza in clinical laboratories have been increasing since mid-January. This season, the percentage of outpatient ILI visits has reached

4.3% at the beginning of February. The peak ILI activity for the past two A(H1N1)pdm09-predominant seasons was 3.6% during the 2015–16 season and 4.6% during the 2013–14 season. Influenza-associated hospitalization rates and P&I-attributed mortality have been relatively low this season and are consistent with what has been observed during previous seasons when influenza A(H1N1)pdm09 viruses predominated (4,5). During most seasons, including this season, adults aged ≥65 years have the highest hospitalization rates, followed by children aged <5 years. Severity indicators demonstrate that, as of February 2, 2019, the severity of influenza activity has been low; however preliminary cumulative in-season prevalence estimates indicate that influenza has caused 155,000–186,000 hospitalizations and 9,600–15,900 deaths. Current influenza forecasts^{††††} predict that elevated influenza activity in parts of the United States will continue for several more weeks.

Most of the influenza viruses characterized during this time are antigenically similar to the cell culture-propagated reference viruses representing the 2018–19 Northern Hemisphere influenza vaccine viruses. However, genetic diversity among currently circulating influenza A(H1N1)pdm09 viruses belonging to clade 6B.1 viruses has increased, suggesting ongoing evolution of these viruses. Increased circulation and testing of 3C.3a viruses has contributed to a recent increasing proportion of A(H3N2) viruses that are antigenically distinct from the reference virus representing the A(H3N2) vaccine component. The majority of influenza viruses collected since October 1, 2018, and tested (>99%) displayed susceptibility to oseltamivir and peramivir, and all tested viruses displayed susceptibility to zanamivir.

The 2018–19 season is the first season that CDC has reported preliminary estimates of the prevalence of influenza in the United States during the season, and prevalence estimates will be updated each week over the remainder of the season. CDC estimates that since the 2010–11 season, during an influenza season, influenza virus infection has caused 9.3 million–49 million symptomatic illnesses, 4.3 million–23 million medical visits, 140,000–960,000 hospitalizations, and 12,000–79,000 deaths^{§§§§}.

Health care providers should continue to offer and encourage vaccination to all unvaccinated persons aged ≥6 months as long as influenza viruses are circulating (3). Interim estimates of vaccine effectiveness based on data collected during November 23, 2018–February 2, 2019, indicate that, overall, the influenza vaccine has been 47% (95% confidence interval = 34%–57%) effective in preventing medically attended acute respiratory virus infection across all age groups and specifically was 46% (30%–58%) effective in preventing medical

^{****} <https://www.cdc.gov/flu/about/burden/how-cdc-estimates.htm>.

^{††††} <https://www.cdc.gov/flu/weekly/flu-sight/index.html>.

^{§§§§} <https://www.cdc.gov/flu/about/burden/past-seasons.html>.

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

CDC collects, compiles, and analyzes data on influenza activity and viruses in the United States.

What is added by this report?

Influenza activity in the United States remained elevated through February 2, 2019, and is expected to continue for several more weeks. Compared with recent influenza seasons, as of February 2, 2019, severity this season has been low, with a lower percentage of outpatient visits for influenza-like illness, lower rates of hospitalization, and fewer deaths attributed to pneumonia and influenza.

What are the implications for public health practice?

Influenza vaccination remains the most effective way to prevent influenza illness. Influenza antiviral medications are an important adjunct to vaccination in the treatment and prevention of influenza.

visits associated with influenza A(H1N1)pdm09 (6). Annual influenza vaccination is the first and best defense against influenza infection. Depending on the vaccine formulation (trivalent or quadrivalent), influenza vaccines can protect against three or four different influenza viruses. With vaccine effectiveness in the range of 30%–60%, influenza vaccination prevents millions of infections and medical visits and tens of thousands of influenza-associated hospitalizations each year in the United States.^{¶¶¶} During the 2017–18 season, vaccination averted an estimated 7.1 million illnesses, 3.7 million medical visits, 109,000 influenza-associated hospitalizations, and 8,000 influenza-associated deaths (7). In addition, influenza vaccination has been found to reduce deaths, intensive care unit admissions and length of stay, and overall duration of hospitalization among hospitalized influenza patients (8).

Influenza antiviral medications are an important adjunct to vaccination in the treatment and prevention of influenza. Treatment as soon as possible with influenza antiviral medications is recommended for patients with confirmed or suspected influenza who have severe, complicated, or progressive illness; who require hospitalization; or who are at high risk for influenza complications. Providers should not rely on less sensitive assays such as rapid antigen detection influenza diagnostic tests to inform treatment decisions (9). Four influenza antiviral drugs are approved by the Food and Drug Administration (FDA) for treatment of acute uncomplicated influenza within 2 days of illness onset and are recommended for use in the United States during the 2018–19 season: oseltamivir, zanamivir, peramivir, and baloxavir, which was approved by the FDA on October 24, 2018 (10).

Influenza surveillance reports for the United States are posted online weekly (<https://www.cdc.gov/flu/weekly>). Additional information regarding influenza viruses, influenza surveillance, influenza vaccine, influenza antiviral medications, and novel influenza A infections in humans is available online (<https://www.cdc.gov/flu>).

Acknowledgments

State, county, city, and territorial health departments and public health laboratories; U.S. World Health Organization collaborating laboratories; National Respiratory and Enteric Virus Surveillance System laboratories; U.S. Outpatient Influenza-Like Illness Surveillance Network sites; National Center for Health Statistics, CDC; World Health Organization, FluNet; LaShondra Berman, Elisabeth Blanchard, Roxana Cintron, Juliana DaSilva, Juan De la Cruz, Angie Foust, Lizheng Guo, Norman Hassell, Shoshona Le, Ji Liu, Brian Lynch, Ewelina Lyszkowicz, Vasily Mishin, Janná Murray, Ha Nguyen, Kyung Park, Thomas Rowe, Sujatha Seenu, Samuel Shepard, Bo Shu, Catherine Smith, Thomas Stark, Alma Trujillo, Malania Wilson, Influenza Division, National Center for Immunization and Respiratory Diseases, CDC.

Corresponding author: Lenee Blanton, LBlanton@cdc.gov, 404–639-3747.

^{¶¶¶}Influenza Division, National Center for Immunization and Respiratory Diseases, CDC.

All authors have completed and submitted the ICMJE form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

References

1. Biggerstaff M, Kniss K, Jernigan DB, et al. Systematic assessment of multiple routine and near real-time indicators to classify the severity of influenza seasons and pandemics in the United States, 2003–2004 through 2015–2016. *Am J Epidemiol* 2018;187:1040–50. <https://doi.org/10.1093/aje/kwx334>
2. World Health Organization. Laboratory methodologies for testing the antiviral susceptibility of influenza viruses: neuraminidase inhibitor (NAI). Geneva, Switzerland: World Health Organization; 2019. https://www.who.int/influenza/gisrs_laboratory/antiviral_susceptibility/nai_overview/en/
3. Grohskopf LA, Sokolow LZ, Broder KR, Walter EB, Fry AM, Jernigan DB. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices—United States, 2018–19 influenza season. *MMWR Recomm Rep* 2018;67(No. RR-3). <https://doi.org/10.15585/mmwr.rr6703a1>
4. Davlin SL, Blanton L, Kniss K, et al. Influenza activity—United States, 2015–16 season and composition of the 2016–17 influenza vaccine. *MMWR Morb Mortal Wkly Rep* 2016;65:567–75. <https://doi.org/10.15585/mmwr.mm6522a3>
5. Epperson S, Blanton L, Kniss K, et al.; Influenza Division, National Center for Immunization and Respiratory Diseases, CDC. Influenza activity—United States, 2013–14 season and composition of the 2014–15 influenza vaccines. *MMWR Morb Mortal Wkly Rep* 2014;63:483–90.
6. Doyle J, Flannery B, Chung JR, et al. Interim estimates of 2018–19 seasonal influenza vaccine effectiveness—United States, February 2019. *MMWR Morb Mortal Wkly Rep* 2019;68:135–9.

^{¶¶¶} <https://www.cdc.gov/flu/about/disease/2016-17.htm>.

7. Rolfes MA, Flannery B, Chung J, et al. U.S. Flu VE Network, the Influenza Hospitalization Surveillance Network (FluSurv-NET), and the Assessment Branch, Immunization Services Division, CDC. Effects of influenza vaccination in the United States during the 2017–18 influenza season. *Clin Infect Dis* 2019. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciz075/5305915?guestAccessKey=1e115fb7-2c0f-4e9f-8a79-3b0b09adb6b3>
8. Arriola C, Garg S, Anderson EJ, et al. Influenza vaccination modifies disease severity among community-dwelling adults hospitalized with influenza. *Clin Infect Dis* 2017;65:1289–97. <https://doi.org/10.1093/cid/cix468>
9. Fiore AE, Fry A, Shay D, Gubareva L, Bresee JS, Uyeki TM. Antiviral agents for the treatment and chemoprophylaxis of influenza—recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2011;60(No. RR-1).
10. Food and Drug Administration. FDA approves new drug to treat influenza (press release). Washington, DC: US Department of Health and Human Services, Food and Drug Administration; 2018. <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm624226.htm>

Interim Estimates of 2018–19 Seasonal Influenza Vaccine Effectiveness — United States, February 2019

Joshua D. Doyle, MD, PhD^{1,2}; Jessie R. Chung, MPH²; Sara S. Kim, MPH²; Manjusha Gaglani, MBBS³; Chandni Raiyani, MPH³; Richard K. Zimmerman, MD⁴; Mary Patricia Nowalk, PhD⁴; Michael L. Jackson, PhD⁵; Lisa A. Jackson, MD⁵; Arnold S. Monto, MD⁶; Emily T. Martin, PhD⁶; Edward A. Belongia, MD⁷; Huong Q. McLean, PhD⁷; Angie Foust, MS²; Wendy Sessions, MPH²; LaShondra Berman, MS²; Rebecca J. Garten, PhD²; John R. Barnes, PhD²; David E. Wentworth, PhD²; Alicia M. Fry, MD²; Manish M. Patel, MD²; Brendan Flannery, PhD²

In the United States, annual vaccination against seasonal influenza is recommended for all persons aged ≥ 6 months (<https://www.cdc.gov/flu/protect/whoshouldvax.htm>). Effectiveness of seasonal influenza vaccine varies by season. During each influenza season since 2004–05, CDC has estimated the effectiveness of seasonal influenza vaccine to prevent laboratory-confirmed influenza associated with medically attended acute respiratory illness (ARI). This interim report uses data from 3,254 children and adults enrolled in the U.S. Influenza Vaccine Effectiveness Network (U.S. Flu VE Network) during November 23, 2018–February 2, 2019. During this period, overall adjusted vaccine effectiveness against all influenza virus infection associated with medically attended ARI was 47% (95% confidence interval [CI] = 34%–57%). For children aged 6 months–17 years, overall vaccine effectiveness was 61% (44%–73%). Seventy-four percent of influenza A infections for which subtype information was available were caused by A(H1N1)pdm09 viruses. Vaccine effectiveness was estimated to be 46% (30%–58%) against illness caused by influenza A(H1N1)pdm09 viruses. CDC recommends that health care providers continue to administer influenza vaccine because influenza activity is ongoing and the vaccine can still prevent illness, hospitalization, and death associated with currently circulating influenza viruses, or other influenza viruses that might circulate later in the season. During the 2017–18 influenza season, in which influenza A(H3N2) predominated, vaccination was estimated to prevent 7.1 million illnesses, 3.7 million medical visits, 109,000 hospitalizations, and 8,000 deaths (1). Vaccination can also reduce the severity of influenza-associated illness (2). Persons aged ≥ 6 months who have not yet been vaccinated this season should be vaccinated.

Methods used by the U.S. Flu VE Network have been published previously (3). At five study sites (Michigan, Pennsylvania, Texas, Washington, and Wisconsin), patients aged ≥ 6 months seeking outpatient medical care for an ARI with cough within 7 days of illness onset were enrolled. Study enrollment began after local surveillance identified increasing weekly influenza activity or one or more laboratory-confirmed cases of influenza per week for 2 consecutive weeks. Patients were eligible for enrollment if they met the following criteria: 1) were aged ≥ 6 months on September 1, 2018, and thus

eligible for vaccination; 2) reported an ARI with cough with onset ≤ 7 days; and 3) had not been treated with influenza antiviral medication (e.g., oseltamivir) during this illness. After obtaining informed consent from patients or their guardians, participants or their proxies were interviewed to collect demographic data, information on general and current health status and symptoms, and 2018–19 influenza vaccination status. Nasal and oropharyngeal swabs (or nasal swabs alone for children aged < 2 years) were collected to obtain respiratory specimens. Nasal and oropharyngeal swabs were placed together in a single tube of viral transport medium and tested at U.S. Flu VE Network laboratories using CDC's real-time reverse transcription–polymerase chain reaction (real-time RT-PCR) protocol for detection and identification of influenza viruses. Participants (including children aged < 9 years, who require 2 vaccine doses during their first vaccination season) were considered vaccinated if they received ≥ 1 dose of any seasonal influenza vaccine ≥ 14 days before illness onset, according to medical records and registries (at the Wisconsin site); medical records and self-report (at the Pennsylvania, Texas, and Washington sites); or self-report only (at the Michigan site). Vaccine effectiveness against all influenza virus types combined and against viruses by type/subtype was estimated as $100\% \times (1 - \text{odds ratio})$.^{*} Estimates were adjusted for study site, age group, sex, race/ethnicity, self-rated general health, number of days from illness onset to enrollment, and month of illness (4-week intervals) using logistic regression. Interim vaccine effectiveness estimates for the 2018–19 season were based on patients enrolled through February 2, 2019.

Among the 3,254 children and adults with ARI enrolled at the five study sites from November 23, 2018, through February 2, 2019, a total of 465 (14%) tested positive for influenza virus by real time RT-PCR, including 456 (98%) for influenza A viruses and nine (2%) for influenza B viruses (Table 1). Among 394 subtyped influenza A viruses, 293 (74%) were A(H1N1)pdm09 viruses, and 101 (26%) were A(H3N2) viruses. Of the eight influenza B viruses with lineage information available, four belonged to the B/Victoria

^{*} $100\% \times (1 - \text{odds ratio})$ [ratio of odds of being vaccinated among outpatients with influenza-positive test results to the odds of being vaccinated among outpatients with influenza-negative test results].

TABLE 1. Influenza test results and seasonal vaccination status among patients with medically attended acute respiratory illness (N = 3,254), by selected characteristics — U.S. Influenza Vaccine Effectiveness Network, November 23, 2018—February 2, 2019*

Characteristic	Test result status			Vaccination status [†]		
	Influenza-positive no. (%)	Influenza-negative no. (%)	P-value [§]	No. of patients	Vaccinated No. (%)	P-value [§]
Overall	465 (14)	2,789 (86)	—	3,254	1,789 (55)	—
Study site						
Michigan	76 (15)	438 (85)	0.006	514	314 (61)	<0.001
Pennsylvania	101 (17)	511 (83)		612	335 (55)	
Texas	72 (10)	637 (90)		709	327 (46)	
Washington	171 (16)	915 (84)		1,086	647 (60)	
Wisconsin	45 (14)	288 (86)		333	166 (50)	
Sex						
Male	208 (16)	1,128 (84)	0.08	1,336	704 (53)	0.03
Female	257 (13)	1,660 (87)		1,917	1,084 (57)	
Age group						
6 mos–8 yrs	118 (15)	689 (85)	0.03	807	453 (56)	<0.001
9–17 yrs	55 (19)	237 (81)		292	120 (41)	
18–49 yrs	166 (15)	932 (85)		1,098	461 (42)	
50–64 yrs	75 (13)	520 (87)		595	369 (62)	
≥65 yrs	51 (11)	411 (89)		462	386 (84)	
Race/Ethnicity[¶]						
White	296 (14)	1,895 (86)	0.33	2,191	1,275 (58)	<0.001
Black	63 (17)	318 (83)		381	165 (43)	
Other race	53 (15)	290 (85)		343	199 (58)	
Hispanic	51 (16)	277 (84)		328	143 (44)	
Self-rated health status						
Fair/Poor	21 (9)	223 (91)	0.003	244	145 (59)	0.12
Good	105 (13)	723 (87)		828	475 (57)	
Very good	177 (14)	1,050 (86)		1,227	651 (53)	
Excellent	162 (17)	791 (83)		953	517 (54)	
Illness onset to enrollment (days)						
<3	191 (19)	795 (81)	<0.001	986	509 (52)	0.01
3–4	176 (15)	1,037 (85)		1,213	666 (55)	
5–7	98 (9)	957 (91)		1,055	614 (58)	
Influenza test result						
Negative	—	2,789	—	2,789	1,591 (57)	—
Influenza B positive	9 (2)	—		9	3 (33)	
B/Yamagata	4 (50)**	—		4	2 (50)	
B/Victoria	4 (50)**	—		4	1 (25)	
B lineage pending	1 (—)	—		1	0 (0)	
Influenza A positive	456 (98)	—		456	195 (43)	
A (H1N1)pdm09	293 (74) ^{††}	—		293	125 (43)	
A (H3N2)	101 (26) ^{††}	—		101	42 (42)	
A subtype pending	62 (—)	—		62	28 (45)	

* Sex was unknown for one patient, race/ethnicity for 11 patients, and self-rated health status for two patients.

[†] Defined as having received ≥1 dose of influenza vaccine ≥14 days before illness onset. A total of 78 participants who received the vaccine ≤13 days before illness onset were excluded from the study sample.

[§] The chi-square statistic was used to assess differences between the numbers of persons with influenza-negative and influenza-positive test results, in the distribution of enrolled patient and illness characteristics, and in differences between groups in the percentage vaccinated.

[¶] Patients were categorized into one of four mutually exclusive racial/ethnic populations: white, black, other race, and Hispanic. Persons identifying as Hispanic might have been of any race. Persons identifying as white, black, or other race were non-Hispanic.

** Percentage for which lineage information was available (n = 8).

^{††} Percentage for which subtype information was available (n = 394).

lineage and four belonged to the B/Yamagata lineage. The proportion of patients with influenza differed by study site, age group, self-rated health status, and interval from illness onset to enrollment. The percentage of all ARI patients who were vaccinated ranged from 46% to 61% among study sites and differed by study site, sex, age group, race/ethnicity, and interval from illness onset to enrollment.

Among participants, 43% of those with influenza had received the 2018–19 seasonal influenza vaccine, compared with 57% of influenza-negative participants (Table 2). The adjusted vaccine effectiveness against medically attended ARI caused by all influenza virus types combined was 47% (95% CI = 34%–57%). Vaccine effectiveness for all ages was 46% (30%–58%) against medically attended ARI caused by

TABLE 2. Number and percentage outpatients with acute respiratory illness and cough (N = 3,254) receiving 2018–19 seasonal influenza vaccine, by influenza test result status, age group, and vaccine effectiveness* against all influenza A and B and against virus type A(H1N1)pdm09 — U.S. Influenza Vaccine Effectiveness Network, November 23, 2018–February 2, 2019

Influenza type/Age group	Influenza-positive		Influenza-negative		Vaccine effectiveness*	
	Total	Vaccinated no. (%)	Total	Vaccinated no. (%)	Unadjusted % (95% CI)	Adjusted % (95% CI) [†]
Influenza A and B						
Overall	465	198 (43)	2,789	1,591 (57)	44 (32 to 54)	47 (34 to 57) [§]
Age group						
6 mos–17 yrs	173	58 (34)	926	515 (56)	60 (43 to 71)	61 (44 to 73) [§]
18–49 yrs	166	58 (35)	932	403 (43)	30 (1 to 50)	37 (9 to 56) [§]
≥50 yrs	126	82 (65)	931	673 (72)	29 (-6 to 52)	24 (-15 to 51)
Influenza A(H3N2)						
Overall	101	42 (42)	2,789	1,591 (57)	46 (20 to 64)	44 (13 to 64) [§]
Influenza A(H1N1)pdm09						
Overall	293	125 (43)	2,789	1,591 (57)	44 (29 to 56)	46 (30 to 58) [§]
Age group						
6 mos–17 yrs	106	37 (35)	926	515 (56)	57 (35 to 72)	62 (40 to 75) [§]
18–49 yrs	113	38 (34)	932	403 (43)	33 (0 to 56)	45 (14 to 64) [§]
≥50 yrs	74	50 (68)	931	673 (72)	20 (-33 to 52)	8 (-59 to 46)

* Vaccine effectiveness was estimated as $100\% \times (1 - \text{odds ratio [ratio of odds of being vaccinated among outpatients with influenza-positive test results to the odds of being vaccinated among outpatients with influenza-negative test results]})$; odds ratios were estimated using logistic regression.

[†] Adjusted for study site, age group, sex, race/ethnicity, self-rated general health, number of days from illness onset to enrollment, and month of illness (4-week intervals) using logistic regression.

[§] Statistically significant at $p < 0.05$.

A(H1N1)pdm09 virus infection and 44% (13%–64%) against influenza A(H3N2) virus infection. Among children aged 6 months–17 years, vaccine effectiveness against all influenza virus types was 61% (44%–73%), and effectiveness against influenza A(H1N1)pdm09 was 62% (40%–75%). Among adults ≥50 years, vaccine effectiveness against all influenza types and influenza A(H1N1)pdm09 was 24% (-15% to 51%) and 8% (-59% to 46%), respectively; neither were significant.

