

## International Overdose Awareness Day — August 31, 2016

August 31 is International Overdose Awareness Day, a global event that aims to raise awareness that overdose death is preventable. Goals include providing awareness regarding the risk for overdose, providing information on community services, and preventing and reducing drug-related harm by supporting evidence-based policy and practice (<http://www.overdoseday.com>).

In 2015, the Drug Enforcement Administration and CDC released alerts identifying illicitly manufactured fentanyl as a threat to public health and safety (1,2). Although fentanyl is available as a prescription medication for treating severe pain, including cancer-related pain, the current epidemic of synthetic opioid-involved overdose deaths largely involves illicitly manufactured fentanyl that is mixed with or sold as heroin (1,3).

In contrast to the 2005–2007 fentanyl overdose outbreak, when deaths were confined to several states, the current epidemic is unprecedented in scope and, as described in a report in this issue of *MMWR*, multiple states in several regions of the United States are reporting substantial increases in fatal synthetic opioid-involved overdoses, primarily driven by fentanyl-involved overdose deaths. Further information and data about fentanyl from CDC are available at <http://www.cdc.gov/drugoverdose/opioids/fentanyl.html>.

### References

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## Fentanyl Law Enforcement Submissions and Increases in Synthetic Opioid-Involved Overdose Deaths — 27 States, 2013–2014

R. Matthew Gladden, PhD<sup>1</sup>; Pedro Martinez, MPH<sup>1</sup>; Puja Seth, PhD<sup>1</sup>

In March and October 2015, the Drug Enforcement Administration (DEA) and CDC, respectively, issued nationwide alerts identifying illicitly manufactured fentanyl (IMF) as a threat to public health and safety (1,2). IMF is unlawfully produced fentanyl, obtained through

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illicit drug markets, includes fentanyl analogs, and is commonly mixed with or sold as heroin (1,3,4). Starting in 2013, the production and distribution of IMF increased to unprecedented levels, fueled by increases in the global supply, processing, and distribution of fentanyl and fentanyl-precursor chemicals by criminal organizations (3). Fentanyl is a synthetic opioid 50–100 times more potent than morphine (2).<sup>\*</sup> Multiple states have reported increases in fentanyl-involved overdose (poisoning) deaths (fentanyl deaths) (2). This report examined the number of drug products obtained by law enforcement that tested positive for fentanyl (fentanyl submissions) and synthetic opioid-involved deaths other than methadone (synthetic opioid deaths), which include fentanyl deaths and deaths involving other synthetic opioids (e.g., tramadol). Fentanyl deaths are not reported separately in national data. Analyses also were conducted on data from 27 states<sup>†</sup> with consistent death certificate reporting of the drugs involved in overdoses. Nationally, the number of fentanyl submissions and synthetic opioid deaths increased by

426% and 79%, respectively, during 2013–2014; among the 27 analyzed states, fentanyl submission increases were strongly correlated with increases in synthetic opioid deaths. Changes in fentanyl submissions and synthetic opioid deaths were not correlated with changes in fentanyl prescribing rates, and increases in fentanyl submissions and synthetic opioid deaths were primarily concentrated in eight states (high-burden states). Reports from six of the eight high-burden states indicated that fentanyl-involved overdose deaths were primarily driving increases in synthetic opioid deaths. Increases in synthetic opioid deaths among high-burden states disproportionately involved persons aged 15–44 years and males, a pattern consistent with previously documented IMF-involved deaths (5). These findings, combined with the approximate doubling in fentanyl submissions during 2014–2015 (from 5,343 to 13,882) (6), underscore the urgent need for a collaborative public health and law enforcement response.

Data were analyzed from four sources: 1) fentanyl submission data from the DEA National Forensic Laboratory Information System (NFLIS), which systematically collects drug identification results from drug cases submitted for analysis to forensic laboratories<sup>§</sup>; 2) synthetic opioid deaths, calculated using the National Vital Statistics System multiple cause-of-death mortality files<sup>¶</sup>;

<sup>\*</sup>Additional information on approved fentanyl products and their indications is available at <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.SearchAction&SearchTerm=fentanyl&SearchType=BasicSearch>.

<sup>†</sup>Arkansas, California, Colorado, Connecticut, Florida, Illinois, Iowa, Kentucky, Massachusetts, Maine, Maryland, Minnesota, Missouri, Nevada, New Hampshire, New York, North Carolina, Ohio, Oklahoma, Oregon, Tennessee, Texas, Utah, Virginia, Washington, West Virginia, and Wisconsin.

<sup>§</sup>Data were extracted July 1, 2016; additional information on NFLIS is available at <http://www.deadiversion.usdoj.gov/nflis/>.

<sup>¶</sup>[http://www.cdc.gov/nchs/nvss/mortality\\_public\\_use\\_data.htm](http://www.cdc.gov/nchs/nvss/mortality_public_use_data.htm).

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3) national and state fentanyl prescription data that are estimated from IMS Health's National Prescription Audit collecting 87% of retail prescriptions in the United States\*\*; and 4) medical examiner/coroner reports or death certificate data from states with a high burden of synthetic opioid deaths (i.e., a 1-year increase in synthetic opioid deaths exceeding two per 100,000 residents, or a 1-year increase of  $\geq 100$  synthetic opioid deaths during 2013–2014). Synthetic opioid deaths were identified using the following *International Classification of Diseases, 10th Revision* codes: 1) an underlying cause-of-death code of X40–44 (unintentional), X60–64 (suicide), X85 (homicide), or Y10–Y14 (undetermined intent) and 2) a multiple cause-of-death code of T40.4. In 2014, any information on the specific drug or drugs involved in a drug overdose were reported for approximately 80% of drug overdose deaths; this proportion varied over time and by state (7). State analyses were limited to 27 states meeting the following criteria: 1)  $>70\%$  of drug overdose deaths reported at least one specific drug in 2013 and 2014; 2) the change in the percentage of overdose deaths reporting at least one specific drug from 2013 to 2014 was  $<10\%$ <sup>††</sup>; 3)  $\geq 20$  synthetic opioid deaths occurred during 2013 and 2014; and 4) fentanyl submissions were reported in 2013 and 2014.<sup>§§</sup> These 27 states accounted for 75% of synthetic opioid deaths in the United States in 2014. Analyses compared changes in the crude rate of fentanyl submissions, fentanyl prescriptions, and synthetic opioid deaths during 2013–2014 using Pearson correlations. States were classified as high-burden if they experienced a 1-year increase in synthetic opioid deaths exceeding two per 100,000 residents or a 1-year increase of  $\geq 100$  synthetic opioid deaths during 2013–2014. Additional evidence from published state medical examiner/coroner or death certificate reports was reviewed to understand whether increases in synthetic opioid deaths were being primarily driven by fentanyl deaths and not by other synthetic opioids. Demographic characteristics of synthetic opioid deaths for high-burden and low-burden states were described.

During 2013–2014, fentanyl submissions in the United States increased by 426%, from 1,015 in 2013 to 5,343 in 2014, and synthetic opioid deaths increased by 79%, from 3,105 in 2013

to 5,544 in 2014.<sup>¶¶</sup> In contrast, fentanyl prescription rates remained relatively stable (Figure 1). Although changes in fentanyl submissions and synthetic opioid death rates from 2013–2014 among the 27 states were highly correlated ( $r = 0.95$ ) (Figure 2), changes in state-level synthetic opioid deaths were not correlated with changes in fentanyl prescribing (data not shown). During 2013–2014, the synthetic opioid crude death rate in the eight high-burden states increased 174%, from 1.3 to 3.6 per 100,000, and the fentanyl submissions rate increased by 1,000% from 0.5 to 5.5 per 100,000 (Table). Six of the eight high-burden states reported increases in synthetic opioid death rates exceeding 2.0 per 100,000 population, and seven states reported increases in deaths of  $\geq 100$ .<sup>\*\*\*</sup> The eight high-burden states were located in the Northeast (Massachusetts, Maine, and New Hampshire), Midwest (Ohio), and South (Florida, Kentucky, Maryland, and North Carolina). Six of the eight states published data on fentanyl deaths from 2013 and 2014.<sup>†††</sup> Combining results across the state reports, total fentanyl deaths during 2013–2014 increased by 1,008, from 392 (2013) to 1,400 (2014), and the increase in total fentanyl deaths was of nearly the same magnitude as the increase in 966 synthetic opioid deaths in these states (589 [2013], 1,555 [2014]). This finding indicates that increases in fentanyl deaths were driving the increases in synthetic opioid deaths in these six states. Among high-burden states, all demographic groups experienced substantial increases in synthetic opioid death rates. Increases of  $>200\%$  occurred among males (227%); persons aged 15–24 years (347%), 25–34 years

<sup>¶¶</sup> Reported drug submissions to NFLIS decreased from 1.54 million in 2013 to 1.51 million in 2014 suggesting that the increase in fentanyl submissions was not driven by general increases in drug submissions to NFLIS. <https://www.nflis.deadiversion.usdoj.gov/DesktopModules/ReportDownloads/Reports/NFLIS2014AR.pdf>.

<sup>\*\*\*</sup> Six states reported increases of more than two synthetic opioid deaths per 100,000 residents (Kentucky [2.4], Maine [3.0], Maryland [2.2], Massachusetts [5.2], New Hampshire [9.1], and Ohio [3.7]), and seven of the eight states reported increases of  $\geq 100$  in synthetic opioid deaths (Florida [143], Kentucky [103], Maryland [137], Massachusetts [355], New Hampshire [121], North Carolina [100], and Ohio [423]).

<sup>†††</sup> The following reports are from seven of the eight high-burden states: 1) *Florida*: <https://www.fdle.state.fl.us/cms/MEC/Publications-and-Forms/Documents/Drugs-in-Deceased-Persons/2014-Annual-Drug-Report-FINAL.aspx>; 2) *Maine*: <http://pub.lucidpress.com/NDEWSFentanyl/>; 3) *Maryland*: [http://bha.dhmh.maryland.gov/OVERDOSE\\_PREVENTION/Documents/2015.05.19%20-%20Annual%20OD%20Report%202014\\_merged%20file%20final.pdf](http://bha.dhmh.maryland.gov/OVERDOSE_PREVENTION/Documents/2015.05.19%20-%20Annual%20OD%20Report%202014_merged%20file%20final.pdf); 4) *Massachusetts*: <http://www.mass.gov/eohhs/docs/dph/quality/drugcontrol/county-level-pmp/data-brief-overdose-deaths-may-2016.pdf>; 5) *New Hampshire*: <http://nhpr.org/post/nh-medical-examiner-least-10-drug-overdoses-2016-86-cases-pending>, [http://mediad.publicbroadcasting.net/p/nhpr/files/201604/drug\\_data\\_update\\_from\\_nh\\_medical\\_examiner\\_s\\_office\\_4-14-16\\_3\\_.pdf](http://mediad.publicbroadcasting.net/p/nhpr/files/201604/drug_data_update_from_nh_medical_examiner_s_office_4-14-16_3_.pdf); 6) *Ohio*: <http://www.medscape.com/viewarticle/851502>; and 7) *Kentucky*: <http://www.mc.uky.edu/kiprc/programs/kdopp/reports/2015-drug-overdose-deaths.pdf>. Other jurisdictions also reporting sharp increases in fentanyl deaths include 1) *Pennsylvania*: [https://www.dea.gov/divisions/phi/2015/phi111715\\_attach.pdf](https://www.dea.gov/divisions/phi/2015/phi111715_attach.pdf), [https://www.dea.gov/divisions/phi/2016/phi071216\\_attach.pdf](https://www.dea.gov/divisions/phi/2016/phi071216_attach.pdf); 2) *New York City*: <https://a816-health30ssl.nyc.gov/sites/nycchan/Lists/AlertUpdateAdvisoryDocuments/Fentanyl-HAN-advisory.pdf>; and 3) *Rhode Island*: <http://www.slideshare.net/OPUNITE/rx16-federal-tues2001gladden2halpin3green>.

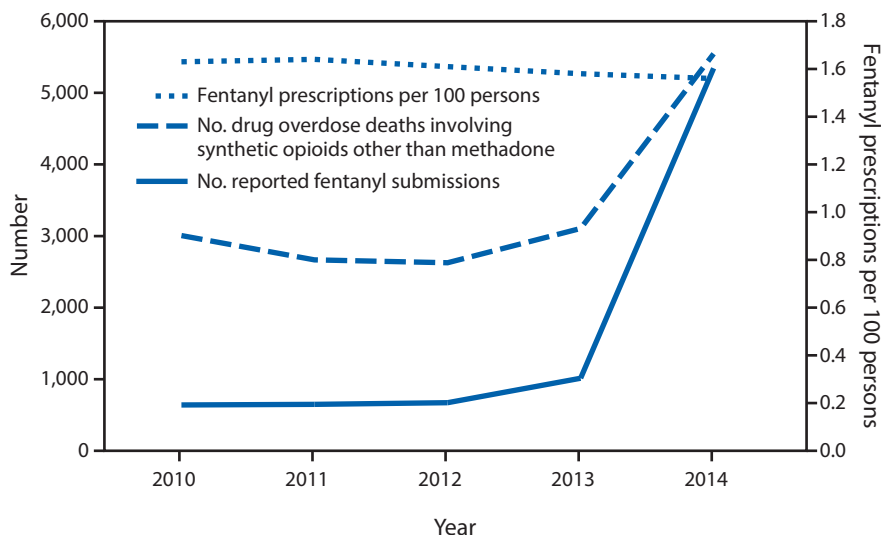
\*\* IMS Health's National Prescription Audit is a trademarked product. [http://www.imshealth.com/files/web/IMSH%20Institute/NPA\\_Data\\_Brief-.pdf](http://www.imshealth.com/files/web/IMSH%20Institute/NPA_Data_Brief-.pdf).

<sup>††</sup> The analysis excluded states whose reporting of any specific drug or drugs involved in an overdose changed by  $>10\%$  from 2013 to 2014. These states were excluded because drug specific overdose numbers and rates, including the number and rate synthetic opioid-involved overdose deaths, were expected to change substantially from 2013 to 2014 because of changes in reporting.

<sup>§§</sup> 38 states reported specific drugs on  $\geq 70\%$  of drug overdoses in 2013 and 2014, but only 36 of these states experienced changes in drug reporting of  $<10$  percentage points from 2013 to 2014. Among these 36 states, only 30 reported  $\geq 20$  synthetic opioid-involved overdose deaths in 2013 and 2014, and 27 of these 30 states had fentanyl submissions in both 2013 and 2014.



**FIGURE 1. Trends in number of drug overdose deaths involving synthetic opioids other than methadone,\* number of reported fentanyl submissions,<sup>†</sup> and rate of fentanyl prescriptions<sup>§</sup> — United States, 2010–2014**



\* Synthetic opioid–involved (other than methadone) overdose deaths are deaths with an *International Classification of Diseases, 10th Revision* underlying cause-of-death of X40–44 (unintentional), X60–64 (suicide), X85 (homicide), or Y10–Y14 (undetermined intent) and a multiple cause-of-death of T40.4 (poisoning by narcotics and psychodysleptics [hallucinogens]; other synthetic narcotics).

<sup>†</sup> Drug products obtained by law enforcement that tested positive for fentanyl are referred to as fentanyl submissions. Reports were supplied by the Drug Enforcement Administration's National Forensic Laboratory Information System and downloaded July 1, 2016.

<sup>§</sup> National estimates supplied by IMS National Prescription Audit and include short and long-acting fentanyl prescriptions.

(248%), and 35–44 (230%) years; Hispanics (290%), and persons living in large fringe metro areas (230%).<sup>§§§</sup> The highest rates of synthetic opioid deaths in 2014 were among males (5.1 per 100,000); non-Hispanics whites (4.6 per 100,000); and persons aged 25–34 years (8.3 per 100,000), 35–44 years (7.4 per 100,000), and 45–54 years (5.7 per 100,000) (Table).

## Discussion

In the 27 states meeting analysis criteria, synthetic opioid deaths sharply increased in the eight high-burden states, and complementary data suggest this increase can be attributed to fentanyl. Six of the eight high-burden states reported substantial increases in fentanyl deaths during 2013–2014, based on medical examiner/coroner data or literal text searches of death certificates. The high potency of fentanyl and the possibility of rapid death after fentanyl administration (8), coupled with the extremely sharp 1-year increase in fentanyl

<sup>§§§</sup> Large fringe metro counties are located in metropolitan statistical areas (MSAs) of  $\geq 1$  million population that did not qualify as large central metro counties. Large central metro counties are MSAs of  $\geq 1$  million population that 1) contain the entire population of largest principal city of the MSA, 2) have their entire population contained in the largest principal city of the MSA, or 3) contain at least 250,000 inhabitants of any principal city of the MSA.

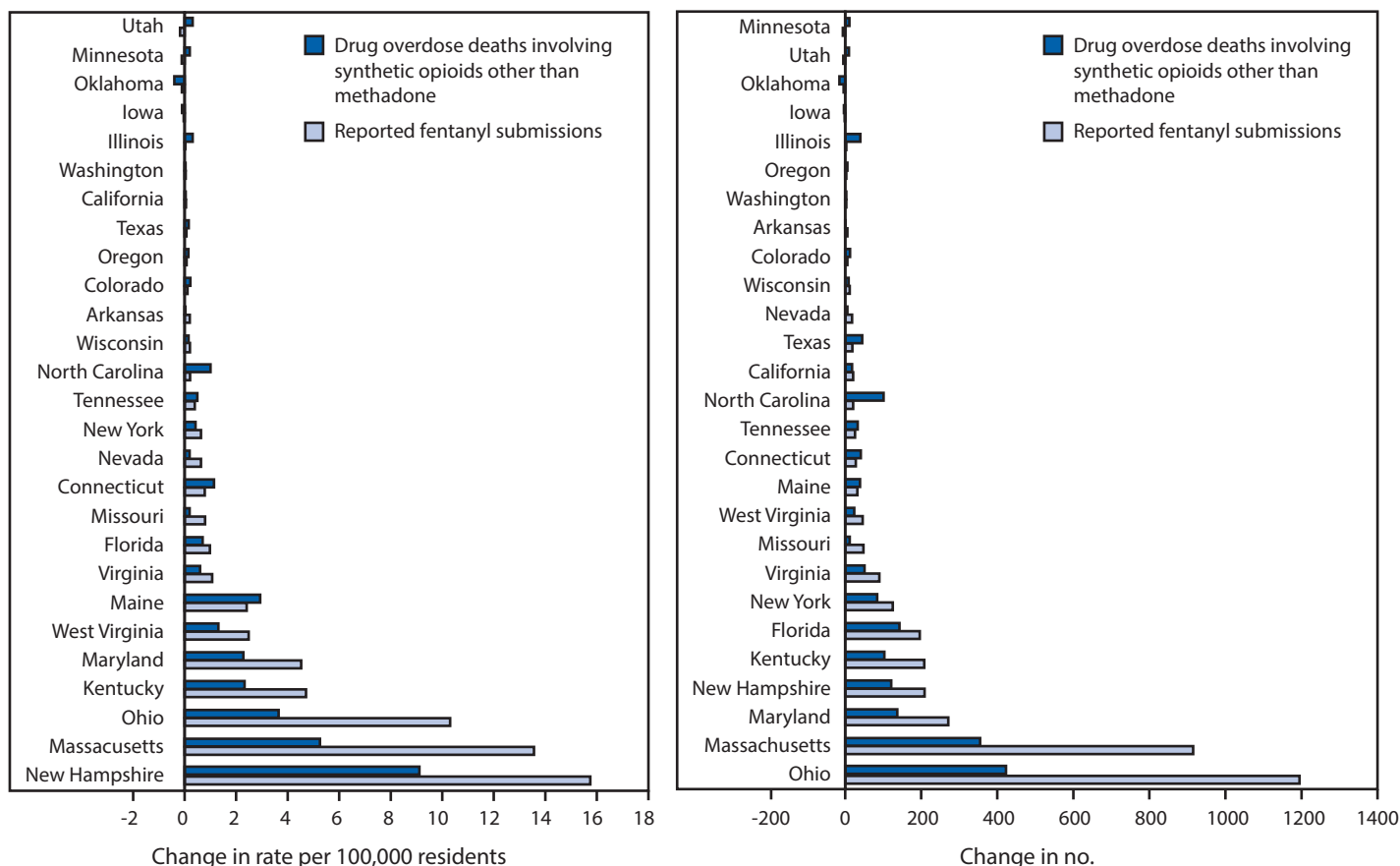
deaths in high-burden states, highlights the need to understand the factors driving this increase.

IMF production and distribution began increasing in 2013 and has grown to unprecedented levels in 2016 (3). For example, there were approximately eight times as many fentanyl submissions in 2015 as there were in 2006 during the last multistate outbreak involving IMF (3). DEA has not reported a sharp increase in pharmaceutical fentanyl being diverted from legitimate medical use to illegal uses (4). Given the strong correlation between increases in fentanyl submissions (primarily driven by IMF) (3,4) and increases in synthetic opioid deaths (primarily fentanyl deaths), and uncorrelated stable fentanyl prescription rates, it is hypothesized that IMF is driving the increases in fentanyl deaths. Findings from DEA (3,4), state, and CDC investigations (5) documenting the role of IMF in the observed increases in fentanyl deaths further support this hypothesis. The demographics of synthetic opioid deaths are rapidly changing and are consistent with the changes in demographics of persons using heroin, in particular, increasing use among non-Hispanic white men aged 25–44 years (9).

Historically, the heroin market in the United States has been divided along the Mississippi River, with Mexican black tar and brown powder heroin being sold in the west and white powder heroin being sold in the east. IMF is most commonly mixed with or sold as white powder heroin (4). The concentration of high-burden states east of the Mississippi River is consistent with reports of IMF distribution in white powder heroin markets (3,4).

An urgent, collaborative public health and law enforcement response is needed to address the increasing problem of IMF and fentanyl deaths. Recently released fentanyl submissions data indicate that 15 states experienced  $>100$  fentanyl submissions in 2015. This is up from 11 states in 2014 (6). The national increase of 8,539 in fentanyl submissions from 2014 (5,343) to 2015 (13,882) (6) exceeded the increase of 4,328 from 2013 to 2014. This finding coupled with the strong correlation between fentanyl submissions and fentanyl-involved overdose deaths observed in Ohio and Florida (5) and supported by this report likely indicate the problem of IMF is rapidly expanding. Recent (2016) seizures of large numbers of counterfeit pills containing IMF indicate that states where persons commonly use diverted prescription pills, including opioid pain relievers, might begin to experience increases in fentanyl deaths (3) because many counterfeit pills are

**FIGURE 2. Change in the rate per 100,000 residents and number of overdose deaths involving synthetic opioids other than methadone\* and reported fentanyl submissions<sup>†</sup> — 27 states,<sup>§</sup> 2013–2014**



\* Synthetic opioid-involved (other than methadone) overdose deaths are deaths with an *International Classification of Diseases, 10th Revision* underlying cause-of-death of X40–44 (unintentional), X60–64 (suicide), X85 (homicide), or Y10–Y14 (undetermined intent) and a multiple cause-of-death of T40.4 (poisoning by narcotics and psychodysleptics [hallucinogens]: other synthetic narcotics).

<sup>†</sup> Drug products obtained by law enforcement that tested positive for fentanyl are referred to as fentanyl submissions. Reports were supplied by the Drug Enforcement Administration National Forensic Laboratory Information System and downloaded July 1, 2016.

<sup>§</sup> Change in rate of synthetic opioid-involved overdose deaths from 2013–2014 was significant for Connecticut, Florida, Kentucky, Maine, Maryland, Massachusetts, Ohio, New Hampshire, New York, North Carolina, Texas, and Virginia using gamma or z-tests.

deceptively sold as and hard to distinguish from diverted opioid pain relievers. Finally, the approximate tripling of heroin-involved overdose deaths since 2010 highlights the need for interventions targeting the illicit opioid market.<sup>¶¶</sup>

The findings in this report are subject to at least four limitations. First, national vital statistics data only report synthetic opioid deaths. A review of state-level reports in six of eight high-burden states indicated that the increase in fentanyl deaths was the primary factor driving increases in synthetic opioid deaths during 2013–2014. Because synthetic opioid deaths include deaths involving synthetic opioids besides fentanyl, the absolute number of synthetic opioid deaths occurring in a year such as 2014 should not be considered a proxy for the

number of fentanyl deaths in a year. Second, law enforcement drug submissions might vary over time and geographically because of differences or changes in law enforcement testing practices and drug enforcement activity, which might underestimate or overestimate the number of fentanyl submissions in certain states. Third, findings and implications are restricted to 27 states. Finally, testing for fentanyl deaths might vary across states because toxicologic testing protocols for drug overdoses vary across states and local jurisdictions.

The Secretary of Health and Human Services has launched an initiative to reduce opioid misuse, abuse, and overdose by expanding medication-assisted treatment, increasing the availability and use of naloxone, and promoting safer opioid prescribing (10). Efforts should focus on 1) improving timeliness

<sup>¶¶</sup> <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6450a3.htm>.

TABLE. Number and crude rates per 100,000 persons of synthetic opioid deaths (overdose deaths involving synthetic opioids other than methadone),\* by sex, age group,<sup>†</sup> race and Hispanic origin,<sup>§</sup> reported fentanyl submissions,<sup>¶</sup> and 2013 urbanization\*\* — eight high-burden states<sup>††</sup> and 19 low-burden states,<sup>§§</sup> 2013 and 2014

| Decedent characteristic       | High-burden states (n = 8) |      |       |      |   | Low-burden states (n = 19) |      |       |      |   |
|-------------------------------|----------------------------|------|-------|------|---|----------------------------|------|-------|------|---|
|                               | 2013                       |      | 2014  |      | Percentage increase<br>in rate, 2013–2014 | 2013                       |      | 2014  |      | Percentage increase<br>in rate, 2013–2014 |
|                               | No.                        | Rate | No.   | Rate |   | No.                        | Rate | No.   | Rate |   |
| All                           | 803                        | 1.32 | 2,225 | 3.63 | 174 <sup>¶¶</sup>                         | 1,559                      | 0.94 | 1,948 | 1.16 | 24 <sup>¶¶</sup>                          |
| <b>Sex</b>                    |                            |      |       |      |   |                            |      |       |      |   |
| Female                        | 342                        | 1.1  | 705   | 2.25 | 104 <sup>¶¶</sup>                         | 741                        | 0.88 | 828   | 0.97 | 11 <sup>¶¶</sup>                          |
| Male                          | 461                        | 1.56 | 1,520 | 5.09 | 227 <sup>¶¶</sup>                         | 818                        | 0.99 | 1,120 | 1.35 | 36 <sup>¶¶</sup>                          |
| <b>Age groups (yrs)</b>       |                            |      |       |      |   |                            |      |       |      |   |
| 15–24                         | 53                         | 0.66 | 237   | 2.92 | 347 <sup>¶¶</sup>                         | 137                        | 0.59 | 153   | 0.65 | 12  |
| 25–34                         | 185                        | 2.38 | 656   | 8.28 | 248 <sup>¶¶</sup>                         | 302                        | 1.29 | 438   | 1.84 | 43 <sup>¶¶</sup>                          |
| 35–44                         | 170                        | 2.23 | 560   | 7.36 | 230 <sup>¶¶</sup>                         | 316                        | 1.45 | 415   | 1.9  | 31 <sup>¶¶</sup>                          |
| 45–54                         | 242                        | 2.8  | 494   | 5.75 | 106 <sup>¶¶</sup>                         | 429                        | 1.88 | 534   | 2.35 | 25 <sup>¶¶</sup>                          |
| 55–64                         | 131                        | 1.66 | 229   | 2.85 | 71 <sup>¶¶</sup>                          | 292                        | 1.45 | 309   | 1.51 | 4   |
| ≥65                           | 21                         | 0.22 | 48    | 0.48 | 121 <sup>¶¶</sup>                         | 80                         | 0.36 | 84    | 0.4  | 11  |
| <b>Race/Ethnicity</b>         |                            |      |       |      |   |                            |      |       |      |   |
| White, non-Hispanic           | 711                        | 1.71 | 1,925 | 4.62 | 170 <sup>¶¶</sup>                         | 1,338                      | 1.35 | 1,653 | 1.67 | 23 <sup>¶¶</sup>                          |
| Black, non-Hispanic           | 61                         | 0.65 | 172   | 1.79 | 178 <sup>¶¶</sup>                         | 82                         | 0.49 | 136   | 0.79 | 64 <sup>¶¶</sup>                          |
| Other, non-Hispanic           | —***                       | —*** | 22    | 0.94 | —***                                      | 33                         | 0.25 | 42    | 0.31 | 22  |
| Hispanic                      | 23                         | 0.31 | 93    | 1.23 | 290 <sup>¶¶</sup>                         | 102                        | 0.27 | 110   | 0.29 | 6   |
| <b>2013 urbanization</b>      |                            |      |       |      |   |                            |      |       |      |   |
| Large central metro           | 156                        | 1.08 | 429   | 2.95 | 171 <sup>¶¶</sup>                         | 483                        | 0.72 | 577   | 0.85 | 18 <sup>¶¶</sup>                          |
| Large fringe metro            | 246                        | 1.3  | 822   | 4.31 | 230 <sup>¶¶</sup>                         | 304                        | 0.84 | 442   | 1.21 | 44 <sup>¶¶</sup>                          |
| Medium metro                  | 202                        | 1.32 | 567   | 3.67 | 178 <sup>¶¶</sup>                         | 314                        | 1.06 | 406   | 1.36 | 28 <sup>¶¶</sup>                          |
| Small metro                   | 54                         | 1.45 | 98    | 2.61 | 80 <sup>¶¶</sup>                          | 133                        | 1.03 | 201   | 1.54 | 50 <sup>¶¶</sup>                          |
| Micropolitan                  | 87                         | 1.61 | 214   | 3.95 | 146 <sup>¶¶</sup>                         | 154                        | 1.33 | 188   | 1.62 | 22  |
| Noncore                       | 58                         | 1.93 | 95    | 3.17 | 64 <sup>¶¶</sup>                          | 171                        | 1.83 | 134   | 1.44 | -21 <sup>¶¶</sup>                         |
| Reported fentanyl submissions | 293                        | 0.48 | 3,340 | 5.46 | 1,029 <sup>¶¶</sup>                       | 417                        | 0.25 | 855   | 0.51 | 103 <sup>¶¶</sup>                         |

Source: CDC Wonder Multiple-Cause-of-Death Data at <http://wonder.cdc.gov/mcd.html>.

\* Synthetic opioid-involved (other than methadone) overdose deaths are deaths with an *International Classification of Diseases, 10th Revision* underlying cause-of-death of X40–44 (unintentional), X60–64 (suicide), X85 (homicide), or Y10–Y14 (undetermined intent) and a multiple cause-of-death of T40.4.

† Synthetic opioid-involved overdose deaths involving persons aged ≤14 years are not reported because cells have nine or fewer deaths. Also, a small number of synthetic opioid-involved overdose deaths do not report age of the decedent.

