

State Laws Regarding Indoor Public Use, Retail Sales, and Prices of Electronic Cigarettes — U.S. States, Guam, Puerto Rico, and U.S. Virgin Islands, September 30, 2017

Kristy Marynak, MPP¹; Brandon Kenemer, MPH¹; Brian A. King, PhD¹; Michael A. Tynan¹; Allison MacNeil, MPH¹; Elizabeth Reimels, JD¹

Electronic cigarettes (e-cigarettes) are the most frequently used tobacco product among U.S. youths, and past 30-day e-cigarette use is more prevalent among high school students than among adults (1,2). E-cigarettes typically deliver nicotine, and the U.S. Surgeon General has concluded that nicotine exposure during adolescence can cause addiction and can harm the developing adolescent brain (2). Through authority granted by the Family Smoking Prevention and Tobacco Control Act, the Food and Drug Administration (FDA) prohibits e-cigarette sales to minors, free samples, and vending machine sales, except in adult-only facilities (3). States, localities, territories, and tribes maintain broad authority to adopt additional or more stringent requirements regarding tobacco product use, sales, marketing, and other topics (2,4). To understand the current e-cigarette policy landscape in the United States, CDC assessed state and territorial laws that 1) prohibit e-cigarette use and conventional tobacco smoking indoors in restaurants, bars, and worksites; 2) require a retail license to sell e-cigarettes; 3) prohibit e-cigarette self-service displays (e.g., requirement that products be kept behind the counter or in a locked box); 4) establish 21 years as the minimum age of purchase for all tobacco products, including e-cigarettes (tobacco-21); and 5) apply an excise tax to e-cigarettes. As of September 30, 2017, eight states, the District of Columbia (DC), and Puerto Rico prohibited indoor e-cigarette use and smoking in indoor areas of restaurants, bars, and worksites; 16 states, DC, and the U.S. Virgin Islands required a retail license to sell e-cigarettes; 26 states prohibited e-cigarette self-service displays; five states, DC, and Guam had tobacco-21 laws; and eight states, DC, Puerto Rico, and the U.S. Virgin Islands taxed e-cigarettes. Sixteen states had none of the assessed laws. A comprehensive approach that combines state-level strategies to reduce youths'

initiation of e-cigarettes and population exposure to e-cigarette aerosol, coupled with federal regulation, could help reduce health risks posed by e-cigarettes among youths (2,5).

Effective and enacted dates for laws enacted as of September 30, 2017, were obtained from the CDC State Tobacco Activities Tracking and Evaluation (STATE) System for the 50 states,

INSIDE

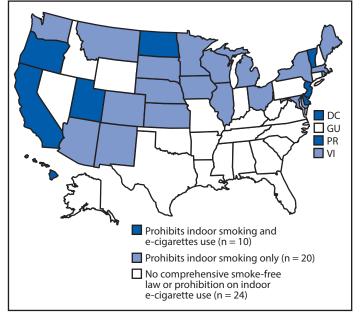
1347	Health and Development at Age 19–24 Months of 19 Children Who Were Born with Microcephaly and Laboratory Evidence of Congenital Zika Virus Infection During the 2015 Zika Virus Outbreak — Brazil, 2017
1352	Large Outbreak of <i>Neisseria meningitidis</i> Serogroup C — Nigeria, December 2016–June 2017
1357	Introduction of Inactivated Poliovirus Vaccine and Impact on Vaccine-Associated Paralytic Poliomyelitis — Beijing, China, 2014–2016
1362	Notes from the Field: Tuberculosis Control Activities After Hurricane Harvey — Texas, 2017
1364	Notes from the Field: Monitoring Out-of-State Patients During a Hurricane Response Using Syndromic Surveillance — Tennessee, 2017
1366	Announcement
1366	Notice to Readers
1367	QuickStats

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



U.S. Department of Health and Human Services Centers for Disease Control and Prevention DC, Puerto Rico, the U.S. Virgin Islands, and Guam.* Legislation information is collected quarterly from the Westlaw online legal research database and is analyzed, coded, and entered into STATE by CDC.[†] State laws and regulations prohibiting self-service displays of e-cigarettes were obtained from the Tobacco Control Legal Consortium (6); effective and enacted dates and territory laws were reviewed in the Westlaw database and on territory websites.

As of September 30, 2017, eight states, DC, and Puerto Rico prohibited indoor e-cigarette use and conventional tobacco smoking in worksites, restaurants, and bars (Figure 1). E-cigarette self-service display restrictions were the most commonly enacted of the five types of laws (26 states), followed by retail license requirements (16 states, DC, and the U.S. Virgin Islands) (Table). Tobacco-21 was the least common law, taking effect in California, Hawaii, and DC in 2016; in Maine, New Jersey, and Oregon in 2017; and in Guam in 2018. Eight states, DC, Puerto Rico, and the U.S. Virgin Islands taxed e-cigarettes, with approaches varying by state. Five of these tax laws have been adjusted since enactment: California, Minnesota, and the U.S. Virgin Islands increased the tax rate, and Kansas and DC decreased the tax rate. FIGURE 1. States and territories with and without laws* prohibiting smoking and use of e-cigarettes in indoor areas of private worksites, restaurants, and bars — United States, September 30, 2017



Abbreviations: DC = District of Columbia; GU = Guam; PR = Puerto Rico; VI = U.S. Virgin Islands.

* A comprehensive state smoke-free law is defined as one that prohibits smoking in indoor areas of private worksites, restaurants, and bars.

The number of newly enacted laws increased from four to 16 during 2013–2014 and from 16 to 21 during 2014–2015, but decreased from 21 to 15 during 2015–2016. Eight laws were

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 2017;66:[inclusive page numbers].

Centers for Disease Control and Prevention

Brenda Fitzgerald, MD, Director William R. Mac Kenzie, MD, Acting Associate Director for Science Joanne Cono, MD, ScM, 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)

Sonja A. Rasmussen, MD, MS, *Editor-in-Chief* Charlotte K. Kent, PhD, MPH, *Executive Editor* Jacqueline Gindler, MD, *Editor* Teresa F. Rutledge, *Managing Editor* Douglas W. Weatherwax, *Lead Technical Writer-Editor* Soumya Dunworth, PhD, Kristy Gerdes, MPH, 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, Paul D. Maitland, Terraye M. Starr, Moua Yang, *Information Technology Specialists*

MMWR Editorial Board

Timothy F. Jones, MD, *Chairman* 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 King K. Holmes, MD, PhD Robin Ikeda, MD, MPH Rima F. Khabbaz, MD Phyllis Meadows, PhD, MSN, RN Jewel Mullen, MD, MPH, MPA Jeff Niederdeppe, PhD Patricia Quinlisk, MD, MPH Patrick L. Remington, MD, MPH Carlos Roig, MS, MA William L. Roper, MD, MPH William Schaffner, MD

^{*} Guam, Puerto Rico, and the U.S. Virgin Islands are the only U.S. territories tracked in STATE System as of June 2017. Additional territories will be added to STATE in the future. https://www.cdc.gov/STATESystem/.

[†] http://legalsolutions.thomsonreuters.com/law-products/westlaw-legal-research/.

TABLE. State laws regarding indoor public use, retail sales, and prices of electronic cigarettes — U.S. states and Guam, Puerto Rico, and U.S. Virgin Islands, enacted as of September 30, 2017

State/Territory	Prohibits e-cigarette use in worksites, restaurants, and bars	e-cigarettes	quired to sellSelf-servicee-cigarettesdisplays ofover thee-cigarettes		E-cigarette tax (tax rate)	Summary of laws [†] enacted as of September 30, 2017	
Alabama	§	_	_	_	_	_	
Alaska	_	_	_	_	_	_	
Arizona	_	_	_	_	_	_	
Arkansas	_	May 1, 2015	Jul 22, 2015	_	_	RL, SS	
California	Jun 9, 2016	Jan 1, 2017	Jun 9, 2016	Jun 9, 2016 [¶]	4/1/2017; (27.3% wholesale cost) 7/1/2017; (65.08% wholesale cost)**	EF, RL, SS, T-21, T	
Colorado	_	_	_	_	_	_	
Connecticut	_	Mar 1, 2016	_	_	_	RL	
Delaware	Oct 5, 2015		Jun 12, 2014	_	1/1/2018; \$0.05 per fluid mL	EF, SS, T	
District of Columbia	Nov 18,2016	Oct 22, 2015	_	Nov 29, 2016	10/1/2015 (67% wholesale sales price) 10/1/2016 (65% wholesale sales price)**	EF, RL, T-21, T	
lorida	_	_	Jul 1, 2014	_		SS	
Georgia	_	_	_	_	_	_	
Buam	_	_	_	Jan 1, 2018 ^{††}	_	T-21	
lawaii	Jan 1, 2016	_	Jul 1, 2014	Jan 1, 2016	_	EF, SS, T-21	
daho	_	_	Jul 1, 2012	_	_	SS	
llinois	—	_	Jan 1, 2015	_	—	SS	
ndiana	—	Jul 1, 2015	Jul 1, 2013	_	—	RL, SS	
owa		Jul 1, 2014	Jul 1, 2014	—	—	RL, SS	
Kansas	_	Jul 1, 2012	Jul 1, 2012	_	Jan 1, 2017 (\$0.20 per mL of consumable material) Jul 1, 2017 (\$0.05 per mL of consumable material)**	RL, SS, T	
Kentucky		—	—	_	_	—	
ouisiana	—	May 28, 2014	May 5, 2014		Jul 1, 2015 (\$0.05 per liquid mL of nicotine)	RL, SS, T	
Maine	—	Nov 1, 2017	Mar 3, 2016*	Nov 1, 2017 ^{§§}	—	RL, SS, T-21	
Maryland	—	Oct 1, 2017		—	—	RL	
Massachusetts	_	—	Sep 25, 2015*	—	—	SS	
Vichigan Vinnesota	_	 Aug 1, 2014	 Jul 1, 2014	_		RL, SS, T	
Vississippi	_	_	_	_		_	
Nissouri	_	_	_	_	_	_	
Nontana	_	Jan 1, 2016	_	_	_	RL	
Vebraska	_		Feb 27, 2015	_	_	SS	
Vevada	_	_		_	_	_	
New Hampshire	_	_	_	_	_	_	
lew Jersey	Jul 11, 2010	_	_	Nov 1, 2017	_	EF, T-21	
New Mexico		_	Jun 19, 2015		_	SS	
New York	_	_	Dec 29, 2014	_	_	SS	

See table footnotes on page 1344.

enacted during January–September 2017 (Figure 2). A total of 72 laws were enacted in 34 states, DC, and three territories during January 2010–September 2017. Sixteen states did not have any of the five assessed laws, and California was the only state with all five of the assessed laws.

Discussion

Several states have enacted laws related to e-cigarettes in recent years, ranging from tobacco-21 laws in five states, DC, and Guam, to self-service display restrictions in approximately half of the states. Legislative activity increased during 2013–2015, peaked in 2015, and has since slowed. One third of states did not have any of the five assessed laws. State, local, and territorial strategies to reduce youths' initiation of e-cigarettes and population exposure to e-cigarette aerosol, including educational initiatives, coupled with federal regulation of tobacco product manufacturing, labeling, and marketing, could help reduce the risks of e-cigarettes on population health, especially among young persons (2,5).

	Effective date				_	
State/Territory	Prohibits e-cigarette use in worksites, restaurants, and bars	e-cigarettes	Self-service displays of e-cigarettes prohibited*	Sales of tobacco products including e-cigarettes to persons aged <21 yrs prohibited	E-cigarette tax (tax rate)	Summary of laws [†] enacted as of September 30, 2017
North Carolina	_	_	—	_	Jun 1, 2015 (\$0.05 per fluid mL)	Т
North Dakota	Dec 6, 2012	_	Aug 1, 2015	—		EF, SS
Ohio	—	—	_	_	—	
Oklahoma	—	—	Nov 1, 2014	—	—	SS
Oregon	Jan 1, 2016	—	May 26, 2015	Aug 9, 2017	—	EF, SS, T-21
Pennsylvania	—	Jul 13, 2016	—	—	Jul 13, 2016 (40% purchase price)	RL, T
Puerto Rico	Apr 11, 2011	—	—	—	May 29, 2017 (\$3.00 per e-cigarette)	EF, T
Rhode Island	—	Jan 1, 2015	_	—	—	RL
South Carolina	—	—	_	—	_	—
South Dakota	—	—	Jul 1, 2014	—	—	SS
Tennessee	—	—	_	—	—	—
Texas	—	—	Oct 1, 2015	—	—	SS
U.S. Virgin Islands	—	May 16, 2014	—	—	Oct 15, 2014 (20% cost price) Mar 23, 2016 (45% cost price)**	RL, T
Utah	May 8, 2012	Jul 1, 2015	Jul 1, 2015	—	_	EF, RL, SS
Vermont	Jul 1, 2016	Jul 1, 2013	Jan 1, 2017	_	_	EF, RL, SS
Virginia	_	_	_	_	_	
Washington	_	Jun 28, 2016	Jun 28, 2016	—	—	RL, SS
West Virginia	_	_	_	_	Jul 1, 2016 (\$0.075 per fluid mL)	Т
Wisconsin	_	_	_	_		
Wyoming	—	—	Mar 13, 2013	—	_	SS
Total	8 states, DC, and Puerto Rico	16 states, DC, and U.S Virgin Islands	26 states	5 states, DC, and Guam	8 states, DC, Puerto Rico and U.S. Virgin Islands	_

TABLE. (*Continued*) State laws regarding indoor public use, retail sales, and prices of electronic cigarettes — U.S. states and Guam, Puerto Rico, and U.S. Virgin Islands, enacted as of September 30, 2017

Abbreviations: EF = E-cigarette free indoor air law; RL = retail license; SS = self-service; T = excise tax; T-21 = sales to persons aged <21 years prohibited.

