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Mumps Outbreaks at Four Universities — Indiana, 2016

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From February to April 2016, the Indiana State Department of Health (ISDH) confirmed mumps outbreaks at four universities (three public and one private). All universities were located within 65 miles of Indianapolis; however, epidemiologic links among outbreaks were limited. ISDH and local health departments investigated the outbreaks and initiated control measures at all universities. A protocol describing recommended testing for mumps, testing priorities during the outbreak, and a preauthorization process for submitting specimens to the ISDH Laboratory (ISDHL) was developed and disseminated to providers and public health partners (*1*). Outbreaks at each university were declared over after two incubation periods* elapsed without identified cases; the last outbreak ended September 10, 2016. Among the 281 confirmed and probable cases identified, 216 (76.9%) persons had documentation of presumptive evidence of immunity† (*2*). At some universities, documentation of receipt of 2 doses of measles, mumps, rubella vaccine (MMR), which is a criterion for evidence of immunity, was not available and required substantial personnel time to verify. Implementation of policies for excluding susceptible persons from classes and other group settings was also difficult. The laboratory testing protocol increased the percentage of specimens testing positive and improved case detection. Outbreak-specific laboratory testing guidance on specimen collection for mumps confirmation and standardized vaccination documentation in highly vaccinated settings could aid outbreak management. Evaluation of exclusion policies might also be necessary. In 2018, the Advisory Committee on Immunization Practices (ACIP) published a recommendation that persons previously vaccinated with 2 doses of MMR who are determined by public health authorities to be part of a group at increased risk for infection during a mumps outbreak receive a third dose of MMR (*3*).

Investigation and Results

On January 20, 2016, a student with unknown mumps vaccination history was evaluated at university A's student health center for parotid swelling. The student reported a possible mumps exposure at a university outside Indiana, where a large mumps outbreak was occurring. Mumps immunoglobulin M (IgM) testing was negative, but continuing parotitis motivated the university to request reverse transcription–polymerase chain reaction (RT-PCR) testing at ISDHL 2 days later, and results were positive for mumps. By February 17, 2016, two additional cases at university A were confirmed by RT-PCR. On January 25, a fully vaccinated student was evaluated at university B's student health center with parotid swelling, headache, and fever. Mumps was suspected and reported to ISDH; however, laboratory testing was not conducted. On February 12, three additional mumps cases with epidemiologic links to the index case were confirmed by RT-PCR at

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

* The range of the incubation period for mumps virus is 12–25 days after exposure (https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6204a1.htm). Two incubation periods were calculated using the maximum of the range, totaling 50 days from the final date of exposure of a university-affiliated case.

† Presumptive evidence of immunity to mumps includes any of the following: documentation of age-appropriate vaccination with a live mumps virus–containing vaccine, laboratory evidence of mumps immunity, laboratory confirmation of disease, or birth before 1957.

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university B. On March 11, three cases were confirmed by RT-PCR at university C, with no epidemiologic links among the patients or to any outside case. On April 2, three cases (one confirmed by RT-PCR and two epidemiologically linked) were identified at university D; all patients reported possible exposures to mumps during a spring break trip to Florida 2 weeks before symptom onset. Additional mumps cases occurred in all four universities and in the surrounding community, with the last onset date among university-affiliated cases on July 18, 2016.

Mumps RT-PCR testing was made available through the ISDHL. IgM testing was only offered through commercial laboratories. A protocol was developed to assist providers in ordering the right testing according to the time elapsed from symptom onset, collecting the correct specimens, and obtaining preauthorization for testing at ISHDL. Preauthorization required consultation with an ISDH epidemiologist to ensure patients with suspected mumps met clinical and epidemiologic criteria for testing and to ascertain exposure information to prioritize testing of specimens from patients without epidemiologic links to other cases or suspected cases in new settings. Odds ratios and comparison of proportions chi-squared tests were calculated to evaluate the impact of specimen collection timing and dissemination of testing guidance on specimen positivity. A subset of RT-PCR–positive specimens was sent to CDC's Viral Vaccine Preventable Diseases Branch for genotyping.

A total of 281 mumps cases (237 laboratory confirmed and 44 probable) were identified in all four outbreaks from January to September 2016. Among these cases, 179 (63.7%) occurred in university students or staff members (university-affiliated cases) and 102 (36.3%) in community members not affiliated with any of the universities (community cases) (Figure 1). Epidemiologic links to university cases were only identified in 25.5% of community cases. Signs and symptoms experienced by patients included parotitis (276, 98.2%), fever (109, 38.8%), headache (74, 26.3%), earache (60, 21.4%), jaw pain (16, 5.7%), malaise/body aches (11, 3.9%), and sore throat (10, 3.6%). Complications from mumps were infrequent, with one report of meningitis and five reports of orchitis.

Receipt of 2 doses of MMR was documented for 152 (84.9%) of 179 university-affiliated cases and 53 (52.0%) of 102 community cases; 11 (3.9%) of the 281 cases had documentation of a positive immunoglobulin G titer. Twelve cases (4.3%) had documentation of ≥3 doses of MMR administered >4 weeks before parotid swelling onset. In six cases in which complications occurred, the persons had each received 2 doses of MMR. Seven vaccination clinics were held across three schools, and 5,273 doses of MMR were administered, most (3,106; 59%) at highly attended clinics at university B. Based on high 2-dose MMR coverage at each university, many of these doses likely were third doses.

ISDHL tested specimens from 490 suspected cases for confirmation by RT-PCR, 209 (42.6%) of which were positive. Among 407 cases of suspected mumps for which RT-PCR results and onset dates were available, 53.1% (146/275) of specimens collected within 2 days of parotitis onset were positive; this

