

## Suicide Rates by Industry and Occupation — National Violent Death Reporting System, 32 States, 2016

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In 2017, nearly 38,000 persons of working age (16–64 years) in the United States died by suicide, which represents a 40% rate increase (12.9 per 100,000 population in 2000 to 18.0 in 2017) in less than 2 decades.\* To inform suicide prevention, CDC analyzed suicide data by industry and occupation among working-age decedents presumed to be employed at the time of death from the 32 states participating in the 2016 National Violent Death Reporting System (NVDRS).<sup>†,§</sup> Compared with rates in the total study population, suicide rates were significantly higher in five major industry groups: 1) Mining, Quarrying, and Oil and Gas Extraction (males); 2) Construction (males); 3) Other Services (e.g., automotive repair) (males); 4) Agriculture, Forestry, Fishing, and Hunting (males); and 5) Transportation and Warehousing (males and females). Rates were also significantly higher in six major occupational groups: 1) Construction and Extraction (males and females); 2) Installation, Maintenance, and Repair (males); 3) Arts, Design, Entertainment, Sports, and Media (males); 4) Transportation and Material Moving (males and females); 5) Protective Service (females); and 6) Healthcare Support (females). Rates for detailed occupational groups (e.g., Electricians or Carpenters within the Construction and Extraction major group) are presented and provide insight into the differences in suicide rates within major occupational groups. CDC's Preventing Suicide: A Technical Package of

Policy, Programs, and Practices (1) contains strategies to prevent suicide and is a resource for communities, including workplace settings.

NVDRS combines data on violent deaths, including suicide, from death certificates, coroner/medical examiner reports, and law enforcement reports. Industry and occupation coding experts used CDC's National Institute for Occupational Safety

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\* <https://www.cdc.gov/injury/wisqars>.

† <https://www.cdc.gov/violenceprevention/nvdrs>.

§ In 2016, 32 states participated in NVDRS: Alaska, Arizona, Colorado, Connecticut, Georgia, Hawaii, Illinois, Indiana, Iowa, Kansas, Kentucky, Maine, Maryland, Massachusetts, Michigan, Minnesota, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, Utah, Vermont, Virginia, Washington, and Wisconsin. That year, Illinois, Pennsylvania, and Washington each collected data on ≥80% of violent deaths in the state, in accordance with requirements under which the state was funded for NVDRS; therefore, presented data likely underestimate suicide deaths and rates.



and Health Industry and Occupation Computerized Coding System (NIOCCS 3.0)<sup>¶</sup> to assign 2010 U.S. Census civilian industry and occupation codes for 20,975 suicide decedents aged 16–64 years from the 32 states participating in the 2016 NVDRS, using decedents' usual industry and occupation as reported on death certificates. Industry (the business activity of a person's employer or, if self-employed, their own business) and occupation (a person's job or the type of work they do) are distinct ways to categorize employment (2).

Suicide rates were analyzed for industry and occupational groups by sex. Population counts by occupation for rate denominators were states' civilian, noninstitutionalized current job population counts (for persons aged 16–64 years) from the 2016 American Community Survey Public Use Microdata Sample.\*\* Replicate weight standard errors for those counts were used to calculate 95% confidence intervals (CIs) for suicide rates (3). Rates were calculated by U.S. Census code for major industry groups, major occupational groups, and detailed occupational groups with  $\geq 20$  decedents; detailed occupational groups are typically more homogenous in terms of employee income, work environment, and peer group. Rates were not calculated for detailed industry groups because many decedents' industry was classifiable only by major group. The following decedents were excluded from rate calculations: military workers (327); unpaid workers (2,863); those whose

other NVDRS data sources (e.g., law enforcement reports) indicated no employment at time of death (i.e., unemployed, disabled, incarcerated, homemaker, or student) (4) (1,783); and those not residing in the analysis states (223). A total of 15,779 decedents, including 12,505 (79%) males and 3,274 (21%) females, were included in the analysis. The analysis was conducted using Stata (version 15, StataCorp) and SAS (version 9.4, SAS Institute) statistical software.

Industry and occupational groups with suicide rates significantly ( $\alpha = 0.05$ ) higher than the study population (i.e., all industries or occupations: 27.4 males [95% CI = 26.9–27.9] and 7.7 females [95% CI = 7.5–8.0] per 100,000 population) were identified when the group's 95% CI exceeded the study population rate point estimate. Treating the population rate as a constant is reasonable when variance is small and is required for one-sample inference that recognizes the nonindependence of individual industry and occupation groups relative to the study population.

The five major industry groups with suicide rates higher than the study population by sex included 1) Mining, Quarrying, and Oil and Gas Extraction (males: 54.2 per 100,000 civilian non-institutionalized working population, 95% CI = 44.0–64.3); 2) Construction (males: 45.3, 95% CI = 43.4–47.2); 3) Other Services (e.g., automotive repair; males: 39.1, 95% CI = 36.1–42.0); 4) Agriculture, Forestry, Fishing, and Hunting (males: 36.1, 95% CI = 31.7–40.5); and 5) Transportation and Warehousing (males: 29.8, 95% CI = 27.8–31.9; females: 10.1, 95% CI = 7.9–12.8) (Table 1) (Supplementary Table 1, <https://stacks.cdc.gov/view/cdc/84274>). The six major occupational

<sup>¶</sup> <https://wwwn.cdc.gov/nioccs3>.

\*\* <https://www.census.gov/programs-surveys/acs/data/pums.html>.

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**TABLE 1. Suicide rates\* for persons working in major industry and occupational groups meeting reporting criteria, by sex — National Violent Death Reporting System, 32 states,† 2016§**

Census code¶	Major group	Sex rate (95% CI)	
		Male	Female
<b>Total</b>	<b>All industries or occupations</b>	<b>27.4 (26.9–27.9)</b>	<b>7.7 (7.5–8.0)</b>
<b>Industry</b>			
0170–0290	Agriculture, Forestry, Fishing, and Hunting	36.1 (31.7–40.5)**	NC††
0370–0490	Mining, Quarrying, And Oil and Gas Extraction	54.2 (44.0–64.3)**	NC
0770	Construction	45.3 (43.4–47.2)**	9.4 (6.5–13.2)
1070–3990	Manufacturing	23.6 (22.5–24.8)	7.3 (6.3–8.2)
4070–4590	Wholesale Trade	11.8 (10.1–13.5)	NC
4670–5790	Retail Trade	21.3 (20.0–22.6)	6.8 (6.1–7.5)
6070–6390	Transportation and Warehousing	29.8 (27.8–31.9)**	10.1 (7.9–12.8)**
0570–0690	Utilities	26.3 (21.9–30.7)	NC
6470–6780	Information	19.6 (16.9–22.3)	6.7 (4.7–9.1)
6870–6990	Finance and Insurance	15.1 (13.3–16.8)	6.0 (5.0–6.9)
7070–7190	Real Estate and Rental and Leasing	16.6 (13.8–19.4)	7.1 (5.0–9.7)
7270–7490	Professional, Scientific, and Technical Services	17.6 (16.2–19.0)	6.4 (5.4–7.3)
7570	Management of Companies and Enterprises	NC	NC
7580–7790	Administrative and Support and Waste Management Services	25.9 (23.7–28.1)	5.2 (3.9–6.7)
7860–7890	Educational Services	9.3 (8.1–10.4)	3.9 (3.4–4.4)
7970–8470	Health Care and Social assistance	18.7 (17.0–20.4)	7.5 (7.0–8.0)
8560–8590	Arts, Entertainment, and Recreation	27.4 (24.0–30.8)	9.7 (7.4–12.4)
8660–8690	Accommodation and Food Services	22.9 (21.2–24.6)	7.8 (6.9–8.7)
8770–9290	Other Services	39.1 (36.1–42.0)**	8.8 (7.5–10.0)
9370–9590	Public Administration	23.1 (21.1–25.1)	7.5 (6.2–8.8)
<b>Occupation</b>			
0010–0430	Management	17.5 (16.4–18.6)	5.7 (5.0–6.5)
0500–0950	Business and Financial Operations	11.5 (10.0–13.0)	4.7 (3.8–5.5)
1000–1240	Computer and Mathematical	16.2 (14.5–17.9)	6.4 (4.5–8.9)
1300–1560	Architecture and Engineering	23.2 (20.6–25.7)	8.2 (4.7–13.4)
1600–1965	Life, Physical, and Social science	21.4 (16.3–27.6)	5.3 (3.0–8.6)
2000–2060	Community and Social Service	15.4 (11.7–20.0)	6.2 (4.7–8.2)
2100–2160	Legal	16.3 (12.1–21.7)	7.9 (5.4–11.2)
2200–2550	Education, Training, and Library	9.9 (8.3–11.6)	3.9 (3.3–4.6)
2600–2960	Arts, Design, Entertainment, Sports, and Media	32.0 (28.2–35.8)**	8.8 (6.7–11.5)
3000–3540	Healthcare Practitioners and Technical	23.6 (20.8–26.3)	8.5 (7.6–9.4)
3600–3655	Healthcare Support	23.6 (17.0–32.1)	10.6 (9.2–12.1)**
3700–3955	Protective Service	26.4 (23.7–29.1)	14.0 (9.9–19.2)**
4000–4160	Food Preparation and Serving Related	21.1 (19.2–22.9)	7.8 (6.7–8.8)
4200–4250	Building and Grounds Cleaning and Maintenance	26.7 (24.4–29.0)	6.9 (5.3–8.7)
4300–4650	Personal Care and Service	25.0 (21.2–28.8)	8.4 (7.2–9.5)
4700–4965	Sales and Related	20.7 (19.3–22.1)	7.1 (6.3–7.8)
5000–5940	Office and Administrative Support	14.2 (12.9–15.5)	5.4 (4.9–5.9)
6000–6130	Farming, Fishing, and Forestry	31.4 (25.6–37.1)	NC
6200–6940	Construction and Extraction	49.4 (47.2–51.6)**	25.5 (15.7–39.4)**
7000–7630	Installation, Maintenance, and Repair	36.9 (34.6–39.3)**	NC
7700–8965	Production	27.5 (25.9–29.2)	6.8 (5.6–8.1)
9000–9750	Transportation and Material Moving	30.4 (28.8–32.0)**	12.5 (10.2–14.7)**

**Abbreviations:** CI = confidence interval; NC = not calculated.

\* Per 100,000 civilian, noninstitutionalized working persons aged 16–64 years.

† Alaska, Arizona, Colorado, Connecticut, Georgia, Hawaii, Illinois, Indiana, Iowa, Kansas, Kentucky, Maine, Maryland, Massachusetts, Michigan, Minnesota, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, Utah, Vermont, Virginia, Washington, and Wisconsin.

§ Number of suicide decedents = 15,779.

¶ Census Bureau 2012 industry and 2010 occupational codes from the 2016 American Community Survey, translated from National Institute for Occupational Safety and Health Industry and Occupation Computerized Coding System codes using Census Bureau definitions (<https://www.census.gov/topics/employment/industry-occupation/guidance/code-lists.html>).

\*\* Statistically higher than population rate (all industries or occupations) based on 95% CI of industry or occupational group rate not containing the total population rate point estimate.

†† NC indicates that rate was not calculated because the number of decedents was <20.

groups with higher rates included 1) Construction and Extraction (males: 49.4, 95% CI = 47.2–51.6; females: 25.5, 95% CI = 15.7–39.4); 2) Installation, Maintenance, and Repair (males: 36.9, 95% CI = 34.6–39.3); 3) Arts, Design, Entertainment, Sports, and Media (males: 32.0, 95% CI = 28.2–35.8); 4) Transportation and Material Moving (males: 30.4, 95% CI = 28.8–32.0; females: 12.5, 95% CI = 10.2–14.7); 5) Protective Service (females: 14.0, 95% CI = 9.9–19.2); and 6) Healthcare Support (females: 10.6, 95% CI = 9.2–12.1).

Rates could be calculated for 118 detailed occupational groups for males and 32 for females (Supplementary Table 2, <https://stacks.cdc.gov/view/cdc/84275>). Some occupational groups with suicide rates significantly higher than those of the study population were only identifiable through observation at the detailed group level (Table 2). Among males, these detailed groups included the following seven groups: 1) Fishing and hunting workers (part of the Farming, Fishing, and Forestry major occupational group); 2) Machinists (Production major group); 3) Welding, soldering, and brazing workers (Production major group); 4) Chefs and head cooks (Food Preparation and Serving Related major group); 5) Construction managers (Management major group); 6) Farmers, ranchers, and other agricultural managers (Management major group); and 7) Retail salespersons (Sales and Related major group). Among females, these detailed groups included the following five groups: 1) Artists and related workers (Arts, Design, Entertainment, Sports, and Media major group); 2) Personal care aides (Personal Care and Service major group); 3) Retail salespersons (Sales and Related major group); 4) Waiters and waitresses (Food Preparation and Serving Related major group); and 5) Registered nurses (Healthcare Practitioners and Technical major group). Groups with highest rate point estimates (e.g., female Artists and related workers and male Fishing and hunting workers) also had wide 95% CIs (Table 2), based on relatively low numbers of decedents and relatively small working populations (Supplementary Table 2, <https://stacks.cdc.gov/view/cdc/84275>).

## Discussion

This report used data from 32 states to provide updated population-level suicide rates for major occupational groups and new information on suicide rates for major industry groups and detailed occupational groups. Estimates for most major occupational groups are similar, although not directly comparable, to previous estimates that were based on 2015 NVDRS data from 17 states (4). Recent NVDRS expansion to 50 states might facilitate direct comparisons over time by industry and occupation nationwide. These findings highlight opportunities for targeted prevention strategies and further

investigation of work-related factors that might increase risk of suicide. Previous research indicates suicide risk is associated with low-skilled work (5), lower education (6), lower absolute and relative socioeconomic status (7), work-related access to lethal means (8), and job stress, including poor supervisory and colleague support, low job control, and job insecurity (9). Industry, labor, and professional associations, as well as employers, and state and local health departments can use this information to focus attention and resources on suicide prevention. Future research might examine these and other risk factors among the industries and occupations identified in this report as having high suicide rates.

This report estimated suicide rates comprehensively for industry and occupational groups meeting sample size criteria and identified groups with rates higher than the study's population rate. Although relative comparisons of suicide rates in this manner are useful for prevention purposes, these results should not overshadow the essential fact that the suicide rate in the U.S. working-age population overall has increased by 40% in less than 2 decades. Therefore, all industry sectors and occupational groups can contribute to reducing suicide incidence.

The findings in this report are subject to at least five limitations. First, this study did not address confounding factors that might account for different suicide rates among and within industry or occupational groups. Second, it did not address suicide among unemployed decedents, military or unpaid workers, or those aged >64 years (9). Third, the numerator and denominator data were not a direct match for calculating rates; death certificates reflect decedents' usual industry and occupation, and available population size data refer to the number of persons by current job. Fourth, the results are based on data from 32 states and are therefore not nationally representative. Finally, three states contributing to the 2016 NVDRS did not collect data on all violent deaths. Other limitations of NVDRS analysis using death certificate industry and occupation data have been described previously (4).