* Self-service display laws include regulations for Maine and Massachusetts, as reviewed by the Tobacco Control Legal Consortium.

⁺ EF: state law prohibits e-cigarette use in indoor areas of private worksites, restaurants, and bars; RL: state law requires retailer to purchase a license to sell e-cigarettes; SS: state law prohibits self-service displays of e-cigarettes; T: state law applies tax to e-cigarettes; T-21: state law prohibits sales of tobacco products, including e-cigarettes, to persons aged <21 years.

[§] Dashes indicate that laws related to these topics were not accessed for this state.

In California, the law prohibiting sales to persons <21 years of age does not apply to the sale, giving, or furnishing of tobacco products to active duty military personnel who are aged ≥18 years.</p>

** In California, District of Columbia, Kansas, Minnesota, and U.S. Virgin Islands, legislation was updated to reflect changes in the excise tax rates. The effective dates presented represent the original and updated laws.

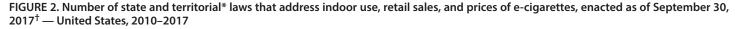
^{††} Guam's T-21 law has been enacted but will not take effect until 2018.

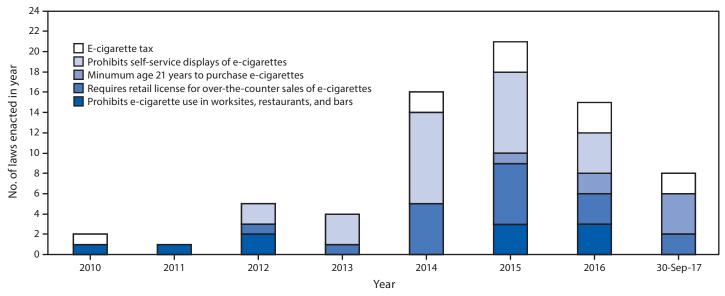
^{§§} Maine's provisions for raising the minimum age of sale of tobacco to 21 years will not begin to be enforced until July 2018. In addition, persons who had attained 18 years of age as of July 1, 2018, will continue to be allowed to buy tobacco products.

On October 23, 2017, New York became the ninth state to include e-cigarettes in its comprehensive smoke-free indoor air law.[§] Thus, one third of the 27 states and DC with comprehensive smoke-free laws that prohibit conventional tobacco smoking in restaurants, worksites, and bars also prohibit e-cigarette use in these venues. Therefore, approximately 75.4% of the U.S. population (an estimated 243.6 million U.S. residents, including 55.7 million children) live in states in which bystanders can be exposed to secondhand e-cigarette aerosol in indoor

public spaces. Previous research indicates that one in four U.S. middle and high school students reported past-month exposure to e-cigarette aerosol in a public place in 2015 (7). This exposure is of public health concern because the U.S. Surgeon General has concluded that e-cigarette aerosol is not harmless water vapor, and environmental studies have documented harmful and potentially harmful ingredients in secondhand e-cigarette aerosol, including nicotine, heavy metals, ultra-fine particulate matter, and volatile organic compounds (2). Including e-cigarettes in comprehensive smoke-free laws can prevent involuntary exposures to secondhand e-cigarette aerosol, especially among vulnerable populations such as youths

[§] New York Senate Bill No. 2543 was enacted on October 23, 2017, and became effective on November 22, 2017. This population estimate includes New York's law, but the law is otherwise excluded from the present study's findings because it was enacted after the September 30, 2017 cutoff date.





* Guam, Puerto Rico, and U.S. Virgin Islands.

⁺ In California, District of Columbia, Kansas, Minnesota, and U.S. Virgin Islands, legislation was updated in later years to reflect changes in tax rates. To avoid duplication, this figure presents the enacted dates only of the original law.

and pregnant women; simplify enforcement of smoke-free policies; and reduce the potential for the renormalization of tobacco product use (2).

The remaining types of laws assessed in this study leverage conventional smoking prevention strategies for youths, which have the potential to prevent youths' e-cigarette access (2,5). Licensing requirements for tobacco retailers and manufacturers can increase the incentive to comply with tobacco-related laws, including those prohibiting sales to youths (2). In addition, restricting self-service tobacco displays can reduce youths' tobacco access by reducing theft and increasing interactions between customers and retailers (8). Increasing the minimum age of tobacco product sales to 21 years is a potential prevention strategy, because 95% of adult smokers begin before age 21, and young adulthood represents a critical period when many smokers progress from experimental to regular tobacco use (9). Finally, substantial increases in conventional cigarette prices reduce consumption, especially among youths. To date, data are limited on the impact of e-cigarette taxes on conventional cigarette use; however, similar to conventional cigarettes, e-cigarette price increases would be expected to reduce use by youths (2,5). Further evaluations of the effectiveness of these strategies can help inform public health practice and planning (2,5).

FDA is authorized to regulate the manufacturing, sales, distribution, and marketing of tobacco products sold in the United States. In May 2016, the agency asserted jurisdiction over products that meet the definition of a tobacco product,

including e-cigarettes. FDA generally cannot restrict public tobacco use, tax tobacco products, or establish a minimum age for tobacco sales above age 18 years (2). However, the Family Smoking Prevention and Tobacco Control Act ensures that localities, states, territories, and tribes can continue to play a central role in tobacco prevention and control policies by preserving their authority to regulate sales, marketing, advertising, and use of tobacco products by persons of any age.[¶] Thus, state, local, territorial, and tribal tobacco control strategies are an important complement to federal regulation, which can help reduce the public health risks of e-cigarettes, particularly among young persons (2).

The findings in this report are subject to at least two limitations. First, STATE does not account for local laws, bills under consideration, regulations, opinions of attorneys general, or case law decisions for tobacco control topics other than preemption. For example, at least 400 localities prohibit indoor e-cigarette use and smoking in worksites, restaurants, and bars,** and at least 200 localities have tobacco-21 laws.^{††} Second, statutory requirements and definitions vary across states. For example, although 26 states have laws or regulations prohibiting self-service displays of e-cigarettes, only three of these states (California, Iowa, and New Mexico) prohibit all

[¶] https://www.gpo.gov/fdsys/pkg/PLAW-111publ31/content-detail.html.

^{**} http://www.no-smoke.org/pdf/ecigslaws.pdf.

^{††} https://www.tobaccofreekids.org/content/what_we_do/state_local_issues/ sales_21/states_localities_MLSA_21.pdf.

self-service displays of e-cigarettes; the remaining 21 states restrict self-service displays to adult-only facilities or tobacco specialty stores and vape shops (6). Moreover, some states have regulated e-cigarettes by expanding the statutory definition of a tobacco product to include e-cigarettes, regardless of nicotine content, to simplify enforcement (2). However, some states define the products as alternative nicotine or vapor products that are exempt from other tobacco product laws, such as licensure requirements and taxes (2).

Given that cigarettes and other combusted tobacco products are responsible for the overwhelming burden of tobacco-related death and disease in the United States (5), the Surgeon General has recommended actions to uphold and accelerate strategies proven to prevent and reduce combustible tobacco smoking among youths and adults, while simultaneously preventing youths' use of emerging tobacco products such as e-cigarettes (2). A comprehensive tobacco control framework, which includes strategies to prevent all tobacco product use by youths and public exposure to secondhand tobacco smoke and e-cigarette aerosol, is important to protect the public's health (2,5).

Acknowledgments

Kisha-Ann S. Williams, Debbie Yembra, Carter Consulting, Inc., Atlanta, Georgia; Ryan Patrick, Hya Qasmieh, MayaTech Corporation, Silver Spring, Maryland; Mark D. Meaney, Tobacco Control Legal Consortium at the Public Health Law Center, St. Paul, Minnesota; Sara E. Wilczek, University at Buffalo School of Public Health and Health Professions, New York.

Conflict of Interest

No conflicts of interest were reported.

¹Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, CDC.

Corresponding author: Kristy Marynak, kmarynak@cdc.gov, 770-488-5493.

References

- Jamal A, Gentzke A, Hu SS, et al. Tobacco use among middle and high school students—United States, 2011–16. MMWR Morb Mortal Wkly Rep 2017;66:597–603. https://doi.org/10.15585/mmwr.mm6623a1
- US Department of Health and Human Services. E-cigarette use among youth and young adults: a report of the Surgeon General. 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
- 3. Food and Drug Administration. 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; restrictions on the sale and distribution of tobacco products and required warning statements for tobacco products. 81 Fed. Reg. 28974 (2016). https://www.federalregister. gov/documents/2016/05/10/2016-10685/deeming-tobacco-products-to-besubject-to-the-federal-food-drug-and-cosmetic-act-as-amended-by-the

Summary

What is already known about this topic?

E-cigarettes are the most commonly used tobacco product among U.S. youths. E-cigarettes typically deliver nicotine, and the U.S. Surgeon General has concluded that nicotine exposure during adolescence can cause addiction and can harm the developing adolescent brain. In addition to federal regulation, states, localities, territories, and tribes maintain broad authority to adopt additional or more stringent requirements regarding tobacco product use, sales, marketing, and other topics.

What is added by this report?

As of September 30, 2017, eight states, the District of Columbia (DC), and Puerto Rico prohibited indoor e-cigarette use and smoking in restaurants, bars, and worksites; 26 states prohibited e-cigarette self-service displays; 16 states, DC, and the U.S. Virgin Islands required a retail license to sell e-cigarettes; five states, DC, and Guam had tobacco-21 laws; and eight states, DC, Puerto Rico, and the U.S. Virgin Islands taxed e-cigarettes. Sixteen states had no such laws.

What are the implications for public health practice?

State, local, and territorial strategies to reduce youths' initiation of e-cigarettes and population exposure to e-cigarette aerosol, which include educational initiatives, coupled with federal regulation of tobacco product manufacturing, labelling, and marketing, could help reduce e-cigarettes' public health risks, especially among young persons.

- Marynak K, Holmes CB, King BA, Promoff G, Bunnell R, McAfee T. State laws prohibiting sales to minors and indoor use of electronic nicotine delivery systems—United States, November 2014. MMWR Morb Mortal Wkly Rep 2014;63:1145–50.
- U.S. Department of Health and Human Services. The health consequences of smoking—50 years of progress: a report of the Surgeon General. Atlanta, GA: US Department of Health and Human Services, CDC; 2014. https:// www.surgeongeneral.gov/library/reports/50-years-of-progress/full-report.pdf
- Tobacco Control Legal Consortium. U.S. e-cigarette regulation: a 50-state review. St. Paul, MN: Tobacco Control Legal Consortium; 2017. http:// www.publichealthlawcenter.org/sites/default/files/E-Cigarette-Legal-Landscape-50-State-Review-March-2017.pdf
- Wang TW, Marynak KL, Agaku IT, King BA. Secondhand exposure to electronic cigarette aerosol among U.S. Youths. JAMA Pediatr 2017;171:490–2. https://doi.org/10.1001/jamapediatrics.2016.4973
- Changelab Solutions. Self-service display of tobacco products: a model ordinance. Oakland, CA: Changelab Solutions; 2017. http://www. changelabsolutions.org/publications/self-service-display-tobacco-products
- Institute of Medicine. Public health implications of raising the minimum age of legal access to tobacco products. Washington, DC: National Academies of Sciences, Institute of Medicine; 2015. http://iom. nationalacademies.org/Reports/2015/TobaccoMinimumAgeReport.aspx

Health and Development at Age 19–24 Months of 19 Children Who Were Born with Microcephaly and Laboratory Evidence of Congenital Zika Virus Infection During the 2015 Zika Virus Outbreak — Brazil, 2017

Ashley Satterfield-Nash, DrPH¹; Kim Kotzky, MPH¹; Jacob Allen, MPH²; Jeanne Bertolli, PhD³; Cynthia A. Moore, MD, PhD³; Isabela Ornelas Pereira⁴; André Pessoa, MD⁵; Flavio Melo, MD⁶; Ana Carolina Faria e Silva Santelli, MD⁷; Coleen A. Boyle, PhD³; Georgina Peacock, MD³

In November 2015, the Brazilian Ministry of Health (MOH) declared the Zika virus outbreak a public health emergency after an increase in microcephaly cases was reported in the northeast region of the country (1). During 2015–2016, 15 states in Brazil with laboratory-confirmed Zika virus transmission reported an increase in birth prevalence of microcephaly (2.8 cases per 10,000 live births), significantly exceeding prevalence in four states without confirmed transmission (0.6 per 10,000) (2). Although children with microcephaly and laboratory evidence of Zika virus infection have been described in early infancy (3), their subsequent health and development have not been well characterized, constraining planning for the care and support of these children and their families. The Brazilian MOH, the State Health Secretariat of Paraíba, and CDC collaborated on a follow-up investigation of the health and development of children in northeastern Brazil who were reported to national surveillance with microcephaly at birth. Nineteen children with microcephaly at birth and laboratory evidence of Zika virus infection were assessed through clinical evaluations, caregiver interviews, and review of medical records. At follow-up (ages 19-24 months), most of these children had severe motor impairment, seizure disorders, hearing and vision abnormalities, and sleep difficulties. Children with microcephaly and laboratory evidence of Zika virus infection have severe functional limitations and will require specialized care from clinicians and caregivers as they age.

