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Frequency of Use Among Middle and High School Student Tobacco Product Users — United States, 2015–2017

Gabriella M. Anic, PhD[1]; Michael D. Sawdey, PhD[1]; Ahmed Jamal, MBBS[2]; Katrina F. Trivers, PhD[2]

Tobacco product use during adolescence increases the risk for lifelong nicotine addiction and immediate adverse health effects (*1*,*2*). During 2011–2017, current use of cigarettes, cigars, smokeless tobacco, and pipe tobacco decreased significantly among middle and high school students, but current use of e-cigarettes increased significantly from 1.5% to 11.7% (*3*). In 2017, an estimated 19.6% of high school students (2.95 million) and 5.6% of middle school students (0.67 million) were current users of any tobacco product; e-cigarettes were the most commonly used tobacco product for both middle (3.3%) and high (11.7%) school students (*3*). The Food and Drug Administration (FDA) and CDC analyzed combined data from the 2015–2017 National Youth Tobacco Surveys (NYTS) to determine past 30-day (current) frequency of use of cigarettes, e-cigarettes, cigars, smokeless tobacco, and hookahs among U.S. high school and middle school students. During 2015–2017, the proportion of students currently using tobacco products who used a product for ≥20 of the past 30 days ranged from 14.0% of cigar smokers to 38.7% of smokeless tobacco users among high school students and from 13.1% of e-cigarette users to 24.5% of hookah smokers among middle school students. Among current users, use of two or more tobacco products ranged from 76.7% (e-cigarettes) to 90.9% (hookahs) among those using the product ≥20 of the preceding 30 days, from 68.0% (e-cigarettes) to 84.2% (hookahs) among those using the product for 6 to 19 of the preceding 30 days, and from 48.8% (e-cigarettes) to 77.2% (cigarettes) among those using the product for 1 to 5 of the preceding 30 days. Sustained implementation of proven tobacco control strategies focusing on all types of tobacco products, in coordination with the regulation of tobacco products by FDA, are needed to reduce tobacco product initiation and use among U.S. youths.

NYTS is a cross-sectional, school-based, pencil-and-paper survey administered to U.S. middle (grades 6–8) and high (grades 9–12) school students (*4*). A three-stage cluster sampling procedure was used to generate a nationally representative sample of U.S. students attending public and private schools in grades 6–12. Data were combined from the 2015 (17,711), 2016 (20,675), and 2017 (17,872) NYTS to provide a sufficient sample size to assess different categories of use frequency. Response rates for 2015–2017 were 63.4%, 71.6%, and 68.1%, respectively. Information on current use (≥1 day in the past 30 days) was collected for the following tobacco products: cigarettes, cigars (cigars, cigarillos, or little cigars), smokeless tobacco products (chewing tobacco, snuff, dip, snus, or dissolvable tobacco products), e-cigarettes, hookahs (water pipes used to smoke tobacco), pipe tobacco, and bidis (small imported cigarettes wrapped in a leaf). Information on frequency of use (number of days used in the past 30 days) was collected for

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five tobacco products: cigarettes, cigars, smokeless tobacco, e-cigarettes, and hookahs. Frequency of hookah smoking was collected only in 2016 and 2017; the other four products were assessed in 2015, 2016, and 2017. Frequency of use information was not collected in any of the surveys for pipe tobacco, bidis, and certain specific smokeless tobacco products (snus and dissolvable tobacco products). Response options describing self-reported frequency of use were "0 days," "1–2 days," "3–5 days," "6–9 days," "10–19 days," "20–29 days," and "all 30 days." Frequent use was defined as using a product for ≥20 of the preceding 30 days. Multiple tobacco product use was defined as any past 30-day use of two or more tobacco products among current users of cigarettes, cigars, e-cigarettes, smokeless tobacco, and hookahs separately. Students with missing responses for frequency of use were excluded from the analysis.* Students missing data on current use of individual products were considered nonusers of that product. National prevalence estimates were calculated with 95% confidence intervals, and weighted population counts were rounded down to the nearest 10,000; all estimates were time-averaged over the pooled survey years. Survey weights were used to account for the complex survey design and adjusted for nonresponse.

During 2015–2017, among high school students who were current users of each product, the prevalence of frequent use (≥20 of the past 30 days) was as follows: 28.4% of cigarette smokers (330,000), 17.4% of e-cigarette users (330,000), 14.0% of cigar smokers (160,000), 38.7% of smokeless tobacco users (260,000), and 16.7% of hookah smokers (60,000) (Table). Among middle school students, the prevalence of frequent use was 17.5% of cigarette smokers (40,000), 13.1% of e-cigarette users (60,000), 13.2% of cigar smokers (20,000), 21.5% of smokeless tobacco users (30,000), and 24.5% of hookah smokers (20,000). High school student current users who used the product 1–5 of the past 30 days accounted for 50.3% of cigarette smokers, 61.4% of e-cigarette users, 70.8% of cigar smokers, 45.2% of smokeless tobacco users, and 66.3% of hookah smokers. The proportion of middle school current users who used the product 1–5 of the past 30 days was 67.4% of cigarette smokers, 68.4% of e-cigarette users, 71.2% of cigar smokers, 56.0% of smokeless tobacco users, and 61.8% of hookah users.

Among middle and high school students who used any of these five products on ≥20 of the preceding 30 days, multiple tobacco products were used by 87.5% of cigarette smokers, 76.7% of e-cigarette users, 81.6% of cigar smokers, 77.0% of smokeless tobacco users, and 90.9% of hookah smokers (Figure). Similarly, for middle and high school students who currently used a product for 1–5 of the preceding 30 days, multiple tobacco product use was reported for 77.2% of cigarette smokers, 48.8% of e-cigarette users, 72.0% of cigar smokers, 72.4% of smokeless tobacco users, and 70.5% of hookah smokers.

*The ranges of proportions of those with missing responses for frequency of use questions were 2.1%–2.5% for cigarettes, 1.5%–2.3% for e-cigarettes, 2.1%–3.1% for cigars, 1.9%–3.2% for smokeless tobacco products, and 2.7%–3.4% for hookahs.

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TABLE. Frequency of use (number of days of use during the preceding 30 days) among middle and high school students currently using cigarettes, e-cigarettes, cigars, smokeless tobacco, and hookahs* — National Youth Tobacco Survey, United States, 2015–2017

	Cigarettes		E-cigarettes		Cigars		Smokeless tobacco		Hookahs†	
Days of use	% (95% CI)	Estimated no. of users§	% (95% CI)	Estimated no. of users§	% (95% CI)	Estimated no. of users§	% (95% CI)	Estimated no. of users§	% (95% CI)	Estimated no. of users§
High school										
1–2	35.9 (33.2–38.6)	440,000	41.3 (38.8–43.9)	790,000	51.7 (49.1–54.2)	610,000	32.9 (29.5–36.5)	220,000	49.2 (45.0–53.4)	190,000
3–5	14.4 (12.8–16.3)	170,000	20.1 (18.2–22.0)	380,000	19.2 (17.4–21.2)	220,000	12.3 (10.3–14.5)	80,000	17.1 (14.2–20.5)	60,000
6–9	8.9 (7.6–10.3)	100,000	10.7 (9.4–12.1)	200,000	7.9 (6.7–9.3)	90,000	7.2 (5.7–9.1)	50,000	11.1 (8.6–14.1)	40,000
10–19	12.5 (10.9–14.2)	150,000	10.5 (9.4–11.9)	200,000	7.2 (6.1–8.6)	80,000	8.9 (7.2–11.0)	60,000	5.9 (4.4–7.8)	20,000
20–29	8.9 (7.5–10.6)	100,000	5.3 (4.5–6.4)	100,000	3.5 (2.8–4.4)	40,000	6.5 (5.0–8.4)	40,000	3.7 (2.6–5.2)	10,000
30	19.4 (17.1–22.0)	230,000	12.1 (10.6–13.7)	230,000	10.5 (9.0–12.3)	120,000	32.2 (27.8–37.0)	220,000	13.0 (10.1–16.6)	50,000
Middle school										
1–2	48.7 (43.0–54.3)	120,000	50.8 (47.2–54.5)	250,000	57.5 (51.2–63.6)	110,000	45.2 (38.6–51.9)	80,000	41.6 (33.7–49.9)	50,000
3–5	18.8 (14.4–24.2)	40,000	17.6 (15.0–20.5)	80,000	13.7 (10.2–18.0)	20,000	10.8 (8.0–14.3)	10,000	20.2 (15.0–26.6)	20,000
6–9	7.9 (5.4–11.5)	20,000	9.9 (8.2–12.0)	50,000	10.3 (7.0–14.8)	20,000	15.1 (10.6–21.0)	20,000	10.2 (6.9–14.7)	10,000
10–19	7.1 (5.0–9.8)	10,000	8.6 (6.7–10.9)	40,000	5.3 (3.4–8.2)	10,000	7.5 (4.2–13.0)	10,000	—¶	—¶
20–29	4.8 (2.9–7.7)	10,000	4.2 (3.0–5.9)	20,000	—¶	—¶	—¶	—¶	—¶	—¶
30	12.8 (10.0–16.3)	30,000	8.9 (7.1–11.1)	40,000	11.3 (8.2–15.4)	20,000	17.9 (13.1–23.9)	30,000	20.9 (15.4–27.9)	20,000

Abbreviation: CI = confidence interval.

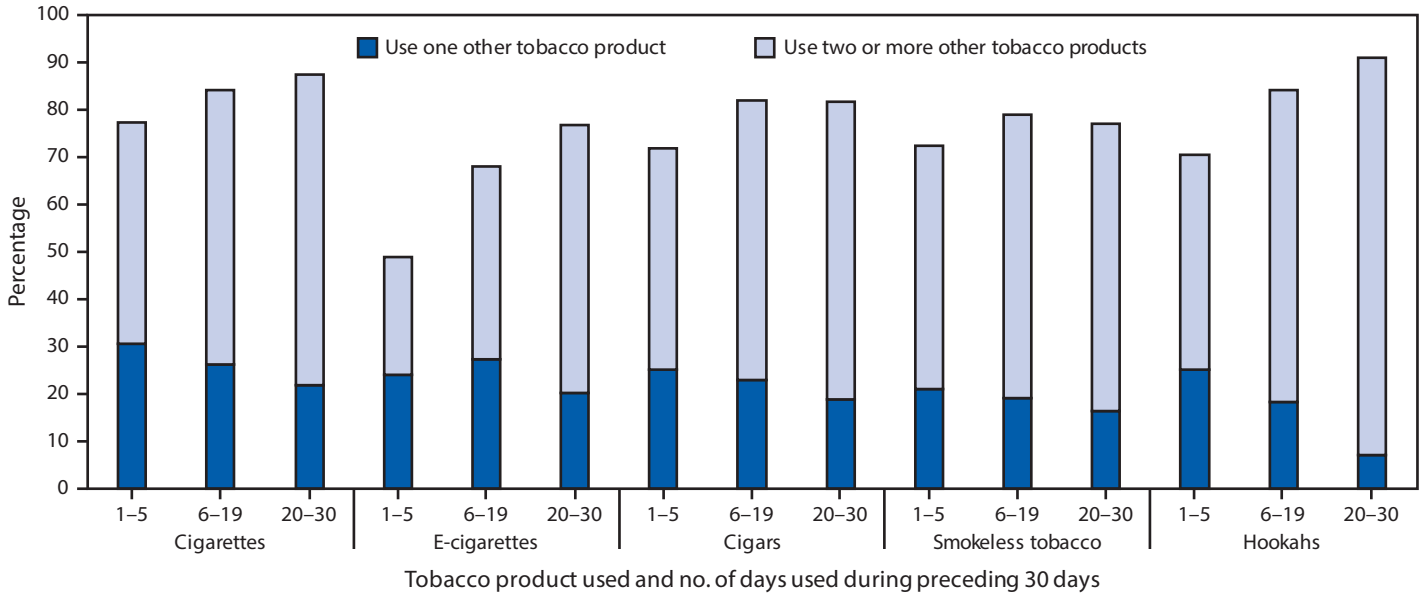
* Frequency of current use of cigarettes, e-cigarettes, cigars (defined as cigars, cigarillos, or little cigars), smokeless tobacco (defined as chewing tobacco, snuff, or dip), and hookahs was determined by asking participants on how many days they used each of these tobacco products during the preceding 30 days.The percentages given indicate the proportion of users for each product (e.g., 35.9% of cigarette users use that product 1–2 days per month.)