All industries and occupations can benefit from a comprehensive approach to suicide prevention. CDC's Preventing Suicide: A Technical Package of Policy, Programs, and Practices (1) provides strategies with the best available evidence to prevent suicide and can serve as a resource for communities and employers. Workplace-specific strategies include 1) promoting help-seeking; 2) integrating workplace safety and health and wellness programs to advance the overall well-being of workers; 3) referring workers to financial and other helping services; 4) facilitating time off and benefits to cover supportive services; 5) training personnel to detect and appropriately respond to suicide risk; 6) creating opportunities for employee social connectedness; 7) reducing access to lethal means among persons at risk; and 8) creating a crisis response plan sensitive to the



**TABLE 2. Detailed occupational groups meeting reporting criteria with male and female suicide rates\* higher† than the population rate (all occupations) and associated major occupational groups and rates — National Violent Death Reporting System, 32 states,§ 2016¶**

Sex/Census code**	Detailed occupational group	Rate (95% CI)†	Census code**	Part of major occupational group	Rate (95% CI)
<b>Male</b>					
6100	Fishing and hunting workers	119.9 (60.9–215.6)†	6000–6130	Farming, Fishing, and Forestry	31.4 (25.6–37.1)
2750	Musicians, singers, and related workers	96.5 (63.7–141.1)†	2600–2960	Arts, Design, Entertainment, Sports, and Media	32.0 (28.2–35.8)†
2600	Artists and related workers	93.5 (60.7–138.5)†	2600–2960	Arts, Design, Entertainment, Sports, and Media	32.0 (28.2–35.8)†
6530	Structural iron and steel workers	79.0 (43.5–134.0)†	6200–6940	Construction and Extraction	49.4 (47.2–51.6)†
7360	Millwrights	78.7 (39.8–142.4)†	7000–7630	Installation, Maintenance, and Repair	36.9 (34.6–39.3)†
6220	Brickmasons, blockmasons, stonemasons, and reinforcing iron and rebar workers	67.6 (45.7–97.0)†	6200–6940	Construction and Extraction	49.4 (47.2–51.6)†
6515	Roofers	65.2 (46.1–90.0)†	6200–6940	Construction and Extraction	49.4 (47.2–51.6)†
7200	Automotive service technicians and mechanics	64.8 (57.4, 72.3)†	7000–7630	Installation, Maintenance, and Repair	36.9 (34.6–39.3)†
8030	Machinists	64.2 (53.1–75.3)†	7700–8965	Production	27.5 (25.9–29.2)
6260	Construction laborers	62.0 (56.7–67.3)†	6200–6940	Construction and Extraction	49.4 (47.2–51.6)†
7010	Computer, automated teller, and office machine repairers	60.8 (41.8–86.1)†	7000–7630	Installation, Maintenance, and Repair	36.9 (34.6–39.3)†
6240	Carpet, floor, and tile installers and finishers	55.2 (35.3–83.1)†	6200–6940	Construction and Extraction	49.4 (47.2–51.6)†
7150	Automotive body and related repairers	54.9 (34.4–83.9)†	7000–7630	Installation, Maintenance, and Repair	36.9 (34.6–39.3)†
6230	Carpenters	54.7 (49.0–60.4)†	6200–6940	Construction and Extraction	49.4 (47.2–51.6)†
8140	Welding, soldering, and brazing workers	53.6 (45.2–62.1)†	7700–8965	Production	27.5 (25.9–29.2)
6320	Construction equipment operators except paving, surfacing, and tamping equipment operators	52.8 (42.2–63.4)†	6200–6940	Construction and Extraction	49.4 (47.2–51.6)†
9620	Laborers and freight, stock, and material movers, hand	51.5 (47.1–55.8)†	9000–9750	Transportation and Material Moving	30.4 (28.8–32.0)†
4000	Chefs and head cooks	47.8 (38.3–57.2)†	4000–4160	Food Preparation and Serving Related	21.1 (19.2–22.9)
0220	Construction managers	45.7 (38.4–53.1)†	0010–0430	Management	17.5 (16.4–18.6)
6355	Electricians	44.0 (37.7–50.2)†	6200–6940	Construction and Extraction	49.4 (47.2–51.6)†
6200	First-line supervisors of construction trades and extraction workers	44.0 (37.4–50.5)†	6200–6940	Construction and Extraction	49.4 (47.2–51.6)†
0205	Farmers, ranchers, and other agricultural managers	43.2 (34.9–51.5)†	0010–0430	Management	17.5 (16.4–18.6)
6420	Painters and paperhangers	36.6 (29.4–43.9)†	6200–6940	Construction and Extraction	49.4 (47.2–51.6)†
6440	Pipelayers, plumbers, pipefitters, and steamfitters	35.4 (28.7–42.1)†	6200–6940	Construction and Extraction	49.4 (47.2–51.6)†
4760	Retail salespersons	31.3 (27.7–35.0)†	4700–4965	Sales and Related	20.7 (19.3–22.1)
9130	Driver/sales workers and truck drivers	30.4 (27.8–33.0)†	9000–9750	Transportation and Material Moving	30.4 (28.8–32.0)†
Total	All occupations	27.4 (26.9–27.9)			
<b>Female</b>					
2600	Artists and related workers	45.5 (25.7–75.5)†	2600–2960	Arts, Design, Entertainment, Sports, and Media	8.8 (6.7–11.5)
9620	Laborers and freight, stock, and material movers, hand	20.9 (14.9–28.8)†	9000–9750	Transportation and Material Moving	12.5 (10.2–14.7)†
4610	Personal care aides	12.1 (9.0–16.0)†	4300–4650	Personal Care and Service	8.4 (7.2–9.5)
4760	Retail salespersons	11.5 (9.3–13.7)†	4700–4965	Sales and Related	7.1 (6.3–7.8)
4110	Waiters and waitresses	11.3 (9.1–13.4)†	4000–4160	Food Preparation and Serving Related	7.8 (6.7–8.8)
3600	Nursing, psychiatric, and home health aides	10.2 (8.3–12.0)†	3600–3655	Healthcare Support	10.6 (9.2–12.1)†
3255	Registered nurses	10.1 (8.6–11.6)†	3000–3540	Healthcare Practitioners and Technical	8.5 (7.6–9.4)
Total	All occupations				7.7 (7.5–8.0)

**Abbreviation:** CI = confidence interval.

\* Per 100,000 civilian, noninstitutionalized working persons aged 16–64 years.

† Statistically higher than population rate (all occupations) based on 95% CI of occupational group rate not containing the total population rate point estimate.

§ Alaska, Arizona, Colorado, Connecticut, Georgia, Hawaii, Illinois, Indiana, Iowa, Kansas, Kentucky, Maine, Maryland, Massachusetts, Michigan, Minnesota, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, Utah, Vermont, Virginia, Washington, and Wisconsin.

¶ Number of suicide decedents = 15,779.

\*\* Census Bureau 2012 industry and 2010 occupational codes from the 2016 American Community Survey, translated from National Institute for Occupational Safety and Health Industry and Occupation Computerized Coding System codes using Census Bureau definitions (<https://www.census.gov/topics/employment/industry-occupation/guidance/code-lists.html>).

needs of coworkers, friends, family, and others who might themselves be at risk (1,10). Other community-based strategies include strengthening economic supports, strengthening access and delivery of care, teaching coping and problem-solving

skills, and responsibly reporting suicide (e.g., not providing details) (1). Further workplace prevention resources are available at <https://workplacesuicideprevention.com/> and

## References

## Summary

## What is already known about this topic?

Suicide among the U.S. working-age population (ages 16–64 years) is increasing; in 2017, nearly 38,000 persons died by suicide.

## What is added by this report?

National Violent Death Reporting System data from 32 states were used to calculate suicide rates for major industry and occupational groups and detailed occupational groups. Five industry groups and six major occupational groups had higher suicide rates than did the overall study population. Suicide rates for detailed occupational groups provide insight into subcategories within major groups.

## What are the implications for public health practice?

Opportunities exist for targeted and broadscale prevention. CDC's Preventing Suicide: A Technical Package of Policy, Programs, and Practices provides strategies to prevent suicide and can serve as a resource for communities and employers.

<https://theactionalliance.org/communities/workplace> and help is available at 1-800-273-TALK (8255).

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Susan Burton, Matt Hirst, Jeff Purdin, Marie Haring Sweeney, Division of Field Studies and Engineering, National Institute for Occupational Safety and Health, CDC; the 32 states that added industry and occupation data to the 2016 National Violent Death Reporting System.

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## Trends in HIV-2 Diagnoses and Use of the HIV-1/HIV-2 Differentiation Test — United States, 2010–2017

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Since 2014, the recommended laboratory testing algorithm for diagnosing human immunodeficiency virus (HIV) infection has included a supplemental HIV-1/HIV-2 differentiation test to confirm infection type on the basis of the presence of type-specific antibodies (1). Correctly identifying HIV-1 and HIV-2 infections is vital because their epidemiology and clinical management differ. To describe the percentage of diagnoses for which an HIV-1/HIV-2 differentiation test result was reported and to categorize HIV type based on laboratory test results, 2010–2017 data from CDC's National HIV Surveillance System (NHSS) were analyzed. During 2010–2017, a substantial increase in the number of HIV-1/HIV-2 differentiation test results were reported to NHSS, consistent with implementation of the HIV laboratory-based testing algorithm recommended in 2014. However, >99.9% of all HIV infections identified in the United States were categorized as HIV-1, and the number of HIV-2 diagnoses (mono-infection or dual-infection) remained extremely low (<0.03% of all HIV infections). In addition, the overall number of false positive HIV-2 test results produced by the HIV-1/HIV-2 differentiation increased. The diagnostic value of a confirmatory antibody differentiation test in a setting with sensitive and specific screening tests and few HIV-2 infections might be limited. Evaluation and consideration of other HIV tests approved by the Food and Drug Administration (FDA) that might increase efficiencies in the CDC and Association of Public Health Laboratories–recommended HIV testing algorithm are warranted.

Worldwide, the majority of HIV infections are HIV-1. HIV-2 occurs predominantly in West Africa, but has been reported in other countries, including the United States (2–4). When last assessed, 166 persons categorized as having HIV-2 infection were reported to CDC as cases of public health importance during 1987–2009 (5). NHSS is a case-based surveillance system for the United States (6); data include patient demographic characteristics, HIV transmission risk category, and laboratory test results. However, HIV infection type is not reported to or determined by NHSS. Consequently, CDC developed a surveillance definition for HIV-2 to determine the number of such cases and to describe the demographics of persons identified with the different HIV infection types in the United States.

For this analysis, the surveillance definitions for type of HIV infection include 1) HIV-2 mono-infection, defined as having an HIV-2-positive nucleic acid test (NAT) result or an HIV-2-positive HIV-1/HIV-2 differentiation test result and no evidence of HIV-1-RNA or DNA\*; 2) HIV-1 and HIV-2 dual-infection, defined as having an HIV-2-positive or HIV-1-positive and HIV-2-positive antibody test result and positive HIV-1 and HIV-2 RNA or DNA test results; or 3) probable HIV-2 infection, defined as having an HIV-2-positive antibody test result (HIV-2 immunoassay or an HIV-1/HIV-2 antigen and antibody test) and no evidence of HIV-1 RNA or DNA. All remaining HIV diagnoses in NHSS were categorized as HIV-1. Data from NHSS were used to summarize patient demographics, HIV transmission risk category, and the number of pregnancies and perinatal transmissions according to HIV type. The estimated annual percentage change (7) was used to calculate the number of HIV diagnoses and the number of patients for whom an HIV-1/HIV-2 differentiation test result was reported to NHSS, both overall and for HIV-1 infections.

Laboratory test results were analyzed for persons with HIV infection diagnosed during 2010–2017 and reported to NHSS through December 2018. Two HIV-1/HIV-2 differentiation tests were available to U.S. laboratories during the analysis period: Multispot HIV-1/HIV-2 Rapid Test (Bio-Rad Laboratories), which was approved by FDA in 2004 and discontinued in 2016, and Geenius HIV-1/HIV-2 Supplemental Assay (Bio-Rad Laboratories), which was approved by FDA in 2014. However, in NHSS data, which of the HIV-1/HIV-2 differentiation tests was used cannot be determined.

During 2010–2017, of 327,700 diagnosed HIV infections in the United States, 327,502 (99.94%) were HIV-1. The remaining 198 (0.06%) diagnosed infections were classified as HIV-2 mono-infection (n = 102), dual HIV-1 and HIV-2 infection (n = 11), or probable but unconfirmed HIV-2 infections (n = 85) (Table 1). Demographic characteristics of persons with HIV-1 infection varied substantially from those with HIV-2 infection (including HIV-2, HIV-2 probable but unconfirmed, or dual HIV-1 and HIV-2 infection) (Table 2). Persons with HIV-2 infection were as likely to be female as

\*A positive quantitative or qualitative nucleic acid test result or molecular sequence data for an HIV-1 genotypic drug-resistance test.

**TABLE 1. Number of HIV diagnoses among persons aged ≥13 years, by diagnosis type — National HIV Surveillance System (NHSS), United States and six dependent areas,\* 2010–2017**

Diagnosis year	No.	Diagnosis type			
		HIV-1 <sup>†</sup>	HIV-2 <sup>§</sup>	HIV-2, probable, but unconfirmed <sup>¶</sup>	Dual HIV-1/HIV-2 <sup>**</sup>
2010	44,086	44,066	7	13	0
2011	42,285	42,265	12	4	4
2012	41,467	41,443	9	12	3
2013	39,987	39,978	7	2	0
2014	40,667	40,635	22	9	1
2015	40,406	40,378	13	14	1
2016	40,121	40,085	18	18	0
2017	38,681	38,652	14	13	2
<b>Total</b>	<b>327,700</b>	<b>327,502</b>	<b>102</b>	<b>85</b>	<b>11</b>
<b>EAPC (95% CI)</b>		<b>-0.03 (-0.03 to -0.02)</b>	<b>12.0 (2.8 to 22.1)</b>	<b>11.4 (1.4 to 22.3)</b>	<b>-7.8 (-28.9 to 19.7)</b>

**Abbreviations:** CI = confidence interval; EAPC = estimated annual percentage change; HIV = human immunodeficiency virus.

\* Data from CDC's National HIV Surveillance System (NHSS) collected through December 2018.

<sup>†</sup> Diagnoses in NHSS with no evidence of an HIV-2, HIV-2 probable but unconfirmed, or dual HIV-1 and HIV-2 infections.

<sup>§</sup> Diagnoses in NHSS with HIV-2 RNA or an HIV-2 positive differentiation test and no evidence of HIV-1 RNA or DNA.

<sup>¶</sup> Diagnoses in NHSS with an HIV-2 positive antibody test and no evidence of HIV-1 RNA or DNA.

\*\* Diagnoses in NHSS with HIV-1 and HIV-2 RNA or DNA.

male, were more frequently older, non-Hispanic black, had HIV infection attributed to heterosexual contact, had been born in countries where HIV-2 infection is endemic, and resided in the northeastern United States at the time of diagnosis. Among the 11 cases classified as dual HIV-1 and HIV-2 infection, six were among men, and five were among women. Eight persons were identified as having emigrated from a country where HIV-2 is endemic. Among the 99 women with confirmed or probable HIV-2 infection, nine had evidence of a pregnancy during or after diagnosis; however, no perinatal HIV-2 transmissions were reported to NHSS.

The number of persons with HIV infection whose report to NHSS included an HIV-1/HIV-2 differentiation test result increased by an estimated 21.2% per year (95% confidence interval [CI] = 21.0–21.4) during 2010–2017 (Table 3). Concurrently, the number of confirmed and probable HIV-2 infections increased by an estimated 12.0% per year (95% CI = 2.8–22.1) and 11.4% per year (95% CI = 1.4–22.3), respectively, during 2010–2017 (Table 1). Although the number of HIV-1/HIV-2 differentiation test results continued to increase during 2014–2017 by an estimated 6.4% per year (95% CI = 6.2%–6.9%), the number of persons with confirmed or probable HIV-2 infections did not change with an estimated annual percentage change including zero, -9.5% per year (95% CI = -27.1% to 12.3%) and 14.3% per year (95% CI = -10.1% to 45.4%), respectively.<sup>†</sup> Among persons with confirmed HIV-1 infection, 356 included false-positive HIV-2 results from an HIV-1/HIV-2 differentiation test (Table 3), and the number of false positive reports increased an estimated 18.8% per year (95% CI = 13.3–24.5) relative

to all HIV diagnoses. However, the number of false positive reports relative to those whose report to NHSS included an HIV-1/HIV-2 differentiation test decreased during the study period by 6.2% (95% CI = -10.7% to -1.5%) (Table 3).

## Discussion

These results are consistent with the previously reported findings from 1987–2009 that HIV-2 remains a rare diagnosis in the United States (5). Use of the HIV-1/HIV-2 differentiation test increased steadily throughout the study period, although after 2014 the number of confirmed or probable HIV-2 infections remained stable. The number of persons with confirmed HIV-1 infection who had a false-positive HIV-2 test result by using the HIV-1/HIV-2 differentiation test was greater than the total number of confirmed and probable HIV-2 diagnoses combined. In these cases, HIV antibody cross-reactivity likely caused the false-positive reaction and necessitated additional time and testing to resolve (8).