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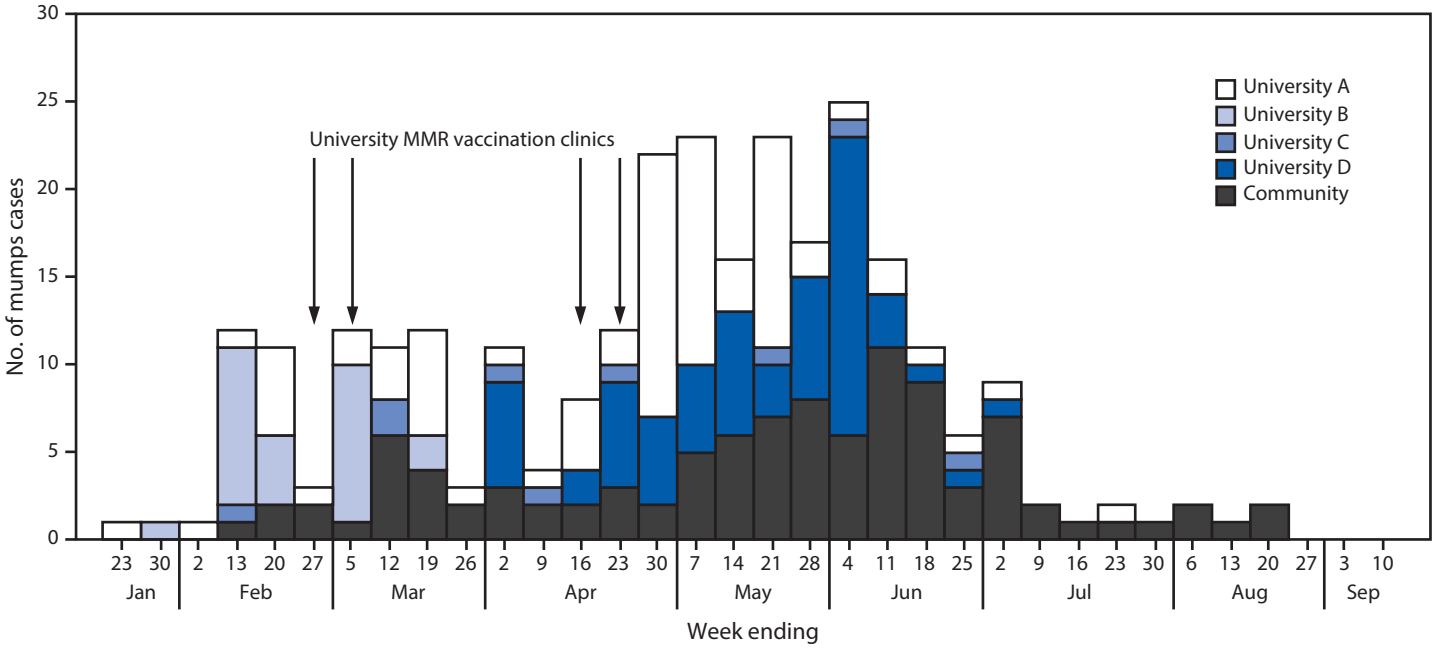
FIGURE 1. Number of confirmed (N = 237) and probable (N = 44) mumps cases associated with outbreaks at four universities, by week of onset and dates of MMR vaccination clinics — Indiana, January–September 2016



Abbreviation: MMR = measles, mumps, and rubella vaccine.

decreased slightly to 47.7% (63/132) for specimens collected ≥3 days after parotitis onset, and the change was not statistically significant (Table). Among 63 cases for which IgM results and onset dates were available, 34.3% (11/32) of specimens collected within 2 days of parotitis onset were positive; the rate of positivity increased to 61.3% (19/31) for specimens collected ≥3 days after parotitis onset (p<0.05). Among 18 cases for which specimens were collected within 5 days of parotitis onset and a RT-PCR test was positive, six had results that were IgM positive. Persons in 16 of these cases had received 2 MMR doses, and those in two cases had received a single dose. Weekly percent positivity of specimens submitted to ISDHL increased significantly from an average of 25.8% in the weeks before dissemination of the laboratory testing protocol to an average of 37.8% (p = 0.005) in the weeks after dissemination (Figure 2). CDC provided genotyping for 142 specimens; 140 (98.6%) were type G (the most common genotype circulating in the United States), and two were unable to be genotyped.

TABLE. Positivity of patient specimens for mumps, by testing method and time from symptom onset to specimen collection — Indiana, 2016

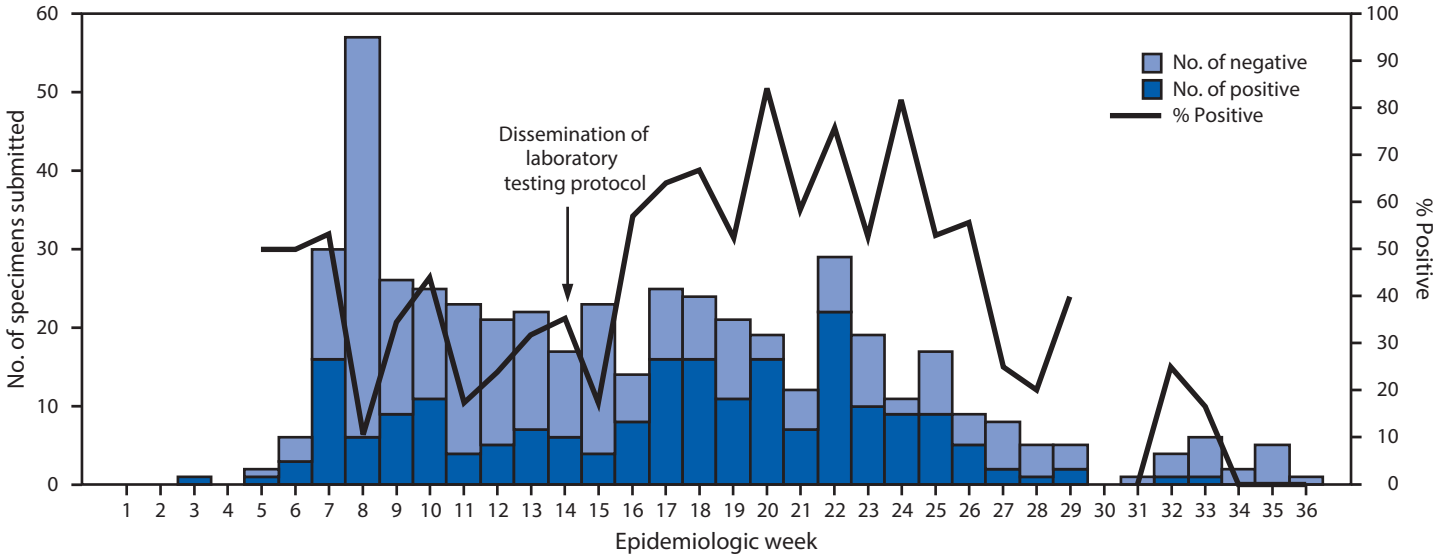
Time from onset to specimen collection	Result no. (%)		OR (95% CI)†
	Positive	Negative/ Indeterminate*	
RT-PCR			
0–2 days	146 (53.1)	129 (46.9)	0.81 (0.53–1.22)
≥3 days	63 (47.7)	69 (52.3)	
IgM			
0–2 days	11 (34.3)	21 (65.6)	3.02 (1.08–8.44)§
≥3 days	19 (61.3)	12 (38.7)	

Abbreviations: CI = confidence interval; IgM = immunoglobulin M; OR = odds ratio; RT-PCR = reverse transcription–polymerase chain reaction.
* RT-PCR values were considered indeterminate if replicates were discordant on two separate runs. Three specimens were ruled indeterminate.
† ORs and 95% CIs were calculated for test results relative to time from symptom onset to specimen collection, with specimen collection ≥3 days after symptom onset as the reference.
§ Significant at p<0.05 level.