† Hookah estimates were based on data from 2016 and 2017. Frequency of hookah smoking was not asked in the 2015 survey.

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

¶ Data are statistically unreliable because the relative standard error was >30%.

FIGURE. Percentage of middle and high school students who were current users of cigarettes, e-cigarettes, cigars, smokeless tobacco, and hookahs, who reported multiple tobacco product use,* by number of days used during the preceding 30 days — National Youth Tobacco Survey, United States, 2015–2017



* Multiple tobacco product use was defined as a current cigarette smoker, e-cigarette user, cigar smoker, smokeless tobacco user, or hookah smoker also using at least one of the following products in the past 30 days: cigarettes; cigars (cigars, cigarillos, or little cigars); smokeless tobacco (chewing tobacco, snuff, or dip); e-cigarettes; hookahs; tobacco pipes; snus; dissolvable tobacco (dissolvables); and bidis.

Discussion

E-cigarettes were the most commonly used tobacco product by middle and high school students in 2017, followed by cigars and cigarettes (*3*.) Use of tobacco products in any form by youths is unsafe, including infrequent use (*1*,*2*). During 2015–2017, the frequency of tobacco product use among current middle and high school users varied by product type and school level. However, for all assessed products, most current users reported using each product for 1–5 of the past 30 days.

The products most commonly used ≥20 of the past 30 days by high school students were smokeless tobacco (38.7%) and cigarettes (28.4%) and by middle school students were hookahs (24.5%) and smokesless tobacco (21.5%).

Any frequency of tobacco product use might lead to symptoms of nicotine dependence (*5*). Symptoms of dependence, including strong cravings (14%), irritability and restlessness when not using tobacco products (11%), strong desire to use the product (6%), and wanting to use the tobacco product within 30 minutes of awakening (1%) have been reported by U.S. adolescent tobacco product users who use a single tobacco product on 1–2 of the previous 30 days (*5*). A high prevalence of multiple tobacco product use was observed for all products, regardless of the number of days that a tobacco product was used. The prevalence of reporting symptoms of nicotine dependence is 2–3 times higher for multiple product users than that for single product users (*5*). Given that nicotine dependence is a major determinant of whether a person becomes a long-term user of tobacco products, reducing experimentation by youths and initiation of all forms of tobacco product use is important to preventing future dependency on, and more frequent use of, these products (*1*,*2*,*6*).

The findings in this report are subject to at least four limitations. First, the data are self-reported; thus, the findings are subject to potential reporting bias. Second, data were not collected on the frequency of using tobacco pipes, snus, dissolvables, bidis, or by type of cigar. Although this precludes reporting frequency of use for these specific products, it should not affect the reported estimates of frequency of use of cigarettes, cigars, e-cigarettes, smokeless tobacco, and hookahs. Third, data were averaged across several years, although there were no significant changes in frequency of use during 2015–2017 for most products.[†] Finally, NYTS only recruited students from public and private schools; therefore, the findings might not be generalizable to youths who are being home-schooled, have dropped out of school, or are in detention centers.

Understanding tobacco product use patterns, including frequency of use and multiple tobacco product use, is important for sustaining implementation of proven tobacco control strategies and regulation of all types of tobacco products. In 2009, FDA was granted immediate authority to regulate cigarettes, cigarette tobacco, roll-your-own tobacco, and smokeless tobacco[§]; in 2016, FDA issued a final rule that extended its regulatory authority to all other tobacco products (*7*). Regulation of tobacco products, along with implementing proven tobacco control and prevention strategies, can reduce the initiation and use of tobacco products among youths. Strategies to reduce youth tobacco product use include increasing the price of tobacco products, implementing advertising and promotion restrictions and national public education media campaigns, and raising the minimum age of purchase for tobacco products to 21 years (*1*,*2*,*8*,*9*). Monitoring the frequency of using tobacco products, including the use of multiple products, is important for informing these strategies to prevent and reduce youth tobacco product use.

Summary

What is already known about this topic?

Most tobacco product use begins during adolescence or young adulthood, increasing the risk for lifelong nicotine addiction and adverse health effects.

What is added by this report?

During 2015–2017, the proportion of students currently using cigarettes, cigars, e-cigarettes, smokeless tobacco, or hookahs who used each product ≥20 of the past 30 days ranged from 14.0% of cigar smokers to 38.7% of smokeless tobacco users among high school students and from 13.1% of e-cigarette users to 24.5% of hookah smokers among middle school students.

What are the implications for public health practice?

Understanding tobacco product use patterns including frequency of use is important for sustained implementation of proven tobacco control strategies and the regulation of tobacco products.

Corresponding author: Gabriella Anic, gabriella.anic@fda.hhs.gov, 240-402-6941.

[1]Office of Science, Center for Tobacco Products, Food and Drug Administration, Beltsville, Maryland; [2]Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, CDC.

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References

1. US Department of Health and Human Services. Preventing tobacco use among youth and young adults: a report of the Surgeon General. Rockville, MD: US Department of Health and Human Services; 2012. https://www.ncbi.nlm.nih.gov/books/NBK99237/pdf/Bookshelf_NBK99237.pdf
2. US Department of Health and Human Services. E-cigarette use among youth and young adults. a report of the Surgeon General. Rockville, MD: US Department of Health and Human Services; 2016. https://e-cigarettes.surgeongeneral.gov/documents/2016_SGR_Full_Report_508.pdf
3. Wang TW, Gentzke A, Sharapova S, Cullen KA, Ambrose BK, Jamal A. Tobacco product use among middle and high school students—United States, 2011–2017. MMWR Morb Mortal Wkly Rep 2018;67:629–33. https://doi.org/10.15585/mmwr.mm6722a3
4. CDC. 2016 National Youth Tobacco Survey: methodology report. Atlanta, GA: US Department of Health and Human Services, CDC; 2017. https://www.cdc.gov/tobacco/data_statistics/surveys/nyts/zip_files/2016-nyts-methodology-report.zip

[†] A chi-squared test found no significant differences across years for the prevalence of infrequent, moderate, and frequent use of e-cigarettes (p = 0.11); cigars (p = 0.44); smokeless tobacco products (p = 0.66); and hookahs (p = 0.80). The prevalence of frequent cigarette smoking decreased during 2015–2017 (p = 0.01).

[§] Family Smoking Prevention and Tobacco Control Act, Pub. L. 111–31, 123 Stat. 1776 (June 22, 2009). https://www.gpo.gov/fdsys/pkg/PLAW-111publ31/pdf/PLAW-111publ31.pdf.

5. Apelberg BJ, Corey CG, Hoffman AC, et al. Symptoms of tobacco dependence among middle and high school tobacco users: results from the 2012 National Youth Tobacco Survey. Am J Prev Med 2014;47(Suppl 1):S4–14. https://doi.org/10.1016/j.amepre.2014.04.013
6. DiFranza JR, Savageau JA, Fletcher K, et al. Symptoms of tobacco dependence after brief intermittent use: the development and assessment of nicotine dependence in youth–2 study. Arch Pediatr Adolesc Med 2007;161:704–10. https://doi.org/10.1001/archpedi.161.7.704
7. US Department of Health and Human Services. Deeming tobacco products to be subject to the Federal Food, Drug, and Cosmetic Act, as amended by the Family Smoking Prevention and Tobacco Control Act. Final Rules. Fed Regist 2016 May 10. 81(90): 28974–29106. https://www.gpo.gov/fdsys/pkg/FR-2016-05-10/pdf/2016-10685.pdf
8. US Department of Health and Human Services. The health consequences of smoking—50 years of progress. a report of the Surgeon General. Rockville, MD: US Department of Health and Human Services; 2014. http://www.surgeongeneral.gov/library/reports/50-years-of-progress/full-report.pdf
9. CDC. Best practices for comprehensive tobacco control programs—2014. Atlanta, GA: US Department of Health and Human Services, CDC; 2014. https://www.cdc.gov/tobacco/stateandcommunity/best_practices/index.htm

Unresolved Splenomegaly in Recently Resettled Congolese Refugees — Multiple States, 2015–2018

Laura D. Zambrano, PhD[1,2]; Olivia Samson[2,3]; Christina Phares, PhD[2]; Emily Jentes, PhD[2]; Michelle Weinberg, MD[2]; Matthew Goers, MD[1,4]; S. Patrick Kachur, MD[5]; Robert McDonald, MD[1,6]; Bozena Morawski, PhD[1,7]; Henry Njuguna, MD[1,8]; Yasser Bakhsh, MBBS[1,9]; Rebecca Laws, PhD[1,9]; Corey Peak, ScD[1,2]; Sally Ann Iverson, DVM[1,10]; Carla Bezold, ScD[1,10]; Hayder Allkhenfr, MBBS[11]; Roberta Horth, PhD[1,11]; Jun Yang, PhD[12]; Susan Miller, MSW[12]; Michael Kacka, MD[13]; Abby Davids, MD[14]; Margaret Mortimer, MSN[14]; Nomana Khan, MBBS[2]; William Stauffer, MD[2,15,*]; Nina Marano, DVM[2,*]

In 2014, panel physicians from the International Organization for Migration (IOM), who conduct Department of State–required predeparture examinations for U.S.-bound refugees at resettlement sites in Uganda, noticed an unusually high number of Congolese refugees with enlarged spleens, or splenomegaly. Many conditions can cause splenomegaly, such as various infections, liver disease, and cancer. Splenomegaly can result in hematologic disturbances and abdominal pain and can increase the risk for splenic rupture from blunt trauma, resulting in life-threatening internal bleeding. On CDC's advice, panel physicians implemented an enhanced surveillance and treatment protocol that included screening for malaria (through thick and thin smears and rapid diagnostic testing), schistosomiasis, and several other conditions; treatment of any condition identified as potentially associated with splenomegaly; and empiric treatment for the most likely etiologies, including malaria and schistosomiasis. CDC recommended further treatment for malaria with primaquine after arrival, after glucose-6-phosphate dehydrogenase testing, to target liver-stage parasites. Despite this recommended treatment protocol, 35 of 64 patients with available follow-up records had splenomegaly that persisted beyond 6 months after resettlement. Among 85 patients who were diagnosed with splenomegaly through abdominal palpation or ultrasound at any point after resettlement, 53 had some hematologic abnormality (leukopenia, anemia, or thrombocytopenia), 16 had evidence of current or recent malaria infection, and eight had evidence of schistosomiasis. Even though primaquine was provided to a minority of patients in this cohort, it should be provided to all eligible patients with persistent splenomegaly, and repeated antischistosomal therapy should be provided to patients with evidence of current or recent schistosomiasis. Given substantial evidence of familial clustering of cases, family members of patients with known splenomegaly should be proactively screened for this condition.

Approximately 6 months before resettlement, all United States–bound refugees undergo a medical examination overseas conducted by panel physicians appointed by the U.S. Department of State, in accordance with technical instructions provided by CDC (*1*). In March and July 2015, among 987 refugees undergoing overseas medical examination in Uganda, 145 (14.7%) bound for 23 U.S. states[†] had palpable but presumably asymptomatic splenomegaly, prompting further investigation. This initial investigation failed to identify a clear etiology, but malaria was considered to be one of the potential causes (*2*). Because of the uncertain etiology, CDC established a mechanism for domestic U.S. clinicians to report postarrival clinical outcomes and receive guidance in the event that case management guidelines changed. The literature published on malaria-associated splenomegaly indicates that the condition usually resolves within months of departure from an area of malaria endemicity (*3*,*4*). However, throughout 2016, it became evident that despite implementation of the diagnostic and treatment protocol,[§] splenomegaly was not resolving in some patients. In response, on April 25, 2017, IOM asked CDC to investigate unresolved splenomegaly (defined as any palpable splenomegaly after arrival) among refugees with a diagnosis of splenomegaly before or after arrival to inform overseas and postarrival screening exams and clinical management. Goals were to describe associated or underlying conditions, clinician management strategies, and clinical outcomes.

CDC contacted the 10 states with the highest number of patients with splenomegaly, as well as Georgia, because of its geographic proximity to CDC. Among these 11 states, nine[¶] agreed to participate. Investigators obtained data through retrospective medical chart abstractions from all available postarrival clinical records and asked participating health care providers about

*These authors contributed equally.

[†] The 23 states were Arizona, California, Connecticut, Florida, Georgia, Idaho, Illinois, Indiana, Kansas, Kentucky, Massachusetts, Michigan, Nevada, New Hampshire, New York, Ohio, Pennsylvania, South Carolina, South Dakota, Texas, Utah, Vermont, and Washington.