Discussion

Influenza activity remains elevated in the United States (4). Overall, influenza A(H1N1)pdm09 viruses have predominated in most of the country, although circulation of influenza A(H3N2) and low levels of influenza B viruses have also been observed. Effectiveness of influenza vaccines in reducing the risk for medically attended influenza illness has ranged from approximately 40%–60% across all ages during seasons when most circulating influenza viruses are antigenically like the recommended influenza vaccine components. The overall interim estimate of 47% vaccine effectiveness against influenza A(H1N1)pdm09 in all age groups is similar to that observed during the most recent A(H1N1)pdm09 predominant season (45%) in 2015–16 (3), but lower than a meta-analysis of vaccine effectiveness against A(H1N1)pdm09 since the 2010–11 season in the United States (5). This interim estimate also is lower than the recently reported interim estimates of 72% effectiveness against A(H1N1)pdm09 in Canada during the 2018–19 season (6) and 78% against A(H1N1)pdm09 in Australia during the 2018 Southern Hemisphere

influenza season (7). The reasons for these differences might include limited sample size caused by low attack rates in some age groups, geographic differences in circulating viruses, and genetic variation within virus subtypes (4). Of note, vaccine effectiveness against A(H1N1)pdm09 among children and adolescents aged 6 months–17 years (62%) was similar to that observed during the 2015–16 season in this age group (49%–63%) (3). Among adults aged ≥50 years, interim estimates of effectiveness were not significant. Vaccine effectiveness against A(H3N2) virus infection was 44% (95% CI = 13%–64%) but a limited number of A(H3N2) viruses were detected. Several more weeks of influenza are likely, and CDC continues to recommend influenza vaccination while influenza viruses are circulating in the community. Vaccination can protect against infection with influenza viruses that are currently circulating, as well as those that may circulate later in the season.

Vaccination remains the best method for preventing influenza and its potentially serious complications, including those that can result in hospitalization and death. In particular, vaccination has been found to reduce the risk for influenza-associated deaths in children (8). During past seasons, including the 2017–18 season, approximately 80% of reported pediatric influenza-associated deaths have occurred in children who were not vaccinated. Vaccination also has been found to reduce the risk for influenza-associated hospitalization in pregnant women (9) and can reduce the risk for cardiac events among persons with heart disease (10). CDC recommends antiviral treatment for any patient with suspected or confirmed influenza who is hospitalized, has severe or progressive illness, or is at high risk

for complications from influenza, regardless of vaccination status or results of point-of-care influenza diagnostic tests.[†] Antiviral treatment also can be considered for any previously healthy symptomatic outpatient not at high risk for complications, with confirmed or suspected influenza, if treatment can be started within 48 hours of illness onset.

The findings in this report are subject to at least four limitations. First, sample sizes are smaller than in recent interim reports, resulting in wide confidence intervals, particularly in adults aged ≥ 50 years. The small sample size also limits the number of age groups included in this analysis. This limitation is common among interim vaccine effectiveness reports during mild or late influenza seasons. End-of-season vaccine effectiveness estimates could change as additional patient data become available or if a change in circulating viruses occurs later in the season. Second, vaccination status included self-report at four of five sites; end-of-season vaccine effectiveness estimates based on updated documentation of vaccination status might differ from interim estimates. For this reason, the type of vaccine received by participants (e.g., egg-based, cell culture-based, or recombinant antigen) is not available at this time, although this information will be updated at the end of the season. Third, an observational study design has greater potential for confounding and bias than do randomized clinical trials. However, the test-negative design is widely used in vaccine effectiveness studies and has been used by the U.S. Flu VE Network to estimate vaccine effectiveness for previous influenza seasons. Finally, the vaccine effectiveness estimates in this report are limited to the prevention of outpatient medical visits rather than more severe illness outcomes, such as hospitalization or death; data from studies measuring vaccine effectiveness against more severe outcomes will be available at a later date.

Vaccination prevents a substantial number of influenza-related illnesses, hospitalizations, and deaths annually. However, better protection and improved vaccination coverage are needed to realize the full potential of influenza vaccines.

[†] A complete summary of guidance for antiviral use is available at <https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm>. Groups at high risk for influenza complications include the following: children aged < 2 years; adults aged ≥ 65 years; persons with chronic pulmonary conditions (including asthma); persons with cardiovascular disease (except hypertension alone); persons with renal, hepatic, or hematologic (including sickle cell) disease; persons with metabolic disorders (including diabetes mellitus); persons with neurologic and neurodevelopmental conditions (including disorders of the brain, spinal cord, peripheral nerves and muscles, such as cerebral palsy, epilepsy [seizure disorders], stroke, intellectual disability [mental retardation], moderate to severe developmental delay, muscular dystrophy, or spinal cord injury); persons with immunosuppression, including that caused by medications or by human immunodeficiency virus infection; women who are pregnant or ≤ 2 weeks postpartum; persons aged < 19 years who are receiving long-term aspirin or salicylate-containing medications; American Indian/Alaska Natives; persons with morbid obesity (i.e., body-mass index ≥ 40); and residents of nursing homes and other chronic-care facilities.

Evaluation of influenza vaccine effectiveness is an essential component of ongoing efforts to improve influenza vaccines. Influenza activity remains elevated in the United States, highlighting the importance of vaccination. CDC will continue to monitor influenza disease throughout the season to better understand the impact of vaccination, identify factors associated with reduced protection, and support efforts to improve influenza vaccines.

Acknowledgments

Alejandro Arroliga, Madhava Beeram, Kelsey Bounds, Wencong Chen, Lydia Clipper, Renee Day, Amanda Drake, Mary Kylberg, Michael Smith, Kempapura Murthy, Teresa Ponder, Michael Reis, Natalie Settele, Jennifer Thomas, Jamie Walkowiak, patients and staff from all participating clinics, Baylor Scott & White Health and Texas A&M University Health Science Center College of Medicine, Temple, Texas; Rose Azrak, G.K. Balasubramani, Todd M. Bear, Duane Eisaman, Heather Eng, Andrew Fackler, Edward Garofolo, Robert Hickey, Philip Iozzi, Monika Johnson, Stephanie Kirk, Jason A. Lyons, Donald B. Middleton, Krissy K. Moehling, Jonathan M. Raviotta, Evelyn C. Reis, Bret Rosenblum, Sean Saul, Theresa Sax, Michael Susick, Joe Suyama, Leonard F. Urbanski, Alexandra Weissman, John V. Williams, University of Pittsburgh Schools of the Health Sciences and University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania; Zoe Kappelman, Erika Kiniry, Lawrence Madziwa, Matt Nguyen, Suzie Park, C. Hallie Phillips, Stacie Wellwood, Kaiser Permanente Washington Health Research Institute, Seattle, Washington; Allen Achkar, Elizabeth Alleman, Trinh Anh Minh, Habeeb Al-Shohate, Gabriela Augustinaitis, Sarah Bauer, Danielle Carroll, Caroline K. Cheng, Robert Deblander III, Michelle Groesbeck, Emileigh Johnson, Anne Kaniclides, Armanda Kimberly, Jenna Kiryakos, Marym Kuril, Lois E. Lamerato, Ryan E. Malosh, Maria Matta, E.J. McSpadden, Madeleine Mendelow, Joshua G. Petrie, Niharika Rajesh, Bryan Richardson, Stephanie Robinson, Hannah Segaloff, Caleb Sokolowski, Rachael Swanson, Rachel Truscon, University of Michigan, Ann Arbor, and Henry Ford Health System, Detroit, Michigan; Elizabeth Armagost, Theresa Balinghasay, Tamara Braund, Deanna Cole, Carrie Curtis, Tom Dalcher, Alicia Easley, Terry Foss, Wayne Frome, Hannah Gourdoux, Gregg Greenwald, Sherri Guzinski, Kayla Hanson, Linda Heeren, Lynn Ivacic, Marie Janz, Tara Johnson, Julie Karl, Jennifer King, Tamara Kronenwetter Koepel, Diane Kohnhorst, Sarah Kopitzke, Erik Kronholm, Marcia Lichtenwald, Carrie Marcis, Karen McGreevey, Jennifer Meece, Nidhi Mehta, Vicki Moon, Madalyn Palmquist, Nan Pan, Rebecca Pilsner, DeeAnn Polacek, Martha Presson, Lauren Putnam, Carla Rottscheit, Crystal Sabatke, Jacklyn Salzwedel, Megan Sauer, Julian Savu, Ram Shrestha, Elisha Stefanski, Patrick Stockwell, Sandy Strey, Marshfield Clinic Research Institute, Marshfield, Wisconsin; Juliana DaSilva, Shoshona Le, Thomas Stark, Influenza Division, National Center for Immunization and Respiratory Diseases, CDC.

References

Summary

What is already known about this topic?

Annual vaccination against seasonal influenza is recommended for all U.S. persons aged ≥ 6 months. Effectiveness of seasonal influenza vaccine varies by season.

What is added by this report?

On the basis of data from the U.S. Influenza Vaccine Effectiveness Network on 3,254 children and adults with acute respiratory illness during November 23, 2018–February 2, 2019, the overall estimated effectiveness of seasonal influenza vaccine for preventing medically attended, laboratory-confirmed influenza virus infection was 47%.

What are the implications for public health practice?

Vaccination remains the best way to protect against influenza and its potentially serious complications. CDC continues to recommend influenza vaccination while influenza viruses are circulating in the community.

Corresponding author: Joshua D. Doyle, JDoyle2@cdc.gov, 404-718-6818.

¹Epidemic Intelligence Service, CDC; ²Influenza Division, National Center for Immunization and Respiratory Diseases, CDC; ³Baylor Scott & White Health, Texas A&M University Health Science Center College of Medicine, Temple, Texas; ⁴University of Pittsburgh Schools of the Health Sciences and University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania; ⁵Kaiser Permanente Washington Health Research Institute, Seattle, Washington; ⁶University of Michigan School of Public Health, Ann Arbor, Michigan; ⁷Marshfield Clinic Research Institute, Marshfield, Wisconsin.

All authors have completed and submitted the ICMJE form for disclosure of potential conflicts of interest. Richard Zimmerman reports grants from Sanofi Pasteur, Pfizer, and Merck & Co., outside the submitted work; Arnold S. Monto reports personal fees from Sanofi Pasteur and Seqirus, outside the submitted work; Emily T. Martin reports personal fees from Pfizer, outside the submitted work; Michael L. Jackson reports grants from Sanofi Pasteur, outside the submitted work; Mary Patricia Nowalk reports grants from Merck & Co, Inc. and Pfizer, outside the submitted work; and Huong Q. McLean reports grants from Seqirus, outside the submitted work. No other potential conflicts of interest were disclosed.

1. Rolfes MA, Flannery B, Chung J, et al. Effects of influenza vaccination in the United States during the 2017–2018 influenza season. *Clin Infect Dis* 2019. Epub February 2, 2019.
2. Arriola C, Garg S, Anderson EJ, et al. Influenza vaccination modifies disease severity among community-dwelling adults hospitalized with influenza. *Clin Infect Dis* 2017;65:1289–97. <https://doi.org/10.1093/cid/cix468>
3. Jackson ML, Chung JR, Jackson LA, et al. Influenza vaccine effectiveness in the United States during the 2015–2016 season. *N Engl J Med* 2017;377:534–43. <https://doi.org/10.1056/NEJMoa1700153>
4. Blanton L, Dugan VG, Elal AIA, et al. Update: influenza activity—United States, September 30, 2018–February 2, 2019. *MMWR Morb Mortal Wkly Rep* 2019;68:125–34.
5. Belongia EA, Simpson MD, King JP, et al. Variable influenza vaccine effectiveness by subtype: a systematic review and meta-analysis of test-negative design studies. *Lancet Infect Dis* 2016;16:942–51. [https://doi.org/10.1016/S1473-3099\(16\)00129-8](https://doi.org/10.1016/S1473-3099(16)00129-8)
6. Skowronski DM, Leir S, Sabaiduc S, et al. Interim estimates of 2018/19 vaccine effectiveness against influenza A(H1N1)pdm09, Canada, January 2019. *Euro Surveill* 2019;24:1900055. <https://doi.org/10.2807/1560-7917.ES.2019.24.4.1900055>
7. Australian Government Department of Health. Information brief: 2018 influenza season in Australia. Canberra, Australia: Australian Government Department of Health; 2016. [http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-ozflu-flucurr.htm/\\$File/2018-Season-Summary.pdf](http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-ozflu-flucurr.htm/$File/2018-Season-Summary.pdf)
8. Flannery B, Reynolds SB, Blanton L, et al. Influenza vaccine effectiveness against pediatric deaths: 2010–2014. *Pediatrics* 2017;139:e20164244. <https://doi.org/10.1542/peds.2016-4244>
9. Thompson MG, Kwong JC, Regan AK, et al. Influenza vaccine effectiveness in preventing influenza-associated hospitalizations during pregnancy: a multi-country retrospective test negative design study, 2010–2016. *Clin Infect Dis* 2018. Epub October 11, 2018.
10. Udell JA, Zawi R, Bhatt DL, et al. Association between influenza vaccination and cardiovascular outcomes in high-risk patients: a meta-analysis. *JAMA* 2013;310:1711–20. PubMed <https://doi.org/10.1001/jama.2013.279206>

Days' Supply of Initial Opioid Analgesic Prescriptions and Additional Fills for Acute Pain Conditions Treated in the Primary Care Setting — United States, 2014

Mallika L. Mundkur, MD¹; Jessica M. Franklin, PhD²; Younathan Abdia, PhD²; Krista F. Huybrechts, PhD²; Elisabetta Patorno, MD, DrPH²; Joshua J. Gagne, PharmD, ScD²; Tamra E. Meyer, PhD¹; Judy Staffa, PhD¹; Brian T. Bateman, MD²

During 2017, opioids were associated with 47,600 deaths in the United States, approximately one third of which involved a prescription opioid (1). Amid concerns that overprescribing to patients with acute pain remains an essential factor underlying misuse, abuse, diversion, and unintentional overdose, several states have restricted opioid analgesic prescribing (2,3). To characterize patterns of opioid analgesic use for acute pain in primary care settings before the widespread implementation of limits on opioid prescribing (2,3), patients filling an opioid analgesic prescription for acute pain were identified from a 2014 database of commercial claims. Using a logistic generalized additive model, the probability of obtaining a refill was estimated as a function of the initial number of days supplied. Among 176,607 patients with a primary care visit associated with an acute pain complaint, 7.6% filled an opioid analgesic prescription. Among patients who received an initial 7-day supply, the probability of obtaining an opioid analgesic prescription refill for nine of 10 conditions was <25%. These results suggest that a ≤7-day opioid analgesic prescription might be sufficient for most, but not all, patients seen in primary care settings with acute pain who appear to need opioid analgesics. However, treatment strategies should account for patient and condition characteristics, which might alternatively reduce or extend the anticipated duration of benefit from opioid analgesic therapy.

This analysis was based on a previously defined cohort used to characterize national patterns of prescribing for acute pain in primary care settings; details of cohort selection are described elsewhere (4). Briefly, adults who filled an opioid analgesic prescription within 7 days of an initial visit for any of 10 common acute pain conditions (back pain with radiculopathy, back pain without radiculopathy, neck pain, joint pain, tendon/bursal pain, muscle strains/sprains, musculoskeletal injury [e.g., ligamentous tears], urinary calculus, headache, and dental pain) evaluated in a primary care setting were identified using 2014 data from a large U.S. nationwide commercial insurer. The cohort excluded patients with history of previous opioid use, substance abuse, cancer, admission to hospice/hospital, or surgery during a baseline claims history of 6 months. Patients filling prescriptions for ≥30 days or for patch formulations also were excluded from this analysis on the assumption that, for these patients, clinicians intended to initiate long-term therapy. Patients who

had <30 days of follow-up or who had multiple pain conditions or multiple opioid analgesic prescriptions associated with the index primary care visit also were excluded. Patients included in the analysis could not have more than one of the 10 acute pain conditions (i.e., only a patient's first visit to a primary care provider that met inclusion criteria for the study was included in the analysis). Two statistical software packages were used to conduct the analyses: SAS (version 9.4; SAS Institute) and R (version 3.5.0; R Foundation for Statistical Computing).

The primary outcome of interest was opioid analgesic refills; any additional fill for oral opioid analgesics during the 30 days after the index fill was considered a refill. Refills were presumed to be an indication that the initial amount of medication prescribed was perceived as insufficient for the treatment of the patient's pain (5). Descriptive statistics concerning the number of days' supply, quantity dispensed, and morphine milligram equivalents of the index dispensing were calculated.

A logistic generalized additive model was fit for the probability of a refill as a smooth function of prescribed days' supply separately for each condition (5,6). Models were first fit without adjustment for covariates, so that the number of days' supply of the initial opioid analgesic fill was the only variable in the model; models were then fit with adjustment for age, sex, and Charlson comorbidity score (an index for estimating mortality from comorbid conditions in longitudinal studies) (7). Age was included in the model using a smooth term to allow for nonlinearity of the association between age and outcome. This model was used to estimate the probability of a refill associated with an initial supply of 3, 5, 7, 14, or 28 days for the average patient with each condition.

Among the 176,607 patients meeting selection criteria with a visit to a primary care setting for an episode of acute pain, a total of 13,440 (7.6%) filled an opioid analgesic prescription within 7 days of the initial visit; the percentage varied by condition, from 1,229 (3.5%) for headache to 302 (27.6%) for dental pain (Table 1). Among patients who filled a prescription for opioid analgesics, the median initial amount filled across conditions ranged from 4–7 days, 20–30 tablets or capsules, and 100–155 morphine milligram equivalents. A total of 2,392 (17.8%) patients who were dispensed an opioid analgesic (i.e., approximately 1% of the full cohort) obtained at least one

refill within 30 days after their initial prescription. Higher unadjusted rates of refills occurred among men (19.3%) than among women (15.8%), as well as among patients with recent history of use of benzodiazepines (26.5%), sedative hypnotics (20.0%), or gabapentin (28.3%), relative to the overall refill rate (17.8%) (Table 1).

The adjusted probability of a refill appeared to decrease with increasing initial prescription duration for some conditions (e.g., back pain with radiculopathy, nephrolithiasis, or dental pain), whereas for other conditions, the adjusted probability of a refill remained relatively constant regardless of the amount initially prescribed (e.g., joint pain or non-radicular back pain) (Table 2). For an initial prescription of 7 days, the adjusted probability of refill ranged from 0.11 (95% confidence interval = 0.09–0.14) for headache to 0.41 (0.19–0.68) for musculoskeletal injury (Table 2).

Discussion

These findings, drawn from the claims of nationwide commercial insurance beneficiaries, indicate that in 2014 the median duration of initial opioid analgesic prescriptions for

acute pain indications in a primary care setting was 4–7 days. Fewer than one in five patients who filled an opioid analgesic prescription received a refill, suggesting that in most cases an initial prescription of this duration was considered sufficient (and possibly even more than necessary) for patients seen in primary care settings with acute pain, consistent with recommendations in the 2016 CDC Guideline for Prescribing Opioids for Chronic Pain (8). These results also suggest that providing a 7-day supply might risk overtreatment for some of these conditions. However, depending upon the specific condition, the probability of receiving a refill after an initial 7-day supply ranged from 0.11–0.41, underscoring the potential variation among patients in time to recovery and variation in clinician practice, as well as possible variation in availability of nonopioid treatment methods. Because legal limits on prescribing are imposed despite such variation, these results suggest that health systems will need to be equipped to provide efficient mechanisms for opioid analgesic refills when they are clinically appropriate (9,10).

The findings in this report are subject to at least four limitations. First, this analysis preceded the implementation of many

TABLE 1. Quantity of opioid analgesics filled after initial visits for acute pain in primary care settings, by patient characteristics — United States, 2014

Characteristic	No. of patients with visit for acute pain	No. of patients with opioid fill within 7 days of initial visit (%)	Index fill: no. of days' supply dispensed,* median (IQR) (10th percentile) (90th percentile)	Index fill: no. of tablets/capsules dispensed,* median (IQR) (10th percentile) (90th percentile)	Index fill total MME dispensed,* median (IQR) (10th percentile) (90th percentile)	No. of patients with ≥1 refill (%)*
Sex						
Women	88,831	5,815 (6.5)	7 (4–10) (3–15)	30 (20–40) (15–60)	150 (100–225) (75–300)	918 (15.8)
Men	87,776	7,625 (8.7)	7 (4–10) (3–15)	30 (20–40) (15–60)	150 (100–225) (75–338)	1,474 (19.3)
Baseline medication						
Benzodiazepines	6,291	810 (12.9)	7 (5–10) (3–15)	30 (20–40) (15–60)	150 (120–250) (90–375)	215 (26.5)
Sedative hypnotics	4,325	375 (8.7)	7 (5–10) (3–15)	30 (21–40) (15–60)	150 (150–300) (100–480)	75 (20.0)
Gabapentinoids	1,515	187 (12.3)	8 (5–13) (4–15)	30 (30–60) (16–75)	200 (150–300) (90–450)	53 (28.3)
Baseline Charlson comorbidity score[†]						
0	152,669	11,680 (7.7)	6 (4–10) (3–15)	30 (20–40) (15–60)	150 (100–225) (75–300)	2,071 (17.7)
1	19,462	1,406 (7.2)	7 (5–10) (3–15)	30 (20–40) (15–60)	150 (120–300) (100–400)	256 (18.2)
2	3,533	279 (7.9)	8 (5–12) (3–15)	30 (30–50) (20–60)	200 (150–300) (100–450)	48 (17.2)
≥3	943	75 (8.0)	8 (5–11) (4–15)	30 (20–50) (15–60)	150 (150–300) (100–450)	17 (22.7)
Pain conditions[§]						
Joint pain	56,474	2,761 (4.9)	7 (5–10) (3–15)	30 (20–40) (15–60)	150 (113–250) (80–400)	521 (18.9)
Back pain without radiculopathy	41,862	5,602 (13.4)	7 (5–10) (3–15)	30 (20–40) (15–60)	150 (100–225) (75–300)	922 (16.5)
Headache	34,718	1,229 (3.5)	6 (4–10) (3–15)	30 (20–40) (12–100)	150 (100–240) (75–600)	144 (11.7)
Neck pain	11,943	1,101 (9.2)	7 (4–10) (3–15)	30 (20–40) (15–60)	150 (100–225) (75–300)	216 (19.6)
Tendonitis/Bursitis	13,371	457 (3.4)	7 (4–10) (3–15)	30 (20–40) (15–60)	150 (100–225) (75–300)	81 (17.7)
Muscular strains/Sprains	9,034	812 (9.0)	5 (3–7) (2–10)	20 (20–30) (12–42)	120 (100–150) (75–300)	132 (16.3)
Back pain with radiculopathy	3,925	684 (17.4)	7 (5–10) (3–15)	30 (20–40) (15–60)	150 (120–225) (100–300)	203 (29.7)
Nephrolithiasis	2,980	422 (14.2)	5 (3–8) (2–10)	26.5 (20–30) (15–50)	150 (100–225) (75–300)	81 (19.2)
Musculoskeletal injury	1,205	70 (5.8)	7 (4–10) (3–15)	30 (20–40) (15–60)	155 (125–225) (95–425)	21 (30.0)
Dental pain	1,095	302 (27.6)	4 (3–6) (2–10)	20 (15–30) (12–30)	100 (75–150) (60–225)	71 (23.5)

Abbreviations: IQR = interquartile range; MME = morphine milligram equivalents.