Public Health Response

Cases were classified according to the Council of State and Territorial Epidemiologists case definition for mumps (*4*), and a mumps outbreak was defined as three or more cases linked by place and time. Cases were considered infectious from 2 days before until 5 days after onset of parotitis. Control measures included isolation recommendations for persons with suspected infections, dissemination of educational materials on case finding, verification of vaccination status for persons and their close contacts in all cases, and MMR vaccination clinics at three of the four universities. Because recent studies on third-dose vaccine effectiveness were limited and had varying results (*5*,*6*), and because there was no formal ACIP recommendation regarding use of a third dose of MMR for persons affected in an outbreak at the time, no university specifically recommended a third dose of MMR to students. However, in addition to recommending to students that they attend clinics for catch-up doses of MMR, students were advised that they

FIGURE 2. Number and percentage of specimens testing positive for mumps by reverse transcription–polymerase chain reaction, by week — Indiana State Department of Health Laboratories, 2016



could receive vaccine if previous MMR vaccination documentation was unavailable or if an additional dose was desired.

Current immunization policies in Indiana require universities to collect immunization information from matriculating students at certain institutions, but guidance on record format and verification is limited (*7*). Each university had different documentation requirements for immunization records. Only two universities (B and D) required documentation of dose and month/day/year administration date, and only university B required provider verification of records.

Although isolation through 5 days after parotid swelling onset was recommended for all patients and exclusion from classes, work, or public gatherings was recommended for contacts without presumptive evidence of immunity, only university B was able to successfully ensure both isolation and exclusion by requiring either off-campus isolation or exclusion at home and providing alternative living arrangements for students who could not isolate or self-exclude off-campus Because most cases were occurring in fully vaccinated persons for whom no exclusion would be recommended by susceptibility-based exclusion policies, the benefit of enforcement was questioned, and it was difficult to garner buy-in to expend already limited personnel resources on enforcing these policies. Affected persons and contacts at universities A and C would have needed to acquire appropriate documentation of immunization from family or providers. Because of time-related difficulties in doing this, only close contacts were required to provide presumptive evidence of immunity for determining if exclusion was needed. At all universities, students without presumptive evidence of immunity were offered the option of receiving a dose of MMR and returning to campus.

Discussion

Mumps is an acute viral illness characterized by parotid gland swelling that can result in more serious complications such as orchitis and encephalitis. A substantial increase in the number of mumps outbreaks and outbreak-associated cases has occurred in the United States since late 2014 (*8*). Four large university mumps outbreaks with considerable community spread occurred in Indiana in 2016, contributing to the 6,366 mumps cases reported nationwide in 2016, the highest number of cases in a decade. In Indiana, epidemiologic links to the university outbreaks or to other cases could not be identified for many community cases. This might indicate gaps in current case finding and linkage methods, asymptomatic transmission, or underreporting of mumps cases during nonoutbreak periods.

Laboratory testing is an important component of confirming mumps cases and outbreaks. Availability of a detailed outbreak-specific testing protocol possibly improved the overall positivity rate of specimens tested at ISDHL during the course of these outbreaks. Detection of mumps virus by RT-PCR was higher among specimens collected ≤2 days from parotid swelling onset, supporting previous findings of higher rates of positivity within 3 days of parotitis onset (*6,9,10*). Results of serologic testing support concerns regarding poor sensitivity of routine diagnostic commercial IgM testing in vaccinated persons in low-incidence settings (*10*).

The occurrence of these outbreaks highlights the need for immunization documentation requirements at institutions of higher education to be standardized and consistent with ACIP and state recommendations for documentation of presumptive evidence of immunity (*2*). As a result of this investigation, both universities A and C implemented requirements for collecting

Summary

What is already known about this topic?

Recently, mumps outbreaks among vaccinated persons in university settings have increased.

What is added by this report?

In 2016, large mumps outbreaks occurred at four Indiana universities. At some universities documentation of receipt of 2 doses of measles, mumps, and rubella vaccine (MMR) was not available and required substantial personnel time to verify. Implementation of policies for excluding susceptible persons from classes and other group settings was also difficult.

What are the implications for public health practice?

Outbreak-specific laboratory testing guidance to partners, standardized vaccination documentation, and evaluation of exclusion policies could aid outbreak management. The Advisory Committee on Immunization Practices currently recommends a third dose of MMR for persons at increased risk during a mumps outbreak.

provider-verified month/day/year immunization records for all matriculating full-time students beginning in fall 2017. Although policies on exposed contact exclusion that are dependent on vaccination status can ease some difficulties in outbreak management by quickly identifying persons without evidence of immunity, these policies may be insufficient for outbreak control at institutions of higher education with high 2-dose MMR coverage (i.e., most persons and contacts are fully vaccinated). A recent ACIP recommendation states that persons previously vaccinated with 2 doses of MMR who are determined by health departments to belong to groups or populations at increased risk during a mumps outbreak be given a third dose of MMR to improve individual protection (*3*). Conducting vaccination clinics to provide these doses could allow multiple individuals to be vaccinated at once at low or no cost to students and staff members and provide an opportunity for health department personnel to educate individuals in the outbreak setting on signs and symptoms of mumps and ways to avoid infection. If outbreak management in populations with high 2-dose coverage continues to be a challenge for public health authorities despite the recommendation for use of a third dose of mumps-containing vaccine during outbreaks, reevaluation of current recommended exclusion measures could be warranted (*1*,*3*). Given the challenges in managing and controlling outbreaks in university settings, documenting and maintaining high 2-dose coverage of MMR in this setting is especially important.

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Conflict of Interest

No conflicts of interest were reported.

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Application of a Tool to Identify Undiagnosed Hypertension — United States, 2016

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Approximately 11 million U.S. adults with a usual source of health care have undiagnosed hypertension, placing them at increased risk for cardiovascular events (*1*–*3*). Using data from the National Health and Nutrition Examination Survey (NHANES), CDC developed the Million Hearts Hypertension Prevalence Estimator Tool, which allows health care delivery organizations (organizations) to predict their patient population's hypertension prevalence based on demographic and comorbidity characteristics (*2*). Organizations can use this tool to compare predicted prevalence with their observed prevalence to identify potential underdiagnosed hypertension. This study applied the tool using medical billing data alone and in combination with clinical data collected among 8.92 million patients from 25 organizations participating in American Medical Group Association (AMGA) national learning collaborative* to calculate and compare predicted and observed adult hypertension prevalence. Using billing data alone revealed that up to one in eight cases of hypertension might be undiagnosed. However, estimates varied when clinical data were included to identify comorbidities used to predict hypertension prevalence or describe observed hypertension prevalence. These findings demonstrate the tool's potential use in improving identification of hypertension and the likely importance of using both billing and clinical data to establish hypertension and comorbidity prevalence estimates and to support clinical quality improvement efforts.

This study used medical billing† and electronic health record (EHR) clinical data collected among 8.92 million patients, aged 18–85 years, who had ≥1 ambulatory office visit for evaluation and management in 2016 within one of 25 AMGA-member organizations. These organizations use the Optum One population health analytic tool§ and pool billing and clinical data as part of a national learning collaborative.