[§] The predeparture diagnostic protocol developed for the investigation of the original cohort included abdominal ultrasonography and laboratory testing for common causes of splenomegaly. CDC recommended that after arrival, malaria testing be repeated in symptomatic patients and further laboratory or radiologic testing be conducted as needed. The treatment protocol included predeparture administration of artemethur-lumefantrine (at the time of diagnosis and immediately before departure) and praziquantel. CDC recommended all patients with splenomegaly receive primaquine after arrival, after testing for normal glucose-6-phosphate dehydrogenase levels. More information on these methods can be found in Goers et al. (https://www.cdc.gov/mmwr/volumes/65/wr/mm6535a5.htm).

[¶] Eight of the 10 states with the highest number of patients with splenomegaly (Arizona, California, Idaho, New York, Pennsylvania, South Carolina, Utah, and Washington) and Georgia agreed to participate.

additional cases of splenomegaly among all arriving Congolese refugees. Investigators also collected laboratory results suggestive of potential etiologies, such as total immunoglobulin M for differential diagnosis of tropical splenomegaly (*5*); available malaria testing results (by smear microscopy, rapid diagnostic testing, or molecular testing); stool specimen testing; urinalyses; and serological evidence of prior schistosomiasis with current eosinophilia (*6*); and then recorded clinical progress and hematologic and hepatic outcomes.

Overall, 135 Congolese refugees with splenomegaly who resettled within the nine states during April 2015–May 2017 were identified; 90 (66.6%) patients were clustered in 22 families. Postarrival medical records were available for 117 (87%) patients, including 96 who received a diagnosis overseas (86 from the original cohort identified prospectively by IOM and an additional 10 patients who were identified by retrospective review of medical records by domestic clinicians) and 21 patients who received a diagnosis domestically (Table 1) (Figure).** Clinicians in New York identified six cases by proactively screening family members of patients with known splenomegaly. All initial domestic screening examinations occurred within 90 days of arrival, as recommended by CDC (*7*). At this postarrival examination, splenomegaly was noted for 64 (66.7%) of 96 patients who received a diagnosis overseas and 21 patients with a domestic diagnosis, resulting in a total of 85 patients who had splenomegaly after their arrival.

Among all 85 patients with splenomegaly at their initial examination, 64 (75.3%) had at least one clinic visit (for any condition) >6 months after arrival. Among these 64 patients, median duration between arrival and the last visit when splenomegaly was noted was 9.0 months (range = 0.3–27.9 months), and 35 (54.7%) had persistent splenomegaly, defined as a palpable spleen 6 months after departing an area with endemic malaria.

** Among the 31 patients classified as having splenomegaly after arrival, 23 originated in Uganda and eight in Tanzania. Data are pending for an additional 11 patients with splenomegaly who arrived from Uganda, Tanzania, and Burundi.

Hematologic, Hepatic, and Infectious Disease Screening

Predeparture or postarrival laboratory results were available for 84 of 85 refugees with documented splenomegaly and 24 of 32 without documented splenomegaly at their initial domestic exam (Table 2). Among the 84 with splenomegaly, 53 (63.1%) had a hematologic abnormality, such as anemia (43 of 83, 51.8%), leukopenia (16 of 79, 20.3%), or thrombocytopenia (19 of 34, 55.9%). Elevated liver enzymes, including alanine transaminase or aspartate transaminase, were present in 11 (20.0%) of 55 patients, and elevated alkaline phosphatase was present in 31 (53.5%) of 58 patients with available results. Among the 46 patients who were screened for malaria by thin or thick smear after arrival, six (13.0%) were smear-positive; two of these six patients had evidence of infection with *Plasmodium falciparum*, four had evidence of infection with *Plasmodium vivax* or *Plasmodium ovale*, and two had coinfection with *Plasmodium malariae* and *P. vivax* or *P. ovale*. Among 30 refugees with splenomegaly after arrival for whom *Schistosoma* immunoglobulin G results were available, 15 (50.0%) had evidence of prior infection; among 13 with both *Schistosoma* immunoglobulin G results and an eosinophil count, eight (61.5%) had eosinophilia (Table 2).

Treatment

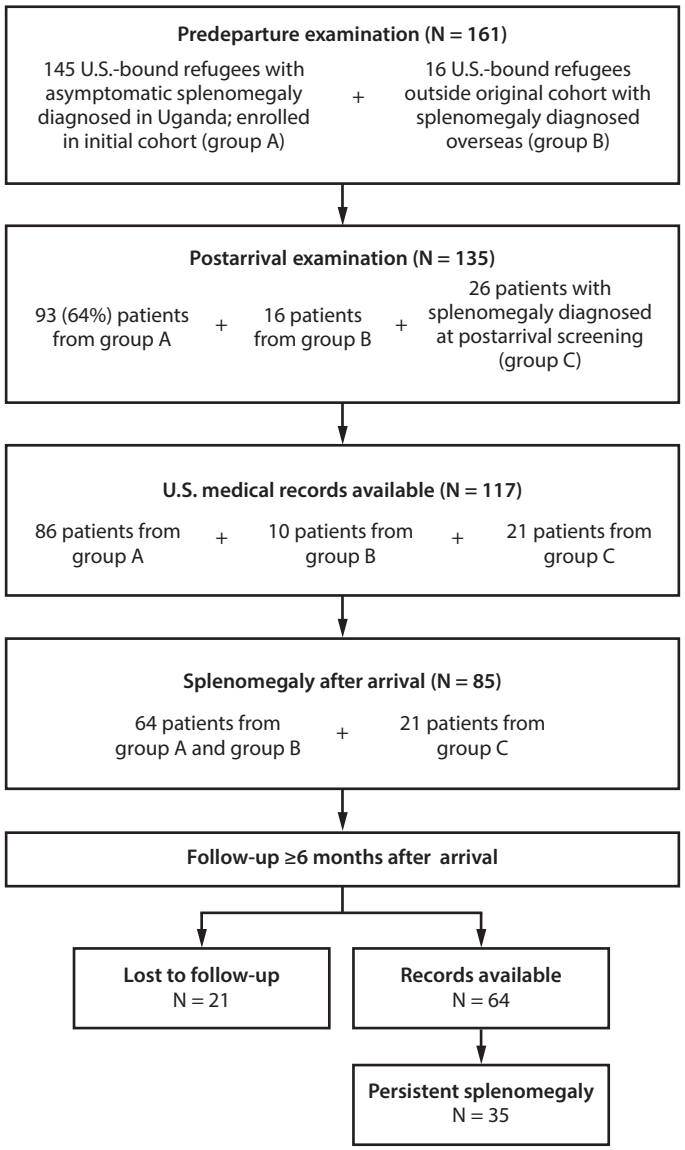
All patients were treated empirically with praziquantel for schistosomiasis and at least 1 dose of artemether-lumefantrine for malaria before departure. Although CDC recommended

TABLE 1. States of resettlement of Congolese refugees* with splenomegaly — United States, 2015–2018

State	Diagnosed overseas		Diagnosed domestically and identified after arrival	Total no. included in investigation†	No. with splenomegaly at initial exam
	Member of original cohort (identified prospectively)	Identified retrospectively after arrival			
Arizona	12	2	0	14	5
California	12	0	1	13	9
Georgia	1	2	0	3	3
Idaho§	13	1	0	14	11
New York	12	1	9	22	18
Pennsylvania	11	1	0	12	4
South Carolina	6	0	7	13	11
Utah	13	3	2	18	18
Washington	6	0	2	8	6
Total	**86**	**10**	**21**	**117**	**85**

* Patients with splenomegaly in a cohort investigated overseas (https://www.cdc.gov/mmwr/volumes/65/wr/mm6535a5.htm?s_cid=mm6535a5) and cases identified after arrival across the eight most affected states and Georgia are shown, along with the total number of patients included in this investigation and number of patients with splenomegaly identified at the initial exam.
† Eighteen additional records from Idaho are pending.
§ Data collection is ongoing in Idaho; case records have been submitted for 14 of 32 known cases in the state.

FIGURE. Number of Congolese refugees with unresolved splenomegaly, by stage of resettlement — United States, 2015–2018[*,†,§]



* Among refugees receiving predeparture examinations (N = 161), 145 resettling to 23 states were enrolled in the intial cohort (Group A). https://www.cdc.gov/mmwr/volumes/65/wr/mm6535a5.htm?s_cid=mm6535a5_w.

† Among refugees receiving postarrival examinations (N = 135), 93 resettled in nine participating states: Arizona, California, Georgia, Idaho, New York, Pennsylvania, South Carolina, Utah, and Washington (group A).

§ Group C patients were screened in six states: California, Idaho, New York, South Carolina, Utah, and Washington.

treatment with primaquine after arrival for all Congolese refugees with splenomegaly (*2*), only 31 (26.5%) of 117 patients had documentation of primaquine administration in their postarrival medical charts, and none had documentation of completion of the 14-day regimen. Among the 31 patients who received primaquine, 29 (93.6%) had a clinic visit >6 months after arrival, compared with 43 (50.0%) of 86 patients who did not receive primaquine. Among these 29 patients, the median duration of observed splenomegaly was 12.4 months after arrival (range = 0.3–24.1 months), and 20 (69.0%) met the definition for persistent splenomegaly. Three patients received praziquantel after arrival.

Discussion

Few data, beyond anecdotal clinician reports, exist on tropical splenomegaly, and patients' anticipated clinical course is still largely unknown, particularly after relocation to nontropical environments. In contrast to what has been reported previously (*3*,*4*), many of the patients in this report had persistent splenomegaly long after arrival, despite receipt of a short course of malaria treatment and removal from an area with endemic malaria, indicating that the clinical course of tropical splenomegaly is still poorly understood. Malaria might still be the predominant underlying etiology, particularly given the presence of species including *P. vivax* and *P. ovale*, which can cause relapsing disease, in some refugees. The original recommendation (*2*) remains unchanged: all refugees of Congolese origin with splenomegaly should receive presumptive treatment with primaquine after arrival in the United States. Despite this recommendation, two thirds of refugees identified with splenomegaly in this investigation did not receive primaquine. Lack of awareness among domestic physicians, need for repeated visits for glucose-6-phosphate dehydrogenase testing, a long (14-day) course, safety concerns, and availability of primaquine might have contributed to inconsistent administration.

The majority of patients with persistent splenomegaly had some combination of hematologic abnormalities, potentially caused by splenic sequestration. Many patients also had elevated liver transaminases, suggesting a need to monitor hepatic complications in this population. In light of the high proportion of patients with evidence of prior *Schistosoma* infection (47%) or eosinophilia (22%), it is important for physicians to consider further screening and diagnostic evaluation through stool and urine examination for ova or urinalysis for red blood cells. Among patients with persistent splenomegaly and clinical indicators of *Schistosoma* infection, such as eosinophilia without any other known cause, clinicians should consider repeating antischistosomal therapy with praziquantel. In addition, because etiology might be multifactorial or patient-specific, clinicians also need to consider further diagnostic testing in cases of persistent splenomegaly for Epstein-Barr virus, autoimmune disorders, or oncologic/hematologic etiologies.

The findings in this report are subject to at least four limitations. First, because data were obtained from clinic visits that occurred at irregular intervals, these findings likely underestimate the duration of splenomegaly in this population. Second, because of loss to follow-up, this investigation cannot estimate the actual proportion of patients whose condition resolved after their initial

screening exam. Third, data quality varied widely across clinics, and diagnostic information from U.S.-based clinics (particularly more sensitive molecular diagnostics) was unavailable in most instances. Finally, considering the 21 cases of splenomegaly identified after U.S. arrival, the condition was likely underdiagnosed. Increased awareness and emphasis on careful spleen examination might improve sensitivity of predeparture detection.

Despite published reports suggesting that resolution would follow malaria treatment and removal from an area with endemic malaria (*3*,*4*), this analysis found that splenomegaly persisted after arrival in many Congolese refugees, in some cases beyond 2 years. Associated pathologic conditions, such as anemia and thrombocytopenia, also were prevalent. Clinicians caring for such patients both predeparture and postarrival need to be aware of the high prevalence of splenomegaly in this population. Given familial clustering and additional cases identified through proactive family screening, both overseas and domestic clinicians could consider screening family members of Congolese refugees with splenomegaly. Congolese refugees found to have splenomegaly should be treated with primaquine, if eligible; counseled on the condition and precautions (e.g., avoidance of contact sports); followed closely; and referred for specialty care if they fail to respond to treatment. Multiple etiologies are possible, but there is likely a predominant underlying infection and immune response. Future investigations might further reveal associated pathologies and etiologies of tropical splenomegaly in this population.