* Among patients with at least one fill for opioids for an episode of acute pain.

[†] An index for estimating mortality from comorbid conditions in longitudinal studies. <https://www.ncbi.nlm.nih.gov/pubmed/3558716>.

[§] Additional detail regarding *International Classification of Diseases, Ninth Revision* codes used to define conditions. <https://www.ncbi.nlm.nih.gov/pubmed/28971545>.

TABLE 2. Crude and adjusted* probabilities of refill by number of days initially supplied and acute pain condition

Condition	No. of days initially supplied (95% CI)				
	3	5	7	14	28
Joint pain					
Crude	0.20 (0.18–0.23)	0.20 (0.18–0.22)	0.20 (0.18–0.22)	0.18 (0.16–0.21)	0.12 (0.05–0.24)
Adjusted	0.20 (0.17–0.22)	0.20 (0.18–0.22)	0.20 (0.18–0.22)	0.18 (0.16–0.22)	0.12 (0.05–0.25)
Back pain without radiculopathy					
Crude	0.17 (0.16–0.19)	0.17 (0.16–0.18)	0.16 (0.15–0.17)	0.15 (0.13–0.17)	0.12 (0.09–0.17)
Adjusted	0.16 (0.14–0.18)	0.16 (0.14–0.17)	0.15 (0.14–0.17)	0.14 (0.12–0.16)	0.11 (0.08–0.16)
Headache					
Crude	0.14 (0.11–0.17)	0.13 (0.11–0.15)	0.12 (0.097–0.14)	0.10 (0.07–0.15)	0.12 (0.03–0.38)
Adjusted	0.13 (0.10–0.16)	0.12 (0.093–0.14)	0.11 (0.086–0.14)	0.09 (0.07–0.14)	0.10 (0.02–0.31)
Neck pain					
Crude	0.22 (0.18–0.25)	0.21 (0.18–0.24)	0.20 (0.18–0.22)	0.17 (0.13–0.22)	0.13 (0.06–0.26)
Adjusted	0.25 (0.20–0.30)	0.23 (0.19–0.28)	0.22 (0.19–0.26)	0.19 (0.14–0.25)	0.13 (0.06–0.26)
Tendonitis/Bursitis					
Crude	0.17 (0.12–0.22)	0.17 (0.13–0.21)	0.17 (0.14–0.21)	0.18 (0.12–0.26)	0.21 (0.07–0.48)
Adjusted	0.17 (0.12–0.23)	0.17 (0.13–0.22)	0.18 (0.14–0.22)	0.19 (0.12–0.27)	0.21 (0.07–0.49)
Muscular strains/Sprains					
Crude	0.17 (0.13–0.20)	0.16 (0.13–0.19)	0.15 (0.12–0.18)	0.13 (0.07–0.21)	0.09 (0.02–0.31)
Adjusted	0.16 (0.13–0.20)	0.16 (0.13–0.19)	0.15 (0.12–0.18)	0.13 (0.07–0.22)	0.09 (0.02–0.32)
Back pain with radiculopathy					
Crude	0.31 (0.24–0.39)	0.33 (0.27–0.40)	0.28 (0.21–0.35)	0.21 (0.12–0.34)	—†
Adjusted	0.24 (0.16–0.35)	0.27 (0.20–0.36)	0.21 (0.14–0.30)	0.15 (0.07–0.29)	—†
Nephrolithiasis					
Crude	0.21 (0.16–0.26)	0.20 (0.16–0.25)	0.20 (0.15–0.25)	0.18 (0.08–0.35)	0.15 (0.02–0.61)
Adjusted	0.22 (0.15–0.31)	0.22 (0.15–0.29)	0.21 (0.14–0.30)	0.19 (0.08–0.39)	0.16 (0.02–0.65)
Musculoskeletal injury					
Crude	0.26 (0.12–0.47)	0.49 (0.27–0.72)	0.37 (0.18–0.62)	0.41 (0.13–0.77)	—†
Adjusted	0.21 (0.086–0.44)	0.55 (0.30–0.79)	0.41 (0.19–0.68)	0.48 (0.15–0.84)	—†
Dental pain					
Crude	0.27 (0.21–0.33)	0.23 (0.19–0.29)	0.20 (0.14–0.28)	0.12 (0.04–0.31)	0.04 (0.003–0.39)
Adjusted	0.27 (0.21–0.33)	0.23 (0.18–0.29)	0.20 (0.14–0.28)	0.12 (0.04–0.31)	0.04 (0.003–0.39)

Abbreviation: CI = confidence interval.

* Adjusted for age, sex, and Charlson comorbidity score. <https://www.ncbi.nlm.nih.gov/pubmed/3558716>. Probabilities calculated for the “average patient.”

† Estimate is not informative because of sparse data. 28 days’ supply estimates are outside the range of data for most conditions.

prescribing limits on opioids (2,3). Accordingly, compared with filling behaviors observed during the period assessed by this study (i.e., 2014), observed filling behaviors in more recent years might be distinct, potentially influenced by factors external to the patient-physician interaction, including policies enforced by states, health systems, or private stakeholders. Second, although absence of a refill was used as a surrogate for adequacy of the initially dispensed supply for controlling pain, in addition to a need for additional opioid therapy, opioid refills might reflect physical dependence, withdrawal, or the need for additional pain control that could possibly be managed by nonopioid alternatives. Third, refills within 30 days of an initial opioid fill were presumed to be for treatment of the same pain condition as the initial fill, although given the lack of direct linkage between the diagnostic and prescription claims, this assumption could not be verified. Finally, certain patient characteristics, such as male sex and recent use of benzodiazepenes, were associated with higher refill rates; however, these associations should be interpreted with caution because

these factors might be associated with conditions requiring longer duration of treatment rather than being independent risk factors for additional fills. Although efforts were made to stratify analyses on distinct pain etiologies targeted by opioid analgesic prescribing in the primary care setting, some heterogeneity with respect to etiology, duration, and severity of pain within these categories is likely.

Future research could aim to further clarify the natural history of acute pain across a range of settings and conditions and to identify the risks and benefits of opioid analgesic use for acute pain through in-depth prospective interviews with patients. Simultaneously, research to evaluate the impact of recent opioid analgesic prescribing guidelines upon patient-centered outcomes including, but not limited to, adequacy of pain control, misuse of opioids, or development of opioid use disorder, is needed. Such measures might help determine whether existing strategies to regulate opioid analgesic prescribing result in an acceptable benefit-to-harms ratio. The findings in this report suggest that for several acute pain conditions

References

- Scholl L, Seth P, Kariisa M, Wilson N, Baldwin G. Drug and opioid-involved overdose deaths—United States, 2013–2017. *MMWR Morb Mortal Wkly Rep* 2018;67:1419–27. <https://doi.org/10.15585/mmwr.mm675152e1>
- Baker-White A. A look at state legislation limiting opioid prescriptions. Arlington, VA: Association of State and Territorial Health Officials; 2017. <http://www.astho.org/StatePublicHealth/A-Look-at-State-Legislation-Limiting-Opioid-Prescriptions/2-23-17/>
- American College of Physicians. Opioid prescribing: states aim to limit opioid prescriptions. Philadelphia, PA: American College of Physicians; 2018. <https://acpinternist.org/archives/2016/10/laws.htm>
- Mundkur ML, Rough K, Huybrechts KF, et al. Patterns of opioid initiation at first visits for pain in United States primary care settings. *Pharmacoepidemiol Drug Saf* 2018;27:495–503. <https://doi.org/10.1002/pds.4322>
- Scully RE, Schoenfeld AJ, Jiang W, et al. Defining optimal length of opioid pain medication prescription after common surgical procedures. *JAMA Surg* 2018;153:37–43. <https://doi.org/10.1001/jamasurg.2017.3132>
- Wood SN. Fast stable restricted maximum likelihood and marginal likelihood estimation of semiparametric generalized linear models. *J R Stat Soc B* 2011;73:3–36. <https://doi.org/10.1111/j.1467-9868.2010.00749.x>
- Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373–83. [https://doi.org/10.1016/0021-9681\(87\)90171-8](https://doi.org/10.1016/0021-9681(87)90171-8)
- Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *JAMA* 2016;315:1624–45. <https://doi.org/10.1001/jama.2016.1464>
- Bateman BT, Choudhry NK. Limiting the duration of opioid prescriptions: balancing excessive prescribing and the effective treatment of pain. *JAMA Intern Med* 2016;176:583–4. <https://doi.org/10.1001/jamainternmed.2016.0544>
- Drug Enforcement Administration. Electronic prescriptions for controlled substances (EPCS): general questions and answers. Washington, DC: US Department of Justice, Drug Enforcement Administration; 2010. https://www.deadiversion.usdoj.gov/ecomm/e_rx/faq/faq.htm

Summary

What is already known about this topic?

The prescribed duration of opioid analgesics for acute pain in the primary care setting varies by patient and condition.

What is added by this report?

For 10 acute pain conditions commonly managed in primary care settings, the probability of obtaining a refill after an initial 7-day opioid analgesic prescription ranged from 11% (headache) to 41% (musculoskeletal injury), with refill probability <25% for most conditions.

What are the implications for public health practice?

Initial opioid analgesic prescriptions of ≤7 days' duration appear sufficient for many patients seen in primary care settings with acute pain. Treatment strategies should account for patient- and condition-specific characteristics, which might reduce or extend duration of benefit from opioid analgesic therapy.

evaluated in primary care settings, opioid analgesics, when provided to treat pain, can generally be prescribed for durations of ≤7 days. However, health systems must anticipate variation in patient, condition, and other contextual characteristics that will influence the duration and intensity of pain and adopt mechanisms to ensure that additional access to both pharmacologic and nonpharmacologic therapy is available when required.

Acknowledgments

Food and Drug Administration, Silver Spring, Maryland.

Corresponding author: Mallika Mundkur, mallika.mundkur@fda.hhs.gov, 301-796-3677.

¹Office of Surveillance and Epidemiology, Center for Drug Evaluation and Research, Food and Drug Administration, Silver Spring, Maryland; ²Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts.

All authors have completed and submitted the ICMJE form for disclosure of potential conflicts of interest. Brian Bateman reports grants from the Food and Drug Administration (FDA) during the conduct of the study; grants to Brigham and Women's Hospital (BWH) from the National Institutes of Health, Pfizer, GSK, Baxalta, Lilly, and Pacira, and personal fees from Aetion, outside the submitted work. Elisabetta Patorno reports a career development grant K08AG055670 from the National Institute on Aging. She is investigator of investigator-initiated grants to BWH from Boehringer Ingelheim and GSK, outside the topic of the submitted work. Jessica Franklin reports grants from FDA during the conduct of the study. Joshua Gagne reports grants from Eli Lilly and Company and Novartis Pharmaceuticals Corporation to BWH and is a consultant to Aetion, Inc. and Optum, Inc., for work unrelated to the study. Krista Huybrechts reports grants from FDA during the conduct of the study and grants to BWH from Lilly, GlaxoSmithKline, and Pfizer Boehringer Ingelheim outside the submitted work. No other potential conflicts of interest were disclosed.

Increased Methamphetamine, Injection Drug, and Heroin Use Among Women and Heterosexual Men with Primary and Secondary Syphilis — United States, 2013–2017

Sarah E. Kidd, MD¹; Jeremy A. Grey, PhD¹; Elizabeth A. Torrone, PhD¹; Hillard S. Weinstock, MD¹

During 2013–2017, the national annual rate of reported primary and secondary (P&S) syphilis cases in the United States increased 72.7%, from 5.5 to 9.5 cases per 100,000 population (1). The highest rates of P&S syphilis are seen among gay, bisexual, and other men who have sex with men (collectively referred to as MSM) (2), and MSM continued to account for the majority of cases in 2017 (1). However, during 2013–2017, the P&S syphilis rate among women increased 155.6% (from 0.9 to 2.3 cases per 100,000 women), and the rate among all men increased 65.7% (from 10.2 to 16.9 cases per 100,000 men), indicating increasing transmission between men and women in addition to increasing transmission between men (1). To further understand these trends, CDC analyzed national P&S syphilis surveillance data for 2013–2017 and assessed the percentage of cases among women, men who have sex with women only (MSW), and MSM who reported drug-related risk behaviors during the past 12 months. Among women and MSW with P&S syphilis, reported use of methamphetamine, injection drugs, and heroin more than doubled during 2013–2017. In 2017, 16.6% of women with P&S syphilis used methamphetamine, 10.5% used injection drugs, and 5.8% used heroin during the preceding 12 months. Similar trends were seen among MSW, but not among MSM. These findings indicate that a substantial percentage of heterosexual syphilis transmission is occurring among persons who use these drugs, particularly methamphetamine. Collaboration between sexually transmitted disease (STD) control programs and partners that provide substance use disorder services will be important to address recent increases in heterosexual syphilis.

P&S syphilis case report data were extracted from the National Notifiable Diseases Surveillance System, the system through which CDC receives syphilis and other notifiable sexually transmitted disease data from all 50 states and the District of Columbia. P&S syphilis case report data include demographic information and also risk factor information, such as information about sex partners and drug use within the past 12 months, which is obtained through case interviews or investigation by the local health department.

For this analysis, men with syphilis were categorized as MSM if they reported having sex with any male partner in the last 12 months; men who reported having sex with only female partners in the last 12 months were categorized as MSW.

To assess drug-related behaviors, the following are included in the case report data as separate yes/no variables: use of injection drugs, methamphetamines, heroin, cocaine, crack, nitrates/poppers, erectile dysfunction drugs, other drugs, no drugs; and sex with a person who injects drugs within the last 12 months. The percentage of persons reporting use of each drug or behavior was calculated separately, using those with a “yes” response to the relevant variable as the numerator. For the injection drug use and sex with a person who injects drugs variables, the percentage of persons reporting these behaviors was calculated among persons with “yes” or “no” responses for that behavior (i.e., those with missing or unknown responses were excluded from the denominator). Because some local health departments collected data on the remaining drug use variables (e.g., methamphetamine and heroin use) differently and did not routinely report “no” responses to these variables, persons with missing and unknown responses for these remaining drug use variables were included in the denominator if they had a “yes” response to any of these variables and also did not have a “no” response to any of these variables (i.e., for these persons, missing and unknown responses were assumed to be “no” responses). SAS statistical software (version 9.3, SAS Institute Inc.) was used for all analyses.

During 2013–2017, the percentage of persons with P&S syphilis who reported methamphetamine use, sex with a person who injects drugs, injection drug use, or heroin use within the past 12 months more than doubled among women and MSW (Table 1). The percentage of persons with P&S syphilis reporting methamphetamine use increased from 6.2% to 16.6% among women, and from 5.0% to 13.3% among MSW, but decreased from 9.2% to 8.0% among MSM. The percentage of persons with P&S syphilis reporting sex with a person who injects drugs increased from 5.5% to 12.4% among women and from 3.6% to 9.3% among MSW, but increased only slightly among MSM (from 4.3% to 5.2%). Injection drug use increased from 4.0% to 10.5% among women with P&S syphilis and from 2.8% to 6.3% among MSW, but remained stable at 3.5% among MSM. Heroin use increased from 2.1% to 5.8% among women with P&S syphilis and from 0.8% to 2.7% among MSW, but remained relatively stable (increased from 0.7% to 0.8%) among MSM.

TABLE 1. Prevalence* of selected drug-related behaviors among women, men who have sex with women only (MSW), and men who have sex with men (MSM) with reported primary or secondary syphilis — National Notifiable Diseases Surveillance System, United States, 2013–2017

Behavior during past 12 months	No. (%)				
	2013	2014	2015	2016	2017
Used methamphetamine					
Women	69 (6.2)	92 (6.8)	184 (10.6)	317 (13.7)	456 (16.6)
MSW	88 (5.0)	151 (7.4)	194 (7.6)	347 (11.1)	482 (13.3)
MSM	805 (9.2)	867 (8.7)	855 (7.5)	1,039 (7.9)	1,132 (8.0)
Total†	987 (7.9)	1,136 (7.9)	1,253 (7.4)	1,738 (8.5)	2,106 (9.6)
Had sex with person who injects drugs					
Women	64 (5.5)	113 (8.3)	135 (7.9)	217 (9.9)	325 (12.4)
MSW	64 (3.6)	119 (5.8)	167 (6.4)	201 (6.6)	325 (9.3)
MSM	368 (4.3)	495 (5.0)	537 (4.7)	594 (4.6)	725 (5.2)
Total†	499 (4.2)	734 (5.3)	847 (5.2)	1,015 (5.5)	1,380 (6.7)
Used injection drugs					
Women	44 (4.0)	81 (6.1)	119 (7.0)	179 (8.1)	281 (10.5)
MSW	48 (2.8)	78 (3.7)	96 (3.6)	152 (4.8)	230 (6.3)
MSM	288 (3.5)	365 (3.6)	345 (2.9)	406 (3.1)	514 (3.5)
Total†	388 (3.5)	534 (3.8)	569 (3.4)	745 (3.9)	1,042 (4.9)
Used heroin					
Women	23 (2.1)	42 (3.1)	59 (3.4)	109 (4.7)	156 (5.8)
MSW	15 (0.8)	37 (1.8)	44 (1.7)	66 (2.1)	97 (2.7)
MSM	57 (0.7)	49 (0.5)	78 (0.7)	102 (0.8)	117 (0.8)
Total†	95 (0.8)	131 (0.9)	182 (1.1)	279 (1.4)	375 (1.7)

* Calculated among persons for whom data for that behavior were reported (persons with missing or unknown responses were excluded from the denominator).

† Includes case records with unknown sex and men with unknown data on sex of sex partner.

Among women with P&S syphilis, increases in methamphetamine use, sex with a person who injects drugs, injection drug use, and heroin use were observed in every region of the United States (Table 2). Among MSW with P&S syphilis, the increase in sex with a person who injects drugs was observed in every region, and the increases in methamphetamine, injection drug, and heroin use occurred in all regions except the Northeast (Table 3). Although trends were generally similar across regions, the prevalence of these behaviors among women and MSW with P&S syphilis varied considerably by region. In 2017, the percentages of both women and MSW reporting these behaviors were highest in the West and lowest in the Northeast. In the West, methamphetamine use during the past 12 months was reported by 34.8% of women with P&S syphilis and 25.0% of MSW with P&S syphilis. In addition, 22.6% of women with P&S syphilis in the West had sex with a person who injects drugs, and 21.2% used injection drugs (Table 2). In contrast, <3% of women or MSW with P&S syphilis in the Northeast reported these behaviors in 2017 (Table 2) (Table 3). Additional data on other behaviors and characteristics reported among persons with P&S syphilis, such as number of sex partners, HIV status, and other drug use data, are available online in a supplemental syphilis surveillance report (<https://www.cdc.gov/std/stats17/syphilis2017/>).

Discussion

Since reaching a historic low in the United States in 2000–2001, the annual national rate of reported P&S syphilis cases has increased, and the rate in 2017 (9.5 per 100,000 population) was the highest reported since 1993 (1). Until 2013, the increase was primarily among MSM, and rates of P&S syphilis among women remained low and relatively stable (3). However, during 2013–2017, the P&S syphilis rate increased among both men and women (1). This report demonstrates that, during this same period, the prevalences of methamphetamine use, sex with a person who injects drugs, injection drug use, and heroin use within the past 12 months more than doubled among MSW and women with P&S syphilis, but not among MSM with P&S syphilis.