The Zika Outcomes and Development in Infants and Children (ZODIAC) investigation sought to compile a comprehensive description of health and development among children aged >12 months who were born with microcephaly and participated in a 2016 case-control investigation. The case-control investigation assessed the association of Zika virus infection and microcephaly among children aged 1–7 months, living in Paraíba state. The children and their caregivers were evaluated by multidisciplinary teams at two state clinics in Campina Grande and João Pessoa (macroregions 1 and 2) in Paraíba state during August–October 2017. This report describes a subsample of 19 children, aged 19–24 months, who participated in ZODIAC and were born with microcephaly and with laboratory evidence of Zika virus infection.

All children in the ZODIAC investigation were born from October 1, 2015 through January 31, 2016, and were reported to the Registro de Eventos de Saúde Pública (RESP)-Microcefalias, Brazil's national microcephaly registry. For infants to be eligible for the 2016 case-control investigation, their mothers must have resided in Paraíba state for at least 80% of their pregnancy. For the ZODIAC investigation, microcephaly was defined as head circumference below the third percentile for gestational age and sex, according to INTERGROWTH 21st standards (4). Subsequent measurements are reported in standard deviations (SD) to better characterize growth deficiencies (5). Laboratory evidence of Zika virus infection was defined as a positive test for Zika virus immunoglobulin M (IgM) and virus specific-neutralizing antibodies or a positive test for Zika virus-specific neutralizing antibodies in an infant sample (6). Samples were obtained at age 1-7 months in the 2016 case-control investigation, and any evidence of infection was assumed to be prenatal in origin. Results of prenatal and newborn testing to rule out other congenital infections were available for some infants and their mothers.

ZODIAC data were collected through clinical evaluations, caregiver interviews, and review of medical records. Licensed physicians performed growth, ophthalmologic and physical exams, and a neurologic assessment. Physicians were trained to use the Hammersmith Infant Neurological Examination (HINE), a standardized neurologic exam, to assess neuromotor function and visual and auditory responses (7). Trained interviewers administered screening and assessment instruments to the primary caregiver (usually the mother) regarding the child's health and development, including a seizure screener (8), the Ages and Stages Questionnaires (ASQ-3),* and the Ages and Stages Social-Emotional Questionnaires (ASQ:SE).[†] Data were captured in REDCap, a secure web application.

1347

^{*}A series of 21 parent-completed questionnaires designed to screen the developmental performance of children aged 1–66 months in the areas of communication, gross motor skills, fine motor skills, problem solving, and personal-social skills. The age-appropriate questionnaire is completed by the parent or caregiver (http://agesandstages.com).

[†]A series of nine age-appropriate parent-completed questionnaires designed to screen young children for social-emotional issues during the first 6 years of life for seven social-emotional areas: self-regulation, compliance, adaptive functioning, autonomy, affect, social-communication, and interaction with people (http://agesandstages.com).

The families of 278 previously studied children residing in the ZODIAC investigation catchment area were eligible for inclusion; 122 children were enrolled, including 19 who were aged <24 months and who had both microcephaly at birth and laboratory evidence of Zika virus infection. Among the 19 children, 11 had a blood specimen that tested positive for Zika virus-specific IgM antibodies and neutralizing antibodies against Zika virus, and eight had only neutralizing antibodies against Zika virus. Among the eight with neutralizing antibodies only, seven had at least one test for other congenital infections; one had a positive Toxoplasma immunoglobulin G (IgG) antibody result and one had positive rubella virus and cytomegalovirus IgG results. Both had negative IgM antibody results for these infections; the first had brain imaging findings consistent with congenital Zika virus infection and the second had no record of imaging.

The median age at follow-up evaluation was 22 months (range = 19–24 months); 10 were male and nine were female. At the time of assessment, 15 children (seven males and eight females) had head circumference measurements more than 3 SDs below the mean for their age and sex (Table 1) (Table 2). Four children had an increase in head circumference for age from birth measurements: three males had head circumference within 1 SD below the mean and one female had head circumference within 1 SD above the mean. Thirteen children (six males and seven females) had length measurements 1–3 SDs below the mean, and 13 children (six males and seven females) had negative means and seven females) had weight measurements 1 to >3 SDs below the mean for their age and sex.

Eleven children screened positive for nonfebrile seizures, indicating possible seizure disorder (Table 2) (Table 3). Caregivers reported that eight children were previously hospitalized, including six hospitalized for bronchitis/pneumonia, and that 10 children had frequent sleeping difficulties and nine had eating or swallowing challenges. Thirteen children had an impaired response to auditory stimuli. Four children had retinal abnormalities and 11 had an impaired response to visual stimuli. Fifteen children did not pass the ASQ-3 age interval questionnaire designed for a child aged 6 months. Fifteen children had a global score below 40 on the HINE, indicating severe motor impairment, including 14 who had findings consistent with cerebral palsy (7). Outcomes including feeding challenges, sleeping difficulties, severe motor impairment, vision and hearing abnormalities, and seizures tended to co-occur. All children had at least one of these outcomes, 12 had three to five of these outcomes, and two had all six outcomes. Four children (infant number 16, 17, 18, and 19) (Table 2) had typical growth and development at follow-up and might have been misclassified at birth.

TABLE 1. Growth measurements* of children aged 19–24 months with confirmed or probable congenital Zika virus infection^{†,§} and microcephaly classification at birth^{¶,**} — Paraíba, Brazil, August–October 2017

	No. (%)			
Growth	Male (n = 10)	Female (n = 9)		
Head circumference ^{††}				
>3 SD below mean for age and sex ^{§§}	7 (70)	8 (89)		
Length ^{¶¶}				
1–3 SD below mean for age and sex***	6 (60)	7 (78)		
Weight ⁺⁺⁺				
1 to >3 SD below mean for age and sex ^{§§§}	6 (60)	7 (78)		

Abbreviation: SD = standard deviation.

* http://www.who.int/childgrowth/standards/en.

- ⁺ Confirmed congenital Zika virus infection was indicated by a positive Zika virus-specific immunoglobulin M [IgM] capture enzyme-linked immunosorbent assay [MAC-ELISA] result on infant cerebrospinal fluid [CSF] or serum) and positive plaque reduction neutralization testing (PRNT). Serologic evidence without confirmation via PRNT indicated probable congenital Zika virus infection.
- [§] http://jcm.asm.org/content/38/5/1823.full.pdf+html.
- ¹ Microcephaly at birth was defined according to the internationally accepted definition, head circumference below the 3rd percentile for gestational age and sex, from the standards for newborns and references for very preterm infants compiled by the International Fetal and Newborn Growth Consortium for the 21st Century.
- ** https://intergrowth21.tghn.org/.
- ⁺⁺ http://www.who.int/childgrowth/standards/hc_for_age/en/.
- ^{§§} Of the remaining males, three (30%) had a head circumference equal to the mean or up to 1 SD below the mean, and of the remaining females, one (11%) had a head circumference equal to the mean or up to 1 SD above the mean.
- ^{¶¶} http://www.who.int/childgrowth/standards/height_for_age/en/.
- *** Of the remaining males, the length of 4 (40%) was equal to the mean or up to 3 SDs above the mean, and of the remaining females, the length of 2 (22%) was equal to the mean or up to 1 SD above the mean.
- ⁺⁺⁺ http://www.who.int/childgrowth/standards/weight_for_age/en/.
- ^{§§§} Of the remaining males, the weight of 3 (30%) was equal to the mean or up to 2 SDs above the mean; the weight of 1 (10%) male was >3 SDs above the mean. Of the remaining females, the weight of 2 (22%) was equal to the mean or up to 2 SDs above the mean.

Discussion

As of September 2017, 2,986 newborns with microcephaly in Brazil were reported to RESP and 2,959 cases are being monitored (9). Children with Zika virus-associated microcephaly face medical and functional challenges that span many areas of development. Previous reports established a baseline of poor health outcomes at birth, including severe brain and ophthalmologic abnormalities, and other serious central nervous system abnormalities (3). This report expands on initial findings by demonstrating that specific outcomes, such as severe motor impairment and impaired visual and auditory response to stimuli, affect the majority of children with evidence of congenital Zika virus infection and microcephaly and become more apparent as these children age. Approximately three quarters of young children affected by Zika virus infection in this analysis had at least three of the specified co-occurring outcomes. Many of the initial findings

Infant no.	Sex	Birth HC ^{**} (%)	ZODIAC HC ^{††} (Z score)	ZODIAC weight ^{§§} (Z score)	Brain imaging consistent with CZS		Seizures	Eating challenges	Sleep challenges	Severe motor impairment	Vision limitation	Hearing abnormalities	ASQ-3 age interval ^{¶¶}
1	F	<3rd	-7.85	-1.68	Yes	IgM +; NAb +	Yes	Yes	Yes	Yes	Yes	Yes	<6 months
2	F	<3rd	-7.21	-0.98	Yes	IgM +; NAb +	No	No	Yes	Yes	Yes	Yes	<6 months
3	F	<3rd	-7.08	-4.47	Yes	IgM +; NAb +	Yes	No	Yes	Yes	No	No	<6 months
4	М	<3rd	-4.88	-2.40	Yes	NAb + only	No	Yes	No	Yes	No	Yes	<6 months
5	М	<3rd	-4.20	1.90	Yes	NAb + only	Yes	No	Yes	Yes	Yes	Yes	<6 months
6	F	<3rd	-5.36	-0.86	Yes	IgM +; NAb +	No	No	No	Yes	No	Yes	<6 months
7	F	<3rd	-8.02	-1.56	Yes	NAb + only	Yes	Yes	No	Yes	Yes	No	<6 months
8	М	<3rd	-5.75	-4.11	Yes	IgM +; NAb +	Yes	No	No	Yes	No	Yes	<6 months
9	М	<3rd	-5.83	-1.46	Yes	IgM +; NAb +	No	Yes	No	Yes	Yes	Yes	<6 months
10	F	<3rd	-6.65	-1.23	Yes	IgM +; NAb +	Yes	Yes	Yes	Yes	Yes	Yes	<6 months
11	F	<3rd	-5.67	-0.91	Yes	NAb + only	Yes	Yes	No	Yes	Yes	Yes	<6 months
12	М	<3rd	-3.69	3.52	Yes	IgM +; NAb +	Yes	No	Yes	Yes	Yes	Yes	<6 months
13	М	<3rd	-7.03	-2.36	Yes	IgM +; NAb +	Yes	No	Yes	Yes	Yes	Yes	<6 months
14	F	<3rd	-8.45	0.18	Yes	IgM +; NAb +	Yes	Yes	No	Yes	Yes	Yes	<6 months
15	М	<3rd	-6.29	-1.60	Yes	IgM +; NAb +	Yes	Yes	No	Yes	Yes	Yes	<6 months
16	М	<3rd	-0.68	1.52	No record	NAb + only	No	No	Yes	No	No	No	>6 months
17	М	<3rd	-0.18	-0.87	No record	NAb + only	No	No	Yes	No	No	No	>6 months
18	F	<3rd	0.23	1.28	No anomaly	NAb + only	No	Yes	No	No	No	No	>6 months
19	М	<3rd	-0.09	1.14	No record	NAb + only	No	No	Yes	No	No	No	>6 months

TABLE 2. Growth parameters,^{*} evaluations, and medical and developmental conditions for 19 infants aged 19–24 months with confirmed or probable congenital Zika virus infection,^{†,§} and microcephaly classification^{1,**} at birth — ZODIAC investigation, Paraíba, Brazil, August–October 2017

Abbreviations: ASQ-3 = Ages and Stages-III Questionnaire; CZS = congenital Zika syndrome; F = female; HC = head circumference; IgM = immunoglobulin M; M = male; NAb = neutralizing antibodies; ZODIAC = Zika Outcomes and Development in Infants and Children.