Summary

What is already known about this topic?

Since 2014, a large number of resettling Congolese refugees have been found to have splenomegaly, which has not resolved in some patients despite treatment.

What is added by this report?

Despite recommendations, most refugees with splenomegaly did not have documented receipt of primaquine after resettlement. Most patients were clustered within families. Approximately 50% of patients with available medical records had persistent splenomegaly >6 months after arrival; 63% of patients with splenomegaly had a hematologic abnormality.

What are the implications for public health practice?

Eligible Congolese refugees with splenomegaly should be treated with primaquine, followed closely, and referred for specialty care if they fail to respond to treatment, and their family members should be proactively screened for splenomegaly.

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TABLE 2. Underlying conditions and clinical sequelae in Congolese refugees with splenomegaly diagnosed predeparture or post-arrival in the United States, by presence of splenomegaly at the initial domestic exam after arrival — nine states,* 2015–2018

		Initial domestic exam			
		Splenomegaly (n = 85)§		No splenomegaly (n = 32)¶	
Laboratory test results	Reference range†	No. tested	No. with condition (%)	No. tested	No. with condition (%)
Elevated total IgM**	46–304 mg/dL	27	12 (44.4)	0	0
Malaria (smear or RDT-positive)	N/A	55	16 (29.1)	19	10 (52.6)
Elevated *Schistosoma* IgG	≥0.20 OD	30	15 (50.0)	4	1 (25.0)
Eosinophilia	≥500 cells/μL	77	21 (27.3)	21	5 (23.8)
Among *Schistosoma* IgG(+)	—	13	8 (61.5)	1	0 (0)
Among *Schistosoma* IgG(-)	—	15	2 (13.3)	2	1 (50.0)
Other hematologic abnormality	N/A	84	53 (63.1)	24	11 (45.8)
Leukopenia	<4,000 cells/μL	79	16 (20.3)	24	3 (12.5)
Anemia (hemoglobin)	F: ≤12.0 g/dL; M: ≤14.0 g/dL	83	43 (51.8)	24	10 (41.7)
Thrombocytopenia	<150,000 platelets/μL	34	19 (55.9)	8	3 (37.5)
Elevated alkaline phosphatase	>147 IU/L	58	31 (53.5)	12	8 (66.7)
Elevated transaminases	>40 IU/L	55	11 (20.0)	11	1 (9.1)
Elevated AST	—	55	9 (16.4)	11	1 (9.1)
Elevated ALT	—	55	8 (14.6)	11	1 (9.1)

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; F = females; IgG = immunoglobulin G; IgM = immunoglobulin M; M = males; OD = optical density; RDT = rapid diagnostic test.

* Arizona, California, Idaho, New York, Pennsylvania, South Carolina, Utah, Washington, and Georgia.

† In the absence of laboratory reference ranges from all laboratories the highest cutoff value reported was used, which might have sacrificed sensitivity.

§ Includes 63 patients with a diagnosis of splenomegaly overseas who had splenomegaly noted at their initial domestic exam and 21 patients who received a diagnosis of splenomegaly domestically. Eighty-five patients had splenomegaly on arrival, but laboratory records were absent for one.

¶ Includes 24 patients with available laboratory results who received a diagnosis of splenomegaly overseas, none of whom had splenomegaly noted at their initial domestic exam, excluding eight patients for whom laboratory results were not available.

** Total IgM is used for in the diagnosis of hyperreactive malarial splenomegaly syndrome.

Moses Muyumbe, Agency for New Americans, Boise, Idaho; Zeze Rwasama, College of Southern Idaho Refugee Center, Twin Falls, Idaho; Melinda Bauman, Tanis Maxwell, South Central Public Health District, Twin Falls, Idaho; Debra Blog, Stephen E. Hughes, Patricia Kirshenbaum, New York State Department of Health; Leena Anil, Atmaram Nambiar, Sharon Watkins, Pennsylvania Department of Health; Catherine Brett, Elizabeth Carter, Dan Drociuk, Alison Jamison-Haggwood, Stephanie Sophie Lee, South Carolina Department of Health and Environmental Control; Allyn Nakashima, Rachel Ashby, Utah Department of Health; Diane Chapman, Karl Kirby, St. Mark's Family Medicine Clinic, Salt Lake City, Utah; Scott Lindquist, Jasmine Matheson, Laura Newman, Washington State Department of Health; Lori Kelley, Yakima Valley Farm Workers Clinic, Unify Health, Spokane, Washington; Abdoulaye Bangoura, Amanda Dam, Lucy Tantum, Division of Global Migration and Quarantine, National Center for Emerging and Zoonotic Diseases, CDC.

Corresponding author: Laura D. Zambrano, lzambrano@cdc.gov, 404-498-1483.

[1]Epidemic Intelligence Service, CDC; [2]Division of Global Migration and Quarantine, National Center for Emerging and Zoonotic Infectious Diseases, CDC; [3]Oak Ridge Institute for Science and Education, Oak Ridge, Tennessee; [4]Division of Global Health Protection, Center for Global Health, CDC; [5]Division of Parasitic Diseases and Malaria, Center for Global Health, CDC; [6]New York State Department of Health; [7]Idaho Department of Health and Welfare; [8]Washington State Department of Health, Tumwater, Washington; [9]California Department of Public Health, Richmond, California; [10]Arizona Department of Health Services; [11]Utah Department of Health; [12]Pennsylvania Department of Human Services; [13]South Carolina Department of Health and Environmental Control; [14]Family Medicine Residency of Idaho, Boise, Idaho; [15]University of Minnesota, Minneapolis.

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References

1. CDC. Technical instructions for panel physicians and civil surgeons: technical instructions for panel physicians. Atlanta, GA: US Department of Health and Human Services, CDC; 2018. https://www.cdc.gov/immigrantrefugeehealth/exams/ti/panel/technical-instructions-panel-physicians.html
2. Goers M, Ope MO, Samuels A, et al. Splenomegaly of unknown etiology in Congolese refugees applying for resettlement to the United States—Uganda, 2015. MMWR Morb Mortal Wkly Rep 2016;65:943–4. https://doi.org/10.15585/mmwr.mm6535a5
3. Bisoffi Z, Leoni S, Angheben A, et al. Chronic malaria and hyper-reactive malarial splenomegaly: a retrospective study on the largest series observed in a non-endemic country. Malar J 2016;15:230. https://doi.org/10.1186/s12936-016-1274-x
4. Leoni S, Buonfrate D, Angheben A, Gobbi F, Bisoffi Z. The hyper-reactive malarial splenomegaly: a systematic review of the literature. Malar J 2015;14:185. https://doi.org/10.1186/s12936-015-0694-3
5. Alkadarou T, Musa A, Alkadarou A, et al. Immunological characteristics of hyperreactive malarial splenomegaly syndrome in sudanese patients. J Trop Med 2013;2013:961051. https://doi.org/10.1155/2013/961051
6. Leite LA, Domingues AL, Lopes EP, et al. Relationship between splenomegaly and hematologic findings in patients with hepatosplenic schistosomiasis. Rev Bras Hematol Hemoter 2013;35:332–6. https://doi.org/10.5581/1516-8484.20130098
7. CDC. Immigrant and refugee health: guidelines for the U.S. domestic medical examination for newly arriving refugees. Atlanta, GA: US Department of Health and Human Services, CDC; 2014. https://www.cdc.gov/immigrantrefugeehealth/guidelines/domestic/domestic-guidelines.html

Low and Decreasing Prevalence and Rate of False Positive HIV Diagnosis — Chókwè District, Mozambique, 2014–2017

Daniel Shodell, MD[1]; Robert Nelson, MPH[2]; Duncan MacKellar, DrPH[2]; Ricardo Thompson, PhD[3]; Isabelle Casavant, MPH[1]; Didier Mugabe, MD[3]; Sherri Pals, PhD[2]; Dawud Ujamaa, MS[2]; Juvencio Bonzela[3]; Judite Cardoso[4]; Salvador Machava[3]; Carlos Lourenço, MD[3]; Chunfu Yang, PhD[2]; Bharat Parekh, PhD[2]; Ishani Pathmanathan, MD[2]; Andrew F. Auld, MD[2]; Stelio Tamele, MD[5]; Manuel Antonio Ouane, MD[5]; Vania Macome, MPH[6]; Noela Chicuecue, MD[7]; Guita Amane[7]; Luciana Kohatsu, PhD[1]; Nely Honwana[1]; Stanley Wei, MD[1]; Peter R. Kerndt, MD[1]; Edgar Monterroso, MD[1]; Alfredo Vergara, PhD[1]

In 2017, rapid human immunodeficiency virus (HIV) testing services enabled the HIV diagnosis and treatment of approximately 15.3 million persons with HIV infection in sub-Saharan Africa with life-saving antiretroviral therapy (ART) (*1*). Although suboptimal testing practices and misdiagnoses have been reported in sub-Saharan Africa and elsewhere, trends in population burden and rate of false positive HIV diagnosis (false diagnosis) have not been reported (*2*,*3*). Understanding the population prevalence and trends of false diagnosis is fundamental for guiding rapid HIV testing policies and practices. To help address this need, CDC analyzed data from 57,655 residents aged 15–59 years in the Chókwè Health and Demographic Surveillance System (CHDSS) in Mozambique to evaluate trends in the rate (the percentage of false diagnoses among retested persons reporting a prior HIV diagnosis) and population prevalence of false diagnosis. From 2014 to 2017, the observed rate of false diagnosis in CHDSS decreased from 0.66% to 0.00% (p<0.001), and the estimated population prevalence of false diagnosis decreased from 0.08% to 0.01% (p = 0.0016). Although the prevalence and rate of false diagnosis are low and have decreased significantly in CHDSS, observed false diagnoses underscore the importance of routine HIV retesting before ART initiation and implementation of comprehensive rapid HIV test quality management systems (*2*,*4*,*5*).

Located in Gaza Province of southern Mozambique, CHDSS conducts annual demographic surveillance of approximately 100,000 residents of Chókwè District. In 2017, an estimated 25.6% of residents aged 15–59 years had HIV infection (*6*). During 2014–2017, staff members visited all CHDSS households in each of four surveillance rounds and offered a brief survey and HIV testing to household members aged 15–59 years. In the first surveillance round (April 2014–April 2015), all consenting participants who reported a prior HIV diagnosis were tested in accordance with the national rapid HIV test algorithm (NRTA). In subsequent surveillance rounds, consenting participants who reported a prior HIV diagnosis were offered, but not required, to test for HIV infection. Dried blood spots from participants with NRTA-negative or indeterminate results who reported a prior diagnosis of HIV infection were tested at CDC with a serologic testing algorithm followed by ultrasensitive HIV-1 gp41 total nucleic acid polymerase chain reaction, if negative by serology (Figure) (*7*). Before delivering CDC-confirmed HIV-negative test results, participants were reinterviewed to verify their prior HIV diagnosis and were retested a second time in accordance with the NRTA. Participants who confirmed their prior diagnosis and retested HIV-negative were informed that they had been misdiagnosed, provided counseling and psychosocial support, and disengaged from HIV care in coordination with their HIV care provider.