These findings indicate that a substantial percentage of heterosexual syphilis transmission is occurring among persons who use methamphetamine, inject drugs or have sex with persons who inject drugs, or who use heroin, and that heterosexual syphilis and drug use are intersecting epidemics. A linkage between heterosexual syphilis and drug use has been observed previously. In the late 1980s and early 1990s, increases in heterosexual syphilis were associated with crack cocaine use (4,5). Drug use, particularly use of methamphetamine and injection drugs, is associated with sexual behaviors that increase the risk for acquiring syphilis and other sexually transmitted

TABLE 2. Prevalence* of selected drug-related behaviors among women with reported primary and secondary syphilis, by U.S. Census region† — National Notifiable Diseases Surveillance System, United States, 2013–2017

Behavior during past 12 months/Region	No. (%)				
	2013	2014	2015	2016	2017
Used methamphetamine					
West	50 (21.7)	63 (19.2)	119 (26.8)	230 (30.7)	310 (34.8)
Midwest	1 (0.8)	6 (3.4)	11 (6.6)	18 (7.7)	31 (13.0)
South	18 (2.7)	22 (3.0)	54 (5.5)	68 (6.0)	112 (8.0)
Northeast	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.5)	3 (1.4)
Total women	69 (6.2)	92 (6.8)	184 (10.6)	317 (13.7)	456 (16.6)
Had sex with person who injects drugs					
West	28 (14.5)	50 (18.4)	56 (16.6)	104 (20.8)	140 (22.6)
Midwest	10 (4.9)	17 (6.8)	13 (4.7)	37 (11.7)	57 (16.4)
South	26 (3.8)	39 (5.4)	62 (6.5)	71 (6.0)	122 (8.6)
Northeast	0 (0.0)	7 (6.0)	4 (2.8)	5 (2.6)	6 (2.7)
Total women	64 (5.5)	113 (8.3)	135 (7.9)	217 (9.9)	325 (12.4)
Used injection drugs					
West	19 (17.3)	36 (19.5)	47 (17.0)	73 (14.5)	134 (21.2)
Midwest	9 (4.5)	12 (5.0)	17 (6.5)	33 (10.6)	43 (12.5)
South	16 (2.2)	32 (4.1)	53 (5.2)	67 (5.6)	98 (6.7)
Northeast	0 (0.0)	1 (0.8)	2 (1.4)	6 (3.0)	6 (2.6)
Total women	44 (4.0)	81 (6.1)	119 (7.0)	179 (8.1)	281 (10.5)
Used heroin					
West	8 (3.5)	15 (4.6)	15 (3.4)	40 (5.4)	67 (7.8)
Midwest	1 (0.8)	8 (4.5)	7 (4.2)	14 (6.0)	9 (3.8)
South	14 (2.1)	18 (2.4)	36 (3.7)	49 (4.3)	75 (5.4)
Northeast	0 (0.0)	1 (0.8)	1 (0.7)	6 (3.1)	5 (2.3)
Total women	23 (2.1)	42 (3.1)	59 (3.4)	109 (4.7)	156 (5.8)

* Calculated among persons for whom data for that behavior were reported (persons with missing or unknown responses were excluded from the denominator).

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

diseases, including having multiple sex partners or concurrent sexual partnerships, inconsistent condom use, and exchange of sex for drugs or money (6–8). In addition, among persons who use drugs, stigma and mistrust of the health care system along with other social determinants of health (e.g., unstable housing, poverty, incarceration, and lack of health insurance or a medical home) might contribute to decreased health care utilization and reluctance or inability to identify and locate sex partners, resulting in delays in diagnosis and treatment (4,5). These complications likely contribute to increasing syphilis incidence in communities and pose significant challenges to syphilis prevention and control efforts.

Pilot projects have demonstrated the feasibility and benefit of implementing substance use disorder interventions in STD clinics (9,10). STD programs should consider partnering with substance use disorder prevention and treatment programs and other organizations that provide services to persons who use drugs in the local community. Heterosexual networks and sexual risk behaviors are linked with drug use, and STD programs should work with substance use programs to facilitate referrals to substance use disorder treatment services when

needed and to integrate STD and substance use disorder prevention and treatment services when possible. Substance use disorder programs and other community organizations that provide services to persons who use drugs can also provide opportunities for STD prevention and case-finding, through promotion of safer sex practices, condom distribution, and testing for syphilis and other sexually transmitted infections.

The findings in this report are subject to at least three limitations. First, syphilis case report data do not include data on opioid use other than heroin, so it was not possible to assess nonheroin opioid use among persons with syphilis. Second, cases with incomplete data on variables of interest were excluded from this analysis. Overall, depending on the year and variable, 18%–25% of reported cases of P&S syphilis among women, MSW, and MSM were missing data on methamphetamine use, sex with a person who injects drugs, injection drug use, or heroin use during 2013–2017. If persons whose records had missing data were less likely to have a risk factor, it is possible that this analysis overestimated the prevalence of these risk factors among persons with syphilis. Finally, because of stigma surrounding these risk behaviors, some persons might

TABLE 3. Prevalence* of selected drug-related behaviors among men who have sex with women only (MSW) with reported primary and secondary syphilis, by U.S. Census region† — National Notifiable Diseases Surveillance System, United States, 2013–2017

Behavior during past 12 months/Region	No. (%)				
	2013	2014	2015	2016	2017
Used methamphetamine					
West	55 (13.4)	112 (19.5)	121 (18.1)	232 (24.8)	313 (25.0)
Midwest	2 (1.1)	6 (2.4)	20 (8.1)	27 (8.5)	36 (11.6)
South	29 (2.9)	31 (3.0)	52 (3.8)	86 (5.6)	130 (7.6)
Northeast	2 (1.1)	2 (1.0)	1 (0.4)	2 (0.6)	3 (0.8)
Total MSW	88 (5.0)	151 (7.4)	194 (7.6)	347 (11.1)	482 (13.3)
Had sex with person who injects drugs					
West	19 (6.1)	56 (12.5)	61 (11.8)	80 (13.0)	126 (14.9)
Midwest	8 (2.5)	14 (3.5)	29 (6.2)	29 (6.0)	55 (11.5)
South	34 (3.4)	44 (4.5)	71 (5.2)	84 (5.3)	133 (7.6)
Northeast	3 (1.7)	5 (2.2)	6 (2.2)	8 (2.1)	11 (2.6)
Total MSW	64 (3.6)	119 (5.8)	167 (6.4)	201 (6.6)	325 (9.3)
Used injection drugs					
West	18 (10.2)	34 (8.5)	39 (8.8)	69 (10.2)	118 (13.0)
Midwest	3 (0.9)	6 (1.5)	13 (2.8)	24 (5.2)	22 (4.7)
South	24 (2.3)	35 (3.2)	39 (2.6)	51 (3.1)	85 (4.7)
Northeast	3 (1.6)	3 (1.3)	5 (1.7)	8 (2.0)	5 (1.1)
Total MSW	48 (2.8)	78 (3.7)	96 (3.6)	152 (4.8)	230 (6.3)
Used heroin					
West	4 (1.0)	12 (2.1)	16 (2.4)	26 (2.8)	48 (3.9)
Midwest	0 (0.0)	4 (1.6)	2 (0.8)	9 (2.8)	7 (2.3)
South	9 (0.9)	21 (2.1)	23 (1.7)	24 (1.6)	40 (2.4)
Northeast	2 (1.1)	0 (0.0)	3 (1.2)	7 (2.2)	2 (0.5)
Total MSW	15 (0.8)	37 (1.8)	44 (1.7)	66 (2.1)	97 (2.7)

* Calculated among persons for whom data for that behavior were reported (persons with missing or unknown responses were excluded from the denominator).

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

have been reluctant to disclose drug use, leading to misclassification and underestimates of the true percentage of persons with syphilis who used these drugs.

The recent increases in heterosexual syphilis, together with the concurrent increases in percentage of persons with P&S syphilis reporting methamphetamine use, sex with a person who injects drugs, injection drug use, and heroin use, are causes for concern. Heterosexual syphilis and drug use, particularly methamphetamine use, are connected and interrelated epidemics in the United States. Collaboration between STD control programs and partners that provide services for persons with substance use disorders will be essential to address recent increases in heterosexual syphilis and link patients to clinical and prevention services.

Corresponding author: Sarah E. Kidd, skidd@cdc.gov, 404-639-8314.

¹Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, CDC.

All authors have completed and submitted the ICMJE form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

Summary

What is already known about this topic?

During 2013–2017, the primary and secondary (P&S) syphilis rate increased 72.7% nationally and 155.6% among women.

What is added by this report?

During 2013–2017, reported methamphetamine, injection drug, and heroin use increased substantially among women and heterosexual men with P&S syphilis.

What are the implications for public health practice?

Heterosexual syphilis transmission and drug use, particularly methamphetamine use, are intersecting epidemics. Collaboration between sexually transmitted disease control programs and substance use disorder services providers will be essential to address recent increases in heterosexual syphilis transmission. Linking syphilis patients with substance use disorders to behavioral health services and providing syphilis screening for persons receiving substance use disorder services are needed to address these co-occurring conditions.

References

1. CDC. Sexually transmitted disease surveillance, 2017. Atlanta, GA: US Department of Health and Human Services, CDC; 2018. <https://www.cdc.gov/std/stats17/default.htm>
2. de Voux A, Kidd S, Grey JA, et al. State-specific rates of primary and secondary syphilis among men who have sex with men—United States, 2015. *MMWR Morb Mortal Wkly Rep* 2017;66:349–54. <https://doi.org/10.15585/mmwr.mm6613a1>
3. Patton ME, Su JR, Nelson R, Weinstock H; CDC. Primary and secondary syphilis—United States, 2005–2013. *MMWR Morb Mortal Wkly Rep* 2014;63:402–6.
4. Rolfs RT, Goldberg M, Sharrar RG. Risk factors for syphilis: cocaine use and prostitution. *Am J Public Health* 1990;80:853–7. <https://doi.org/10.2105/AJPH.80.7.853>
5. Gunn RA, Montes JM, Toomey KE, et al. Syphilis in San Diego County 1983–1992: crack cocaine, prostitution, and the limitations of partner notification. *Sex Transm Dis* 1995;22:60–6. <https://doi.org/10.1097/00007435-199501000-00010>
6. CDC. Methamphetamine use and HIV risk behaviors among heterosexual men—preliminary results from five northern California counties, December 2001–November 2003. *MMWR Morb Mortal Wkly Rep* 2006;55:273–7.
7. Zule WA, Costenbader EC, Meyer WJ Jr, Wechsberg WM. Methamphetamine use and risky sexual behaviors during heterosexual encounters. *Sex Transm Dis* 2007;34:689–94. <https://doi.org/10.1097/01.olq.0000260949.35304.22>
8. Flom PL, Friedman SR, Kottiri BJ, et al. Stigmatized drug use, sexual partner concurrency, and other sex risk network and behavior characteristics of 18- to 24-year-old youth in a high-risk neighborhood. *Sex Transm Dis* 2001;28:598–607. <https://doi.org/10.1097/00007435-200110000-00006>
9. Gryczynski J, Nordeck CD, Mitchell SG, et al. Pilot studies examining feasibility of substance use disorder (SUD) screening and treatment linkage at urban sexually transmitted disease (STD) clinics. *J Addict Med* 2017;11:350–6. <https://doi.org/10.1097/ADM.0000000000000327>
10. Yu J, Appel B, Rogers M, et al. Integrating intervention for substance use disorder in a healthcare setting: practice and outcomes in New York City STD clinics. *Am J Drug Alcohol Abuse* 2016;42:32–8. <https://doi.org/10.3109/00952990.2015.1094478>

Transmission Patterns in a Low HIV-Morbidity State — Wisconsin, 2014–2017

Katarina M. Grande, MPH¹; Casey L. Schumann, MS¹; M. Cheryl Bañez Ocfemia, MPH²; James M. Vergeront, MD¹; Joel O. Wertheim, PhD³; Alexandra M. Oster, MD²

Public health interviews (i.e., partner services), during which persons with diagnosed human immunodeficiency virus (HIV) infection name their sexual or needle-sharing partners (named partners), are used to identify HIV transmission networks to guide and prioritize HIV prevention activities. HIV sequence data, generated from provider-ordered drug resistance testing, can be used to understand characteristics of molecular clusters, a group of sequences for which each sequence is highly similar (linked) to all other sequences, and assess whether named partners are plausible HIV transmission partners. Although molecular data in higher HIV-morbidity states have been analyzed (1–3), few analyses exist for lower morbidity states (4), such as Wisconsin, which reported 4.6 HIV diagnoses per 100,000 persons aged ≥13 years in 2016 (5). The Wisconsin Division of Public Health (DPH) analyzed HIV sequence data generated from provider-ordered drug resistance testing and collected through routine HIV surveillance to identify molecular clusters and describe demographic and transmission risk characteristics among pairs of persons whose sequences were highly genetically similar (i.e., molecular linkages). In addition, overlap between partner linkages identified during public health interviews and molecular linkages was assessed. Overall, characteristics of molecular clusters in Wisconsin mirrored those from states with more HIV diagnoses, particularly in that most molecular linkages were observed among persons of the same race (78.2% of non-Hispanic blacks [blacks] linked to other blacks), the same transmission risk (90.2% of men who have sex with men [MSM] linked to other MSM), and the same age group (59.2% of persons aged 20–29 years linked to other persons aged 20–29 years). Among named partner linkages identified during interviews in which both persons also had a reported sequence, overlap of named partner and molecular linkages was moderate: 33.8% of named partners were plausible transmission partners according to available molecular data. Analysis of HIV sequence data is a useful tool for characterizing transmission patterns not immediately apparent using traditional public health interview data, even in a state with lower HIV morbidity. Prevention recommendations generated from national data (e.g., targeting preexposure prophylaxis for HIV-negative persons at high risk and implementing measures to maintain viral suppression among persons with HIV infection) also are relevant in a lower HIV-morbidity state.

HIV sequence data derived from standard drug resistance testing are reportable by laboratories to the Wisconsin DPH

and are maintained in a secure surveillance database. HIV-1 sequence data reported in Wisconsin during 2014–2017 for persons with HIV infection diagnosed through August 15, 2017, were analyzed using Secure HIV-TRACE (Secure HIV TRAnsmiSSion Cluster Engine).^{*} This web-based application performed pairwise comparisons of HIV-1 protease and partial reverse transcriptase to measure sequence relatedness and identify sequences that were highly genetically similar at a genetic distance of ≤0.015 substitutions per site (6,7). Pairs of closely related sequences formed molecular linkages, and a group of ≥2 linked sequences was considered a molecular cluster; these procedures are described elsewhere (1,6). Weights were applied to persons who had multiple molecular linkages so that each person was counted once (1). Analysis also was conducted to describe race/ethnicity, transmission risk, and age at diagnosis among pairs of persons whose sequences were linked (1). Multiple imputation using standard surveillance approaches was used to assign a transmission category for persons with missing risk factor information. Findings for linkages by race/ethnicity and transmission category were compared with previously published estimates from national analyses (1,8).

Named partner data and linkages were obtained through Wisconsin's PartnerServicesWeb, a CDC-developed database containing the results of public health interviews for persons with diagnosed HIV infection. To compare named partner linkages and molecular linkages, only named partnerships for which both persons had a reported HIV sequence were included in the analysis. These named partner linkages then were matched to the molecular linkages to determine whether named partners also had highly genetically similar sequences. SAS (version 9.3; SAS Institute) was used to conduct all analyses.

Using findings from a national analysis (1) as a comparison group, molecular linkages were examined for overall characteristics, sex, race, transmission category, and age partnerships. Among 1,401 persons who had HIV sequences reported to the Wisconsin DPH during 2014–2017, 433 (30.9%) had a molecular linkage to at least one other person (Table 1), representing 703 unique molecular linkages and 119 clusters (range = 2–20 persons per cluster). Among the 433 persons with one or more molecular linkages at the genetic distance threshold of ≤0.015, most were male (88.5%), black (57.3%), MSM (80.8%), and aged 20–29 years (50.3%) (Table 2).

^{*} Secure HIV-TRACE is a web-based tool developed by CDC with the University of California, San Diego and Temple University to detect, analyze, and visualize HIV molecular clusters.

TABLE 1. Comparison of human immunodeficiency virus (HIV) molecular clusters* identified in Wisconsin† and HIV molecular clusters — U.S. National HIV Surveillance System (NHSS),[§] Wisconsin, 2014–2017

Characteristic	No. of molecular clusters identified in Wisconsin	No. of molecular clusters identified in NHSS
No. of persons included in analysis	1,401	40,950
No. of persons with ≥1 molecular linkage	433	12,910
No. of links per person, median (range)	2 (1–13)	1 (1–83)
No. of clusters* in data set (persons per cluster, range)	119 (2–20)	3,584 (2–85)

* A molecular cluster describes a set of ≥2 linked sequences in which each sequence is connected, either directly or indirectly, to all other sequences.

† Analysis included HIV-1 genetic sequences reported through August 15, 2017, to the Wisconsin Division of Public Health for persons with HIV infection diagnosed during 2014–2017.

[§] <http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00126334-201512010-00017>.

Analysis of molecular partnerships by race/ethnicity revealed that blacks and non-Hispanic whites most commonly linked with persons of their own racial group (78.2% and 54.5%, respectively), whereas a minority of Hispanic/Latino persons linked with other Hispanics/Latinos (31.7%) (Table 3). Partnerships by transmission category indicated that MSM most commonly had molecular linkages with other MSM (90.2%) (Table 3). MSM who injected drugs also were primarily linked to MSM (88.3%).

Persons aged 20–29 years at diagnosis, the largest age group in the data set, were most likely to have molecular linkages with others aged 20–29 years (59.2%) (Table 3). Persons aged 13–19 years also were commonly linked with persons aged 20–29 years (58.2%). Among the 123 black MSM aged 20–29 years, 57.7% were molecularly linked to other persons aged 20–29 years (Table 3), and 19.2% were linked to persons aged 13–19 years. Among 139 named partner linkages identified during public health interviews in which both persons each had a reported sequence, 47 (33.8%) also had a molecular linkage, indicating that the named partners were plausible transmission partners.

Discussion

These findings from Wisconsin, that approximately one of every three persons with a reported HIV sequence was molecularly linked to at least one other person, largely align with those found in a national analysis, for which most data originated from states with higher HIV morbidity (1,8). The Wisconsin data also revealed that most molecular linkages occurred among persons of the same racial/ethnic, transmission risk, and age groups, with the highest percentages of same partnerships observed among blacks, MSM, and persons aged

TABLE 2. Comparison of persons identified as part of human immunodeficiency virus (HIV) molecular clusters* in Wisconsin† and persons identified as part of HIV molecular clusters — U.S. National HIV Surveillance System (NHSS),[§] Wisconsin, 2014–2017

Characteristic	No. of persons identified as part of molecular clusters in Wisconsin (%)	No. of persons identified as part of molecular clusters in NHSS (%)
Total persons with ≥1 molecular linkage	433 (100)	12,910 (100)
Sex		
Male	383 (88.5)	11,232 (87.0)
Female	50 (11.5)	1,678 (13.0)
Race/Ethnicity[¶]		
Black, non-Hispanic	248 (57.3)	5,445 (42.2)
White, non-Hispanic	112 (25.9)	3,992 (30.9)
Hispanic/Latino [¶]	55 (12.7)	2,884 (22.3)
Other**	18 (4.2)	589 (4.6)
Transmission category^{††}		
MSM	350 (80.8)	9,839 (76.2)
MSM who inject drugs	15 (3.5)	496 (3.8)
Men who inject drugs	5 (1.2)	309 (2.4)
Women who inject drugs	9 (2.1)	268 (2.1)
Heterosexual males	11 (2.5)	583 (4.5)
Heterosexual females	39 (9.0)	1,409 (10.9)
Other	3 (0.7)	6 (0.5)
Age at HIV diagnosis (yrs)		
<13	3 (0.7)	N/A
13–19	53 (12.2)	1,162 (9.0)
20–29	218 (50.3)	5,954 (46.1)
30–39	74 (17.1)	3,172 (24.6)
40–49	53 (12.2)	1,841 (14.3)
50–59	29 (6.7)	656 (5.1)
≥60	3 (0.7)	125 (1.0)

Abbreviations: MSM = men who have sex with men; N/A = not applicable.

* A molecular cluster describes a set of ≥2 linked sequences in which each sequence is connected, either directly or indirectly, to all other sequences.

† Analysis included HIV-1 genetic sequences reported through August 15, 2017, to the Wisconsin Division of Public Health for persons with HIV infection diagnosed during 2014–2017.

[§] <http://pt.wkhealth.com/pt/re/lwwgateway/landingpage.htm?sid=WKPTLP:landingpage&an=00126334-201512010-00017>.

[¶] Hispanics/Latinos can be of any race.

** Persons of other races/ethnicities include Asian, American Indian/Alaska Native, and multiple races.

†† Data have been statistically adjusted to account for missing transmission category using multiple imputation; therefore, values might not sum to column totals.

20–29 years. These findings also were consistent with findings from the national analysis (1,8) and validate the generalizability of characteristics of national molecular surveillance data to Wisconsin. Therefore, surveillance strategies to combine sequence data and interview data in identifying clusters are equally useful in states with lower HIV morbidity.

It is important to note that directionality cannot be inferred from molecular surveillance data alone, nor is it the intent of molecular cluster analysis to confirm transmission relationships. Rather, the patterns of persons with genetically related

TABLE 3. Comparison of potential transmission partnerships identified in human immunodeficiency virus (HIV) molecular clusters* in Wisconsin† and potential transmission partnerships — U.S. National HIV Surveillance System (NHSS),[§] Wisconsin, 2014–2017

Characteristic	Molecular clusters identified in Wisconsin		Molecular clusters identified in NHSS	
	Total no. of persons	No. of partnerships (row %)	Total no. of persons	No. of partnerships (row %)
Same-race partnerships[¶]				
Black, non-Hispanic	248	194 (78.2)	5,445	4,410 (81.0)
White, non-Hispanic	112	61 (54.5)	3,992	2,475 (62.0)
Hispanic/Latino**	55	17 (31.7)	2,884	1,500 (52.0)
Transmission category^{††} partnerships				
Among MSM, linkages to MSM	350	316 (90.2)	9,839	8,658 (88.0)
Among MSM who inject drugs, linkages to MSM	15	13 (88.3)	496	377 (76.0)
Among heterosexual females, linkages to MSM	39	12 (31.5)	1,409	409 (29.0)
Same-age group^{§§} partnerships (yrs)				
<13	3	0 (0.0)	N/A	N/A
13–19	53	8 (15.1)	N/A	N/A
20–29	218	129 (59.2)	N/A	N/A
30–39	74	12 (16.2)	N/A	N/A
40–49	53	8 (15.1)	N/A	N/A
50–59	29	6 (20.7)	N/A	N/A
≥60	3	0 (0.0)	N/A	N/A
Same-age group^{§§} partnerships of black MSM (yrs)				
<13	0	0 (0.0)	N/A	N/A
13–19	42	8 (19.0)	N/A	N/A
20–29	123	71 (57.7)	N/A	N/A
30–39	30	6 (20.0)	N/A	N/A
40–49	10	1 (10.0)	N/A	N/A
50–59	4	0 (0.0)	N/A	N/A
≥60	0	0 (0.0)	N/A	N/A

Abbreviations: MSM = men who have sex with men; N/A = not applicable.