* http://www.who.int/childgrowth/standards/en.

⁺ Confirmed congenital Zika virus infection was indicated by a positive Zika virus-specific IgM capture enzyme-linked immunosorbent assay result on infant cerebrospinal fluid or serum) and positive plaque reduction neutralization testing (PRNT). Serologic evidence without confirmation via PRNT indicated probable congenital Zika virus infection.

[§] http://jcm.asm.org/content/38/5/1823.full.pdf+html.

[¶] Microcephaly at birth was defined according to the internationally accepted definition, head circumference below the 3rd percentile for gestational age and sex from the standards for newborns and references for very preterm infants compiled by the International Fetal and Newborn Growth Consortium for the 21st Century. ** https://intergrowth21.tghn.org/.

thtp://www.who.int/childgrowth/standards/hc_for_age/en/.

§§ http://www.who.int/childgrowth/standards/weight_for_age/en/.

^{¶1} The ASQ-3 is a series of 21 parent-completed questionnaires designed to screen the developmental performance of children aged 1–66 months in the areas of communication, gross motor skills, fine motor skills, problem solving, and personal-social skills (http://agesandstages.com); based on ASQ-3 screening, an age interval of <6 months indicates that the child's parent-reported developmental progress has not advanced beyond that typical of an infant at age 6 months.</p>

identified at birth remain present at ages 19–24 months, and these children are falling far behind in achievement of ageappropriate developmental milestones, indicating the need for long-term follow-up and support.

The findings in this report are subject to at least four limitations. First, although all children with microcephaly recruited into the 2016 case-control investigation from selected areas of Paraíba state were offered enrollment in the ZODIAC investigation, not all families chose to participate. Consequently, the findings might not be representative of all children with microcephaly associated with congenital Zika virus infection. Second, errors in head circumference measurement at birth and passive transfer of maternal antibodies might have led to misidentification and might explain the divergent observations for the four children showing more typical development. Additionally, some of the parent-assessment findings, such as those from the seizure screener, were not medically verified. Finally, the ages of infants in the original case-control investigation ranged from 1 to 7 months at the time of blood collection, and it is possible that the laboratory results for some infants reflected postnatal, rather than prenatal, exposure. TABLE 3. Health and developmental outcomes of 19 children aged 19–24 months with confirmed or probable congenital Zika virus infection,^{*,†} and microcephaly classification^{§,¶} at birth — Paraíba, Brazil, August–October 2017

Outcome	No. (%)
Medical findings	
Seizures**, ^{††}	11 (58)
Retinal abnormalities ^{§§}	4 (21)
Hospitalization**	8 (42)
Pneumonia/Bronchitis	6 (75)
Intestinal infection	1 (14)
High fever	1 (14)
Failure to thrive/feed	1 (14)
Functional outcomes	
Sleeping difficulties**	10 (53)
Feeding difficulties**	9 (47)
Impaired response to auditory stimuli (hearing asymmetric or no response) ^{¶¶}	13 (68)
Impaired response to visual stimuli ^{¶¶}	11 (58)
Neurologic outcomes ^{¶¶}	
Severe motor impairment ^{¶¶}	15 (79)
Cerebral palsy***	14 (74)

* Confirmed congenital Zika virus infection was indicated by a positive Zika virus-specific immunoglobulin M capture enzyme-linked immunosorbent assay result on infant cerebrospinal fluid or serum and positive plaque reduction neutralization testing (PRNT) at birth. Serologic evidence without confirmation via PRNT indicated probable congenital Zika virus infection.

⁺ http://jcm.asm.org/content/38/5/1823.full.pdf+html.

[§] Microcephaly at birth was defined according to the internationally accepted definition, head circumference below the 3rd percentile for gestational age and sex from the standards for newborns and references for very preterm infants compiled by the International Fetal and Newborn Growth Consortium for the 21st Century.

[¶] https://intergrowth21.tghn.org/.

** Reported by the caregiver.

- ⁺⁺ https://doi.org/10.1016/j.pediatrneurol.2015.09.016.
- §§ Retinal abnormalities were identified by ophthalmologic exam.
- ^{¶¶} Motor function, functional hearing, and functional vision were assessed using the Hammersmith Infant Neurologic Exam (HINE). A global score below 40 on the HINE is associated with severe motor impairment, according to findings published in 2016 (https://doi.org/10.1111/dmcn.12876).

*** Cerebral palsy was identified by neurologist.

This report provides information on the ongoing challenges facing children with severe congenital Zika virus syndrome; these children will require specialized care from clinicians and caregivers as they age. These findings allow for anticipation of medical and social service needs of affected children and their families, including early intervention services, and planning for resources to support these families in health care and community settings in Brazil, the United States, and other countries. Children with disabilities related to congenital Zika virus infection will need multidisciplinary care from various pediatric subspecialists (10). Long-term follow-up and measurement of developmental progression of children affected by Zika virus can inform intervention services and sub-specialities needed to provide optimal care for these children.

Summary

What is already known about this topic?

Congenital Zika virus infection has been linked to increased rates of microcephaly and a unique pattern of birth defects among infants. Although children with microcephaly and laboratory evidence of Zika virus infection have been described in early infancy, the subsequent health and development in young children have not been well characterized, constraining planning for the care of these children.

What is added by this report?

The growth and development of 19 children, aged 19–24 months, with laboratory evidence of Zika virus infection were thoroughly assessed. All children had at least one adverse outcome including feeding challenges, sleeping difficulties, severe motor impairment, vision and hearing abnormalities, and seizures, and these outcomes tended to co-occur.

What are the implications for public health practice?

Children with microcephaly and laboratory evidence of Zika virus infection face medical and functional challenges that span many areas of development, some of which become more evident as children age. They will continue to require specialized care from clinicians and caregivers. These data allow for anticipation of medical and social services needs of affected children and families, such as early intervention services, and planning for resources to support these families in healthcare and community settings.

Acknowledgments

Alanna dos Santos Delfino, Analine de Souza Bandeira Correia, Bruna Valerio Correia, Camila Carla de Arruda Silva, Camille Harden, Camille Smith, Charles Rose, Christine Coeli Moreira da Silva, Claudia Ferreira Rineiro Leao, Cláudia Luciana de Sousa Mascena Veras, Eric Dziuban, Erlane Marques Ribeiro, J. Erin Staples, Joria Guerreiro, Larissa Ribeiro Do Amaral, Maria Celeste Dantas Jotha De Lima, Myrian Carvalho, Daniele Ribeiro Magalhães Camelo, Eliza Gordon-Lipkin, Fabio Ramon Bezerra Clementino, Flawber Antonio Cruz, Georgia Medeiros Lopes De Souza Lucio, Isadora Silveira Xavier, Ivanice Jacinto da Silva, Jeanete Romao dos Santos, Jennita Reefhuis, Juliana Carneiro Monteiro Wanderley, Juliana Sousa Soares De Araujo, Kallytuana Mell Silva Sarmento, Karla Naraiane de Araujo, Karoline Marques Dantas, Mariana Bernardo Bezerra, Mariana Braatz Krueger, Michael Fox, Nathalie Maitre, Nevin Krishna, Pâmela Rodrigues Barbosa, Patricia Karla Guimaraes Brito, Priscila Leal Leite, Rafaela Domingos da Cunha, Rafaela Soares Barros de Menezes, Rafaella Alves Sarmento Costa, Rebecca Bitsko, Renato Girade, Renato Lima, Rogeirio Alves de Santana, Saile Cavalcante Kerbage, Suzanne Gilboa, Thalita Analyane Bezerra de Albuquerque, Thayse Elaine Costa Figueiredo, Vandezita Dantas De Medeiros Mazzaro, Virginia Batista de Morais.

Conflict of Interest

Ana Carolina Faria e Silva Santelli received funding through an Interagency Agreement between the United States Agency for International Development and CDC for work on Zika during conduct of the study. No other conflicts of interest were reported.

Corresponding author: Ashley Satterfield-Nash, yev6@cdc.gov, 404-498-6084.

References

- Pan American Health Organization. Timeline of emergence of Zika virus in the Americas. Washington DC: Word Health Organization, Pan American Health Organization; 2016. http://www.paho.org/hq/index. php?option=com_content&view=article&id=11959:timeli ne-of-emergence-of-zika-virus-in-the-americas&Itemid=41711&lang=en
- Kleber de Oliveira W, Cortez-Escalante J, De Oliveira WT, et al. Increase in reported prevalence of microcephaly in infants born to women living in areas with confirmed Zika virus transmission during the first trimester of pregnancy—Brazil, 2015. MMWR Morb Mortal Wkly Rep 2016;65:242–7. https://doi.org/10.15585/mmwr.mm6509e2
- Moore CA, Staples JE, Dobyns WB, et al. Characterizing the pattern of anomalies in congenital Zika syndrome for pediatric clinicians. JAMA Pediatr 2017;171:288–95. https://doi.org/10.1001/jamapediatrics.2016.3982

- 4. International Fetal and Newborn Growth Consortium for the 21st Century. Standards for newborns and references for very preterm infants. Oxford, United Kingdom: International Fetal and Newborn Growth Consortium for the 21st Century; 2017. https://intergrowth21.tghn.org/
- 5. World Health Organization. Child growth standards. Head circumference for age. Geneva, Switzerland: World Health Organization; 2017. http://www.who.int/childgrowth/standards/hc_for_age/en/
- Martin DA, Muth DA, Brown T, Johnson AJ, Karabatsos N, Roehrig JT. Standardization of immunoglobulin M capture enzyme-linked immunosorbent assays for routine diagnosis of arboviral infections. J Clin Microbiol 2000;38:1823–6.
- Romeo DM, Ricci D, Brogna C, Mercuri E. Use of the Hammersmith Infant Neurological Examination in infants with cerebral palsy: a critical review of the literature. Dev Med Child Neurol 2016;58:240–5. https:// doi.org/10.1111/dmcn.12876
- Douglass LM, Kuban K, Tarquinio D, et al. A novel parent questionnaire for the detection of seizures in children. Pediatr Neurol 2016;54:64–69. e1. https://doi.org/10.1016/j.pediatrneurol.2015.09.016
- Secretaria de Vigilância em Saúde, Ministério da Saúde. Integrated monitoring of changes in growth and development related to Zika virus infection and other infectious etiologies, up to Epidemiological week 38 of 2017.Brasília, Brazil: Ministry of Health Brazil, Secretaria de Vigilância em Saúde, Ministério da Saúde; 2017. http://portalarquivos2. saude.gov.br/images/pdf/2017/novembro/16/2017-036.pdf
- Adebanjo T, Godfred-Cato S, Viens L, et al. Update: interim guidance for the diagnosis, evaluation, and management of infants with possible congenital Zika virus infection—United States, October 2017. MMWR Morb Mortal Wkly Rep 2017;66:1089–99. https://doi.org/10.15585/ mmwr.mm6641a1

¹Oak Ridge Institute for Science and Education, Oak Ridge, Tennessee; ²Eagle Global Scientific, San Antonio, Texas; ³National Center on Birth Defects and Developmental Disabilities, CDC; ⁴Ministry of Health Brazil; ⁵Hospital Infantil Albert Sabin, Fortaleza, Ceará, Brazil; ⁶Hospital Regional de Guarabira/ Governo do Estado da Paraíba, Paraíba, Brazil; ⁷Center for Global Health, CDC Brazil.

Large Outbreak of *Neisseria meningitidis* Serogroup C — Nigeria, December 2016–June 2017

Chimeremma Nnadi MD, PhD¹; John Oladejo, MBBS²; Sebastian Yennan, MPH²; Adesola Ogunleye, DDS²; Chidinma Agbai, MPH³; Lawal Bakare, MBBS²; Mohammed Abdulaziz, MBBS⁴; Amina Mohammed, MBBS⁵; Mary Stephens, MBBS⁶; Kyadindi Sumaili, MPH⁷; Olivier Ronveaux, MBBS⁸; Helen Maguire, MBBS⁹; Debra Karch, PhD¹⁰; Mahmood Dalhat, MBBS¹¹; Martin Antonio, PhD¹²; Andre Bita, MBBS¹³; Ifeanyi Okudo, MBBS⁶; Patrick Nguku, MBBCH¹¹; Ryan Novak, PhD¹⁴; Omotayo Bolu, MD¹⁵; Faisal Shuaib DrPH⁵; Chikwe Ihekweazu, MBBS²

On February 16, 2017, the Ministry of Health in Zamfara State, in northwestern Nigeria, notified the Nigeria Centre for Disease Control (NCDC) of an increased number of suspected cerebrospinal meningitis (meningitis) cases reported from four local government areas (LGAs). Meningitis cases were subsequently also reported from Katsina, Kebbi, Niger, and Sokoto states, all of which share borders with Zamfara State, and from Yobe State in northeastern Nigeria. On April 3, 2017, NCDC activated an Emergency Operations Center (EOC) to coordinate rapid development and implementation of a national meningitis emergency outbreak response plan. After the outbreak was reported, surveillance activities for meningitis cases were enhanced, including retrospective searches for previously unreported cases, implementation of intensified new case finding, and strengthened laboratory confirmation. A total of 14,518 suspected meningitis cases were reported for the period December 13, 2016–June 15, 2017. Among 1,339 cases with laboratory testing, 433 (32%) were positive for bacterial pathogens, including 358 (82.7%) confirmed cases of Neisseria meningitidis serogroup C. In response, approximately 2.1 million persons aged 2-29 years were vaccinated with meningococcal serogroup C-containing vaccines in Katsina, Sokoto, Yobe, and Zamfara states during April–May 2017. The outbreak was declared over on June 15, 2017, after high-quality surveillance yielded no evidence of outbreak-linked cases for 2 consecutive weeks. Routine highquality surveillance, including a strong laboratory system to test specimens from persons with suspected meningitis, is critical to rapidly detect and confirm future outbreaks and inform decisions regarding response vaccination.