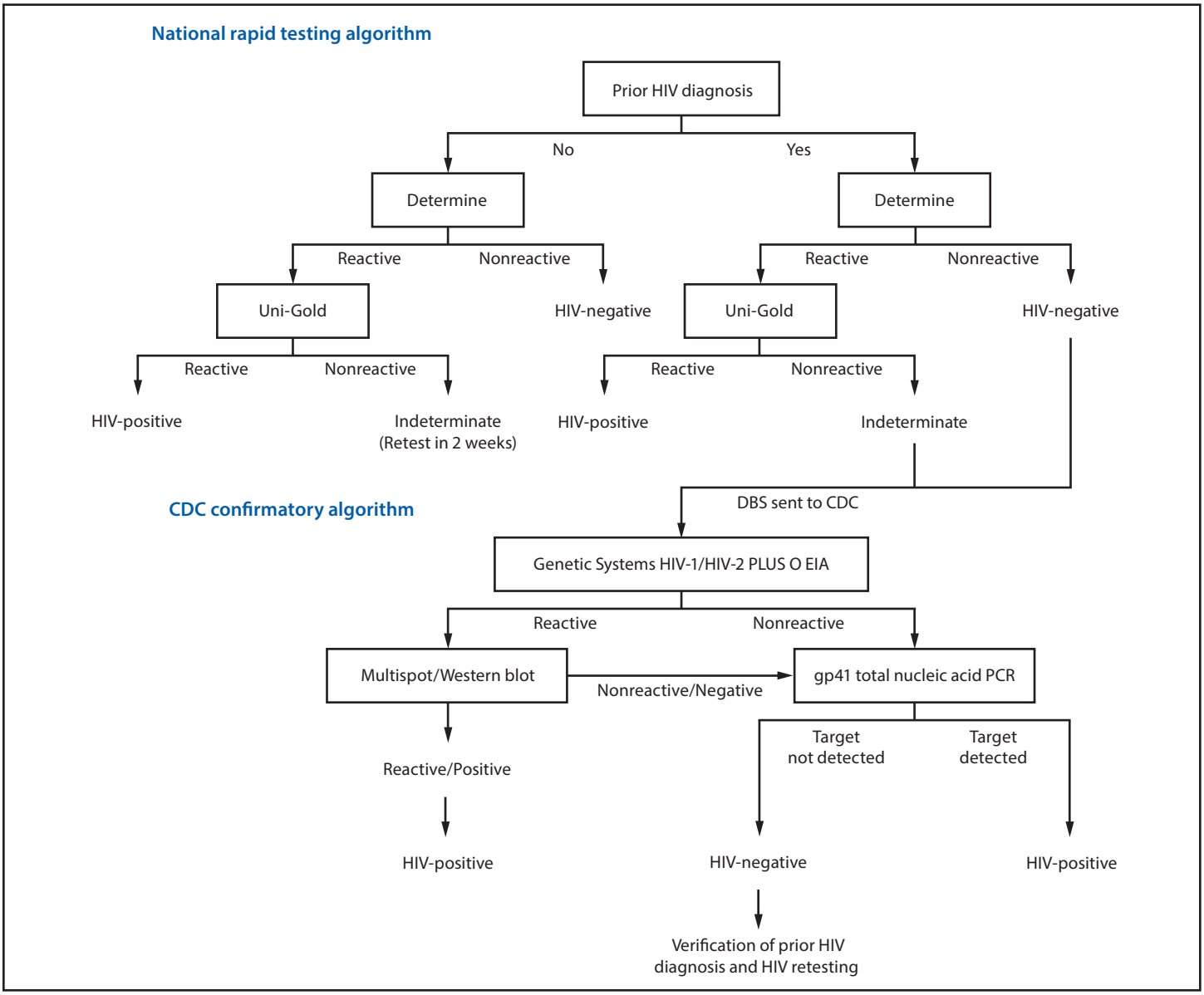
To estimate the prevalence of false diagnosis in the second and subsequent surveillance rounds, cases were imputed by applying the observed cumulative false diagnosis rate to nontested participants who reported a prior HIV diagnosis. Logistic regression was used to test for linear trends in the observed rate and estimated prevalence of false diagnosis across surveillance rounds, adjusting for within-household correlation. Maximum expected cases, rates, and prevalence of false diagnosis were calculated using the World Health Organization (WHO) prequalification lower 95% confidence limits for sensitivity and specificity for Determine* and Uni-Gold† rapid HIV tests (*8*,*9*). Excess cases were calculated as the difference between total estimated and maximum expected false diagnoses.

During 2014–2017, among 57,655 CHDSS residents aged 15–59 years, 43,496 (75.4%) participated in at least one round of surveillance (Table 1). Prior HIV diagnosis, based on the Mozambique national HIV testing algorithm (Figure), was reported by 8,608 (19.8%) participants, among whom 5,568 (64.7%) were tested for HIV. Of those tested, >99.0% in all demographic groups were NRTA-positive, including 4,698 (99.6%) of 4,719 participants who reported being on ART.

CDC confirmatory testing was conducted on specimens from 45 of 46 NRTA-negative or indeterminate participants who initially reported a prior HIV diagnosis. All 41 NRTA-negative participants tested HIV-negative at CDC; three of four NRTA-indeterminate participants tested HIV-positive, and one tested HIV-negative. Of 42 CDC-confirmed HIV-negative participants, 39 were recontacted, and 12 (31%) verified that they had never tested HIV-positive. Reasons for initial misclassification included interviewer error, or participant

* https://www.who.int/diagnostics_laboratory/documents/guidance/determine.pdf.
† https://www.who.int/diagnostics_laboratory/documents/guidance/uni_gold.pdf.

FIGURE. National rapid* and CDC confirmatory HIV testing algorithms for survey participants aged 15–59 years who reported having received a prior HIV diagnosis — Chókwè Health Demographic Surveillance System (CHDSS), Chókwè, Mozambique, 2014–2017



Abbreviations: DBS = dried blood spot; EIA = enzyme immunoassay; gp41 = glycoprotein 41; HIV = human immunodeficiency virus; PCR = polymerase chain reaction.
* The Mozambique national rapid test algorithm refers to the use of Determine followed by Uni-Gold in accordance with national HIV testing guidelines. Prior HIV diagnosis is defined as reporting during the CHDSS survey of 1) ever having tested HIV-positive, 2) testing HIV-positive at the last test, or 3) currently or ever receiving HIV care.

misunderstanding, perceived need to report a diagnosis to receive services, or mental illness. Among the 27 recontacted participants who confirmed their prior HIV diagnosis, all retested NRTA-negative a median of 170 days (interquartile range = 142–263 days) after their survey encounter. Overall, 31 participants were classified as having received a false diagnosis, including one participant who had insufficient specimen for confirmatory testing and three CDC-confirmed HIV-negative participants lost to follow-up (Table 2).

During 2014–2017, the observed rate of false diagnosis in CHDSS decreased from 0.66% to 0.00% ($p<0.001$), and estimated prevalence of false diagnosis decreased from 0.08% to 0.01% ($p = 0.0016$) (Table 2). The cumulative observed false diagnosis rate and estimated prevalence of false diagnosis were 0.56% and 0.11%, respectively. Compared with maximum expectations based on WHO prequalification studies, 44 excess false diagnoses were estimated overall, decreasing from 20 in the first round (2014–2015) to three in the fourth round (2017) (Table 2).

TABLE 1. National rapid and CDC confirmatory HIV test outcomes among survey participants aged 15–59 years who reported having received a prior HIV diagnosis, by selected characteristics and round of participation — Chókwè Health Demographic Surveillance System (CHDSS), Mozambique, 2014–2017

Characteristic	CHDSS residents and survey participants			National rapid HIV testing algorithm			CDC confirmatory testing		
	No. of residents*	Survey participants† no. (%)	Prior HIV diagnosis§ no. (%)	HIV tested¶ no. (%)	HIV-positive no. (%)	HIV-negative/ indet,** no. (%)	DBS tested†† no. (%)	HIV-positive§§ no. (%)	HIV-negative¶¶ no. (%)
All survey rounds									
Total	**57,655**	**43,496 (75.4)**	**8,608 (19.8)**	**5,568 (64.7)**	**5,534 (99.4)**	**34 (0.6)**	**33 (97.1)**	**3 (9.1)**	**30 (90.9)**
Sex									
Female	35,378	28,339 (80.1)	6,755 (23.8)	4,471 (66.2)	4,444 (99.4)	27 (0.6)	26 (96.3)	1 (3.8)	25 (96.2)
Male	22,277	15,157 (68.0)	1,853 (12.2)	1,097 (59.2)	1,090 (99.4)	7 (0.6)	7 (100.0)	2 (28.6)	5 (71.4)
Age group (yrs)									
15–24	26,306	19,886 (75.6)	1,073 (5.4)	614 (57.2)	609 (99.2)	5 (0.8)	5 (100.0)	0 (—)	5 (100.0)
25–34	13,482	9,678 (71.8)	2,637 (27.2)	1,639 (62.2)	1,634 (99.7)	5 (0.3)	5 (100.0)	0 (—)	5 (100.0)
35–59	17,867	13,932 (78.0)	4,898 (35.2)	3,315 (67.7)	3,291 (99.3)	24 (0.7)	23 (95.8)	3 (13.0)	20 (87.0)
Survey round* **									
1 (2014–2015)	51,362	24,947 (48.6)	3,169 (12.7)	3,169 (100.0)	3,145 (99.2)	24 (0.8)	23 (95.8)	3 (13.0)	20 (87.0)
2 (2015–2016)	47,823	24,455 (51.1)	2,623 (10.7)	1,232 (47.0)	1,226 (99.5)	6 (0.5)	6 (100.0)	0 (—)	6 (100.0)
3 (2016–2017)	47,624	24,178 (50.8)	1,865 (7.7)	805 (43.2)	801 (99.5)	4 (0.5)	4 (100.0)	0 (—)	4 (100.0)
4 (2017)	48,556	20,302 (41.8)	951 (4.7)	362 (38.1)	362 (100.0)	0 (—)	0 (—)	0 (—)	0 (—)

Abbreviations: DBS = dried blood spots; HIV = human immunodeficiency virus; indet = indeterminate.

* Approximately 102,500 persons of all ages were residents in CHDSS during round 1. For each survey round, counselors visited each household in CHDSS (20,122 households in round 1) and offered all available household members aged 15–59 years the opportunity to participate in a brief survey and to test for HIV.

† Totals for sex and age groups include residents who participated in any one of four survey rounds. For these characteristics, counts are unique individuals. Survey rounds 2, 3, and 4 include some residents who participated in a prior survey round. Within each round, counts reflect unique individuals. The sum of rounds include repeat participants.

§ Reporting during the survey of ever having tested HIV-positive, testing HIV-positive at the last test, or currently or ever receiving HIV care. Percentages are of survey participants. Participants who reported a prior HIV diagnosis in more than one round are counted only once in the round in which they first reported receiving a prior HIV diagnosis. Including repeat participants, 4,778 (20%), 5,440 (22%), and 4,539 (22%) residents reported a prior HIV diagnosis in survey rounds 2, 3, and 4, respectively. Excludes 12 participants who on follow-up were verified not to have received a prior HIV diagnosis.

¶ In round 1, counselors collected a 1-mL whole blood specimen from all consenting participants who reported a prior HIV diagnosis. Specimens were tested for HIV at the CHDSS research laboratory by trained laboratory technicians in accordance with the national rapid test algorithm. In rounds 2–4, consenting participants who reported a prior HIV diagnosis were encouraged but not required to test for HIV if they had not previously tested HIV-positive as part of CHDSS. Participants who reported a prior diagnosis and who consented to test were HIV tested at home by trained counselors in accordance with the national rapid HIV test algorithm. Percentages are of participants who reported a prior HIV diagnosis.

** Four participants tested HIV-indeterminate.

†† Excludes 12 participants who on follow-up were verified not to have received a prior HIV diagnosis. Dried blood spots of participants who reported a prior HIV diagnosis and who tested HIV-negative or indeterminate by the national rapid test algorithm were shipped on dry ice and tested at CDC in accordance with a standard confirmatory testing algorithm.

§§ All had tested HIV-indeterminate by the national rapid testing algorithm.

¶¶ Of 27 (90%) persons contacted at follow-up, 27 (100%) retested HIV-negative in accordance with the national rapid HIV test algorithm a median of 170 days (interquartile range = 142–263 days) from their survey encounter.

*** Round 1: April 2014–April 2015; round 2: May 2015–January 2016; round 3: March 2016–March 2017; round 4: April 2017–November 2017.

Discussion

False positive HIV diagnosis can result in severe individual and public health consequences, including separation from spouse and family, unnecessary care and treatment, and public distrust in HIV testing. Accurate estimation of the population burden and trends in false diagnosis is therefore critical for guiding rapid HIV testing policies and practices. In a high HIV prevalence district in Mozambique, among 5,568 residents who reported a prior HIV diagnosis, including 4,719 on ART, nearly all (>99.0%) tested HIV-positive with the Mozambique NRTA. Both the low observed rate (0.66%) and estimated prevalence (0.08%) of false diagnosis in the first round of surveillance (2014–2015) decreased to nearly zero by the fourth round (2017). Nonetheless, applying the estimated cumulative false diagnosis prevalence of 0.11% to the estimated 100,421 residents aged 15–64 years in Chókwè District, 110 residents might have ever received a false diagnosis.