* A molecular cluster describes a set of ≥2 linked sequences in which each sequence is connected, either directly or indirectly, to all other sequences.

† Analysis included HIV-1 genetic sequences reported through August 15, 2017, to the Wisconsin Division of Public Health for persons with HIV infection diagnosed during 2014–2017.

§ <http://pt.wkhealth.com/pt/re/lwwgateway/landingpage.htm?sid=WKPTLP:landingpage&an=00126334-201512010-00017>.

¶ Persons of other races represented <5% of the clustered sample and were not analyzed independently.

** Hispanics/Latinos can be of any race.

†† Data have been statistically adjusted to account for missing transmission category using multiple imputation; therefore, values might not sum to column totals.

§§ Age group is based on the person's age at HIV diagnosis. Same-age group partnerships were not assessed in Oster et al. <https://www.ncbi.nlm.nih.gov/pubmed/26302431>.

sequences are helpful in viewing population-level patterns of transmission and guiding prevention activities.

The findings in this report are subject to at least four limitations. First, the molecular clusters identified do not include all persons in the transmission network because not all persons with HIV infection know their status, some with diagnosed infection are not linked to HIV medical care, and some linked to care did not receive antiretroviral resistance testing or did not have their sequence reported. Second, in states with long-standing molecular reporting, two thirds of persons who are linked to care within 3 months of diagnosis have received drug resistance testing, although this linkage is less likely among older persons and black persons, and in areas with smaller populations (9). The demographics of persons who did not receive resistance testing were not assessed in the Wisconsin data set but could be a limitation if the national linkage biases exist in Wisconsin. Third, the comparison of molecular linkages with named partner linkages was limited to persons who

named partners and might not be representative of all persons with HIV infection in Wisconsin. Finally, imputation was used for persons with missing risk information (13%), which could affect the estimates.

Because most new diagnoses of HIV infection in Wisconsin occur in clinical outpatient settings rather than testing sites (10), it is common for a person with newly diagnosed HIV infection to already be established in care and have had resistance testing completed by the time a public health interview is conducted. This situation makes it possible for public health personnel to prioritize follow-up and intensive prevention measures (e.g., referral and linkage to preexposure prophylaxis for HIV-negative partners at high risk) for members of rapidly expanding clusters and their partners. Despite relatively low overlap between molecular data and named partner data, the results of public health interviews are still important for identifying persons at high risk for acquiring HIV infection, identifying undiagnosed HIV infection, and ensuring that

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

Identifying named partners through public health interviews is an important strategy for interrupting human immunodeficiency virus (HIV) transmission. Analyzing HIV molecular sequence data also can identify networks of potential transmission partners.

What is added by this report?

Most molecular linkages in Wisconsin were among persons within the same racial/ethnic, risk, and age groups. Among named partner linkages where both persons had an HIV sequence available, 33.8% also had a molecular linkage and were deemed plausible transmission partners.

What are the implications for public health practice?

Supplementing named partner data with molecular data might detect HIV transmission networks not elucidated through traditional public health interviews and identify opportunities for prevention in rapidly growing clusters of HIV infections in states with lower HIV morbidity.

persons with diagnosed HIV infection are engaged in HIV medical care. The combination of public health interview and molecular sequence data is a powerful new tool for understanding HIV transmission networks and identifying population- or individual-level interventions to reduce HIV transmission and improve health outcomes.

Acknowledgments

Council of State and Territorial Epidemiologists (CSTE) MMWR Intensive Training Program; John Moran, CSTE, Atlanta, Georgia; Mary Wedig, Wisconsin State Lab of Hygiene; Sergei Kosakovsky Pond, Steven Weaver, Temple University, Philadelphia, Pennsylvania.

Corresponding author: Katarina M. Grande, kgrande@publichealthmdc.com, 608-640-9430.

¹Division of Public Health, AIDS/HIV Program, Wisconsin Department of Health Services; ²Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, CDC; ³Department of Medicine, University of California, San Diego.

All authors have completed and submitted the ICMJE form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

References

- Oster AM, Wertheim JO, Hernandez AL, Ocfemia MC, Saduvala N, Hall HI. Using molecular HIV surveillance data to understand transmission between subpopulations in the United States. *J Acquir Immune Defic Syndr* 2015;70:444–51. <https://doi.org/10.1097/QAI.0000000000000809>
- Wertheim JO, Kosakovsky Pond SL, Forgione LA, et al. Social and genetic networks of HIV-1 transmission in New York City. *PLoS Pathog* 2017;13:e1006000. <https://doi.org/10.1371/journal.ppat.1006000>
- Little SJ, Kosakovsky Pond SL, Anderson CM, et al. Using HIV networks to inform real time prevention interventions. *PLoS One* 2014;9:e98443. <https://doi.org/10.1371/journal.pone.0098443>
- Chan PA, Hogan JW, Huang A, et al. Phylogenetic investigation of a statewide HIV-1 epidemic reveals ongoing and active transmission networks among men who have sex with men. *J Acquir Immune Defic Syndr* 2015;70:428–35. <https://doi.org/10.1097/QAI.0000000000000786>
- CDC. Diagnoses of HIV infection in the United States and dependent areas, 2016. HIV surveillance report, 2016, vol. 28. Atlanta, GA: US Department of Health and Human Services, CDC; 2017. <https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-2016-vol-28.pdf>
- Kosakovsky Pond SL, Weaver S, Leigh Brown AJ, Wertheim JO. HIV-TRACE (transmission cluster engine): a tool for large scale molecular epidemiology of HIV-1 and other rapidly evolving pathogens. *Mol Biol Evol* 2018;35:1812–9. <https://doi.org/10.1093/molbev/msy016>
- CDC. Detecting, investigating, and responding to HIV transmission clusters: a guide for health departments. Atlanta, GA: US Department of Health and Human Resources, CDC; 2018. <https://www.cdc.gov/hiv/pdf/funding/announcements/ps18-1802/CDC-HIV-PS18-1802-AttachmentE-Detecting-Investigating-and-Responding-to-HIV-Transmission-Clusters.pdf>
- Whiteside YO, Song R, Wertheim JO, Oster AM. Molecular analysis allows inference into HIV transmission among young men who have sex with men in the United States. *AIDS* 2015;29:2517–22. <https://doi.org/10.1097/QAD.0000000000000852>
- Dasgupta S, Hall HI, Hernandez AL, Ocfemia MCB, Saduvala N, Oster AM. Receipt and timing of HIV drug resistance testing in six U.S. jurisdictions. *AIDS Care* 2017;29:1567–75. <https://doi.org/10.1080/09540121.2017.1316356>
- Wisconsin Department of Health Services. Wisconsin HIV surveillance annual review. Madison, WI: Wisconsin Department of Health Services; 2017. <https://www.dhs.wisconsin.gov/publications/p00484-16.pdf>

Recommendations of the Advisory Committee on Immunization Practices for Use of Hepatitis A Vaccine for Persons Experiencing Homelessness

Mona Doshani, MD¹; Mark Weng, MD¹; Kelly L. Moore, MD²; José R. Romero, MD³; Noele P. Nelson, MD, PhD¹

Hepatitis A (HepA) vaccination is recommended routinely for children at age 12–23 months, for persons who are at increased risk for hepatitis A virus (HAV) infection, and for any person wishing to obtain immunity. Persons at increased risk for HAV infection include international travelers to areas with high or intermediate hepatitis A endemicity, men who have sex with men, users of injection and noninjection drugs, persons with chronic liver disease, person with clotting factor disorders, persons who work with HAV-infected primates or with HAV in a research laboratory setting, and persons who anticipate close contact with an international adoptee from a country of high or intermediate endemicity (1–3). Persons experiencing homelessness are also at higher risk for HAV infection and severe infection-associated outcomes. On October 24, 2018, the Advisory Committee on Immunization Practices (ACIP)* recommended that all persons aged 1 year and older experiencing homelessness be routinely immunized against HAV. The ACIP Hepatitis Vaccines Work Group conducted a systematic review of the evidence for administering vaccine to persons experiencing homelessness, which included a set of criteria assessing the benefits and adverse events associated with vaccination. HepA vaccines are highly immunogenic, and >95% of immunocompetent adults develop protective antibody within 4 weeks of receipt of 1 dose of the vaccine (1). HAV infections are acquired primarily by the fecal-oral route by either person-to-person transmission or via ingestion of contaminated food or water. Among persons experiencing homelessness, effective implementation of alternative strategies to prevent exposure to HAV, such as strict hand hygiene, is difficult because of living conditions among persons in this population. Integrating routine HepA vaccination into health

care services for persons experiencing homelessness can reduce the size of the at-risk population over time and thereby reduce the risk for large-scale outbreaks.

Introduction

In 2017 in the United States, 1.42 million persons used an emergency shelter or transitional housing program at some point during the year (4). Estimates of homelessness are higher when unsheltered persons are considered. Some studies estimate that 2.3 million to 3.5 million persons experience homelessness each year (5), and persons of color are disproportionately affected (4,5). In 2017, on a single night, an estimated 553,742 persons experienced homelessness in the United States, approximately 35% of whom were in unsheltered locations (4). Although the number of persons experiencing homelessness has declined overall since 2007, the number of unsheltered persons experiencing homelessness in major cities has increased, and disparities remain (4). Persons experiencing homelessness are at 1.5 to 11.5 times the risk for mortality compared with the general population (6). Homelessness has been associated with substantial health inequalities, including shorter life expectancy; poor access to health care, resulting in delayed clinical presentation; higher morbidity; and greater use of acute hospital services, often for preventable conditions (6,7).

HAV infection is associated with poor sanitation and hygiene and is transmitted by the ingestion of contaminated food or water or by direct contact with an infectious person. Congregate living conditions, both within and outside shelters, increase the risk for disease transmission, which can result in outbreaks (6). Recent outbreaks with direct HAV transmission among persons reporting homelessness signal a shift in HAV infection epidemiology in the United States (8). During 2017, a total of 1,521 outbreak-associated HAV cases were reported from California, Kentucky, Michigan, and Utah, with 1,073 (71%) hospitalizations and 41 (3%) deaths; the majority of infections were among persons reporting homelessness or injection or noninjection drug use (8). The person-to-person HAV outbreaks involving persons who use drugs or persons experiencing homelessness are ongoing, and case counts and geographic dispersion increased substantially in 2018.† As of October 12, 2018, approximately 7,000 outbreak-associated cases had been reported from 12 states (8).

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

† <https://www.cdc.gov/hepatitis/outbreaks/2017March-HepatitisA.htm>.

Hepatitis A vaccines are critical to the prevention of HAV infection among persons experiencing homelessness. Detectable antibodies persist for at least 20 years after HepA vaccination in childhood (9), and antibodies persist for an estimated 40 years or longer based on mathematical modeling and anti-HAV kinetic studies (9). Although recommended as a 2-dose series, evidence of protection for up to 11 years exists for 1 dose of single-antigen vaccine (10); clinical and outbreak response experience suggests that lifelong protection is possible after 1 dose. Owing to limited access to health care and historically low rates of insurance coverage, the majority of adults who experience homelessness have low rates of immunization coverage with vaccines routinely recommended for adults. Community health centers provide preventive and primary health services to meet the specific needs of persons experiencing homelessness, including vaccination. Street or shelter-based interventions for targeted populations have been used as efficient methods for vaccinating persons experiencing homelessness during outbreaks (11). Thirty-six states and the District of Columbia have expanded Medicaid under the Affordable Care Act, providing an increase in coverage and access to care among persons experiencing homelessness; an estimated 77% had access to some form of insurance in 2017 (12).

This report provides recommendations for use of HepA vaccine among persons experiencing homelessness and updates previous ACIP recommendations for HepA vaccine that did not include homelessness as an indication for use of HepA vaccine for preexposure protection against HAV infection (1).

Methods

During February 2018–October 2018, the ACIP Hepatitis Vaccines Work Group[§] held monthly conference calls to review and discuss relevant scientific evidence[¶] supporting inclusion of homelessness as an indication for HepA vaccine. The work group evaluated the quality of evidence related to the benefits and harms of administering HepA vaccine to persons experiencing homelessness using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework (<https://www.cdc.gov/vaccines/acip/recs/grade/table-refs.html>).

[§]The ACIP Hepatitis Vaccines Work Group comprises professionals from academic medicine (family medicine, internal medicine, pediatrics, obstetrics, infectious disease, occupational health, and preventive medicine specialists), federal and state public health entities, and medical societies.

[¶]In preparation for ACIP deliberation, the scientific literature was searched using PubMed, Medline and EMBASE databases for reports published from January 1, 2000, through April 25, 2018. Search terms excluded studies in nonhumans. Studies were also excluded if they were published earlier than 2000, included only vaccines not licensed in the United States, did not address the population of interest (homeless) or if relevant data could not be extracted. There were no language restrictions on initial searches and articles from any country were included.

At the October 2018 ACIP meeting, the following proposed recommendations were presented to the committee: all persons aged 1 year and older experiencing homelessness should be routinely immunized against hepatitis A. After a period for public comment, the recommendations were approved unanimously by the voting ACIP members.**

Summary of Key Findings

Homelessness as an indication for hepatitis A vaccination.

Little is known about HAV seroprevalence among homeless populations in the United States. Review of the literature found few studies that considered homelessness as an independent risk factor. Based on the evidence to recommendations framework, other considerations were assessed, such as recent HAV outbreaks (8), HAV-related hospitalizations and deaths, treatment costs for liver transplants, and the benefits and costs associated with HepA vaccination (<https://www.cdc.gov/vaccines/acip/recs/grade/table-refs.html>). These studies concluded that the benefits of vaccinating persons experiencing homelessness were substantial and the cost and risk of vaccinating persons experiencing homelessness is much lower than the risk of not vaccinating.

The clinical trial and observational studies that were included in the GRADE review had several limitations, and some did not report any quantitative data. The studies had limitations in design and execution. No comparison/control groups were present, and there was a serious risk of bias, inconsistency, indirectness, and imprecision. Only one study was found with vaccine immunogenicity data among the homeless population, and it reported on a non-U.S. population.

GRADE quality of evidence summary for HepA vaccine among homeless persons. The evidence assessing benefits and harms of administering HepA vaccine to prevent HAV infection in persons experiencing homelessness was determined to be GRADE evidence type 4 (i.e., evidence from clinical experience and observations, observational studies with important limitations, or randomized controlled trials with several major limitations) for benefits and for harms. The balance of consequences for the evidence to recommendation framework was determined to be that desirable consequences clearly outweigh undesirable consequences in most settings (<https://www.cdc.gov/vaccines/acip/recs/grade/table-refs.html>).

Recommendation for Hepatitis A Vaccine for Persons Experiencing Homelessness

All persons aged 1 year and older experiencing homelessness should be routinely immunized against hepatitis A (Box 1). Routine vaccination consists of a 2-dose schedule or a 3-dose schedule when combined hepatitis A and B vaccine is administered.

** Eleven members voted in favor, with none opposed, none abstained, and none recused.

BOX1. Recommendations for routine preexposure use of hepatitis A vaccine — Advisory Committee on Immunization Practices

- All children at age 12–23 months.
- Persons traveling to or working in countries that have high or intermediate HAV endemicity.
- Persons who anticipate close contact with an international adoptee from a country of high or intermediate endemicity during the first 60 days following arrival of the adoptee in the United States.
- Men who have sex with men.
- Users of injection and noninjection drugs.
- Persons with chronic liver disease.
- Persons with clotting factor disorders.
- Persons who work with HAV-infected primates or with HAV in a research laboratory setting.
- Persons experiencing homelessness.
- Anyone wishing to obtain immunity.

Sources: CDC. Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices. *MMWR Recomm Rep* 2006;55(No. RR-7).

CDC. Updated recommendations from the Advisory Committee on Immunization Practices (ACIP) for use of hepatitis A vaccine in close contacts of newly arriving international adoptees. *MMWR Morb Mortal Wkly Rep* 2009;58:1006–7.

Nelson NP, Link-Gelles R, Hofmeister MG, et al. Update: Recommendations of the Advisory Committee on Immunization Practices for use of hepatitis a vaccine for postexposure prophylaxis and for preexposure prophylaxis for international travel. *MMWR Morb Mortal Wkly Rep* 2018;67:1216–20.

BOX2. Homeless definition: U.S. Department of Health and Human Services

A homeless person is defined as an individual

- who lacks housing (without regard to whether the individual is a member of a family), including an individual whose primary residence during the night is a supervised public or private facility (e.g., shelter) that provides temporary living accommodations and an individual who is a resident in transitional housing;
- without permanent housing who may live on the streets; stay in a shelter, mission, single-room occupancy facility, abandoned building or vehicle; or in any other unstable or nonpermanent situation;
- who is “doubled up,” a term that refers to a situation where individuals are unable to maintain their housing situation and are forced to stay with a series of friends and/or extended family members.

In addition, previously homeless individuals who are to be released from a prison or a hospital may be considered homeless if they do not have a stable housing situation to which they can return. A recognition of the instability of an individual’s living arrangements is critical to the definition of homelessness.

Sources: National Health Care for the Homeless Council. <https://www.nhchc.org/faq/official-definition-homelessness/>.

U.S. Department of Health and Human Services [Section 330 of the Public Health Service Act (42 U.S.C., 254b)].

HRSA/Bureau of Primary Health Care, Program Assistance Letter 99–12, Health Care for the Homeless Principles of Practice.

Clinical Considerations

Concern about loss to follow-up before HepA vaccine series completion should not be a deterrent to initiating the vaccine series in persons experiencing homelessness. One dose of HepA vaccine provides personal protection and can contribute to herd immunity, although long-term protection might be suboptimal (10).

Multiple definitions of homelessness have been published in the United States; however, the definitions are similar in content. The U.S. Department of Health and Human Services definition is used for the purpose of this recommendation (Box 2). Because of the difficulty distinguishing the type of homelessness a person is experiencing (e.g., sheltered versus unsheltered) and

the associated risks for HAV infection, all persons experiencing homelessness should routinely receive HepA vaccine.

Rationale for Recommendation

Advantages of HepA vaccine for persons experiencing homelessness. Persons experiencing homelessness might have difficulty implementing recommended nonvaccine strategies to protect themselves from exposure (e.g., access to clean toilet facilities, regular handwashing, and avoidance of crowded living conditions). For this reason, vaccination is the most reliable protection from HAV infection for persons experiencing homelessness. HepA vaccination of persons experiencing homelessness will provide individual protection and increase herd immunity over time, reducing the risk of large-scale, person-to-person outbreaks in this population. The

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

Hepatitis A (HepA) vaccine is highly safe and effective, and a complete HepA vaccine series provides long-term protection against hepatitis A virus (HAV) infection. Person-to-person HAV outbreaks among persons using drugs or experiencing homelessness are widespread and ongoing.

What is added by this report?

All persons aged ≥ 1 year experiencing homelessness should be routinely immunized against HAV. Vaccination of homeless persons facilitates integration of HepA vaccine into routine preventive services.

What are the implications for public health practice?

HepA vaccination of homeless persons would improve protection of persons at increased risk of exposure to HAV and complications of hepatitis A disease and reduce the risk for large-scale outbreaks by increasing immunity to HAV among homeless persons living in congregate settings where HAV can spread readily.

recommendation facilitates routine HepA vaccination of persons experiencing homelessness through facilities that already provide health care services for the homeless population.

Acknowledgment

Doug Campos-Outcalt, MD, Department of Family, Community and Preventive Medicine, University of Arizona College of Medicine, Phoenix, Arizona.

ACIP Hepatitis Vaccines Work Group

Membership as of October 24, 2018: Kelly Moore, MD, Nashville, Tennessee (chair); Natali Aziz, MD, Stanford, California; Sharon Balter, MD, Los Angeles, California; Elizabeth Barnett, MD, Boston, Massachusetts; Susan Even, MD, Columbia, Missouri; Darci Everett, MD, Silver Spring, Maryland; Echezona Ezeanolue, MD, Las Vegas, Nevada; Christine Finley, Burlington, Vermont; Robert Frenck, MD, Cincinnati, Ohio; Sharon Frey, MD, St. Louis, Missouri; Kathleen Harriman, PhD, Richmond, California; Susan Lett, MD, Jamaica Plain, Massachusetts; Marian Major, PhD, Silver Spring, Maryland; Brian McMahon, MD, Anchorage, Alaska; David Nace, MD, Pittsburgh, Pennsylvania; Greg Poland, MD, Rochester, Minnesota; Arthur Reingold, MD, Berkeley, California; Pamela Rockwell, DO, Ann Arbor, Michigan; José Romero, MD, Little Rock, Arkansas; Jennifer Rosen, MD, New York City, New York; Ann Thomas, MD, Portland, Oregon; David Weber, MD, Chapel Hill, North Carolina; Matthew Zahn, MD, Orange, California; Jennifer Zipprich, PhD, Richmond, California.

Work Group Contributors

Maria Cano, MD; Mona Doshani, MD; Penina Haber, MPH; Aaron Harris, MD; Beth Hibbs, MPH; Megan Hofmeister, MD;

David Kim, MD; Alaya Koneru, MPH; Andrew Kroger, MD; Noele Nelson, MD, PhD; Jeff Nemhauser, MD; Tina Objio, MSN, MHA; Sarah Schillie, MD; Phil Spradling, MD; Tureka Watson, MS; Mark Weng, MD, CDC.

Corresponding author: Noele P. Nelson, nnelson@cdc.gov, 404-718-8576.