§ Data for Hispanic origin should be interpreted with caution; studies comparing Hispanic origin on death certificates and on census surveys have indicated inconsistent reporting on Hispanic ethnicity. Numbers might not sum to the total because the ethnicity and race of some synthetic opioid-involved overdose deaths are not known.

¶ Drug products obtained by law enforcement that tested positive for fentanyl are referred to as fentanyl submissions. Reports were supplied by the Drug Enforcement Administration's National Forensic Laboratory Information System and downloaded July 1, 2016.

\*\* Categories of 2013 NCHS Urban-Rural Classification Scheme for Counties ([http://www.cdc.gov/nchs/data/series/sr\\_02/sr02\\_166.pdf](http://www.cdc.gov/nchs/data/series/sr_02/sr02_166.pdf)): *Large central metro*: Counties in metropolitan statistical areas (MSAs) of ≥1 million population that 1) contain the entire population of largest principal city of the MSA, or 2) have their entire population contained in the largest principal city of the MSA, or 3) contain at least 250,000 inhabitants of any principal city of the MSA; *Large fringe metro*: Counties in MSAs of ≥1 million population that did not qualify as large central metro counties; *Medium metro*: Counties in MSAs of populations of 250,000–999,999; *Small metro*: Counties in MSAs of populations less than 250,000; *Micropolitan (nonmetropolitan counties)*: counties in micropolitan statistical areas; *Noncore (nonmetropolitan counties)*: nonmetropolitan counties that did not qualify as micropolitan.

†† High-burden states (n = 8) include Florida, Kentucky, Maine, Maryland, Massachusetts, New Hampshire, North Carolina, and Ohio.

§§ Low-burden states (n = 19) include Arkansas, California, Colorado, Connecticut, Illinois, Iowa, Minnesota, Missouri, Nevada, New York, Oklahoma, Oregon, Tennessee, Texas, Utah, Virginia, Washington, West Virginia, and Wisconsin.

¶¶ Statistically significant at p<0.05 level. Gamma tests were used if cell count was less than 100 in 2013 or 2014, and z-tests were used if cell counts were ≥100 in both 2013 and 2014.

\*\*\* Cells with nine or fewer deaths are not reported and rates based on <20 deaths are not considered reliable and not reported. When rate for a year is suppressed, change in rate is also not reported.

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

In 2015, the Drug Enforcement Administration and CDC issued nationwide alerts identifying illicitly manufactured fentanyl (IMF) as a threat. Beginning in 2013, the distribution of IMF increased to unprecedented levels. Individual states have reported increases in fentanyl-involved overdose deaths (fentanyl deaths).

**What is added by this report?**

During 2013–2014, the number of drug products obtained by law enforcement that tested positive for fentanyl (fentanyl submissions) increased by 426%, and synthetic opioid-involved overdose deaths (excluding methadone) increased by 79% in the United States. Changes in synthetic opioid-involved overdose deaths among 27 states were highly correlated with fentanyl submissions but not correlated with fentanyl prescribing. Eight high-burden states were identified, and complementary data indicate increases in these states are primarily attributable to fentanyl, supporting the argument that IMF is driving increases in fentanyl deaths.

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

An urgent, collaborative public health and law enforcement response is needed, including 1) improving timeliness of opioid surveillance to facilitate faster identification and response to spikes in fentanyl overdoses; 2) expanding testing for fentanyl and fentanyl analogues in high-burden states; 3) expanding evidence-based harm reduction and naloxone access; 4) implementing programs that increase linkage and access to medication-assisted treatment; 5) increasing collaboration between public health and public safety; and 6) planning rapid response in high-burden states and states beginning to experience increases in fentanyl submissions or deaths.

of opioid surveillance to facilitate faster identification and response to spikes in fentanyl overdoses; 2) expanding testing for fentanyl and fentanyl analogs by physicians, treatment programs, and medical examiners/coroners in high-burden states; 3) expanding evidence-based harm reduction and expanding naloxone access, with a focus on persons using heroin; 4) implementing programs that increase linkage and access to medication-assisted treatment, with a focus on persons using heroin; 5) increasing collaboration between public health and public safety; and 6) planning rapid response in high-burden states and states beginning to experience increases in fentanyl submissions or deaths.

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Tamara Haegerich, PhD, Nina Shah, MS, Division of Unintentional Injury Prevention, National Center for Injury Prevention and Control, CDC.

<sup>1</sup>Division of Unintentional Injury Prevention, National Center for Injury Prevention and Control, CDC.

Corresponding author: R. Matthew Gladden, [mgladden@cdc.gov](mailto:mgladden@cdc.gov), 770-488-4276.

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## Increases in Fentanyl-Related Overdose Deaths — Florida and Ohio, 2013–2015

Alexis B. Peterson, PhD<sup>1,2,3</sup>; R. Matthew Gladden, PhD<sup>2</sup>; Chris Delcher, PhD<sup>4</sup>; Erica Spies, PhD<sup>1,5</sup>; Amanda Garcia-Williams, PhD<sup>1,5</sup>; Yanning Wang, MS<sup>4,6</sup>; John Halpin, MD<sup>2</sup>; Jon Zibbell, PhD<sup>2</sup>; Carolyn Lullo McCarty, PhD<sup>1,7,8</sup>; Jolene DeFiore-Hyrmer, MPH<sup>8</sup>; Mary DiOrio, MD<sup>8</sup>; Bruce A. Goldberger, PhD<sup>6</sup>

In March and October 2015, the Drug Enforcement Administration (DEA) and CDC issued nationwide alerts identifying fentanyl, particularly illicitly manufactured fentanyl (IMF), as a threat to public health and safety (1,2). IMF is pharmacologically similar to pharmaceutical fentanyl (PF), but is unlawfully produced in clandestine laboratories, obtained via illicit drug markets, and includes fentanyl analogs. Fentanyl is a synthetic opioid 50–100 times more potent than morphine and approved for the management of surgical/postoperative pain, severe chronic pain, and breakthrough cancer pain.\* DEA's National Forensic Laboratory Information System (NFLIS) collects drug identification results from drug cases analyzed by federal, state, and local forensic laboratories throughout the United States.† In 2014, 80% of fentanyl submissions (i.e., drug products obtained by law enforcement that tested positive for fentanyl) in NFLIS were identified from 10 states, including Florida and Ohio (2), and seven of these 10 states reported sharp increases in fentanyl-related overdose deaths (fentanyl deaths) (3). This report presents findings of increased fentanyl deaths during 2013–2015 from investigations conducted by the University of Florida and the Ohio Department of Public Health, in collaboration with CDC. Analyses examined the association between trends in fentanyl-related law enforcement submissions and fentanyl deaths and describes groups at risk for fentanyl death using medical examiner and coroner reports. The marked increases in fentanyl death in Florida and Ohio during 2013–2015 were closely associated with parallel increases in fentanyl submissions, with the largest impact on persons who use heroin, consistent with reports that IMF is commonly mixed with or sold as heroin (1,4). In Ohio, circumstances associated with fentanyl deaths included a current diagnosed mental health disorder<sup>§</sup> and recent release from an institution such as a jail, rehabilitation facility, or hospital.

Three different analyses are reported. The first analysis compared trends in fentanyl deaths, fentanyl submissions, and fentanyl prescribing during January 2013–June 2015, using 1) medical examiner and coroner reports in Florida and death certificates in Ohio, 2) NFLIS data in both states, and

3) prescription drug monitoring program data (E-FORCSE in Florida<sup>¶</sup> and OARRS in Ohio<sup>\*\*</sup>) that track the prescribing and dispensing of controlled substances (schedules II, III, and IV drugs). Data on overdose deaths involving fentanyl analogs were also available for the first half of 2015 in Florida. The second analysis used medical examiner data to compare demographic and toxicologic characteristics of fentanyl deaths in Florida before (2010–2012) and during (2013–2014) the marked increase in fentanyl submissions. For the third analysis, the Ohio Department of Health conducted an in-depth review of medical examiner and coroner reports of fentanyl deaths, including toxicology panel findings, medical history, drug abuse history, and overdose scene characteristics occurring in 14 high-burden counties (Butler, Clark, Clermont, Cuyahoga, Fayette, Hamilton, Lucas, Miami, Montgomery, Ross, Scioto, Stark, Summit, and Warren) in 2014. These counties were selected based on a high number and/or rate of fentanyl deaths and geographic diversity (urban versus rural) and accounted for 73% of Ohio's fentanyl deaths reported on death certificates during January–December 2014. Data from Ohio's medical examiners and coroners were abstracted from the Ohio Violent Death Reporting System.

During 2013–2014, fentanyl submissions increased 494% in Florida (from 33 to 196) and 1,043% in Ohio (from 109 to 1,246), concurrent with a 115% increase in fentanyl deaths in Florida (from 185 to 397) and a 526% increase in Ohio (from 84 to 526) (Figure). In Florida, fentanyl submissions and fentanyl deaths gradually increased during May–November 2014, with a sharp increase during December 2014–February 2015, before returning to levels consistent with July–November 2014 during March–June 2015. Ohio's fentanyl deaths and fentanyl submissions spiked during November 2013–March 2014, followed by a sharp decline in April–May 2014, and then a gradual and continuous rise during June 2014–May 2015. In contrast, fentanyl prescription rates for the full year increased only 5% in Florida (from 19.3 in 2013 to 20.3 in 2014 per 1,000 population) and declined 7% in Ohio over the same period (from 21.6 to 20.1) (Figure).

Florida's fentanyl death rates increased approximately 250% among persons aged 14–34 years from 2010–2012

\* <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.SearchAction&SearchTerm=fentanyl&SearchType=BasicSearch>.

† <http://www.deadiversion.usdoj.gov/nflis/>.

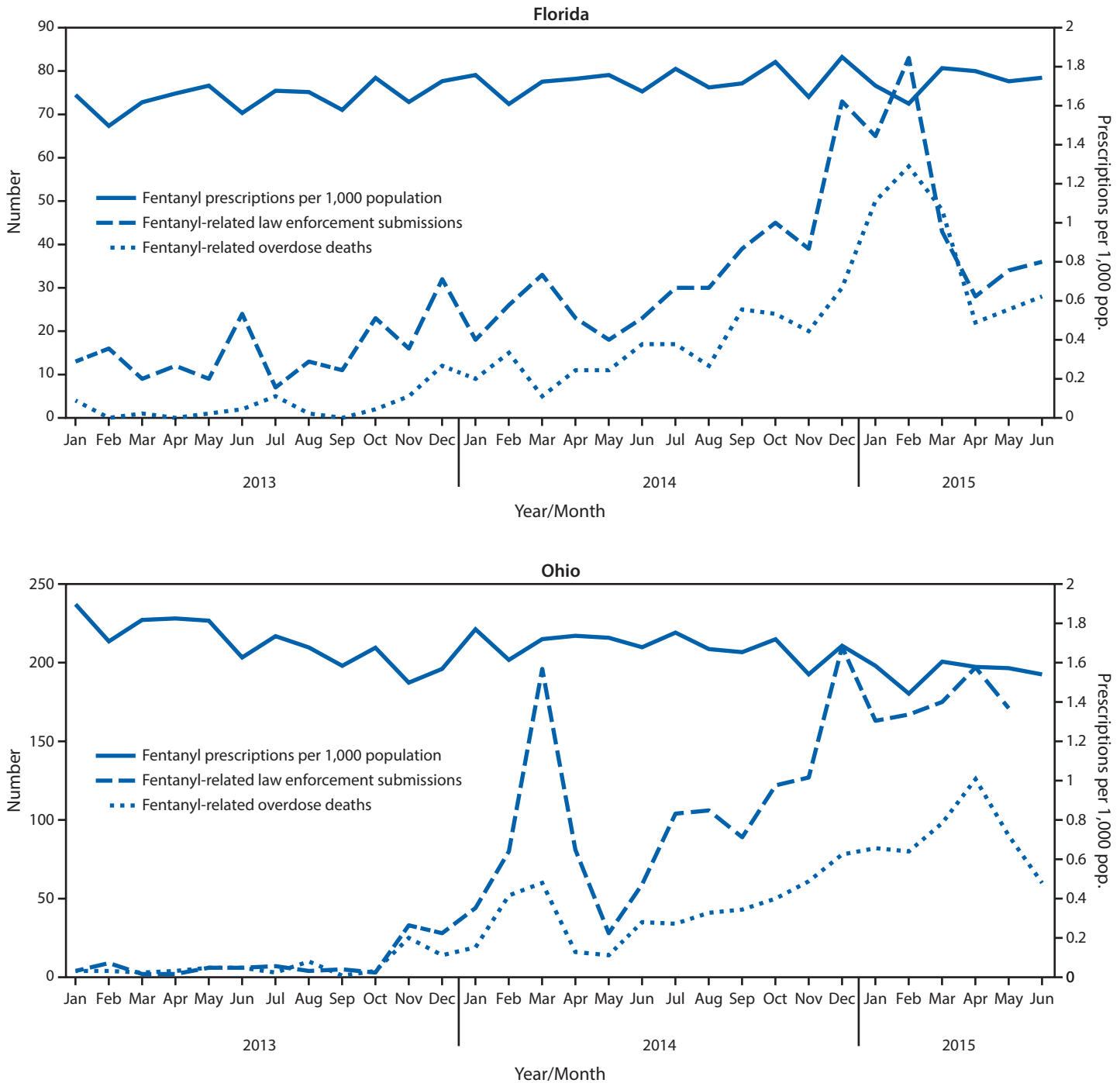
§ The decedent had been identified during the death investigation as having a mental health disorder or syndrome listed in the Diagnostic and Statistical Manual, Version IV (DSM-IV). Alcohol and other substance dependence are excluded from this variable.

¶ Additional information regarding the Electronic-Florida Online Reporting of Controlled Substance Evaluation Program (E-FORCSE) is available at <http://www.floridahealth.gov/statistics-and-data/e-forcse/>.

\*\* Additional information regarding the Ohio Automated Rx Reporting System (OARRS) is available at <https://www.ohiopmp.gov/Portal/Default.aspx>.



**FIGURE. Number of fentanyl-related law enforcement submissions\* and overdose deaths, and rate of fentanyl prescriptions — Florida and Ohio, January 2013–June 2015**



\* Drug products obtained by law enforcement that tested positive for fentanyl. Florida submissions data downloaded April 20, 2016, and Ohio data downloaded November 17, 2015, from the Drug Enforcement Administration’s National Forensic Laboratory Information System.

to 2013–2014, followed by increases among persons aged 35–50 years, males, and whites of 143.2%, 162.9%, and 122.5%, respectively (Table 1). The highest fentanyl death rates in Florida during 2013–2014 occurred among persons aged 26–34 years (3.2 per 100,000) and 35–50 years (2.9), males (2.5), and whites

(2.1). Similarly, the highest fentanyl death rates in Ohio’s 14 high-burden counties occurred among persons aged 25–34 years (10.5 per 100,000) and 35–44 years (9.2), males (5.6), and whites (4.2) as well as persons who were never married/single (8.4) and had less than a high school diploma (9.9) (Table 2).

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TABLE 1. Demographic characteristics and toxicology findings for fentanyl-related overdose decedents — Florida, 2010–2012, 2013–2014, and January–June, 2015

| Demographic characteristics/<br>Toxicology findings   | 2010–2012<br>(N = 379) |                                 | 2013–2014<br>(N = 582) |                                 | Jan–Jun 2015<br>(N = 289) | % change<br>from 2010–2012 to<br>2013–2014 |
|---|------------------------|---------------------------------|------------------------|---------------------------------|---------------------------|--|
|   | No. (%)                | Mean annual rate<br>per 100,000 | No. (%)                | Mean annual rate<br>per 100,000 | No. (%)                   |  |
| <b>Total</b>  | <b>379 (100)</b>       | <b>0.9</b>                      | <b>582 (100)</b>       | <b>1.6</b>                      | <b>289 (100)</b>          | <b>122.1*</b>                              |
| <b>Age group (yrs)</b>                                |                        |                                 |                        |                                 |                           |  |
| Mean (SD)   | 45.4 (12.3)            | —                               | 41.1 (12.1)            | —                               | 40.0 (11.6)               | —  |
| 14–25   | 26 (6.9)               | 0.3                             | 59 (10.1)              | 1.0                             | 36 (12.5)                 | 247.4*                                     |
| 26–34   | 56 (14.8)              | 0.9                             | 141 (24.2)             | 3.2                             | 70 (24.2)                 | 257.0*                                     |
| 35–50   | 147 (38.8)             | 1.2                             | 235 (40.4)             | 2.9                             | 118 (40.8)                | 143.2*                                     |
| >50   | 150 (39.6)             | 0.7                             | 147 (25.3)             | 1.0                             | 65 (22.5)                 | 37.0*                                      |
| <b>Sex</b>  |                        |                                 |                        |                                 |                           |  |
| Female  | 163 (43.0)             | 0.7                             | 189 (32.5)             | 1.1                             | 84 (29.1)                 | 67.6*                                      |
| Male  | 216 (57.0)             | 0.9                             | 393 (67.5)             | 2.5                             | 205 (70.9)                | 162.9*                                     |
| <b>Race/Ethnicity<sup>†</sup></b>                     |                        |                                 |                        |                                 |                           |  |
| White   | 359 (94.7)             | 0.9                             | 549 (94.3)             | 2.1                             | 270 (93.4)                | 122.5*                                     |
| Black   | 14 (3.7)               | Exc                             | 25 (4.3)               | 0.5                             | 16 (5.5)                  | —  |
| Other   | 6 (1.6)                | Exc                             | 8 (1.4)                | Exc                             | Exc                       | —  |
| <b>Polysubstance use at time of death<sup>§</sup></b> |                        |                                 |                        |                                 |                           |  |
| Prescription opioids <sup>¶</sup>                     | 212 (55.9)             | —                               | 243 (41.8)             | —                               | 104 (36.0)                | -25.4*                                     |
| Benzodiazepines <sup>**</sup>                         | 198 (52.2)             | —                               | 289 (49.7)             | —                               | 107 (37.0)                | -5.0                                       |
| Other substances <sup>††</sup>                        |                        |                                 |                        |                                 |                           |  |
| Morphine <sup>§§</sup>                                | 25 (6.6)               | —                               | 165 (28.4)             | —                               | 93 (32.2)                 | 329.8*                                     |
| Amphetamines  | 14 (3.7)               | —                               | 30 (5.2)               | —                               | 18 (6.2)                  | 39.5                                       |
| <b>Illicit substances</b>                             |                        |                                 |                        |                                 |                           |  |
| Cocaine or Heroin                                     | 66 (17.4)              | —                               | 242 (41.6)             | —                               | 158 (54.7)                | 139.1*                                     |
| Cocaine   | 66 (17.4)              | —                               | 190 (32.6)             | —                               | 121 (41.9)                | 87.5*                                      |
| Heroin  | 0 (0.0)                | —                               | 109 (18.7)             | —                               | 79 (27.3)                 | —  |
| Cannabinoids  | 30 (7.9)               | —                               | 61 (10.5)              | —                               | 49 (17.0)                 | 32.4                                       |
| <b>Alcohol</b>  |                        |                                 |                        |                                 |                           |  |
| Ethanol   | 75 (19.8)              | —                               | 133 (22.9)             | —                               | 63 (21.8)                 | 15.5                                       |

Abbreviations: Exc = data excluded; SD = standard deviation.

\* p<0.05.

<sup>†</sup> Information on Hispanic ethnicity was not available; thus, racial categories include Hispanics and non-Hispanics.

<sup>§</sup> Substances consistently reported to the surveillance system during study period: alprazolam, amphetamine, buprenorphine, cannabinoids, carisoprodol/meprobamate, chlordiazepoxide, clonazepam, cocaine, codeine, diazepam, estazolam, ethanol, fentanyl, flunitrazepam, flurazepam, y-hydroxybutyric acid, helium, heroin, hydrocodone, hydromorphone, ketamine, lorazepam, meperidine, methadone, methamphetamine, midazolam, morphine, nitrous oxide, nordiazepam, oxazepam, oxycodone, oxymorphone, phencyclidine, temazepam, tramadol, triazolam, and zolpidem.

<sup>¶</sup> Prescription opioids: buprenorphine, codeine, hydrocodone, hydromorphone, meperidine, methadone, oxycodone, oxymorphone, tramadol. Morphine is reported separately.

<sup>\*\*</sup> Benzodiazepines: alprazolam, chlordiazepoxide, clonazepam, diazepam, estazolam, flunitrazepam, flurazepam, lorazepam, midazolam, nordiazepam, oxazepam, temazepam, and triazolam.

<sup>††</sup> Includes drugs that are either prescription or illicit drugs.

<sup>§§</sup> Includes decedents who ingested prescription morphine and might include deaths involving heroin.

In Florida, from 2010–2012 to 2013–2014, the percentage of fentanyl deaths testing positive for other illicit substances increased significantly; in particular, fentanyl deaths testing positive for cocaine increased from 17% to 33%, and fentanyl deaths testing positive for heroin increased from 0% to 19%. This trend continued into the first half of 2015, with 55% of fentanyl decedents testing positive for heroin or cocaine compared with 42% during 2013–2014. The percentage of fentanyl deaths testing positive for morphine in Florida increased significantly from 2010–2012 (7%) to 2013–2014 (28%) (Table 1). Finally, fentanyl analogs were implicated in 49 fatal drug overdoses in Florida during January–June 2015,

including acetyl fentanyl (26), butyryl fentanyl (five), and beta-hydroxythiofentanyl (18).

In Ohio’s 14 high-burden counties, 56% of fentanyl deaths tested positive for heroin or cocaine in 2014, with 39% testing positive for heroin and 23% for cocaine (Table 2). In-depth examination of medical examiner and coroner records in these high-burden counties revealed that emergency medical services responded to 82% of fentanyl deaths, at least one bystander was present in 72% of cases, and 41% of decedents received treatment in the field with naloxone (Table 2). Other characteristics of fentanyl deaths included current diagnosed mental health disorder (25%) and recent release (within 30 days) from a jail, hospital, or treatment facility (10.3%) (Table 2).

**TABLE 2. Selected characteristics of fentanyl-related overdose decedents (N = 456) — 14 Ohio counties, 2014**

| Characteristic  | No. (%)    | Rate per 100,000 |
|---|------------|------------------|
| <b>Sex*</b>   |            |                  |
| Female  | 137 (30.0) | 2.3              |
| Male  | 319 (70.0) | 5.6              |
| <b>Race*</b>  |            |                  |
| White   | 407 (89.3) | 4.2              |
| Black   | 43 (9.4)   | 2.8              |
| <b>Age group (yrs)*</b>   |            |                  |
| 15–24   | 48 (10.5)  | 3.1              |
| 25–34   | 154 (33.8) | 10.5             |
| 35–44   | 130 (28.5) | 9.2              |
| 45–54   | 79 (17.3)  | 4.9              |
| ≥55   | 45 (9.9)   | 1.3              |
| <b>Marital status*</b>  |            |                  |
| Never married/Single  | 244 (54.0) | 8.4              |
| Divorced, separated, widowed  | 130 (28.8) | 6.8              |
| Married   | 78 (17.3)  | 1.7              |
| <b>Education (≥25 yrs)*</b>   |            |                  |
| Less than high school diploma   | 86 (21.5)  | 9.9              |
| High school or General Educational Development  | 212 (53.0) | 7.9              |
| Some college  | 58 (14.5)  | 3.6              |
| Associate's degree or higher  | 44 (11.0)  | 1.7              |
| <b>Current diagnosed mental health disorder†</b>  |            |                  |
| Yes   | 103 (25.0) | —                |
| No  | 309 (75.0) | —                |
| <b>Recent (in preceding 30 days) release from a jail, rehabilitation facility, or hospital‡</b> |            |                  |
| Overall   | 47 (10.3)  | —                |
| Jail, prison, or detention facility   | 19 (40.4)  | —                |
| Residential substance use disorder treatment  | 16 (34.0)  | —                |
| Hospital  | 9 (19.1)   | —                |
| <b>Response to fentanyl overdose¶</b>   |            |                  |
| Bystanders present  | 251 (72.3) | —                |
| Emergency medical services responded  | 375 (82.2) | —                |
| Naloxone administered   | 161 (40.8) | —                |
| <b>Polysubstance use at time of death**</b>   |            |                  |
| Tested positive for cocaine   | 105 (23.0) | —                |
| Tested positive for heroin  | 177 (38.8) | —                |

\* Because of the low number of missing values for each of these variables, percentages for these were calculated for fentanyl deaths with known information.

† "Yes" indicates that the decedent had been identified during the death investigation as having a mental health disorder or syndrome listed in the *Diagnostic and Statistical Manual, Version IV (DSM-IV)*. Alcohol and other substance dependence are excluded from this variable.

‡ Type of institution was not known for one decedent, and fewer than five decedents had been released from other types of facilities.

¶ Information was abstracted from death scene investigations and might be underestimated.

\*\* Fewer than five decedents did not have toxicology information.

## Discussion

The findings in this report suggest the need to improve fentanyl death surveillance with a focus on distinguishing deaths involving IMF and PF, and enhancing public health support of persons using heroin through increased access to medication-assisted treatment and expanded access to the opioid antagonist

naloxone. Although toxicologic panels cannot distinguish IMF from PF, the findings suggest that the surges in fentanyl deaths in Florida and Ohio during 2013–2015 were closely related to increases in the IMF supply, as opposed to diverted PF. This is supported by multiple factors including 1) the stability in prescribing and dispensing of PF in Florida and Ohio, even as fentanyl deaths sharply increased; 2) the implication of acetyl fentanyl and beta-hydroxythiofentanyl, both illicitly produced fentanyl analogs, in a significant number of fentanyl deaths in Florida; 3) recent DEA reports linking most U.S. fentanyl deaths to IMF (4); 4) demographic characteristics of fentanyl decedents in Ohio and changes in the demographic characteristics of fentanyl decedents from 2010–2012 to 2013–2014 in Florida were similar to heroin decedents nationally; and 5) interviews with persons using illicit drugs in Ohio indicating that fentanyl appears to be mixed with or sold as heroin.†† DEA reports have noted that IMF is often mixed with heroin, and then sold as a heroin product on the illicit market (1,4). In Ohio and Florida, a substantial proportion of fentanyl decedents tested positive for heroin (39% and 19%, respectively); it is likely that this represents an underascertainment, because heroin is quickly metabolized to morphine, thus morphine-positive fentanyl deaths can indicate prescription morphine or metabolism of heroin (5).

The changing demographics of fentanyl decedents in Florida from 2010–2012 to 2013–2014 and the demographics of fentanyl decedents in Ohio in 2014 mirror the evolving demographics of persons who use heroin in the United States.§§ Risk profiles changed notably during the current epidemic, with fentanyl deaths in Florida increasing almost 2.5 times faster among men (163%) than women (68%), with the most rapidly increasing rate among persons aged 14–34 years. In contrast, U.S. death rates involving prescription opioids are highest among persons aged 45–54 years, a slightly older group than this cohort of fentanyl decedents (6). In addition, the demographic of fentanyl decedents in Ohio closely matched those of heroin overdose decedents, but diverged from prescription opioid overdose decedents.

The findings in this report are subject to at least five limitations. First, since toxicologic panels cannot distinguish between PF and IMF, this study does not provide precise counts of overdoses involving IMF compared with PF. Second, the numbers and rates of fentanyl deaths are underestimated because not all overdose deaths were tested for fentanyl and testing for fentanyl analogs is not systematic statewide in either state. Third, NFLIS data might vary over time and geography because of differences or changes in law enforcement testing practices

†† <http://mha.ohio.gov/Portals/0/assets/Research/OSAM-TRI/January2015-fullReport.pdf>.

§§ <http://www.cdc.gov/nchs/products/databriefs/db190.htm>.

## Summary

### What is already known about this topic?

In 2015, the Drug Enforcement Agency and CDC issued nationwide alerts identifying increases in fentanyl-related overdose deaths (fentanyl deaths) in multiple states. Although prescription fentanyl can be diverted for misuse, most fentanyl overdoses and deaths have been linked to illicitly manufactured fentanyl (IMF), including fentanyl analogs. Multiple states that experienced increases in law enforcement submissions to laboratories of drug products that tested positive for fentanyl during 2013–2014 also reported sharp increases in fentanyl deaths.

### What is added by this report?

Analyses of 2013–2015 data from Florida and Ohio indicated that sharp increases in fentanyl deaths were associated with significant increases in the supply of IMF in these states, with fentanyl analogs detected in the Florida illicit market. Novel circumstances surrounding fentanyl mortality included current diagnosed mental health disorder and release from an institutional facility (e.g., a jail, treatment facility, or hospital) within the preceding 30 days. The risk profiles of fentanyl overdose decedents were similar to those of persons dying from heroin overdose.

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

The rapid increases in fentanyl deaths in Florida and Ohio illustrate the need to intensify efforts to expand use of naloxone. Increased naloxone access, particularly among community members, is critical given fentanyl's potency and the possibility of causing rapid death. The relationship between fentanyl deaths and increases in the supply of IMF suggests that law enforcement testing data on drug cases could serve as an early warning system to detect variations in overdose risk related to changes in the drug supply. Multidisciplinary strategies from public health agencies, harm reduction communities, emergency medical services, law enforcement, and treatment services for substance use disorders might have the greatest impact on public health, given the close relationship between fentanyl mortality and confiscation of IMF.

and enforcement activity. Fourth, part of this investigation was limited to abstraction of information collected during the medical examiner and coroner death investigation, and information collected might vary among counties within both states. Finally, analysis of medical examiner and coroner records was limited to high-burden counties in Ohio, and findings might not be generalizable to the entire state.

The rapid increase in fentanyl deaths indicates the need for timely surveillance and response. The relationship between fentanyl deaths and fentanyl submissions in both Florida and Ohio suggests that fentanyl submissions data could act as an early warning system to identify changes in the illicit drug supply. Distinguishing whether an overdose involves IMF

or PF is critical for targeted interventions because overdose risk profiles differ. Additional work is needed to determine the extent to which medical examiners and coroners can use decedents' substance use history, scene evidence (e.g., white powder consistent with IMF or patches consistent with PF), toxicology (e.g., presence of heroin or cocaine), and prescription drug monitoring program data to distinguish IMF from PF overdoses. Similar to national NFLIS data, Florida began detecting increases in fentanyl analog submissions in 2015. Because the lethality of fentanyl analogs vary, increased testing for analogs in areas experiencing large numbers of fentanyl deaths or increases in overdose deaths might be needed.

The U.S. Department of Health and Human Services has launched an initiative to reduce opioid misuse and overdose by expanding medication-assisted treatment, increasing the availability and use of naloxone, and promoting safer opioid prescribing.<sup>¶¶</sup> Past misuse of prescription opioids is the strongest risk factor for heroin initiation and use, particularly among persons who report past-year dependence or abuse (7).