Although HIV-2 is rare, correct diagnosis is vital for ensuring correct clinical management. Persons with HIV-2 who have an incorrect HIV-1 diagnosis and are treated with nonnucleoside reverse-transcriptase inhibitors, to which HIV-2 is intrinsically resistant, might fail to suppress an HIV-2 viral load (9). Without commercially available HIV-2 viral load tests, HIV-2 infection might not be recognized, or might require additional testing to determine HIV status. This step might include having to send specimens to specialized laboratories that perform a laboratory-developed HIV-2 NAT.

The findings in this report are subject to at least three limitations. First, the definition used to define HIV-2 infection using test results entered into the Enhanced HIV/AIDS Reporting

<sup>†</sup> 2014–2017 total HIV diagnoses = 159,875.



**TABLE 2. Characteristics of persons aged ≥13 years with diagnosed HIV infection — National HIV Surveillance System (NHSS), United States and six dependent areas,\* 2010–2017**

Characteristic	No. (%)	
	HIV-1 <sup>†</sup>	HIV-2 <sup>§</sup>
<b>Total</b>	<b>327,502 (100)</b>	<b>198 (100)</b>
<b>Age group (yrs)</b>		
13–24	71,893 (22)	20 (10.1)
25–34	100,937 (30.8)	30 (15.2)
35–44	67,462 (20.6)	35 (17.7)
45–54	55,957 (17.1)	46 (23.2)
≥55	31,253 (9.5)	67 (33.8)
<b>Sex</b>		
Male	262,520 (80.2)	99 (50.0)
Female	64,982 (19.8)	99 (50.0)
<b>Race/Ethnicity</b>		
Black, non-Hispanic	141,712 (43.3)	147 (74.2)
White, non-Hispanic	84,848 (25.9)	15 (7.6)
Hispanic	80,291 (24.5)	21 (10.6)
Other	20,651 (6.3)	15 (7.6)
<b>Transmission category</b>		
Male-to-male sexual contact	210,250 (64.2)	50 (25.3)
Heterosexual contact	84,063 (25.7)	121 (61.1)
Injection-drug use (IDU)	20,966 (6.4)	23 (11.6)
Male-to-male sexual contact/IDU	11,613 (3.5)	2 (1.0)
Other	610 (0.2)	2 (1.0)
<b>Birth country</b>		
United States	205,370 (62.7)	44 (22.2)
Other countries	70,647 (21.6)	37 (18.7)
Unknown	48,222 (14.7)	28 (14.1)
Countries where HIV-2 is endemic <sup>¶</sup>	3,263 (1)	89 (44.9)
<b>U.S. Census region of residence at diagnosis</b>		
South	163,204 (49.8)	62 (31.3)
West	61,380 (18.7)	16 (8.1)
Northeast	55,593 (17)	109 (55.1)
Midwest	42,069 (12.8)	11 (5.6)
U.S. dependent areas	5,256 (1.6)	0 (—)

**Abbreviation:** HIV = human immunodeficiency virus.

\* Data from CDC's National HIV Surveillance System (NHSS) collected through December 2018.

<sup>†</sup> Diagnoses in NHSS with no evidence of HIV-2, HIV-2 probable but not confirmed, or dual HIV-1 and HIV-2 infections.

<sup>§</sup> Diagnoses in NHSS of HIV-2, HIV-2 probable but not confirmed, or dual HIV-1 and HIV-2 infections.

<sup>¶</sup> Angola, Benin, Burkina Faso, Cape Verde, Côte d'Ivoire, the Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Mozambique, Niger, Nigeria, Sao Tome, Senegal, Sierra Leone, and Togo.

System,<sup>§</sup> (an application for collecting, storing, and retrieving HIV-related data), was developed for use with surveillance data to report epidemiologic trends. Identification of type of HIV diagnosis for the management of patients might require additional diagnostic tests that are beyond the scope of this study. Second, for 61 (33%) HIV-2 diagnoses (probable and confirmed) with missing HIV-1 NAT results, the possibility of HIV-2 infection or identification of dual infection could not be ruled out. An HIV-2 NAT might also have helped confirm these infections, but no FDA-approved commercially available

<sup>§</sup> <https://doi.org/10.3886/ICPSR34725.v1>.

## Summary

### What is already known about this topic?

Since 2014, CDC has recommended using an antibody-based HIV-1/HIV-2 differentiation test as part of a laboratory-based algorithm to confirm HIV-1 and HIV-2 infections.

### What is added by this report?

During 2010–2017, use of the HIV-1/HIV-2 differentiation test increased, but the number of confirmed HIV-2 diagnoses remained <0.1%. In addition, the overall number of false positive HIV-2 test results produced by the HIV-1/HIV-2 differentiation increased.

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

CDC recommends that laboratories continue to follow the laboratory-based algorithm with the HIV-1/HIV-2 differentiation test as the second step. However, updates to the laboratory-based testing algorithm merit consideration in the United States where HIV-2 infections remain rare.

test exists. Moreover, HIV-2 infection results in lower levels of circulating virus compared with those of HIV-1 infection. Finally, evidence of pregnancy in women with HIV infection is underreported to NHSS (10). Although this can result in an underestimation of the number of pregnant women with HIV-2, reporting of perinatal HIV infection is robust, thus increasing the likelihood that perinatal HIV-2 infection would have been recognized.

Despite increasing use of the HIV-1/HIV-2 differentiation test, few HIV-2 infections are diagnosed in the United States. CDC continues to recommend that laboratories follow the laboratory-based algorithm with the HIV-1/HIV-2 differentiation test as the second step. Use of an HIV-1 NAT in the algorithm would likely distinguish type of HIV infection for the majority of diagnoses in the United States. Follow-up testing of specimens that remain ambiguous regarding HIV type after testing with an HIV-1 NAT is also recommended.<sup>¶</sup> However, updates to the laboratory-based testing algorithm merit consideration in the United States. This could include development of new FDA-approved tests to reduce the time to HIV diagnosis and treatment, primarily for HIV-1, but in rare cases, for HIV-2.

<sup>¶</sup> <https://stacks.cdc.gov/view/cdc/50872>.

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**TABLE 3. HIV differentiation testing for persons aged ≥13 years with diagnosed HIV infection — National HIV Surveillance System (NHSS), United States and six dependent areas,\* 2010–2017**

Diagnosis year	No. of HIV diagnoses	No. (%)		
		Overall persons tested with an HIV-1/HIV-2 differentiation test	Persons with diagnosed HIV-1, <sup>†</sup> tested with an HIV-1/HIV-2 differentiation test	Persons with diagnosed HIV-1, <sup>†</sup> tested with an HIV-1/HIV-2 differentiation test that was falsely positive for HIV-2 <sup>§</sup>
2010	44,086	8,761 (19.9)	8,755 (19.9)	26 (0.3)
2011	42,285	8,865 (21.0)	8,850 (20.9)	23 (0.3)
2012	41,467	9,997 (24.1)	9,987 (24.1)	19 (0.3)
2013	39,987	14,105 (35.3)	14,099 (35.3)	25 (0.2)
2014	40,667	26,147 (64.3)	26,120 (64.3)	68 (0.3)
2015	40,406	31,576 (78.2)	31,551 (78.1)	87 (0.3)
2016	40,121	32,346 (80.6)	32,313 (80.6)	65 (0.2)
2017	38,681	31,458 (81.3)	31,432 (81.3)	43 (0.1)
<b>Total</b>	<b>327,700</b>	<b>163,255 (49.8)</b>	<b>163,107 (49.8)</b>	<b>356 (0.2)</b>
<b>EAPC (95% CI)</b>		<b>21.2 (21.0 to 21.4)</b>	<b>21.2 (21.1 to 21.4)</b>	<b>-6.2 (-10.7 to -1.5)</b>

**Abbreviations:** CI = confidence interval; EAPC = estimated annual percentage change; HIV = human immunodeficiency virus.

\* Data from CDC's National HIV Surveillance System (NHSS) collected through December 2018.

<sup>†</sup> Diagnoses in NHSS with no evidence of an HIV-2, HIV-2 probable but unconfirmed, or dual HIV-1 and HIV-2 infection.

<sup>§</sup> Percentage of those who ever received an HIV-1/HIV-2 differentiation test.

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## Population-Based Surveillance for Birth Defects Potentially Related to Zika Virus Infection — 22 States and Territories, January 2016–June 2017

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Zika virus infection during pregnancy can cause congenital brain and eye abnormalities and is associated with neurodevelopmental abnormalities (1–3). In areas of the United States that experienced local Zika virus transmission, the prevalence of birth defects potentially related to Zika virus infection during pregnancy increased in the second half of 2016 compared with the first half (4). To update the previous report, CDC analyzed population-based surveillance data from 22 states and territories to estimate the prevalence of birth defects potentially related to Zika virus infection, regardless of laboratory evidence of or exposure to Zika virus, among pregnancies completed during January 1, 2016–June 30, 2017. Jurisdictions were categorized as those 1) with widespread local transmission of Zika virus; 2) with limited local transmission of Zika virus; and 3) without local transmission of Zika virus. Among 2,004,630 live births, 3,359 infants and fetuses with birth defects potentially related to Zika virus infection during pregnancy were identified (1.7 per 1,000 live births, 95% confidence interval [CI] = 1.6–1.7). In areas with widespread local Zika virus transmission, the prevalence of birth defects potentially related to Zika virus infection during pregnancy was significantly higher during the quarters comprising July 2016–March 2017 (July–September 2016 = 3.0; October–December 2016 = 4.0; and January–March 2017 = 5.6 per 1,000 live births) compared with the reference period (January–March 2016) (1.3 per 1,000). These findings suggest a fourfold increase (prevalence ratio [PR] = 4.1, 95% CI = 2.1–8.4) in birth defects potentially related to Zika virus in widespread local transmission areas during January–March 2017 compared with that during January–March 2016, with the highest prevalence (7.0 per 1,000 live births) in February 2017. Population-based birth defects surveillance is critical for identifying infants and fetuses with birth defects potentially related to Zika virus regardless of whether Zika virus testing was conducted, especially given the high prevalence of asymptomatic disease. These data can be used to inform follow-up care and services as well as strengthen surveillance.

State and territorial health departments, in collaboration with CDC, conducted population-based surveillance for birth defects potentially related to Zika virus infection during pregnancy.\* As previously described (4), data from medical records were abstracted for live births and pregnancy losses with any potentially Zika-related birth defect. Clinical expert review of verbatim descriptions was used to confirm case inclusion, and cases were assigned to one of four mutually exclusive categories.† Because the case definition for birth defects potentially related to Zika virus infection has been updated to exclude neural tube defects (NTDs) and other early brain malformations and consequences of central nervous system dysfunction (5), the prevalence of cases with 1) brain abnormalities and/or microcephaly and 2) eye abnormalities without mention of a brain abnormality are reported. Prevalence estimates for NTDs and other early brain malformations during the study period, compared with brain and eye abnormalities in areas with

\* With population-based surveillance of birth defects potentially related to Zika virus infection, information is collected on all infants who have birth defects that might be related to Zika virus infection. This includes infants who have not been exposed to Zika virus and might have the same birth defects for other reasons. <https://www.cdc.gov/pregnancy/zika/research/birth-defects.html>.

† 1) Brain abnormalities and/or microcephaly (congenital microcephaly [head circumference <3rd percentile for gestational age and sex, and documentation of microcephaly or a small head in the medical record], intracranial calcifications, cerebral atrophy, abnormal cortical gyral patterns [e.g., polymicrogyria, lissencephaly, pachygyria, schizencephaly, gray matter heterotopia], corpus callosum abnormalities, cerebellar abnormalities, porencephaly, hydranencephaly, ventriculomegaly/hydrocephaly [excluding “mild” ventriculomegaly without other brain abnormalities], fetal brain disruption sequence [collapsed skull, overlapping sutures, prominent occipital bone, scalp rugae], other major brain abnormalities); 2) neural tube defects and other early brain malformations (anencephaly/acrania, encephalocele, spina bifida, holoprosencephaly); 3) eye abnormalities without mention of a brain abnormality (microphthalmia/anophthalmia, coloboma, cataract, intraocular calcifications, chorioretinal anomalies [e.g., atrophy and scarring, gross pigmentary changes, excluding retinopathy of prematurity]; optic nerve atrophy, pallor, and other optic nerve abnormalities); 4) consequences of central nervous system dysfunction (arthrogryposis, clubfoot with associated brain abnormalities, congenital hip dysplasia with associated brain abnormalities, and congenital sensorineural hearing loss).

widespread local transmission, are presented to support the updated case definition.<sup>§</sup> Prevalence was calculated using the number of monthly live births reported by each jurisdiction.

Jurisdictions included in this report submitted data to CDC for the entire period (January 2016–June 2017). Jurisdictions were aggregated by level of local transmission of Zika virus: 1) widespread local transmission of Zika virus (Puerto Rico and the U.S. Virgin Islands); 2) limited local transmission of Zika virus (southern Florida counties and Texas Public Health Region 11); and 3) without local transmission of Zika virus.<sup>¶</sup>

Prevalence estimates for birth defects per 1,000 live births were calculated by group for each quarter. A PR (compared with the reference period, January–March 2016) was calculated for each quarter. PRs and CIs were calculated using Poisson regression. SAS (version 9.4; SAS Institute) was used to conduct all analyses.

During January 1, 2016–June 30, 2017, among 2,004,630 live births, 3,359 infants and fetuses with a birth defect potentially related to Zika virus infection were delivered to residents of the 22 jurisdictions, including 2,813 (83.7%) with brain abnormalities and/or microcephaly and 546 (16.3%) with eye abnormalities without mention of a brain abnormality (overall prevalence = 1.7 per 1,000 live births; 95% CI = 1.6–1.7) (Table 1). During the reference period, in areas with widespread local Zika transmission, limited local transmission, and without local transmission, prevalences were 1.3, 2.2, and 1.7 per 1,000 live births, respectively (Table 2).

The prevalence of birth defects potentially related to Zika virus infection in widespread local transmission areas was significantly higher in three periods during July 2016–March 2017 compared with that during the reference period. Prevalence increased fourfold (PR = 4.1, 95% CI = 2.1–8.4) during January–March 2017 (5.6 per 1,000 live births), compared with that during the reference period (1.3 per 1,000) (Table 2), reaching a peak prevalence of 7.0 per 1,000 live births in February 2017 (Figure). In areas with limited local transmission, there was a 20% (PR = 1.2, 95% CI = 0.9–1.7) increase during October–December 2016 (2.7 per 1,000 live births) compared with that during the reference period (2.2 per 1,000),

**TABLE 1. Population-based counts and prevalence of infants and fetuses with birth defects potentially related to Zika virus infection during pregnancy — 22 U.S. jurisdictions,\* January 1, 2016–June 30, 2017**

Characteristic	Brain abnormalities and/or microcephaly <sup>†</sup> (n = 2,813 [83.7%])	Eye abnormalities without brain abnormalities <sup>§</sup> (n = 546 [16.3%])	Total (N = 3,359 [100%])
<b>Prevalence<sup>¶</sup> (95% CI)</b>	1.4 (1.4–1.5)	0.3 (0.3–0.3)	1.7 (1.6–1.7)
<b>Eye abnormalities, no. (%)</b>	289 (10.3)	—	835 (24.9)
<b>Pregnancy outcome**</b>			
Live birth, no. (%)	2,667 (95.7)	537 (99.3)	3,204 (96.3)
Neonatal death (≤28 days), no. (% of live births)	138 (5.2)	9 (1.7)	147 (4.6)
Pregnancy loss, <sup>††</sup> no. (%)	119 (4.3)	4 (0.7)	123 (3.7)
<b>Zika virus laboratory testing for mothers or infants</b>			
Positive, no. (%)	64 (2.3)	9 (1.6)	73 (2.2)
Negative, no. (%)	103 (3.7)	15 (2.7)	118 (3.5)
No laboratory testing performed/NA, <sup>§§</sup> no. (%)	2,646 (94.1)	522 (95.6)	3,168 (94.3)

**Abbreviations:** CI = confidence interval; NA = not applicable.

\* 22 U.S. jurisdictions included births that occurred in California (selected counties), Florida (selected southern counties), Georgia (selected metropolitan Atlanta counties), Hawaii, Illinois, Indiana, Iowa, Louisiana, Massachusetts, Minnesota, New Jersey, New York (excluding New York City residents), North Carolina (selected regions), Oklahoma, Puerto Rico, Rhode Island, South Carolina, Texas (Public Health Regions 10, 11), the U.S. Virgin Islands, Utah, Vermont, and Virginia. Total live births = 2,004,630.