¹Division of Viral Hepatitis, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, CDC; ²Department of Health Policy, Vanderbilt University School of Medicine, Nashville, Tennessee; ³Pediatric Infectious Diseases Section, University of Arkansas for Medical Sciences and Arkansas Children's Hospital, Little Rock, Arkansas.

All authors have completed and submitted the ICMJE form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

References

1. Fiore AE, Wasley A, Bell BP; Advisory Committee on Immunization Practices (ACIP). Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2006;55(No. RR-7).
2. CDC; Advisory Committee on Immunization Practices. Updated recommendations from the Advisory Committee on Immunization Practices (ACIP) for use of hepatitis A vaccine in close contacts of newly arriving international adoptees. *MMWR Morb Mortal Wkly Rep* 2009;58:1006–7.
3. Nelson NP, Link-Gelles R, Hofmeister MG, et al. Update: recommendations of the Advisory Committee on Immunization Practices for use of hepatitis A vaccine for postexposure prophylaxis and for preexposure prophylaxis for international travel. *MMWR Morb Mortal Wkly Rep* 2018;67:1216–20. <https://doi.org/10.15585/mmwr.mm6743a5>
4. US Department of Housing and Urban Development. 2017 annual homeless assessment report (AHAR). Washington, DC: US Department of Housing and Urban Development; 2018. <https://www.hudexchange.info/homelessness-assistance/ahar/#2017-reports>
5. Koh HK, O'Connell JJ. Improving health care for homeless people. *JAMA* 2016;316:2586–7. <https://doi.org/10.1001/jama.2016.18760>
6. Gambatese M, Marder D, Begier E, et al. Programmatic impact of 5 years of mortality surveillance of New York City homeless populations. *Am J Public Health* 2013;103(Suppl 2):S193–8. <https://doi.org/10.2105/AJPH.2012.301196>
7. Baggett TP, O'Connell JJ, Singer DE, Rigotti NA. The unmet health care needs of homeless adults: a national study. *Am J Public Health* 2010;100:1326–33. <https://doi.org/10.2105/AJPH.2009.180109>
8. Foster M, Ramachandran S, Myatt K, et al. Hepatitis A virus outbreaks associated with drug use and homelessness—California, Kentucky, Michigan, and Utah, 2017. *MMWR Morb Mortal Wkly Rep* 2018;67:1208–10. <https://doi.org/10.15585/mmwr.mm6743a3>
9. Theeten H, Van Herck K, Van Der Meer O, Crasta P, Van Damme P, Hens N. Long-term antibody persistence after vaccination with a 2-dose Havrix (inactivated hepatitis A vaccine): 20 years of observed data, and long-term model-based predictions. *Vaccine* 2015;33:5723–7. <https://doi.org/10.1016/j.vaccine.2015.07.008>
10. Ott JJ, Wiersma ST. Single-dose administration of inactivated hepatitis A vaccination in the context of hepatitis A vaccine recommendations. *Int J Infect Dis* 2013;17:e939–44. <https://doi.org/10.1016/j.ijid.2013.04.012>
11. Badiaga S, Raoult D, Brouqui P. Preventing and controlling emerging and reemerging transmissible diseases in the homeless. *Emerg Infect Dis* 2008;14:1353–9. <https://doi.org/10.3201/eid1409.080204>
12. National Health Care for the Homeless Council. Health insurance at HCH programs, 2017. Nashville, TN: National Health Care for the Homeless Council; 2018. <https://www.nhchc.org/wp-content/uploads/2018/11/health-insurance-hch-programs-2017.pdf>

Vital Signs: Tobacco Product Use Among Middle and High School Students — United States, 2011–2018

Andrea S. Gentzke, PhD¹; MeLisa Creamer, PhD¹; Karen A. Cullen, PhD²; Bridget K. Ambrose, PhD²; Gordon Willis, PhD³; Ahmed Jamal, MBBS¹; Brian A. King, PhD¹

On February 11, 2019, this report was posted as an MMWR Early Release on the MMWR website (<https://www.cdc.gov/mmwr>).

Abstract

Introduction: Tobacco use is the leading cause of preventable disease and death in the United States; nearly all tobacco product use begins during youth and young adulthood.

Methods: CDC, the Food and Drug Administration, and the National Cancer Institute analyzed data from the 2011–2018 National Youth Tobacco Surveys to estimate tobacco product use among U.S. middle and high school students. Prevalence estimates of current (past 30-day) use of seven tobacco products were assessed; differences over time were analyzed using multivariable regression (2011–2018) or t-test (2017–2018).

Results: In 2018, current use of any tobacco product was reported by 27.1% of high school students (4.04 million) and 7.2% of middle school students (840,000); electronic cigarettes (e-cigarettes) were the most commonly used product among high school (20.8%; 3.05 million) and middle school (4.9%; 570,000) students. Use of any tobacco product overall did not change significantly during 2011–2018 among either school level. During 2017–2018, current use of any tobacco product increased 38.3% (from 19.6% to 27.1%) among high school students and 28.6% (from 5.6% to 7.2%) among middle school students; e-cigarette use increased 77.8% (from 11.7% to 20.8%) among high school students and 48.5% (from 3.3% to 4.9%) among middle school students.

Conclusions and Implications for Public Health Practice: A considerable increase in e-cigarette use among U.S. youths, coupled with no change in use of other tobacco products during 2017–2018, has erased recent progress in reducing overall tobacco product use among youths. The sustained implementation of comprehensive tobacco control strategies, in coordination with Food and Drug Administration regulation of tobacco products, can prevent and reduce the use of all forms of tobacco products among U.S. youths.

Introduction

Tobacco use is the leading cause of preventable disease and death in the United States; nearly all tobacco product use begins during youth and young adulthood (1,2). Cigarette smoking among U.S. youths has steadily declined over the past 2 decades (1,2). However, recent changes to the tobacco product landscape (3) and the introduction of new electronic cigarette (e-cigarette) devices have shifted the types of tobacco products used by youths (4). Since 2014, e-cigarettes have been the most commonly used tobacco product among U.S. middle and high school students (5).

Although e-cigarettes have the potential to benefit adult smokers if used as a complete substitute for combustible tobacco smoking (1), the use of any form of tobacco product by youths is unsafe (3). E-cigarettes typically contain nicotine (3,4). The Surgeon General has concluded that exposure to nicotine during adolescence can cause addiction and harm the developing adolescent brain (3). This report provides the most

recent national estimates of tobacco product use among U.S. middle and high school students.

Methods

The National Youth Tobacco Survey (NYTS) is an annual cross-sectional, voluntary, school-based, self-administered, pencil-and-paper survey of U.S. middle school (grades 6–8) and high school (grades 9–12) students.* A three-stage cluster sampling procedure is used to generate a nationally representative sample of U.S. students attending public and private schools in grades 6–12. This report used data from eight NYTS waves (2011–2018); sample sizes (response rates) were 18,866 (72.7%) in 2011; 24,658 (73.6%) in 2012; 18,406 (67.8%) in 2013; 22,007 (73.3%) in 2014; 17,711 (63.4%) in 2015; 20,675 (71.6%) in 2016; 17,872 (68.1%) in 2017; and 20,189 (68.2%) in 2018.

*https://www.cdc.gov/tobacco/data_statistics/surveys/nyts/index.htm.

Participants were asked about use of seven tobacco products: cigarettes, cigars (cigars, little cigars, and cigarillos), smokeless tobacco,[†] e-cigarettes,[§] hookahs,[¶] pipe tobacco,^{**} and bidis.^{††} Current use of each product was defined as use on ≥ 1 day during the past 30 days. Any tobacco product use was defined as current use of one or more of the seven assessed tobacco products. Use of ≥ 2 tobacco product types was defined as current use of two or more of the seven assessed tobacco products. Any combustible tobacco product use was defined as current use of one or more of the following: cigarettes, cigars, hookahs, pipe tobacco, and bidis. Among respective users, frequent tobacco product use, defined as use on ≥ 20 of the past 30 days, was assessed for cigarettes, cigars, smokeless tobacco, e-cigarettes, and hookahs.^{§§}

Data were weighted to account for the complex survey design and adjusted for nonresponse. National prevalence estimates with 95% confidence intervals were computed; population

totals were estimated from extrapolated probability weights. In 2018, current use estimates were determined for any tobacco product overall, ≥ 2 tobacco products, any combustible tobacco product, and individual tobacco products, overall and by selected demographics (sex and race/ethnicity) within each school level (middle and high school). The presence of linear and nonlinear (quadratic) trends during 2011–2018 were assessed, adjusting for sex, race/ethnicity, and grade level.^{¶¶} Differences in current and frequent tobacco product use during 2017–2018 were assessed by t-test. For all analyses, p-values < 0.05 were considered statistically significant.

Results

In 2018, 27.1% of high school students (an estimated 4.04 million) reported current use of any tobacco product, including 13.9% (2.07 million; 51.3% of current tobacco product users) who used any combustible tobacco product and 11.3% (1.68 million; 41.7% of current tobacco product users) who used ≥ 2 tobacco product types (Table). E-cigarettes were the most commonly used tobacco product among high school students (20.8%), followed by cigarettes (8.1%), cigars (7.6%), smokeless tobacco (5.9%), hookahs (4.1%), and pipe tobacco (1.1%). Use of any tobacco product, ≥ 2 tobacco products, e-cigarettes, cigarettes, cigars, smokeless tobacco, and pipe tobacco was higher among males than females ($p < 0.05$). Among high school students, use of any tobacco product was reported by 32.4% of non-Hispanic whites (whites), 21.7% of Hispanics, 18.4% of non-Hispanic students of other races, and 17.4% of non-Hispanic blacks (blacks). E-cigarettes were the most commonly used tobacco product among white (26.8%) and Hispanic (14.8%) high school students; cigars were the most commonly used tobacco product among black high school students (9.2%).

In 2018, 7.2% (an estimated 840,000) of middle school students reported current use of any tobacco product, including 3.3% (380,000; 45.8% of current tobacco product users) who used any combustible tobacco product and 2.4% (270,000; 33.3% of current tobacco product users) who used ≥ 2 tobacco products (Table). Among middle school students, the most commonly used tobacco product was e-cigarettes (4.9%), followed by cigarettes (1.8%), smokeless tobacco (1.8%), cigars (1.6%), hookahs (1.2%), and pipe tobacco (0.3%). Use of smokeless tobacco, any tobacco product, and ≥ 2 tobacco products was higher among males than females ($p < 0.05$). Among middle school students, use of any tobacco product

[†] Beginning in 2015, the definition of smokeless tobacco included chewing tobacco/snuff/dip, snus, and dissolvable tobacco to reflect this class of tobacco products better. Thus, estimates for individual smokeless tobacco products (chewing tobacco/snuff/dip, snus, and dissolvable tobacco) are not reported.

[§] During 2011–2013, e-cigarette use was assessed by the question “In the past 30 days, which of the following products have you used on at least one day?” and the response option, “Electronic cigarettes or e-cigarettes such as Ruyan or NJOY.” In 2014, current use of e-cigarettes was assessed by the question “During the past 30 days, on how many days did you use e-cigarettes such as Blu, 21st Century Smoke, or NJOY?” During 2015–2018, e-cigarette questions were preceded by an introductory paragraph defining the product. In 2015, current use of e-cigarettes was assessed by the question “During the past 30 days, on how many days did you use electronic cigarettes or e-cigarettes?” During 2016–2018, current use of e-cigarettes was assessed by the question “During the past 30 days, on how many days did you use e-cigarettes?”

[¶] During 2011–2015, current hookah smoking was assessed by the question “In the past 30 days, which of the following products have you used on at least one day?” Hookah was the fourth or fifth response option during 2011–2013, the first option in 2014, and the fourth option in 2015. During 2016–2018, hookah questions were preceded by an introductory paragraph defining the product; current hookah smoking was assessed by the question “In the past 30 days, on how many days did you smoke tobacco in a hookah or waterpipe?”

^{**} During 2011–2013, pipe tobacco use was assessed by the question “During the past 30 days, on how many days did you smoke tobacco in a pipe?” During 2014–2018, current use of pipe tobacco was assessed by the question “In the past 30 days, which of the following products have you used on at least one day?” and the response option “Pipes filled with tobacco (not waterpipe).” Pipe tobacco was the second response option available in 2014, the fifth option in 2015, and the second option during 2016–2018.

^{††} In 2018, bidis was assessed by the question, “In the past 30 days, which of the following tobacco products have you used on at least one day?” and the response option, “Bidis (small brown cigarettes wrapped in a leaf).” Beginning in 2018, prevalence estimates are not provided for bidis by school level, sex, or race/ethnicity. However, use of bidis is captured in the composite measures of any tobacco product use, ≥ 2 tobacco products use, and use of combustible tobacco products to maintain consistent definitions over time.

^{§§} Frequency of use data were available during 2011–2018 for cigarettes, cigars, and smokeless tobacco products (chewing tobacco, snuff, dip, only). Frequency of use data were available only for certain years for e-cigarettes (2014–2018), hookahs (2016–2018), and pipe tobacco (2011–2013). Frequency of use data were unavailable for bidis, snus, and dissolvable tobacco products during 2011–2018.

^{¶¶} Trends were assessed using multivariable-adjusted regression analysis. A test for linear trend was significant if an overall statistically significant decrease or increase occurred during the study period. Data also were assessed for the presence of nonlinear (quadratic) trends. A significant nonlinear trend indicated that the rate of change accelerated or decelerated across the study period.

TABLE. Estimated prevalence of tobacco product use in the past 30 days, by product,* school level, sex, and race/ethnicity† — National Youth Tobacco Survey, United States, 2018

School level/ Tobacco product	% (95% CI)							Estimated no. of users [§]	Total % (95% CI)
	Sex		Race/Ethnicity						
	Female	Male	White, non-Hispanic	Black, non-Hispanic	Hispanic	Other race, non-Hispanic			
High school students									
Any tobacco product [¶]	24.9 (22.9–26.9)	29.1 (27.1–31.3)	32.4 (30.4–34.4)	17.4 (14.5–20.7)	21.7 (19.4–24.1)	18.4 (15.0–22.4)	4,040,000	27.1 (25.3–29.0)	
Any combustible tobacco**	13.0 (11.3–15.0)	14.6 (13.3–16.0)	14.7 (13.0–16.6)	13.2 (10.8–15.9)	13.7 (11.8–15.7)	8.1 (5.8–11.1)	2,070,000	13.9 (12.6–15.4)	
≥2 Tobacco products ^{††}	9.3 (8.0–10.9)	13.1 (11.7–14.6)	13.6 (12.1–15.4)	5.5 (4.0–7.5)	9.9 (8.4–11.5)	6.3 (4.1–9.6)	1,680,000	11.3 (10.1–12.6)	
E-cigarettes	18.8 (16.7–21.1)	22.6 (20.6–24.8)	26.8 (24.7–29.0)	7.5 (5.5–10.2)	14.8 (12.9–17.0)	14.5 (10.8–19.1)	3,050,000	20.8 (18.8–22.9)	
Cigarettes	7.3 (6.1–8.7)	8.8 (7.6–10.2)	9.9 (8.5–11.6)	3.2 (2.3–4.6)	7.2 (5.8–8.8)	4.4 (2.5–7.6)	1,180,000	8.1 (7.1–9.3)	
Cigars	6.0 (4.9–7.4)	9.0 (8.1–10.0)	7.8 (6.7–9.1)	9.2 (6.8–12.4)	7.3 (5.9–9.1)	3.4 (2.0–5.7)	1,100,000	7.6 (6.7–8.6)	
Smokeless tobacco	3.3 (2.7–4.0)	8.4 (6.9–10.1)	7.6 (6.2–9.2)	2.2 (1.4–3.3)	4.2 (3.3–5.4)	3.0 (1.7–5.3)	870,000	5.9 (5.0–7.0)	
Hookahs	4.1 (3.2–5.3)	4.0 (3.4–4.8)	3.3 (2.6–4.1)	3.7 (2.7–5.2)	6.0 (4.7–7.7)	4.1 (2.8–6.1)	590,000	4.1 (3.5–4.9)	
Pipe tobacco	0.8 (0.6–1.2)	1.4 (1.1–1.8)	1.1 (0.8–1.6)	— ^{§§}	1.4 (0.9–2.1)	—	160,000	1.1 (0.9–1.4)	
Middle school students									
Any tobacco product [¶]	6.3 (5.4–7.4)	8.0 (6.9–9.3)	6.6 (5.5–7.8)	6.8 (5.2–9.0)	9.5 (8.0–11.2)	3.8 (2.1–6.6)	840,000	7.2 (6.3–8.1)	
Any combustible tobacco**	2.9 (2.2–3.7)	3.7 (2.9–4.6)	2.5 (1.7–3.4)	4.4 (3.0–6.3)	4.7 (3.9–5.7)	—	380,000	3.3 (2.7–4.0)	
≥2 Tobacco products ^{††}	1.9 (1.4–2.5)	2.8 (2.2–3.5)	2.1 (1.5–3.0)	1.5 (0.8–2.7)	3.6 (2.9–4.4)	—	270,000	2.4 (1.9–2.9)	
E-cigarettes	4.8 (3.9–5.7)	5.1 (4.2–6.2)	4.9 (4.0–5.9)	3.0 (2.1–4.2)	6.6 (5.1–8.5)	—	570,000	4.9 (4.2–5.8)	
Cigarettes	1.5 (1.1–2.0)	2.1 (1.6–2.7)	1.6 (1.1–2.4)	—	2.4 (1.8–3.1)	—	200,000	1.8 (1.4–2.2)	
Cigars	1.6 (1.2–2.1)	1.7 (1.3–2.3)	1.1 (0.7–1.6)	2.9 (1.8–4.5)	2.2 (1.6–2.9)	—	190,000	1.6 (1.3–2.1)	
Smokeless tobacco	0.9 (0.6–1.3)	2.7 (2.1–3.6)	1.8 (1.3–2.6)	—	2.2 (1.7–3.0)	—	210,000	1.8 (1.5–2.3)	
Hookahs	1.0 (0.7–1.4)	1.5 (1.0–2.1)	0.8 (0.5–1.3)	—	2.2 (1.6–3.0)	—	140,000	1.2 (0.9–1.6)	
Pipe tobacco	0.4 (0.2–0.6)	0.3 (0.2–0.5)	—	—	0.6 (0.4–1.0)	—	30,000	0.3 (0.2–0.5)	

Abbreviations: CI = confidence interval; e-cigarettes = electronic cigarettes.

* Past 30-day use of e-cigarettes was determined by asking, "During the past 30 days, on how many days did you use e-cigarettes?" Past 30-day use of cigarettes was determined by asking, "During the past 30 days, on how many days did you smoke cigarettes?" Past 30-day use of cigars was determined by asking, "During the past 30 days, on how many days did you smoke cigars, cigarillos, or little cigars?" Past 30-day use of hookah was determined by asking, "During the past 30 days, on how many days did you smoke tobacco in a hookah or waterpipe?" Smokeless tobacco was defined as use of chewing tobacco, snuff, dip, snus, and/or dissolvable tobacco products. Past 30-day use of smokeless tobacco was determined by asking the following question for use of chewing tobacco, snuff, and dip: "During the past 30 days, on how many days did you use chewing tobacco, snuff, or dip?" and the following question for use of snus and dissolvable tobacco products: "In the past 30 days, which of the following products did you use on at least one day?" Responses from these questions were combined to derive overall smokeless tobacco use. Past 30-day use of pipe tobacco (not hookahs) was determined by asking, "In the past 30 days, which of the following products have you used on at least one day?"

† Blacks, whites, and others are non-Hispanic; Hispanic persons could be of any race.

§ Estimated total number of users was rounded down to the nearest 10,000 persons.

¶ Any tobacco product use was defined as use of any tobacco product (e-cigarettes, cigarettes, cigars, smokeless tobacco, hookahs, pipe tobacco, and/or bidis) on ≥1 day in the past 30 days.

** Any combustible tobacco product use was defined as use of cigarettes, cigars, hookahs, pipe tobacco, and/or bidis on ≥1 day in the past 30 days.

†† ≥2 tobacco products use was defined as use of ≥2 tobacco products (e-cigarettes, cigarettes, cigars, smokeless tobacco, hookahs, pipe tobacco, and/or bidis) on ≥1 day in the past 30 days.

§§ Dashes indicate that data are statistically unreliable because samples size was <50 or relative standard error was >0.3.

was reported by 9.5% of Hispanics, 6.8% of blacks, 6.6% of whites, and 3.8% of non-Hispanic students of other races. E-cigarettes were the most commonly used tobacco product among Hispanic (6.6%), white (4.9%), and black (3.0%) middle school students.