The rapid increase in fentanyl deaths in Florida and Ohio illustrates the high potency of fentanyl, with the possibility of rapid death (8), highlighting the importance of quickly recognizing an overdose, calling 9-1-1 promptly, facilitating rapid administration of  $\geq 1$  naloxone doses, and the need to expand naloxone availability. The presence of bystanders in Ohio suggests the opportunity to improve overdose response including increasing support for community naloxone distribution programs. In Ohio, naloxone was administered in four of 10 cases. Multiple doses of naloxone and/or emergency medical treatment might be needed to reverse a fentanyl overdose. Community members might want to have several naloxone doses available and should be instructed to call 9-1-1 immediately, even when administering naloxone (2).<sup>\*\*\*</sup>

Linkage and access to treatment and to naloxone are needed for persons at high risk. In Ohio, a significant percentage of fentanyl deaths involved persons recently released from an institution and persons with a current diagnosed mental health disorder, placing both groups at increased risk for overdose. Persons recently released from an institution are at particularly high risk for opioid overdose because of lowered opioid tolerance resulting from abstinence during residential treatment or incarceration (9). Interventions such as provision of naloxone and continuation of medication-assisted treatment after release have been shown to be effective for this group (10).

¶¶ [https://aspe.hhs.gov/sites/default/files/pdf/107956/ib\\_OpioidInitiative.pdf](https://aspe.hhs.gov/sites/default/files/pdf/107956/ib_OpioidInitiative.pdf).  
 \*\*\* <http://store.samhsa.gov/shin/content//SMA16-4742/SMA16-4742.pdf>.



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<sup>1</sup>Epidemic Intelligence Service, CDC; <sup>2</sup>Division of Unintentional Injury Prevention, National Center for Injury Prevention and Control, CDC; <sup>3</sup>Division of Analysis, Research, and Practice Integration, National Center for Injury Prevention and Control, CDC; <sup>4</sup>Department of Health Outcomes and Policy, College of Medicine, University of Florida, Gainesville, Florida; <sup>5</sup>Division of Violence Prevention, National Center for Injury Prevention and Control, CDC; <sup>6</sup>Department of Pathology, Immunology, and Laboratory Medicine, College of Medicine, University of Florida, Gainesville, Florida; <sup>7</sup>Division of Scientific Education and Professional Development, CDC; <sup>8</sup>Ohio Department of Health.

Corresponding authors: Alexis Peterson, [apeterson4@cdc.gov](mailto:apeterson4@cdc.gov), 770-488-0767; R. Matthew Gladden, [mgladden@cdc.gov](mailto:mgladden@cdc.gov), 770-488-4276.

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## National, Regional, State, and Selected Local Area Vaccination Coverage Among Adolescents Aged 13–17 Years — United States, 2015

Sarah Reagan-Steiner, MD<sup>1</sup>; David Yankey, MS<sup>1</sup>; Jenny Jeyarajah, MS<sup>2</sup>; Laurie D. Elam-Evans, PhD<sup>1</sup>; C. Robinette Curtis, MD<sup>1</sup>; Jessica MacNeil, MPH<sup>3</sup>; Lauri E. Markowitz, MD<sup>4</sup>; James A. Singleton, PhD<sup>1</sup>

The Advisory Committee on Immunization Practices (ACIP) recommends that adolescents aged 11–12 years routinely receive vaccines to prevent diseases, including human papillomavirus (HPV)-associated cancers, pertussis, and meningococcal disease (1). To assess vaccination coverage among adolescents in the United States, CDC analyzed data collected regarding 21,875 adolescents through the 2015 National Immunization Survey-Teen (NIS-Teen).<sup>\*</sup> During 2014–2015, coverage among adolescents aged 13–17 years increased for each HPV vaccine dose among males, including  $\geq 1$  HPV vaccine dose (from 41.7% to 49.8%), and increased modestly for  $\geq 1$  HPV vaccine dose among females (from 60.0% to 62.8%) and  $\geq 1$  quadrivalent meningococcal conjugate vaccine (MenACWY) dose (from 79.3% to 81.3%). Coverage with  $\geq 1$  HPV vaccine dose was higher among adolescents living in households below the poverty level, compared with adolescents in households at or above the poverty level.<sup>†</sup> HPV vaccination coverage ( $\geq 1$ ,  $\geq 2$ , or  $\geq 3$  doses) increased in 28 states/local areas among males and in seven states among females. Despite limited progress, HPV vaccination coverage remained lower than MenACWY and tetanus, diphtheria, and acellular pertussis vaccine (Tdap) coverage, indicating continued missed opportunities for HPV-associated cancer prevention.

NIS-Teen monitors vaccination coverage among adolescents aged 13–17 years in the 50 states, District of Columbia (DC),

selected local areas, and territories<sup>§</sup> using a random-digit-dialed sample of landline and cell phone numbers.<sup>¶</sup> Through telephone interviews with adolescents' parents/guardians, information is collected on adolescent, maternal, and household sociodemographic characteristics and vaccination providers. After receiving respondent consent, questionnaires are mailed to all identified vaccination providers to obtain immunization information from medical records.<sup>\*\*</sup> All coverage estimates are based on provider-reported vaccination histories from adolescents with adequate provider data. In 2015, national estimates included information regarding 21,875 adolescents (10,508 females and 11,367 males).<sup>††</sup> NIS-Teen methodology, including methods for weighting and synthesizing provider-reported vaccination histories, has been described separately ([ftp://ftp.cdc.gov/pub/Health\\_Statistics/NCHS/Dataset\\_Documentation/NIS/NISTEENPUF14\\_DUG.pdf](ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NIS/NISTEENPUF14_DUG.pdf)). A revised adequate provider data definition was implemented in 2014 and retrospectively applied to 2013 NIS-Teen data for purposes of comparability (<http://www.cdc.gov/vaccines/imz-managers/coverage/nis/teen/apd-report.html>). Statistical comparisons were made using t-tests on weighted data to

<sup>§</sup> Local areas that received Federal Section 317 immunization funds were sampled separately: Chicago, Illinois; New York, New York; Philadelphia County, Pennsylvania; Bexar County, Texas; and Houston, Texas. Two local areas (in Texas) were oversampled: El Paso County and Hidalgo County. Three territories were sampled separately in 2015: Guam, Puerto Rico, and the U.S. Virgin Islands.

<sup>¶</sup> All identified cellular telephone households were eligible for interview. Sampling weights were adjusted for dual-frame (landline and cellular telephone), nonresponse, noncoverage, and overlapping samples of mixed telephone users. A description of NIS-Teen dual-frame survey methodology and its effect on reported vaccination estimates is available at <http://www.cdc.gov/vaccines/imz-managers/coverage/nis/child/dual-frame-sampling.html>.

<sup>\*\*</sup> The overall Council of American Survey Research Organizations (CASRO) response rate was 33.0%. Response rates for the landline and cell phone samples were 56.4% and 29.8%, respectively. For completed interviews in the states and local areas, 4,784 landline calls (53.4%) and 17,091 cell phone calls (48.9%) had adequate provider data. Overall, for states and local areas, 22% of completed interviews with adequate provider data were from landlines and 78% were from cell phones. For U.S. territories, the landline and cell phone sample CASRO rates were 52.1% and 22.6% for Guam, 57.8% and 37.4% for Puerto Rico, and 69.6% and 41.5% for the U.S. Virgin Islands, respectively. The CASRO response rate is the product of three other rates: 1) the resolution rate (the proportion of telephone numbers that can be identified as either for business or residence), 2) the screening rate (the proportion of qualified households that complete the screening process), and 3) the cooperation rate (the proportion of contacted eligible households for which a completed interview is obtained).

<sup>††</sup> Adolescents from Guam (192 females and 227 males), Puerto Rico (158 females and 181 males), and the U.S. Virgin Islands (222 females and 236 males) were excluded from the national estimates.

<sup>\*</sup> Eligible participants were born during January 1997–February 2003. Tdap represents coverage with  $\geq 1$  Tdap dose at or after age 10 years. DMenACWY represents coverage with the quadrivalent meningococcal conjugate vaccine or meningococcal-unknown type vaccine. ACIP published Category B recommendations for the use of serogroup B meningococcal (MenB) vaccines in October 2015 (<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6441a3.htm>), with administration preferred at ages 16–18 years. Coverage with MenB vaccines is not included in 2015 NIS-Teen vaccination coverage estimates. HPV vaccination coverage represents receipt of any HPV vaccine and does not distinguish among 9-valent (9vHPV), quadrivalent (4vHPV), or bivalent (2vHPV) vaccines. Some adolescents might have received more than the 3 recommended HPV vaccine doses. Except as noted, coverage estimates for  $\geq 1$  and  $\geq 2$  varicella vaccine doses were obtained among adolescents with no history of varicella disease. Influenza vaccination coverage data are not included in this report but are available online at <http://www.cdc.gov/flu/fluaxview/index.htm>.

<sup>†</sup> Adolescents were classified as being below the federal poverty level if their total family income was less than the federal poverty level specified for the applicable family size and number of children aged <18 years. All others were classified as at or above the poverty level. Poverty status was unknown for 767 adolescents (<http://www.census.gov/topics/income-poverty/poverty.html>).

account for the complex survey design. Differences were considered statistically significant at  $p < 0.05$ .

## National Vaccination Coverage

In 2015, among males, coverage with  $\geq 1$  HPV vaccine dose was 49.8% and with  $\geq 3$  doses was 28.1%; among females coverage with  $\geq 1$  dose was 62.8% and with  $\geq 3$  doses was 41.9% (Table 1) (Figure 1). During 2014–2015, among males, coverage with each HPV vaccine dose increased, with percentage point increases of 8.1 for  $\geq 1$  dose, 7.6 for  $\geq 2$  doses, and 6.5 for  $\geq 3$  doses. Among females, coverage with  $\geq 1$  HPV vaccine dose increased modestly (2.8 percentage points). Among all adolescents, coverage with  $\geq 1$  MenACWY dose increased 2.0 percentage points to 81.3%. Among adolescents aged 17 years, coverage with  $\geq 2$  MenACWY doses increased 4.8 percentage points to 33.3%; an additional 5.3% (95%

confidence interval [CI] = 4.4%–6.4%) received their first MenACWY dose on or after their 16th birthday.

In 2015, among all adolescents (females and males combined), HPV vaccination coverage with  $\geq 1$  dose was 56.1% (95% CI = 54.9%–57.4%), with  $\geq 2$  doses was 45.4% (95% CI = 44.2%–46.7%), and with  $\geq 3$  doses was 34.9% (95% CI = 33.7%–36.1%). Among all adolescents, coverage with  $\geq 1$  HPV vaccine dose was 30.3 percentage points lower than coverage with  $\geq 1$  Tdap dose and 25.2 percentage points lower than coverage with  $\geq 1$  MenACWY dose.

## Vaccination Coverage by Selected Characteristics

In 2015,  $\geq 1$ -dose HPV vaccination coverage among females aged 13 years was lower than coverage among females aged  $\geq 15$  years, but was similar among males in all age groups (Table 1). Although HPV vaccination coverage remained

**TABLE 1. Estimated vaccination coverage with selected vaccines and doses among adolescents aged 13–17\* years, by age at interview — National Immunization Survey–Teen (NIS-Teen), United States, 2015**

| Vaccine/Dose  | Age (yrs)                       |                                 |                                 |                                 |                                 | Total                              |                                    |
|---|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|------------------------------------|------------------------------------|
|   | 13<br>(n = 4,476)<br>% (95% CI) | 14<br>(n = 4,567)<br>% (95% CI) | 15<br>(n = 4,445)<br>% (95% CI) | 16<br>(n = 4,403)<br>% (95% CI) | 17<br>(n = 3,984)<br>% (95% CI) | 2015<br>(n = 21,875)<br>% (95% CI) | 2014<br>(n = 20,827)<br>% (95% CI) |
| Tdap <sup>†</sup> $\geq 1$ dose                         | 86.5 ( $\pm 2.0$ )              | 88.7 ( $\pm 1.7$ )              | 86.0 ( $\pm 2.2$ )              | 85.0 ( $\pm 2.5$ )              | 85.6 ( $\pm 2.2$ )              | 86.4 ( $\pm 1.0$ )                 | 87.6 ( $\pm 0.9$ )                 |
| MenACWY <sup>§</sup>                                    |                                 |                                 |                                 |                                 |                                 |                                    |                                    |
| $\geq 1$ dose   | 79.2 ( $\pm 2.4$ )              | 81.9 ( $\pm 2.4$ )              | 81.3 ( $\pm 2.3$ )              | 81.4 ( $\pm 2.4$ )              | 82.5 ( $\pm 2.1$ ) <sup>¶</sup> | 81.3 ( $\pm 1.0$ ) <sup>**</sup>   | 79.3 ( $\pm 1.1$ )                 |
| $\geq 2$ doses <sup>††</sup>                            | —                               | —                               | —                               | —                               | 33.3 ( $\pm 2.7$ )              | 33.3 ( $\pm 2.7$ ) <sup>**</sup>   | 28.5 ( $\pm 2.8$ )                 |
| HPV <sup>§§</sup> vaccine                               |                                 |                                 |                                 |                                 |                                 |                                    |                                    |
| Females   |                                 |                                 |                                 |                                 |                                 |                                    |                                    |
| $\geq 1$ dose   | 56.4 ( $\pm 4.2$ )              | 61.2 ( $\pm 4.0$ )              | 62.7 ( $\pm 4.0$ ) <sup>¶</sup> | 63.0 ( $\pm 3.9$ ) <sup>¶</sup> | 70.6 ( $\pm 3.5$ ) <sup>¶</sup> | 62.8 ( $\pm 1.8$ ) <sup>**</sup>   | 60.0 ( $\pm 1.9$ )                 |
| $\geq 2$ doses  | 42.6 ( $\pm 4.2$ )              | 49.0 ( $\pm 4.1$ ) <sup>¶</sup> | 53.1 ( $\pm 4.1$ ) <sup>¶</sup> | 54.2 ( $\pm 4.0$ ) <sup>¶</sup> | 61.7 ( $\pm 3.9$ ) <sup>¶</sup> | 52.2 ( $\pm 1.8$ )                 | 50.3 ( $\pm 1.9$ )                 |
| $\geq 3$ doses  | 29.5 ( $\pm 3.9$ )              | 37.3 ( $\pm 4.0$ ) <sup>¶</sup> | 44.1 ( $\pm 4.0$ ) <sup>¶</sup> | 44.2 ( $\pm 3.9$ ) <sup>¶</sup> | 54.4 ( $\pm 4.0$ ) <sup>¶</sup> | 41.9 ( $\pm 1.8$ )                 | 39.7 ( $\pm 1.9$ )                 |
| Males   |                                 |                                 |                                 |                                 |                                 |                                    |                                    |
| $\geq 1$ dose   | 48.7 ( $\pm 3.9$ )              | 47.0 ( $\pm 4.2$ )              | 51.4 ( $\pm 3.9$ )              | 51.5 ( $\pm 4.0$ )              | 50.4 ( $\pm 3.8$ )              | 49.8 ( $\pm 1.8$ ) <sup>**</sup>   | 41.7 ( $\pm 1.8$ )                 |
| $\geq 2$ doses  | 36.7 ( $\pm 3.8$ )              | 38.5 ( $\pm 4.1$ )              | 40.4 ( $\pm 3.7$ )              | 38.6 ( $\pm 3.8$ )              | 40.9 ( $\pm 3.8$ )              | 39.0 ( $\pm 1.7$ ) <sup>**</sup>   | 31.4 ( $\pm 1.7$ )                 |
| $\geq 3$ doses  | 24.9 ( $\pm 3.5$ )              | 27.7 ( $\pm 3.9$ )              | 28.6 ( $\pm 3.3$ )              | 30.6 ( $\pm 3.6$ ) <sup>¶</sup> | 28.8 ( $\pm 3.3$ )              | 28.1 ( $\pm 1.6$ ) <sup>**</sup>   | 21.6 ( $\pm 1.6$ )                 |
| MMR $\geq 2$ doses                                      | 91.5 ( $\pm 1.6$ )              | 91.4 ( $\pm 1.7$ )              | 90.7 ( $\pm 1.9$ )              | 89.1 ( $\pm 2.0$ )              | 90.7 ( $\pm 1.4$ )              | 90.7 ( $\pm 0.8$ )                 | 90.7 ( $\pm 0.8$ )                 |
| Hepatitis B vaccine $\geq 3$ doses                      | 91.0 ( $\pm 1.9$ )              | 91.8 ( $\pm 1.7$ )              | 91.7 ( $\pm 2.0$ )              | 89.7 ( $\pm 2.1$ )              | 91.4 ( $\pm 1.3$ )              | 91.1 ( $\pm 0.8$ )                 | 91.4 ( $\pm 0.7$ )                 |
| Varicella   |                                 |                                 |                                 |                                 |                                 |                                    |                                    |
| History of varicella <sup>¶¶</sup>                      | 10.9 ( $\pm 1.6$ )              | 16.5 ( $\pm 2.5$ ) <sup>¶</sup> | 15.9 ( $\pm 2.1$ ) <sup>¶</sup> | 20.5 ( $\pm 2.3$ ) <sup>¶</sup> | 25.6 ( $\pm 2.6$ ) <sup>¶</sup> | 17.8 ( $\pm 1.0$ ) <sup>**</sup>   | 21.0 ( $\pm 1.1$ )                 |
| No history of varicella                                 |                                 |                                 |                                 |                                 |                                 |                                    |                                    |
| $\geq 1$ dose vaccine                                   | 95.4 ( $\pm 1.5$ )              | 95.3 ( $\pm 1.8$ )              | 93.9 ( $\pm 2.1$ )              | 94.3 ( $\pm 1.9$ )              | 95.7 ( $\pm 1.1$ )              | 94.9 ( $\pm 0.8$ )                 | 95.2 ( $\pm 0.6$ )                 |
| $\geq 2$ doses vaccine                                  | 86.8 ( $\pm 2.0$ )              | 84.4 ( $\pm 2.4$ )              | 82.6 ( $\pm 2.6$ ) <sup>¶</sup> | 79.2 ( $\pm 2.9$ ) <sup>¶</sup> | 82.2 ( $\pm 2.3$ ) <sup>¶</sup> | 83.1 ( $\pm 1.1$ ) <sup>**</sup>   | 81.0 ( $\pm 1.2$ )                 |
| History of varicella or received $\geq 2$ doses vaccine | 88.3 ( $\pm 1.8$ )              | 86.9 ( $\pm 2.0$ )              | 85.4 ( $\pm 2.3$ )              | 83.4 ( $\pm 2.4$ ) <sup>¶</sup> | 86.8 ( $\pm 1.8$ )              | 86.1 ( $\pm 0.9$ )                 | 85.0 ( $\pm 0.9$ )                 |

**Abbreviations:** CI = confidence interval; HPV = human papillomavirus; MenACWY = quadrivalent meningococcal conjugate vaccine; MMR = measles, mumps, and rubella vaccine; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine.

\* Adolescents (n = 21,875) in the 2015 NIS-Teen were born during January 1997–February 2003.

<sup>†</sup> Includes percentages receiving Tdap vaccine at or after age 10 years.

<sup>§</sup> Includes percentages receiving MenACWY or meningococcal–unknown-type vaccine.

<sup>¶</sup> Statistically significant difference ( $p < 0.05$ ) in estimated vaccination coverage by age; reference group was adolescents aged 13 years.

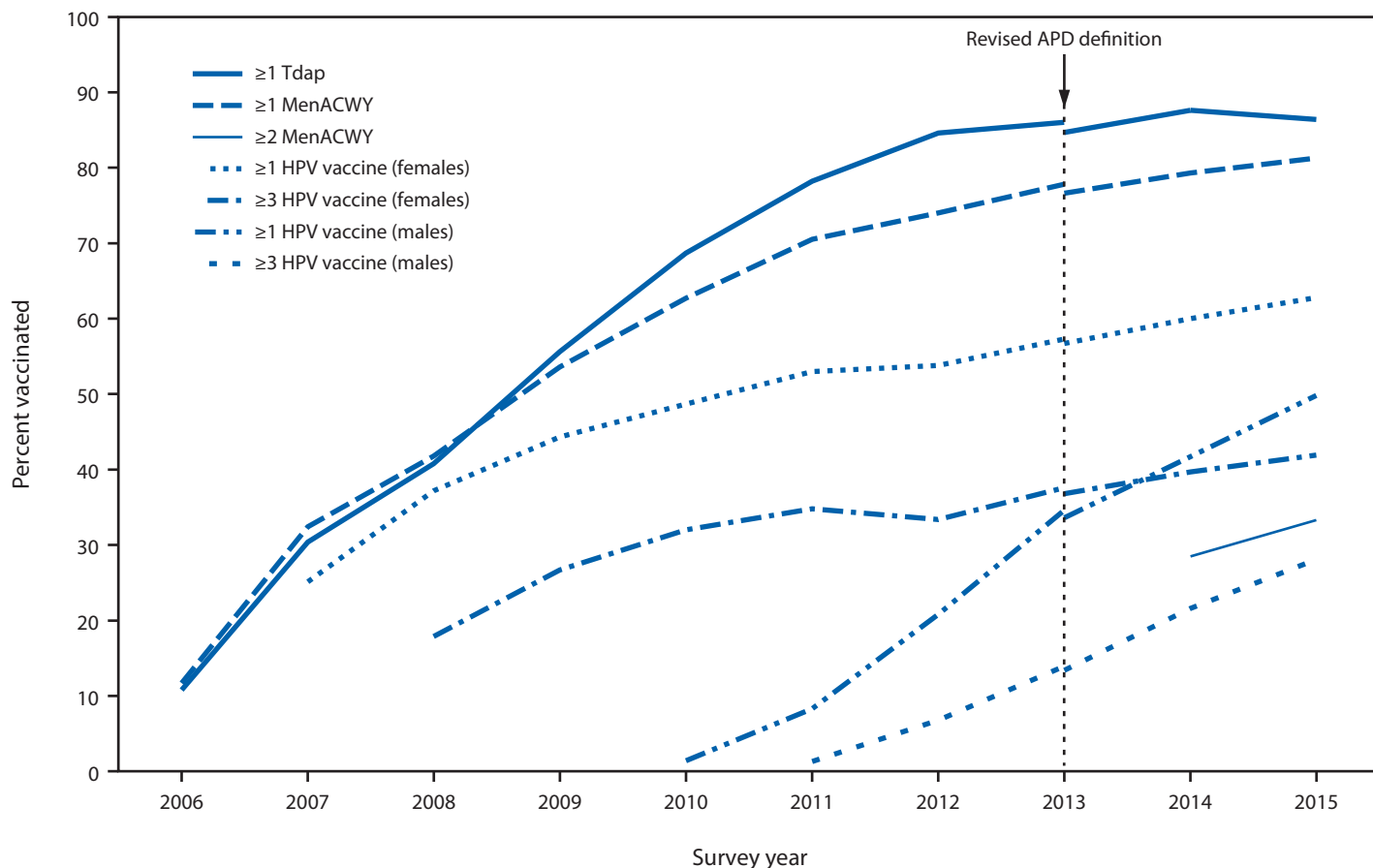
<sup>\*\*</sup> Statistically significant difference ( $p < 0.05$ ) compared with 2014 NIS-Teen estimates.

<sup>††</sup>  $\geq 2$  doses of MenACWY or meningococcal–unknown-type vaccine. Calculated only among adolescents who were 17 years of age at interview (n = 3,984); does not include adolescents who received their first dose of MenACWY vaccine at or after age 16 years.

<sup>§§</sup> HPV vaccine, 9-valent (9vHPV), quadrivalent (4vHPV), or bivalent (2vHPV). Percentages in the table are reported separately for females only (n = 10,508) and for males only (n = 11,367). Coverage with  $\geq 1$  HPV vaccine dose among all adolescents (females and males combined) aged 13–17 years was 56.1% (95% CI = 54.9%–57.4%); with  $\geq 2$  doses was 45.4% (95% CI = 44.2%–46.7%), and with  $\geq 3$  doses was 34.9% (95% CI = 33.7%–36.1%). 9vHPV, 4vHPV, or 2vHPV are recommended for females and 9vHPV or 4vHPV are recommended for males. Some adolescents might have received more than the 3 recommended HPV vaccine doses.

<sup>¶¶</sup> By parent/guardian report or provider records.

**FIGURE 1. Estimated vaccination coverage with selected vaccines and doses\* among adolescents aged 13–17 years, by survey year — National Immunization Survey-Teen, United States, 2006–2015†**



**Abbreviations:** ACIP = Advisory Committee on Immunization Practices; APD = adequate provider data; HPV = human papillomavirus; MenACWY = quadrivalent meningococcal conjugate vaccine; NIS-Teen = National Immunization Survey-Teen; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine, \* *Tdap*: ≥1 dose Tdap at or after age 10 years; ≥1 *MenACWY*: ≥1 dose MenACWY or meningococcal-unknown type vaccine; ≥2 *doses MenACWY*: ≥2 doses MenACWY or meningococcal-unknown type vaccine, calculated only among adolescents aged 17 years at time of interview (does not include adolescents who received their first dose of MenACWY at or after 16 years of age); ≥1 *HPV vaccine*: ≥1 dose HPV vaccine, 9-valent (9vHPV), quadrivalent (4vHPV) or bivalent (2vHPV); ACIP recommends 9vHPV, 4vHPV or 2vHPV for females and 9vHPV or 4vHPV for males (the routine ACIP recommendation was made for females in 2006 and for males in 2011); ≥3 *HPV vaccine*: ≥3 doses HPV vaccine.

† NIS-Teen implemented a revised APD definition in 2014 and retrospectively applied the revised APD definition to 2013 data. Estimates using different APD definitions may not be directly comparable.

higher among females than among males, the percentage point difference in coverage estimates decreased over time (Figure 1). Coverage with each HPV vaccine dose and with ≥1 MenACWY dose was higher among Hispanic adolescents than among non-Hispanic white (white) adolescents; however, coverage with ≥2 measles, mumps, and rubella vaccine (MMR) doses and ≥3 hepatitis B vaccine doses was lower among Hispanic adolescents (Table 2). Coverage with ≥1 HPV vaccine dose was higher among non-Hispanic black (black) adolescents, compared with white adolescents. Adolescents living below the federal poverty level had higher ≥1- and ≥2-dose HPV vaccination coverage than did adolescents living at or above the poverty level. Among subgroups stratified by race/ethnicity and poverty status, ≥1-dose HPV vaccination coverage was higher

among Hispanic and black adolescents living below the poverty level compared with white adolescents living at or above the poverty level, and higher for black males compared to white males among those living at or above the poverty level. §§

§§ Among females, ≥1-dose HPV vaccination coverage estimates stratified by race/ethnicity and poverty status were: 72.9% (95% CI = 63.7%–80.4%) for Hispanic females below the poverty level, 72.3% (95% CI = 65.1%–78.6%) for non-Hispanic black females below the poverty level, and 59.3% (95% CI = 56.9%–61.5%) for non-Hispanic white females at or above the poverty level (reference group). Among males, ≥1-dose HPV vaccination coverage estimates were 70.8% (95% CI = 64.2%–76.6%) for Hispanic males below the poverty level, 60.2% (95% CI = 51.9%–68.0%) for non-Hispanic black males below the poverty level, 51.9% (95% CI = 45.5%–58.3%) for non-Hispanic black males at or above the poverty level, and 43.4% (95% CI = 41.2%–45.6%) for non-Hispanic white males at or above the poverty level (reference group).



## State-Specific Vaccination Coverage

In 2015, vaccination coverage varied among the 50 states and DC (Table 3). Among males,  $\geq 1$ -dose HPV vaccination coverage ranged from 34.8% (Kentucky) to 80.6% (Rhode Island) (Figure 2), and among females, from 47.7% (Wyoming) to 87.9% (Rhode Island) (Figure 3). Among males,  $\geq 3$ -dose HPV vaccination coverage ranged from 16.0% (Tennessee) to 58.1% (Rhode Island), and among females, from 24.4% (Mississippi) to 68.0% (Rhode Island). Coverage with  $\geq 1$  Tdap

dose ranged from 69.7% (Alaska) to 97.1% (Rhode Island) and for  $\geq 1$  MenACWY dose ranged from 55.3% (Mississippi) to 97.7% (Rhode Island).