<sup>†</sup> Congenital microcephaly (head circumference <3rd percentile for gestational age and sex and documentation of microcephaly or a small head in the medical record), intracranial calcifications, cerebral atrophy, abnormal cortical gyral patterns (e.g., polymicrogyria, lissencephaly, pachygyria, schizencephaly, gray matter heterotopia), corpus callosum abnormalities, cerebellar abnormalities, porencephaly, hydranencephaly, ventriculomegaly/hydrocephaly (excluding “mild” ventriculomegaly without other brain abnormalities), fetal brain disruption sequence (collapsed skull, overlapping sutures, prominent occipital bone, scalp rugae), and other major brain abnormalities.

<sup>§</sup> Microphthalmia/anophthalmia, coloboma, cataract, intraocular calcifications, and chorioretinal anomalies (e.g., atrophy and scarring, gross pigmentary changes, excluding retinopathy of prematurity); optic nerve atrophy, pallor, and other optic nerve abnormalities.

<sup>¶</sup> Per 1,000 live births.

\*\* Thirty-two unknown pregnancy outcomes not included.

<sup>††</sup> Included miscarriages, fetal deaths, and terminations. Not all programs reported pregnancy losses.

<sup>§§</sup> Included cases where no testing was performed or testing status was unknown.

although the increase was not significant (Table 2). In areas without local transmission, there was also no significant difference in the prevalence of birth defects potentially related to Zika virus infection between the reference period and any of the subsequent quarters (Table 2). In widespread local Zika virus transmission areas, the significant prevalence increase was limited to brain abnormalities and/or microcephaly and eye abnormalities without mention of a brain abnormality; the prevalence of NTDs and other early brain malformations remained flat during the study period (Supplementary Figure, <https://stacks.cdc.gov/view/cdc/84198>).

<sup>§</sup> Overall and in each jurisdictional group, there were no changes in the prevalence of NTDs and other early brain malformations during January 2016–June 2017.

There were 1,170 cases of NTDs and other early brain malformations and 1,547 cases of consequences of central nervous system dysfunction in this period.

<sup>¶</sup> Areas with limited local transmission of Zika virus: southern Florida counties and Texas Public Health Region 11 (<https://www.cdc.gov/media/releases/2017/s0313-risk-of-zika-transmission-florida.html>, <https://emergency.cdc.gov/han/han00393.asp>, <https://emergency.cdc.gov/han/han00399.asp>). Areas without local transmission of Zika virus: California [selected counties], Georgia [selected metropolitan Atlanta counties], Hawaii, Illinois, Indiana, Iowa, Louisiana, Massachusetts, Minnesota, New Jersey, New York [excluding New York City residents], North Carolina [selected regions], Oklahoma, Rhode Island, South Carolina, Texas Public Health Region 10, Utah, Vermont, and Virginia.



**TABLE 2. Prevalence of birth defects potentially related to Zika virus infection\* during pregnancy, by level of local transmission of Zika virus and quarter — 22 U.S. jurisdictions, January 1, 2016–June 30, 2017**

Characteristic	Areas with widespread local transmission <sup>†</sup> (n = 129 [3.8%])		Areas with limited local transmission <sup>§</sup> (n = 340 [10.1%])		Areas without local transmission <sup>¶</sup> (n = 2,890 [86.0%])	
	Prevalence**	PR <sup>††</sup> (95% CI)	Prevalence**	PR <sup>††</sup> (95% CI)	Prevalence**	PR <sup>††</sup> (95% CI)
<b>Quarter</b>						
Jan–Mar 2016	1.3	Reference	2.2	Reference	1.7	Reference
Apr–Jun 2016	2.5	1.9 (0.9–4.0)	2.0	0.9 (0.6–1.3)	1.7	1.0 (0.9–1.1)
Jul–Sep 2016	3.0	2.3 (1.1–4.8)	2.0	0.9 (0.6–1.3)	1.7	1.0 (0.9–1.1)
Oct–Dec 2016	4.0	3.0 (1.4–6.1)	2.7	1.2 (0.9–1.7)	1.5	0.9 (0.8–1.0)
Jan–Mar 2017	5.6	4.1 (2.1–8.4)	1.9	0.8 (0.6–1.2)	1.5	0.9 (0.8–1.0)
Apr–Jun 2017	2.0	1.5 (0.7–3.5)	2.1	1.0 (0.7–1.4)	1.5	0.9 (0.8–1.0)
<b>Zika virus laboratory testing for mothers or infants</b>						
Positive, no. (%)	50 (38.8%)		7 (2.1%)		16 (0.6%)	
Negative, no. (%)	55 (42.6%)		27 (7.9%)		36 (1.3%)	
No laboratory testing performed/ NA, <sup>§§</sup> no. (%)	24 (18.6%)		306 (90.0%)		2,838 (98.2%)	

**Abbreviations:** CI = confidence interval; NA = not applicable; PR = prevalence ratio.

\* Fetuses and infants included those with 1) brain abnormalities and/or microcephaly or 2) eye abnormalities without mention of a brain abnormality included in the brain abnormalities and/or microcephaly category.

<sup>†</sup> Jurisdictions with widespread local transmission of Zika virus during 2016–2017 included Puerto Rico and the U.S. Virgin Islands. Total live births for areas with widespread local transmission = 42,358.

<sup>§</sup> Jurisdictions with limited local transmission of Zika virus during 2016–2017 included southern Florida counties and Texas Public Health Region 11. Total live births for areas with limited local transmission = 156,613.

<sup>¶</sup> Jurisdictions without local transmission of Zika virus during 2016–2017 included California (selected counties), Georgia (selected metropolitan Atlanta counties), Hawaii, Illinois, Indiana, Iowa, Louisiana, Massachusetts, Minnesota, New Jersey, New York (excluding New York City residents), North Carolina (selected regions), Oklahoma, Rhode Island, South Carolina, Texas Public Health Region 10, Utah, Vermont, and Virginia. Total live births for areas without local transmission = 1,805,659.

\*\* Per 1,000 live births.

<sup>††</sup> Compared with reference, January–March 2016.

<sup>§§</sup> Included cases where no testing was performed or testing status was unknown.

Overall, most cases (3,168 [94.3%]) had no reported laboratory testing of maternal, placental, fetal, or infant specimens. Among the remaining 191 cases, laboratory evidence of confirmed or possible Zika virus infection was reported in at least one specimen for 73 (2.2%) cases, and 118 (3.5%) had negative Zika virus laboratory testing. In widespread local transmission areas, laboratory testing at any time in at least one specimen was reported for 105 of 129 (81.4%) cases; among the 105 cases with laboratory testing, 50 (47.6%) had laboratory evidence of confirmed or possible Zika virus infection.

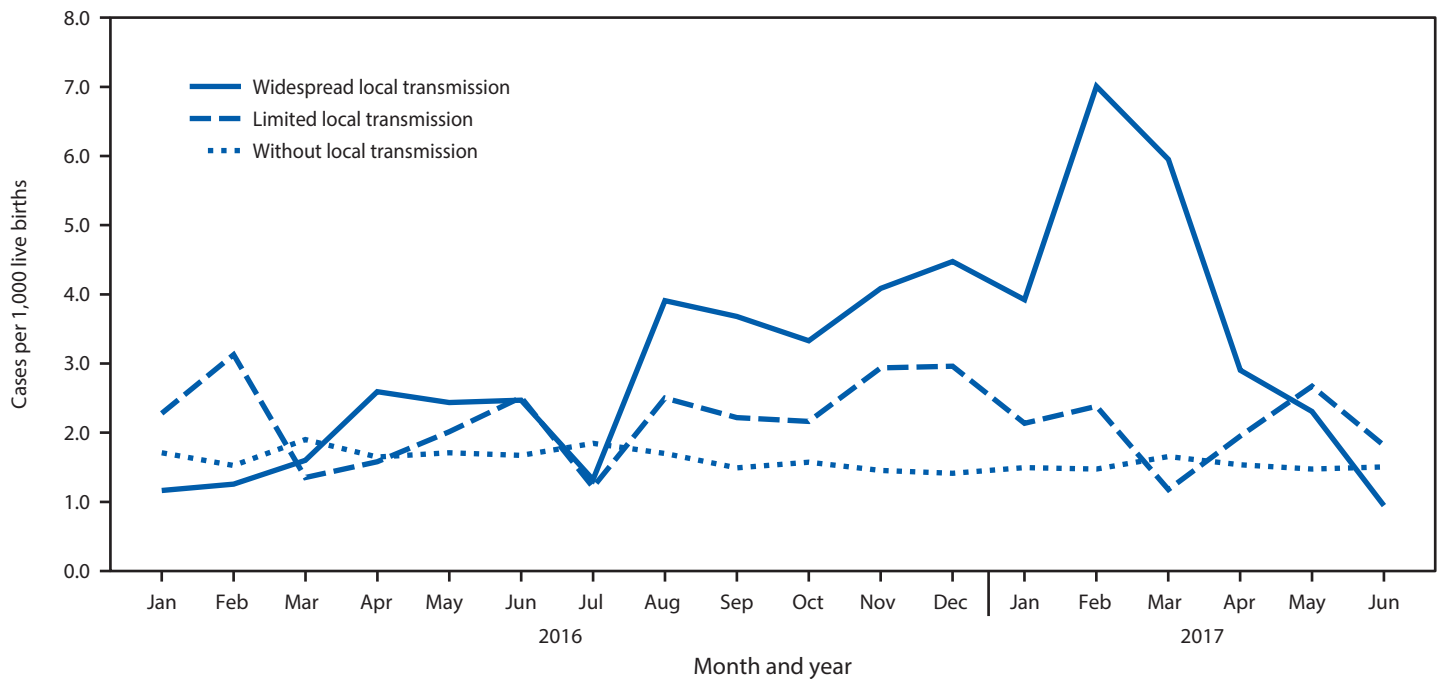
### Discussion

The peak occurrence of birth defects potentially related to Zika virus infection in areas with widespread local transmission occurred in February 2017, 6 months after the reported peak of the Zika virus outbreak in these areas in August 2016 (6). This is consistent with other findings regarding the time between the peak of a Zika virus outbreak and recognition of an increase in potentially Zika-related birth defects (7). Approximately one half (47.6%) of cases with laboratory test results available in areas with widespread local transmission had confirmed or possible laboratory evidence of infection. In areas with limited local transmission, the prevalence increased 20% during October–December 2016, although not significantly; no increase was observed in areas without local transmission.

Compared with the previous report (4), this analysis added seven more jurisdictions (including one with widespread local transmission) and reported 18 months of data from monitoring births potentially affected by the outbreak. The previous report grouped widespread and limited local transmission areas together, reporting a 21% increase in prevalence for these areas combined (4). Stratification by local transmission levels provides support that the significant increase in prevalence is exclusive to widespread local Zika virus transmission areas. Further, the baseline prevalence of birth defects potentially related to Zika virus infection during the reference period in the 22 jurisdictions is consistent with the baseline prevalence for three jurisdictions before Zika virus was introduced in the Region of the Americas (5).

The findings in this report are subject to at least four limitations. First, results might not be generalizable beyond the included jurisdictions because jurisdictions might differ in population demographics and case-finding methodology. Second, heightened awareness can result in better identification of affected infants. For example, there might have been more extensive implementation of recommendations for eye exams in widespread local transmission areas. Third, categorization of areas with limited local transmission included regions of Florida and Texas that were larger than the actual areas of local transmission, which might mask any increase in Zika-related

**FIGURE. Prevalence of birth defects potentially related to Zika virus infection during pregnancy,\* by level of local Zika virus transmission and month — 22 U.S. jurisdictions, January 2016–June 2017<sup>†,§,¶</sup>**



\* Fetuses and infants included those with 1) brain abnormalities and/or microcephaly or 2) eye abnormalities without mention of a brain abnormality included in brain abnormalities and/or microcephaly category.

<sup>†</sup> Jurisdictions with widespread local transmission of Zika virus during 2016–2017 included Puerto Rico and the U.S. Virgin Islands.

<sup>§</sup> Jurisdictions with limited local transmission of Zika virus during 2016–2017 included southern Florida counties and Texas Public Health Region 11.

<sup>¶</sup> Jurisdictions without local transmission of Zika virus during 2016–2017 included California (selected counties), Georgia (selected metropolitan Atlanta counties), Hawaii, Illinois, Indiana, Iowa, Louisiana, Massachusetts, Minnesota, New Jersey, New York (excluding New York City residents), North Carolina (selected regions), Oklahoma, Rhode Island, South Carolina, Texas Public Health Region 10, Utah, Vermont, and Virginia.

birth defects in smaller geographic areas where transmission occurred. Finally, the majority of cases did not have Zika virus testing reported. In widespread local transmission areas, approximately three quarters of cases had at least one sample tested, although the relatively high prevalence of negative results could reflect that timing might not have been optimal for detection of Zika virus in many cases. However, nearly half of those tested had laboratory evidence of Zika virus infection.

During the Zika virus outbreak, population-based birth defects surveillance programs were adapted to monitor birth defects potentially related to Zika virus infection during pregnancy. Use of population-based birth defects surveillance programs and the U.S. Zika Pregnancy and Infant Registry provide an example of a complementary approach in ascertaining both exposures and outcomes to better monitor new and emerging threats during pregnancy and impact on infants (8). Birth defects surveillance was important for identifying infants with birth defects potentially related to Zika virus infection whose mothers were not tested during pregnancy or were not tested at a time when infection could be detected. Health departments can use these data to inform referral services for

### Summary

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

In states and territories with documented local Zika virus transmission, the prevalence of birth defects potentially related to Zika virus infection during pregnancy increased 21% during the second half of 2016 compared with that in the first half.

#### What is added by this report?

In U.S. territories with widespread local Zika virus transmission, the prevalence of birth defects potentially related to Zika virus infection increased fourfold during January–March 2017 compared with January–March 2016.

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

During the Zika virus outbreak, birth defects surveillance programs adapted to rapidly identify Zika-related birth defects regardless of laboratory evidence. These data provide more complete information on all infants affected and allow planning for care.

affected infants and program planning. These findings underscore the important role of birth defects surveillance programs in preparing for emerging public health threats to pregnant women and infants.

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## Variation in Tdap and Influenza Vaccination Coverage Among Pregnant Women by Insurance Type — Florida, 2016–2018

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Infants are at increased risk for pertussis-associated morbidity and mortality, and pregnant women and their infants are more likely than other patient populations to experience severe influenza-related illness (1,2). The Advisory Committee on Immunization Practices (ACIP) recommends that all women receive the tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine during each pregnancy, preferably during the early part of gestational weeks 27–36 (3). ACIP also recommends that women who are or might be pregnant during the influenza season receive the inactivated influenza vaccine at any time during pregnancy (4). Despite these recommendations, coverage with Tdap and influenza vaccines during pregnancy has been low, with approximately one half of women receiving each vaccine and only one third receiving both, based on a survey during March–April 2019 (5). Data obtained through a retrospective chart review of randomly selected pregnant women who delivered at the University of Florida Health Shands Hospital in Gainesville, Florida, from January 1, 2016, to December 31, 2018, were analyzed to assess vaccination coverage by insurance type. Because the Florida Medicaid policy at that time did not cover these vaccines during pregnancy, the hospital system offered Tdap and influenza vaccines at no additional cost to mothers during the immediate postpartum hospital stay. Among 341 women, 68.6% of privately insured and 13.4% with Medicaid received Tdap during pregnancy, and among 316 women, 70.4% of privately insured and 35.6% with Medicaid received influenza vaccine during pregnancy. Many women, especially those with Medicaid, were vaccinated in the immediate postpartum period, when vaccination was available at no cost, increasing Tdap vaccination rates to 79.3% for privately insured and 51.7% for women with Medicaid; influenza vaccination rates rose to 72.0% for privately insured and 43.5% for women with Medicaid. These data suggest that the state Medicaid policy to not cover these vaccines during pregnancy might have significantly reduced coverage among its enrollees.