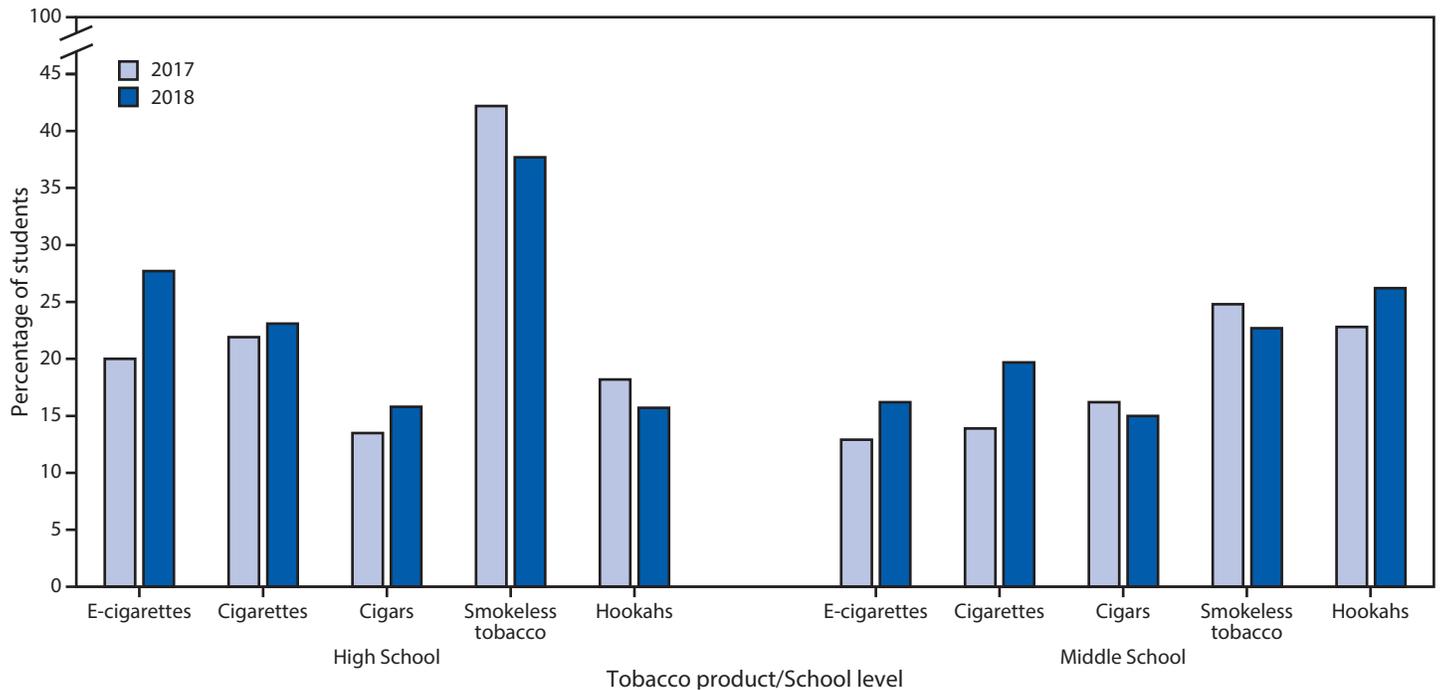
In 2018, frequent use among current product users in high school was 37.7% for smokeless tobacco, 27.7% for e-cigarettes, 23.1% for cigarettes, 15.8% for cigars, and 15.7% for hookahs (Figure 1). During 2017–2018, frequent e-cigarette use increased significantly by 38.5% among current e-cigarette users (from 20.0% to 27.7%); no significant change in frequent use was observed for other tobacco products. Among middle school students, frequent use among current product users was 26.2% for hookahs, 22.7% for smokeless tobacco, 19.7% for cigarettes, 16.2% for e-cigarettes, and

15.0% for cigars in 2018; no significant change in frequent use was observed for any product during 2017–2018.

Among current users of any tobacco product in 2018, exclusive use of e-cigarettes was reported by 42.0% of high school students and 42.7% of middle school students. However, among high school students who reported currently using ≥2 tobacco products, the most common combinations reported were "e-cigarettes + cigarettes" (14.8%); "e-cigarettes + cigars" (13.3%); and "e-cigarettes + smokeless tobacco" (9.0%). Among middle school students who reported currently using ≥2 tobacco products, the most common combinations reported were "e-cigarettes + cigarettes" (14.4%); "e-cigarettes + cigars" (9.1%); and "cigarettes + e-cigarettes + cigars + smokeless tobacco + hookah" (8.8%).

Among high school students, during 2011–2018, no significant trend in the reported use of any tobacco product overall

FIGURE 1. Frequent use* of selected tobacco products† among U.S. middle and high school students who currently used each tobacco product‡ — National Youth Tobacco Survey, 2017–2018¶



Abbreviation: e-cigarettes = electronic cigarettes.

* Frequent tobacco product use defined as use of each respective tobacco product on ≥ 20 of the past 30 days.

† Frequency of use during the past 30 days was not available for pipe tobacco in the 2017 or 2018 surveys.

‡ Among youths who currently report using each respective tobacco product, defined as a response other than "0 days" to each of the following questions: *E-cigarettes*: "During the past 30 days, on how many days did you use e-cigarettes?"; *Cigarettes*: "During the past 30 days, on how many days did you smoke cigarettes?"; *Cigars*: "During the past 30 days, on how many days did you smoke cigars, cigarillos, or little cigars?"; *Smokeless tobacco*: "During the past 30 days, on how many days did you use chewing tobacco, snuff, or dip?"; *Hookahs*: "During the past 30 days, on how many days did you smoke tobacco in a hookah or waterpipe?" For all questions, answer choices included, "0 days, 1 or 2 days, 3 to 5 days, 6 to 9 days, 10 to 19 days, 20 to 29 days, and All 30 days."

¶ During 2017–2018, a significant increase in frequent use of e-cigarettes was observed only among high school students ($p < 0.05$). No significant changes were observed for any other tobacco product during 2017–2018 among middle or high school students.

was observed (Figure 2). However, changes were observed for individual tobacco products over this period. A significant nonlinear increase in current e-cigarette use occurred from 2011 (1.5%) to 2018 (20.8%). During 2011–2018, significant linear declines in combustible tobacco product use (from 21.8% to 13.9%) and ≥ 2 tobacco product use (from 12.0% to 11.3%) occurred; by product type, significant linear declines occurred for cigars (from 11.6% to 7.6%), smokeless tobacco (from 7.9% to 5.9%), and pipe tobacco (from 4.0% to 1.1%). A significant nonlinear decline was observed for cigarettes (from 15.8% to 8.1%). A significant nonlinear change during 2011–2018 was observed for hookahs (from 4.1% to 4.1%).

Among middle school students, no significant change in use of any tobacco product overall occurred during 2011–2018 (Figure 3). However, changes for individual tobacco products were observed. A significant nonlinear increase in e-cigarette use occurred (from 0.6% to 4.9%) during 2011–2018. A significant linear decline was observed for combustible tobacco product use (from 6.4% to 3.3%), ≥ 2 tobacco products use (from 3.8% to 2.4%), cigarettes (from 4.3% to 1.8%), cigars

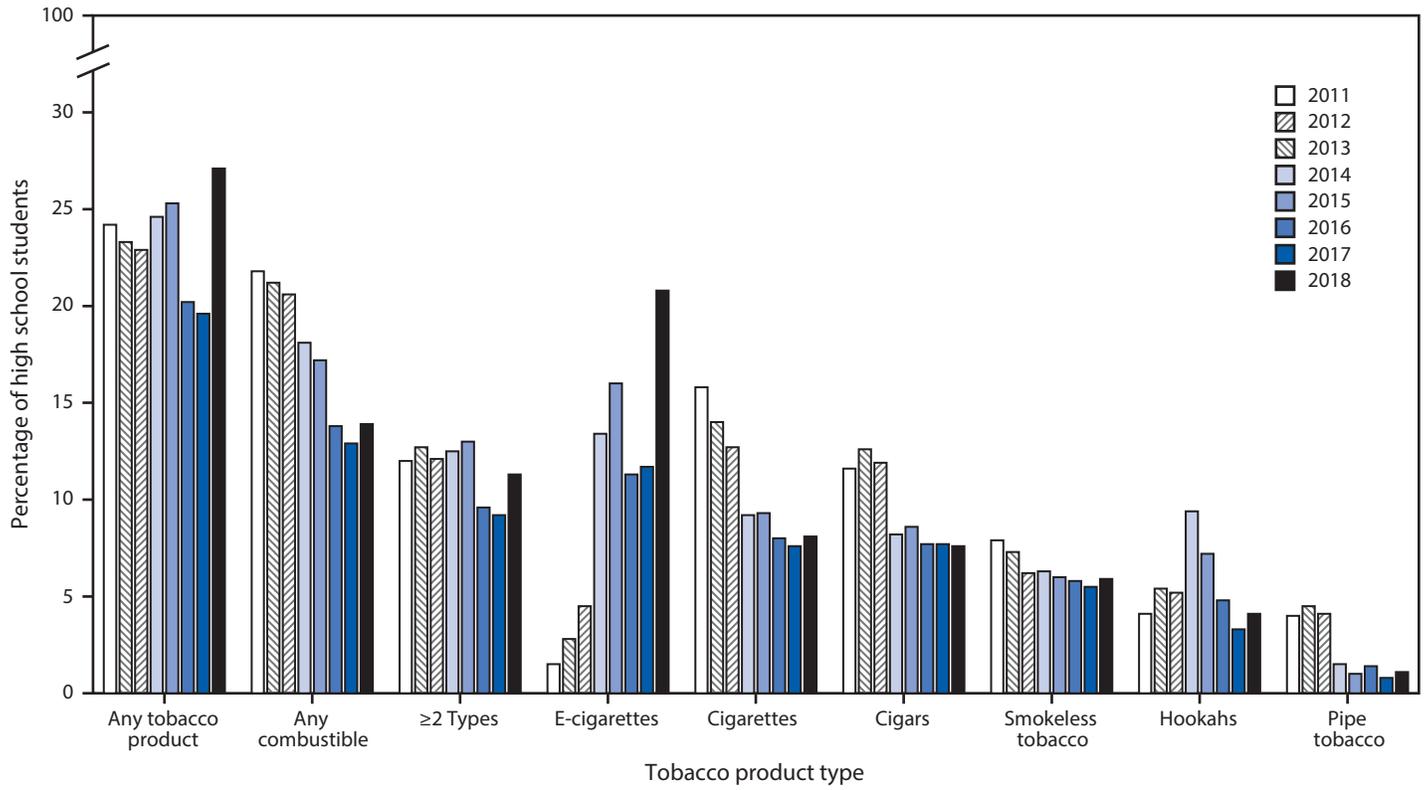
(from 3.5% to 1.6%), smokeless tobacco (from 2.7% to 1.8%), and pipe tobacco (from 2.2% to 0.3%); a significant nonlinear change occurred for hookah smoking (from 1.0% to 1.2%).

During 2017–2018, use of any tobacco product increased significantly by 38.3% (from 19.6% to 27.1%) among high school students (Figure 2) and by 28.6% (from 5.6% to 7.2%) among middle school students (Figure 3). Current use of ≥ 2 tobacco products increased significantly by 22.8% (from 9.2% to 11.3%) among high school students. Current e-cigarette use increased significantly by 77.8% (from 11.7% to 20.8%) among high school students and by 48.5% (from 3.3% to 4.9%) among middle school students during 2017–2018; no significant changes in use of other tobacco products was observed during this period, irrespective of grade level.

Conclusions and Comment

In 2018, approximately one in four U.S. high school students and one in 14 middle school students reported current use of any tobacco product. Among both high school and middle school students, current use of e-cigarettes increased

FIGURE 2. Estimated percentage of high school students who currently use any tobacco product,* any combustible tobacco product,† ≥ 2 tobacco product types,‡ and selected tobacco products — National Youth Tobacco Survey, 2011–2018^{¶,**,††}



Abbreviation: e-cigarettes = electronic cigarettes.

* Any tobacco product use was defined as use of e-cigarettes, cigarettes, cigars, hookahs, smokeless tobacco, pipe tobacco and/or bidis (small brown cigarettes wrapped in a leaf) on ≥ 1 day in the past 30 days.

† Any combustible tobacco product use was defined as use of cigarettes, cigars, hookahs, pipe tobacco, and/or bidis on ≥ 1 day in the past 30 days.

‡ Use of ≥ 2 tobacco product types was defined as use of ≥ 2 of the following tobacco products: e-cigarettes, cigarettes, cigars, hookahs, smokeless tobacco, pipe tobacco, and/or bidis on ≥ 1 day in the past 30 days.

¶ During 2017–2018, current use of any tobacco product, ≥ 2 types of tobacco products, and e-cigarettes significantly increased ($p < 0.05$).

** During 2011–2018, current use of combustible tobacco products, ≥ 2 types of tobacco products, cigars, smokeless tobacco, and pipe tobacco exhibited linear decreases ($p < 0.05$). Current use of cigarettes exhibited a nonlinear decrease ($p < 0.05$). Current use of hookahs exhibited a nonlinear change ($p < 0.05$). Current use of e-cigarettes exhibited a nonlinear increase ($p < 0.05$). No significant trend in use of any tobacco product overall was observed.

†† Beginning in 2015, the definition of smokeless tobacco included chewing tobacco/snuff/dip, snus, and dissolvable tobacco to better reflect this class of tobacco products. Thus, estimates for individual smokeless tobacco products (chewing tobacco/snuff/dip, snus, and dissolvable tobacco) are not reported. This definition was applied across all years (2011–2018) for comparability purposes.

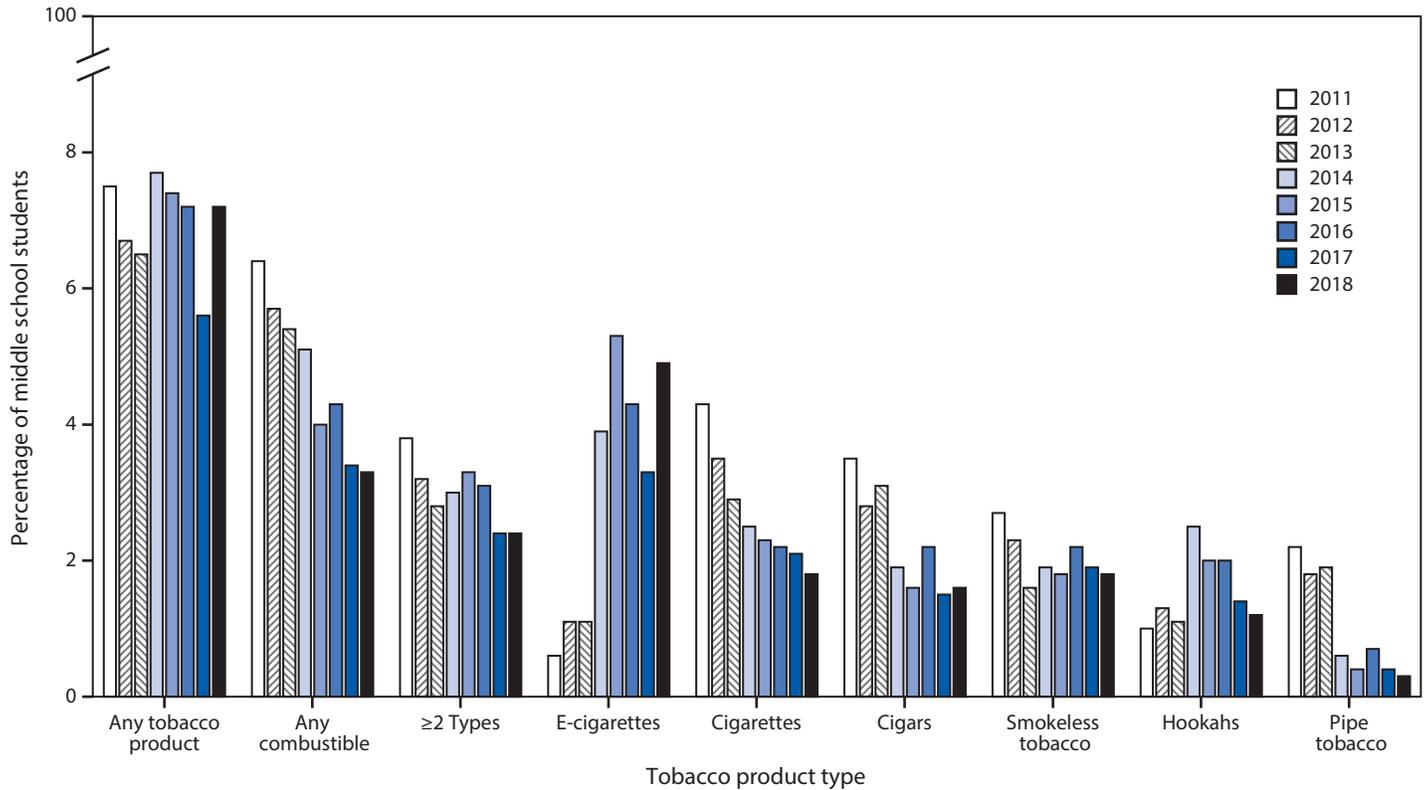
considerably between 2017 and 2018, reaching epidemic proportions, according to the U.S. Surgeon General (4); approximately 1.5 million more youths currently used e-cigarettes in 2018 (3.6 million) compared with 2017 (2.1 million) (5). However, no significant change in current use of combustible tobacco products, such as cigarettes and cigars, was observed in recent years (5) or during 2017–2018. This indicates that e-cigarettes were the driver of the observed increase in any tobacco product use. The recent changes in patterns of use of e-cigarettes and other tobacco products during 2017–2018 erased the decline in any tobacco product use that occurred in previous years (5).

E-cigarettes have been the most commonly used tobacco product among U.S. youths since 2014 (5). Before 2018, the

prevalence of e-cigarette use by U.S. high school students had peaked in 2015 before declining by 29% during 2015–2016 (from 16% to 11.3%) (6); this decline was the first ever recorded for e-cigarette use among youths in the NYTS since monitoring began, and it was subsequently sustained during 2016–2017 (5). However, current e-cigarette use increased by 77.8% among high school students and 48.5% among middle school students during 2017–2018, erasing the progress in reducing e-cigarette use, as well as any tobacco product use, that had occurred in prior years (7).

This recent increase in e-cigarette use among youths is consistent with observed increases in sales of the e-cigarette JUUL (8), a USB-shaped e-cigarette device with a high nicotine content that can be used discreetly and is available in flavors that can appeal

FIGURE 3. Estimated percentage of middle school students who currently use any tobacco product,* any combustible tobacco product,† ≥ 2 tobacco product types,‡ and selected tobacco products — National Youth Tobacco Survey, 2011–2018^{¶,**,††}



Abbreviation: e-cigarettes = electronic cigarettes.

* Any tobacco product use was defined as use of e-cigarettes, cigarettes, cigars, hookahs, smokeless tobacco, pipe tobacco and/or bidis (small brown cigarettes wrapped in a leaf) on ≥ 1 day in the past 30 days.

† Any combustible tobacco product use was defined as use of cigarettes, cigars, hookahs, pipe tobacco, and/or bidis on ≥ 1 day in the past 30 days.

‡ Use of ≥ 2 tobacco product types was defined as use of ≥ 2 of the following tobacco products: e-cigarettes, cigarettes, cigars, hookahs, smokeless tobacco, pipe tobacco, and/or bidis on ≥ 1 day in the past 30 days.

¶ During 2017–2018, current use of any tobacco product and e-cigarettes significantly increased ($p < 0.05$).

** During 2011–2018, current use of combustible tobacco products, ≥ 2 tobacco products, cigarettes, cigars, smokeless tobacco, and pipe tobacco exhibited significant linear decreases ($p < 0.05$). Use of e-cigarettes exhibited a significant nonlinear increase ($p < 0.05$), and use of hookahs exhibited a nonlinear change ($p < 0.05$). No significant trend in use of any tobacco product overall was observed.

†† Beginning in 2015, the definition of smokeless tobacco included chewing tobacco/snuff/dip, snus, and dissolvable tobacco to better reflect this class of tobacco products. Thus, estimates for individual smokeless tobacco products (chewing tobacco/snuff/dip, snus, and dissolvable tobacco) are not reported. This definition was applied across all years (2011–2018) for comparability purposes.

to youths. A single prefilled liquid nicotine JUUL pod contains as much nicotine as a pack of cigarettes (9). Media reports and a survey indicate that JUUL devices are being used among youths in schools, including inside bathrooms and classrooms.*** JUUL entered the U.S. market in 2015 and subsequently became a commonly used tobacco product among U.S. youths (10). Sales of JUUL increased by approximately 600% during 2016–2017 (8) and increased even further through 2018 (10). By December 2017, JUUL held the largest market share of any e-cigarette (8). Thus, given that NYTS is fielded annually in the spring, the 2018 data are the first to reflect the impact of rising

sales of JUUL and other USB-shaped devices on e-cigarette and overall tobacco product use among U.S. youths.

Any form of tobacco product use among youths, irrespective of frequency, is unsafe (1–4). During 2017–2018, frequent e-cigarette use increased significantly by 38.5% among high school student users. Thus, in addition to more youths using e-cigarettes overall, current e-cigarette users also are using them more frequently.

Furthermore, among current tobacco product users, approximately 40% of high school students and one third of middle school students reported currently using more than one tobacco product; the prevalence of using two or more tobacco products

*** <https://www.cdc.gov/tobacco/infographics/youth/pdfs/e-cigarettes-usb-flash-508.pdf>; <https://truthinitiative.org/news/nearly-1-5-youth-say-they-have-seen-juul-used-school>.

increased significantly by 22.8% among high school students during 2017–2018. E-cigarettes were the most commonly reported product used in combination with other products among both middle and high school students in 2018. Most e-cigarettes contain nicotine (11), which is highly addictive and can harm the developing adolescent brain (3). Among youths, symptoms of nicotine dependence are increased in multiple tobacco product users than in single product users (12). In addition, some evidence suggests that e-cigarette use increases the risk for ever using cigarettes among youths, and that e-cigarette use might increase the frequency and intensity of subsequent cigarette smoking (13).

Differences in individual tobacco product use were also observed across population groups. In 2018, e-cigarettes were the most commonly used product among all racial/ethnic groups except black high school students, among whom cigars were the most commonly reported product. Targeted advertising of cigars in locations with a greater proportion of black residents, a relatively lower price, and the availability of cigars for purchase as a single unit might contribute to higher cigar smoking among blacks (14).