Compared with 2014, HPV vaccination coverage among males ( $\geq 1$ ,  $\geq 2$ , or  $\geq 3$  doses) increased in 28 states/local areas (e.g., range for  $\geq 1$  HPV vaccine dose = 10.5–24.7 percentage points). Among females, HPV vaccination coverage ( $\geq 1$ ,  $\geq 2$ , or  $\geq 3$  doses) increased in seven states: Hawaii ( $\geq 2$ ,  $\geq 3$  doses), Kansas ( $\geq 2$  doses), Nevada ( $\geq 1$ ,  $\geq 2$  doses), New Jersey ( $\geq 1$ ,

**TABLE 2. Estimated vaccination coverage among adolescents aged 13–17 years,\* by race/ethnicity,<sup>†</sup> poverty level,<sup>§</sup> and selected vaccines and doses — National Immunization Survey–Teen (NIS-Teen), United States, 2015**

| Vaccine/Dose  | Race/Ethnicity  |   |                                    |   |   |                                       | Poverty status                                |  |
|---|---|---|------------------------------------|---|---|---------------------------------------|---|--|
|   | White, non-Hispanic (n = 12,835)<br>% (95% CI) <sup>¶</sup> | Black, non-Hispanic (n = 2,228)<br>% (95% CI) | Hispanic (n = 4,610)<br>% (95% CI) | American Indian/Alaska Native, non-Hispanic (n = 290)<br>% (95% CI) | Asian, non-Hispanic (n = 751)<br>% (95% CI) | Multiracial (n = 1,074)<br>% (95% CI) | Below poverty level (n = 4,544)<br>% (95% CI) | At or above poverty level (n = 16,564)<br>% (95% CI) |
| <b>Tdap**<math>\geq 1</math> dose</b>                             | 86.6 ( $\pm 1.1$ )  | 86.0 ( $\pm 2.6$ )                            | 85.3 ( $\pm 2.8$ )                 | 87.6 ( $\pm 5.6$ )  | 86.0 ( $\pm 4.8$ )                          | 90.6 ( $\pm 2.7$ ) <sup>††</sup>      | 85.0 ( $\pm 2.1$ )                            | 87.0 ( $\pm 1.1$ )                                   |
| <b>MenACWY<sup>§§</sup></b>                                       |   |   |                                    |   |   |                                       |   |  |
| $\geq 1$ dose   | 79.5 ( $\pm 1.2$ )  | 81.7 ( $\pm 3.0$ )                            | 85.0 ( $\pm 2.6$ ) <sup>††</sup>   | 83.9 ( $\pm 5.9$ )  | 83.3 ( $\pm 5.3$ )                          | 80.8 ( $\pm 5.3$ )                    | 82.6 ( $\pm 2.1$ )                            | 80.5 ( $\pm 1.2$ )                                   |
| $\geq 2$ doses <sup>¶¶</sup>                                      | 30.8 ( $\pm 3.1$ )  | 33.6 ( $\pm 6.3$ )                            | 37.9 ( $\pm 8.1$ )                 | 35.0 ( $\pm 20.3$ )   | 37.1 ( $\pm 15.0$ )                         | 40.7 ( $\pm 11.3$ )                   | 36.5 ( $\pm 6.9$ )                            | 32.2 ( $\pm 2.9$ )                                   |
| <b>HPV*** vaccine</b>   |   |   |                                    |   |   |                                       |   |  |
| <b>Females</b>  |   |   |                                    |   |   |                                       |   |  |
| $\geq 1$ dose   | 59.2 ( $\pm 2.1$ )  | 66.9 ( $\pm 4.4$ ) <sup>††</sup>              | 68.4 ( $\pm 4.8$ ) <sup>††</sup>   | 70.5 ( $\pm 11.4$ )   | 63.8 ( $\pm 9.0$ )                          | 62.0 ( $\pm 8.3$ )                    | 70.0 ( $\pm 4.1$ ) <sup>†††</sup>             | 60.4 ( $\pm 2.0$ )                                   |
| $\geq 2$ doses  | 49.4 ( $\pm 2.1$ )  | 51.9 ( $\pm 4.8$ )                            | 57.8 ( $\pm 4.9$ ) <sup>††</sup>   | 55.4 ( $\pm 14.3$ )   | 58.1 ( $\pm 9.4$ )                          | 51.1 ( $\pm 8.0$ )                    | 56.6 ( $\pm 4.1$ ) <sup>†††</sup>             | 50.5 ( $\pm 2.1$ )                                   |
| $\geq 3$ doses  | 39.6 ( $\pm 2.1$ )  | 40.8 ( $\pm 4.6$ )                            | 46.2 ( $\pm 4.9$ ) <sup>††</sup>   | 38.7 ( $\pm 12.9$ )   | 53.5 ( $\pm 9.8$ ) <sup>††</sup>            | 42.5 ( $\pm 7.7$ )                    | 44.4 ( $\pm 3.9$ )                            | 41.3 ( $\pm 2.1$ )                                   |
| <b>Males</b>  |   |   |                                    |   |   |                                       |   |  |
| $\geq 1$ dose   | 43.8 ( $\pm 2.0$ )  | 54.0 ( $\pm 4.9$ ) <sup>††</sup>              | 58.9 ( $\pm 5.0$ ) <sup>††</sup>   | 58.5 ( $\pm 12.5$ ) <sup>††</sup>                                   | 49.6 ( $\pm 9.9$ )                          | 58.8 ( $\pm 6.9$ ) <sup>††</sup>      | 61.1 ( $\pm 3.9$ ) <sup>†††</sup>             | 46.0 ( $\pm 2.0$ )                                   |
| $\geq 2$ doses  | 34.9 ( $\pm 1.9$ )  | 37.1 ( $\pm 4.4$ )                            | 47.8 ( $\pm 4.9$ ) <sup>††</sup>   | 48.6 ( $\pm 12.2$ ) <sup>††</sup>                                   | 39.8 ( $\pm 10.1$ )                         | 46.8 ( $\pm 7.2$ ) <sup>††</sup>      | 46.7 ( $\pm 4.1$ ) <sup>†††</sup>             | 36.3 ( $\pm 1.9$ )                                   |
| $\geq 3$ doses  | 25.2 ( $\pm 1.7$ )  | 26.0 ( $\pm 3.8$ )                            | 35.0 ( $\pm 4.5$ ) <sup>††</sup>   | 34.6 ( $\pm 11.1$ )   | 30.7 ( $\pm 9.9$ )                          | 30.6 ( $\pm 6.4$ )                    | 31.0 ( $\pm 3.8$ )                            | 27.4 ( $\pm 1.7$ )                                   |
| <b>MMR <math>\geq 2</math> doses</b>                              | 91.7 ( $\pm 0.8$ )  | 91.9 ( $\pm 2.2$ )                            | 88.1 ( $\pm 2.2$ ) <sup>††</sup>   | 91.1 ( $\pm 4.7$ )  | 87.5 ( $\pm 4.5$ )                          | 90.5 ( $\pm 3.0$ )                    | 89.5 ( $\pm 1.8$ )                            | 90.9 ( $\pm 0.9$ )                                   |
| <b>Hepatitis B vaccine <math>\geq 3</math> doses</b>              | 92.5 ( $\pm 0.8$ )  | 92.5 ( $\pm 2.2$ )                            | 87.4 ( $\pm 2.6$ ) <sup>††</sup>   | 93.1 ( $\pm 3.9$ )  | 89.2 ( $\pm 3.9$ )                          | 90.6 ( $\pm 3.0$ )                    | 90.3 ( $\pm 1.8$ )                            | 91.1 ( $\pm 1.0$ )                                   |
| <b>Varicella</b>  |   |   |                                    |   |   |                                       |   |  |
| History of varicella <sup>§§§</sup>                               | 18.1 ( $\pm 1.2$ )  | 14.3 ( $\pm 2.2$ ) <sup>††</sup>              | 19.6 ( $\pm 3.0$ )                 | 22.3 ( $\pm 6.9$ )  | 16.4 ( $\pm 4.4$ )                          | 17.0 ( $\pm 3.8$ )                    | 18.9 ( $\pm 1.9$ )                            | 17.4 ( $\pm 1.2$ )                                   |
| No history of varicella   |   |   |                                    |   |   |                                       |   |  |
| $\geq 1$ dose vaccine   | 95.4 ( $\pm 0.8$ )  | 95.3 ( $\pm 2.3$ )                            | 93.1 ( $\pm 2.4$ )                 | 96.0 ( $\pm 2.6$ )  | 94.0 ( $\pm 3.6$ )                          | 96.7 ( $\pm 1.8$ )                    | 94.8 ( $\pm 1.7$ )                            | 94.7 ( $\pm 0.9$ )                                   |
| $\geq 2$ doses vaccine  | 82.8 ( $\pm 1.3$ )  | 84.9 ( $\pm 3.0$ )                            | 82.3 ( $\pm 3.0$ )                 | 86.9 ( $\pm 6.5$ )  | 84.5 ( $\pm 5.2$ )                          | 82.7 ( $\pm 5.8$ )                    | 85.4 ( $\pm 2.2$ ) <sup>†††</sup>             | 82.2 ( $\pm 1.3$ )                                   |
| History of varicella or received $\geq 2$ doses varicella vaccine | 85.9 ( $\pm 1.1$ )  | 87.1 ( $\pm 2.6$ )                            | 85.7 ( $\pm 2.5$ )                 | 89.8 ( $\pm 5.1$ )  | 87.1 ( $\pm 4.3$ )                          | 85.7 ( $\pm 5.0$ )                    | 88.2 ( $\pm 1.8$ ) <sup>†††</sup>             | 85.3 ( $\pm 1.1$ )                                   |

**Abbreviations:** CI = confidence interval; HPV = human papillomavirus; MenACWY = quadrivalent meningococcal conjugate vaccine; MMR = measles, mumps, and rubella vaccine; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine.

\* Adolescents (n = 21,875) in the 2015 NIS-Teen were born during January 1997–February 2003.

<sup>†</sup> Adolescents' race/ethnicity were reported by their parents or guardians. Adolescents identified in this report as white, black, Asian, American Indian/Alaska Native, or multiracial were reported by the parents or guardians as non-Hispanic. Adolescents identified as multiracial had more than one race category selected. Adolescents identified as Hispanic might be of any race. Native Hawaiian or other Pacific Islanders were not included in the table because of small sample sizes.

<sup>§</sup> Adolescents were classified as below poverty level if their total family income was less than the federal poverty level specified for the applicable family size and number of children aged <18 years. All others were classified as at or above the poverty level (<http://www.census.gov/topics/income-poverty/poverty.html>). Poverty status was unknown for 767 adolescents; these adolescents were not included in the estimates by poverty status.

<sup>¶</sup> Estimates with 95% CI half-widths >10 might not be reliable.

\*\* Includes percentages receiving Tdap vaccine at or after age 10 years.

<sup>††</sup> Statistically significant difference (p<0.05) in estimated vaccination coverage by race/ethnicity; reference group was non-Hispanic white adolescents.

<sup>§§</sup> Includes percentages receiving MenACWY and meningococcal-unknown type vaccine.

<sup>¶¶</sup>  $\geq 2$  doses of MenACWY or meningococcal-unknown type vaccine. Calculated only among adolescents who were 17 years of age at interview (n = 3,984). Does not include adolescents who received their first dose of MenACWY vaccine at or after age 16 years.

<sup>\*\*\*</sup> HPV vaccine, 9-valent (9vHPV), quadrivalent (4vHPV), or bivalent (2vHPV). Percentages are reported separately for females only (n = 10,508) and for males only (n = 11,367). 9vHPV, 4vHPV, or 2vHPV are recommended for females, and 9vHPV or 4vHPV are recommended for males. Some adolescents might have received more than the 3 recommended HPV vaccine doses.

<sup>†††</sup> Statistically significant difference (p<0.05) in estimated vaccination coverage by poverty level; reference group was adolescents living at or above poverty level.

<sup>§§§</sup> By parent/guardian report or provider records.

**TABLE 3. Estimated vaccination coverage with selected vaccines and doses\* among adolescents aged 13–17 years,† by HHS Regions and state, selected local areas, or territories — National Immunization Survey-Teen (NIS-Teen), United States, 2015**

| HHS Region/State/<br>Territory | All adolescents (n = 21,875)                     |                                       | Females (n = 10,508)               |                                    |                                   | Males (n = 11,367)                 |                                    |                                    |
|--------------------------------|--|---------------------------------------|------------------------------------|------------------------------------|-----------------------------------|------------------------------------|------------------------------------|------------------------------------|
|                                | ≥1 Tdap <sup>§</sup><br>% (95% CI) <sup>¶¶</sup> | ≥1 MenACWY <sup>¶</sup><br>% (95% CI) | ≥1 HPV <sup>**</sup><br>% (95% CI) | ≥2 HPV <sup>††</sup> % (95%<br>CI) | ≥3 HPV <sup>§</sup><br>% (95% CI) | ≥1 HPV <sup>**</sup><br>% (95% CI) | ≥2 HPV <sup>††</sup><br>% (95% CI) | ≥3 HPV <sup>§§</sup><br>% (95% CI) |
| <b>United States overall</b>   | <b>86.4 (±1.0)</b>                               | <b>81.3 (±1.0)***</b>                 | <b>62.8 (±1.8)***</b>              | <b>52.2 (±1.8)</b>                 | <b>41.9 (±1.8)</b>                | <b>49.8 (±1.8)***</b>              | <b>39.0 (±1.7)***</b>              | <b>28.1 (±1.6)***</b>              |
| <b>Region I</b>                | <b>92.3 (±2.1)</b>                               | <b>89.7 (±2.3)</b>                    | <b>73.0 (±4.6)</b>                 | <b>63.1 (±5.1)</b>                 | <b>53.7 (±5.2)</b>                | <b>65.8 (±4.6)***</b>              | <b>55.2 (±4.8)***</b>              | <b>40.8 (±4.6)***</b>              |
| Connecticut                    | 93.7 (±3.0)                                      | 93.5 (±3.1)                           | 70.9 (±6.2)                        | 64.3 (±8.7)                        | 55.2 (±9.1)                       | 65.3 (±7.8)***                     | 58.2 (±8.1)***                     | 42.0 (±8.3)***                     |
| Maine                          | 87.7 (±4.0)                                      | 77.7 (±5.3)                           | 66.0 (±8.3)                        | 53.9 (±8.7)                        | 44.1 (±8.6)                       | 65.8 (±7.9)***                     | 58.7 (±8.3)***                     | 46.7 (±8.4)***                     |
| Massachusetts                  | 91.2 (±4.1)                                      | 89.5 (±4.4)                           | 73.5 (±8.6)                        | 63.0 (±9.5)                        | 52.8 (±9.7)                       | 63.0 (±8.8)                        | 50.9 (±9.1)                        | 35.2 (±8.5)                        |
| New Hampshire                  | 92.4 (±3.9)                                      | 87.7 (±4.4)                           | 74.2 (±8.8)                        | 59.7 (±10.0)                       | 51.4 (±10.0)                      | 69.8 (±7.9)***                     | 55.1 (±9.0)                        | 47.1 (±9.1)***                     |
| Rhode Island                   | 97.1 (±1.6)***                                   | 97.7 (±1.5)                           | 87.9 (±4.9)***                     | 77.9 (±6.7)                        | 68.0 (±7.4)***                    | 80.6 (±5.8)***                     | 66.6 (±7.1)                        | 58.1 (±7.4)***                     |
| Vermont                        | 95.8 (±2.4)                                      | 84.4 (±4.3)                           | 68.7 (±8.1)                        | 59.1 (±8.3)                        | 54.4 (±8.4)                       | 66.1 (±7.6)***                     | 56.9 (±7.9)***                     | 41.1 (±7.8)                        |
| <b>Region II</b>               | <b>88.4 (±2.4)</b>                               | <b>89.3 (±2.2)***</b>                 | <b>64.5 (±5.0)***</b>              | <b>56.4 (±5.2)***</b>              | <b>46.5 (±5.3)***</b>             | <b>57.2 (±5.0)***</b>              | <b>46.8 (±5.0)***</b>              | <b>35.7 (±4.7)***</b>              |
| New Jersey                     | 87.2 (±4.4)                                      | 95.7 (±2.4)                           | 69.0 (±7.8)***                     | 56.3 (±8.6)***                     | 45.0 (±8.8)                       | 50.9 (±8.8)***                     | 41.4 (±8.7)***                     | 30.9 (±8.3)                        |
| New York (NY)                  | 89.0 (±2.9)                                      | 86.2 (±3.1)***                        | 62.3 (±6.4)                        | 56.4 (±6.5)                        | 47.3 (±6.6)                       | 60.3 (±6.1)***                     | 49.4 (±6.1)***                     | 38.1 (±6.9)***                     |
| NY-City of New York            | 90.6 (±3.5)                                      | 84.8 (±4.6)                           | 65.3 (±8.7)                        | 60.0 (±9.1)                        | 46.1 (±9.3)                       | 72.3 (±7.4)***                     | 60.1 (±8.5)***                     | 47.9 (±8.7)                        |
| NY-rest of state               | 88.0 (±4.2)                                      | 87.1 (±4.0)***                        | 60.3 (±8.8)                        | 54.1 (±9.0)                        | 48.0 (±9.1)                       | 52.6 (±8.5)                        | 42.6 (±8.3)                        | 31.7 (±7.6)                        |
| <b>Region III</b>              | <b>87.4 (±2.4)</b>                               | <b>84.6 (±2.7)</b>                    | <b>63.0 (±4.8)</b>                 | <b>53.9 (±5.0)</b>                 | <b>44.2 (±4.9)</b>                | <b>51.1 (±4.7)</b>                 | <b>43.0 (±4.6)***</b>              | <b>32.9 (±4.4)***</b>              |
| Delaware                       | 88.7 (±3.8)                                      | 87.5 (±4.1)                           | 67.6 (±8.4)                        | 60.9 (±8.9)                        | 52.8 (±9.1)                       | 62.9 (±7.6)                        | 53.2 (±8.0)                        | 43.0 (±8.0)                        |
| District of Columbia           | 81.3 (±5.0)                                      | 90.9 (±3.4)                           | 76.5 (±7.7)                        | 67.5 (±8.7)                        | 58.8 (±9.2)                       | 73.0 (±7.8)                        | 57.6 (±8.9)                        | 40.9 (±8.7)                        |
| Maryland                       | 86.5 (±4.5)                                      | 87.3 (±4.4)                           | 66.0 (±9.0)                        | 61.7 (±9.1)                        | 43.7 (±9.3)                       | 55.0 (±9.4)                        | 46.6 (±9.5)                        | 31.3 (±8.9)                        |
| Pennsylvania (PA)              | 91.7 (±2.7)                                      | 94.7 (±2.1)                           | 62.2 (±7.7)                        | 56.4 (±7.7)                        | 47.8 (±7.7)                       | 55.9 (±7.1)                        | 48.2 (±7.1)***                     | 38.3 (±6.9)***                     |
| PA-Philadelphia                | 86.1 (±4.6)                                      | 91.2 (±3.5)                           | 79.3 (±6.8)                        | 68.1 (±8.1)                        | 58.6 (±8.5)                       | 79.5 (±7.1)***                     | 61.2 (±8.6)                        | 43.4 (±9.1)***                     |
| PA-rest of state               | 92.5 (±3.0)                                      | 95.2 (±2.3)                           | 60.0 (±8.6)                        | 54.9 (±8.7)                        | 46.4 (±8.7)                       | 52.8 (±8.0)                        | 46.5 (±8.0)***                     | 37.7 (±7.8)***                     |
| Virginia                       | 82.2 (±6.4)†††                                   | 66.8 (±7.7)                           | 61.2 (±11.1)                       | 43.9 (±11.4)                       | 38.5 (±11.0)                      | 40.1 (±10.6)                       | 32.0 (±9.9)                        | 25.7 (±9.3)                        |
| West Virginia                  | 85.8 (±4.1)***                                   | 86.0 (±4.3)                           | 62.0 (±8.6)                        | 49.7 (±8.8)                        | 39.2 (±8.6)                       | 45.3 (±8.5)                        | 36.6 (±8.3)                        | 27.1 (±7.6)                        |
| <b>Region IV</b>               | <b>86.9 (±1.9)</b>                               | <b>75.1 (±2.4)</b>                    | <b>59.4 (±3.8)</b>                 | <b>45.0 (±3.9)</b>                 | <b>35.9 (±3.7)</b>                | <b>43.7 (±3.8)***</b>              | <b>33.7 (±3.6)***</b>              | <b>22.5 (±3.0)***</b>              |
| Alabama                        | 93.3 (±3.2)                                      | 72.1 (±5.8)                           | 57.7 (±9.2)                        | 50.4 (±9.3)                        | 40.8 (±9.3)                       | 39.4 (±8.6)***                     | 30.3 (±8.3)***                     | 22.6 (±7.9)***                     |
| Florida                        | 87.3 (±4.9)                                      | 70.4 (±6.4)                           | 62.5 (±9.6)                        | 44.6 (±9.7)                        | 36.8 (±9.3)                       | 45.3 (±9.9)                        | 33.2 (±9.1)                        | 19.8 (±6.9)                        |
| Georgia                        | 90.2 (±4.0)                                      | 87.0 (±4.6)***                        | 54.4 (±9.5)                        | 38.7 (±8.9)†††                     | 32.3 (±8.4)†††                    | 51.0 (±8.5)                        | 42.5 (±8.4)***                     | 27.5 (±7.6)                        |
| Kentucky                       | 84.0 (±4.7)                                      | 79.0 (±5.2)                           | 57.4 (±8.6)                        | 47.2 (±8.7)                        | 36.2 (±8.5)                       | 34.8 (±8.2)                        | 25.2 (±7.5)                        | 17.1 (±6.1)                        |
| Mississippi                    | 74.7 (±5.3)                                      | 55.3 (±6.0)***                        | 52.4 (±8.0)                        | 37.2 (±7.7)                        | 24.4 (±6.6)                       | 38.9 (±8.9)***                     | 29.6 (±8.5)***                     | 21.4 (±8.0)                        |
| North Carolina                 | 93.4 (±3.0)                                      | 78.5 (±5.1)                           | 65.7 (±8.5)                        | 53.5 (±8.9)                        | 37.8 (±8.7)†††                    | 48.0 (±8.6)                        | 40.3 (±8.5)                        | 29.8 (±8.0)                        |
| South Carolina                 | 77.8 (±5.5)                                      | 69.0 (±5.9)                           | 53.7 (±9.0)                        | 43.3 (±9.0)                        | 34.3 (±8.5)                       | 35.1 (±8.3)                        | 26.4 (±7.7)                        | 21.0 (±7.5)                        |
| Tennessee                      | 79.7 (±5.4)                                      | 76.7 (±5.6)                           | 59.7 (±8.7)                        | 46.7 (±9.0)                        | 38.9 (±8.8)***                    | 38.2 (±8.9)                        | 26.0 (±8.1)                        | 16.0 (±6.8)                        |
| <b>Region V</b>                | <b>85.8 (±1.9)</b>                               | <b>83.9 (±1.9)***</b>                 | <b>62.0 (±3.6)</b>                 | <b>50.9 (±3.6)</b>                 | <b>41.0 (±3.6)</b>                | <b>47.1 (±3.5)***</b>              | <b>36.0 (±3.3)</b>                 | <b>26.2 (±2.9)***</b>              |
| Illinois (IL)                  | 89.1 (±3.0)                                      | 79.0 (±3.8)                           | 62.0 (±5.9)                        | 52.0 (±6.1)                        | 40.2 (±6.0)                       | 44.3 (±6.3)                        | 34.3 (±6.0)                        | 26.8 (±5.6)                        |
| IL-Chicago                     | 87.2 (±4.7)                                      | 82.8 (±5.1)                           | 70.8 (±8.2)                        | 62.1 (±9.0)                        | 47.7 (±9.6)                       | 68.1 (±9.0)                        | 53.9 (±9.7)                        | 41.6 (±9.7)***                     |
| IL-rest of state               | 89.5 (±3.5)                                      | 78.1 (±4.4)                           | 60.0 (±7.0)                        | 49.9 (±7.2)                        | 38.6 (±7.0)                       | 39.1 (±7.4)                        | 29.9 (±6.9)                        | 23.6 (±6.4)                        |
| Indiana                        | 89.7 (±4.0)                                      | 92.3 (±3.4)                           | 53.7 (±9.0)                        | 43.1 (±8.8)                        | 30.9 (±8.0)†††                    | 43.2 (±9.0)***                     | 34.3 (±8.6)***                     | 27.5 (±8.1)***                     |
| Michigan                       | 74.0 (±5.5)                                      | 95.0 (±2.5)                           | 67.6 (±8.3)                        | 56.9 (±8.9)                        | 47.2 (±9.2)                       | 52.3 (±8.3)                        | 40.2 (±8.2)                        | 28.6 (±7.2)                        |
| Minnesota                      | 90.4 (±3.9)                                      | 83.6 (±4.8)***                        | 65.5 (±8.8)                        | 51.3 (±8.9)                        | 44.5 (±8.8)                       | 57.1 (±8.7)                        | 36.2 (±8.3)                        | 22.4 (±6.6)                        |
| Ohio                           | 86.7 (±5.1)                                      | 76.1 (±6.0)                           | 61.0 (±9.9)                        | 47.8 (±9.9)                        | 37.8 (±9.4)                       | 43.7 (±9.0)                        | 32.0 (±8.1)                        | 21.0 (±6.7)                        |
| Wisconsin                      | 88.0 (±4.1)                                      | 81.6 (±4.6)                           | 60.5 (±8.7)                        | 53.2 (±8.9)                        | 47.3 (±8.9)                       | 46.4 (±8.1)                        | 42.1 (±8.1)                        | 33.5 (±7.8)                        |
| <b>Region VI</b>               | <b>86.1 (±1.9)</b>                               | <b>86.4 (±1.7)</b>                    | <b>60.5 (±3.8)***</b>              | <b>50.2 (±3.9)</b>                 | <b>39.5 (±3.7)</b>                | <b>44.1 (±3.6)</b>                 | <b>34.7 (±3.3)***</b>              | <b>26.0 (±3.0)***</b>              |
| Arkansas                       | 91.2 (±3.4)***                                   | 81.5 (±4.6)***                        | 63.5 (±8.4)                        | 49.4 (±8.9)                        | 34.0 (±8.4)                       | 44.2 (±8.1)                        | 28.9 (±7.2)                        | 16.4 (±5.8)                        |
| Louisiana                      | 91.0 (±3.4)                                      | 90.9 (±3.6)                           | 60.3 (±8.6)                        | 53.3 (±8.9)                        | 39.3 (±8.8)                       | 49.5 (±7.9)                        | 39.1 (±7.8)                        | 30.5 (±7.4)                        |
| New Mexico                     | 85.9 (±4.2)                                      | 72.5 (±5.3)                           | 66.7 (±7.6)                        | 55.6 (±7.8)                        | 40.6 (±7.5)                       | 54.3 (±8.5)                        | 49.9 (±8.5)***                     | 40.3 (±8.2)***                     |
| Oklahoma                       | 84.4 (±4.8)                                      | 68.1 (±6.4)                           | 58.1 (±10.0)                       | 43.4 (±9.9)                        | 32.2 (±9.1)                       | 52.9 (±8.9)                        | 40.1 (±9.0)                        | 35.7 (±8.9)***                     |
| Texas (TX)                     | 85.1 (±2.6)                                      | 89.6 (±2.2)                           | 60.1 (±5.1)***                     | 50.4 (±5.2)                        | 40.9 (±5.0)                       | 41.4 (±4.8)                        | 32.9 (±4.4)                        | 24.0 (±3.8)                        |
| TX-Bexar County                | 85.7 (±4.5)                                      | 88.5 (±4.3)                           | 56.2 (±8.5)                        | 46.5 (±8.6)                        | 32.8 (±8.2)                       | 40.3 (±9.0)                        | 28.9 (±8.3)                        | 19.9 (±7.2)                        |
| TX-City of Houston             | 83.3 (±5.3)                                      | 87.2 (±4.8)                           | 66.9 (±10.1)                       | 58.1 (±10.7)                       | 42.8 (±10.8)                      | 58.6 (±9.6)                        | 46.4 (±10.0)                       | 22.7 (±8.0)                        |
| TX-El Paso County              | 83.4 (±3.9)                                      | 85.5 (±3.8)†††                        | 75.4 (±6.6)                        | 64.6 (±7.1)                        | 52.2 (±7.4)                       | 60.7 (±7.2)                        | 47.8 (±7.2)                        | 34.4 (±6.6)                        |
| TX-Hidalgo County              | 81.3 (±4.0)                                      | 88.8 (±3.3)                           | 66.9 (±6.7)                        | 56.7 (±7.1)                        | 40.7 (±7.0)                       | 52.3 (±7.3)                        | 43.7 (±7.2)                        | 34.1 (±6.8)                        |
| TX-rest of state               | 85.4 (±3.2)                                      | 90.1 (±2.7)                           | 58.9 (±6.4)                        | 49.1 (±6.4)                        | 41.0 (±6.3)                       | 38.7 (±5.8)                        | 30.9 (±5.3)                        | 23.5 (±4.7)                        |
| <b>Region VII</b>              | <b>86.3 (±2.6)***</b>                            | <b>70.7 (±3.4)***</b>                 | <b>60.2 (±5.1)***</b>              | <b>49.3 (±5.3)***</b>              | <b>37.9 (±5.1)</b>                | <b>44.8 (±5.0)***</b>              | <b>34.6 (±4.8)***</b>              | <b>24.4 (±4.5)***</b>              |
| Iowa                           | 85.5 (±4.6)***                                   | 75.0 (±5.3)***                        | 66.7 (±8.0)                        | 62.3 (±8.2)                        | 49.8 (±8.6)                       | 48.0 (±8.7)***                     | 37.0 (±8.2)                        | 23.9 (±7.2)                        |
| Kansas                         | 87.3 (±4.2)***                                   | 63.7 (±5.9)                           | 50.9 (±8.8)                        | 43.6 (±8.6)***                     | 31.7 (±8.0)                       | 36.0 (±8.1)                        | 26.3 (±7.4)                        | 18.5 (±6.7)                        |
| Missouri                       | 85.7 (±4.9)                                      | 69.7 (±6.5)                           | 59.3 (±10.0)                       | 43.4 (±10.4)                       | 31.5 (±9.7)                       | 44.7 (±9.8)***                     | 33.7 (±9.5)***                     | 25.1 (±9.1)***                     |
| Nebraska                       | 87.7 (±4.1)                                      | 78.1 (±4.8)                           | 67.3 (±7.9)                        | 55.5 (±8.5)                        | 48.2 (±8.6)                       | 54.3 (±7.9)***                     | 46.9 (±7.8)***                     | 32.2 (±7.2)                        |
| <b>Region VIII</b>             | <b>87.5 (±2.2)</b>                               | <b>76.6 (±2.7)***</b>                 | <b>57.8 (±4.9)</b>                 | <b>47.9 (±4.9)</b>                 | <b>36.8 (±4.7)</b>                | <b>52.0 (±4.8)***</b>              | <b>42.6 (±5.0)***</b>              | <b>28.7 (±4.7)***</b>              |
| Colorado                       | 93.3 (±2.9)                                      | 85.6 (±4.3)***                        | 65.3 (±8.2)                        | 57.7 (±8.6)                        | 46.0 (±8.7)                       | 63.2 (±8.4)***                     | 52.7 (±9.0)***                     | 37.1 (±8.8)***                     |
| Montana                        | 89.5 (±3.7)                                      | 65.8 (±5.4)                           | 55.0 (±8.5)                        | 41.8 (±8.3)                        | 34.8 (±8.0)                       | 46.0 (±8.0)***                     | 33.3 (±7.7)***                     | 21.7 (±6.8)                        |
| North Dakota                   | 88.9 (±4.5)                                      | 91.6 (±4.0)                           | 70.5 (±8.2)                        | 60.9 (±9.0)                        | 47.1 (±9.1)                       | 62.3 (±8.9)***                     | 53.1 (±9.1)***                     | 38.4 (±8.6)***                     |
| South Dakota                   | 72.4 (±5.8)                                      | 55.5 (±6.3)                           | 53.2 (±9.1)                        | 42.3 (±8.9)                        | 32.4 (±8.7)                       | 39.2 (±8.5)                        | 28.6 (±7.8)                        | 22.0 (±7.2)                        |

See table footnotes on next page.