Observed hypertension prevalence was defined using three case definitions that use increasing amounts of billing and clinical data collected during the observation year. The first hypertension case definition included patients with at least one diagnosis code for hypertension¶ on a billing claim. Patients without a diagnosis code on a billing claim, but who had a diagnosis code for "hypertension" on their EHR problem list** met the hypertension criteria for the second case definition. Additional patients were added who did not meet criteria for the first two case definitions, but who had elevated in-office blood pressure (BP) readings, defined as a single reading ≥160/100 mm Hg or two readings on different days ≥140/90 mm Hg. The first and second case definitions reflect documented diagnoses of hypertension. The BP criteria in the third case definition align with national recommendations for diagnosing hypertension††; however, patients who meet this definition alone are not considered to have a hypertension diagnosis and might not have hypertension upon further assessment.

Predicted hypertension prevalence was determined by applying the Hypertension Prevalence Estimator Tool to the organizations' data; development and validation of the tool are described elsewhere (*2*). The tool requires input of the patient population's demographic characteristics (i.e., distribution by sex, race/ethnicity, and age group) with the option§§ of

* All AMGA Analytics for Improvement (A4i) participants use the Optum One population health and risk analytics platform. Optum collects longitudinal data on approximately 95 million patients and 175 million claims. These data represent a subset of this larger database. The 25 organizations included in this analysis are AMGA members that vary in size (70–3,000 FTE physicians) and serve in total approximately 25 million patients; 52% are integrated delivery systems. Among the 8.92 million adult patients aged 18–85 years assessed in this study, 51% had commercial health insurance, 36% had some form of Medicare coverage, 5% had Medicaid coverage, 0.9% were uninsured, and 7% had some other form of health insurance or were missing information (<1%). Additional information about the learning collaborative is available at http://www.amga.org/wcm/A4I/wcm/AboutAMGA/CF/Anceta/A4I/index_a4i.aspx?hkey=9429bbc5-72d9-4eb7-9cfa-f80d8bc40cc2.

† Billing data consist of outbound administrative claims, collected longitudinally.

§ https://www.optum.com/solutions/prod-nav/performance-analytics.html.

¶ *International Classification of Diseases* (ICD), *Tenth Revision, Clinical Modification* (ICD-10-CM) code of I10, I11.X, I12.X, or I13.X (reflects ICD, *Ninth Revision, Clinical Modification* (ICD-9-CM) codes of 401.X, 402.X, 403.X, or 404.X).

** Same codes as designated for claims to identify hypertension or the three comorbidities. Organizations typically use ICD-10-CM codes in their problem list documentation, including all 25 AMGA member organizations. Some organizations might use other nomenclature (e.g. SNOMED-CT) or still rely on text-based fields.

†† The blood pressure thresholds used align with those recommended in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7) (https://www.ncbi.nlm.nih.gov/books/NBK9630/), and the ≥140/90 mm Hg threshold to identify hypertension is used by Million Hearts for national hypertension surveillance and in the development of the Hypertension Prevalence Estimator Tool.

§§ Organizations that do not have access to accurate comorbidity data are still able to use the Million Hearts Hypertension Prevalence Estimator Tool (https://nccd.cdc.gov/MillionHearts/Estimator/). If no accurate comorbidity data are available, the comorbidity profile of the organization's patient population is estimated using NHANES data that are based on the organization's patient population's age, gender, and race/ethnicity characteristics. If limited accurate comorbidity data are available, organizations can use their own data for some conditions (e.g., diabetes and chronic kidney disease), but allow the tool to provide estimates for the other conditions (e.g., obesity) using NHANES data that are based on their patient population's age, gender, and race/ethnicity characteristics.

providing the prevalence of three comorbidities within the patient population that aid in predicting hypertension prevalence (i.e., the presence of none, one, or two or more of the following conditions: obesity, diabetes, and chronic kidney disease). Similar to identifying hypertension, comorbidities were identified during the observation year using 1) medical billing claims only[¶¶]; 2) problem list diagnosis codes; or 3) other clinical data.[***]

The observed hypertension prevalence and the 95% confidence intervals of the predicted hypertension prevalence, calculated with and without use of organization-specific information on comorbidity prevalence, were compared overall and by organization using each case definition.

A total of 8.92 million patient records were included, with patient populations ranging from 50,000 to 1.02 million across the 25 organizations. Nearly 40% of patients were aged 45–64 years; 57% were female, and 74% were non-Hispanic white (range = 47%–90%) (Table 1). Overall, 5.9% of patients with ≥1 office visit during 2016 had no BP reading recorded (range = 0.3%–15.9%) (Supplementary Figure, https://stacks.cdc.gov/view/cdc/54153).

Comorbidity prevalence and predicted and observed hypertension prevalence varied overall and by organization depending on the evidence used (Table 2) (Table 3) (Supplementary Figure, https://stacks.cdc.gov/view/cdc/54153). Overall obesity prevalence increased from 10.7% using billing data alone to 45.0% using all three data sources (Table 2). Use of billing data alone indicated that 4.4% of patients had 2–3 comorbidities; the addition of problem list data alone and in combination with other clinical data increased detection of 2–3 comorbidities to 5.7% and 14.3%, respectively. Prevalence of 2–3 comorbidities ranged from 8.3% to 18.1% across organizations using all three data sources.

With the addition of each data source to identify hypertension and the comorbidities, overall observed hypertension prevalence increased from 29.1% to 30.0% to 36.0% (range = 2.60–3.21 million patients), and overall predicted hypertension prevalence increased from 33.2% to 33.9% to 39.5% (range = 2.96–3.52 million patients), respectively (Table 2) (Table 3) (Supplementary Figure, https://stacks.cdc.gov/view/cdc/54153). Differences between the estimates for observed and predicted hypertension prevalence ranged from 3.5 to 4.1 percentage points, representing a range of 312,000 to 366,000, or one in eight to one in 11 patients who potentially have undiagnosed hypertension. Across the 25 organizations, observed hypertension prevalence ranged from 24.2% to 46.1%, predicted hypertension prevalence ranged from 35.5% to 47.6%, and the difference between the two ranged from 1.0 to 13.8 percentage points, with predicted prevalence always higher than observed prevalence.

Removing organization-specific comorbidity data from the information used to predict hypertension prevalence and relying on the NHANES-based comorbidity estimates provided in the Estimator Tool resulted in an overall predicted hypertension prevalence of 38.5% and increased the difference between observed and predicted prevalence from 2.5 to 9.4 percentage points, depending on the data sources used to identify hypertension (Table 2).