Background

All northern Nigeria states lie within the sub-Saharan "Meningitis Belt," a region of 26 countries that experiences the largest burden of meningococcal disease, with annual epidemics reported during the December–June dry season. Meningitis causes severe illness, and if not detected and treated quickly, could lead to permanent disability that puts a significant burden on families. In many settings, approximately 10% of meningitis cases ultimately result in death. Before introduction of the meningococcal serogroup A conjugate vaccine (MenAfriVac) in 2013 (1), Nigeria experienced some of the largest epidemics of meningococcal meningitis, including the 1996 *N. meningitidis* serogroup A (NmA) epidemic that resulted in 109,580 suspected cases and 11,717 reported deaths (2). In 2013, a new strain of *N. meningitidis* serogroup C (NmC) emerged in Nigeria, resulting in small focal outbreaks during 2014–2016 (3,4). In 2015, this strain of NmC entered neighboring Niger, resulting in the largest ever global epidemic of serogroup C meningitis (5), until the 2016–2017 Nigeria epidemic described in this report. Molecular sequencing of bacterial isolates from patients in the region has confirmed the expansion of this new strain of serogroup C in five countries in the region (Ryan Novak, National Center for Immunization and Respiratory Diseases, CDC, personal communication, 2017).

Case Definition and Incidence Thresholds for Response

A suspected case of meningitis was defined as the sudden onset of fever (>100.4°F [>38.0°C]) and at least one meningeal sign, including neck stiffness or altered consciousness in any person, or a bulging anterior fontanelle in children aged <18 months (6). Available cerebrospinal fluid (CSF) or blood specimens from patients meeting the suspected meningitis case definition were transported to a designated laboratory for confirmation by culture, latex agglutination, or real-time-polymerase chain reaction (PCR) tests. World Health Organization (WHO) Meningitis Outbreak Response Guidelines were used to identify geographic areas at risk for epidemics to guide response (6). Attack rates of suspected meningitis cases reported weekly by LGAs were calculated. WHO recommends that a set of preparedness activities be implemented when the attack rate of suspected meningitis in an LGA crosses a defined "Alert" threshold, and additional response activities at a defined "Epidemic" threshold (Table 1).

Outbreak Investigation

Two outbreak investigation teams were deployed to Zamfara and Sokoto states to augment routine surveillance, forward available CSF specimens to a designated laboratory for analysis, verify the extent of the outbreak, and gather specific information regarding the affected population to guide response. The

TABLE 1. Guidelines for incidence thresholds and interventions for detection and control of epidemic meningococcal meningitis based on
population size of the local government area in countries in Africa with endemic disease* — World Health Organization

Incidence threshold	Popula			
	<30,000	- Interventions		
Alert	Two suspected cases in 1 week or increase in incidence compared with nonepidemic years	Three suspected cases per 100,000 population per week (two or more cases in 1 week)	 Inform authorities, 2) strengthen surveillance, investigate, 4) confirm (including laboratory), treat cases, 6) prepare for eventual response 	
Epidemic	Five suspected cases in 1 week [†] or doubling of number of cases in a 3-week period	10 suspected cases per 100,000 population per week	1) Conduct mass vaccination [§] within 4 weeks of crossing epidemic threshold, 2) distribute treatment to health centers, 3) treat according to epidemic protocol, 4) inform the public	

* Guidelines adapted from http://apps.who.int/iris/handle/10665/144727.

⁺ In special situations such as mass gatherings, refugees, displaced persons or closed institutions, two confirmed cases in a week should prompt mass vaccination. [§] If an area neighboring one targeted for vaccination is considered to be at risk (e.g., cases early in the dry season, no recent relevant vaccination campaign, or high

population density), it should be included in a vaccination program.

first meningitis cases, a 21-case cluster in a village in Zurmi LGA of Zamfara State, were reported to the State Ministry of Health in December 2016; however, the cluster was not reported to NCDC until February 2017, after the outbreak had spread to four other LGAs in Zamfara, and to Katsina, Kebbi, Niger, and Sokoto states. During December 2016–June 2017, among Nigeria's 37 state-level jurisdictions, 26 (70%) reported suspected meningitis cases, with peak incidence during reporting week 15 (April 16–22, 2017) (Figure). Meningitis incidence in 56 LGAs met the alert threshold and in 38 met the epidemic threshold. Overall, 14,518 suspected cases and 1,166 deaths (case-fatality ratio = 8.0%), were reported during the outbreak; 7,140 (49%) cases were reported from Zamfara State, and 6,792 (47%) occurred in children aged 5-14 years (Table 2). Confirmatory laboratory testing was conducted for specimens from 1,339 (9%) suspected meningitis patients; among these, 433 (32.3%) were laboratory-confirmed as bacterial meningitis, including 358 (82.7%) with NmC (Table 2).

Early Outbreak Response Activities

Following initial investigations, including health facility register reviews and analysis of community informant reports, NCDC activated the meningitis EOC on April 3, 2017 to coordinate outbreak response strategies and operations across the entire country in collaboration with country partner agencies, including WHO, CDC, the Africa Centre for Disease Control and Prevention, the United Nations Children's Fund (UNICEF) and the Africa Field Epidemiology Network. To ensure that suspected meningitis cases were rapidly detected and investigated, meningitis surveillance, according to WHO's Africa Region Guidelines for Enhanced Meningitis Surveillance, was strengthened in all states, regardless of whether states reported cases. EOCs were also activated to coordinate outbreak response activities in Sokoto and Zamfara states, the two states at the epicenter of the outbreak. Rapid response teams of epidemiologists and clinicians were deployed from the national EOC to support states with at least one LGA meeting the defined outbreak threshold.

Early outbreak response activities were hampered by difficulty in accessing some of the more rural and remote communities experiencing the outbreak. A limited capacity for CSF specimen collection among health care workers, deficiencies in the laboratory systems, including a lack of basic test kits and limited resources to support timely and appropriate specimen transportation from health facilities to a laboratory with PCR or culture capacity, contributed to delayed case identification. Additionally, the human resources needed to support effective outbreak detection and response were limited in some of the states with the largest case numbers, necessitating the recruitment and deployment of a large contingent of ad hoc technical support personnel from the national level to support outbreak control activities in these states.

Outbreak Response Vaccination

The National Primary Health Care Development Agency, responsible for vaccination activities in Nigeria, received meningococcal C-containing vaccines through the International Coordinating Group on Vaccine Provision in April 2017, 2 months after the outbreak was first widely reported. Because of limited vaccine supplies, vaccine use was prioritized to the most affected LGAs in Katsina, Sokoto, Yobe, and Zamfara states (6) where approximately 2.1 million (84.4%) of an estimated 2.5 million persons at risk (based on the WHO guidelines) aged 2–29 years were vaccinated. Extensive social mobilization activities, including outreach to community leaders and engagement on social and traditional media helped raise awareness and facilitate desired behavior change, including vaccine acceptance and avoidance of overcrowding, thereby reducing potential for continued transmission.

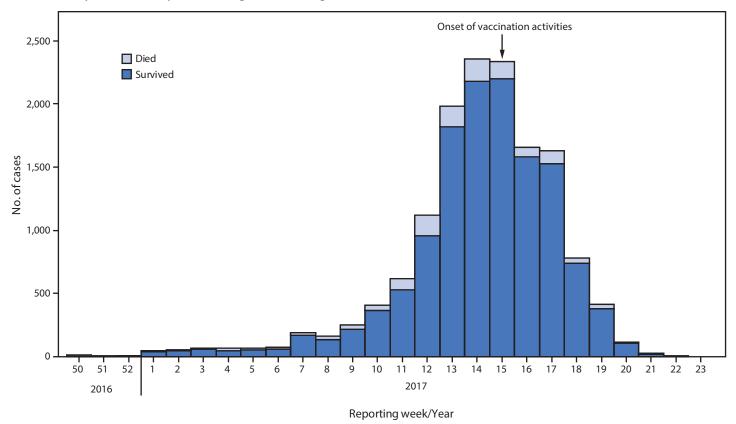


FIGURE. Weekly number of suspected meningitis cases — Nigeria, December 2016–June 2017*

* Reporting week 15 corresponds to April 16–22, 2017; week 21 corresponds to June 4–10, 2017.

Discussion

The outbreak likely represents the largest global outbreak of NmC. Response measures implemented during the outbreak, including improved case finding and management as well as mass vaccination campaigns, might have contributed to the outbreak control. However, the large number of cases and prolonged duration of the outbreak highlight key lessons for meningitis outbreak prevention, detection, and response in Nigeria and other countries in the meningitis belt. Timely and appropriate use of meningococcal vaccines is effective in preventing and limiting the spread of meningococcal meningitis outbreaks. The introduction of the meningococcal A conjugate vaccine against NmA in Nigeria and other countries in the meningitis belt represents a major milestone in meningitis outbreak control and has contributed to significant reductions in NmA infections (7,8). However, laboratory data from this and other recent outbreaks point to the evolving regional meningitis epidemiology with increasing proportions of epidemics attributable to bacterial meningitis pathogens other than NmA, for which meningococcal A conjugate vaccine provides no protection (3,4). These findings suggest an urgent need to

expand availability of multivalent vaccines that are effective against non-A serogroups.

In Nigeria, meningitis is classified as an epidemic-prone disease, requiring immediate notification, investigation, and necessary action (9); significant lapses in reporting in the early stages of this outbreak (from December 2016 to February 2017) might have contributed to its large size and wide reach. Additionally, limited capacity for CSF specimen collection, a lack of test kits, and inadequate resources to support timely and appropriate specimen transportation from health facilities to a laboratory with PCR or culture capacity contributed to the low percentage of confirmed meningitis cases. Similarly, delays in case finding, reporting and investigation, especially in the more remote areas, limited timely outbreak response. These meningitis surveillance system weaknesses merit further investigation, with remediating action implemented to prevent future reoccurrence. Because delayed access to meningococcal vaccines might have contributed to the prolonged outbreak duration, a careful examination of country vaccine requisition processes, and International Coordinating Group on Vaccine Provision protocols for vaccine requests, approval, delivery and use, is needed.

TABLE 2. Characteristics of patients in 14,518 suspected cerebrospinal
meningitis cases — Nigeria, December 2016–June 2017

Characteristic	No. (%)
Sex	
Male	7,802 (53.7)
Female	6,699 (46.2)
Missing/Unknown	17 (0.1)
Age group (yrs)	
<1	219 (1.5)
1–4	1,796 (12.4)
5–14	6,792 (46.8)
≥15	5,667 (39.1)
Missing/Unknown	44 (0.3)
State	
Zamfara	7,140 (49.2)
Sokoto	4,980 (34.3)
Katsina	915 (6.3)
Yobe	415 (2.9)
Kebbi	142 (1.0)
Niger	131 (0.9)
Other	795 (5.5)
Meningococcal serogroup or other identified	organism* ^{,†}
A	27 (6.2)
В	1 (0.2)
C	358 (82.7)
W	1 (0.2)
X§	
Y	0 (0)
Unknown	32 (7.4)
Haemophilus influenzae (type b)	5 (1.2)
Streptococcus pneumoniae	9 (2.1)

* Total number of laboratory specimens tested = 1,339; 433 specimens yielded meningococcal or nonmeningococcal organisms. A total of 129 test results were invalid or missing, and the rest were classified as negative for any organisms tested.

[†] Cases confirmed by any of the following tests: latex agglutination, polymerase chain reaction, or culture.

§ Laboratory tests not available to detect Neisseria meningitidis serogroup X.

A surveillance and outbreak response system is most effective when the capacity to prevent, detect, and appropriately respond to outbreaks is available (10). In Nigeria, the human resource capacity to support an effective outbreak response varied widely within and between states, and was severely limited in some of the most at-risk states and LGAs. In low human resource capacity settings, evolving and refining new models for effective and timely outbreak detection and response, including scaling up emergency Rapid Response Team deployment where needed, is critical. In Nigeria, an opportunity exists for improved response coordination with lessons learned from EOCs established for coordination of polio eradication activities and response to Ebola virus disease, as well as leveraging trained personnel from the Nigeria Field Epidemiology and Laboratory Training Program. In the longer term, building adequate health care worker capacity at all national and subnational surveillance system levels will be essential to a timely and effective outbreak response. Functional laboratory systems are

Summary

What is already known about this topic?