The findings in this report are subject to at least three limitations. First, changes in the wording and placement of survey questions for certain tobacco products during 2011–2018 might limit comparability of estimates between years. Second, data were self-reported and might be subject to recall and response bias. Finally, findings might not be generalizable to all youths, including those who are home-schooled, have dropped out of school, or are enrolled in alternative schools. However, in 2016, nearly 97% of students aged 10–17 years were enrolled in school.^{†††}

Several factors continue to promote and influence tobacco product use among youths, including exposure to tobacco product advertising and imagery through various media, as well as the availability of flavored tobacco products (2,3,15,16). The sustained and comprehensive implementation of population-based strategies, in coordination with the regulation of tobacco products by the Food and Drug Administration (17), and continued research investments and cessation-related initiatives, including Smokefree Teen by the National Institutes of Health's National Cancer Institute^{§§§} can reduce all forms of

^{†††} <https://www.census.gov/data/tables/2016/demo/school-enrollment/2016-cps.html>.

^{§§§} The National Cancer Institute created Smokefree.gov to help smokers quit smoking. Smokefree.gov is a part of an effort by the U.S. Department of Health and Human Services to reduce smoking rates in the United States, particularly among certain populations. Smokefree Teen (<https://teen.smokefree.gov/>) is part of the Smokefree.gov initiative, with the goal to reduce the number of youths who use tobacco.

Summary

What is already known about this topic?

Tobacco use is the leading cause of preventable disease and death in the United States; nearly all tobacco product use begins during youth and young adulthood.

What is added by this report?

In 2018, 4.04 million high school students and 840,000 middle school students currently used any tobacco product; e-cigarettes were the most commonly used product. Driven by an increase in e-cigarette use, current tobacco product use significantly increased among high school and middle school students during 2017–2018, erasing the decline in tobacco product use among youths that occurred in previous years.

What are the implications for public health practice?

Sustained implementation of proven population-based strategies, in coordination with Food and Drug Administration regulation of tobacco products, is important for reducing tobacco product use and initiation among U.S. youths.

tobacco product use and initiation among U.S. youths (1–3). As a direct result of the considerable increase in e-cigarette use among youths during 2017–2018 (7), in November 2018, the Food and Drug Administration announced several proposed new steps to protect youths, including restricting sales of flavored e-cigarettes (other than tobacco, menthol, mint, or nonflavored) to physical locations with age restrictions or online with heightened age verification procedures, and plans to advance notices of proposed rulemaking that would ban menthol cigarettes and cigars and all other flavored cigars (18). Additional strategies to reduce tobacco product use among youths include increasing the price of tobacco products, implementing comprehensive smoke-free policies, implementing advertising and promotion restrictions and national antitobacco public education media campaigns, and implementing and enforcing policies that raise the minimum age of purchase for tobacco products to 21 years (1,3,19,20).

Corresponding author: Andrea S. Gentzke, AGentzke@cdc.gov, 770-488-5493.

¹Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, CDC; ²Center for Tobacco Products, Food and Drug Administration, Silver Spring, Maryland; ³Tobacco Control Research Branch, National Cancer Institute, National Institutes of Health, Rockville, Maryland.

All authors have completed and submitted the ICMJE form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

References

1. US Department of Health and Human Services. The health consequences of smoking—50 years of progress. Atlanta, GA: US Department of Health and Human Services, CDC; 2014. <https://www.surgeongeneral.gov/library/reports/50-years-of-progress/full-report.pdf>
2. US Department of Health and Human Services. Preventing tobacco use among youth and young adults. Atlanta, GA: US Department of Health and Human Services, CDC; 2012. https://www.cdc.gov/tobacco/data_statistics/sgr/2012/index.htm
3. US Department of Health and Human Services. E-cigarette use among youth and young adults. Atlanta, GA: US Department of Health and Human Services, CDC; 2016. https://www.cdc.gov/tobacco/data_statistics/sgr/e-cigarettes/pdfs/2016_sgr_entire_report_508.pdf
4. US Department of Health and Human Services. Surgeon General's advisory on e-cigarette use among youth. Washington, DC: US Department of Health and Human Services, Office of the Surgeon General; 2018. <https://e-cigarettes.surgeongeneral.gov/documents/surgeon-generals-advisory-on-e-cigarette-use-among-youth-2018.pdf>
5. Wang TW, Gentzke A, Sharapova S, Cullen KA, Ambrose BK, Jamal A. Tobacco product use among middle and high school students—United States, 2011–2017. *MMWR Morb Mortal Wkly Rep* 2018;67:629–33. <https://doi.org/10.15585/mmwr.mm6722a3>
6. Jamal A, Gentzke A, Hu SS, et al. Tobacco use among middle and high school students—United States, 2011–2016. *MMWR Morb Mortal Wkly Rep* 2017;66:597–603. <https://doi.org/10.15585/mmwr.mm6623a1>
7. Cullen KA, Ambrose BK, Gentzke AS, Apelberg BJ, Jamal A, King BA. Notes from the field: increase in e-cigarette use and any tobacco product use among middle and high school students—United States, 2011–2018. *MMWR Morb Mortal Wkly Rep* 2018;67:1276–7. <https://doi.org/10.15585/mmwr.mm6745a5>
8. King BA, Gammon DG, Marynak KL, Rogers T. Electronic cigarette sales in the United States, 2013–2017. *JAMA* 2018;320:1379–80. <https://doi.org/10.1001/jama.2018.10488>
9. Campaign for Tobacco Free Kids. JUUL and youth: rising e-cigarette popularity. Washington, DC: Campaign for Tobacco Free Kids; 2018. <https://www.tobaccofreekids.org/assets/factsheets/0394.pdf>
10. Vallone DM, Bennett M, Xiao H, Pitzer L, Hair EC. Prevalence and correlates of JUUL use among a national sample of youth and young adults. *Tob Control* 2018. Epub October 29, 2018. <https://tobaccocontrol.bmj.com/content/early/2018/10/30/tobaccocontrol-2018-054693>
11. Marynak KL, Gammon DG, Rogers T, Coats EM, Singh T, King BA. Sales of nicotine-containing electronic cigarette products: United States, 2015. *Am J Public Health* 2017;107:702–5. <https://doi.org/10.2105/AJPH.2017.303660>
12. Apelberg BJ, Corey CG, Hoffman AC, et al. Symptoms of tobacco dependence among middle and high school tobacco users: results from the 2012 National Youth Tobacco Survey. *Am J Prev Med* 2014;47(Suppl 1):S4–14. <https://doi.org/10.1016/j.amepre.2014.04.013>
13. National Academies of Sciences, Engineering, and Medicine. Public health consequences of e-cigarettes. Washington, DC: The National Academies Press; 2018.
14. Corey CG, Dube SR, Ambrose BK, King BA, Apelberg BJ, Husten CG. Cigar smoking among U.S. students: reported use after adding brands to survey items. *Am J Prev Med* 2014;47(Suppl 1):S28–35. <https://doi.org/10.1016/j.amepre.2014.05.004>
15. Tsai J, Walton K, Coleman BN, et al. Reasons for electronic cigarette use among middle and high school students—National Youth Tobacco Survey, United States, 2016. *MMWR Morb Mortal Wkly Rep* 2018;67:196–200. <https://doi.org/10.15585/mmwr.mm6706a5>
16. Marynak K, Gentzke A, Wang TW, Neff L, King BA. Exposure to electronic cigarette advertising among middle and high school students—United States, 2014–2016. *MMWR Morb Mortal Wkly Rep* 2018;67:294–9. <https://doi.org/10.15585/mmwr.mm6710a3>
17. Food and Drug Administration, US Department of Health and Human Services. Deeming tobacco products to be subject to the federal food, drug, and cosmetic act, as amended by the family smoking prevention and tobacco control act; regulations on the sale and distribution of tobacco products and required warning statements for tobacco products. *Fed Regist* 2016;81:28973–9106 <https://www.federalregister.gov/documents/2016/05/10/2016-10685/deeming-tobacco-products-to-be-subject-to-the-federal-food-drug-and-cosmetic-act-as-amended-by-the>
18. Food and Drug Administration. Statement from FDA Commissioner Scott Gottlieb, M.D., on proposed new steps to protect youth by preventing access to flavored tobacco products and banning menthol in cigarettes [press release]. Washington, DC: Food and Drug Administration; 2018. <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm625884.htm>
19. CDC. Best practices for comprehensive tobacco control programs—2014. Atlanta, GA: US Department of Health and Human Services, CDC; 2014. https://www.cdc.gov/tobacco/stateandcommunity/best_practices/index.htm
20. U.S. National Cancer Institute, World Health Organization. The economics of tobacco and tobacco control. NCI Tobacco Control monograph 21. Bethesda, MD: US Department of Health and Human Services, National Institutes of Health, National Cancer Institute; 2016.

Notes from the Field

Assessment of State-Level Influenza Season Severity — Minnesota and Utah, 2017–18 Influenza Season

Michelle M. Hughes, PhD^{1,2}; Joshua D. Doyle MD, PhD^{1,2};
Keegan McCaffrey³; Melissa McMahon, MPH⁴;
Melanie Spencer, MPH⁵; Karen Martin, MPH⁴; Gregg M. Reed, MPH³;
Anna E. Carmack, MD⁶; Shikha Garg, MD²; Melissa Rolfes, PhD²;
Carrie Reed, PhD²; Matthew Biggerstaff, ScD²

The U.S. 2017–18 influenza season was a high-severity season, with the highest number of outpatient visits for influenza-like illness* (ILI) since the 2009–10 pandemic and the highest rate of influenza-associated hospitalizations since surveillance expanded to include adult hospitalizations during the 2005–06 season (1). The severe season was characterized by reports of strained emergency departments and hospitals and spot shortages of influenza antiviral medications (2). Influenza activity can vary widely across geographic regions (3), and local severity assessments might better guide public health actions and health care needs and support the development of tailored communication messages to prevent influenza morbidity and mortality. CDC assesses influenza season severity at the national level (4),[†] but the applicability of this approach at state or local levels has not been tested.

In February 2018, field investigations were conducted in Minnesota and Utah to identify potential indicators of state-level influenza activity and pilot a state-level approach to assessing influenza season severity in real time. Indicators were selected using three criteria: 1) availability of data for 2017–18 and at least five previous influenza seasons; 2) completeness and representativeness of data on observed influenza seasonality; and 3) timeliness. Two indicators selected in both states were weekly ILI activity (percentage of outpatient visits to sentinel providers for ILI) and influenza-associated hospitalizations (counts or population-based rates). A third indicator included weekly counts of influenza-associated deaths in Minnesota and weekly percentage of specimens testing positive for influenza reported by sentinel clinical laboratories in Utah. Using state-level data from five earlier seasons (2012–13 through 2016–17) and following previously published procedures (3), indicator-specific intensity thresholds (ITs) for a 50% chance (IT₅₀), 10% chance (IT₉₀), and a 2% chance (IT₉₈)

*Fever (temperature $\geq 100^{\circ}\text{F}$ [37.8°C]) and a cough and/or a sore throat without a known cause other than influenza.

[†]Nationally, CDC assesses flu severity using three indicators: 1) percentage of visits to outpatient clinics for ILI; 2) the rates of influenza-associated hospitalizations; and 3) the percentage of deaths resulting from pneumonia or influenza that occurred during each season.

of observing higher values during the 2017–18 season were calculated. Severity was classified as low, moderate, high, or very high if at least two of three indicators peaked during the 2017–18 season below their IT₅₀ value, between their IT₅₀ and IT₉₀ values, between their IT₉₀ and IT₉₈ values, and above their IT₉₈ value, respectively.

The interim severity of the 2017–18 influenza season (assessed in mid-February 2018) for both Minnesota and Utah was categorized as high. As an example of one of the three indicators, influenza-associated hospitalizations through the end of the 2017–18 season (May 2018) peaked above the IT₉₀ (Minnesota) and IT₉₈ (Utah) values (Figure). End-of-season severity assessments for both states remained high, aligning with national trends and the subsequent high severity classification for the entire United States (1).

The national severity assessment framework was successfully adapted for use in Minnesota and Utah. Utah is piloting the report of the weekly severity assessments for the 2018–19 season (5). Additional states might find this method useful for improving local public health messaging, preparedness, and response during an influenza season and in the event of a pandemic. CDC continues to develop resources to support local assessments of influenza season severity; interested jurisdictions are encouraged to contact CDC's Influenza Division for assistance.

Corresponding author: Michelle M. Hughes, MHughes7@cdc.gov, 404-639-3747.

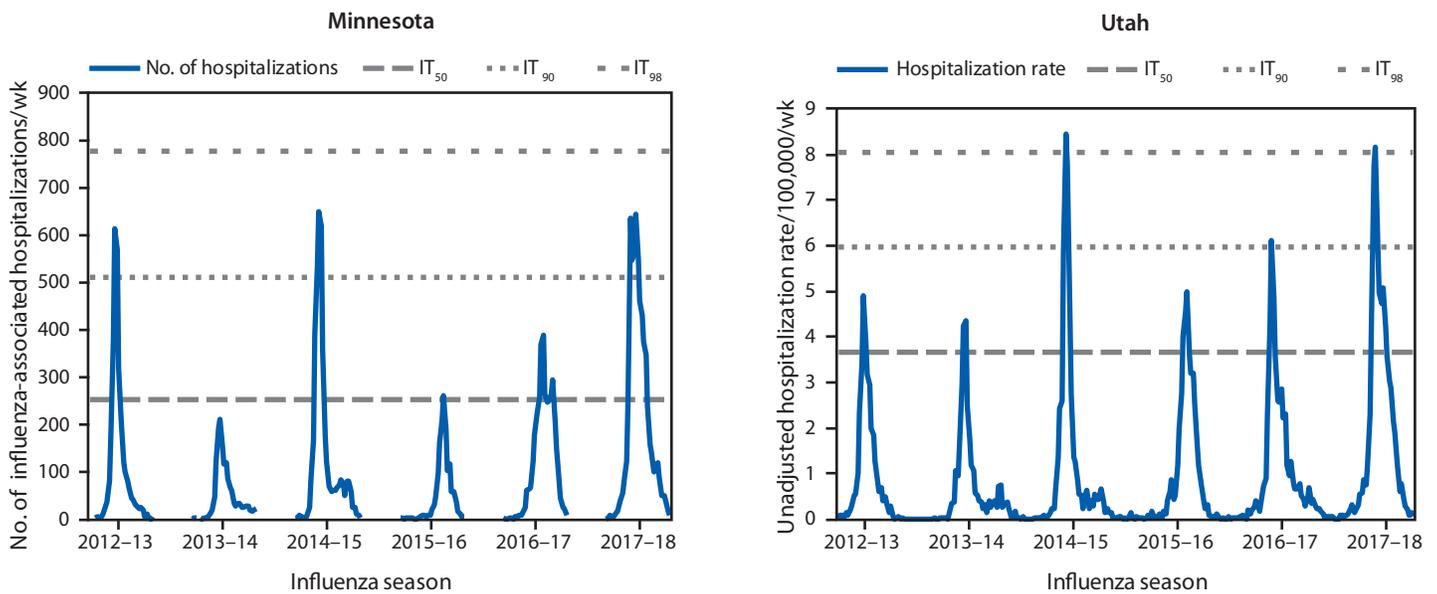
¹Epidemic Intelligence Service, CDC; ²Influenza Division, National Center for Immunization and Respiratory Diseases, CDC; ³Utah Department of Health; ⁴Minnesota Department of Health; ⁵Salt Lake County Health Department, Salt Lake City, Utah; ⁶University of Maryland Medical Center, Baltimore, Maryland.

All authors have completed and submitted the ICMJE form for disclosure of potential conflicts of interest. Keegan McCaffrey reports grants from the Council of State and Territorial Epidemiologists during the course of the study. No other potential conflicts of interest were disclosed.

References

- Garten R, Blanton L, Elal AIA, et al. Update: influenza activity in the United States during the 2017–18 season and composition of the 2018–19 influenza vaccine. *MMWR Morb Mortal Wkly Rep* 2018;67:634–42. <https://doi.org/10.15585/mmwr.mm6722a4>
- Uyeki TM, Fowler RA, Fischer WA 2nd. Gaps in the clinical management of influenza: a century since the 1918 pandemic. *JAMA* 2018;320:755–6. <https://doi.org/10.1001/jama.2018.8113>
- Dahlgren FS, Shay DK, Izurieta HS, et al. Patterns of seasonal influenza activity in U.S. core based statistical areas, described using prescriptions of oseltamivir in Medicare claims data. *Epidemics* 2018; 18:30014–8. [PubMed https://doi.org/10.1016/j.epidem.2018.08.002](https://doi.org/10.1016/j.epidem.2018.08.002)

FIGURE. Influenza-associated hospitalization indicators and intensity thresholds — Minnesota^{*,†} and Utah,^{§,¶} 2012–18 influenza seasons



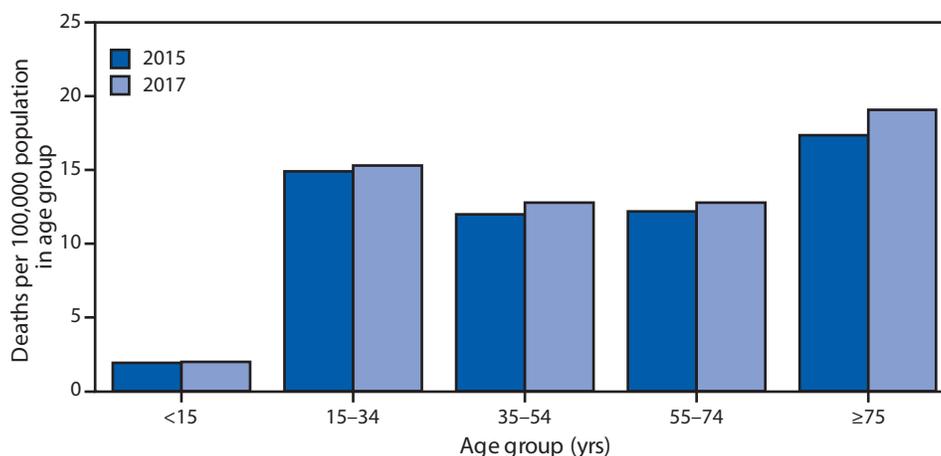
Abbreviations: IT₅₀ = intensity threshold at which there is a 50% chance of observing a higher value during 2017–18 based on historical (2012–13 through 2016–17) peak values; IT₉₀ = intensity threshold at which there is a 10% chance of observing a higher value during 2017–18 based on historical (2012–13 through 2016–17) peak values; IT₉₈ = intensity threshold at which there is a 2% chance of observing a higher value during 2017–18 based on historical (2012–13 through 2016–17) peak values.
^{*} Reported to the Minnesota Department of Health.
[†] Minnesota intensity thresholds: IT₅₀ = 255; IT₉₀ = 511; IT₉₈ = 778.
[§] Reported to the Utah Department of Health.
[¶] Utah intensity thresholds: IT₅₀ = 3.66; IT₉₀ = 5.99; IT₉₈ = 8.06.

4. Biggerstaff M, Kniss K, Jernigan DB, et al. Systematic assessment of multiple routine and near-real time indicators to classify the severity of influenza seasons and pandemics in the United States, 2003–2004 through 2015–2016. *Am J Epidemiol* 2018;187:1040–50. <https://doi.org/10.1093/aje/kwx334>
5. Utah Department of Health. Influenza weekly updates: 2018–2019 influenza season severity measures. Salt Lake City, UT: Utah Department of Health; 2018; <http://health.utah.gov/epi/diseases/influenza/surveillance/>

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Death Rates* for Motor Vehicle Traffic Injury,[†] by Age Group — National Vital Statistics System, United States, 2015 and 2017



* Rates are deaths per 100,000 population in specified age group.

[†] Motor vehicle traffic injuries are identified as underlying cause of death with *International Classification of Diseases, Tenth Revision* (ICD-10) codes V02-V04 (.1,.9), V09.2,V12-V14 (.3-.9), V19 (.4-.6), V20-V28 (.3-.9), V29-V79 (.4-.9), V80 (.3-.5), V81.1, V82.1, V83-V86 (.0-.3), V87 (.0-.8), and V89.2.

From 2015 to 2017, death rates for motor vehicle traffic injury increased for persons aged ≥ 15 years. For infants and children aged < 15 years there was no statistically significant change from 2015 to 2017, and this group had the lowest death rate (2.0 deaths per 100,000) in 2017. The highest death rate in 2017 was for persons aged ≥ 75 years (19.1), followed by a 15.3 death rate for persons aged 15–34 years, and 12.8 for persons aged 35–54 and 55–74 years.

Source: National Vital Statistics System. Underlying cause of death data, 1999–2017. <https://wonder.cdc.gov/ucd-icd10.html>.

Reported by: Jiaquan Xu, MD, jiaquanxu@cdc.gov, 301-458-4086.

For more information on this topic, CDC recommends: <https://www.cdc.gov/motorvehiclesafety/index.html>.

Morbidity and Mortality Weekly Report

The *Morbidity and Mortality Weekly Report (MMWR)* Series is prepared by the Centers for Disease Control and Prevention (CDC) and is available free of charge in electronic format. To receive an electronic copy each week, visit *MMWR* at <https://www.cdc.gov/mmwr/index.html>.

Readers who have difficulty accessing this PDF file may access the HTML file at <https://www.cdc.gov/mmwr/index2019.html>. Address all inquiries about the *MMWR* Series, including material to be considered for publication, to Executive Editor, *MMWR* Series, Mailstop E-90, CDC, 1600 Clifton Rd., N.E., Atlanta, GA 30329-4027 or to mmwrq@cdc.gov.

All material in the *MMWR* Series is in the public domain and may be used and reprinted without permission; citation as to source, however, is appreciated.

MMWR and *Morbidity and Mortality Weekly Report* are service marks of the U.S. Department of Health and Human Services.

Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

References to non-CDC sites on the Internet are provided as a service to *MMWR* readers and do not constitute or imply endorsement of these organizations or their programs by CDC or the U.S. Department of Health and Human Services. CDC is not responsible for the content of these sites. URL addresses listed in *MMWR* were current as of the date of publication.

ISSN: 0149-2195 (Print)