**TABLE 3. (Continued) Estimated vaccination coverage with selected vaccines and doses\* among adolescents aged 13–17 years,† by HHS Regions and state, selected local areas, or territories — National Immunization Survey-Teen (NIS-Teen), United States, 2015**

| HHS Region/State/<br>Territory | All adolescents (n = 21,875)                     |                                       | Females (n = 10,508)               |                                    |                                    | Males (n = 11,367)                 |                                    |                                    |
|--------------------------------|--|---------------------------------------|------------------------------------|------------------------------------|------------------------------------|------------------------------------|------------------------------------|------------------------------------|
|                                | ≥1 Tdap <sup>§</sup><br>% (95% CI) <sup>¶¶</sup> | ≥1 MenACWY <sup>¶</sup><br>% (95% CI) | ≥1 HPV <sup>**</sup><br>% (95% CI) | ≥2 HPV <sup>††</sup> % (95%<br>CI) | ≥3 HPV <sup>§§</sup><br>% (95% CI) | ≥1 HPV <sup>**</sup><br>% (95% CI) | ≥2 HPV <sup>††</sup><br>% (95% CI) | ≥3 HPV <sup>§§</sup><br>% (95% CI) |
| Utah                           | 82.0 (±5.2)                                      | 71.5 (±5.8)                           | 47.8 (±9.4)                        | 35.9 (±8.8)                        | 24.6 (±7.7)                        | 40.9 (±8.9)***                     | 33.7 (±8.7)***                     | 19.9 (±7.6)                        |
| Wyoming                        | 87.9 (±4.1)                                      | 58.7 (±6.4)                           | 47.7 (±9.6)                        | 37.6 (±9.4)                        | 26.5 (±8.7)                        | 37.1 (±8.8)                        | 30.8 (±8.5)***                     | 18.8 (±6.9)                        |
| <b>Region IX</b>               | <b>83.3 (±4.4)</b>                               | <b>78.7 (±4.6)</b>                    | <b>67.3 (±7.6)</b>                 | <b>59.2 (±7.8)</b>                 | <b>47.6 (±7.8)</b>                 | <b>56.8 (±7.7)</b>                 | <b>41.3 (±7.6)</b>                 | <b>29.0 (±7.1)</b>                 |
| Arizona                        | 86.6 (±3.8)                                      | 87.6 (±3.8)                           | 68.3 (±7.4)                        | 56.1 (±8.1)                        | 44.2 (±8.3)                        | 51.3 (±8.2)                        | 40.6 (±8.2)***                     | 27.0 (±7.3)***                     |
| California                     | 82.5 (±5.6)                                      | 77.2 (±5.9)                           | 66.7 (±9.6)                        | 59.7 (±9.9)                        | 48.4 (±9.9)                        | 58.5 (±9.8)                        | 41.8 (±9.7)                        | 29.5 (±9.0)                        |
| Hawaii                         | 79.6 (±4.9)                                      | 78.7 (±5.0)                           | 71.3 (±8.0)                        | 64.1 (±8.4)***                     | 52.4 (±8.8)***                     | 62.5 (±8.0)                        | 50.2 (±8.4)                        | 36.2 (±8.1)                        |
| Nevada                         | 88.3 (±4.3)                                      | 78.0 (±5.3)***                        | 72.0 (±7.8)***                     | 57.6 (±9.0)***                     | 42.5 (±9.2)                        | 44.5 (±8.8)                        | 31.9 (±8.1)                        | 23.7 (±7.2)                        |
| <b>Region X</b>                | <b>85.3 (±2.7)</b>                               | <b>75.1 (±3.2)</b>                    | <b>65.3 (±5.0)</b>                 | <b>53.4 (±5.2)</b>                 | <b>43.6 (±5.2)</b>                 | <b>49.5 (±5.0)</b>                 | <b>41.9 (±5.0)***</b>              | <b>29.5 (±4.6)***</b>              |
| Alaska                         | 69.7 (±5.8)                                      | 55.7 (±6.2)                           | 57.0 (±8.7)                        | 46.3 (±8.7)                        | 36.9 (±8.4)                        | 41.6 (±8.5)                        | 30.3 (±7.8)                        | 18.8 (±6.4)                        |
| Idaho                          | 82.5 (±5.2)***                                   | 81.4 (±5.2)                           | 57.3 (±8.9)                        | 43.5 (±9.0)                        | 30.3 (±8.2)                        | 44.2 (±8.9)                        | 36.4 (±8.6)***                     | 26.4 (±7.9)                        |
| Oregon                         | 89.4 (±3.8)                                      | 75.2 (±5.5)                           | 70.0 (±8.1)                        | 55.4 (±9.0)                        | 48.9 (±9.0)                        | 58.6 (±8.4)***                     | 48.2 (±8.7)***                     | 35.7 (±8.5)***                     |
| Washington                     | 85.3 (±4.5)                                      | 75.4 (±5.1)                           | 65.8 (±8.1)                        | 55.8 (±8.4)                        | 45.1 (±8.4)                        | 46.8 (±8.0)                        | 41.2 (±7.8)                        | 28.0 (±7.1)                        |
| <b>Range<sup>§§§</sup></b>     | <b>(69.7–97.1)</b>                               | <b>(55.3–97.7)</b>                    | <b>(47.7–87.9)</b>                 | <b>(35.9–77.9)</b>                 | <b>(24.4–68.0)</b>                 | <b>(34.8–80.6)</b>                 | <b>(25.2–66.6)</b>                 | <b>(16.0–58.1)</b>                 |
| <b>Territory</b>               |  |                                       |                                    |                                    |                                    |                                    |                                    |                                    |
| Guam                           | 79.6 (±4.6)                                      | 76.2 (±4.8)                           | 68.9 (±7.8)                        | 50.5 (±8.3)                        | 37.0 (±7.9)                        | 52.2 (±7.8)                        | 38.0 (±7.6)                        | 22.4 (±6.4)                        |
| Puerto Rico                    | 82.5 (±5.2)                                      | 87.9 (±4.3)                           | 77.4 (±7.8)                        | 52.7 (±9.7)                        | 42.0 (±9.4)                        | 68.1 (±8.6)                        | 44.3 (±9.1)                        | 30.8 (±8.7)                        |
| U.S. Virgin Islands            | 82.0 (±4.0)                                      | 56.0 (±5.4)                           | 40.4 (±7.7)                        | 25.8 (±6.9)                        | 16.4 (±5.9)                        | 35.5 (±7.1)                        | 18.6 (±5.5)                        | 11.8 (±4.6)                        |

**Abbreviations:** CI = confidence interval; HHS = U.S. Department of Health and Human Services; HPV = human papillomavirus; MenACWY = quadrivalent meningococcal conjugate vaccine; MMR = measles, mumps, rubella vaccine; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine.

\* Estimates for additional measures, including MMR, hepatitis B, and varicella vaccines are available (<http://www.cdc.gov/vaccines/vaxview/teenvaxview>).

† Adolescents (n = 21,875) in the 2015 NIS-Teen were born during January 1997–February 2003.

§ ≥1 dose Tdap at or after age 10 years.

¶ ≥1 dose of MenACWY or meningococcal-unknown type vaccine.

\*\* ≥1 dose HPV vaccine, 9-valent (9vHPV), quadrivalent (4vHPV), or bivalent (2vHPV). Percentages are reported separately for females only (n = 10,508) and males only (n = 11,367). 9vHPV, 4vHPV, or 2vHPV are recommended for females, and 9vHPV or 4vHPV are recommended for males.

†† ≥2 doses of HPV vaccine, including 9vHPV, 4vHPV or 2vHPV.

§§ ≥3 doses of HPV vaccine, including 9vHPV, 4vHPV or 2vHPV. Some adolescents might have received more than the 3 recommended HPV vaccine doses.

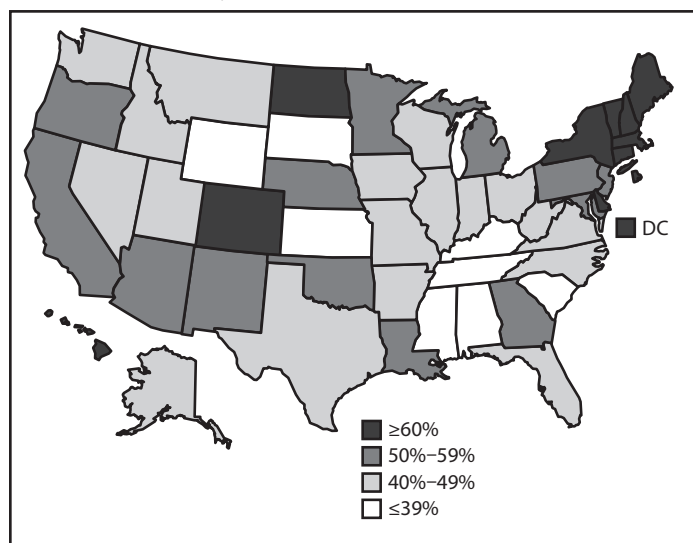
¶¶ Estimates with 95% CI half-widths >10 might not be reliable.

\*\*\* Statistically significant (p<0.05) percentage point increase from 2014.

††† Statistically significant (p<0.05) percentage point decrease from 2014.

§§§ Range excludes all selected local areas and territories.

**FIGURE 2. Estimated vaccination coverage with ≥1 dose of HPV vaccine\* among male adolescents aged 13–17 years† — National Immunization Survey-Teen,<sup>§</sup> United States, 2015**



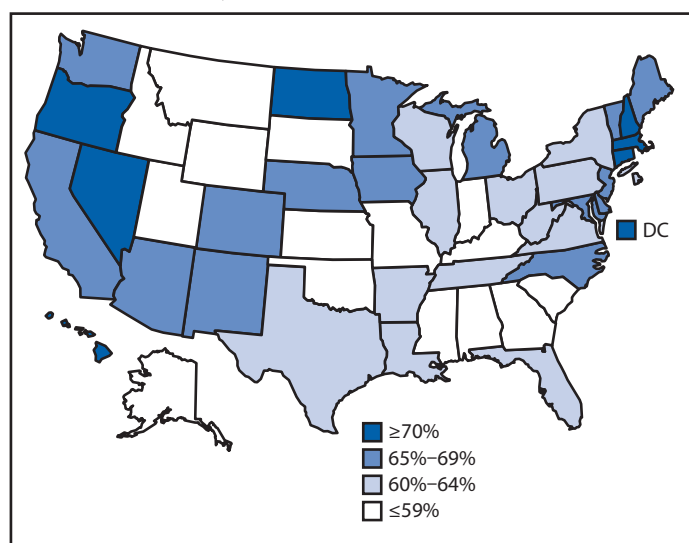
**Abbreviation:** HPV = human papillomavirus.

\* The Advisory Committee on Immunization Practices recommends 9-valent or quadrivalent HPV vaccine for males.

† National coverage = 50% (n = 11,367); percentages reported among males only.

§ Includes male adolescents born January 1997 through February 2003.

**FIGURE 3. Estimated vaccination coverage with ≥1 dose of HPV vaccine\* among female adolescents aged 13–17 years† — National Immunization Survey-Teen,<sup>§</sup> United States, 2015**



**Abbreviation:** HPV = human papillomavirus.

\* The Advisory Committee on Immunization Practices recommends 9-valent, quadrivalent, or bivalent HPV vaccine for females.

† National coverage = 63% (n = 10,508); percentages reported among females only.

§ Includes female adolescents born January 1997 through February 2003.

≥2 doses), Rhode Island (≥1, ≥3 doses), Tennessee (≥3 doses), and Texas (≥1 dose) (e.g., range for ≥1 HPV vaccine dose = 9.4–21.0 percentage points). Three states experienced decreases in ≥3-dose HPV vaccination coverage among females (Georgia, Indiana, and North Carolina; range = 13.5–16.2 percentage points). No decreases in HPV vaccination coverage were observed among males.

### Healthy People 2020 Targets Among Adolescents Aged 13–15 Years

In 2015, the *Healthy People 2020* target (80%) for adolescents aged 13–15 years<sup>¶¶</sup> was met nationally for the fifth survey year for ≥1 dose of Tdap (87.1% [95% CI = 85.9%–88.2%]) and, for the first survey year, for ≥1 dose of MenACWY (80.8% [95% CI = 79.4%–82.1%]). Targets were not met for ≥3 HPV doses (target 80%) in males (27.1% [95% CI = 25.1%–29.2%]) or females (37.1% [95% CI = 34.8%–39.5%]) or ≥2 varicella vaccine doses (target = 90%) (84.6% [95% CI = 83.2%–85.9%]).

### Discussion

In 2015, coverage with each HPV vaccine dose increased among males, however, among females, ≥1-dose HPV vaccination coverage increased only modestly, and no change was observed in coverage with ≥2 and ≥3 HPV doses. During 2015, as in previous years, coverage with ≥1 HPV vaccine dose was lower than coverage with Tdap and MenACWY, two other vaccines routinely recommended at age 11–12 years. These gaps in coverage demonstrate ongoing missed opportunities for HPV vaccination at visits when other recommended vaccines are administered. A revised Healthcare Effectiveness Data and Information Set (HEDIS) measure will be implemented in 2017 to assess receipt of Tdap, MenACWY, and HPV vaccines by age 13 years in both females and males combined in one composite indicator (2), enabling health plans to evaluate their performance in administering these vaccines to adolescents.

Each year in the United States, an estimated 24,600 newly diagnosed cancers are attributable to the two high-risk HPV types targeted by all currently licensed HPV vaccines, and an additional 3,800 are attributable to the five additional high-risk HPV types included in the 9-valent HPV vaccine (3). Improvement in HPV vaccination coverage among adolescents

### Summary

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

To prevent diseases, including human papillomavirus (HPV)-associated cancers, pertussis, and meningococcal disease, routine immunization of adolescents aged 11–12 years is recommended by the Advisory Committee on Immunization Practices. During 2006–2014, national coverage with ≥1 dose of tetanus-diphtheria-acellular pertussis vaccine (Tdap) and ≥1 dose of quadrivalent meningococcal conjugate vaccine (MenACWY) increased annually. Since 2007, among females, HPV vaccination coverage has lagged behind Tdap and MenACWY coverage, with gaps of 28 and 17 percentage points, respectively, in 2014. HPV vaccination coverage among males has increased annually since 2011, but remains lower than coverage among females.

#### What is added by this report?

In 2015, vaccination coverage among adolescents aged 13–17 years increased for each HPV vaccine dose among males, ≥1 HPV vaccine dose among females, and ≥1 MenACWY among all adolescents. HPV vaccination coverage continues to be lower than Tdap and MenACWY coverage. Wide variation in coverage by state was observed for all vaccines assessed. In 2015, 28 states and local areas achieved increases in HPV vaccination coverage among males, and seven states achieved increases among females.

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

Although national-level ≥1-dose HPV vaccination coverage increased in 2015 among adolescents, it remained lower than Tdap and MenACWY coverage. This suggests that HPV vaccine is not being routinely administered at visits when other recommended vaccines are given, and demonstrates ongoing missed opportunities for the prevention of HPV-associated outcomes, including cancers. Routine age-appropriate administration of all recommended vaccines to adolescents aged 11–12 years, and strong, consistent recommendations by clinicians are important to maintaining high vaccination coverage for Tdap and MenACWY vaccines and improving HPV vaccination coverage.

is needed to decrease the number of future HPV-associated cancers (4). Strong clinician recommendations for HPV vaccination, and coadministration of the first HPV vaccine dose with Tdap and MenACWY vaccine at age 11–12 years during the same visit, would improve HPV vaccination coverage. Reasons for low HPV vaccination coverage, particularly among younger adolescents, include lack of a strong clinician recommendation for HPV vaccine at age 11–12 years, recommending vaccination inconsistently based on perceived risk for adolescents' HPV exposure, or not recommending coadministration of routine vaccines (5,6). Clinicians also might overestimate parental concerns and underestimate HPV vaccine demand (7). Resources for clinicians to facilitate optimal communication with parents and adolescents regarding HPV and other recommended vaccines are available at <http://www.cdc.gov/hpv/>.

<sup>¶¶</sup> *Healthy People 2020* targets for vaccination coverage among adolescents aged 13–15 years are 80.0% for ≥1 Tdap, ≥1 MenACWY, and ≥3 HPV vaccine doses among females and males, and 90.0% for ≥2 varicella vaccine doses (<https://www.healthypeople.gov/2020/topics-objectives/topic/immunization-and-infectious-diseases/objectives>). State and selected local area-level coverage estimates for vaccines included in the *Healthy People 2020* objectives among adolescents aged 13–15 years will be available at <http://www.cdc.gov/vaccines/vaxview/teenvaxview>.



At a national level,  $\geq 1$  and  $\geq 2$  HPV and  $\geq 2$  varicella vaccination coverage estimates among adolescents living below the federal poverty level were higher than among those living at or above the poverty level. Coverage with other vaccines was similar by poverty status. Differences in HPV vaccination coverage by race/ethnicity and poverty status have been observed previously (8). Higher HPV vaccination coverage among adolescents living below the poverty level might, in part, be because of the routine provision of strong recommendations for HPV vaccination and consistent coadministration of vaccines by clinicians caring for adolescents from lower income households (5,6). Other factors might include clinicians' participation in, and adolescents' eligibility for, the Vaccines for Children (VFC) program<sup>\*\*\*</sup> and differential vaccine acceptance by poverty status.

Many states and local areas achieved increases in HPV vaccination coverage. In 2014–2015, CDC provided technical assistance and Prevention and Public Health Fund (PPHF) resources to immunization programs and national partner organizations to implement interventions for improving HPV vaccination coverage.<sup>†††</sup> Activities included clinician education, clinical practice quality improvement strategies (e.g., CDC's Assessment, Feedback, Incentives, and eXchange programmatic initiative [<http://www.cdc.gov/vaccines/programs/afix/index.html>]), patient reminder/recall (9), communication campaigns, and stakeholder engagement.<sup>†††</sup> Measurable impact of quality improvement activities at a clinical practice level can be achieved in short time horizons, but the impact of programmatic interventions on population-level vaccination coverage outcomes can take time to occur and be difficult to sustain. Also, because NIS-Teen assesses vaccination coverage among adolescents aged 13–17 years, the impact of activities targeted at improving HPV vaccination at the recommended age of 11–12 years will not be measurable until at least 1–2 years after implementation. However, evidence suggests that multifaceted interventions that emphasize providing strong recommendations for routine, on-time vaccination at age 11–12 years might be effective in improving HPV vaccination delivery (9,10).

<sup>\*\*\*</sup> Children and adolescents aged  $\leq 18$  years who are Medicaid-eligible, uninsured, or American Indian/Alaska Native (as defined by the Indian Health Care Improvement Act) are eligible to receive vaccines from providers through the VFC program. Children categorized as "underinsured" (because their health plans do not include coverage for recommended vaccinations) are eligible to receive VFC vaccines if they are served by a rural health clinic or federally qualified health center or under an approved deputization agreement. (<http://www.cdc.gov/vaccines/programs/vfc/providers/eligibility.html>).

<sup>†††</sup> CDC provided PPHF resources to 22 state and local immunization programs, the Academic Pediatric Association, American Academy of Pediatrics, American Cancer Society, the National Area Health Education Center Organization, and National Association of County and City Health Officials (<http://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2015-10/hpv-03-curtis.pdf>).

The findings in this report are subject to at least five limitations. First, the overall household response rate was 33.0% (56.4% for the landline and 29.8% for the cell phone samples), and only 53.4% of landline-completed and 48.9% of cell phone-completed interviews had adequate provider data. Second, bias in estimates might remain even after adjustment for household and provider nonresponse and phoneless households.<sup>§§§</sup> Weights have been adjusted for the increasing number of cell phone-only households over time. Nonresponse bias might change, which could affect comparisons of estimates between survey years. Third, estimates stratified by state/local area and those stratified by race/ethnicity might be unreliable because of small sample sizes. Fourth, multiple statistical tests were conducted, and a small number might be significant because of chance alone. Finally,  $\geq 2$ -dose MenACWY coverage likely underestimates the proportion of adolescents who receive  $\geq 2$  MenACWY doses. Adolescents might receive their second MenACWY dose after age 17 years (1); because NIS-Teen includes adolescents aged 13–17 years, receipt of MenACWY at age  $\geq 18$  years cannot be captured in coverage estimates.

Widespread improvement in HPV vaccination coverage among males was observed in 2015 suggesting that clinicians are increasingly administering HPV vaccine to males in accordance with ACIP recommendations. However, HPV vaccination coverage among adolescents remains lower than vaccination coverage with Tdap and the first MenACWY vaccine dose, demonstrating that HPV vaccine is not consistently coadministered with other recommended vaccines, and that missed opportunities for HPV-associated cancer prevention are occurring. A revised HEDIS measure planned for implementation in 2017 will enable improved assessment of receipt of Tdap, MenACWY, and HPV vaccines by age 13 years among adolescents covered by U.S. health plans (2). Resources are available to help clinicians effectively communicate with parents and adolescents regarding the importance of HPV vaccination. Tools are available for immunization programs and partner organizations, including cancer prevention stakeholders, to improve awareness of and demand for vaccines recommended for adolescents, including HPV vaccine. Interventions aimed at improving HPV vaccination coverage are ongoing. To optimize protection of adolescents against vaccine-preventable diseases, including HPV-associated cancers, it is important for clinicians to consistently recommend and coadminister Tdap, MenACWY, and HPV vaccines at age 11–12 years.

<sup>§§§</sup> A total survey error model of 2011 NIS-Teen that included comparison with provider-reported data from National Health Interview Survey participants indicated coverage estimates were 2.9–5.9 percentage points higher as a result of noncoverage and household nonresponse error; however, these estimates of bias might be too high because they do not account for possible underascertainment of vaccination status (<http://www.amstat.org/meetings/jsm/2012/onlineprogram/abstractdetails.cfm?abstractid=304324> and <http://www.cdc.gov/vaccines/imz-managers/coverage/nis/child/downloads/total-survey-error-NIS-2011.pdf>).

<sup>1</sup>Immunization Services Division, National Center for Immunization and Respiratory Diseases, CDC; <sup>2</sup>Carter Consulting, Inc., Atlanta, Georgia; <sup>3</sup>Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, CDC; <sup>4</sup>Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, CDC.

Corresponding author: Sarah Reagan-Steiner, sreagansteiner@cdc.gov, 404-639-2811.

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## Fractional-Dose Inactivated Poliovirus Vaccine Immunization Campaign — Telangana State, India, June 2016

Sunil Bahl, MD<sup>1</sup>; Harish Verma, MBBS, DCH<sup>2</sup>; Pankaj Bhatnagar, MD<sup>3</sup>; Pradeep Haldar, MBBS<sup>4</sup>; Asish Satapathy, MBBS<sup>3</sup>; K. N. Arun Kumar, MBBS<sup>3</sup>; Jennifer Horton, MD<sup>2</sup>; Concepcion F. Estivariz, MD<sup>5</sup>; Abhijeet Anand, MBBS<sup>5</sup>; Roland Sutter, MD<sup>2</sup>

Wild poliovirus type 2 was declared eradicated in September 2015 (1). In April 2016, India, switched from use of trivalent oral poliovirus vaccine (tOPV; containing types 1, 2, and 3 polio vaccine viruses), to bivalent OPV (bOPV; containing types 1 and 3), as part of a globally synchronized initiative to withdraw Sabin poliovirus type 2 vaccine. Concurrently, inactivated poliovirus vaccine (IPV) was introduced into India's routine immunization program to maintain an immunity base that would mitigate the number of paralytic cases in the event of epidemic transmission of poliovirus type 2 (2,3). After cessation of use of type 2 Sabin vaccine, any reported isolation of vaccine-derived poliovirus type 2 (VDPV2) would be treated as a public health emergency and might need outbreak response with monovalent type 2 oral vaccine, IPV, or both (4). In response to identification of a VDPV2 isolate from a sewage sample collected in the southern state of Telangana in May 2016, India conducted a mass vaccination campaign in June 2016 using an intradermal fractional dose (0.1 ml) of IPV (fIPV). Because of a global IPV supply shortage, fIPV, which uses one fifth of regular intramuscular (IM) dose administered intradermally, has been recommended as a response strategy for VDPV2 (5). Clinical trials have demonstrated that fIPV is highly immunogenic (6,7). During the 6-day campaign, 311,064 children aged 6 weeks–3 years were vaccinated, achieving an estimated coverage of 94%. With appropriate preparation, an emergency fIPV response can be promptly and successfully implemented. Lessons learned from this campaign can be applied to successful implementation of future outbreak responses using fIPV.

On June 7, 2016, a VDPV2 isolate with 10 nucleotide changes from the corresponding OPV strain was reported in an environmental surveillance sample collected from a sewage site on May 16, 2016. The sample was collected from the Amberpet sewage treatment plant, which receives sewage from parts of the Hyderabad and Rangareddy districts of Telangana state (Figure). No cases of acute flaccid paralysis (AFP) caused by poliovirus were reported and an active search of medical records in health care facilities identified no unreported AFP cases in Hyderabad and Rangareddy districts in the preceding 6 months. The last reported case of wild poliovirus case in Telangana state occurred in 2007, and no VDPVs had been reported from any sampling site since initiation of environmental sampling in Hyderabad in April 2016.

Following the outbreak response protocol for a VDPV2 event (4), which calls for an immediate vaccination response and after a joint national (Governments of India and Telangana State) and international (Global Polio Eradication Initiative [GPEI]) review, a decision was made to conduct a campaign using fIPV. The target group for the fIPV campaign was children aged 6 weeks–3 years. The campaign was limited to areas from which sewage drains to the Amberpet sewage treatment plant and that were considered to be at high risk for a potential circulating VDPV (cVDPV) outbreak, based on coverage of routine immunization and quality of earlier polio vaccination campaigns (i.e., Hyderabad city/district), and areas adjoining slum and migrant populations at high risk in the Rangareddy district.

In contrast to the house-to-house approach used for OPV campaigns, during which OPV is administered to targeted children directly at their home or other points where they are encountered (e.g., bus stops or public markets), the fIPV campaign was implemented using a “fixed site” approach, in which parents and caretakers bring children to a convenient neighborhood location for vaccination. The campaign was implemented June 20–25, 2016, within the recommended maximum 14-day interval to conduct a response after the initial confirmation of VDPV (4).

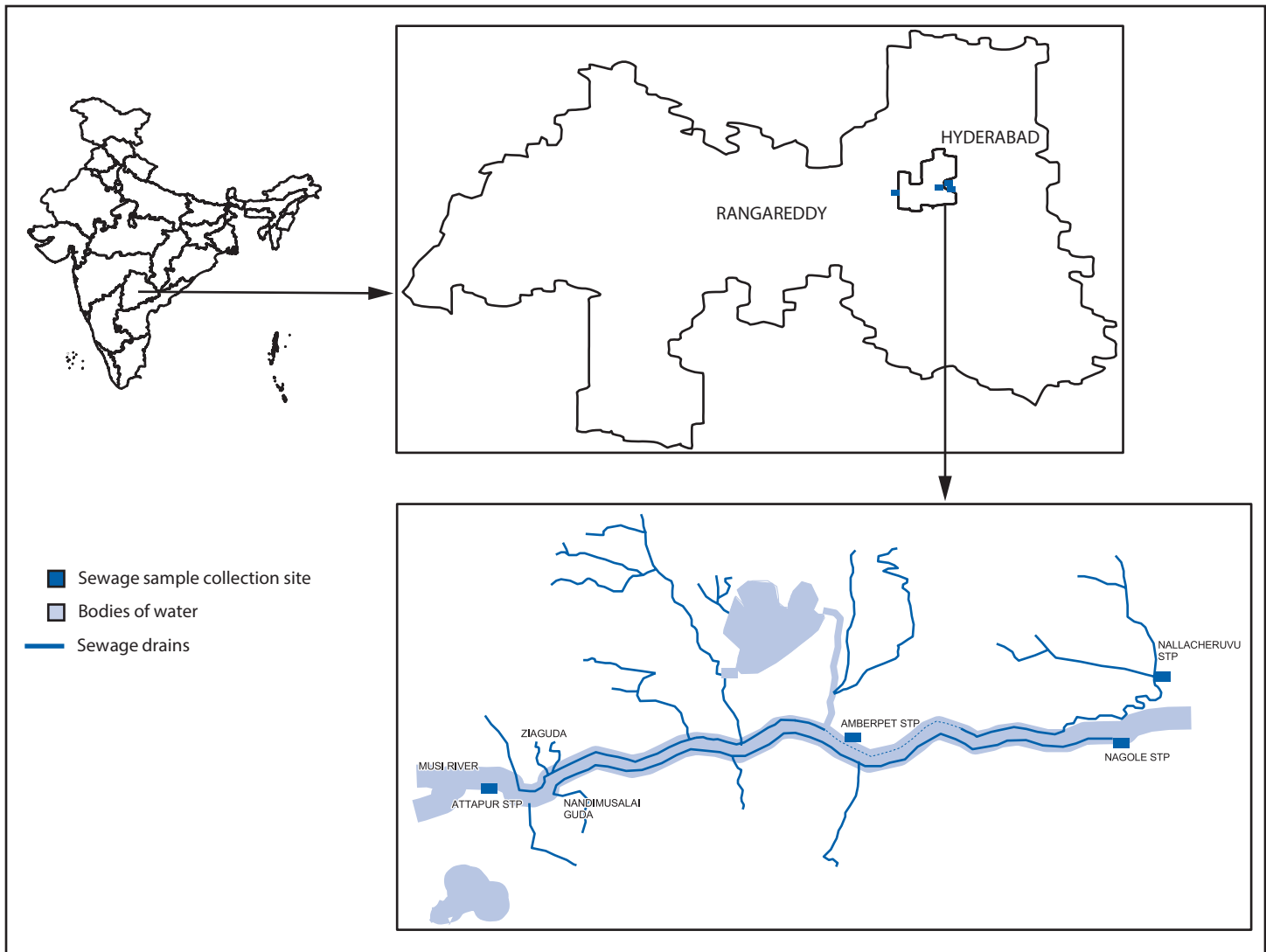
### Campaign Planning and Implementation

Twenty-nine surveillance medical officers from World Health Organization-India's National Polio Surveillance Project were deployed to support the development of campaign microplans and to conduct precampaign training and campaign monitoring. Existing microplans\* developed for previous OPV campaigns were adapted for the fIPV campaign. A rapid house-to-house survey was conducted to enumerate all eligible children and to inform families about the campaign. The target population was estimated to be 291,305.

A total of 5,373 immunization sessions were organized during 6 days (Table 1); the number of daily sessions ranged from 719 to 1,227. A total of 1,038 vaccinators supported implementation of the campaign, with 638 vaccinators mobilized from neighboring districts. At least one four-member team that included one vaccinator (an auxiliary nurse midwife),

\* [http://www.who.int/immunization/sage/9\\_Final\\_RED\\_280909.pdf](http://www.who.int/immunization/sage/9_Final_RED_280909.pdf).

FIGURE. Sewage sample collection sites — Hyderabad and Rangareddy Districts, India, May 2016



**Abbreviation:** STP = sewage treatment plant.

two community mobilizers, and one volunteer managed each session. Auxiliary nurse midwives administer all injectable vaccines during routine immunization sessions. A 1-day training session was organized to instruct all vaccination staff members supporting the fIPV campaign. Social mobilization for the campaign was conducted through print and electronic media, posters, invitation slips to parents of eligible children indicating day and place of immunization sessions, banners, microphone announcements, and community mobilizers.

The IPV vials used in the campaign were 10-IM-dose vials (5 ml per vial) manufactured by Shantha Biotech (Hyderabad, India) with 0.1 ml withdrawn for each fIPV vaccination. Therefore, each 10-IM-dose vial could potentially vaccinate 50 children with fIPV. The multi-dose vial policy permitted

use of open IPV vials for up to 28 days from the date of first use (8); partially used opened vials returned at the end of each campaign day were the first priority for use during the next day. A 0.1-ml dose of fIPV was administered intradermally on the lateral aspect of the right upper arm using an autodisable needle and syringe (with a 0.1-ml mark). An autodisable needle/syringe is a “fixed system,” in which the needle cannot be removed from the syringe; this system reduces vaccine wastage from the syringe. After vaccination, the nail of the left fifth finger of each vaccine recipient was marked with an indelible marker pen. Parents and caregivers were asked to report any adverse events occurring within a week of receiving the vaccine, including illness, hospitalizations, or death.