Meningococcal disease caused by *Neisseria meningitidis* causes severe illness, and could lead to permanent disability or death if not quickly detected and treated. The largest global burden of meningococcal disease is in sub-Saharan Africa, where annual epidemics caused mainly by *N. meningitidis* serogroup A were previously common. After the introduction of meningococcal A vaccines in 2013, meningitis caused by serogroup A declined. However, *N. meningitidis* serogroup C (NmC) has now emerged as a cause of large outbreaks.

What is added by this report?

During December 2016–June 2017, the largest global epidemic of meningitis caused by NmC occurred in northern Nigeria, with 14,518 suspected cases and 1,166 deaths reported. An emergency operations center coordinated rapid development and implementation of an emergency outbreak response plan, including administration of meningococcal serogroup C– containing vaccines to >2 million persons. Multiple logistical challenges were encountered during the response; the outbreak was declared over in June 2017.

What are the implications for public health practice?

National and regional evaluations of the outbreak response have outlined recommendations for improving meningitis outbreak prevention, timely detection, and response in Nigeria. Implementation of these recommendations will be key to reducing future meningitis outbreaks. Expanding availability of multivalent vaccines that are effective against non-A serogroups of *N. meningitidis* might prevent future outbreaks in this region.

pivotal to meningitis case confirmation and provide guidance for critical outbreak response activities, including decisions on appropriate vaccine use.

With the outbreak now declared over, efforts to improve surveillance and outbreak preparedness for meningitis need to continue. Recently concluded national and regional evaluations of the outbreak response have articulated recommendations for improving meningitis outbreak prevention, timely detection, and response in Nigeria, and implementation of these recommendations is needed at all levels of the public health system. Additionally, conducting a review of the implementation of current meningitis outbreak alert and epidemic thresholds in Nigeria, including an assessment of sub-LGA–level sensitivity to outbreaks at the current thresholds could help to ensure optimal and timely detection at the lower levels. Developing and introducing conjugate vaccines effective against non-A meningococcal serogroups might help reduce the risk for future non-serogroup A meningococcal meningitis outbreaks.

Acknowledgments

Government and partner support staff members.

Conflict of Interest

No conflicts of interest were reported.

Corresponding author: Chimeremma Nnadi, wgq4@cdc.gov, 404-906-6316.

References

- 1. World Health Organization. Meningococcal meningitis. Fact sheet. Geneva, Switzerland: World Health Organization; 2017. http://www. who.int/mediacentre/factsheets/fs141/en/
- Mohammed I, Nasidi A, Alkali AS, et al. A severe epidemic of meningococcal meningitis in Nigeria, 1996. Trans R Soc Trop Med Hyg 2000;94:265–70. https://doi.org/10.1016/S0035-9203(00)90316-X

- 3. Chow J, Uadiale K, Bestman A, et al. Invasive meningococcal meningitis serogroup C outbreak in northwest Nigeria, 2015—third consecutive outbreak of a new strain. PLoS Curr 2016;8:8.
- 4. Funk A, Uadiale K, Kamau C, Caugant DA, Ango U, Greig J. Sequential outbreaks due to a new strain of *Neisseria meningitidis* serogroup C in northern Nigeria, 2013–14. PLoS Curr 2014;6:6.
- Sidikou F, Zaneidou M, Alkassoum I, et al. Emergence of epidemic *Neisseria meningitidis* serogroup C in Niger, 2015: an analysis of national surveillance data. Lancet Infect Dis 2016;16:1288–94. https://doi. org/10.1016/S1473-3099(16)30253-5
- World Health Organization. Meningitis outbreak response in sub-Saharan Africa. WHO guideline. Geneva, Switzerland: World Health Organization; 2014. http://www.who.int/csr/resources/publications/ meningitis/guidelines2014/en/
- Trotter CL, Lingani C, Fernandez K, et al. Impact of MenAfriVac in nine countries of the African meningitis belt, 2010–15: an analysis of surveillance data. Lancet Infect Dis 2017;17:867–72. https://doi. org/10.1016/S1473-3099(17)30301-8
- Sambo L, Chan M, Davis S, et al. A vaccine meets its promise: success in controlling epidemic meningitis in sub-Saharan Africa. Clin Infect Dis 2015;61(Suppl 5):S387–8. https://doi.org/10.1093/cid/civ490
- Nigeria Centre for Disease Control. Technical guidelines for integrated disease surveillance and response in Nigeria. Abuja, Nigeria: Nigeria Centre for Disease Control; 2016. http://www.ncdc.gov.ng/themes/ common/docs/protocols/4_1476085948.pdf
- Lo TQ, Marston BJ, Dahl BA, De Cock KM. Ebola: anatomy of an epidemic. Annu Rev Med 2017;68:359–70. https://doi.org/10.1146/ annurev-med-052915-015604

¹Global Immunization Division, CDC; ²Nigeria Centre for Disease Control, Abuja, Nigeria; ³Federal Ministry of Health, Abuja, Nigeria; ⁴Africa Centre for Disease Control, Addis Ababa, Ethiopia; ⁵National Primary Health Care Development Agency, Abuja, Nigeria; ⁶Nigeria Country Office, World Health Organization, Abuja, Nigeria; ⁷Nigeria Country Office, United Nations Children's Fund Abuja, Nigeria; ⁸World Health Organization, Geneva, Switzerland; ⁹Public Health England, London, United Kingdom; ¹⁰Center for Global Health, Global Rapid Response Team, CDC; ¹¹Nigeria Office, Africa Field Epidemiology Network, Kampala, Uganda; ¹²Medical Research Council, Vaccines and Immunity Theme, Banjul, Gambia; ¹³World Health Organization Inter-country Support Team for West Africa, Ouagadougou, Burkina Faso; ¹⁴Meningitis and Vaccine Preventable Diseases Branch, National Center for Respiratory and Infectious Diseases, CDC; ¹⁵CDC, Nigeria Country Office, Abuja.

Introduction of Inactivated Poliovirus Vaccine and Impact on Vaccine-Associated Paralytic Poliomyelitis — Beijing, China, 2014–2016

Dan Zhao, MD¹; Rui Ma, MD¹; Tao Zhou, MD¹; Fan Yang, MD¹; Jin Wu, MD²; Hao Sun³; Fang Liu, MD⁴; Li Lu, MD¹; Xiaomei Li¹; Shuyan Zuo, MD⁵; Wei Yao⁶; JianYin⁶

When included in a sequential polio vaccination schedule, inactivated polio vaccine (IPV) reduces the risk for vaccineassociated paralytic poliomyelitis (VAPP), a rare adverse event associated with receipt of oral poliovirus vaccine (OPV). During January 2014, the World Health Organization (WHO) recommended introduction of at least 1 IPV dose into routine immunization schedules in OPV-using countries (1). The Polio Eradication and Endgame Strategic Plan 2013-2018 recommended completion of IPV introduction in 2015 and globally synchronized withdrawal of OPV type 2 in 2016 (2). Introduction of 1 dose of IPV into Beijing's Expanded Program on Immunization (EPI) on December 5, 2014 represented China's first province-wide IPV introduction. Coverage with the first dose of polio vaccine was maintained from 96.2% to 96.9%, similar to coverage with the first dose of diphtheria and tetanus toxoids and pertussis vaccine (DTP) (96.5%–97.2%); the polio vaccine dropout rate (the percentage of children who received the first dose of polio vaccine but failed to complete the series) was 1.0% in 2015 and 0.4% in 2016. The use of 3 doses of private-sector IPV per child decreased from 18.1% in 2014, to 17.4% in 2015, and to 14.8% in 2016. No cases of VAPP were identified during 2014-2016. Successful introduction of IPV into the public sector EPI program was attributed to comprehensive planning, preparation, implementation, robust surveillance for adverse events after immunization (AEFI), and monitoring of vaccination coverage. This evaluation provided information that helped contribute to the expansion of IPV use in China and in other OPV-using countries.

OPV has been employed in China's EPI system for decades, leading to certification of China's polio-free status in 2000.* After elimination of wild-type polio in China, VAPP, a rare occurrence of paralysis associated with a mutated vaccine virus that occurs in an OPV recipient or a close unvaccinated or nonimmune contact of the OPV recipient, emerged as an unacceptable risk: during 2010–2014, an average of one case of VAPP (reporting rate 7.16 per million first OPV doses) occurred annually among previously healthy children in Beijing. A majority of VAPP occurs in infancy, associated with the first OPV dose (1). IPV provides immunity against wild polioviruses, but cannot cause VAPP and greatly reduces

* http://www.wpro.who.int/china/mediacentre/factsheets/polio/en/.

the risk for VAPP associated with subsequent OPV doses. Countries that have previously introduced at least 1 IPV dose before vaccination with OPV have rapidly eliminated VAPP (1). IPV has been available in China's private sector since 2009. After completion of immunogenicity studies (3–5), Beijing introduced IPV into the public sector EPI program in December 2014 as part of a sequential schedule that included 1 dose of IPV at age 2 months, followed by 3 doses of trivalent OPV at ages 3, 4, and 48 months. After the global synchronized withdrawal of all Sabin type 2 vaccines in April 2016, trivalent OPV was replaced with bivalent OPV, which contains types 1 and 3 oral polio vaccine viruses.

Preparation for IPV introduction included addressing financial constraints, establishing a management structure, and developing an operational plan. The Beijing municipal government secured RMB18.9 million yuan (\$US 2.9 million) for IPV procurement and program operations. During April–November 2014, the Beijing provincial health authorities developed a comprehensive work plan with technical guidelines for cold chain capacity assessment, training, risk communication, frequently asked questions, logistics materials (e.g., vaccines, forms), supply and distribution, and surveillance for polio vaccine utilization and AEFIs. During November 2014, health authorities issued an official circular that detailed responsibilities of various agencies and stated an objective to achieve 98.0% coverage with IPV. Information about the new IPV/OPV schedule was disseminated through the Beijing Municipal Authority's website. Posters describing IPV and the availability of free vaccinations were posted on December 5, 2014, the first day that government-supplied IPV was offered. Health care workers were the primary sources of information about IPV introduction. Health care workers in vaccination clinic training workshops focused on immunogenicity, safety, and risk communication regarding the sequential schedule. Training materials included a polio fact sheet with frequently asked questions for parents, the new immunization schedule, eligibility criteria for IPV catch-up vaccination, and correct vaccine administration technique. Training was completed 2-7 days before IPV was introduced.

In December 2015, a program evaluation was conducted at the provincial level CDC (Beijing CDC), four subordinate district level CDCs, and 12 health facilities, by using the WHO Post Introduction Evaluation (PIE) tool (6). This tool is a systematic method for evaluating the effect of introducing a vaccine on a country's existing immunization system. Beijing CDC surveyed 83 health care workers who were vaccinating children and 40 parents or guardians whose children were offered IPV. Polio vaccine utilization data were obtained from Beijing's Immunization Planning Information System. Beijing CDC compared the proportions of eligible children receiving IPV and OPV before routine IPV introduction (December 2013–November 2014) and after IPV introduction (December 2014–November 2015) to assess utilization and preferences regarding polio vaccines and compared the polio vaccine and DTP dropout rates in 2015 and 2016 among children aged 1 year (born during October–November 2014 and 2015, respectively).

Adequate cold chain storage capacity was identified in all 12 surveyed sites. In addition to manual temperature recording, nine of the 12 surveyed health facilities were using a system that alerts vaccine mangers of temperature excursions. Oversight regarding IPV introduction was incorporated into routine supervision, with priority placed on vaccine usage and management. During the 6 months before the PIE, each surveyed health facility reported receiving 1–4 supervisory visits by district CDC personnel. Vaccine wastage data were reported by health facilities to district CDCs on a monthly basis. Median OPV and IPV wastage rates were 2.3% (range = 0%–5.3%) and 0.03% (range = 0%–1.2%), respectively.

Among the 83 health care worker survey respondents, 77 (93%) received training, and 80 (96%) responded correctly to questions about the immunization schedule, proper injection technique, contraindications to vaccination, and common AEFIs; all health care workers knew the appropriate anatomic site for injecting IPV. At least two of the following messages were relayed to parents by 72 (87%) health care workers: the vaccine name, the disease prevented, the sequential IPV/OPV schedule, the benefits of IPV, common AEFIs, how to report AEFIs, and the need to bring the child's vaccination card to each visit. Among 40 parents or guardians whose children were offered IPV at the health facility, 13 (33%) knew what IPV and poliomyelitis were; among these 13 persons the primary sources of information about IPV were health care workers (seven), the Internet (four), and friends or relatives (two).