As with all diagnostic tests that have excellent, but not perfect performance, false positive HIV diagnoses are expected even when testing is conducted in accordance with standard procedures and with approved, multitest algorithms (*2*,*3*). Compared with WHO prequalification expectations, 20 excess false diagnoses were observed in the first round of surveillance, decreasing to an estimated three cases in the fourth round. Although reasons for excess false diagnoses are unclear, findings from the CHDSS are consistent with reports suggesting that the specificity of the Determine rapid HIV test can be lower than manufacturer claims (*2*,*3*,*10*). Observed reductions in excess false diagnoses might be attributed to improved rapid HIV test practices and quality management systems or

TABLE 2. Number of observed, estimated, and maximum expected false positive HIV diagnosis (false diagnosis) cases, and rates and prevalence of false diagnosis among survey participants aged 15–59 years, by selected characteristics and surveillance round — Chókwè Health Demographic Surveillance System (CHDSS), Mozambique, 2014–2017

	False diagnosis rate*		False diagnosis prevalence		Maximum expected false diagnosis outcomes†			
Characteristic	No. of observed cases	False diagnosis rate§ % (95% CI)	Total estimated no. of cases¶	False diagnosis prevalence** % (95% CI)	No. of expected cases††	False diagnosis rate§§ %	False diagnosis prevalence¶¶ %	No. of excess cases***
Total	**31**	**0.56 (0.36–0.75)**	**48**	**0.11 (0.08–0.13)**	**4**	**0.047**	**0.009**	**44**
Sex								
Female	26	0.58 (0.36–0.80)	39	0.13 (0.10–0.17)	3	0.041	0.011	36
Male	5	0.46 (0.06–0.85)	9	0.07 (0.04–0.09)	1	0.058	0.006	8
Age group (yrs)								
15–24	5	0.81 (0.10–1.53)	9	0.04 (0.02–0.06)	2	0.179	0.010	7
25–34	5	0.31 (0.04–0.57)	9	0.10 (0.05–0.14)	1	0.029	0.010	8
35–59	21	0.63 (0.36–0.90)	31	0.22 (0.15–0.28)	1	0.024	0.007	30
Survey round†††								
1 (2014–2015)	21	0.66 (0.38–0.94)§§§	21	0.08 (0.04–0.12)¶¶¶	1	0.047	0.004	20
2 (2015–2016)	6	0.49 (0.10–0.87)§§§	14	0.05 (0.02–0.08)¶¶¶	1	0.047	0.004	13
3 (2016–2017)	4	0.50 (0.01–0.98)§§§	10	0.04 (0.02–0.07)¶¶¶	1	0.047	0.004	9
4 (2017)	0	0.00 (0.00–0.01)§§§	3	0.01 (0.00–0.03)¶¶¶	0	0.047	0.000	3

Abbreviations: CI = confidence interval; HIV = human immunodeficiency virus.

* Includes 27 persons who reported a prior HIV-positive diagnosis and tested HIV-negative in accordance with the national rapid test and CDC confirmatory test algorithms, and at follow-up a median of 170 days (interquartile range = 142–263 days) from their survey encounter, retested HIV-negative in accordance with the national rapid HIV test algorithm, and reaffirmed that they had received a prior HIV-positive diagnosis. Also includes four participants who reported a prior HIV-positive diagnosis and tested HIV-negative in accordance with the national rapid test algorithm, but who had insufficient specimen for testing at CDC (one participant), or were confirmed HIV-negative at CDC but were lost to follow-up for retesting and confirmation of reported prior HIV diagnosis (three participants). Excludes 12 participants who on follow-up were verified not to have received a prior HIV diagnosis.

† Maximum outcomes were calculated using standard formulae and reported lower 95% confidence limits (LCL) for sensitivity (SENS) and specificity (SPEC) from World Health Organization prequalification studies: Alere Determine HIV-1/2 (D): WHO report PQDx 0033–013–00 (https://www.who.int/diagnostics_laboratory/evaluations/pq-list/hiv-rdts/160712_amended_final_public_report_0033_013_00_v5.pdf); LCL for sensitivity and specificity for Determine are 99.10 (SENSDLCL) and 97.80 (SPECDLCL), respectively. Uni-Gold HIV (U): WHO report PQDx 0149–052–00 (https://www.who.int/diagnostics_laboratory/evaluations/pq-list/hiv-rdts/171103_amended_final_pqpr_0149_052_00_v7.pdf); LCL for sensitivity and specificity for Uni-Gold are 98.70 (SENSULCL) and 99.20 (SPECULCL), respectively.

§ 1 – positive predictive value of self-reported prior HIV-positive diagnosis (PPVSRDx); PPVSRDx = (No. prior HIV diagnoses – No. observed false diagnoses)/No. prior HIV diagnoses.

¶ Includes 17 false diagnosis cases imputed for rounds 2–4, calculated by applying the overall and demographic subgroup-specific false diagnosis rates to nontested survey participants who reported having received a prior HIV-positive diagnosis. Sum of estimated cases by age group (49) does not equal total estimated cases (48) because of rounding error.

** Total false diagnoses/survey participants, weighted to CHDSS census age-group, sex, and urban/rural distribution.

†† Prior HIV diagnosis x Maximum expected false diagnosis rate, rounded up to the nearest integer. Sum of expected cases by survey round (3) does not equal total expected cases (4) because of rounding error.

§§ 1 – lowest expected positive predictive value (PPV) of national rapid test algorithm (PPVNRTA-LE). PPVNRTA-LE = (PREV*SENSNRTA-LE) / [(PREV*SENSNRTA-LE) + (1-PREV)(1- SPECDLCL)(1-SPECULCL)]; SENSNRTA-LE = SENSDLCL*SENSULCL. PREV = observed round 1 HIV prevalence: total, 27.8%; female, 30.3%; male, 23.6%; aged 15–24 years, 9.1%; aged 25–34 years, 38.5%; aged 35–59 years, 43.1%; rounds 1–4, 27.8%.

¶¶ Maximum expected false diagnoses/survey participants, weighted to CHDSS census age-group, sex, and geographic distribution.

*** Difference between total estimated and maximum expected false diagnosis cases. Sum of estimated cases by age group (45) and survey round (45) does not equal total estimated cases (44) because of rounding error.

††† Round 1: April 2014–April 2015; round 2: May 2015–January 2016; round 3: March 2016–March 2017; round 4: April 2017–November 2017.

§§§ Test for linear trend: p<0.001. Round 4 one-sided 97.5% upper confidence limit is estimated using Clopper-Pearson method. https://jamanetwork.com/journals/jama/fullarticle/385438.

¶¶¶ Test for linear trend: p = 0.0016.

increased client-initiated retesting among persons who are diagnosed (*4*). Provider-initiated retesting before ART initiation as recommended by WHO was not routinely implemented during this period (2014–2017) and most likely does not account for observed reductions in false HIV diagnoses (*2*).

Notably, the observed cumulative rate of false positive HIV diagnosis in the CHDSS (0.56%) is less than one fifth the median false diagnosis rate (3.1%) reported in a recent systematic review of 30 studies (*3*). Findings of the low cumulative and decreasing rate of false diagnosis in the CHDSS are reassuring, and caution should be exercised in interpreting results of this systematic review. Higher rates of false diagnosis reported in many studies might be attributed to the use of suboptimal testing strategies such as a third rapid test as a tiebreaker to rule in HIV infection and lack of verification of HIV diagnostic claims (*3*). Lack of verification might be a particularly important limitation, as nearly one third of reinterviewed CHDSS participants who were initially classified as having had a false positive HIV diagnosis were verified to have never received an HIV diagnosis. Studies that do not include follow-up procedures to verify self-reported HIV diagnoses might substantially overreport false diagnosis.

After being informed of their misdiagnosis, nearly all contacted participants expressed relief that they were not infected

Summary

What is already known about this topic?

A systematic review of studies conducted in sub-Saharan Africa suggests higher than expected rates of false positive human immunodeficiency virus (HIV) diagnosis (false diagnosis) using rapid tests.

What is added by this report?

From 2014 to 2017, the rate and population prevalence of false diagnosis in Chókwè District, Mozambique, decreased from 0.66% to 0.00% and from 0.08% to 0.01%, respectively. The cumulative false diagnosis rate was 0.56%, less than one fifth the median rate (3.1%) reported in the systematic review.

What are the implications for public health practice?

Low and decreasing prevalence and rate of false diagnosis are reassuring and underscore caution in extrapolating results of the systematic review. Nonetheless, observed false diagnoses underscore the need for routine HIV retesting before initiation of antiretroviral therapy and implementation of comprehensive rapid HIV test quality management systems.

and no longer needed HIV care. At the request of one participant, the psychologist and medical officer from the local health authority confirmed the client's status with concerned family members; no other follow-up support services were requested. All contacted participants were successfully disengaged from HIV care, including 16 who were on ART. Public concerns about the accuracy of HIV testing and reductions in uptake of rapid HIV testing services in Chókwè District have not been reported.

The findings in this report are subject to at least four limitations. First, after the first round, fewer than half of participants who claimed a prior diagnosis were tested for HIV. Estimated cases and prevalence of false diagnosis, however, is conservative because imputed cases were based on the higher cumulative false diagnosis rate rather than lower round-specific rates, and participants who did not complete all testing and prior-diagnosis verification steps were assumed to have received false diagnoses. Second, surveillance of quality management system activities among facility and community rapid HIV test providers was not conducted, and the potential impact of these activities on reducing the rate and prevalence of false diagnosis is unknown. Third, it is possible that some HIV-infected participants who were receiving ART might have false negative test results because of loss of detectable antibody (*2*,*3*,*7*). Total nucleic acid polymerase chain reaction is not 100% sensitive, and retesting negative does not rule out HIV infection for patients on ART (*7*). Participants who discontinued ART are being retested periodically. Finally, this study was conducted in a high HIV prevalence district in southern Mozambique. Because the positive predictive value of diagnostic tests depends, in part, on disease prevalence, other areas and districts of Mozambique might have higher rates of false diagnosis attributed to lower HIV prevalence alone.

Low and decreasing trends in the estimated prevalence of false positive HIV diagnosis in CHDSS indicate that residents in Chókwè District have received high-quality rapid HIV testing services, and that HIV care and ART is provided near universally to only those in need. However, observed false diagnoses in Chókwè District underscore the importance of routine retesting and confirmation of HIV infection for all patients before ART initiation, and implementation of comprehensive quality management systems to ensure appropriate training, supervision, proficiency testing, and external quality assessment of rapid HIV test providers (*2*,*4*,*5*).

Corresponding author: Duncan MacKellar, DMackellar@cdc.gov, 404-639-6199.

[1]CDC Country Office, Maputo, Mozambique; [2]Division of Global HIV and TB, Center for Global Health, CDC; [3]Chókwè Health Research and Training Center, National Institute of Health, Chókwè, Mozambique; [4]Jhpiego, Johns Hopkins University, Maputo, Mozambique; [5]Chókwè District Public Health Directorate, Chókwè, Mozambique; [6]FHI 360, Maputo, Mozambique; [7]Mozambique Ministry of Health, Maputo, Mozambique.