Pertussis and influenza are associated with substantial morbidity and mortality among infants. Pertussis-related mortality is highest among newborns, who receive the first dose of the diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccination series at age 2 months (1). Influenza vaccine is recommended for all infants aged ≥6 months (4). During the period before infants are eligible for vaccination, they rely

upon passively acquired transplacental maternal antibodies for protection against these vaccine-preventable diseases. Pregnant women are also at increased risk for severe influenza-associated illness and death (2). To provide protection for both mothers and infants, maternal immunization with Tdap is recommended during pregnancy and with influenza vaccine before or during pregnancy, rather than during the postpartum period; vaccination during the postpartum period has been shown to be less effective in preventing infant pertussis (6).

Data for this analysis were obtained through a retrospective review of charts of women who delivered a live birth at the University of Florida Health Shands Hospital during 2016–2018. A computer-generated, random selection of 450 women was obtained from the population of 6,949 women with Medicaid or private insurance at the time of their delivery. Among these women, 109 (24.2%) were excluded because they did not meet certain eligibility criteria: 13 (2.9%) were aged <18 years at initial visit, 84 (18.7%) received no prenatal care at University of Florida Health, and 12 (2.6%) delivered at less than 30 weeks' gestation, thus leaving an initial analytic sample of 341. An additional 25 women for whom the influenza vaccine was not indicated (because of receipt of vaccine just before pregnancy, allergy to a vaccine component, or nonavailability of the vaccine because of late presentation to prenatal care in the brief summer window when vaccine was not available) were excluded from the analysis of influenza vaccination, leaving 316 women in the analysis of influenza vaccination. Women who were not pregnant during influenza season were not specifically excluded; however, a few women were excluded if the vaccine was unavailable when they were seen for prenatal care, effectively excluding women who were seen outside of influenza season.

The primary outcomes assessed were receipt of Tdap and influenza vaccines during pregnancy. The primary predictor was insurance status (Medicaid versus private insurance). Secondary outcomes included receipt of Tdap and influenza vaccines during pregnancy or in the immediate postpartum period (before delivery hospital discharge). Although postpartum vaccination was examined to estimate the number of women who would be responsive to vaccination if financial barriers were removed, other factors might have contributed to this decision. Descriptive statistics for demographic and prenatal care characteristics were calculated overall and by



insurance type. Characteristics for which statistically significant differences existed by insurance type were included as covariates in subsequent multivariate analyses.

Unadjusted and adjusted logistic regression models were used to estimate the relationships between insurance type and receipt of Tdap and influenza vaccines during pregnancy\* and receipt of Tdap and influenza vaccines in the immediate postpartum period. The models were adjusted for race, age, parity, gestational age at delivery, trimester at initiation of prenatal care, and completion of recommended prenatal initiation studies as a proxy for establishing prenatal care and third trimester laboratory studies. Unadjusted odds ratios (ORs) and adjusted odds ratios (aORs) were calculated, comparing Medicaid insurance with private insurance with respect to odds of these vaccination outcomes. Robust standard errors were calculated for both specifications, and Hosmer-Lemeshow tests were calculated to indicate goodness of model fit. Analyses were conducted with SPSS (version 25; IBM), and a priori alpha levels were set at 0.05.

\* All women who received Tdap during pregnancy were included, including eight who received Tdap outside of the recommended gestational age of 27–36 weeks.

Approximately one half of women in the randomly selected sample were white (52.5%), a majority were non-Hispanic (88.0%) and Medicaid enrolled (58.9%), and approximately one third were pregnant for the first time (37%) (Table 1). Overall, 76.2% of women initiated prenatal care during the first trimester, 88.5% completed laboratory tests at both initiation of prenatal care and during the third trimester,<sup>†</sup> and 61.9% had a vaginal delivery; however, these rates significantly varied by insurance type, with lower rates among women with Medicaid.

Among 341 women eligible to receive Tdap, 215 (63.1%) received it, including 123 (36.1%) who were vaccinated during pregnancy and 92 (27.0%) who were vaccinated during the immediate postpartum period (Table 2). This varied significantly by insurance type: 96 of 140 (68.6%) women with private insurance and 27 of 201 (13.4%) with Medicaid received Tdap during the recommended time (27–36 weeks' gestation)

<sup>†</sup> Laboratory tests at initiation of prenatal care included complete blood count (CBC), urinalysis (UA), and screening for syphilis, rubella, human immunodeficiency virus (HIV), hepatitis B, gonorrhea, and chlamydia. Laboratories during the third trimester included CBC, UA, glucose tolerance test, and screening for syphilis, rubella, HIV, and hepatitis B.

**TABLE 1. Characteristics of Medicaid-insured and privately insured pregnant women who received tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine (N = 341) and influenza vaccine (N = 316)\* during pregnancy — University of Florida Health, Gainesville, Florida, 2016–2018**

Characteristic	No. (%)		
	Overall (N = 341)	Medicaid-insured (n = 201)	Privately insured (n = 140)
Maternal age at delivery, mean (SD)	28.7 (5.5)	27.2 (5.4) <sup>†</sup>	30.9 (5.1)
Weeks of gestation at delivery, mean (SD)	38.7 (1.8)	38.5 (2.0) <sup>†</sup>	39.0 (1.6)
<b>Maternal race</b>			
White	179 (52.5)	91 (45.3) <sup>†</sup>	88 (62.9)
Black or African American	100 (29.3)	77 (38.3) <sup>†</sup>	23 (16.4)
Other	62 (18.2)	33 (16.4)	29 (20.7)
<b>Maternal ethnicity</b>			
Hispanic or Latino	38 (11.1)	25 (12.4)	13 (9.3)
Non-Hispanic or Latino	300 (88.0)	175 (87.1)	125 (89.3)
Unknown	3 (0.9)	1 (0.5)	2 (1.4)
<b>Parity</b>			
1	127 (37.2)	67 (33.3)	60 (42.9)
2	111 (32.6)	56 (27.9) <sup>†</sup>	55 (39.3)
≥3	103 (30.2)	78 (38.8) <sup>†</sup>	25 (17.9)
<b>Prenatal care initiation (trimester)</b>			
1st	260 (76.2)	130 (64.7) <sup>†</sup>	130 (92.9)
2nd	66 (19.4)	57 (28.3) <sup>†</sup>	9 (6.4)
3rd	15 (4.4)	14 (7.0) <sup>†</sup>	1 (0.7)
<b>Mode of delivery</b>			
Standard vaginal delivery	211 (61.9)	124 (61.7)	87 (62.1)
Operational vaginal delivery	12 (3.5)	6 (3.0)	6 (4.3)
Caesarean	118 (34.6)	71 (35.3)	47 (33.6)
<b>Completion of prenatal laboratory tests</b>			
Prenatal care initiation laboratory tests	304 (89.1)	168 (83.6) <sup>†</sup>	136 (97.1)
3rd trimester laboratory tests	339 (99.4)	199 (99.0)	140 (100.0)

**Abbreviation:** SD = standard deviation.

\* A total of 25 women for whom the vaccine was not indicated because of documented receipt before pregnancy, allergy to a vaccine component, or lack of availability of the vaccine during prenatal care were excluded from the analysis of influenza vaccination, leaving 316 women in the analysis of influenza vaccination.

<sup>†</sup> Indicates statistically significant difference ( $p < 0.05$ ) between Medicaid-insured women and privately insured women.

during pregnancy (OR = 0.07; 95% CI = 0.04–0.12, p<0.001). Among women who received Tdap, 77 (74.0%) of those with Medicaid and 15 (13.5%) of those with private insurance received the vaccine in the immediate postpartum period (Table 2) (Figure). Overall, 111 (79.3%) women with private insurance and 104 (51.7%) women with Medicaid received Tdap either during pregnancy or the immediate postpartum period (OR = 0.28; 95% CI = 0.17–0.46, p<0.001).

Influenza vaccine was received by 54.8% of 316 vaccine-eligible women, including 49.4% who received the vaccine during pregnancy and 5.4% who received it during the immediate postpartum period. Overall, 88 of 125 (70.4%) women with private insurance and 68 of 191 (35.6%) women with Medicaid received influenza vaccine during pregnancy (OR = 0.23; 95% CI = 0.14–0.38, p<0.001);

overall, 90 (72.0%) women with private insurance and 83 (43.5%) with Medicaid received influenza vaccine during pregnancy or the immediate postpartum period (OR = 0.30; 95% CI = 0.18–0.49, p<0.001).

Adjusting for patient demographic and prenatal care characteristics did not change these associations. Compared with women who had private insurance, the odds of receiving Tdap during pregnancy were significantly lower among those with Medicaid (aOR = 0.09; 95% CI = 0.05–0.17, p<0.001) (Table 2). Similarly, the odds of receiving influenza vaccine during pregnancy were significantly lower among women with Medicaid than among those with private insurance (aOR = 0.30; 95% CI = 0.17–0.54, p = 0.007). Hosmer-Lemeshow tests indicated that the data were consistent with the assumed model (all p-values >0.10) for all model specifications.

**TABLE 2. Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) and influenza vaccination coverage among pregnant women, by insurance type — University of Florida Health, Gainesville, Florida, 2016–2018**

Vaccine/Time of receipt	No.(%)			Bivariate analysis*		Multivariate analysis*†	
	Total (N = 341)	Medicaid insurance (n = 201)	Private insurance (n = 140)	OR (95% CI)	p-value	aOR (95% CI)	p-value
<b>Tdap</b>							
During pregnancy	123 (36.1)	27 (13.4)	96 (68.6)	0.07 (0.04–0.12)	<0.001	0.09 (0.05–0.17)	<0.001
Overall <sup>§</sup>	215 (63.1)	104 (51.7)	111 (79.3)	0.28 (0.17–0.46)	<0.001	0.30 (0.17–0.53)	<0.001
<b>Influenza<sup>¶</sup></b>							
During pregnancy	156 (49.4)	68 (35.6)	88 (70.4)	0.23 (0.14–0.38)	<0.001	0.30 (0.17–0.54)	<0.007
Overall <sup>§</sup>	173 (54.8)	83 (43.5)	90 (72.0)	0.30 (0.18–0.49)	<0.001	0.38 (0.22–0.67)	<0.001

**Abbreviations:** aOR = adjusted odds ratio; CI = confidence interval; OR = unadjusted odds ratio.

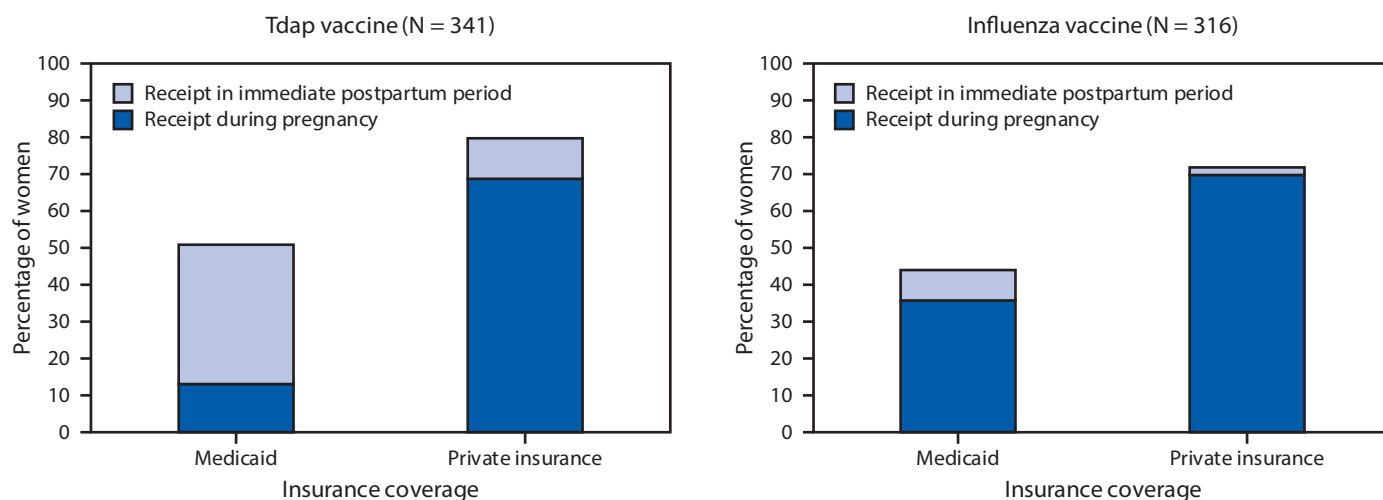
\* Reference group = private insurance.

† Multivariate analyses adjusted for race, age, parity, gestational age at delivery, trimester of prenatal care initiation, and completion of recommended prenatal initiation studies and third trimester laboratory studies.

§ Receipt during pregnancy or immediate postpartum period.

¶ Ten Medicaid-insured women and 15 privately-insured women were excluded from analyses of influenza vaccination because of documentation of receipt before pregnancy, allergy to vaccine components, or lack of availability of the vaccine during prenatal care, leaving an influenza sample of 316.

**FIGURE. Percentage of pregnant women receiving tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccination and influenza vaccination, by insurance type and timing of receipt relative to pregnancy — University of Florida Health, 2016–2018**



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

Vaccination with influenza and tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccines during pregnancy can decrease the risk for influenza and pertussis-associated complications among women and infants, yet vaccination rates remain low. Before 2019, Florida's Medicaid-covered pregnancy-related services did not include these vaccines; one hospital system covered these vaccines in the immediate postpartum period.

**What is added by this report?**

Among pregnant women who delivered at a Florida health system during 2016–2018, fewer Medicaid-insured than privately insured women received Tdap and influenza vaccines during pregnancy; many women chose to receive vaccination immediately postpartum when provided for free.

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

Medicaid benefits for Tdap and influenza vaccination during pregnancy might increase vaccination coverage.

**Discussion**

In a random sample of 341 mothers who delivered at a large, quaternary care and referral academic health center in Florida during 2016–2018, a significantly smaller percentage of Medicaid-insured women received Tdap and influenza vaccines during pregnancy than did privately insured women. This finding is consistent with previous studies demonstrating lower vaccination rates among Medicaid-insured pregnant women (7,8). However, few studies have included information on receipt of Tdap and influenza vaccines during the postpartum period. Results from this analysis show that compared with privately insured pregnant women, a significantly larger proportion of pregnant women with Medicaid received Tdap and influenza vaccines during the immediate postpartum period, a strategy that confers less protection for infants (6).

Under Florida Medicaid guidelines in place during 2016–2018, vaccines, including Tdap and influenza, were not included in the covered pregnancy-related services for pregnant women aged  $\geq 18$  years, although Tdap and influenza vaccines were administered in this hospital system in the immediate postpartum period at no additional cost to Medicaid patients. Approximately three fourths of Medicaid-insured women in this study who received Tdap were vaccinated during the immediate postpartum period, suggesting that Medicaid-insured women might receive the Tdap and influenza vaccines as recommended during pregnancy if cost barriers were removed. Florida Medicaid's lack of coverage for recommended immunizations during pregnancy might have contributed to the lower vaccination rates among Medicaid-insured pregnant women in this study.

The findings in this report are subject to at least four limitations. First, the analyses are limited by the accuracy of the vaccination records available in the patient electronic health records; a vaccine administered at an outside site might not be documented. Second, there is likely to be variation in the number of times a patient was offered these vaccines depending on provider preference and the number of prenatal visits completed (5). Third, although the analysis estimated the number of women who would be responsive to vaccination if financial barriers were removed, other factors might have contributed to this decision. Finally, this study was performed at a single university medical center in Florida and might not be generalizable to other settings or states.