TABLE 1. Patient characteristics of 25 health care delivery organizations participating in application of Million Hearts Hypertension Prevalence Estimator Tool — United States, 2016

Characteristic	Overall population	Range
No. of patients included in analyses,* millions	8.92	0.05–1.02
Age group (yrs), %		
18–44	34.2	25.6–39.4
45–64	39.5	36.1–42.6
65–74	16.9	13.8–22.9
75–85	9.4	7.4–14.7
Sex, %		
Women	57.3	52.6–61.1
Men	42.7	38.9–47.4
Race/Ethnicity %		
White, non-Hispanic	73.9	46.9–90.3
Black, non-Hispanic	7.1	0.4–20.2
Hispanic	3.4	0.7–9.4
Other	10.5	1.7–34.9
Missing	5.1	0.4–15.0

* Aged 18–85 years with a least one ambulatory care visit during 2016.

Discussion

Application of the Million Hearts Hypertension Prevalence Estimator Tool using billing and clinical data collected from approximately 9 million U.S. adult patients within multispecialty medical groups and integrated systems across the country revealed that up to one in eight patients with hypertension might not have received a diagnosis. Across the 25 organizations assessed, the difference between predicted and observed hypertension prevalence was as high as 13.8 percentage points, and the percentage of patients with an outpatient visit who did not have a documented BP measurement during the observation period was as high as 15.9%. The identification of lower than anticipated hypertension prevalence or BP screening rates allows organizations to evaluate and refine systems of care to

[¶¶] ICD-10-CM codes of E66.09, E66.1, E66.8, E66.9, E66.01, E66.2, Z68.3X, Z68.4X, Z68.54, or R93.9 for obesity (reflects ICD-9-CM codes of 278.00, 278.01, 278.03, V85.3X, V85.4X, V85.54, or 793.91); ICD-10-CM codes of E10.X or E11.X for diabetes (ICD-9-CM: 250.X); and ICD-10-CM codes of I12.X, I13.X, or N18.X for chronic kidney disease (ICD-9-CM: 403.X, 404.X, or 585.X).

[***] Body mass index ≥30 kg/m2 for obesity; hemoglobin A1c of ≥6.5%, fasting plasma glucose of ≥126 mg/dL, plasma glucose conducted on the same day as a lipid panel of ≥126 mg/dL (assumes fasting), or a glucose tolerance test of ≥200 mg/dL for diabetes; and an estimated glomerular filtration rate of <60 mL/min per 1.73 m2 for chronic kidney disease.

TABLE 2. Variation in observed and predicted hypertension prevalence with increasing levels of medical billing and clinical data used, overall and across health care delivery organizations (HDOs) (n = 8.92 million) participating in application of Million Hearts Hypertension Prevalence Estimator Tool — United States, 2016

	Overall total			Range across HDOs*		
Prevalence	Claims	Claims or problem list	Claims with problem list and clinical criteria	Claims	Claims or problem list	Claims with problem list and clinical criteria
Comorbidity prevalence, %						
Obesity	10.7	13.1	45.0	4.6 to 34.7	7.2 to 35.2	29.6 to 51.4
Diabetes	11.3	12.9	16.4	6.0 to 13.8	6.8 to 17.5	9.2 to 21.8
Chronic kidney disease	3.4	4.4	7.4	1.2 to 5.2	1.4 to 6.3	3.6 to 9.3
Combined prevalence of the above conditions						
0 conditions	79.4	76.2	48.3	59.6 to 86.5	58.2 to 84.4	41.5 to 63.7
1 condition	16.3	18.1	37.5	11.2 to 31.5	12.8 to 32.5	27.4 to 42.4
2–3 conditions	4.4	5.7	14.3	2.3 to 8.9	2.8 to 9.3	8.3 to 18.1
Hypertension prevalence						
Observed, %	29.1	30.0	36.0	17.1 to 35.4	18.3 to 37.8	24.2 to 46.1
No. (millions)	2.60	2.68	3.21	0.02 to 0.05	0.02 to 0.06	0.03 to 0.07
Predicted† using organization-specific comorbidity data, % (95% CI)	33.2 (33.2–33.3)	33.9 (33.9–34.0)	39.5 (39.5–39.5)	30.2 to 40.1	30.9 to 41.4	35.5 to 47.6
Percentage point difference,§ (95% CI)	4.1 (4.1–4.2)	3.9 (3.9–4.0)	3.5 (3.5–3.6)	0.0 to 14.7	0.4 to 13.9	1.0 to 13.8
No. of additional patients identified	366,000	348,000	312,000	24 to 65,000	731 to 67,100	267 to 57,700
Predicted† not using organization-specific comorbidity data,¶ % (95% CI)	38.5 (38.5–38.6)	38.5 (38.5–38.6)	38.5 (38.5–38.6)	35.4 to 46.2	35.4 to 46.2	35.4 to 46.2
Percentage point difference,§ (95% CI)	9.4 (9.4–9.5)	8.5 (8.5–8.6)	2.5 (2.5–2.6)	-21.1 to 4.0	-19.9 to 2.8	-14.0 to 2.8
No. of additional patients identified	838,000	758,000	223,000	2,910 to 119,000	1,770 to 114,000	130 to 57,800

Abbreviation: CI = confidence interval.

* Range of values calculated across the 25 health care delivery organizations participating in the American Medical Group Association's national learning collaborative; 95% CIs are not provided for the predicted hypertension prevalence estimates.

† Based on Million Hearts Hypertension Prevalence Estimator Tool.

§ Compared with observed prevalence. Observed prevalence was always less than predicted prevalence.

¶ The comorbidity profile of the health care delivery organization's patient population is estimated using National Health and Nutrition Examination Survey databased on the organization's patient population's age, gender, and race/ethnicity characteristics.

improve the diagnosis and management of hypertension (*3*). This could include, as an initial step, reassessing patients who had a single in-office BP ≥160/100 mm Hg or two readings on different days ≥140/90 mm Hg to establish, if warranted, a documented diagnosis and to ensure provision of appropriate hypertension treatment. This is a conservative approach, and recent guidelines (*4*) might suggest even lower thresholds. One report found that approximately one in three patients who met the BP criteria alone and were able to be reassessed received a diagnosis of hypertension (*5*).

This report reinforces the utility of using multiple data sources to identify patients in potential need of chronic disease management and to estimate the prevalence of chronic conditions. In addition, these findings indicate how the identification of patients for inclusion in clinical registries or quality improvement measure reporting††† depend on the data types (i.e., medical billing data alone or in combination with clinical data) used to detect the targeted conditions. Higher comorbidity and observed hypertension prevalence were found when clinical data were included with billing data for case ascertainment, particularly for obesity. Billing data are generated to initiate payment for services rendered, and some conditions might not be prioritized for treatment or billing because of patients' competing health needs or limited reimbursement. Therefore, use of billing data alone to describe the prevalence of hypertension and other chronic conditions or to predict hypertension prevalence likely underrepresents the burden (*6*–*8*). If organizations are unable to use all three data sources to describe their comorbidity prevalence (in particular obesity prevalence), they might consider using the nonorganization-specific comorbidity estimates provided in the Hypertension Prevalence Estimator Tool to predict their hypertension prevalence. When the nonorganization specific comorbidity estimates were applied, the predicted hypertension prevalence typically was closest to the observed hypertension prevalence determined using all available billing and clinical data.