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References

1. Joint United Nations Programme on HIV. AIDS info database. Geneva, Switzerland: Joint United Nations Programme on HIV; 2018. http://aidsinfo.unaids.org/
2. World Health Organization. Consolidated guidelines on HIV testing services. Geneva, Switzerland: World Health Organization; 2015. https://www.who.int/hiv/pub/guidelines/hiv-testing-services/en/
3. Johnson CC, Fonner V, Sands A, et al. To err is human, to correct is public health: a systematic review examining poor quality testing and misdiagnosis of HIV status. J Int AIDS Soc 2017;20(Suppl 6):21755–71. https://doi.org/10.7448/IAS.20.7.21755
4. Parekh BS, Kalou MB, Alemnji G, Ou CY, Gershy-Damet GM, Nkengasong JN. Scaling up HIV rapid testing in developing countries: comprehensive approach for implementing quality assurance. Am J Clin Pathol 2010;134:573–84. https://doi.org/10.1309/AJCPTDIMFR00IKYX
5. World Health Organization. Handbook: improving the quality of HIV-related point-of-care testing: ensuring the reliability and accuracy of test results. Geneva, Switzerland: World Health Organization; 2015. https://www.who.int/hiv/pub/toolkits/handbook-point-of-care-testing/en/
6. Nelson R, Casavant I, Thompson R, et al. Trends in HIV diagnostic coverage & prevalence of undiagnosed infection in a high burden district with annual home-based HIV testing: findings from the Chókwè Health Demographic Surveillance System (CHDSS), Chókwè District, Mozambique, 2014–2017 [Poster]. Presented at the International AIDS Conference (AIDS 2018); July 23–27, 2018; Amsterdam, Netherlands.
7. Yang C, Li M, Cowart F, et al. Characterization of human immunodeficiency virus type-1 from HIV-1 seropositive cases with undetectable viremia. J Clin Virol 2004;30:224–8. https://doi.org/10.1016/j.jcv.2003.11.007

8. World Health Organization. WHO prequalification of diagnostic programme public report. Product: Alere Determine HIV-1/2. Number: PQDx 0033–013–00. Geneva, Switzerland: World Health Organization; 2016. https://www.who.int/diagnostics_laboratory/evaluations/pq-list/hiv-rdts/public_report/en/
9. World Health Organization. WHO prequalification of diagnostic programme public report. Product: Uni-Gold HIV. Number: PQDx 0149–052–00. Geneva, Switzerland: World Health Organization; 2012. https://www.who.int/diagnostics_laboratory/evaluations/pq-list/hiv-rdts/public_report/en/
10. Kroidl I, Clowes P, Mwalongo W, et al. Low specificity of determine HIV1/2 RDT using whole blood in south west Tanzania. PLoS One 2012;7:e39529. https://doi.org/10.1371/journal.pone.0039529

Influenza Activity — United States, September 30–December 1, 2018

Alicia P. Budd, MPH[1]; Anwar Isa Abd Elal[1]; Noreen Alabi, MPH[1]; John Barnes, PhD[1]; Lenee Blanton, MPH[1]; Lynnette Brammer, MPH[1]; Erin Burns, MA[1]; Charisse N. Cummings, MPH[1]; Vivien G. Dugan, PhD[1]; Shikha Garg, MD[1]; Rebecca Garten, PhD[1]; Lisa A. Grohskopf, MD[1]; Larisa Gubareva, PhD[1]; Krista Kniss, MPH[1]; Natalie Kramer[1]; Alissa O'Halloran, MSPH[1]; Wendy Sessions, MPH[1]; Calli Taylor, MPH[1]; David E. Wentworth, PhD[1]; Xiyan Xu, MD[1]; Alicia M. Fry, MD[1]; Jacqueline Katz, PhD[1]; Daniel Jernigan, MD[1]

Influenza activity in the United States was low during October 2018, and, although it increased slowly during November, activity remains low across most of the country.* During the week ending December 1, 2018, the percentage of outpatient visits for influenza-like illness† (ILI) was equal to the national baseline§ (Figure) and was at or slightly above the region-specific baseline in four of the 10 U.S. Department of Health and Human Services regions¶ (Regions 4 and 7–9). The majority of jurisdictions experienced minimal or low ILI activity since September 30; however, two experienced moderate ILI activity, and two experienced high ILI activity** during the week ending December 1. The percentage of deaths attributed to pneumonia and influenza remains below the epidemic threshold,†† and the rate of influenza-associated hospitalizations remains low. Five laboratory-confirmed, influenza-associated pediatric deaths occurring since September 30 have been reported to CDC. During the week ending December 1, the majority of jurisdictions (40 states, the District of Columbia, Puerto Rico, and U.S. Virgin Islands) reported sporadic or local geographic spread of influenza activity, nine states reported regional activity, and one state reported widespread activity.§§

Influenza A(H1N1)pdm09 viruses have been reported most frequently (67% of all viruses and 81% of subtyped influenza A viruses) by U.S. public health laboratories since September 30, 2018 (Table), but A(H3N2) and influenza B viruses also were reported. The majority of influenza viruses characterized during this period were genetically and antigenically similar to the cell-grown reference viruses representing the 2018–19 Northern Hemisphere influenza vaccine viruses.¶¶ No viruses with resistance to oseltamivir, zanamivir, or peramivir have been identified.

The timing of influenza activity often varies; however, influenza activity will increase in coming weeks and is likely to peak during December–February. Annual influenza vaccination is recommended for all persons aged ≥6 months who do not have contraindications (*1*). Multiple influenza vaccines are approved and recommended for use during the 2018–19 season, and vaccination should continue to be offered as long as influenza viruses are circulating and unexpired vaccine is available. For the 2018–19 season, manufacturers projected they would supply the United States with 163–168 million doses

* Data as of December 7, 2018.

† Defined as a fever (temperature ≥100°F [≥37.8°C], oral or equivalent) and cough or sore throat, without a known cause other than influenza.

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

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

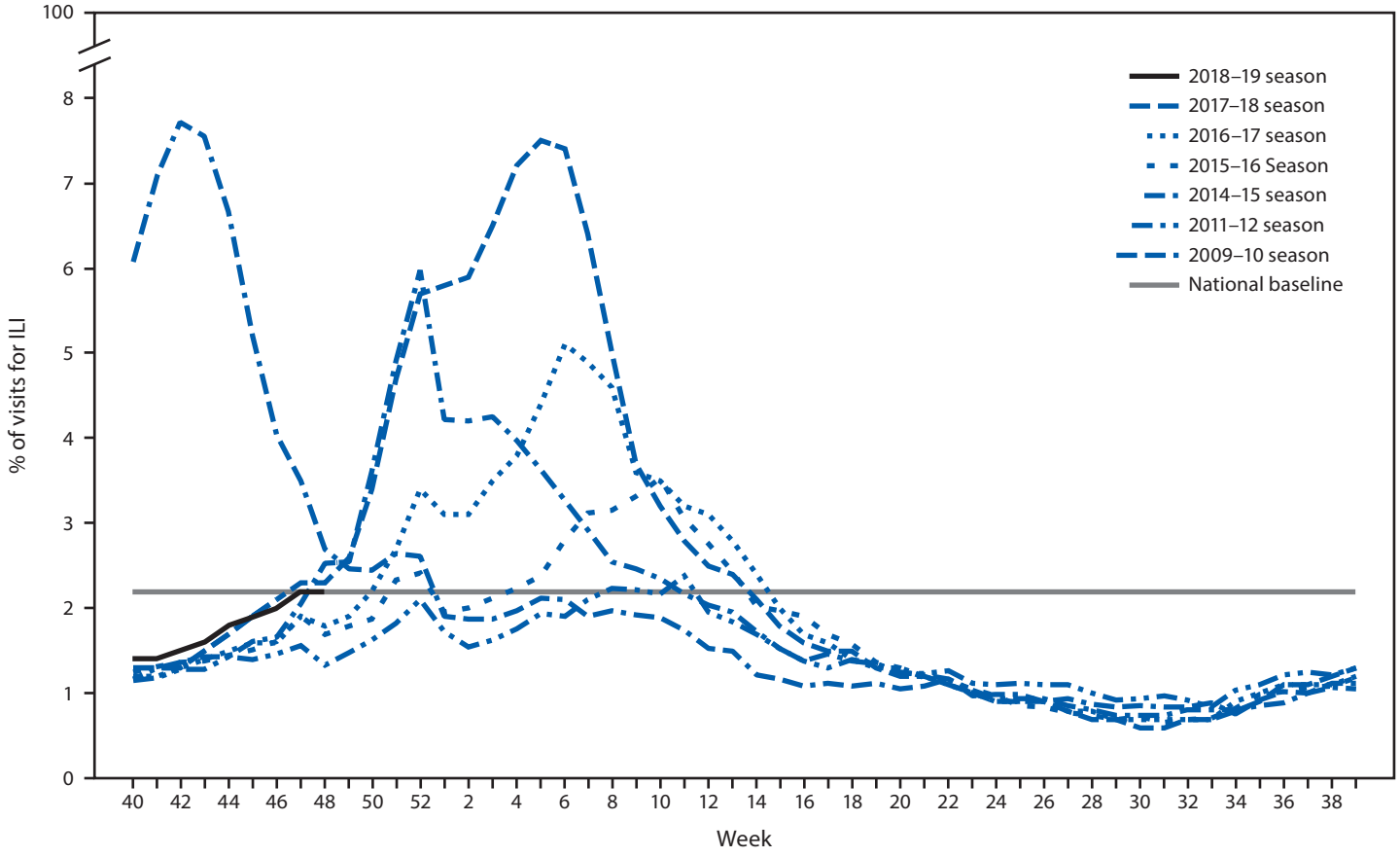
** Activity levels are based on the percentage of outpatient visits in a jurisdiction attributed to ILI and are compared with the average percentage of ILI visits that occur during weeks with little or no influenza virus circulation. Activity levels range from minimal, corresponding to ILI activity from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

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

§§ Levels of activity are 1) no activity; 2) sporadic: isolated laboratory-confirmed influenza cases or a laboratory-confirmed outbreak in one institution, with no increase in activity; 3) local: increased ILI or two or more institutional outbreaks (ILI or laboratory-confirmed influenza) in one region of the state, with recent laboratory evidence of influenza in that region; virus activity no greater than sporadic in other regions; 4) regional: increased ILI activity or institutional outbreaks (ILI or laboratory-confirmed influenza) in two or more outbreaks, but less than half of the regions in the state with recent laboratory evidence of influenza in those regions; and 5) widespread: increased ILI activity or institutional outbreaks (ILI or laboratory-confirmed influenza) in at least half the regions in the state, with recent laboratory evidence of influenza in the state. During the week ending December 1, 2018, nine states (California, Connecticut, Georgia, Kentucky, Louisiana, Nevada, New York, Oregon, and Vermont) reported regional activity, and one state (Massachusetts) reported widespread activity.

¶¶ The recommended Northern Hemisphere 2018–19 trivalent influenza vaccine composition includes an A/Michigan/45/2015 (H1N1)pdm09-like virus, an A/Singapore/INFIMH-16-0019/2016 (H3N2)-like virus, and a B/Colorado/06/2017-like (Victoria lineage virus), with an additional influenza B virus (B/Phuket/3073/2013-like [Yamagata lineage]) virus recommended for quadrivalent vaccines.

FIGURE. Percentage of visits for influenza-like illness (ILI) — U.S. Outpatient Influenza-like Illness Surveillance Network (ILINet), weekly national summary, 2018–2019* and selected previous seasons



* As of December 7, 2018.

TABLE. Influenza positive specimens reported by U.S. public health laboratories — United States, September 30–December 1, 2018*

Influenza virus type/Subtype or lineage	No. of positive specimens (% of total)
Influenza A viruses	
Influenza A(H1N1)pdm09	740 (67)
Influenza A(H3N2)	176 (16)
Influenza A (subtyping not performed)	92 (8)
Influenza B viruses	
Influenza B Yamagata	60 (5)
Influenza B Victoria	21 (2)
Influenza B (lineage not performed)	22 (2)

* As of December 7, 2018.

of influenza vaccine. As of November 30, 2018, approximately 163.8 million doses had been distributed.

Influenza antiviral medications are an important adjunct to vaccination in the treatment and prevention of influenza. There are four recommended influenza antiviral medications for treatment of influenza this season: oral oseltamivir, inhaled zanamivir, intravenous peramivir, and the newly approved oral baloxavir. Treatment with influenza antiviral medications as close to the onset of illness as possible is recommended for patients with confirmed or suspected influenza who have severe, complicated, or progressive illness; who require hospitalization; or who are at high risk for influenza complications. Some antiviral medications (oseltamivir and zanamivir) can be considered for chemoprophylaxis to prevent influenza in certain situations; however, general seasonal or preexposure antiviral chemoprophylaxis is not recommended. Updated recommendations for use of antiviral drugs are available (https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm).

Influenza surveillance reports for the United States are posted online weekly (https://www.cdc.gov/flu/weekly). Additional information regarding influenza viruses, influenza surveillance, influenza vaccines, and influenza antiviral medications is available online (https://www.cdc.gov/flu).

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Corresponding author: Alicia Budd, abudd@cdc.gov, 404-639-3747.

[1]Influenza Division, National Center for Immunization and Respiratory Diseases, CDC.

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

Reference

1. Grohskopf LA, Sokolow LZ, Broder KR, Walter EB, Fry AM, Jernigan DB. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices—United States, 2018–19 influenza season. MMWR Recomm Rep 2018;67(No. RR-3). https://doi.org/10.15585/mmwr.rr6703a1

Notes from the Field

Follow-Up on 11 Infants Born to Women with Evidence of Zika Virus Infection During Pregnancy — Los Angeles County, 2016

Curtis Croker, MPH[1]; Amy Marutani, MPH[1]; Marita Santos[1]; Susan Hathaway, MPH[1]; Bessie Hwang, MD[1]

Microcephaly and other birth defects have been identified among infants born to women with Zika virus infection during pregnancy (*1*–*4*). In accordance with CDC recommendations (*5*), the Los Angeles County (LAC) Department of Public Health implemented surveillance to assess the health of infants born to women with evidence of Zika virus infection during pregnancy at birth and at ages 2, 6, and 12 months. These recommendations included testing all such infants at birth for Zika virus.