In Florida and other states with traditional Medicaid coverage, each state Medicaid program determines whether maternal vaccinations are provided to pregnant mothers with or without cost sharing.<sup>§</sup> In Florida, Medicaid-insured pregnant women are currently asked to pay for these services themselves or are referred to distant off-site health departments to receive these vaccines on a sliding fee scale. Since the conclusion of this study, Florida announced that as of February 2019 “for enrollees 21 years of age and older (including pregnant women), all (Medicaid) plans elected to cover the influenza vaccine as an expanded benefit.” Removing cost and access barriers that Medicaid-insured women face might increase maternal vaccination coverage in the Medicaid population (9).

<sup>§</sup><https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/MedicareProgramRatesStats/Downloads/MedicareMedicaidSummaries2018.pdf>.

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# Use of Tetanus Toxoid, Reduced Diphtheria Toxoid, and Acellular Pertussis Vaccines: Updated Recommendations of the Advisory Committee on Immunization Practices — United States, 2019

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## Introduction

Since 2005, a single dose of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine has been recommended by the Advisory Committee on Immunization Practices (ACIP) for adolescents and adults (1,2). After receipt of Tdap, booster doses of tetanus and diphtheria toxoids (Td) vaccine are recommended every 10 years or when indicated for wound management. During the October 2019 meeting of ACIP, the organization updated its recommendations to allow use of either Td or Tdap where previously only Td was recommended. These situations include decennial Td booster doses, tetanus prophylaxis when indicated for wound management in persons who had previously received Tdap, and for multiple doses in the catch-up immunization schedule for persons aged  $\geq 7$  years with incomplete or unknown vaccination history. Allowing either Tdap or Td to be used in situations where Td only was previously recommended increases provider point-of-care flexibility. This report updates ACIP recommendations and guidance regarding the use of Tdap vaccines (3).

## Background

Two Tdap vaccines are licensed for use in the United States. Boostrix (GlaxoSmithKline) is approved for a single dose in persons aged  $\geq 10$  years; Adacel (Sanofi Pasteur) is approved for persons aged 10–64 years. Since 2005, a single booster dose of Tdap has been recommended for children and adolescents aged 11–18 years and adults aged 19–64 years (1,2) to increase protection against tetanus, diphtheria, and pertussis. Booster doses of Td have been recommended every 10 years (decennial vaccination) to ensure continued protection against tetanus and diphtheria. These recommendations were expanded to include a single dose of Tdap for adults aged  $\geq 65$  years in 2012 (although only one Tdap product is approved for use in persons aged  $\geq 65$  years, either vaccine administered to a person aged  $\geq 65$  years is considered valid) (4). Pregnant women are recommended to receive a dose of Tdap during each pregnancy to prevent pertussis in infants too young for routine vaccination (off-label use\*) (3). If a tetanus toxoid-containing vaccine is indicated for wound management, Td has been recommended

for nonpregnant persons aged  $\geq 7$  years who had previously received Tdap. For pregnant women, Tdap is recommended in this setting. For previously unvaccinated persons aged  $\geq 7$  years, a 3-dose catch-up immunization schedule included only 1 dose of Tdap, preferably as the first dose in the series (off-label use in children aged 7–9 years), and 2 subsequent Td doses at specified intervals (5). No further doses of Tdap were routinely recommended, with two exceptions: pregnant women should receive Tdap during each pregnancy (off-label use), and children aged 7–10 years who received Tdap as part of the catch-up schedule were recommended to receive the routine adolescent Tdap booster dose at age 11–12 years (1,2). In 2010, ACIP evaluated the safety of administering Tdap at intervals  $< 5$  years after Td administration (6,7) and recommended that the dose of Tdap, when indicated, should not be delayed and should be administered regardless of the interval since the last tetanus or diphtheria toxoid-containing vaccine.

In 2013, ACIP reviewed the most recent safety and immunogenicity data available at that time to inform their recommendations regarding a second routine dose of Tdap. ACIP concluded that a second dose of Tdap would be safe and immunogenic at 5- or 10-year intervals (8–12). However, antipertussis antibodies decline rapidly after the first year (10,13–20), and vaccine effectiveness studies indicated that pertussis protection begins to wane within 2–4 years after receipt of a single Tdap dose (21–23). This likely limits the impact of a second dose of Tdap on the overall burden of pertussis in the United States (24). In addition, Tdap vaccines have an uncertain role in prevention of transmission and in herd protection (25,26). ACIP concluded that the data did not support a general recommendation for a routine second dose of Tdap, given the likely limited public health impact (27).

In January 2019, FDA approved Adacel for a second Tdap dose if administered  $\geq 8$  years after the first Tdap dose and for use for tetanus prophylaxis when indicated for wound management if  $\geq 5$  years have elapsed since the previous receipt of any tetanus toxoid-containing vaccine (28). In light of the new indication for a second dose of Adacel and evidence of Tdap being used frequently in place of Td (29), ACIP reassessed current Tdap recommendations. In October 2019, ACIP recommended that either Tdap or Td vaccines could be used in situations where only Td vaccine had been recommended

\*Off-label use is the use of pharmaceutical drugs for an unapproved indication or in an unapproved age group, dosage, or route of administration.

previously. This report provides recommendations for the use of Td or Tdap for the decennial Td booster, tetanus prophylaxis when indicated for wound management, and catch-up immunization schedule for persons aged  $\geq 7$  years with incomplete or unknown vaccination history.

## Methods

Beginning in September 2018, the ACIP Pertussis Vaccines Work Group participated in monthly telephone conferences to review Tdap vaccination recommendations. A search of clinical trials published during January 2013–June 2019 that examined Tdap vaccination in adolescents and adults who had previously received Tdap was performed, so the work group could review data that had not previously been reviewed by ACIP. Because of limited data on the use of  $>1$  Tdap dose in the catch-up immunization schedule, the work group also considered published and unpublished safety data on receipt of  $>1$  Tdap dose within a 12-month period in both pregnant women and nonpregnant adolescents and adults. Data from public sector orders (CDC, unpublished data, 2019), commercial insurance claims (Truven Health Analytics, unpublished data, 2019), and a published study from the Vaccine Safety Datalink (VSD) (29) were analyzed to assess stakeholders' values attributed to perceived benefits and harms, acceptability, and implementation considerations regarding use of Tdap in place of Td.

Summaries of evidence, including the evidence to recommendations framework (<https://www.cdc.gov/vaccines/acip/recs/grade/tdap-etr.html>) and assessment of programmatic considerations, were presented to ACIP at the October 2018, June 2019, and October 2019 meetings. Proposed recommendations were presented to the committee at the October 2019 meeting, and, after a public comment period, were approved by the voting members as follows: either Td or Tdap should be allowed for use in situations where only Td is currently recommended for the decennial Td booster, tetanus prophylaxis for wound management, and catch-up vaccination, including in pregnant women (14 voted in favor, and none opposed).

## Summary of Key Findings

**Safety and immunogenicity.** Two clinical trials found no increased risk for adverse events among adults who received Tdap, compared with those who received Td 10 years after receipt of the initial Tdap dose (30,31). In addition, the proportion of persons with seroprotective levels of antibodies to tetanus and diphtheria was similar in the Tdap and Td groups. Another clinical trial compared adults receiving a second dose of Tdap 9 years after their initial Tdap dose with adults receiving Tdap for the first time as a control group (32). Solicited adverse events, the most frequent of which were injection site

pain, fatigue, and headache, were higher in the groups receiving a second dose of Tdap. Grade 3 adverse events, defined in this study as redness and swelling with diameter  $>50$  mm, pain, headaches, fatigue, gastrointestinal symptoms preventing normal activity, and fever with temperature  $>104^{\circ}\text{F}(40^{\circ}\text{C})$ , were similar in both groups. A retrospective VSD study identified 68,915 adolescents and adults who had received an initial dose of Tdap and then received another Td-containing vaccine, either a second Tdap (61,394, 89%) or Td (7,521, 11%). There was no statistically significant increase in medical visits for cellulitis, limb swelling, pain in limb, seizure, cranial nerve disorders, paralytic syndromes, encephalopathy, encephalitis, or meningitis among those who received a subsequent dose of Tdap compared with those who received Td (29).

Data on the use of  $>1$  Tdap dose in the catch-up immunization schedule are limited. One double-blind, randomized controlled clinical trial enrolled 460 adults aged  $\geq 40$  years who had not received a diphtheria or tetanus vaccination for  $\geq 20$  years or who had an unknown vaccination history. Subjects were randomized to receive either 3 doses of a Tdap formulation; 1 Tdap-inactivated polio vaccine combination dose, which is not licensed in the United States, followed by 2 Td doses; or 3 Td doses at 0, 1, and 6 months. There was no significant difference in adverse events for subjects receiving 3 Tdap doses, compared with those receiving 3 Td doses, and no significant differences in diphtheria and tetanus seroprotection rates among the three groups (33). An analysis of data collected as part of a published VSD retrospective study (29) identified 13,599 persons who had received an initial dose of Tdap and then received another Td-containing vaccine within 12 months of the previous Tdap dose, either a second Tdap (11,687, 86%) or Td (1,912, 16%). There was no elevated risk for medical visits for adverse events among those who received a subsequent dose of Tdap compared with those who received Td (CDC/VSD, unpublished data, 2019). Among 34,804 reports to the Vaccine Adverse Event Reporting System (VAERS) (34) following receipt of Tdap in nonpregnant and pregnant persons of all ages during January 1, 1990–June 30, 2019, 88 (0.3%) persons had received multiple Tdap doses spaced  $\leq 12$  months apart. Among this small group of reports, 21 (24%) were associated with adverse events, the most frequent of which was injection site reactions (8, 38%) (CDC, unpublished data, 2019).

There are no published data comparing rates of adverse events among pregnant women who received multiple doses of Tdap during a single pregnancy with those who received a single Tdap dose and additional Td doses for catch-up vaccination. A cohort study examining reactogenicity of Tdap in pregnant women included only eight study participants who received  $>1$  Tdap dose within a 12-month period; none

experienced severe reactions or fever (35). A VSD study examining safety of Tdap during pregnancy identified 187 women who had received >1 Tdap dose during a single pregnancy among 633,542 singleton pregnancies screened for potential study inclusion (36). Although these 187 women were excluded from the published study, the authors found similar rates of adverse birth outcomes (i.e., small for gestational age, preterm delivery, and low birthweight) in these women compared with women who had received a single Tdap dose in pregnancy (29,155). Among these 187 women who received >1 Tdap dose during pregnancy, one had a medically attended acute adverse event, which was diagnosed as limb pain and swelling 7 days after vaccination. One woman received 3 Tdap doses during a single pregnancy; she did not experience any adverse events, and her baby was born at term (CDC, unpublished data, 2019).

**Acceptability to patients and providers.** Analysis of commercial insurance claims indicated that Tdap claims were 12 times as high as Td claims in adults aged 19–64 years during 2017 (Truven Health Analytics, unpublished data, 2019). In the same year, there were approximately 10 times the number of Tdap doses (441,075) as Td doses (41,881) ordered by providers for adults as public sector purchases (CDC, unpublished data, 2019). These data, in addition to the one published VSD study (29) documented that Tdap was widely used in place of Td by clinicians in the United States and suggested acceptability to both patients and health care providers.

**Health impact and economic considerations.** Tdap costs more than Td (37). The population-level effectiveness and economic impact of replacing Td with Tdap has been modeled and previously reviewed by ACIP (24). However, this analysis and an updated model of the economic impact of substituting Tdap for the decennial Td booster demonstrated that estimates of cost effectiveness are dependent on values for parameters with a high degree of uncertainty, including pertussis incidence, illness severity, initial vaccine effectiveness, duration of protection, and the impact of Tdap on herd protection (38). Coupling such uncertainty with the evidence for notable widespread use of Tdap in place of Td, programmatic issues were the main consideration in the decision-making process.

## Rationale for Recommendations

In 2013, ACIP did not support a general recommendation for a routine second dose of Tdap; the rationale was described in previously published guidance (3). In 2019, ACIP again concluded that in light of the higher cost of Tdap relative to Td and uncertainty about the impact that receipt of multiple Tdap doses would have on pertussis control and transmission, there continues to be insufficient evidence to preferentially recommend that Tdap replace Td. However, given the reassuring

safety profile and evidence of widespread use of Tdap in place of Td, to allow providers more flexibility, either Tdap or Td was recommended for use in situations when previously only Td was recommended. ACIP recommends that either Td or Tdap be used for the decennial Td booster, tetanus prophylaxis for wound management, and for additional required doses in the catch-up immunization schedule if a person has received at least 1 Tdap dose.

## General Recommendations

**Persons aged 11–18 years.** These persons should receive a single dose of Tdap, preferably at a preventive care visit at age 11–12 years. To ensure continued protection against tetanus and diphtheria, 1 booster dose of either Td or Tdap should be administered every 10 years throughout life.

**Persons aged ≥19 years.** Regardless of the interval since their last tetanus or diphtheria toxoid-containing vaccine, persons aged ≥19 years who have never received a dose of Tdap should receive 1 dose of Tdap. To ensure continued protection against tetanus and diphtheria, booster doses of either Td or Tdap should be administered every 10 years throughout life.

**Pregnant women.** No change has been made to the recommendations for routine Tdap immunization during pregnancy. Pregnant women should receive 1 dose of Tdap during each pregnancy, irrespective of their history of receiving the vaccine. Tdap should be administered at 27–36 weeks' gestation, preferably during the earlier part of this period, although it may be administered at any time during pregnancy (3,5).

## Tetanus Prophylaxis for Wound Management Recommendations

A tetanus toxoid-containing vaccine is indicated for wound management when >5 years have passed since the last tetanus toxoid-containing vaccine dose. If a tetanus toxoid-containing vaccine is indicated for persons aged ≥11 years, Tdap is preferred for persons who have not previously received Tdap or whose Tdap history is unknown. If a tetanus toxoid-containing vaccine is indicated for a pregnant woman, Tdap should be used. For nonpregnant persons with documentation of previous Tdap vaccination, either Td or Tdap may be used if a tetanus toxoid-containing vaccine is indicated. Complete information on tetanus prophylaxis and the use of tetanus immunoglobulin when indicated for wound management is available at <https://www.cdc.gov/mmwr/volumes/67/rr/rr6702a1.htm>.

## Catch-Up Immunization Recommendations

**Persons aged 7–18 years.** If persons aged 7–18 years have never been vaccinated against pertussis, tetanus, or diphtheria,



these persons should receive a series of three tetanus and diphtheria toxoid–containing vaccines, which includes at least 1 Tdap dose. The preferred schedule is 1 dose of Tdap, followed by 1 dose of either Td or Tdap  $\geq 4$  weeks afterward, and 1 dose of either Td or Tdap 6–12 months later. Persons aged 7–18 years who are not fully immunized against tetanus and diphtheria should receive 1 dose of Tdap, preferably as the first dose in the catch-up series; if additional tetanus toxoid–containing doses are required, either Td or Tdap may be used. The vaccination series does not need to be restarted for those with incomplete DTaP history, regardless of the time that has elapsed between doses. The catch-up schedule and minimum intervals between doses are available at <https://www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html>.

**Persons aged  $\geq 19$  years.** If persons aged  $\geq 19$  years have never been vaccinated against pertussis, tetanus, or diphtheria, these persons should receive a series of three tetanus and diphtheria toxoid–containing vaccines, which includes at least 1 Tdap dose. The preferred schedule is 1 dose of Tdap, followed by 1 dose of either Td or Tdap at least 4 weeks afterward, and 1 dose of either Td or Tdap 6–12 months later. Persons aged  $\geq 19$  years who are not fully immunized against tetanus and diphtheria should receive 1 dose of Tdap, preferably as the first dose in the catch-up series; if additional tetanus toxoid–containing doses are required, either Td or Tdap may be used.