The findings in this report are subject to at least four limitations. First, the billing and clinical definitions used align with national standards and guidelines, but variation might exist in how the conditions are diagnosed and documented across

††† For example, inclusion in hypertension registries or in the National Quality Forum's Controlling High Blood Pressure Measure (NQF 0018).

TABLE 3. Observed and predicted prevalence of hypertension among the American Medical Group Association's member health care delivery organizations — United States, 2016

Organization	Medical claims only*		Medical claims plus problem list*		Medical claims plus problem list plus clinical data*		Based on national comorbidity estimates†
	Observed§	Predicted¶	Observed§	Predicted¶	Observed§	Predicted¶	Predicted¶
1	35.4%	40.1%	37.8%	41.4%	46.1%	47.6%	46.2%
2	34.9%	38.5%	35.5%	38.9%	44.3%	44.6%	43.9%
3	34.6%	39.0%	37.0%	39.3%	40.4%	42.4%	40.7%
4	34.2%	34.2%	35.4%	35.0%	41.0%	40.0%	38.2%
5	31.9%	32.4%	32.3%	33.3%	39.3%	40.4%	37.9%
6	31.8%	33.6%	32.6%	34.3%	40.7%	40.1%	38.0%
7	31.4%	34.2%	31.4%	35.0%	38.5%	41.1%	40.8%
8	30.5%	31.5%	30.7%	32.2%	34.9%	36.8%	36.1%
9	30.1%	35.9%	31.5%	36.7%	37.5%	42.2%	40.6%
10	29.6%	35.0%	30.9%	35.3%	38.5%	39.8%	39.1%
11	28.9%	31.1%	29.9%	31.7%	36.8%	38.6%	36.3%
12	28.6%	32.5%	29.2%	33.3%	33.8%	38.4%	37.9%
13	28.5%	32.6%	29.8%	33.5%	34.7%	39.3%	38.1%
14	28.4%	32.3%	29.9%	32.9%	39.3%	40.0%	38.4%
15	28.4%	34.0%	32.9%	34.9%	37.3%	40.8%	39.5%
16	28.3%	30.9%	29.7%	31.7%	33.6%	37.1%	35.4%
17	28.3%	35.4%	28.8%	36.2%	35.0%	41.3%	41.3%
28	28.0%	35.3%	28.9%	35.9%	33.2%	40.0%	41.4%
19	27.5%	30.2%	27.7%	30.9%	33.8%	37.0%	35.9%
20	27.5%	32.9%	28.6%	33.7%	33.5%	39.3%	38.0%
21	24.7%	34.0%	27.2%	34.4%	35.7%	40.7%	39.9%
22	24.5%	32.4%	25.7%	32.7%	30.7%	37.1%	37.5%
23	24.2%	33.1%	24.3%	33.7%	31.4%	39.3%	38.4%
24	22.2%	31.4%	22.7%	31.8%	26.5%	35.5%	37.8%
25	17.1%	31.8%	18.3%	32.2%	24.2%	38.0%	38.2%

* Observed prevalence of the three comorbidities within the organizations' patient population is used to predict hypertension prevalence. Comorbidities were identified based on: 1) "medical claims only": at least one diagnosis code for the condition on an outbound billing claim (*International Classification of Disease, Tenth Revision, Clinical Modification* [ICD-10-CM] code of E66.09, E66.1, E66.8, E66.9, E66.01, E66.2, Z68.3X, Z68.4X, Z68.54, or R93.9 for obesity; E10.X or E11.X for diabetes; and I12.X, I13.X, or N18.X for chronic kidney disease); 2) "medical claims plus problem list": adds additional patients who had a diagnosis code for obesity, diabetes, or chronic kidney disease on their electronic health record (EHR) problem list (same codes as designated for claims); and 3) "medical claims plus problem list & clinical data": adds additional patients who had a body mass index ≥30 kg/m2 for obesity; hemoglobin A1c of ≥6.5%, plasma glucose of ≥126 mg/dL, fasting plasma glucose of ≥126 mg/dL, or a glucose tolerance test of ≥200 mg/dL for diabetes; and an estimated glomerular filtration rate of <60 mL/min per 1.73 m2 for chronic kidney disease.

† Predicted prevalence of the three comorbidities within the organizations' patient population is used to predict hypertension prevalence. Predicted comorbidity prevalence is estimated based on the organization population prevalence of age, gender, and race/ethnicity characteristics and use of National Health and Nutrition Examination Survey data. Using this method does not affect the observed hypertension prevalence; therefore, no observed prevalence values are provided.

§ Defined using: 1) "medical claims only": at least one diagnosis code for hypertension on an outbound billing claim (ICD-10-CM code of I10, I11.X, I12.X, or I13.X); 2) "medical claims plus problem list": adds additional patients who had a diagnosis code for "hypertension" on their EHR problem list (same codes as designated for claims); and 3) "medical claims plus problem list & clinical data": adds additional patients who had elevated in-office blood pressure readings, defined as a single reading ≥160/100 mm Hg or two readings on different days ≥140/90 mm Hg.

¶ Determined by applying the Million Hearts Hypertension Prevalence Estimator Tool to the organizations' data. The predicted hypertension prevalence is estimated based on the distribution of patients by age, gender, race/ethnicity, and predicted or diagnosed comorbidity prevalence (presence of 0, 1, or 2–3 of the following conditions: obesity, diabetes and chronic kidney disease).

organizations. Furthermore, the data were not assessed to ensure appropriate coding or documentation. Both of these factors could potentially lead to variation in disease prevalence estimates, including the degree of prevalence underestimation, and indicate more differences in clinical practice, documentation, and billing than in the actual health status of the population. Second, organizations participating in this national learning collaborative are considered to be high performing; therefore, the differences between predicted and observed hypertension prevalence reported in this study are likely to underestimate quality gaps in other organizations. Third, it was not possible to determine the actual observed hypertension prevalence of this population. To do so would involve further assessment of those patients who either met the clinical definition alone or did not have a BP assessment during the observation period. Finally, new evidence suggests that compared with standardized BP observation, BP readings taken in a clinical setting overestimate systolic BP by an average of 6.4 to 11.8 mm Hg depending on the study setting and independent of "white coat syndrome" or masked hypertension (*9*,*10*)

Improving management of hypertension in health care organizations is multifaceted, requiring interventions across

Summary

What is already known about this topic?

Approximately 11 million U.S. adults with a usual health care source have undiagnosed hypertension. Identification, diagnosis, and treatment of hypertension are needed to decrease the risk for an adverse cardiovascular event.

What is added by this report?

Using the Million Hearts Hypertension Prevalence Estimator Tool to calculate and compare observed and predicted prevalences of hypertension among approximately 9 million U.S. patients revealed that nearly one in eight patients with hypertension might not have received a diagnosis.

What are the implications for public health practice?