## Campaign Monitoring

At least one campaign monitor was assigned to each of the 25 blocks/administrative divisions in the districts of Hyderabad and Rangareddy. Areas selected for monitoring were known locations of residence of disenfranchised, mobile, or migrant populations and other groups for which lower than average routine immunization coverage had been reported. A total of 958 (18%) vaccination sessions were observed during the 6-day campaign (Table 2). All monitored team sessions were organized as planned, and 96% of monitored teams had the vaccinator that was listed in the microplan. Among monitored teams, 97% had adequate supplies to conduct vaccination sessions. Because of high vaccine demand, especially on the first 2 days of the campaign, 6% of monitored teams reported a shortage of IPV vials at some time during the session. No frozen IPV vials were reported to have been observed; IPV is freeze-sensitive, and any vials that are suspected to have been frozen must be discarded (9). Also, on the basis of their observance of vaccine vial monitors (heat-sensitive labels placed on vaccine vials that register cumulative heat exposure), monitors reported that no IPV vials reached the discard point, which implied an overall appropriate maintenance of the cold chain. On the first day of the campaign, a median of 48 fIPV doses (range: 41–50) were extracted from each IPV vial. Monitors noted that no vaccine leakage from the vial caps occurred during monitored sessions. In 93% of observed children, a bleb, indicative of intradermal delivery of fIPV, was observed immediately after vaccination. A median of 73 children (range: 10–148) were vaccinated per session per day during the campaign.

## Postcampaign Evaluation and Coverage

A total of 311,064 children were reported to have been vaccinated during the campaign, representing 107% of the initially estimated target of 291,305 children (Table 1). The reported coverage in Hyderabad was 87% of the estimated target, and in the Rangareddy district, almost twice the number of initially estimated children (185%) received the vaccine. The high reported coverage in Rangareddy was attributed to a large number of children from nontargeted areas that were adjacent to targeted areas who received vaccine during the campaign. After the campaign, a postcampaign assessment was conducted by 46 monitors to check for the likely number of missed children in a given location. Monitors prioritized areas that were known locations of residence of disenfranchised, migrant, or mobile populations. A total of 2,821 children were randomly checked (through finger marking) by monitors as part of a postcoverage monitoring survey, and 94% of assessed children overall were found to have received fIPV during the campaign (Table 2). The main reasons for nonvaccination included the

**TABLE 1. Numbers of fractional dose of inactivated poliovirus vaccine (fIPV)\* vaccination sessions and children (aged 6 weeks–3 years) targeted and vaccinated, and median number of children vaccinated per day in a vaccination session, by district — Telangana, India, June 20–25, 2016**

| District     | No. vaccination sessions conducted | Children aged 6 weeks–3 years |                                       |  |
|--------------|------------------------------------|-------------------------------|---------------------------------------|--|
|              |                                    | No. targeted                  | No. reported vaccinated with fIPV (%) | Median no. vaccinated per day in a session (range) |
| Hyderabad    | 4,360                              | 231,482                       | 200,480 (87)                          | 68 (10–102)  |
| Rangareddy   | 1,013                              | 59,823                        | 110,584 (185)                         | 87 (24–148)  |
| <b>Total</b> | <b>5,373</b>                       | <b>291,305</b>                | <b>311,064 (107)</b>                  | <b>73 (10–148)</b>                                 |

\* Equivalent to one fifth of an intramuscular dose.

**TABLE 2. Monitoring and evaluation of fractional inactivated poliovirus vaccine campaign sessions and children's vaccination status, by district — Telangana, India, June 2016**

| District     | Campaign monitoring |                            |   |   | Post-campaign evaluation  |
|--------------|---------------------|----------------------------|---|---|---|
|              | No. monitors        | No. sessions monitored (%) | Sessions with the vaccinators listed in microplan (%) | Sessions with adequate vaccine/syringes (%) | No. children checked by monitors for vaccination status (% vaccinated)* |
| Hyderabad    | 30                  | 661 (15)                   | (95)  | (98)  | 1,862 (96)  |
| Rangareddy   | 16                  | 297 (29)                   | (98)  | (94)  | 959 (91)  |
| <b>Total</b> | <b>46</b>           | <b>958 (18)</b>            | <b>(96)</b>   | <b>(97)</b>                                 | <b>2,821 (94)</b>   |

\* Based on examination of finger marking (after vaccination, the nail of the fifth finger of the left hand of each vaccine recipient was marked with an indelible marker pen).

child was not available on the day of vaccination (29%), the child was sick (21%), lack of parental awareness (16%), fear of injection (2%), and hesitancy and refusal (6.2%). Four nonserious adverse events, reported within a week after receipt of fIPV, deemed to be unrelated to vaccination.

## Discussion

Although vaccination campaigns with injectable vaccines have been conducted for other diseases, globally, this was the first campaign to use fIPV, which required vaccinators with experience in administering intradermal injections. Overall, this emergency response to a reported VDPV2 event demonstrates that it is feasible to plan and implement a fIPV campaign within 14 days of the reported event and to achieve high reported coverage. Strong government leadership at the national and state levels, well-coordinated technical and operational support from GPEI partners, clearly defined standard operating procedures for outbreak response, and experience implementing OPV campaigns were critical elements to the success of the fIPV campaign in Telangana state, India.

A number of lessons learned from this experience are likely to aid India and other countries in the successful implementation of future fIPV campaigns, as well as emergency campaigns with other injectable vaccines. Meticulous planning to ensure a

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

In April 2016, India withdrew Sabin poliovirus type 2 vaccine as part of a globally synchronized initiative that followed the declaration of eradication of wild poliovirus type 2 in September 2015. After the use of Sabin poliovirus type 2 ceased, any report of isolation of vaccine-derived poliovirus type 2 (VDPV2) would be considered a public health emergency and might require an outbreak response vaccination with monovalent type 2 oral polio vaccine or inactivated poliovirus vaccine (IPV). Global IPV supply shortage has limited the number of available doses of IPV. Fractional IPV (fIPV), administered intradermally using one fifth of regular dose, stretches the limited supplies of IPV and has been recommended as a response strategy for VDPV2 outbreaks.

**What is added by this report?**

In response to a VDPV2 isolation in Telangana, India, a mass vaccination campaign was conducted using fIPV within 14 days of the VDPV2 isolation. A total of 311,064 children were reported to have been vaccinated during the campaign. This was the first mass vaccination campaign to use fIPV, and in a postcoverage monitoring survey, 94% of assessed children were found to have received fIPV during the campaign.

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

This emergency response to a reported VDPV2 event demonstrates the feasibility of planning and implementing an fIPV campaign within 14 days of a reported event and of achieving high reported coverage. Strong government leadership at the national and state levels and well-coordinated technical and operational support from Global Polio Eradication Initiative partners, as well as experience in implementing oral poliovirus campaigns and having clearly defined standard operating procedures for outbreak response were critical elements to the success of the fIPV campaign in Telangana, India.

sufficient number of vaccination sites that are located strategically and availability of an adequate number of vaccinators with experience in intradermal administration of vaccines, coupled with rapid refresher training of these vaccinators, assisted in ensuring good injection practices and high coverage as determined by postcampaign monitoring.

The Emergency Operations Center established by the Indian government was responsible for the overall coordination of the emergency response, with strong support from GPEI partners. Communication technologies, such as group messaging, helped ensure rapid communication among all stakeholders. Progress in all sectors of the campaign area was shared in real-time during the preparatory and implementation phases, as were challenges and barriers, to ensure faster solutions to identified problems.

Sharing accurate and timely information is important in developing a positive partnership with the media. Extensive publicity of the campaign through mass media, the perceived threat of the

return of polio, and the nonavailability of IPV in the private sector, as well as the private sector's promotion of the campaign, all contributed to high community participation and high coverage.

One unanticipated problem was that the number of children identified during precampaign surveys did not match the number of children who reported to the vaccination sites to receive fIPV, especially in Rangareddy, where only about half the number of children who were actually vaccinated were initially targeted. Therefore, when planning for a time-sensitive outbreak response, resource-intensive precampaign surveys should be avoided. Available resources should be diverted to update existing vaccination microplans and develop communication strategies. Strong mobilization measures using community health workers and volunteers on the days of the campaign were effective in achieving high coverage. This large, emergency campaign with an injectable vaccine required a large number of trained vaccinators to be brought in to the targeted area from other districts; this scenario needs to be anticipated in response plans for future similar campaigns.

The experience in Telangana state, India, demonstrates that operational and logistical challenges to an injectable vaccination campaign can be overcome. Through active government and partner coordination, achievement of high vaccination coverage with intradermal fIPV in an emergency campaign setting is possible.

<sup>1</sup>World Health Organization, South-East Asia Regional Office, New Delhi, India; <sup>2</sup>World Health Organization, Geneva, Switzerland; <sup>3</sup>National Polio Surveillance Project, World Health Organization, New Delhi, India; <sup>4</sup>Ministry of Health and Family Welfare, Government of India, New Delhi, India; <sup>5</sup>Global Immunization Division, Center for Global Health, CDC.

Corresponding author: Abhijeet Anand, aanand@cdc.gov, 404-639-1970.

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# Vital Signs: Epidemiology of Sepsis: Prevalence of Health Care Factors and Opportunities for Prevention

Shannon A. Novosad, MD<sup>1,2</sup>; Mathew R.P. Sapiano, PhD<sup>2</sup>; Cheri Grigg, DVM<sup>1,2</sup>; Jason Lake, MD<sup>1,2</sup>; Misha Robyn, DVM<sup>1,4</sup>; Ghinwa Dumyati, MD<sup>3</sup>; Christina Felsen, MPH<sup>3</sup>; Debra Blog, MD<sup>4</sup>; Elizabeth Dufort, MD<sup>4</sup>; Shelley Zansky, PhD<sup>4</sup>; Kathryn Wiedeman, MPH<sup>2</sup>; Lacey Avery, MA<sup>2</sup>; Raymund B. Dantes, MD<sup>2</sup>; John A. Jernigan, MD<sup>2</sup>; Shelley S. Magill, MD<sup>2</sup>; Anthony Fiore, MD<sup>2</sup>; Lauren Epstein, MD<sup>2</sup>

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## Abstract

**Background:** Sepsis is a serious and often fatal clinical syndrome, resulting from infection. Information on patient demographics, risk factors, and infections leading to sepsis is needed to integrate comprehensive sepsis prevention, early recognition, and treatment strategies.

**Methods:** To describe characteristics of patients with sepsis, CDC and partners conducted a retrospective chart review in four New York hospitals. Random samples of medical records from adult and pediatric patients with administrative codes for severe sepsis or septic shock were reviewed.

**Results:** Medical records of 246 adults and 79 children (aged birth to 17 years) were reviewed. Overall, 72% of patients had a health care factor during the 30 days before sepsis admission or a selected chronic condition likely to require frequent medical care. Pneumonia was the most common infection leading to sepsis. The most common pathogens isolated from blood cultures were *Escherichia coli* in adults aged  $\geq 18$  years, *Klebsiella* spp. in children aged  $\geq 1$  year, and *Enterococcus* spp. in infants aged  $< 1$  year; for 106 (33%) patients, no pathogen was isolated. Eighty-two (25%) patients with sepsis died, including 65 (26%) adults and 17 (22%) infants and children.

**Conclusions:** Infection prevention strategies (e.g., vaccination, reducing transmission of pathogens in health care environments, and appropriate management of chronic diseases) are likely to have a substantial impact on reducing sepsis. CDC, in partnership with organizations representing clinicians, patients, and other stakeholders, is launching a comprehensive campaign to demonstrate that prevention of infections that cause sepsis, and early recognition of sepsis, are integral to overall patient safety.

## Introduction

Many different infections can lead to sepsis, a serious and often fatal clinical syndrome that is characterized by organ dysfunction and can be difficult to diagnose (1–3). Sepsis is associated with high morbidity and mortality (1–4) and accounted for \$23.7 billion in health care expenditures in 2013 (5). Identifying specific sepsis prevention strategies is a public health priority.

Evaluations of sepsis epidemiology have typically used death certificate or health services utilization data; these methods have well-described limitations (6,7). Most sepsis initiatives have focused on improving outcomes by promoting protocol-driven approaches that facilitate early recognition and treatment (8). Detailed data regarding underlying conditions, health care factors, types of infections, and pathogens most commonly associated with sepsis could guide development of programs to inform clinicians, patients, and families about prevention of infections that can lead to sepsis. To inform sepsis initiatives and health

communication efforts, CDC partnered with the New York State Department of Health and Emerging Infections Program to perform a medical record assessment to describe clinical characteristics, comorbidities, and potential opportunities for infection prevention among patients with sepsis.

## Methods

A retrospective medical record review at four general, acute care hospitals in New York was performed through CDC's Emerging Infections Program. Patients were eligible for inclusion if they had a hospital admission during October 1, 2012–September 30, 2013 (fiscal year [FY] 2013), or October 1, 2014–September 30, 2015 (FY 2015). The *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) discharge diagnosis codes for severe sepsis (995.92) or septic shock (785.52) were used by hospitals to generate lists of potential cases. A target sample



size of approximately 300 records was selected. The lists of medical records were sorted into random order, and samples of records were selected and reviewed to identify demographic characteristics, underlying conditions, and infections leading to sepsis. Patients' demographic and clinical characteristics were abstracted using a standardized form. Patients whose medical records did not include documentation of sepsis and patients for whom large portions of the medical record were incomplete or missing were excluded.

The first date of clinical documentation of sepsis or a related term in the chart by a clinician was used to classify sepsis cases. The timing of first sepsis documentation was used as a proxy for sepsis onset, and the presence of health care factors prior to the sepsis hospitalization was used to classify cases as community- or health care-associated. Cases were classified as community-associated/community-onset if the initial documentation of sepsis occurred at admission or during the first 3 calendar days of admission, with the date of admission considered to be day 1, and if, during the 30 days preceding admission, there were no health care factors (i.e.,  $\geq 2$  days in a nursing home, long-term or other acute care hospital, receipt of intravenous antimicrobials, peritoneal or hemodialysis, surgery, total parenteral nutrition, chemotherapy, wound therapy, or presence of a central venous catheter). Community-associated/community-onset cases were further categorized based on whether the patient had one or more of a number of selected chronic conditions that might require frequent contact with health care providers for management.\*

Sepsis cases were classified as health care-associated if the initial documentation of sepsis occurred  $\leq 3$  days after admission and health care factors were identified during the preceding 30 days; they were further categorized as nursing home-onset, community-onset, or undetermined-onset, depending on the location from which the patient was admitted to the hospital. Sepsis cases for which the first documentation of sepsis occurred after day 3 of admission were classified as health care-associated/hospital-onset. A descriptive analysis of demographics, clinical characteristics, underlying chronic conditions, pathogens, and infection types among patients with sepsis was performed.

## Results

**Adult patients with sepsis.** Charts of 290 adult patients with sepsis were selected, and reviews were completed for 246 (85%); 44 (15%) records were excluded, most commonly

\*Selected chronic conditions included any of the following: steroid/immunosuppressive therapy, acquired immunodeficiency syndrome, cerebral palsy, hemiplegia, spinal cord injury, paraplegia, quadriplegia, congestive heart failure, chronic obstructive pulmonary disease, cystic fibrosis, chronic ventilator/tracheostomy, leukemia, lymphoma, multiple myeloma, neutropenia, transplant (hematopoietic and solid organ), solid tumor (metastatic and not metastatic), sickle cell disease, cirrhosis, or diabetes mellitus with complications.

because encounter information was missing. The median age of adult patients with sepsis was 69 years; 127 (52%) were male (Table 1). The median length of hospital stay was 9 days. Most patients (238 [97%]) had at least one comorbidity; 87 (35%) had diabetes mellitus, 79 (32%) had cardiovascular disease (including coronary artery disease, peripheral vascular disease, or congestive heart failure), 56 (23%) had chronic kidney disease, and 50 (20%) had chronic obstructive pulmonary disease. The most common illnesses leading to sepsis were pneumonia (85 [35%]), urinary tract infections (62 [25%]), gastrointestinal infections (28 [11%]), and skin/soft tissue infections (26 [11%]) (Table 2). Pathogens were isolated from blood cultures of 75 (30%) patients and from urine cultures of 70 (28%); these groups were not mutually exclusive. The most common pathogens identified from blood were *Staphylococcus* spp. (including both *S. aureus* and coagulase negative *Staphylococcus*), *Escherichia coli*, and *Streptococcus* spp. (Table 3). For 76 (31%) patients with sepsis, no pathogen was identified in any culture or nonculture based tests.

Among the 246 adult patients with sepsis whose records were reviewed, 142 (58%) were classified as health care-associated with 44 (18%) of these hospital-onset and 104 (42%) were classified as community-associated, without health care factors. Among health care-associated sepsis cases, the most common health care factors were acute care hospitalization or nursing home stays of  $\geq 2$  days in the preceding 30 days, which were reported for 44 (18%) and 43 (17%) patients, respectively. Among patients with community-associated sepsis, nearly 50% (20% of all patients with sepsis) had a selected chronic condition likely to lead to frequent encounters with health care providers, such as diabetes mellitus with complications, cancer, or congestive heart failure. Pneumococcal vaccination before the sepsis hospitalization was documented for 108 (44%) patients, and influenza vaccination in the year before admission was documented for 87 (35%) patients.

Among the 155 patients admitted from a private residence, 23 (15%) were discharged to a long-term care facility. Sixty-five (26%) patients died during their sepsis hospitalization, including 47 (representing 72% of deaths) who were aged  $\geq 65$  years, and seven (representing 11% of deaths) who had no health care factors in the 30 days preceding admission.

**Pediatric patients with sepsis.** Records of 88 pediatric patients with sepsis were selected for review, and reviews were completed for 79 (90%), including 31 infants aged  $< 1$  year (39%), and 48 children, aged 1–17 years (61%) (Table 1). At least one comorbidity was present for 62 (78%) pediatric patients, including 25 (81%) infants and 37 (77%) children. The most common comorbidity among infants was congenital heart disease, affecting seven (23%) patients; the most common comorbidities among children were cognitive deficits or cerebral palsy, affecting 18 (38%).

**TABLE 1. Number and percentage of sepsis cases among adult (N = 246) and pediatric (N = 79) patients, by selected characteristics — four acute care hospitals, New York, fiscal years 2013 and 2015**

| Characteristic  | Adult patients<br>(N = 246)*<br>No. (%) | Pediatric patients (N = 79)* |                              |
|---|---|------------------------------|------------------------------|
|   |   | <1 year, (n = 31)<br>No. (%) | ≥1 year, (n = 48)<br>No. (%) |
| Male sex  | 127 (52)                                | 22 (71)                      | 26 (54)                      |
| Age: median, (Q1, Q3) (years)   | 69 (60, 81)                             | —                            | 12 (7, 15)                   |
| Hospital stay: median, (Q1, Q3) (days)  | 9 (5, 18)                               | 19 (7, 37)                   | 11 (7, 19)                   |
| Influenza vaccine received in year preceding sepsis (yes) <sup>†</sup>                                      | 87 (35)                                 | 1 (3)                        | 10 (21)                      |
| Pneumococcal vaccine received (yes)   | 108 (44)                                | 2 (6)                        | 14 (29)                      |
| Comorbidities (any)   | 238 (97)                                | 25 (81)                      | 37 (77)                      |
| Comorbidities (selected) <sup>§</sup>   | 149 (61)                                | 1 (3)                        | 16 (33)                      |
| Health care–associated/Hospital-onset <sup>¶,**</sup>   | 44 (18)                                 | 12 (39)                      | 8 (17)                       |
| Health care–associated/Nursing home-onset <sup>¶,††</sup>   | 34 (14)                                 | —                            | 1 (2)                        |
| Health care–associated/Community-onset <sup>¶,§§</sup>  | 53 (22)                                 | 1 (3)                        | 8 (17)                       |
| Health care–associated/Undetermined-onset <sup>¶,¶¶</sup>   | 11 (4)                                  | 2 (6)                        | 2 (4)                        |
| Community-associated/Community-onset, no health care factors, with selected comorbidities <sup>***</sup>    | 50 (20)                                 | 1 (3)                        | 7 (15)                       |
| Community-associated/Community-onset, no health care factors, without selected comorbidities <sup>†††</sup> | 54 (22)                                 | 15 (48)                      | 22 (46)                      |
| <b>Preadmission location</b>  |   |                              |                              |
| Private residence   | 155 (63)                                | 6 (19)                       | 34 (71)                      |
| Nursing home/SNF  | 44 (18)                                 | —                            | 2 (4)                        |
| Other acute care hospital   | 24 (10)                                 | 14 (45)                      | 12 (25)                      |
| Other/Unknown   | 23 (9)                                  | 11 (35)                      | —                            |
| <b>Discharge disposition</b>  |   |                              |                              |
| Private residence   | 102 (41)                                | 17 (55)                      | 38 (79)                      |
| Nursing home/SNF  | 61 (25)                                 | 1 (3)                        | 4 (8)                        |
| Other acute care hospital   | 2 (<1)                                  | —                            | 1 (2)                        |
| Other/Unknown   | 2 (<1)                                  | 1 (3)                        | —                            |
| Hospice   | 14 (6)                                  | —                            | —                            |
| Died during hospitalization   | 65 (26)                                 | 12 (39)                      | 5 (10)                       |

**Abbreviations:** Q1 = 25th percentile; Q3 = 75th percentile; SNF = skilled nursing facility.

\* Adult and pediatric populations were not sampled proportionally.

† Vaccination in year prior to sepsis diagnosis.

§ Steroid/immunosuppressive therapy, acquired immunodeficiency syndrome, cerebral palsy, hemiplegia, spinal cord injury, paraplegia, quadriplegia, congestive heart failure, chronic obstructive pulmonary disease, cystic fibrosis, chronic ventilator/tracheostomy, leukemia, lymphoma, multiple myeloma, neutropenia, transplant (hematopoietic and solid organ), solid tumor (metastatic and not metastatic), sickle cell disease, cirrhosis, or diabetes mellitus with complications.

¶ Health care–associated cases included any of the following in the preceding 30 days: ≥2 days in a nursing home, long-term acute care hospital or other acute care hospital, intravenous antimicrobials, peritoneal or hemodialysis, surgery, total parenteral nutrition, central venous catheter, wound therapy, or onset after 3 days in the hospital.

\*\* First documentation of sepsis >3 days after admission.

†† Sepsis documented within 3 days of admission; patient was admitted from a nursing home and spent at least 2 calendar days in a nursing home during the preceding 30 days.

§§ Sepsis documented within 3 days of admission; patient was admitted from private residence but had a health care factor in the preceding 30 days.

¶¶ Sepsis documented within 3 days of admission; patient was admitted from another hospital or nursing home and had one other health care exposure (excludes those who were both admitted from a nursing home and spent at least 2 calendar days in a nursing home during preceding 30 days).

\*\*\* Sepsis documented within 3 days of admission; patient had no health care factors in preceding 30 days, with selected comorbidities (steroid/immunosuppressive therapy, acquired immunodeficiency syndrome, cerebral palsy, hemiplegia, spinal cord injury, paraplegia, quadriplegia, congestive heart failure, chronic obstructive pulmonary disease, cystic fibrosis, chronic ventilator/tracheostomy, leukemia, lymphoma, multiple myeloma, neutropenia, transplant (hematopoietic and solid organ), solid tumor (metastatic and not metastatic), sickle cell disease, cirrhosis, or diabetes mellitus with complications).

††† Sepsis documented within 3 days of admission; patient had no health care factors in preceding 30 days, without selected comorbidities.

Among pediatric patients, 34 (43%) had sepsis with health care factors, and 45 (57%) were community-associated sepsis cases without health care factors (Table 1). The most commonly identified health care factor, receipt of intravenous antibiotics in the 30 days preceding sepsis admission, was reported for eight (10%) patients. Selected chronic conditions (Table 1) likely to require frequent medical care were identified in eight (10%) community-associated cases.

Among infections leading to sepsis, respiratory infections were most common, and preceded sepsis in 29% of

all pediatric patients, followed by gastrointestinal infections (24%) (Table 2). Among 41 (52%) patients for whom a pathogen was identified in a blood culture, *Enterococcus* spp. and *Klebsiella* spp. were most commonly identified in infants (14%) and children (9%), respectively (Table 3). In 30 (38%) pediatric patients, sepsis was diagnosed but no pathogen was isolated. Seventeen (22%) pediatric cases died during their sepsis hospitalization, including 12 (39%) infants and five (10%) children.

**TABLE 2. Number and percentage of types of infections among adult (N = 246) and pediatric (N = 79) patients with sepsis — four acute care hospitals, New York, fiscal years 2013 and 2015**

| Type of infection           | Adult patients<br>(N = 246)*<br>No. (%) | Pediatric patients (N=79)       |                                 |
|-----------------------------|---|---------------------------------|---------------------------------|
|                             |   | <1 year,<br>(n = 31)<br>No. (%) | ≥1 year,<br>(n = 48)<br>No. (%) |
| Respiratory tract†          | 86 (35)                                 | 9 (29)                          | 14 (29)                         |
| Urinary tract               | 62 (25)                                 | 1 (3)                           | 4 (8)                           |
| Gastrointestinal§           | 28 (11)                                 | 8 (26)                          | 11 (23)                         |
| Unknown/Undetermined¶       | 32 (13)                                 | 6 (19)                          | 8 (17)                          |
| Skin and soft tissue        | 26 (11)                                 | 1 (3)                           | 3 (6)                           |
| Bloodstream                 | 13 (5)                                  | 8 (26)                          | 6 (13)                          |
| Bone and joint              | 6 (2)                                   | 1 (3)                           | 1 (2)                           |
| Cardiovascular              | 5 (2)                                   | 2 (6)                           | —                               |
| Eye/Ear/Nose/Throat         | 3 (1)                                   | —                               | 2 (4)                           |
| Central nervous system      | 2 (<1)                                  | 1 (3)                           | 2 (4)                           |
| Disseminated systemic viral | 2 (<1)                                  | —                               | 1 (2)                           |
| Surgical site               | 2 (<1)                                  | —                               | —                               |
| None documented             | 22 (9)                                  | —                               | 2 (4)                           |

\* Patients can have more than one type of infection. Adult and pediatric populations were not sampled proportionally.

† Includes upper respiratory infections and pneumonia. Upper respiratory infections in one (<1%) adult, three (33%) <1 year, and zero (0%) ≥1 year. Pneumonia in 85 (99%) adults, six (67%) <1 year, and 14 (100%) ≥1 year.

§ Includes intra-abdominal, gastrointestinal tract, *Clostridium difficile*, and hepatobiliary infections. Intra-abdominal infections in 10 (36%) adults, four (50%) <1 year, and seven (64%) ≥1 year. Gastrointestinal tract infections in five (18%) adults, four (50%) <1 year, and three (27%) ≥1 year. *Clostridium difficile* infections in seven (25%) adults, 0 (0%) <1 year, and one (1%) ≥1 year. Hepatobiliary infections in six (21%) adults, zero (0%) <1 year, and zero (0%) ≥1 year.

¶ Infection documented by health care provider, but source was unknown.

## Conclusions and Comments

The findings from this analysis will inform expansion of efforts by CDC and partners to describe the epidemiology of sepsis, prevent infections that lead to sepsis, and educate clinicians and patients about reducing the risk for sepsis. Patients with sepsis experience severe illness and serious adverse outcomes, including long hospital stays (median = 10 days), discharge to long-term care settings (20%), and death (25%). Similar to other studies (1,9,10), sepsis most commonly occurred among patients with one or more comorbidities, and a majority of patients developed infections leading to sepsis outside a hospital. Among all patients with sepsis, 72% had either a health care factor in the month preceding admission or a chronic condition likely to require frequent contact with the health care system, suggesting that opportunities exist for prevention or earlier recognition of infections leading to sepsis. Although multiple infections and organisms among patients with sepsis were identified in this study and in others (2,11,12), in many cases a specific pathogen is not determined.

Because different types of infections can lead to sepsis, many interventions that are currently viewed as pathogen-specific or disease-specific should also be considered opportunities to prevent sepsis and included in efforts to improve sepsis education. For example, pneumonia is the most common infection causing

**TABLE 3. Number and percentage of types of pathogens commonly isolated\* from blood cultures of adult (N = 225) and pediatric (N = 75) patients with sepsis — four acute care hospitals, New York, fiscal years 2013 and 2015†**

| Type of pathogen                                 | Adult patients<br>(N = 225)<br>No. (%)§ | Pediatric patients (N = 75)     |                                 |
|--|---|---------------------------------|---------------------------------|
|  |   | <1 year<br>(n = 29)<br>No. (%)§ | ≥1 year<br>(n = 46)<br>No. (%)§ |
| <i>Escherichia coli</i>                          | 17 (8)                                  | 2 (7)                           | 3 (7)                           |
| <i>Streptococcus</i> spp.¶                       | 15 (7)                                  | 2 (7)                           | 2 (4)                           |
| Coagulase negative<br><i>Staphylococcus</i> spp. | 14 (6)                                  | 1 (3)                           | —                               |
| <i>Staphylococcus aureus</i>                     | 13 (6)                                  | 3 (10)                          | 1 (2)                           |
| <i>Pseudomonas</i> spp.                          | 3 (1)                                   | 1 (3)                           | 1 (2)                           |
| <i>Bacillus</i> spp.                             | 3 (1)                                   | —                               | —                               |
| <i>Enterococcus</i> spp.                         | 3 (1)                                   | 4 (14)                          | 1 (2)                           |
| <i>Enterobacter</i> spp.                         | 3 (1)                                   | —                               | —                               |
| <i>Candida</i> spp.                              | 1 (<1)                                  | 1 (3)                           | 1 (2)                           |
| <i>Klebsiella</i> spp.                           | 1 (<1)                                  | —                               | 4 (9)                           |

\* Only pathogens isolated from more than two patients (adult and pediatric patients combined) are shown.

† Pathogens isolated from cultures collected from 7 days before through 2 days after the first sepsis documentation in the medical record.

§ Denominator includes all patients with blood cultures (positive or negative); patients could have more than one blood culture or pathogen isolated from the blood.

¶ *Streptococcus* spp. (not further speciated) 7 patients, *Streptococcus pneumoniae* 3 patients, *Streptococcus* Group B 3 patients, *Streptococcus* Group A 3 patients, *Streptococcus* Group D 2 patients.

sepsis (2,11,12), and vaccination is an important and highly effective prevention strategy. Pneumococcal and influenza vaccination have both been shown to have saved thousands of lives, despite suboptimal vaccination coverage in the U.S. population; thousands more deaths could be prevented with better coverage (13–16).

Among those patients for whom sepsis onset was determined, 79.4% were classified as having sepsis onset outside of the hospital (i.e., first medical record documentation of sepsis at admission or in the first 3 hospital days). The majority of patients in this analysis had recent interactions with the health care system before admission. While this likely reflects the vulnerability of chronically ill patients to infection, it also suggests that health care facilities and providers could play a central role in sepsis prevention by providing age-appropriate and condition-appropriate vaccination to all patients and optimizing the health status of patients with chronic conditions. In addition, facility-level interventions are available to reduce the risk for health care–associated infections, such as appropriate hand hygiene and personal protective equipment to limit pathogen spread among patients. The potential impact of facility-level interventions is demonstrated through awareness and prevention efforts focused on infections caused by central line-associated bloodstream infections (CLABSIs). During 1990–2010, it is likely that as many as 198,000 CLABSIs were prevented in intensive care units, attributable at least

in part to the successful and widespread implementation of evidence-based CLABSI prevention measures (17). Finally, efforts to reduce exposure to antibiotic-resistant organisms and disruption of the protective normal microbiome should also be included among sepsis prevention strategies.