All surveyed sites reported that they had sufficient IPV and ancillary supplies (e.g., registration forms, certificates). Although new vaccination cards that included the IPV/OPV sequential schedule were issued to replace the previous cards, five (12.5%) surveyed parents still had the older vaccination cards on which IPV doses were recorded. Used needles and syringes were observed to have been discarded into safety boxes without recapping. Also, in five of the 12 health facilities, health care workers were observed to frequently manually disconnect the needle from syringe.

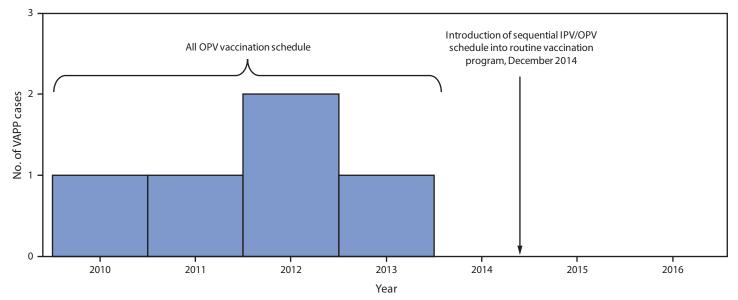
The existing acute flaccid paralysis (AFP) surveillance system, which needs to be sensitive enough to detect one case of AFP per 100,000 children aged <15 years, even in the absence of polio, has detected from 1.1 to 2.3 nonpolio AFP cases per 100,000 children aged <15 years annually during 2010-2016 in Beijing. VAPP cases were initially detected through this system. Since IPV introduction, clinicians, IPV suppliers, and district CDCs have reported any AEFI, including VAPP, after IPV administration through the existing passive, online AEFI surveillance system (7). During the first 2 years after IPV introduction, 115 mild adverse events (fever, local reaction, rash, or angioneurotic edema) and two rare adverse reactions (one case each of anaphylactoid purpura and thrombocytopenic purpura [both patients fully recovered]) were recorded. In addition, 22 adverse events that were determined, after expert panel review, to be unrelated to vaccination (i.e., coincidental events) occurred. These coincidental events included infections, allergies, thrombocytopenia, and infantile spasms. No case of VAPP has been reported since 2014 (Figure 1).

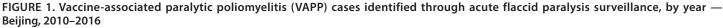
Administrative coverage rates with the first dose of polio vaccines during 2014, 2015, and 2016 were 96.2%, 96.9%, and 97.4%, respectively; these rates were similar to those for the first DTP dose during those years (96.5% [2014], 97.2% [2015], and 97.6% [2016]). The polio vaccine drop-out rate was 1.0% in 2015 and 0.4% in 2016, similar to that for DTP (1.5% [2015], 2.1% [2016]). Before introduction of the sequential IPV/OPV schedule in Beijing, parents could choose IPV or an IPV-containing combination vaccine, such as Pentavalent (Pentaxim, Sanofi Pasteur, France) (which protects against diphtheria, tetanus, pertussis, polio, and Haemophilus influenzae type b) for the second or third polio vaccine dose, at their expense. However, in June 2016, China's national drug and health authorities prohibited IPV for all 3 doses in the private market because of a global IPV shortage, and to ensure that all children could get a first IPV dose.[†] The use of 3 doses of private-sector IPV declined slightly from 18.1% in 2014 to 17.4% in 2015 and to 14.8% in 2016 (Figure 2).

Discussion

IPV introduction using a sequential IPV/OPV schedule in Beijing was associated with a good safety record, no occurrence of VAPP or other serious adverse events, and maintenance of >95% coverage with the first dose of polio vaccine. There was little change in the relatively small percentage of children receiving an all-IPV schedule through the private sector. Given

[†]http://app1.sfda.gov.cn/WS01/CL1368/155900.html.





Abbreviations: IPV = inactivated polio vaccine; OPV = oral poliovirus vaccine.

the current global shortage of IPV (8), it was reassuring that public confidence in the safety of OPV remained high, assuring the availability of 1-dose IPV access. OPV wastage exceeded that of IPV, possibly because infants occasionally spat out the oral dose, which had to be repeated.

Strong public health leadership, good operational planning, secured resources, and budget were critical to successful IPV introduction in Beijing. However, the PIE did identify areas for improvement. For example, two thirds of parents interviewed were not familiar with either IPV or poliomyelitis, possibly because of the short time available for health workers to educate parents and still administer all vaccines. Because health care workers served as the primary sources of information about the sequential schedule to parents, there was a risk that the occurrence of any serious AEFIs might cause parents to lose confidence in the vaccination program, especially if a serious AEFI were to be widely reported by the media (9,10). Thus, large-scale media campaigns, describing the program, and monitoring public concerning the safety of polios vaccines should be reinforced during IPV introduction. In addition, compliance with safe injection practices by health care workers needs improvement through more targeted training.

The findings in this report are subject to at least two limitations. First, as recommended in the PIE tool, 40 parents and 12 health facilities were selected for the survey; however, because of the large population in Beijing and the large annual birth cohort, the small sample might not be representative. Second, although no VAPP cases were reported during the

Summary

What is already known about this topic?

Since 2014, the World Health Organization has recommended that all countries using oral poliovirus vaccine (OPV) introduce at least 1 dose of inactivated polio vaccine (IPV) into routine immunization programs. However, the evaluation of IPV introduction after this global recommendation was limited, including the impact that IPV introduction might have on the existing immunization program. Beijing Municipal Authority implemented the first province-wide IPV introduction in China on December 5, 2014 with a sequential IPV/OPV poliovirus vaccination schedule.

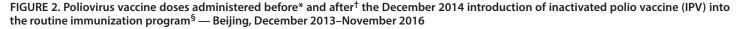
What is added by this report?

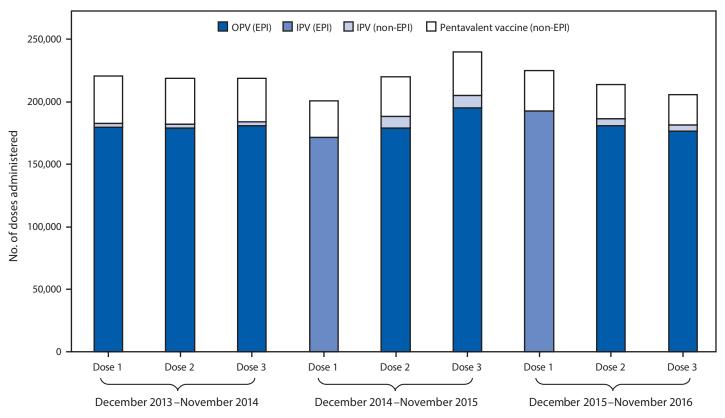
Two years after introduction of the sequential IPV/OPV vaccination schedule in Beijing, a postintroduction evaluation was conducted. The sequential schedule was successfully introduced into the public-sector Expanded Program on Immunization system and was well accepted by parents and providers. Compared with the year preceding IPV introduction, polio vaccination coverage remained high, no adverse effect on coverage with other vaccines occurred, and no cases of vaccine-associated paralytic poliomyelitis have been identified.

What are the implications for public health practice?

Comprehensive IPV introduction plans not only ensure a smooth transition to a new vaccine schedule, but can also help improve the current routine immunization system. Good planning and preparation can lead to high coverage with a new vaccine without negative impact on coverage with other vaccines. The experience in Beijing helped contribute to expansion of IPV use nationwide in China, and can also aid IPV introductions in other OPV-using countries.

1359





Abbreviations: EPI = expanded program on immunization; OPV= oral poliovirus vaccine.

* December 2013–November 2014.

[†] December 2014–November 2016.

[§] The Beijing immunization program provide IPV and OPV in the sequential schedule without charge; however, parents can choose IPV for the second and third doses, or an IPV-containing combination vaccine at their own expense. IPV is standalone Salk-poliovirus strains; Pentavalent vaccine is a combination vaccine containing diphtheria, tetanus, acellular pertussis vaccine, inactivated poliovirus, and *Haemophilus influenzae* type b vaccines.

2 years after IPV introduction, additional time will be needed to assess the impact of the IPV/OPV sequential schedule on VAPP in Beijing.

Successful implementation of the sequential IPV/OPV schedule in Beijing and the findings of the PIE demonstrate the feasibility of implementing the sequential schedule throughout the country, and of introducing another injectable vaccine into the childhood immunization schedule. In addition, surveillance data regarding VAPP from the first 2 years after IPV introduction indicate that, as has been observed in other countries, if IPV is made available in a sequential schedule throughout China, VAPP could be eliminated.

Acknowledgments

Health facilities and CDCs in Huai Rou, Hai Dian, Xi Cheng, and Da Xing districts in Beijing municipality, China; Dr. Lance Rodewald, World Health Organization, Beijing, China.

Conflict of Interest

No conflicts of interest were reported.

¹Beijing CDC, China; ²Shijingshan District of Beijing CDC, China; ³Dongcheng District of Beijing CDC, China; ⁴Chaoyang District of Beijing CDC, China; ⁵World Health Organization Country Office, Beijing, China; ⁶Shenzhen Jin Wei Xin Technology Co., LTD, Shenzhen City, China.

Corresponding authors: Li Lu, lulibj@sina.com; Xiaomei Li, anananlxm@163.com.

References

- 1. World Health Organization. Polio vaccines: WHO position paper, January 2014. Wkly Epidemiol Rec 2014;89:73–92.
- 2. World Health Organization. Polio eradication and endgame strategic plan 2013–2018. Geneva, Switzerland: World Health Organization; 2016. http://www.polioeradication.org/resourcelibrary/strategyandwork.aspx
- Lu L, Li X, Zhang H, et al. Immunogenicity and persistence from different 3-dose schedules of live and inactivated polio vaccines in Chinese infants. Vaccine 2015;33:4653–8. https://doi.org/10.1016/j. vaccine.2014.08.091

- Zhang ZJ, Li J, Wang HH, et al. Safety of different sequential immunization schedules of inactivated poliovirus vaccine and oral poliovirus vaccine primary vaccination [Chinese]. Zhonghua Yu Fang Yi Xue Za Zhi 2013;47:910–5.
- Li XM, Zhang ZJ, Wang HH, et al. Immunogenicity and safety of a booster dose of inactivated polio vaccine [Chinese]. Zhonghua Yu Fang Yi Xue Za Zhi 2013;47:905–9.
- 6. World Health Organization. New vaccine Post-Introduction Evaluation (PIE) Tool. Geneva, Switzerland: World Health Organization; 2017. http://www.who.int/immunization/monitoring_surveillance/resources/ PIE_tool/en/
- Liu D, Wu W, Li K, et al. Surveillance of adverse events following immunization in China: past, present, and future. Vaccine 2015;33:4041–6. https://doi.org/10.1016/j.vaccine.2015.04.060

- World Health Organization. Meeting of the SAGE. Geneva, Switzerland: World Health Organization; 2016. http://www.who.int/immunization/sage/ meetings/2016/april/SAGE_April_2016_Meeting_Web_summary.pdf
- Zhang Y, Wei J, Qi W. Research on the citizens' preference of channels to obtain information in emergency states. Information Science 2012;30:574–8. http://en.cnki.com.cn/Article_en/CJFDTOTAL-QBKX201204020.htm
- 10. Shi L. The integration of interactive interpersonal communication and mass communication-the application of interpersonal communication in mass media [Chinese]. Journal of Southwest University for Nationalities (Humanities & Social Sciences) 2006;10:198–201. http:// en.sss.net.cn/105001011/56.aspx

1361

Tuberculosis Control Activities After Hurricane Harvey — Texas, 2017

Sandra Morris¹; Mark Miner²; Tomas Rodriguez^{1,2}; Richard Stancil³; Dana Wiltz-Beckham⁴; Terence Chorba²

On September 14, 2017, the Texas Department of State Health Services (DSHS) reported that Hurricane Harvey had caused 82 deaths in Texas during August 25–August 30, 2017 (1), with property damage that could total \$180 billion (2). Houston alone received 45 inches of rain from August 24 to September 1, 2017, and some parts of Texas received 60 inches or more. Dozens of inches of rain also fell on the cities of Port Arthur and Beaumont. Several local health departments experienced closures during the week of August 28 and resumed operations the week of September 5 under emergency conditions.

The Texas DSHS uses federal and state funding for tuberculosis (TB) surveillance, prevention, and control activities in eight DSHS health service regions, 31 local health departments, and four binational TB projects. In advance of major storms, TB programs have activated established protocols for providing patients with medications to take on their own, and for providing contact information to give to health departments in case patients become displaced. Line listings of patients are closely monitored to account for all patients after the storm, and treatment duration is frequently extended to allow for medication doses that were missed. Information exchange among neighboring local, regional, or state programs is often necessary.