During 2016, 11 infants were born to women in LAC who met the Council of State and Territorial Epidemiologists case definition (*6*) for confirmed (four infants) or probable (seven infants) Zika virus infection (Table). Follow-up through age 12 months was completed for nine infants; two infants (numbers 3 and 5) were evaluated at birth, and their parents declined to participate after delivery. All infants appeared healthy and normal at the last available assessment, with normal head circumference measurements. Zika virus immunoglobulin M (IgM) testing of serum was completed on eight infants at birth; all test results were negative. Three of these eight infants were also tested for Zika virus RNA in urine and in serum; all test results were negative.

Although no infant had clinical or laboratory evidence of Zika virus infection, there were instances when laboratory or clinical information raised concern for possible Zika-associated birth defects. Zika virus RNA was isolated from the umbilical cord at the time of delivery of infant number 1 (Table); this infant had a negative Zika IgM test and was found to be healthy and normal at birth and at all follow-up visits. A fetal cranial ultrasound obtained for infant number 4 indicated "poor fetal brain development"; however, the mother's amniotic fluid tested negative for Zika virus RNA, the infant tested negative for Zika virus at birth (serum IgM and RNA and urine RNA), and was healthy and normal at all follow-up visits.

TABLE. Follow-up* of 11 infants born to women with Zika virus infection during pregnancy — Los Angeles County, 2016

Maternal, fetal, perinatal, and infant testing	Infant no.										
	1	2	3	4	5	6	7	8	9	10	11
Mother											
Symptomatic	yes	yes	no	no	no	yes	yes	yes	yes	no	no
Zika IgM and PRNT†	positive	positive	positive	positive	positive	positive	positive	positive	positive	positive	positive
Zika RNA by PCR§	—	—	—	—	—	negative	—	negative	—	—	—
Dengue IgM and PRNT¶	negative	positive	negative	negative	positive	positive	positive	positive	negative	positive	positive
Case status	conf.	prob.	conf.	conf.	prob.	prob.	prob.	prob.	conf.	prob.	prob.
Fetus											
Cranial ultrasound	negative	negative	negative	positive	negative	negative	negative	negative	negative	NT	negative
Amniotic fluid (Zika RNA)	NT	NT	NT	negative	NT	NT	negative	NT	NT	NT	NT
Zika RNA in tissue											
Central placenta	negative	negative	NT	negative	negative	NT	negative	negative	negative	NT	negative
Placental membrane	negative	negative	NT	negative	negative	NT	negative	NT	negative	NT	negative
Umbilical cord membrane	positive	negative	NT	negative	NT	NT	negative	NT	negative	NT	negative
Infant	negative	NT	NT	negative	negative	negative	negative	negative	negative	NT	—
Zika IgM (serum)**	negative	NT	NT	negative	negative	negative	negative	negative	negative	NT	negative
Zika RNA by PCR (urine)**	NT	NT	NT	negative	NT	negative	NT	negative	NT	NT	NT
Zika RNA by PCR (serum)**	NT	NT	NT	negative	NT	negative	NT	negative	NT	NT	NT
Apgar score (5 minutes)	9/10	9/10	9/10	9/10	9/10	9/10	9/10	9/10	9/10	9/10	9/10
HC <3rd percentile for age/sex	No	No	No	No	No	Yes	No	Yes	No	No	No
Admitted to NICU	No	No	No	No	No	No	No	Yes	No	No	No
Cranial ultrasound	negative	NT	NT	NT	negative	negative	NT	negative	NT	NT	NT
Age at follow-up (mos)	0,2,6,12	0,2,6,12	0	0,2,6,12	0	0,2,6,12	0,2,6,12	0,2,6,12	0,2,6,12	0,2,5,††12	0,2,6,12

Abbreviations: conf. = confirmed; HC = head circumference; IgM = immunoglobulin M; NICU = neonatal intensive care unit; NT = not tested; PCR = polymerase chain reaction testing; PRNT = plaque reduction neutralization test; prob. = probable.

* At birth and ages 2, 6, and 12 months.

† Zika-specific IgM antibodies and Zika virus-specific neutralizing antibodies in the same or a later specimen. Neutralizing antibodies detected by PRNT.

§ Two mothers had serum collected within 2 weeks of illness onset for PCR testing (number 6 at day 1 and number 8 at day 12). The remaining nine mothers (four symptomatic and five asymptomatic) had serum collected within 2 weeks of returning from an area with endemic Zika virus transmission for PCR testing.

¶ Dengue-specific IgM antibodies and dengue virus-specific neutralizing antibodies in the same or a later specimen. Neutralizing antibodies detected by PRNT.

** Specimens for serum and urine testing were collected within two days of birth.

†† Infant was evaluated at age 5 months, because the mother was unavailable for visit at age 6 months.

The head circumferences at birth of infant number 6 (30 cm) and infant number 8 (31 cm) were below the third percentile for gestational age and sex. Zika virus test results (serum IgM and RNA and urine RNA) were all negative for infant number 6 at birth; the infant received a diagnosis of microcephaly at age 1 week, but head circumference was normal at ages 2, 6, and 12 months, and a cranial ultrasound at age 3 months was unremarkable. A pediatrician classified the infant as normal at age 12 months. Infant number 8 was born at 38 weeks gestation, weighing 2.2 kg. Zika virus test results (serum IgM and RNA and urine RNA) at birth were negative. The infant received a diagnosis of symmetric growth retardation and was admitted to the neonatal intensive care unit for respiratory distress but was discharged home in good health at age 4 days. A pediatrician found this infant to be healthy and with normal head circumference at age 12 months.

Among 11 infants born to women in LAC with evidence of confirmed or probable Zika virus infection during pregnancy, the nine who participated in follow-up through age 12 months had no apparent adverse health effects at that time. Subtler health effects, or health effects occurring later in life, would not be captured with this surveillance activity. In addition, mothers with Zika virus infection who did not seek medical care, as well as those who chose not to participate in, or did not complete, the surveillance, limited the generalizability of these findings. Ongoing assessment of the health of infants born to women with evidence of Zika virus infection during pregnancy is important to assess the public health impact of Zika virus and to guide interventions.

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Martha E. Garcia, Monica Molina, Elizabeth Traub, Acute Communicable Disease Control Program, Department of Health, Los Angeles County, California; Children's Medical Services Program, County Department of Health, Los Angeles County, California; Maternal Child and Adolescent Health Program, Department of Public Health, Los Angeles County, California; staff members, Public Health Laboratory, Department of Public Health, Los Angeles County, California.

[1]Acute Communicable Disease Control Program, Los Angeles County Department of Public Health, Los Angeles, California.

Corresponding author: Curtis Croker, ccroker@ph.lacounty.gov, 213-240-7941.

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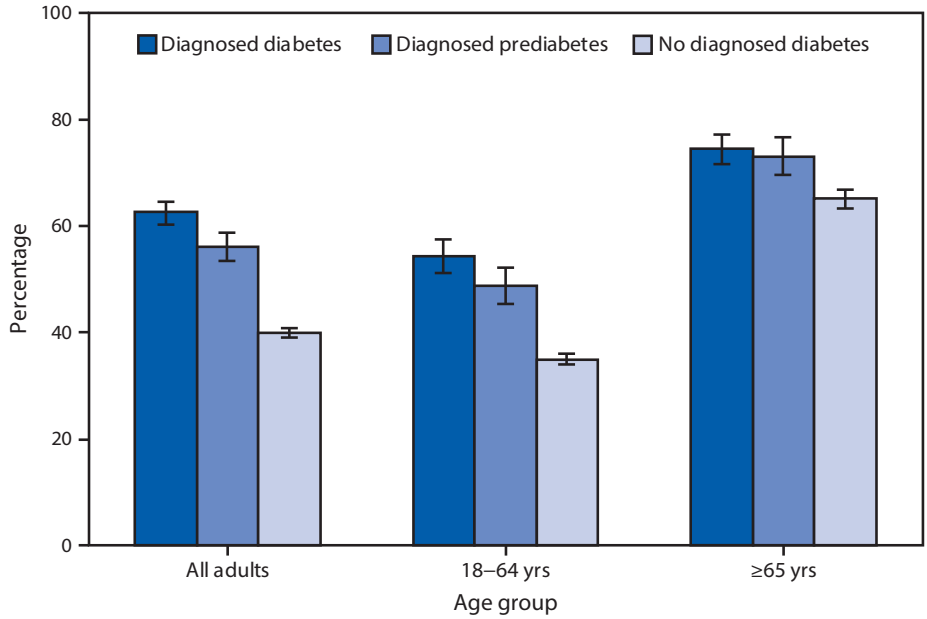
References

1. de Araújo TVB, Rodrigues LC, de Alencar Ximenes RA, et al.; Investigators from the Microcephaly Epidemic Research Group; Brazilian Ministry of Health; Pan American Health Organization; Instituto de Medicina Integral Professor Fernando Figueira; State Health Department of Pernambuco. Association between Zika virus infection and microcephaly in Brazil, January to May, 2016: preliminary report of a case-control study. Lancet Infect Dis 2016;16:1356–63. https://doi.org/10.1016/S1473-3099(16)30318-8
2. Rasmussen SA, Jamieson DJ, Honein MA, Petersen LR. Zika virus and birth defects—reviewing the evidence for causality. N Engl J Med 2016;374:1981–7. https://doi.org/10.1056/NEJMsr1604338
3. 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
4. Cauchemez S, Besnard M, Bompard P, et al. Association between Zika virus and microcephaly in French Polynesia, 2013–15: a retrospective study. Lancet 2016;387:2125–32. https://doi.org/10.1016/S0140-6736(16)00651-6
5. Adebanjo T, Godfred-Cato S, Viens L, et al.; Contributors. 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
6. CDC. Zika virus 2016 case definitions. Atlanta, GA: US Department of Health and Human Services, CDC; 2017. https://wwwn.cdc.gov/nndss/conditions/zika

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage* of Adults Aged ≥18 Years Who Had an Influenza Vaccination† in the Past 12 Months, by Diagnosed Diabetes Status§ and Age Group — National Health Interview Survey,¶ 2017



* With 95% confidence intervals indicated by error bars.
† Based on a response to the question "During the past 12 months, have you had a flu vaccination?" Annual calendar-year estimates of vaccinations differ from seasonal influenza vaccination totals, which reflect vaccinations obtained during the influenza season.
§ Diabetes status was determined by a positive response to the survey question "Have you ever been told by a doctor or health professional that you have diabetes or sugar diabetes?" Women were asked not to include diabetes occurring during pregnancy. Prediabetes status was determined if respondents volunteered that they had borderline diabetes or prediabetes when asked whether they had diabetes or by a positive response to the survey question "Have you ever been told by a doctor or health professional that you have any of the following: prediabetes, impaired fasting glucose, impaired glucose tolerance, borderline diabetes, or high blood sugar?"
¶ Estimates are based on household interviews of a sample of the noninstitutionalized U.S. civilian population aged ≥18 years and are derived from the National Health Interview Survey Sample Adult component.

In 2017, among adults aged ≥18 years, those with a diagnosis of diabetes were more likely to have had an influenza vaccination in the past 12 months than those with a diagnosis of prediabetes (62.5% versus 56.1%); those with no diagnosed diabetes were the least likely to have had an influenza vaccination (40.1%). Among adults aged ≥65 years, influenza vaccination was higher for those with a diagnosis of diabetes (74.5%) or prediabetes (73.0%) than for those with no diagnosed diabetes (65.1%). For adults aged 18–64 years, influenza vaccination rates also were highest for those with diagnosed diabetes (54.3%), followed by those with diagnosed prediabetes (48.7%), and were lowest for those with no diagnosed diabetes (35.0%). Regardless of diabetes status, influenza vaccination rates were higher among those aged ≥65 years than among those aged 18–64 years.

Source: National Health Interview Survey, 2017. https://www.cdc.gov/nchs/nhis.htm.

Reported by: Sarah E. Lessem, PhD, slessem@cdc.gov, 301-458-4209; Robin P. Pendley, DrPH.

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