Sepsis prevention activities led by CDC and partners are focused on five key areas: 1) increasing sepsis awareness among patients, families, and providers and building a coalition of clinical professional partners and patient advocates to work with CDC; 2) promoting early recognition of sepsis and aligning antibiotic stewardship efforts with early recognition; 3) identifying at-risk populations for prevention and early recognition efforts; 4) developing better sepsis surveillance methods to measure the impact of interventions; and 5) preventing infections that lead to sepsis, including infections caused by antibiotic-resistant pathogens. These efforts are being coordinated with partners to reduce sepsis risk, improve patient outcomes, and track progress. Recent sepsis initiatives focused on early recognition and treatment include legislation passed in 2014 in New York requiring hospitals to report a variety of sepsis process measures to the New York State Department of Health, and the Centers for Medicare & Medicaid Services implementation in 2015 of a new policy instrument to improve sepsis care increasing the use of specific and timely medical interventions during the first few critical hours that patients with sepsis are in the hospital or emergency room (18). In addition, the Society for Critical Care Medicine and the European Society of Intensive Care Medicine recently published guidelines intended to improve early recognition of sepsis (3).

The findings in this report are subject to at least five limitations. First, the assessment examined medical records from a small sample of patients and hospitals; characteristics of patients with sepsis could be different elsewhere, although these results are consistent with previous studies. Second, a sample of adult and pediatric records were reviewed, and the numbers of records are not proportional to the actual number of adult and pediatric patients with sepsis in these facilities. Third, to identify patients with sepsis and septic shock, administrative codes were used along with confirmation that at least one provider had documented sepsis in the medical record, rather than application of an objective definition based on physiological or laboratory criteria. Therefore, although this approach has obvious limitations, it reflects the clinical impression of treating providers. Fourth, because this analysis relied on medical records for all information, data might be incomplete. Information on outpatient clinic visits was not collected; therefore, the proportion of patients with sepsis who have health care factors before their sepsis hospitalizations might have been underestimated. Finally, in many patients more than one infectious process was present, and it is possible

that not all of the infections and organisms described actually caused sepsis in an individual patient.

Sepsis is a significant public health and clinical management challenge. CDC continues to work closely with numerous clinical professional organizations and patient advocates and will partner with stakeholders to launch a comprehensive campaign targeting clinicians and the public, demonstrating how steps to prevent and urgently recognize sepsis are critical components of patient safety programs. Routine health care encounters should be used as opportunities to implement interventions that could reduce the risk for infections leading to sepsis. These interventions include increasing vaccination coverage, educating patients and families about early sepsis warning signs, improving infection control programs, and optimizing chronic disease management. In addition, current efforts led by CDC and partners to improve sepsis surveillance will enhance analysis of risk factors and infections leading to sepsis and provide a more objective measure to track trends and evaluate interventions, informing overall prevention, recognition, and treatment efforts.

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<sup>1</sup>Epidemic Intelligence Service, CDC; <sup>2</sup>Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, CDC; <sup>3</sup>Emerging Infections Program, University of Rochester Medical Center, Rochester, New York; <sup>4</sup>New York State Department of Health.

Corresponding author: Lauren H. Epstein, lepstein@cdc.gov, 404-639-8162.

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## Update: Interim Guidance for the Evaluation and Management of Infants with Possible Congenital Zika Virus Infection — United States, August 2016

Kate Russell, MD<sup>1,2</sup>; Sara E. Oliver, MD<sup>1,3</sup>; Lillianne Lewis, MD<sup>1,4</sup>; Wanda D. Barfield, MD<sup>5</sup>; Janet Cragan, MD<sup>6</sup>; Dana Meaney-Delman, MD<sup>7</sup>; J. Erin Staples, MD, PhD<sup>8</sup>; Marc Fischer, MD<sup>8</sup>; Georgina Peacock, MD<sup>9</sup>; Titilope Oduyebo, MD<sup>5</sup>; Emily E. Petersen, MD<sup>5</sup>; Sherif Zaki, MD, PhD<sup>10</sup>; Cynthia A. Moore, MD, PhD<sup>6</sup>; Sonja A. Rasmussen, MD<sup>11</sup>; Contributors

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CDC has updated its interim guidance for U.S. health care providers caring for infants born to mothers with possible Zika virus infection during pregnancy (1). Laboratory testing is recommended for 1) infants born to mothers with laboratory evidence of Zika virus infection during pregnancy and 2) infants who have abnormal clinical or neuroimaging findings suggestive of congenital Zika syndrome and a maternal epidemiologic link suggesting possible transmission, regardless of maternal Zika virus test results. Congenital Zika syndrome is a recently recognized pattern of congenital anomalies associated with Zika virus infection during pregnancy that includes microcephaly, intracranial calcifications or other brain anomalies, or eye anomalies, among others (2). Recommended infant laboratory evaluation includes both molecular (real-time reverse transcription–polymerase chain reaction [rRT-PCR]) and serologic (immunoglobulin M [IgM]) testing. Initial samples should be collected directly from the infant in the first 2 days of life, if possible; testing of cord blood is not recommended. A positive infant serum or urine rRT-PCR test result confirms congenital Zika virus infection. Positive Zika virus IgM testing, with a negative rRT-PCR result, indicates probable congenital Zika virus infection. In addition to infant Zika virus testing, initial evaluation of all infants born to mothers with laboratory evidence of Zika virus infection during pregnancy should include a comprehensive physical examination, including a neurologic examination, postnatal head ultrasound, and standard newborn hearing screen. Infants with laboratory evidence of congenital Zika virus infection should have a comprehensive ophthalmologic exam and hearing assessment by auditory brainstem response (ABR) testing before 1 month of age. Recommendations for follow-up of infants with laboratory evidence of congenital Zika virus infection depend on whether abnormalities consistent with congenital Zika syndrome are present. Infants with abnormalities consistent with congenital Zika syndrome should have a coordinated evaluation by multiple specialists within the first month of life; additional evaluations will be needed within the first year of life, including assessments of vision, hearing, feeding, growth, and neurodevelopmental and endocrine function. Families and caregivers will also need

ongoing psychosocial support and assistance with coordination of care. Infants with laboratory evidence of congenital Zika virus infection without apparent abnormalities should have ongoing developmental monitoring and screening by the primary care provider; repeat hearing testing is recommended. This guidance will be updated when additional information becomes available.

Zika virus infection during pregnancy is a cause of microcephaly and other serious brain anomalies (3); however, the clinical spectrum of the effects of Zika virus infection during pregnancy is not yet known. A wide range of neurologic abnormalities, in addition to microcephaly, has been observed among infants with presumed or confirmed congenital Zika virus infection (2,4). Reported neuroimaging findings include intracranial calcifications; ventriculomegaly and extra-axial fluid; abnormal gyral patterns (e.g., polymicrogyria); decreased brain parenchymal volume; cortical atrophy and malformation; hypoplasia of the cerebellum, cerebellar vermis or brainstem; delayed myelination; and thinning or hypoplasia of the corpus callosum (5,6). Neurologic abnormalities apparent on examination of these infants have included hypertonia, hypotonia, spasticity, hyperreflexia, severe irritability, and seizures (2,4). Zika virus appears to primarily target neural progenitor cells resulting in cell death and disruption of neuronal proliferation, migration and differentiation, which slows brain growth and affects neural cell viability (7–9). Ocular findings reported in infants with presumed or confirmed congenital Zika virus infection have included chorioretinal atrophy or scarring, pigmentary changes, optic nerve hypoplasia, optic disc pallor, increased optic disc cupping, hemorrhagic retinopathy and abnormal retinal vasculature (10–12). Some infants with presumed or confirmed congenital Zika virus infection have had a phenotype consistent with fetal brain disruption sequence, characterized by severe microcephaly, collapse of the skull, overlapping cranial sutures, prominent occipital bone, redundant scalp skin, and severe neurologic impairment (13,14). Other findings seen in infants with congenital Zika virus infection have included clubfoot and contractures of single or multiple joints (arthrogryposis), presumably secondary to central nervous system damage (4).

Experience with other congenital infections can provide insight to guide clinical management until more data emerge

regarding outcomes associated with congenital Zika virus infection. Infants with congenital infections, such as cytomegalovirus (CMV) and rubella, can develop a range of clinical manifestations, including hearing loss, seizures, neurodevelopmental delays and diabetes mellitus later in life (15,16), even without apparent clinical manifestations of congenital infection at birth (17).

Diagnostic testing for congenital Zika virus infection can be challenging. Whereas a positive molecular (rRT-PCR) testing result in an infant can confirm Zika virus infection, a negative result does not exclude infection. Viral shedding can be prolonged in congenital CMV and rubella infections (18,19); however, little is known about the duration of viral shedding in infants with congenital Zika virus infection. IgM results might assist in making the diagnosis, but can be difficult to interpret because of false-positive results occurring from cross-reacting IgM antibodies or nonspecific reactivity (20). Because maternal IgG crosses the placenta, the presence of IgG in an infant specimen cannot be used as evidence of congenital infection.

Currently, there are >1,000 pregnant women with laboratory evidence of possible Zika virus infection in the United States and U.S. territories (<http://www.cdc.gov/zika/geo/pregwomen-uscases.html>). Pediatric health care providers need information to guide appropriate laboratory testing and clinical evaluation and management of infants born to these mothers. On July 21–22, 2016, CDC, in collaboration with the American Academy of Pediatrics (AAP), convened a meeting to obtain individual input from experts and partners to inform the development of guidance for the evaluation and management of infants with congenital Zika virus infection. In attendance were experts in pediatrics, infectious diseases, neurology, developmental and behavioral pediatrics, ophthalmology, audiology, physical medicine and rehabilitation, neonatology, lactation and nutrition, maternal-fetal medicine, clinical genetics, hospitalist medicine, neonatology, and endocrinology, and representatives from principal partner groups (Box 1). Discussion focused on three areas: 1) initial evaluation and laboratory testing of infants born to mothers with laboratory evidence of Zika virus infection during pregnancy, 2) outpatient management and follow-up of infants with microcephaly or other findings consistent with congenital Zika syndrome, and 3) outpatient management and follow-up of infants with laboratory evidence of congenital Zika virus infection but without findings consistent with congenital Zika syndrome.

This guidance aims to assist health care providers in the evaluation and management of infants with congenital Zika virus infection based on currently available data on congenital infections with Zika virus and other pathogens. As more information becomes available, this guidance will be updated.

## Updated Recommendations for the Initial Laboratory Testing and Evaluation of Infants with Possible Congenital Zika Virus Infection

**Infant diagnostic testing.** Laboratory testing for congenital Zika virus infection is recommended for infants born to mothers with laboratory evidence of Zika virus infection, and for infants with findings suggestive of congenital Zika syndrome and a maternal epidemiologic link suggesting possible transmission, regardless of maternal testing results (Figure). Laboratory evidence of maternal Zika virus infection includes Zika virus RNA detected in any maternal clinical specimen by rRT-PCR and positive Zika virus IgM with confirmatory neutralizing antibody titer for Zika virus or flavivirus, not otherwise specified. Zika virus rRT-PCR testing should be performed on both infant serum and urine, and Zika virus IgM enzyme-linked immunosorbent assay (ELISA) should concurrently be performed on infant serum. If cerebrospinal fluid (CSF) is obtained for other studies, rRT-PCR testing for Zika virus RNA and Zika virus IgM should be performed on CSF. Laboratory testing should be performed on infant specimens; cord blood is not recommended because it can yield false positive results through contamination with maternal blood and might also yield false negative results (21). Infant laboratory testing for Zika virus should be performed within the first 2 days after birth; if testing is performed later, distinguishing between congenital, perinatal, and postnatal infection will be difficult. If the timing of infection cannot be determined, infants should be managed as if they have congenital Zika virus infection.

A Zika rRT-PCR positive result in an infant sample confirms the diagnosis of congenital Zika virus infection (Table 1). Zika virus IgM detected in an infant, without detectable Zika virus RNA, should be interpreted as probable congenital Zika virus infection. The plaque reduction neutralization test (PRNT) measures virus-specific neutralizing antibodies and is used to confirm the specificity of the IgM antibodies against Zika virus and rule out a false positive IgM result (20). If the infant's initial sample is IgM-positive, but PRNT was not performed on the mother's sample, PRNT should be performed on the infant's initial sample. However, PRNT cannot distinguish between maternal and infant antibodies. Because of this, it might be necessary to wait until the child is at least age 18 months, when maternal antibodies are expected to wane, to confirm congenital infection. PRNT should be performed on a sample collected from a child aged  $\geq 18$  months whose initial sample was IgM positive if Zika-specific neutralizing antibodies were detected by PRNT on either the infant's or mother's sample. If the infant's initial sample is negative by both IgM ELISA and rRT-PCR but clinical concerns remain (e.g., microcephaly with negative evaluation for other known causes), PRNT at age

**BOX 1. Areas of expertise and organizations represented at the Clinical Evaluation and Management of Infants with Congenital Zika Virus Infection meeting — Atlanta, Georgia, July 21–22, 2016**

**Specialties represented**

Audiology  
 Clinical genetics  
 Critical care  
 Developmental and behavioral pediatrics  
 Endocrinology  
 Hospitalist medicine  
 Infectious disease  
 Lactation and infant feeding  
 Maternal-fetal medicine  
 Neonatology  
 Neurology  
 Nutrition  
 Ophthalmology  
 Orthopedics  
 Pediatrics  
 Physical medicine and rehabilitation

**Partner organizations**

American Academy of Family Physicians  
 American Academy of Pediatrics (including representation from the Puerto Rico chapter)  
 American College of Obstetricians and Gynecologists  
 Association of Maternal & Child Health Programs  
 Family Voices, Inc.  
 March of Dimes  
 National Association of Pediatric Nurse Practitioners  
 Parent to Parent of Georgia  
 Society for Maternal-Fetal Medicine

**Federal agencies**

Administration for Children and Families  
 CDC  
 Centers for Medicare & Medicaid Services  
 Maternal and Child Health Bureau, Health Resources and Services Administration  
 National Institute of Child Health and Human Development, National Institutes of Health  
 Office of the Assistant Secretary for Preparedness and Response

18 months can be considered. If PRNT results at 18 months are negative, the child is considered to not have congenital Zika virus infection. If PRNT results are positive, congenital Zika infection is presumed, but postnatal infection cannot be excluded, especially for children living in an area with active Zika virus transmission.

In many cases, infant laboratory testing results will not be available before hospital discharge. In these cases, infants should be presumed to have congenital Zika virus infection until test results are available. For the purposes of this guidance, infants with confirmed or probable Zika virus infection should be managed in the same manner.

Detection of Zika virus RNA in the placenta can confirm the presence of maternal infection, but cannot distinguish between maternal and congenital infection. For circumstances in which maternal testing was not previously performed, performed more than 12 weeks after exposure (22), or was not definitive (e.g., flavivirus not otherwise specified) (20), a positive placental rRT-PCR result can confirm maternal Zika virus infection. Based on unpublished CDC data, placentas from mothers with Zika virus infection during pregnancy can have detectable Zika virus RNA at the time of delivery, regardless of the timing of maternal infection. Clinical implications for an infant with Zika virus RNA detected in the placenta, in the absence of laboratory evidence of Zika virus in the infant, are unknown.

Limited data are currently available regarding perinatal Zika virus transmission (23). Guidelines for evaluation and management of infants and children with postnatally acquired Zika virus disease (1) will be updated as more information is available.

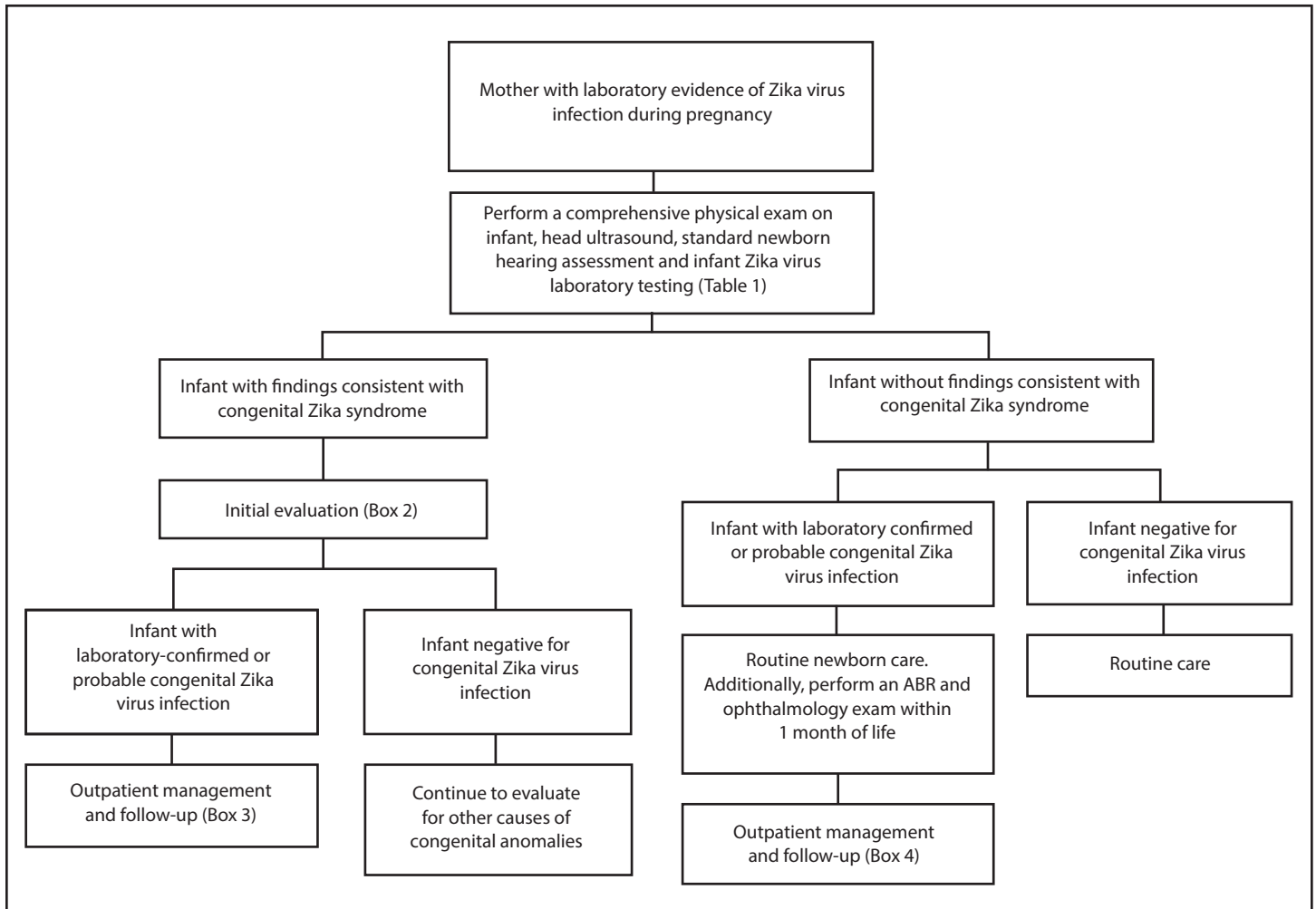
**Clinical evaluation of infants.** Infants born to mothers with laboratory evidence of Zika virus infection should receive a comprehensive physical examination, including precise measurement of head (occipitofrontal) circumference,\* length and weight, assessment of gestational age, and examination for neurologic abnormalities and dysmorphic features (Table 2). A postnatal head ultrasound should be performed on all infants born to mothers with laboratory evidence of Zika virus infection before discharge from the hospital, including those infants with normal prenatal ultrasound findings, because some abnormal findings associated with congenital Zika syndrome might not be readily apparent on prenatal ultrasounds. All infants should receive a hearing screen per universal screening recommendations before hospital discharge. Infants with laboratory evidence of congenital Zika virus infection should be referred for a comprehensive ophthalmologic exam and evaluation of hearing by ABR testing before 1 month of age. Other evaluations should be performed as clinically indicated.

Infants with negative IgM and negative rRT-PCR testing born to a mother with laboratory evidence of Zika virus

\* Standard head circumference charts are based on measurements taken within 24 hours of birth. Additional information on child growth standards is available at <http://www.who.int/childgrowth/en/>. Additional information on head circumference measurement is available at [https://www.cdc.gov/zika/pdfs/microcephaly\\_measuring.pdf](https://www.cdc.gov/zika/pdfs/microcephaly_measuring.pdf).



**FIGURE. Recommended Zika virus testing and evaluation of infants born to mothers with laboratory evidence of Zika virus infection during pregnancy \***



**Abbreviation:** ABR = auditory brainstem response.

\* Laboratory evidence of maternal Zika virus infection includes 1) Zika virus RNA detected by real-time reverse transcription–polymerase chain reaction (rRT-PCR) in any clinical specimen; or 2) positive Zika virus immunoglobulin M (IgM) with confirmatory neutralizing antibody titers. Mothers should be tested by rRT-PCR within 2 weeks of exposure or symptom onset, or by IgM within 2–12 weeks of exposure or symptom onset. Because of the decline in IgM antibody and viral RNA levels over time, negative maternal testing 12 weeks after exposure does not rule out maternal infection. **Source:** Oduyebo T, Igbinosa I, Petersen EE, et al. Update: interim guidance for health care providers caring for pregnant women with possible Zika virus exposure—United States, July 2016. *MMWR Morb Mortal Wkly Rep* 2016;65:739–44. <http://dx.doi.org/10.15585/mmwr.mm6529e1>.

**TABLE 1. Interpretation of results of laboratory testing of infant’s blood, urine and/or cerebrospinal fluid for evidence of congenital Zika virus infection**

| Infant test results* |                      |   |
|----------------------|----------------------|---|
| rRT-PCR              | IgM                  | Interpretation                                |
| Positive             | Positive or Negative | Confirmed congenital Zika virus infection     |
| Negative             | Positive             | Probable congenital Zika virus infection†     |
| Negative             | Negative             | Negative for congenital Zika virus infection† |

**Abbreviations:** rRT-PCR = real-time reverse transcription–polymerase chain reaction; IgM = immunoglobulin M.

\* Infant serum, urine, or cerebrospinal fluid.

† Laboratory results should be interpreted in the context of timing of infection during pregnancy, maternal serology results, clinical findings consistent with congenital Zika syndrome, and any confirmatory testing with plaque reduction neutralization testing (PRNT).

infection should receive routine care, including monitoring of head circumference at every well child visit and age-appropriate developmental screening (24). Health care providers should report information on pregnant women in the United States and the U.S. territories with laboratory evidence of Zika virus infection and their infants (regardless of infant test results) to state, tribal, local, or territorial health departments for inclusion in the U.S. Zika Pregnancy Registry (<http://www.cdc.gov/zika/hc-providers/registry.html>), or the Puerto Rico Zika Active Pregnancy Surveillance System (ZAPSS) (<http://www.cdc.gov/zika/public-health-partners/zapss.html>).

For all infants with abnormal findings consistent with congenital Zika syndrome, an extensive evaluation is recommended

**TABLE 2. Initial evaluation and recommended outpatient management during the first 12 months of life for infants with possible congenital Zika virus infection, based on maternal and infant laboratory tests and infant clinical findings**

| Mother   | Infant clinical exam                                   | Before hospital discharge  | Infant testing   | 2 wks.  | 1 mo. | 2 mos. | 3 mos. | 4–6 mos. | 9 mos. | 12 mos. |
|--|--|--|--|---|-------|--------|--------|----------|--------|---------|
| Laboratory evidence of Zika virus infection*         | No evidence of abnormalities                           | Routine newborn care: PE, HC, weight/length, and neurologic exam<br>Hearing screen<br>Head US<br>Infant Zika virus testing (Table 1)   | Negative for Zika virus infection<br><br>Laboratory evidence of Zika virus infection*        | Routine care, including monitoring of OFC and development at every well child visit and age-appropriate developmental screening |       |        |        |          |        |         |
|  | Abnormalities consistent with congenital Zika syndrome | As above plus:<br>Consider transfer to hospital with subspecialty care<br>CBC, metabolic panel, LFTs, ophthalmology exam<br>ABR<br>Consider advanced neuroimaging (Box 2)                                  | Negative for Zika virus infection<br><br>Laboratory evidence of Zika virus infection*        | Evaluate for other causes of congenital anomalies<br>Further management as clinically indicated                                 |       |        |        |          |        |         |
| Not tested, or tested outside of appropriate window† | No evidence of abnormalities                           | Maternal Zika virus testing†<br>Consider Zika virus placental testing<br>Routine newborn care: PE, HC, weight/length and neurologic exam<br>Hearing screen<br>Head US                                      | Perform infant Zika virus testing if evidence of Zika virus infection on maternal testing*,† | Outpatient management for appropriate infant clinical exam and test results   |       |        |        |          |        |         |
|  | Abnormalities consistent with congenital Zika syndrome | As above, plus:<br>Consider transfer to hospital with subspecialty care.<br>CBC, metabolic panel, LFTs, ophthalmology exam<br>ABR<br>Consider advanced neuroimaging<br>Infant Zika virus testing (Table 1) | Negative for Zika virus infection<br><br>Laboratory evidence of Zika virus infection*        | Evaluate for other causes of congenital anomalies<br>Further management as clinically indicated                                 |       |        |        |          |        |         |

**Abbreviations:** ABR = auditory brainstem response; CBC = complete blood count; LFTs = liver function tests; HC = head (occipitofrontal) circumference; PE = physical examination; rRT-PCR = real-time reverse transcription–polymerase chain reaction; US = ultrasound.

\* Laboratory evidence of maternal Zika virus infection includes 1) Zika virus RNA detected by real-time reverse transcription–polymerase chain reaction (rRT-PCR) in any clinical specimen; or 2) positive Zika virus immunoglobulin M (IgM) with confirmatory neutralizing antibody titers. Confirmatory neutralizing antibody titers are needed in addition to IgM for maternal Zika virus infection.

† Mothers should be tested by rRT-PCR within 2 weeks of exposure or symptom onset, or by IgM within 2–12 weeks of exposure or symptom onset. Because of the decline in IgM antibody titers and viral RNA levels over time, negative maternal testing 12 weeks after exposure does not rule out maternal infection. **Source:** Oduyebo T, Igbinosa I, Petersen EE, et al. Update: interim guidance for health care providers caring for pregnant women with possible Zika virus exposure—United States, July 2016. *MMWR Morb Mortal Wkly Rep* 2016;65:739–44. <http://dx.doi.org/10.15585/mmwr.mm6529e1>. Mothers should be tested by rRT-PCR within 2 weeks of exposure or symptom onset, or by IgM within 2–12 weeks of exposure or symptom onset. Because of the decline in IgM antibody titers and viral RNA levels over time, negative maternal testing 12 weeks after exposure does not rule out maternal infection. <http://dx.doi.org/10.15585/mmwr.mm6529e1>.

(Box 2). Transfer to a facility with access to pediatric subspecialty care might facilitate this evaluation. However, the decision should not be based solely on the presence of maternal Zika virus infection during pregnancy. Health care providers should consider both the immediate needs of the infant and the potential negative impact of possible separation from his or her family. The recommended evaluation includes a complete

blood count and metabolic panel, including liver function tests, a comprehensive examination by an ophthalmologist, ABR testing, and consideration of advanced neuroimaging in consultation with a neurologist. In addition, infants should be evaluated for other causes of microcephaly or intracranial calcifications, including genetic conditions and other congenital infections.

Infants born to mothers with risk factors for maternal Zika virus infection (travel to or residence in an area of Zika virus transmission or sex with a partner who traveled to or resided in such an area) and for whom maternal testing was not performed before delivery, should have a comprehensive physical examination, including standardized measurement of head circumference. Maternal diagnostic testing should be performed (20,22), and testing of the placenta for Zika virus PCR should be considered (<http://www.cdc.gov/zika/hc-providers/test-specimens-at-time-of-birth.html>); infant testing should be performed if maternal testing is consistent with laboratory evidence of Zika virus infection. If an infant appears clinically well, further evaluation, including head ultrasound, ophthalmologic assessment, and infant laboratory Zika virus testing, can be deferred until maternal test results are available. However, if there is concern about infant follow-up, head

**BOX 2. Initial clinical evaluation and management of infants with laboratory evidence of Zika virus infection and abnormalities consistent with congenital Zika syndrome**

- Consultation with:
  - Neurologist for determination of appropriate neuroimaging and additional evaluation.
  - Infectious disease specialist for diagnostic evaluation of other congenital infections (e.g., syphilis, toxoplasmosis, rubella, cytomegalovirus infection, lymphocytic choriomeningitis virus infection, and herpes simplex virus infection).
  - Ophthalmologist for comprehensive eye exam and evaluation for possible cortical visual impairment prior to discharge from the hospital or within 1 month of birth.
  - Endocrinologist for evaluation for hypothalamic or pituitary dysfunction.
  - Clinical geneticist to evaluate for other causes of microcephaly or other anomalies if present.
- Consider consultation with:
  - Orthopedist, physiatrist, or physical therapist for the management of hypertonica, club foot or arthrogryptic-like conditions.
  - Pulmonologist or otolaryngologist for concerns about aspiration.
  - Lactation specialist, nutritionist, gastroenterologist, or speech or occupational therapist for the management of feeding issues.
- Perform auditory brainstem response to assess hearing.
- Perform complete blood count and metabolic panel, including liver function tests.
- Provide family and supportive services.

ultrasound, ophthalmologic assessment and infant Zika virus testing should be performed before hospital discharge. CDC recommends standard precautions in all health care settings to protect both health care personnel and patients from infection with blood-borne pathogens, including Zika virus (25).

Although Zika virus has been detected in breast milk (26), no cases of Zika virus infection associated with breastfeeding have been reported, and current evidence suggests that the benefits of breastfeeding outweigh the theoretical risks of Zika virus transmission. All women with Zika virus infection during pregnancy should be encouraged and supported to breastfeed their infants, regardless of infant Zika virus testing results.

### Outpatient Management of Infants with Laboratory Evidence of Zika Virus Infection and Abnormalities Consistent with Congenital Zika Syndrome

The care of infants with abnormalities consistent with congenital Zika syndrome requires a multidisciplinary team and an established medical home to facilitate the coordination of care, which is critical to ensuring that these infants receive necessary testing and consultations (Box 3), and that abnormal findings are detected and appropriately addressed (27). If abnormalities are noted on prenatal evaluation, counseling specific to congenital Zika syndrome should occur during pregnancy, preferably with the involvement of obstetric and pediatric providers. Before the infant's discharge from the birth hospital, follow-up appointments with specialists and services recommended during initial evaluation should be made. Consideration should be given to using preexisting coordinated multidisciplinary care clinics.

Infants should receive routine preventive pediatric health care, including regularly scheduled immunizations (24). Families of infants with congenital Zika syndrome should receive information that includes discussion of concerns for development, function, feeding and growth, and prognosis. Standardized measurement of growth parameters, including head circumference, weight, and length, should occur regularly through the first year of life.