Directly observed therapy (DOT) of patients taking each dose of their TB medications is a cornerstone of TB control activity, and video-enabled DOT using electronic devices, such as smart phones, has become a useful tool for patients who cannot visit, or be visited by, a health care provider (6). Lessons learned regarding management and follow-up of TB patients on treatment during Hurricane Katrina in 2005 (3) were applied during hurricanes Gustav and Ike in 2008 (4), Sandy in 2012 (5), and Harvey in 2017. Whereas approximately half of the TB patients in New Orleans, Louisiana, fled the state during Hurricane Katrina (3), TB patients in Texas during Hurricane Harvey typically remained close to their usual residence (at home, with relatives, or in shelters).

Immediately after Hurricane Harvey, the DSHS TB program directly contacted all affected regional and local health departments to determine the status of high-priority TB patients (persons with new TB diagnoses, infectious patients, and children), and relayed status of patient care, health care worker safety, and needs of local and regional health departments to CDC. In addition, surveillance questionnaires were distributed to temporary shelters to identify residents or volunteers exhibiting signs and symptoms of TB. Although TB control personnel in Texas were personally affected by the storm's damage, they remained on duty, with some staff members traveling into flooded communities to follow up patients.

A total of 282 TB cases from 17 affected local or regional health departments, including 212 (75%) from one large urban county, were high priority TB cases with confirmed disease. Response efforts by affected local and regional health departments ensured that all but two of the 282 persons were accounted for within a week after the storm began. The remaining two were located the following week and connected to care. Sixty-one patients had already been placed on video-enabled DOT, 30 had TB disease (cases), and 31 had latent TB infection and needed DOT. Fifty-nine (97%) were monitored successfully and did not miss any medication doses. The aforementioned two patients who were lost during the storm and found a week later had TB disease (cases). Although respiratory illnesses among shelter residents were reported, no suspected cases of undiagnosed TB disease were identified.

Each year, the upcoming hurricane season provides opportunities to develop, test, and implement preparedness plans for continuity of patient care. During Hurricane Harvey, the high proportion of patients successfully managed through videoenabled DOT demonstrates that video-enabled DOT can help ensure TB treatment completion when regular treatment options have been disrupted by a major storm or other disasters.

Conflict of Interest

No conflicts of interest were reported.

Corresponding author: Mark Miner, MMiner@cdc.gov, 404-639-8648.

References

- 1. Moravic ER. Texas officials: Hurricane Harvey death toll at 82, "mass casualties have absolutely not happened." The Washington Post. September 14, 2017. https://www.washingtonpost.com/national/texas-officials-hurricane-harvey-death-toll-at-82-mass-casualties-have-absolutely-not-happened/2017/09/14/bff3ffea-9975-11e7-87fc-c3f7ee4035c9_story.html?utm_term=.e1db77bc3069
- Reuters. Hurricane Harvey damages could cost up to \$180 billion. Fortune. September 3, 2017. http://fortune.com/2017/09/03/ hurricane-harvey-damages-cost/

1362

¹Texas Department of State Health Services; ²Division of Tuberculosis Elimination, CDC; ³Houston Health Department, Texas; ⁴Harris County Health Department, Texas.

- 3. CDC. Tuberculosis control activities after Hurricane Katrina—New Orleans, Louisiana, 2005. MMWR Morb Mortal Wkly Rep 2006;55:332–5.
- 4. Miner MC, Burns-Grant G, DeGraw C, Wallace C, Pozsik C, Jereb J. Integrated preparedness for continuity of tuberculosis care after Hurricanes Gustav and Ike: Louisiana and Texas, 2008. Public Health Rep 2010;125:518–9. https://doi.org/10.1177/003335491012500405
- 5. CDC. Tuberculosis control activities before and after Hurricane Sandy northeast and mid-Atlantic states, 2012. MMWR Morb Mortal Wkly Rep 2013;62:206–8.
- 6. Story A, Garfein RS, Hayward A, et al. Monitoring therapy adherence of tuberculosis patients by using video-enabled electronic devices. Emerg Infect Dis 2016;22:538–40. https://doi.org/10.3201/eid2203.151620

Notes from the Field

Monitoring Out-of-State Patients During a Hurricane Response Using Syndromic Surveillance — Tennessee, 2017

Caleb Wiedeman, MPH¹; Julie Shaffner, MS, MPH²; Kelly Squires, MPH¹; Jeffrey Leegon, MS¹; Rendi Murphree, PhD²; Paul E. Petersen, PharmD¹

In late August and early September of 2017, Hurricanes Harvey and Irma swept through the Caribbean and made landfall in the continental United States. As Texas and Florida readied for direct impacts of the storms, nearby states prepared for the arrival of internally displaced persons. During the weeks surrounding the storms, the Tennessee Department of Health (TDH) supported all-hazards situational awareness for public health partners by enhancing syndromic surveillance activities, i.e., the monitoring of symptom combinations or other indicators within a population to inform public health action (1).

TDH collects and analyzes emergency department (ED) data from 70 hospitals across Tennessee using the Electronic Surveillance System for Early Notification of Community-Based Epidemics (ESSENCE) (2). ESSENCE is a tool in the BioSense Platform made available to public health jurisdictions through CDC's National Syndromic Surveillance Program (NSSP) (3). Syndromic surveillance typically supplements disease- or condition-specific surveillance; however, it can also improve situational awareness during an event or disaster.

Before, during, and after the landfalls of Hurricanes Harvey and Irma, the volume of out-of-state patients visiting EDs in Tennessee was monitored to identify any unusual clusters of symptoms or spatial clustering and to assess the real-time impact on the health care system by persons displaced by the storms.

Data were monitored from August 18-September 24, 2017 by querying ESSENCE for patient home postal codes in Texas and Florida. During the monitoring period, Tennessee EDs reported 257,095 total visits, including 277 (0.1%) patient visits by Texas residents and 1,041 (0.4%) visits by Florida residents. The number of ED visits by patients from Texas remained stable during the monitoring period (average 7.3 per day). In contrast, there was an increase in patients from Florida visiting Tennessee EDs beginning 3 days before Hurricane Irma made landfall in the continental United States. The increase peaked on the day of impact in Florida (September 10) at 116 ED visits, and returned to baseline levels (between 10-20 patients per day) within 1 week (Figure). The increase in patients from Florida was evenly distributed across Tennessee, with some clustering around a popular tourism area in East Tennessee. No concerning trends in reported syndromes or chief complaints were identified among Texas or Florida patients. The most frequently occurring chief complaints for these patients were injuries, complaints of chest or back pain, gastrointestinal illness, and respiratory illness, similar to patterns of chief complaints seen in Tennessee residents visiting EDs during the same period.

Syndromic surveillance data are often used to identify clusters of illness based on geography or time (1); TDH was able to use the data to detect changes suggestive of population displacement due to an out of state natural disaster. Although TDH was unable to validate whether patients identified as residents

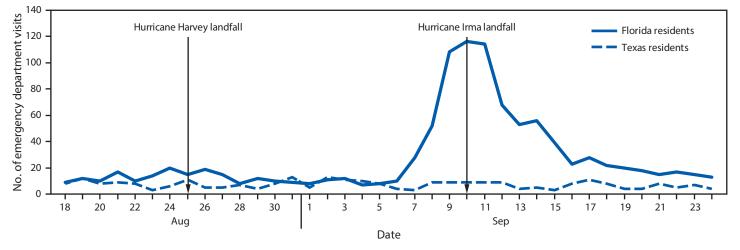


FIGURE. Emergency department visits* by residents of Texas and Florida — Tennessee, August 18–September 24, 2017

* Identified through query of the Electronic Surveillance System for Early Notification of Community-Based Epidemics (ESSENCE).

of Florida were displaced because of Hurricane Irma, the timing of the increase and subsequent decrease in patient ED visits suggested population displacement related to the storm. The absence of a substantial increase in patients with residence in Texas suggested that the effects of Hurricane Harvey were not affecting hospital EDs in Tennessee.

At TDH, ESSENCE is the only easily accessible information source capable of rapidly collecting health information on out-of-state patients. This initiative allowed TDH to observe where and when out-of-state patients were seeking ED care in Tennessee and to monitor the need for targeted messaging and resources to heavily affected areas. Additionally, close surveillance of chief complaints among out-of-state patients provided assurance that no unusual patterns in illness or injury were occurring.

Enhancing syndromic surveillance during these storms was an important strategy for improving situational awareness among public health stakeholders and will be incorporated into future response activities by TDH.

Conflict of Interest

No conflicts of interest were reported.

¹Tennessee Department of Health; ²Division of State and Local Readiness, Office of Public Health Preparedness and Response, CDC.

Corresponding author: Julie Shaffner, wuy2@cdc.gov, 615-532-5118.

References

- 1. Henning KJ. What is syndromic surveillance? MMWR Suppl 2004; 53(Suppl):5–11.
- 2. CDC. National Syndromic Surveillance Program (NSSP): BioSense platform. Atlanta, GA: US Department of Health and Human Services, CDC; 2017. https://www.cdc.gov/nssp/biosense/index.html
- CDC. National Syndromic Surveillance Program (NSSP). Atlanta, GA: US Department of Health and Human Services, CDC; 2017. https:// www.cdc.gov/nssp/index.html

1365

Announcement

Community Preventive Services Task Force Findings for Mobile Phone Applications Used Within Health Care Systems for Self-Management of Type 1 and Type 2 Diabetes

The Community Preventive Services Task Force (CPSTF) recommends mobile phone applications used within health care systems for self-management of type 2 diabetes. "Diabetes Management: Mobile Phone Applications Used Within Healthcare Systems for Type 2 Diabetes Self-Management" is available at https://www.thecommunityguide.org/findings/ diabetes-management-mobile-phone-applications-used-within-healthcare-systems-type-2.

The CPSTF finds insufficient evidence for the intervention approach when used with patients who have type 1 diabetes. "Diabetes Management: Mobile Phone Applications Used Within Healthcare Systems for Type 1 Diabetes Self-Management" is available at https://www.thecommunityguide. org/findings/diabetes-management-mobile-phone-applications-used-within-healthcare-systems-type-1.

Established in 1996 by the U.S. Department of Health and Human Services, the CPSTF is an independent, nonfederal panel of public health and prevention experts whose members are appointed by the director of CDC. The CPSTF provides information for a wide range of persons who make decisions about programs, services, and other interventions to improve population health. Although CDC provides administrative, scientific, and technical support for the CPSTF, the recommendations developed are those of the task force and do not undergo review or approval by CDC.

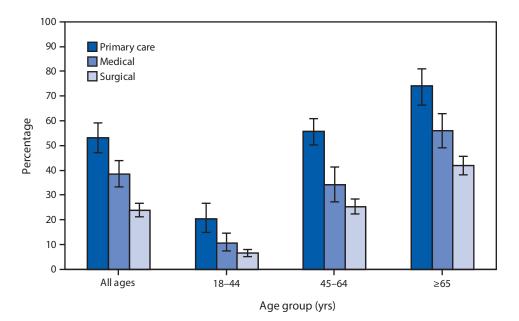
Notice to Readers

Change in MMWR Announcements

Effective January 12, 2018, Announcements will be limited to public health events (e.g., World AIDS Day or Great American Smokeout) that are topically related to Full Reports. Both the Announcement and Full Report will appear on the cover of the issue. Information about other national health observances is available at https://healthfinder.gov/NHO/ default.aspx.

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage* of Visits by Patients Aged ≥18 Years to Office-Based Physicians[†] Made by Patients with ≥2 Selected Diagnosed Chronic Conditions,[§] by Physician Specialty Category and Patient Age Group — National Ambulatory Medical Care Survey, 2015



* With 95% confidence intervals indicated by error bars.

- ⁺ Based on a sample of visits to nonfederally employed office-based physicians who are primarily engaged in direct patient care. Physicians in specialties of anesthesiology, pathology, and radiology are excluded from the survey.
- [§] Defined as visits made by adults with documentation in the medical record of a diagnosis of ≥2 selected chronic conditions, regardless of the diagnosis of the current visit. Selected diagnosed chronic conditions include the 10 most frequent: hypertension; hyperlipidemia; arthritis; diabetes; depression; obesity; cancer; coronary artery disease, ischemic heart disease, and/or history of myocardial infarction; asthma; and chronic kidney disease.

In 2015, the percentage of office-based physician visits by adults with two or more diagnosed chronic conditions was 53.1% for primary care physicians, 38.5% for medical specialists, and 23.9% for surgeons. This pattern was observed for each of the age groups studied. The percentage of visits increased with age group, regardless of specialty category.

Source: National Ambulatory Medical Care Survey, 2015 data. https://www.cdc.gov/nchs/ahcd/ahcd_questionnaires.htm. Reported by: Brian W. Ward, PhD, ijz8@cdc.gov, 301-458-4568; Kelly L. Myrick, PhD; Donald K. Cherry, MS.

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*'s free subscription page at *https://www.cdc.gov/mmwr/mmwrsubscribe.html*. Paper copy subscriptions are available through the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402; telephone 202-512-1800.

Readers who have difficulty accessing this PDF file may access the HTML file at *https://www.cdc.gov/mmwr/index2017.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.

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)