The Hypertension Prevalence Estimator Tool might improve hypertension identification within health care delivery organizations; using both billing and clinical data to establish hypertension and comorbidity prevalence estimates are important to support clinical quality improvement efforts.

multiple systems and within diverse disciplines, including those reviewed in the Guide to Community Preventive Services[§§§] and summarized by the Million Hearts initiative.[¶¶¶] The tool assessed in this report can be used to support the evaluation of the effectiveness of these organizations in identifying hypertension. With recently released updated hypertension guidelines (*4*) that increased the number of persons classified as having hypertension, there is an urgent need for careful and thorough identification and treatment of people with hypertension.

[§§§] https://www.thecommunityguide.org/content/task-force-findings-cardiovascular-disease.

[¶¶¶] https://millionhearts.hhs.gov/tools-protocols/hiding-plain-sight/toolkit.html.

Conflict of Interest

No conflicts of interest were reported.

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Characteristics of Patients for Whom Benznidazole Was Released Through the CDC-Sponsored Investigational New Drug Program for Treatment of Chagas Disease — United States, 2011–2018

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Chagas disease (also known as American trypanosomiasis) is caused by the protozoan parasite *Trypanosoma cruzi* (*1*,*2*). Vectorborne transmission via skin or mucosal contact with the feces of infected triatomine bugs mainly occurs in rural areas of Latin America but has been reported in the southern United States (*3*). The parasite also is transmissible congenitally and via blood transfusion, organ transplantation, and accidental laboratory exposures. The two drugs used for treating Chagas disease are benznidazole and nifurtimox (*1*,*2*), which have been used in Latin America since the 1970s and 1960s, respectively. In the absence of commercially available drugs approved by the Food and Drug Administration (FDA), benznidazole and nifurtimox have been available exclusively through CDC, under Investigational New Drug (IND) treatment protocols. On August 29, 2017, FDA approved a benznidazole product (Chemo Research, SL, in care of Exeltis*) for treatment of Chagas disease (*4*), which became commercially available on May 14, 2018. Therefore, effective May 14, 2018, benznidazole is no longer available through the CDC-sponsored IND program. This report summarizes selected characteristics of patients for whom CDC released benznidazole through that program from October 2011, when the IND went into effect, until mid-May 2018. The majority of the 365 patients included in intention-to-treat analyses were chronically infected adults who were born and became infected in Latin America. Physician requests for benznidazole should now be directed to the drug company Exeltis.† The CDC-sponsored IND for nifurtimox remains in effect to provide an alternative therapeutic option to benznidazole when clinically appropriate. CDC will continue to provide reference diagnostic testing for *T. cruzi* infection and teleconsultative services regarding Chagas disease.

Background

Trypanosoma cruzi infection occurs in two successive phases. The acute phase, which can be life-threatening in immunosuppressed persons, typically lasts for several weeks or months. The subsequent chronic phase, which can be life-threatening (e.g., can cause sudden cardiac death) even in asymptomatic persons, is associated with an estimated 20%–30% lifetime risk of developing cardiac or gastrointestinal disease (*1*,*2*). The number of chronically infected Latin American immigrants in the United States has been estimated to exceed 300,000 (*5*,*6*). Blood-donor screening for serologic evidence of *T. cruzi* infection, which was introduced in the United States in 2007, has resulted in increased detection of asymptomatic, chronically infected persons and has helped raise awareness about Chagas disease, including the importance of diagnostic testing and appropriate antimicrobial therapy for infected persons.

Treatment of Chagas Disease in U.S. Patients

To ensure availability of and access to antimicrobial therapy for eligible U.S. patients, CDC has sponsored expanded-access IND programs for benznidazole (IND 103,359) and nifurtimox (IND 84,422). Both drugs are administered orally, typically for approximately 2 months (benznidazole) or approximately 3–4 months (nifurtimox). Both drugs are commonly associated with adverse events, which tend to be more frequent and bothersome in adults than in children (*1*,*2*). Some patients tolerate one drug better than the other; if one of the drugs is not tolerated, the other can be tried as an alternative.

The CDC-sponsored IND for benznidazole went into effect in October 2011. The IND treatment program used benznidazole manufactured by a Brazilian public pharmaceutical laboratory, Laboratório Farmacêutico do Estado de Pernambuco (LAFEPE), which was the sole producer of benznidazole when the protocol went into effect.

On August 29, 2017, FDA approved benznidazole (Chemo Research, SL, in care of Exeltis) for treatment of Chagas disease in children aged 2–12 years§ (*4*). On May 14, 2018, the FDA-approved benznidazole product became commercially available through an exclusive distributor, Foundation Care. Physician requests for benznidazole for treatment of Chagas disease in U.S. patients (not limited to patients aged 2–12 years) (*7*) should now be directed to Exeltis.

Effective May 14, 2018, benznidazole is no longer available through the CDC-sponsored IND program. However, the

* Exeltis is the U.S. regulatory representative for Chemo Research, SL.
† http://www.benznidazoletablets.com/en/.

§ FDA's multidisciplinary reviews of the benznidazole New Drug Application and the FDA-approved prescribing information are available at https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=209570.

IND will remain in effect through November 2018 to provide sufficient time for patients who were enrolled before the FDA-approved product became commercially available to complete their current treatment course and for their physicians to comply with IND reporting requirements. The CDC-sponsored IND for nifurtimox remains in effect to provide an alternative therapeutic option to benznidazole when clinically appropriate (e.g., for patients who do not tolerate benznidazole therapy).

Characteristics of Patients for Whom Benznidazole Was Released Through the CDC-Sponsored IND Program

From October 2011 until patient enrollment was discontinued in May 2018, CDC released the LAFEPE benznidazole product under the IND for 369 patients, including two patients who received benznidazole prophylaxis after laboratory accidents and two patients determined not to have Chagas disease after benznidazole was released. Data for the remaining 365 patients were included in intention-to-treat analyses. Median patient age was 42.9 years (range = 0.1–76.0 years). Only 32 patients (8.8%) were aged <19 years (Table), including two patients (0.5%) aged 2–12 years (5 years and 9 years) and one neonate with congenital Chagas disease (*8*).

Overall, 319 patients (87.4%) had been born in Latin America, including a total of 261 (71.5%) from El Salvador (117), Mexico (77), or Bolivia (67) (Table). The shipping addresses of the physicians of record for the 365 patients were in 41 states and the District of Columbia; however, seven (16.7%) of the 42 jurisdictions accounted for 263 patients (72.1%): California (111 patients), Texas (40), New York (35), the District of Columbia (22), Massachusetts (21), Virginia (19), and Florida (15).

Only four patients (1.1%) had acute-phase infection (Table). All four were born and became infected in the United States, two via transplantation of solid organs from Central American immigrants, one via congenital transmission from a Bolivian immigrant (*8*), and one via presumptive vectorborne transmission. The other 361 patients (98.9%) had chronic-phase infection, 35 of whom were Latin American immigrants who developed reactivated infection after becoming immunosuppressed in the context of solid organ transplantation (29 patients), infection with human immunodeficiency virus (five), or chemotherapy (one).