Breastfeeding should be encouraged and supported for nutrition and enhanced bonding. Primary care providers should assess the infant for evidence of feeding difficulties and refer for consultations related to lactation, occupational therapy, speech therapy, nutrition, and/or gastroenterology for poor suck, swallowing dysfunction, gastroesophageal reflux, and aspiration. Swallowing dysfunction might not be evident initially and feeding should be monitored closely.

A neurologic examination should be performed at age 1 month and 2 months by a primary care provider and subsequently as

**BOX 3. Outpatient management of infants with laboratory evidence of Zika virus infection and abnormalities consistent with congenital Zika syndrome**

- A medical home should be established, and visits with primary care provider should occur monthly for at least the first 6 months of life.
  - Follow growth parameters; monitor development; provide routine immunizations, anticipatory guidance, and psychosocial support; and ensure infants receive necessary testing and consultations.
- Neurologic examination by the primary care provider at 1 and 2 months of age. Refer to neurology for any abnormalities, or for any parental or provider concerns.
- Refer to developmental specialist and early intervention services.
- Repeat comprehensive ophthalmologic exam at age 3 months, and refer to ophthalmology for any abnormal findings, or for any parental or provider concerns.
- Repeat auditory brainstem response testing at age 4–6 months, and refer to audiology for any abnormal findings, or for any parental or provider concerns.
- Repeat testing for hypothyroidism at age 2 weeks and age 3 months, even if the initial testing results were normal. Refer to endocrinology for any abnormal findings.
- Provide family and supportive services.

needed depending on the infant's clinical status. If not already initiated, neurology referral should occur for evaluation of any abnormalities, including sleep problems and excess irritability. If the ophthalmology exam performed within the first month of life was normal, another exam (including retinal assessment) is recommended at age 3 months. ABR testing is the preferred test to detect hearing loss resulting from neurologic damage. If the initial newborn hearing screen was performed using only otoacoustic emission testing, the infant should be referred for ABR screening before 1 month of age. If the newborn hearing screen was normal, an ABR should be performed at age 4–6 months. If vision or hearing results are abnormal, referrals to appropriate specialists should occur as soon as possible.

Infants with abnormal brain development can be at risk for hypothalamic dysfunction leading to pituitary insufficiency, and early manifestations of endocrine dysfunction might not be detected by routine newborn screening (28). Thyroid screening, including measurement of thyroid stimulation hormone (TSH) and thyroxine (either free T<sub>4</sub> or both total T<sub>4</sub> and estimated free T<sub>4</sub>) should be performed at age 2 weeks and again at age 3 months. If either of these results is abnormal,

further evaluation of pituitary function should be performed by an endocrinologist.

Developmental monitoring should occur at each routine visit, and standardized, validated screening tools should be used to assess the presence of developmental delay (24). Referral to a developmental specialist and early intervention services should occur as soon as possible. It is important that primary care providers continue to monitor the child's development and progress with standardized, validated developmental screening tools to ensure that the child's developmental needs are addressed.

Overall, families and caregivers of infants with congenital Zika syndrome will require ongoing psychosocial assessment and support. Health care providers should work closely with parents to ensure that the care plan that is developed is consistent with the infant's needs and the family's wishes. Monitoring for depression among caregivers should occur during primary care visits, because depression or family stress might be associated with the infant's complex medical needs. Families might also face financial stressors, social stigma, and other forms of discrimination. Existing national and local resources for families of children with complex care needs should be made available to families (29).

Referrals for abnormal findings should occur as clinically indicated, either to a pediatric specialist or a specialist with expertise in the care of children. In areas with limited access to pediatric subspecialty care, the numerous services recommended for infants with congenital Zika syndrome might not be readily available; in these situations, telehealth might be explored as a potential means of providing subspecialty care and support to families in areas with limited access (30).

### **Outpatient Management of Infants with Laboratory Evidence of Zika Virus Infection but Without Abnormalities Consistent with Congenital Zika Syndrome**

Infants with laboratory evidence of Zika virus infection but without apparent abnormalities at birth are recommended to have additional monitoring (Box 4), until further information is available regarding outcomes, because some neurologic sequelae of congenital Zika virus infection (e.g., seizures, cognitive impairment, and vision and hearing abnormalities) might be subtle or have delayed onset. During routine infant follow-up with primary care providers, a standardized, validated developmental screening tool should be used at age 9 months, as currently recommended by the American Academy of Pediatrics (24), or sooner, if there are any developmental concerns. Referral to a developmental specialist and early intervention programs should be considered as soon as caregiver or provider concerns are noted, and additional referrals to specialists should be made as clinically indicated.



A vision screening, including assessment of visual regard, should be performed at each well child visit, and referral to an ophthalmologist should be made for any caregiver or provider concerns. Infants with abnormalities on initial hearing screen should be referred to an audiologist for a complete evaluation. Later development of hearing loss in infants without other clinical findings has been observed in other congenital infections (15); however, the likelihood that an infant with congenital Zika virus infection without clinical findings consistent with congenital Zika syndrome and with an initial normal hearing screen will develop hearing loss is unknown. ABR testing of infants at age 4–6 months can be considered, although the risk from sedation needs to be taken into account. Infants who passed an initial ABR and without an ABR at age 4–6 months should be referred for behavioral audiologic diagnostic testing at age 9 months, or sooner for any hearing concerns. Behavioral audiologic testing is recommended because of the potential need for sedation with ABR testing in infants.

As a critical component of patient care and to facilitate early identification of developmental delays, families should be empowered to be active participants in their child's monitoring and care. Anticipatory guidance provided to caregivers should

**BOX 4. Outpatient management of infants with laboratory evidence of Zika virus infection, but without abnormalities consistent with congenital Zika syndrome**

- A medical home should be established.
  - Follow growth parameters, and perform developmental screening at each well child visit.
  - Emphasize anticipatory guidance for families regarding developmental milestones, feeding and growth, sleep and irritability, and abnormal movements.
- Use a standardized, validated developmental screening tool at 9 months as currently recommended, or earlier for any parental or provider concerns.
- Referral to ophthalmology for comprehensive eye exam within one month of birth. Perform vision screening and assess visual regard at every well child visit, and refer to ophthalmology for any abnormal findings, or for any parental or provider concerns.
- Perform auditory brainstem response within one month of birth. Consider repeat auditory brainstem response at age 4–6 months or perform behavioral diagnostic testing at age 9 months and refer to audiology for any abnormal findings, or for any parental or provider concerns.
- Provide family and supportive services.

emphasize developmental milestones, feeding and growth, sleep, irritability, and seizure recognition.

A disproportionate burden of congenital Zika virus infection might affect families with already limited access to health care. Families might face language and cultural barriers, financial barriers, and inadequate access. Rural populations might have difficulty accessing specialists. Barriers to care for all affected infants and their families should be addressed through linkage to national, state, and local health programs.

### Contributors

Michael Agus, MD, Boston Children's Hospital; Donald B. Bailey, PhD, RTI International; Jim Bale, MD, University of Utah; Katherine A. Beckmann, PhD, Administration for Children and Families; Jatinder Bhatia, MD, Augusta University; Jennifer Bolden Pitre, JD, Family Voices, Inc.; Timothy J. Brei, MD, Seattle Children's Hospital; Lekisha Daniel-Robinson, MSPH, Center for Medicaid and CHIP Services, Centers for Medicare and Medicaid Services; Eric Dziuban, MD, CDC; Marcus Gaffney, MPH, CDC; Dixie D. Griffin, MD, Tift Regional Health System; Alyson B. Goodman, MD, CDC; Manda Hall, MD, Texas Department of State Health Services; R. Phillips Heine, MD, Duke University; Amy Houtrow, MD, PhD, University of Pittsburgh; Lisa Hunter, PhD, Cincinnati Children's Hospital; Susan L. Hyman, MD, University of Rochester Medical Center; Wanda K. Jones, DrPH, Office of the Assistant Secretary for Health; Bill G. Kapogiannis, MD, National Institute of Child Health and Human Development; Sharon S. Lehman, MD, Nemours Children's Health System, Sidney Kimmel Medical College of Thomas Jefferson University; Aaron Lopata, MD, Maternal and Child Health Bureau, Health Resources and Services Administration; Yvonne Maldonado, MD, Stanford University; Edward McCabe, MD, PhD, March of Dimes; Rima McLeod, MD, University of Chicago; Joan Y. Meek, MD, Florida State University College of Medicine; Michael E. Msall, MD, University of Chicago Medicine-Comer Children's Hospital; Lynne M. Mofenson, MD, Elizabeth Glaser Pediatric AIDS Foundation; Sitara Nayak, Parent to Parent of Georgia; Scott Needle, MD, Healthcare Network of Southwest Florida; Susan Reef, MD, CDC; Sydney Rice, MD, University of Arizona; Scott Rivkees, MD, University of Florida; Jeannie Rodriguez, PhD, Emory University; Elizabeth Rosenblum, MD, University of California, San Diego; Pablo Sanchez, MD, Nationwide Children's Hospital; Renate Savich, MD, University of Mississippi Medical Center; Angela Scheuerle, MD, University of Texas Southwestern Medical Center; Lee Segal, MD, University of Wisconsin, Madison; Camille Smith, EdS, CDC; Parminder S. Suchdev, MD, Emory University; V. Fan Tait, MD, American Academy of Pediatrics (AAP); Edwin Trevathan, MD, Vanderbilt University School of Medicine; Camila V. Ventura, MD, Altino Ventura Foundation; Richard Whitley, MD, Children's of Alabama, University of Alabama at Birmingham; Susan Wiley, MD, Cincinnati Children's Hospital Medical Center; Fernando Ysern, MD, Puerto Rico Chapter, AAP.

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<sup>1</sup>Epidemic Intelligence Service, CDC; <sup>2</sup>Influenza Division, National Center for Immunization and Respiratory Diseases, CDC; <sup>3</sup>Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, CDC; <sup>4</sup>Division of Environmental Hazards and Health Effects, National Center for Environmental Health, CDC; <sup>5</sup>Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, CDC; <sup>6</sup>Division of Congenital and Developmental Disorders, National Center on Birth Defects and Developmental Disabilities, CDC; <sup>7</sup>Office of the Director, National Center for Emerging and Zoonotic Infectious Diseases, CDC; <sup>8</sup>Division of Vector-Borne Diseases, National Center for Emerging and Zoonotic Infectious Diseases, CDC; <sup>9</sup>Division of Human Development and Disability, National Center on Birth Defects and Developmental Disabilities, CDC; <sup>10</sup>Infectious Diseases Pathology Branch, Division of High-Consequence Pathogens and Pathology, National Center for Emerging and Zoonotic Infectious Diseases, CDC; <sup>11</sup>Division of Public Health Information Dissemination, Center for Surveillance, Epidemiology, and Laboratory Services, CDC.

Corresponding authors: Kate Russell, [kerussell@cdc.gov](mailto:kerussell@cdc.gov), 404-718-1178; Sara E. Oliver, [seoliver@cdc.gov](mailto:seoliver@cdc.gov), 404-639-1204.

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## Notes from the Field

### Outbreak of Listeriosis Associated with Consumption of Packaged Salad — United States and Canada, 2015–2016

Julie L. Self, PhD<sup>1,2</sup>; Amanda Conrad, MPH<sup>2</sup>; Steven Stroika<sup>2</sup>; Alikeh Jackson, MPH<sup>3</sup>; Laura Burnworth, MPH<sup>2</sup>; Jennifer Beal, MPH<sup>3</sup>; Allison Wellman, MPH<sup>3</sup>; Kelly A. Jackson, MPH<sup>2</sup>; Sally Bidol, MPH<sup>4</sup>; Terri Gerhardt, MS<sup>5</sup>; Meghan Hamel, MSc<sup>6</sup>; Kristyn Franklin, MSc<sup>6</sup>; Christine Kopko<sup>7</sup>; Penelope Kirsch, MSc<sup>7</sup>; Matthew E. Wise, PhD<sup>2</sup>; Colin Basler, DVM<sup>2</sup>

In September 2015, PulseNet, the national molecular subtyping network for foodborne disease surveillance, identified a cluster of *Listeria monocytogenes* (*Listeria*) clinical isolates indistinguishable by two-enzyme pulsed-field gel electrophoresis (PFGE) pattern combination and highly related by whole-genome multilocus sequence typing (wgMLST). A case was defined as isolation of *Listeria* with the outbreak PFGE pattern and highly related by wgMLST with an isolation date on or after July 5, 2015, the isolate date of the earliest case in this cluster.

A standardized *Listeria* Initiative questionnaire (1) was used to gather information about foods consumed in the 4 weeks before illness from seven persons identified by November 30, 2015, with isolation dates occurring July 5, 2015–October 30, 2015. This tool did not include leafy green vegetables and failed to identify a common source for the infections. During December 2015 and January 2016, eight new or previously interviewed patients or their surrogates participated in open-ended interviews or provided shopper card records, and all reported consuming leafy greens in the month before illness onset. Among these, seven (88%) reported romaine and six (75%) reported spinach, higher than national food consumption estimates of 47% ( $p = 0.022$ ) and 24% ( $p = 0.003$ ), respectively (2). Six patients (75%) recalled consuming packaged salad, and three patients (38%) who recalled brands reported packaged salad brands processed by Company A.

The Ohio Department of Agriculture obtained packaged salad processed at Company A's Ohio facility from a store during routine sampling. On January 14, 2016, PulseNet analyzed sequence data from *Listeria* isolated from the packaged salad, and the isolate was highly related to the clinical isolates by wgMLST (median allele differences <10). This molecular finding, combined with the epidemiologic information, led the Food and Drug Administration to initiate an inspection of Company A's Ohio facility on January 16, 2016. Two food samples collected during the inspection yielded *Listeria*, and wgMLST analysis indicated that they were highly related

(median allele differences <10) to clinical and retail product isolates (Figure).

On January 21, 2016, Company A voluntarily halted production at its Ohio facility and conducted a market withdrawal of all packaged salad products from that facility because of possible *Listeria* contamination.\* The market withdrawal included 22 varieties of packaged salads sold under various brand names. Company A issued a voluntary recall of these products on January 27, 2016, which further identified the list of affected products and brand names.†

After the market withdrawal and recall, CDC fielded >450 inquiries about listeriosis from concerned consumers and clinicians, and the CDC outbreak website received >787,000 page views, more views than after any other foodborne illness outbreak to date.§

As of March 28, 2016, there were 19 persons meeting the case definition from nine states (Connecticut, Indiana, Massachusetts, Michigan, Missouri, New Jersey, New York, Ohio, and Pennsylvania) with isolation dates through January 31, 2016. All were hospitalized; one died. One illness in a pregnant woman resulted in a preterm live birth. One otherwise healthy child developed meningitis.

The Public Health Agency of Canada investigated 14 cases of listeriosis associated with this outbreak, with onset dates from May 7, 2015 to February 23, 2016 (3). Six Canadian clinical isolates were compared with U.S. clinical isolates and were highly related by wgMLST. Three cases reported consuming packaged salad processed at the Ohio facility. In January 2016, the Canadian Food Inspection Agency (CFIA) collected 55 packaged salads from stores in Canada representing 12 different products processed at the Ohio facility. CFIA isolated the outbreak strain and issued a food recall warning on January 22, 2016, for all products processed at the Ohio facility and distributed in Canada.¶

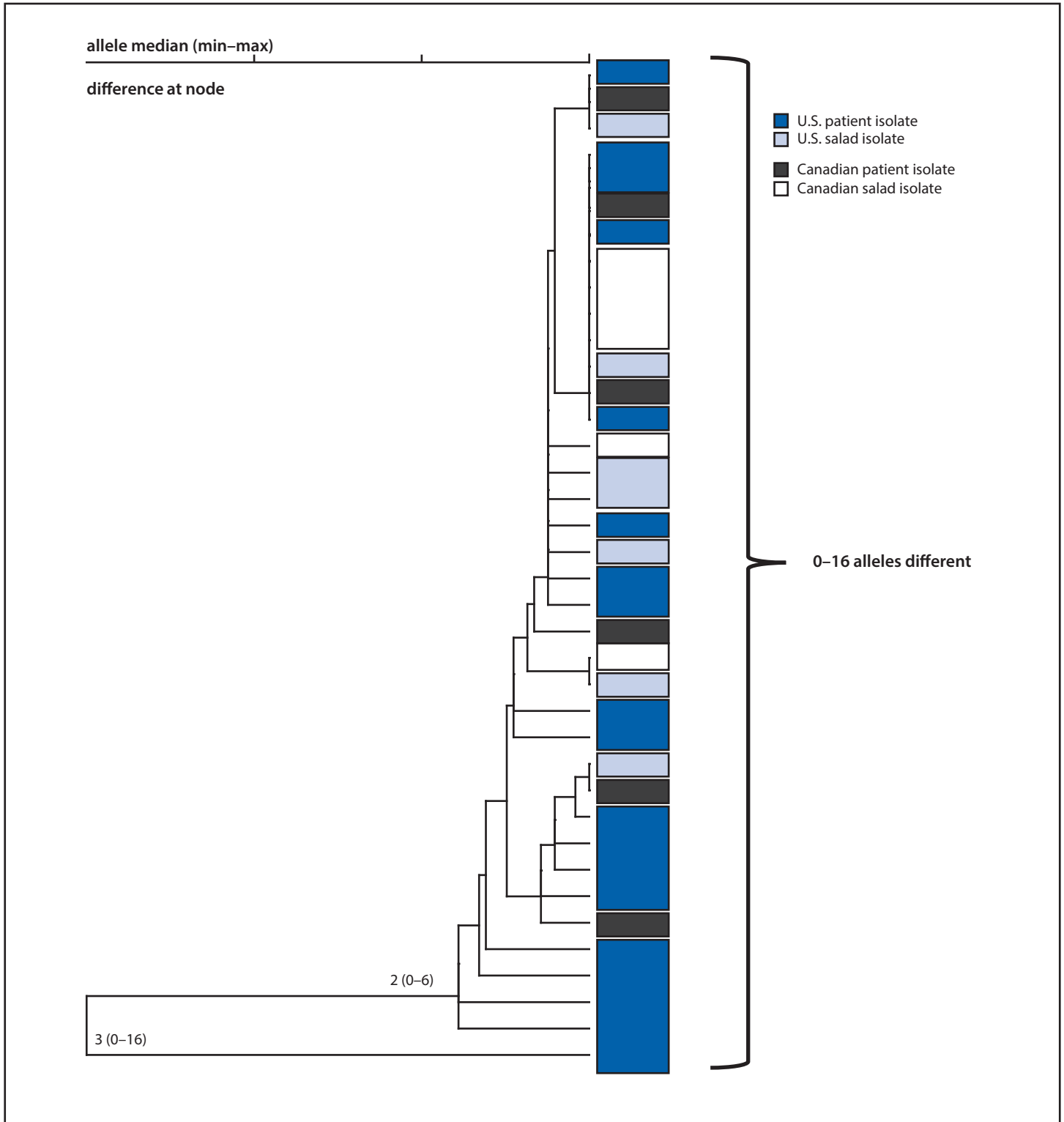
\* Food and Drug Administration. Recall—firm press release: Dole Fresh Vegetables announces voluntary withdrawal for salads. <http://www.fda.gov/Safety/Recalls/ucm482822.htm>.

† Food and Drug Administration. What you need to know about our voluntary recall of salads processed at the Springfield, Ohio facility. <http://www.fda.gov/Safety/Recalls/ucm483588.htm>.

§ CDC. Multistate outbreak of listeriosis linked to packaged salads produced at Springfield, Ohio Dole processing facility. <http://www.cdc.gov/listeria/outbreaks/bagged-salads-01-16/>.

¶ CFIA. Food recall warning—certain Dole brand pre-packaged chopped salads, salad blends and kits and leafy greens and certain PC Organics brand leafy greens recalled due to *Listeria monocytogenes*. <http://www.inspection.gc.ca/about-the-cfia/newsroom/food-recall-warnings/complete-listing/2016-01-22/eng/1453522915084/1453522920123>.

FIGURE. Phylogenetic tree by whole-genome multilocus sequence typing (wgMLST) of *Listeria monocytogenes* isolates\* from patients and salad products with indistinguishable pulsed-field gel electrophoresis patterns — United States and Canada,† July 5, 2015–January 31, 2016



\* By wgMLST, clinical and food isolates from the United States and Canada were closely related because they differed by a median of three alleles, with a range of 0–16 alleles.

† 19 patients from nine U.S. states and six patients from Canada.



The wgMLST analysis identified this listeriosis cluster and provided evidence of the link between contaminated food products and human illness. This allowed timely recall of potentially contaminated food, which might have prevented additional cases of serious illness.

This is the first reported outbreak of listeriosis associated with leafy greens and the eighth reported outbreak of listeriosis associated with fresh produce in the United States; all occurred since 2008 (4).<sup>\*\*</sup> It is unclear whether the appearance of these outbreaks might be attributed to improved outbreak detection, changes in consumer behavior, or changes in production and distribution. Fresh produce processors are advised to review food safety plans and consider incorporating measures to avoid the growth and persistence of *Listeria*.<sup>††</sup> The *Listeria* Initiative questionnaire has been revised to include additional questions about fresh produce to better identify produce vehicles of *Listeria*.

<sup>\*\*</sup> CDC. Foodborne Outbreak Online Database (FOOD Tool). <http://wwwn.cdc.gov/foodborneoutbreaks/>.

<sup>††</sup> Food and Drug Administration. FSMA Final Rule for Preventive Controls for Human Food. <http://www.fda.gov/Food/GuidanceRegulation/FSMA/ucm334115.htm>.

<sup>1</sup>Epidemic Intelligence Service, Division of Scientific Education and Professional Development, Center for Surveillance, Epidemiology, and Laboratory Services, CDC; <sup>2</sup>Division of Foodborne, Waterborne, and Environmental Diseases, National Center for Emerging and Zoonotic Infectious Diseases, CDC; <sup>3</sup>Food and Drug Administration; <sup>4</sup>Michigan Department of Health and Human Service; <sup>5</sup>Ohio Department of Agriculture; <sup>6</sup>Public Health Agency of Canada; <sup>7</sup>Canadian Food Inspection Agency.

Corresponding author: Julie L. Self, [yxj9@cdc.gov](mailto:yxj9@cdc.gov), 404-718-4689.

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## Notes from the Field

### Cluster of Tuberculosis Cases Among Marshallese Persons Residing in Arkansas — 2014–2015

Laura Lester Rothfeldt, DVM<sup>1,2</sup>; Naveen Patil, MD<sup>2,3</sup>; Dirk T. Haselow, MD<sup>2,3,4</sup>; Sandy Hainline Williams, MA<sup>2</sup>; J. Gary Wheeler, MD<sup>2,3,4</sup>; Leonard N. Mukasa, MBChB<sup>2,3</sup>

During early September 2014, the Arkansas Department of Health identified an increased number of tuberculosis (TB) cases among a unique population in a well-circumscribed geographical area in northwest Arkansas. The Compact of Free Association Act of 1985 (Public Law 99-239, amended in 2003 by Public Law 108-188) established the Republic of the Marshall Islands (RMI) as an independent nation, and persons from the RMI can travel freely (with valid RMI passport) to and from the United States as nonimmigrants without visas (1). Marshallese started settling in northwest Arkansas during the early 1990s because of employment and educational opportunities (2). According to the 2010 Census, an estimated 4,300 Marshallese resided in Arkansas (2), mostly within one county which ranked 6th in the United States for counties with the highest percentage of Native Hawaiians and Other Pacific Islanders (3). It is estimated that this number has been growing steadily each year since the 2010 Census; however, obtaining an accurate count is difficult. The RMI is a TB high-incidence country, with a case-rate of 212.7 per 100,000 persons for 2014, whereas the case-rate was 3.1 per 100,000 persons in Arkansas and 2.9 per 100,000 persons in the United States (4,5). Screening for either active TB or latent TB infection (LTBI) is not required for Marshallese entry to the United States (1).

A total of 107 active TB cases have been identified among Marshallese persons residing in Arkansas from 1997 through 2013. Despite establishment of an outreach team during 2002 and a satellite clinic during 2011, TB control among Marshallese residing in Arkansas remains challenging because of the high LTBI burden in this population, resulting in the increased likelihood of the development of active cases and exposure to persons with active disease. Outbreaks were identified during 2004 and again during 2014. During 2014, a total of 23 cases were identified among Marshallese persons, substantially above the average of six cases per year reported during the preceding 9 years. The Arkansas Department of Health identified an additional 11 cases through March 31, 2015, for a total of 34 TB cases, from self-reporting and contact tracing with targeted screening (tuberculin skin test and interferon-gamma release assay [T-Spot.TB test, Oxford Diagnostic Laboratories, Memphis, Tennessee]) of 412 contacts, which identified 165 additional persons (40%) with LTBI. Two deaths were

reported, one of which occurred in a young child who died of TB meningitis after being symptomatic with cough for 3 months and altered mental status for 1 week, prompting an extensive review of contact investigations. Among 34 patients, 33 (97%) resided within two zip codes of a single county. TB incidence among the Marshallese community accounted for 25% of all TB cases in Arkansas for 2014 and 79% of all TB cases in the affected county (Table). Among the 23 patients born in the RMI, 50% developed TB within 2.4 years (95% confidence interval = 1.2–3.1) of arrival in Arkansas.

This cluster is characterized by a high number of cases in children aged ≤15 years (19/34; 55.9%), with 11 of 34 (32.4%) patients aged ≤4 years; 11 of 19 (57.9%) patients aged ≤15 years were born in the United States and had no history of travel outside of the United States. Eight of 14 (57.1%) culture-confirmed, genotyped cases had the G00017 genotype, which constitutes the majority of genotyped TB cases in the RMI (4) and has been found in Arkansas since 2006 (Table). Obtaining a *Mycobacterium tuberculosis* isolate is less common for pediatric TB cases because of the low bacterial load and difficulty in sputum collection, therefore, only two of 19 (10.5%) pediatric cases versus 12 of 15 (80.0%) adult cases were genotyped.

The TB burden in the Marshallese community in Arkansas is substantially higher than that in the rest of the state. During 2014–2015, there was a substantial increase in the number of TB cases reported among Marshallese persons in Arkansas. The majority of these cases occurred among children; cases among children are widely considered to be indicative of ongoing transmission in a community (6). Cases in adults likely resulted from reactivation of LTBI or local acquisition of disease within Arkansas. Efforts to investigate this cluster are ongoing with an emphasis on informing targeted methods to decrease TB-associated morbidity and *M. tuberculosis* transmission.

**TABLE. Demographic and clinical characteristics of reported tuberculosis (TB) cases among Marshallese in Arkansas — January 1, 2014–March 31, 2015 (N = 34)**

| Characteristic   | No. (%)   |
|--|-----------|
| Born in Republic of the Marshall Islands                 | 23 (67.6) |
| Male   | 16 (47.1) |
| Age (yrs)  |           |
| 0–4  | 11 (32.4) |
| 5–15   | 8 (23.5)  |
| ≥16  | 15 (44.1) |
| <i>Mycobacterium tuberculosis</i> culture positive       | 14 (41.2) |
| National TB genotype G00017 (n = 14)                     | 8 (57.1)  |
| Proportion of TB cases in Arkansas, 2014 (n = 93)        | 23 (24.7) |
| Proportion of TB cases in affected county, 2014 (n = 29) | 23 (79.3) |

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<sup>1</sup>Epidemic Intelligence Service, Division of Scientific Education and Professional Development, CDC; <sup>2</sup>Arkansas Department of Health; <sup>3</sup>University of Arkansas for Medical Sciences; <sup>4</sup>Arkansas Children's Hospital.

Corresponding author: Laura Lester Rothfeldt, [laura.k.rothfeldt.mil@mail.mil](mailto:laura.k.rothfeldt.mil@mail.mil), 270-798-4749.

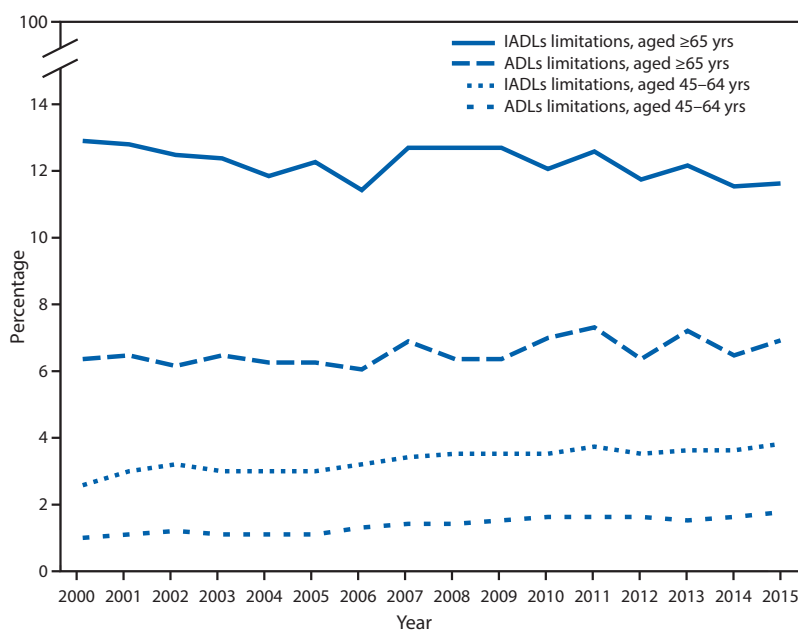
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## QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

## Percentage of Adults Aged $\geq 45$ Years with Activity Limitations, by Age Group and Type of Limitation\* — National Health Interview Survey,<sup>†</sup> United States, 2000–2015



**Abbreviations:** ADLs= activities of daily living; IADLs= instrumental activities of daily living.

\* Limitations in ADLs are based on response to the question, "Because of a physical, mental, or emotional problem, does [person] need the help of other persons with personal care needs, such as eating, bathing, dressing, or getting around inside this home?" Limitations in IADLs are based on response to the question, "Because of a physical, mental, or emotional problem, does [person] need the help of other persons in handling routine needs, such as everyday household chores, doing necessary business, shopping, or getting around for other purposes?"

<sup>†</sup> Estimates are based on household interviews of a sample of the noninstitutionalized U.S. civilian population and are derived from the National Health Interview Survey Family Core component.

The percentage of adults aged 45–64 years with limitations in activities of daily living (ADLs) increased from 1.3% in 2000 to 2.0% in 2015, and the percentage with limitations in instrumental activities of daily living (IADLs) increased from 2.8% to 4.0%. Among adults aged  $\geq 65$  years, the percentage with limitations in ADLs increased from 6.4% to 6.9%, and the percentage with limitations in IADLs decreased from 12.9% to 11.7%.

**Source:** National Health Interview Survey, 2000–2015. <http://www.cdc.gov/nchs/nhis.htm>.

**Reported by:** Ellen A. Kramarow, PhD, [ekramarow@cdc.gov](mailto:ekramarow@cdc.gov), 301-458-4325.









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