### Prevention of Neonatal and Obstetric Tetanus

Pregnant women who have completed the childhood immunization schedule and were last vaccinated  $>10$  years previously should receive a booster dose of tetanus toxoid–containing vaccine to prevent neonatal tetanus. The risk for neonatal tetanus is minimal if a previously unvaccinated woman has received at least 2 properly spaced doses of a tetanus toxoid–containing vaccine during pregnancy; at least 1 of the doses administered during pregnancy should be Tdap, administered according to published guidance (3). If  $>1$  dose is needed, either Td or Tdap may be used. The 3-dose primary series should be completed at the recommended intervals.

### CDC Guidance

**Catch-up immunization.** For persons aged 7–9 years who receive a dose of Tdap as part of the catch-up series, an adolescent Tdap dose should be administered at age 11–12 years. If a Tdap dose is administered at age  $\geq 10$  years, the Tdap dose may count as the adolescent Tdap dose.

### Inadvertent Administration

**Persons aged  $\geq 7$  years.** DTaP is not indicated for persons aged  $\geq 7$  years. If DTaP is administered inadvertently to a fully

vaccinated<sup>†</sup> child aged 7–9 years, an adolescent Tdap dose should be administered at age 11–12 years. If DTaP is administered inadvertently to an undervaccinated child aged 7–9 years, this dose should count as the Tdap dose of the catch-up series, and the child should receive an adolescent Tdap dose at age 11–12 years. If DTaP is administered inadvertently to a person aged  $\geq 10$  years, this dose should count as the adolescent Tdap dose routinely administered at age 11–12 years.

**Fully vaccinated children aged 7–10 years.** If a fully vaccinated child aged 7–9 years receives Tdap, the Tdap dose should not be counted as valid. The adolescent Tdap dose should be administered as recommended when this child is aged 11–12 years. The preferred age at administration for the adolescent Tdap dose is 11–12 years. However, if Tdap is administered at age 10 years, the Tdap dose may count as the adolescent Tdap dose.

### Off-Label Use of Vaccine

Off-label indications based on age and pregnancy status have not changed (Table). New off-label indications for Adacel would include any additional routine or catch-up Td dose beyond a second dose administered  $\geq 8$  years after an initial Tdap dose, if not given for wound prophylaxis within the specified guidance. Any additional doses of Boostrix administered beyond the single licensed dose are considered off-label. The work group did not find any reason to distinguish between these two products in making its recommendations.

**Contraindications and precautions.** Contraindications and precautions are unchanged from previous recommendations (3).

**Reporting of vaccine adverse reactions.** Adverse events occurring after administration of any vaccine should be reported to VAERS. Reports can be submitted to VAERS online, by fax, or by mail. Additional information about VAERS is available by telephone (1-800-822-7967) or online (<https://vaers.hhs.gov>).

### Future Research and Monitoring Priorities

ACIP will continue to review data on Td and Tdap as they become available, examine the necessity and frequency of booster doses for protection against tetanus and diphtheria, and consider any needed policy changes. As with all vaccines, CDC will use VAERS and VSD to monitor adverse events following immunization.

<sup>†</sup> Fully vaccinated is defined as having received 5 valid doses of DTaP or 4 valid doses of DTaP if the fourth dose was administered on or after the fourth birthday.



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

Repeat doses of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine at 5- and 10-year intervals are safe and immunogenic.

**What is added by this report?**

ACIP recommendations have been updated to allow either tetanus and diphtheria toxoids (Td) vaccine or Tdap to be used for the decennial Td booster, tetanus prophylaxis for wound management, and for additional required doses in the catch-up immunization schedule if a person has received at least 1 Tdap dose.

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

Allowing either Tdap or Td to be used in situations where Td only was previously recommended increases provider point-of-care flexibility.

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**TABLE. Food and Drug Administration (FDA)–approved and off-label recommendations for licensed tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) products — United States, 2019**

Licensed Tdap product	FDA-approved indications for use and administration	Off-label uses		
		Decennial Td booster	Tetanus prophylaxis for wound management	Catch-up immunization,* including during pregnancy†
Adacel <sup>§</sup>	Age: 10–64 years	Age: ≥65 years	Age: <10 or ≥65 years	Age: 7–9 years
	Routine booster ≥5 years after a dose of DTaP or Td vaccine, with a second dose ≥8 years after first (any) Tdap dose  Tetanus prophylaxis if ≥5 years have elapsed since the last tetanus-containing vaccine	Any dose beyond second Adacel dose administered ≥8 years after first Tdap dose		>1 Tdap dose
Boostrix <sup>§</sup>	Age: ≥10 years	Any dose if previously received Tdap	Age: <10 years	Age: 7–9 years
	Single dose ≥5 years after a dose of DTaP or Td vaccine  Tetanus prophylaxis if no previous Tdap		Any dose if previously received Tdap	>1 Tdap dose

**Abbreviations:** DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine; Td = tetanus and reduced diphtheria toxoid.

\* Persons with incomplete or unknown vaccination history should receive a single dose of Tdap, preferably as the first dose of the 3-dose catch-up series; if additional tetanus toxoid-containing doses are needed, either Td or Tdap vaccine may be used.

† Both Tdap vaccines may be administered during pregnancy with the same intervals and restrictions (vaccine specific) as would apply to a nonpregnant person.

§ Package inserts for indications and intervals for wound management are available at <https://www.fda.gov/media/119862/download> (Adacel) and <https://www.fda.gov/media/124002/download> (Boostrix).

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## Characteristics of Persons Who Report Using Only Nicotine-Containing Products Among Interviewed Patients with E-cigarette, or Vaping, Product Use–Associated Lung Injury — Illinois, August–December 2019

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In 2019, the United States experienced an outbreak of e-cigarette, or vaping, product use–associated lung injury (EVALI) (1). Most EVALI patients have reported using tetrahydrocannabinol (THC)-containing e-cigarette, or vaping, products obtained from informal sources (2,3), and vitamin E acetate in these products has been closely linked with EVALI (4,5). However, some EVALI patients report using only nicotine-containing products. This study compared demographic, product use, and clinical characteristics of EVALI patients in Illinois who reported using only nicotine-containing e-cigarette, or vaping, products with those of patients who reported using any THC-containing products. Among 121 interviewed Illinois EVALI patients, 17 (14%) reported using only nicotine-containing products, including nine (7%) patients who had no indication of any THC use, based on self-report or toxicology testing. Compared with patients who used any THC-containing products, these nine patients were significantly more likely to be older and female and were less likely to experience constitutional symptoms or to have leukocytosis on initial evaluation. Although vitamin E acetate has been strongly linked with EVALI, evidence is not sufficient to rule out the contribution of other chemicals of concern, including chemicals in either THC- or non-THC-containing products, in some reported EVALI cases. The contributing cause or causes of EVALI for patients reporting use of only nicotine-containing products warrants further investigation.

Medical records were requested for all suspected EVALI cases reported to the Illinois Department of Public Health (IDPH), and clinical information was abstracted using a standardized form. Cases were included in this study if the illness met the EVALI surveillance definition for a confirmed or probable case.\* EVALI patients or their proxies were also asked to complete a structured questionnaire that collected information about demographics and e-cigarette, or vaping, product use. A follow-up interview was attempted with all patients who reported that they did not use THC-containing products on the initial questionnaire to confirm that they used

only nicotine-containing products, and corresponding medical records were reexamined for any indication of THC use (e.g., a positive urine cannabinoid screen or report of smoking combustible marijuana to a health care provider). When available, bronchoalveolar lavage fluid specimens were sent to CDC for laboratory testing. EVALI cases reported during July 20–December 1, 2019, with a completed initial structured questionnaire were included in this analysis.

Among 195 EVALI cases reported to IDPH, 121 patients (62%) had a completed structured questionnaire. These patients were categorized into two analysis groups: those who reported using any THC-containing products and those who reported using no THC-containing products and reported using only nicotine-containing products. The group that reported no THC-containing product use was further stratified into two groups: those with no indication of any THC use after follow-up interview and reexamination of medical records and those who reported no THC-containing e-cigarette, or vaping, product use but who did have evidence of using THC (e.g., disclosed use of combustible marijuana or had a positive urine cannabinoid screen).

Demographic characteristics, use of nicotine-containing products, and clinical characteristics of patients with no indication of any THC use were compared with those who reported any THC-containing product use. To allow replication analyses by other health departments, where access to the follow-up interviews or medical records necessary to define the subgroups compared here might not be available, patients who reported using no THC-containing products (whether or not they had subsequent indication of any THC use) were also compared with those patients who reported using THC-containing products. Differences were assessed using Pearson's chi-squared test or Fisher's exact test for cells with <5 observations. The Wilcoxon rank sum test was used to compare medians. P-values <0.05 were considered statistically significant. Analyses were conducted using SAS (version 9.4; SAS Institute).

Initially, 19 (16%) of 121 interviewed Illinois EVALI patients reported using only nicotine-containing products (Figure), nine of whom participated in a follow-up interview; at that time, two patients (both aged <18 years) disclosed that they used products likely to have contained THC. Both

\* [https://www.cdc.gov/tobacco/basic\\_information/e-cigarettes/severe-lung-disease/health-departments/index.html#primary-case-def](https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease/health-departments/index.html#primary-case-def).



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

Most patients with e-cigarette, or vaping, product use–associated lung injury (EVALI) report using tetrahydrocannabinol (THC)-containing products. However, some report using only nicotine-containing products.

**What is added by this report?**

Among 121 interviewed Illinois EVALI patients, nine who reported using only nicotine-containing products and had no indication of any THC use were more likely to be older, female, and less likely to experience constitutional symptoms or leukocytosis than were patients who used THC-containing products.

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

Although vitamin E acetate has been strongly linked with EVALI, evidence is not sufficient to rule out the contribution of other chemicals of concern, including chemicals in either THC- or non-THC-containing products, in some reported EVALI cases.

patients completed the initial questionnaire with parents present, whereas follow-up interviews were conducted privately (with parental consent). Thus, overall, 104 patients (86%) reported using any THC-containing products, and 17 (14%) reported using only nicotine-containing products. Six of the 17 patients who reported using only nicotine-containing products also reported smoking combustible marijuana, and two other patients had positive urine cannabinoid screens and reported combustible marijuana use to their health care providers; bronchoalveolar lavage fluid from one of these patients was available for testing, and both THC and vitamin E acetate were detected in the fluid. Thus, nine of 121 patients (7%) had no indication of any THC use and constituted the analysis subgroup; three of these patients underwent urine cannabinoid screening and all were negative.

Among 104 patients who reported using any THC-containing products, 46 (44%) were classified as having confirmed EVALI, compared with two of 17 patients (12%) who reported using only nicotine-containing products, and none of nine patients with no indication of any THC use ( $p = 0.01$  for both) (Table 1). For the most part, these nine patients did not meet the minimum criteria for negative infectious disease testing to be classified as a confirmed case, in some instances because infection was not considered in the differential diagnosis. Compared with patients who reported using any THC-containing products, patients with no indication of any THC use were more likely to be female (78% versus 25%;  $p < 0.01$ ) and aged  $\geq 45$  years (33% versus 2%,  $p < 0.01$ ). There were no statistically significant differences in the frequency of use of nicotine-containing products, number

of nicotine-containing products used, or source of the nicotine-containing products.

At initial hospital evaluation, patients with no indication of any THC use were less likely than were patients who reported using any THC-containing products to experience constitutional symptoms (56% versus 96%;  $p < 0.01$ ), have an initial leukocytosis (38% versus 91%;  $p < 0.01$ ), or to have presented to an outpatient provider or emergency department before hospitalization (25% versus 80%;  $p < 0.05$ ) (Table 2). There were no statistically significant differences between patients with no indication of any THC use and those who reported using any THC-containing product in initial vital signs, other initial laboratory results, admission to an intensive care unit, or severe outcome (defined as death or respiratory failure requiring endotracheal intubation and mechanical ventilation).

**Discussion**

Among the 121 EVALI patients included in this analysis, nine (7%) reported using only nicotine-containing e-cigarette, or vaping, products and had no indication of any THC use. EVALI patients who had no indication of any THC use were more likely to be older and female and less likely to have constitutional symptoms and an initial leukocytosis and to have seen an outpatient provider before hospitalization. Vitamin E acetate has been strongly linked to the EVALI outbreak (4); however, before the current EVALI outbreak, there have been case reports of lung injury associated with nicotine-containing e-cigarette, or vaping, product use (6,7). Along with a longstanding baseline rate of emergency department visits from e-cigarette, or vaping, product use identified from syndromic surveillance (8), these findings suggest that some EVALI cases might be associated with the use of nicotine-containing products. Given the different demographics, clinical presentations, and the lack of any indication of exposure to THC-containing products, the contributing cause or causes of EVALI for persons using only nicotine-containing products might differ from the majority of EVALI patients and warrants further investigation.

A small number of EVALI patients in Illinois who initially reported not using THC-containing e-cigarette, or vaping, products were ultimately determined to have used these products through follow-up interview and laboratory testing. These findings demonstrate inconsistencies in patient reporting of THC-containing e-cigarette, or vaping, product use. Empathetic and private questioning might help facilitate accurate reporting, particularly among younger patients (9). In all suspected EVALI patients, providers should consider conducting, with informed consent, urine toxicology testing, including testing for THC (10).

FIGURE. Categorization of patients with confirmed and probable e-cigarette, or vaping, product use–associated lung injury (EVALI), by tetrahydrocannabinol (THC)-containing product use — Illinois, July–December 2019

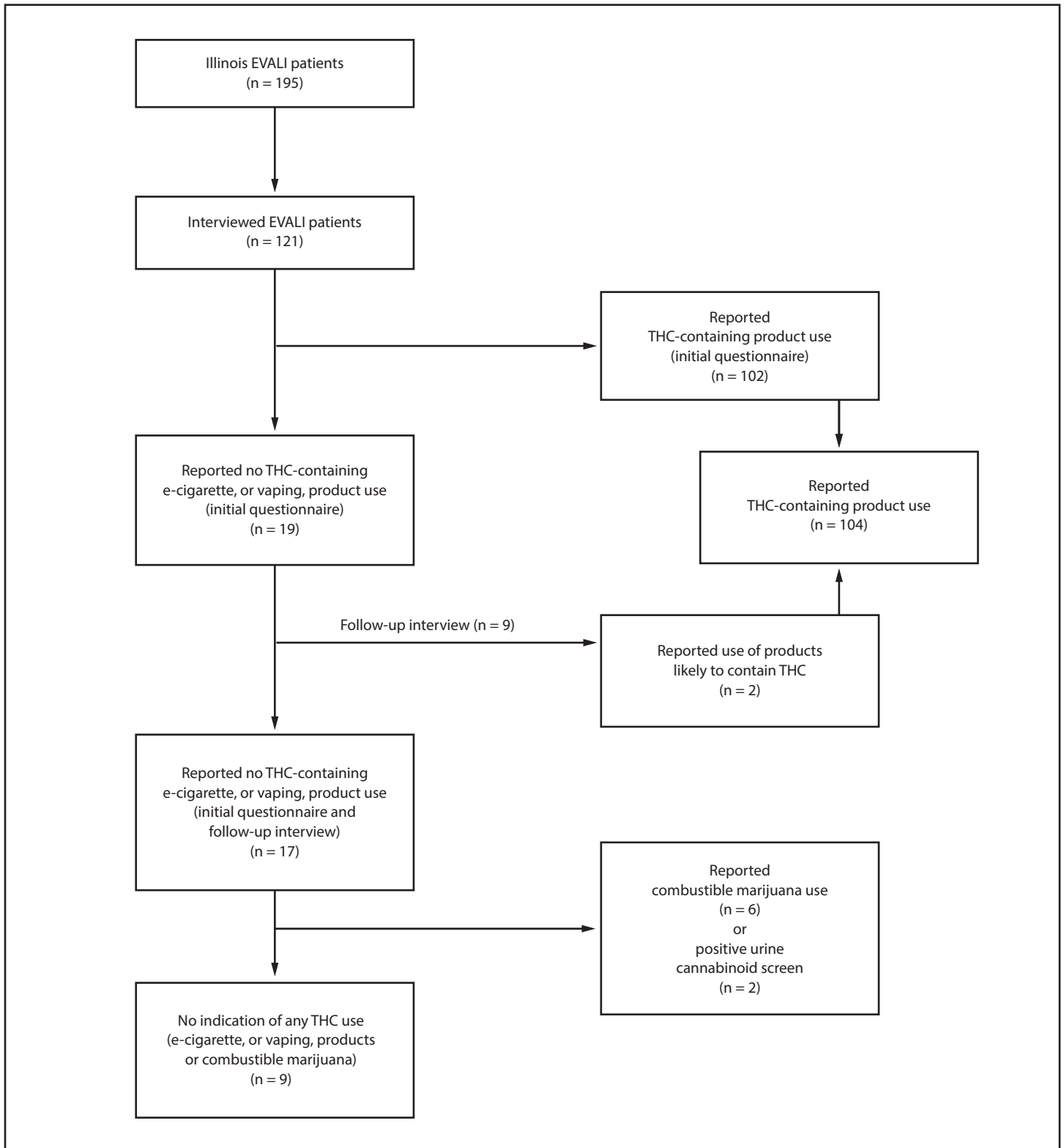


TABLE 1. Demographic characteristics and use of nicotine-containing e-cigarette, or vaping, products among patients with e-cigarette, or vaping, product use–associated lung injury (EVALI), by tetrahydrocannabinol (THC)-containing product use — Illinois, July–December 2019