TABLE. Number (N = 365*) and percentage of patients for whom benznidazole was released through the CDC-sponsored Investigational New Drug program for treatment of Chagas disease, by selected characteristics — United States, October 2011–May 2018†

Characteristic	No.	(%)
Sex		
Female	192	(52.6)
Male	173	(47.4)
Age group (yrs)		
<2	1	(0.3)
2–12	2	(0.5)
13–18	29	(7.9)
19–50	236	(64.7)
>50	97	(26.6)
Country of birth in Latin America§		
Total	**319**	**(87.4)**
El Salvador	117	(32.1)
Mexico	77	(21.1)
Bolivia	67	(18.4)
Guatemala	16	(4.4)
Honduras	14	(3.8)
Brazil	8	(2.2)
Colombia	5	(1.4)
Argentina	4	(1.1)
Ecuador	4	(1.1)
Nicaragua	3	(0.8)
Paraguay	2	(0.5)
Peru	2	(0.5)
Other countries of birth		
United States	43¶	(11.8)
Countries in Europe	2**	(0.5)
Not specified	1	(0.3)
Phase of *Trypanosoma cruzi* infection		
Acute infection	4	(1.1)
Chronic infection, not reactivated	326	(89.3)
Chronic infection, reactivated	35	(9.6)

* Data for four other patients were excluded from these intention-to-treat analyses: two patients who received benznidazole prophylaxis after laboratory accidents and two patients determined not to have Chagas disease after benznidazole was released.
† Effective May 14, 2018, patient enrollment was discontinued.
§ Countries are listed in descending order by number of patients. Most of these patients likely became infected in Latin America, although not necessarily in their country of birth.
¶ Autochthonous, presumptive vectorborne transmission was considered the likely means by which at least 50% of the U.S.-born patients became infected, including one patient with an acute infection.
** One patient became infected in Mexico, and the other patient likely became infected in the United States via presumptive vectorborne transmission.

Conclusion

The majority of patients for whom CDC released benznidazole under the IND were chronically infected adults who were born and became infected in Latin America. Only two patients were aged 2–12 years, the group for which FDA has approved the use of benznidazole. However, FDA-approved drugs can be used for nonapproved indications (i.e., "off label"), in accordance with the practice of medicine (*7*). FDA's approval of benznidazole and the commercial availability of the approved product in the United States likely will increase awareness of Chagas disease and facilitate access to therapy.

CDC will continue to provide reference diagnostic testing for *T. cruzi* infection (https://www.cdc.gov/dpdx) and teleconsultative services regarding Chagas disease. Health care providers and U.S. health departments with questions about Chagas disease may contact CDC Parasitic Diseases Branch Inquiries by telephone (404-718-4745) or e-mail (parasites@cdc.gov).

Summary

What is already known about this topic?

Benznidazole is used to treat Chagas disease, a potentially life-threatening parasitic disease. In October 2011, a CDC-sponsored Investigational New Drug (IND) treatment protocol went into effect to ensure benznidazole availability for eligible U.S. patients.

What is added by this report?

Among 365 patients for whom CDC released benznidazole under the IND, 362 (99%) were aged ≥13 years, 361 (99%) had chronic-phase infection, and 319 (87%) were Latin American immigrants. CDC stopped enrolling patients in the IND program in May 2018, when a benznidazole product approved by the Food and Drug Administration in August 2017 became commercially available.

What are the implications for public health practice?

Physician requests for benznidazole should now be directed to the drug company Exeltis (http://www.benznidazoletablets.com/en/).

The CDC Drug Service may be contacted by telephone (404-639-3670) or e-mail (drugservice@cdc.gov). Physician requests for benznidazole, which is now commercially available in the United States, should be directed to Exeltis at http://www.benznidazoletablets.com/en/ (telephone: 877-303-7181; e-mail: FastAccess@exeltis.com). Additional information about Chagas disease is available on CDC's website at https://www.cdc.gov/parasites/chagas.

Conflict of Interest

No conflicts of interest were reported.

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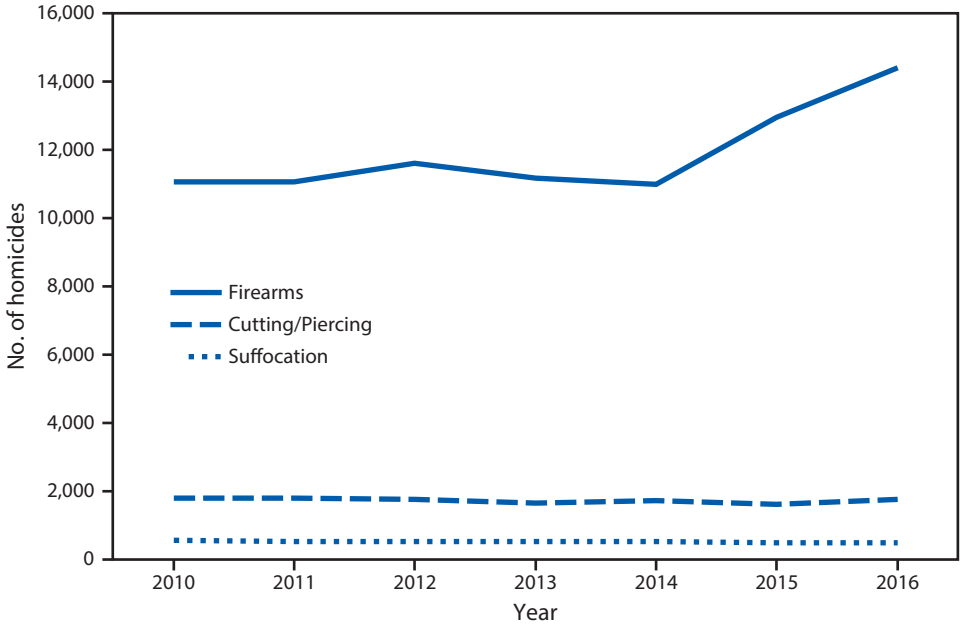
QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Number of Homicides, by the Three Most Common Methods* — United States, 2010–2016



* The three most common methods of homicide are based on numbers of deaths and are identified with *International Classification of Disease, Tenth Revision* (ICD-10) codes X93–X95, U01.4 (firearms), X99 (cutting/piercing), and X91 (suffocation).

During 2010–2016, use of firearms was the most common homicide method in the United States, followed by the use of instruments for cutting and piercing and then suffocation. The number of firearm-related homicides was relatively stable during 2010–2014 (fluctuating between 11,008 and 11,622) but then increased by 31% from 2014 (11,008) to 2016 (14,415). In 2016, the number of homicides involving firearms was approximately eight times the number of those involving cutting and piercing (1,781) and approximately 30 times those involving suffocation (502).

Source: National Vital Statistics System, Underlying Cause of Death Data, 2000–2016. https://wonder.cdc.gov/ucd-icd10.html.

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