Characteristic	No. (%)			No. (%)	
	Reported THC-containing product use* (reference)	Reported no THC-containing product use†	p-value¶	No indication of any THC use§	p-value¶
<b>Total (N = 121)**</b>	<b>104 (86)</b>	<b>17 (14)</b>	—	<b>9 (7)</b>	—
<b>Case status</b>					
Confirmed	46/104 (44)	2/17 (12)	0.01	0/9 (0)	0.01
Probable	58/104 (56)	15/17 (88)		9/9 (100)	
<b>Gender</b>					
Female	26/104 (25)	7/17 (41)	0.2	7/9 (78)	0.003
<b>Age group (yrs)</b>					
13–24	65/104 (63)	7/17 (41)	0.007	2/9 (22)	<0.001
25–44	37/104 (36)	7/17 (41)		4/9 (44)	
45–74	2/104 (2)	3/17 (18)		3/9 (33)	
<b>Race/Ethnicity</b>					
White, non-Hispanic	61/93 (66)	11/16 (69)	0.3	4/9 (44)	0.06
Black, non-Hispanic	6/93 (6)	3/16 (19)		3/9 (33)	
Other, non-Hispanic	9/93 (10)	1/16 (6)		1/9 (11)	
Hispanic	17/93 (18)	1/16 (6)		1/9 (11)	
<b>Nicotine-containing e-cigarette, or vaping, products</b>					
Used nicotine product >5 times per day	35/48†† (73)	8/15 (53)	0.2	4/8 (50)	0.2
Used more than one nicotine product	13/55 (24)	3/17 (18)	0.7	2/9 (22)	1.0
<b>Source of nicotine product (s)§§</b>					
Vape or tobacco shop	22/47 (47)	10/14 (71)	0.1	7/9 (78)	0.1
Convenience store	14/47 (30)	5/14 (36)	0.7	2/9 (22)	1.0
Online	4/47 (9)	1/14 (7)	1.0	1/9 (11)	1.0
Informal source¶¶	11/47 (23)	0/14 (0)	0.06	0/9 (0)	0.2

\* Patients who reported using THC-containing e-cigarette, or vaping, products on initial structured questionnaire or follow-up interview.

† Patients who reported not using THC-containing e-cigarette, or vaping, products on initial structured questionnaire and follow-up interview.

§ Subgroup of patients who reported not using THC-containing products who also had no indication of use of any other THC-containing substance (e.g., reported not smoking combustible marijuana, had negative toxicology testing, if performed).

¶ P-values for comparisons, using Pearson's chi-squared test or Fisher's exact test (for cells with <5 observations). Statistical tests compared EVALI patients who reported THC-containing product use with EVALI patients who reported no THC-containing product use and with EVALI patients with no indication of any THC use.

\*\* Data were not available for all variables for all patients. Differing denominators reflect missing data.

†† Only patients who used nicotine-containing e-cigarette, or vaping, products and reported a frequency of use are included in the denominator.

§§ Six patients reported purchasing nicotine-containing e-cigarette, or vaping, products from more than one source: vape/tobacco shop and convenience store (three) and vape/tobacco shop and online (three).

¶¶ Informal sources of nicotine-containing products include friends, family members, or from in-person or online dealers.

The findings in this report are subject to at least four limitations. First, findings should be interpreted with caution because of the small number of patients who reported not using any THC-containing products. This small sample size limits the statistical power or ability to account for potential confounding factors. Second, product use was self-reported and might be subject to reporting biases, particularly given that recreational use of THC-containing products was illegal in Illinois before January 1, 2020. Moreover, urine toxicology screens and laboratory testing of e-cigarette, or vaping, products were not performed routinely. Thus, the group of 17 patients who reported not using THC-containing products includes both persons with and without exposure to THC; nevertheless, this group was included in this report principally to aid future analyses. The primary comparison in the analysis reported here is between those who report using THC-containing products

and those with no indication of any THC use. Nevertheless, of the nine patients analyzed in this report as having no indication of any THC use, only three were screened for cannabinoids. Third, because EVALI has diverse presentations and an intentionally sensitive surveillance case definition, some non-cases might have been misclassified as cases. Finally, not all EVALI patients were reached for initial or follow-up interview, which could limit generalizability of these findings.

CDC recommends that persons should not use THC-containing e-cigarette, or vaping, products, particularly those obtained from informal sources such as friends, family members, or from in-person or online dealers. Vitamin E acetate is strongly linked to the EVALI outbreak. However, evidence is not sufficient to rule out the contribution of other chemicals of concern, including chemicals in either THC- or non-THC-containing products, in some reported EVALI cases.

**TABLE 2. Clinical characteristics of patients with e-cigarette, or vaping, product use-associated lung injury (EVALI), by reported tetrahydrocannabinol (THC)-containing product use — Illinois, July–December 2019**

Characteristic	No. (%)		p-value <sup>¶</sup>	No. (%)	
	Reported THC-containing product use* (reference)	Reported no THC-containing product use <sup>†</sup>		No indication of any THC use <sup>§</sup>	p-value <sup>¶</sup>
<b>Total (N = 121)**</b>	<b>104 (86)</b>	<b>17 (14)</b>	—	<b>9 (7)</b>	—
<b>Past medical history</b>					
Existing respiratory condition <sup>††</sup>	12/61 (20)	3/14 (21)	1.0	2/7 (29)	0.6
Existing cardiovascular condition <sup>§§</sup>	2/61 (3)	1/14 (7)	0.5	1/7 (14)	0.3
<b>Symptoms reported at presentation</b>					
Any respiratory symptom <sup>¶¶</sup>	99/100 (99)	16/17 (94)	0.3	8/9 (89)	0.2
Any gastrointestinal symptom <sup>***</sup>	88/100 (88)	14/17 (82)	0.5	7/9 (78)	0.3
Any constitutional symptom <sup>†††</sup>	96/100 (96)	13/17 (76)	0.02	5/9 (56)	0.001
<b>Vital signs at presentation</b>					
Hypoxemia (O <sub>2</sub> saturation ≤95% on room air)	66/104 (63)	10/17 (59)	0.7	5/9 (56)	0.7
Tachypnea (RR >20 breaths per minute)	25/66 (38)	7/15 (47)	0.5	3/8 (38)	1.0
Tachycardia (HR >100 beats per minute)	40/68 (59)	7/15 (47)	0.7	4/8 (50)	0.7
Fever (temperature ≥100.4°F [38°C])	21/65 (32)	3/14 (21)	0.5	2/8 (25)	1.0
<b>Initial laboratory results</b>					
Leukocytosis (WBC count >11,000 per mm <sup>3</sup> )	63/69 (91)	9/16 (56)	0.001	3/8 (38)	0.001
with >80% neutrophils	53/63 (84)	5/9 (56)	0.07	1/3 (33)	0.08
Sodium <135 mmol/liter	17/69 (25)	3/16 (19)	0.8	0/8 (0)	0.2
Potassium <3.5 mmol/liter	18/68 (26)	2/15 (13)	0.5	2/7 (29)	1.0
AST or ALT >35 U/liter	27/61 (44)	9/13 (69)	0.1	5/6 (83)	0.1
<b>Clinical course</b>					
Duration of symptoms before hospitalization (median days, range)	7 (1–148)	4 (0–205)	0.04	3 (0–205)	0.1
Outpatient or ED visit before hospitalization	51/64 (80)	3/10 (30)	0.003	1/4 (25)	0.04
Received glucocorticoids	53/55 (96)	8/10 (80)	0.1	5/5 (100)	1.0
Clinical improvement documented after glucocorticoids	16/53 (30)	1/8 (13)	0.4	0/5 (0)	0.3
Admitted to intensive care unit	40/81 (49)	9/17 (53)	0.8	5/9 (56)	1.0
Severe outcome <sup>§§§</sup>	19/90 (21)	7/17 (41)	0.07	4/9 (44)	0.2

**Abbreviations:** ALT = alanine aminotransferase; AST = aspartate aminotransferase; ED = emergency department; HR = heart rate; O<sub>2</sub> = oxygen; RR = respiratory rate; WBC = white blood cell.

\* Patients who reported using THC-containing e-cigarette, or vaping, products on initial structured questionnaire or follow-up interview.

† Patients who reported not using THC-containing e-cigarette, or vaping, products on initial structured questionnaire or follow-up interview.

§ Subgroup of those patients who reported not using THC-containing products who also had no indication of use of any other THC-containing substance (e.g., reported not smoking combustible marijuana, had negative toxicology testing, if performed).

¶ P-values for comparisons, using Pearson's chi-squared test or Fisher's exact test (for cells with <5 observations). Wilcoxon rank sum test used to compare medians. Statistical tests compared EVALI patients who reported THC-containing product use with EVALI patients who reported no THC-containing product use and with EVALI patients with no indication of any THC use.

\*\* Data were not available for all patients. Differing denominators reflect missing data.

†† Existing respiratory conditions include asthma, chronic obstructive pulmonary disease, bronchitis, previous lung cancer and obstructive sleep apnea.

§§ Existing cardiovascular conditions include ischemic heart disease, congestive heart failure and congenital heart disease.

¶¶ Respiratory symptoms include shortness of breath, any cough, pleuritic chest pain.

\*\*\* Gastrointestinal symptoms include nausea, vomiting, diarrhea, abdominal pain.

††† Constitutional symptoms include subjective fever, chills, weight loss, fatigue/malaise.

§§§ Severe outcomes include death or respiratory failure requiring endotracheal intubation and mechanical ventilation.

Vitamin E acetate should not be added to e-cigarette, or vaping, products. In addition, persons should not add any other substances not intended by the manufacturer to e-cigarette, or vaping, products, including products purchased through retail establishments.<sup>†</sup> Adults using nicotine-containing e-cigarette or vaping products as an alternative to cigarettes should not go back to smoking; they should weigh all available information and consider using Food and Drug Administration–approved

cessation medications.<sup>§</sup> They should contact their health care provider if they need help quitting tobacco products, including e-cigarettes, as well as if they have concerns about EVALI. Adults who do not currently use tobacco products should not start using e-cigarette, or vaping, products. Finally, e-cigarette, or vaping, products should never be used by youths, young adults, or pregnant women.

<sup>§</sup> [https://www.cdc.gov/tobacco/campaign/tips/quit-smoking/index.html?s\\_cid](https://www.cdc.gov/tobacco/campaign/tips/quit-smoking/index.html?s_cid).

<sup>†</sup> [https://www.cdc.gov/tobacco/basic\\_information/e-cigarettes/severe-lung-disease/need-to-know/index.html#cdc-recommends](https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease/need-to-know/index.html#cdc-recommends).



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## Update: Characteristics of a Nationwide Outbreak of E-cigarette, or Vaping, Product Use–Associated Lung Injury — United States, August 2019–January 2020

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*On January 17, 2020, this report was posted as an MMWR Early Release on the MMWR website (<https://www.cdc.gov/mmwr>).*

Since August 2019, CDC, the Food and Drug Administration (FDA), state and local health departments, and public health and clinical stakeholders have been investigating a nationwide outbreak of e-cigarette, or vaping, product use–associated lung injury (EVALI) (1). This report updates patient demographic characteristics, self-reported substance use, and hospitalization dates for EVALI patients reported to CDC by states, as well as the distribution of emergency department (ED) visits related to e-cigarette, or vaping, products analyzed through the National Syndromic Surveillance Program (NSSP). As of January 14, 2020, a total of 2,668 hospitalized EVALI cases had been reported to CDC. Median patient age was 24 years, and 66% were male. Overall, 82% of EVALI patients reported using any tetrahydrocannabinol (THC)-containing e-cigarette, or vaping, product (including 33% with exclusive THC-containing product use), and 57% of EVALI patients reported using any nicotine-containing product (including 14% with exclusive nicotine-containing product use). Syndromic surveillance indicates that ED visits related to e-cigarette, or vaping, products continue to decline after sharply increasing in August 2019 and peaking in September 2019. Clinicians and public health practitioners should remain vigilant for new EVALI cases. CDC recommends that persons not use THC-containing e-cigarette, or vaping, products, especially those acquired from informal sources such as friends, family members, or from in-person or online dealers. Vitamin E acetate is strongly linked to the EVALI outbreak and should not be added to any e-cigarette, or vaping, products (2). However, evidence is not sufficient to rule out the contribution of other chemicals of concern, including chemicals in either THC- or non-THC-containing products, in some reported EVALI cases.

States and jurisdictions voluntarily report data on confirmed and probable hospitalized or deceased EVALI patients to CDC weekly using established case definitions\* and data collection tools† (1). Self-reported substances used in e-cigarette, or vaping,

products were assessed among EVALI patients, including the percentage reporting any or exclusive THC-containing product use, any or exclusive nicotine-containing product use, and use of both THC- and nicotine-containing products. To assess trends in possible EVALI-related ED visits, CDC and health departments developed a query to assess exposure to e-cigarette, or vaping, products as a reason for an ED visit§ (3,4).

As of January 14, 2020, all 50 states, the District of Columbia, the U.S. Virgin Islands, and Puerto Rico had reported 2,668 hospitalized EVALI patients (Table). Overall, 66% of patients were male. The median patient age was 24 years (range = 13–85 years), and 76% were aged <35 years. Most EVALI patients were non-Hispanic white (73%), and 15% were Hispanic. Among 2,022 hospitalized patients with information on substances used, 1,650 (82%) reported using any THC-containing product, and 1,162 (57%) reported using any nicotine-containing product; 669 (33%) reported exclusive THC-containing product use, and 274 (14%) reported exclusive nicotine-containing product use.

The weekly number of hospital admissions for EVALI reported to CDC peaked at 215 during the week of September 15, 2019 (Figure 1). Since then, the number of cases reported each week has continued to steadily decline. NSSP data show that the number of possible EVALI-related ED visits sharply increased during August 11–September 8, 2019, by a mean of 26 visits per million each week (95% confidence interval [CI] = 18–33) (Figure 2). The weekly visit rate peaked at 116 per million during the week of September 8, 2019, then decreased by an average of approximately four per million weekly visits (95% CI = 4–5) to 35 per million during the week of January 5, 2020. This remains higher than the rate of 23 per million ED visits during the week of August 18, 2019.

### Discussion

As of January 14, 2020, all 50 states, the District of Columbia, the U.S. Virgin Islands, and Puerto Rico had reported EVALI patients. The majority of EVALI patients were non-Hispanic white, young adults, and male, similar to

\* [https://www.cdc.gov/tobacco/basic\\_information/e-cigarettes/assets/2019-Lung-Injury-Surveillance-Case-Definition-508.pdf](https://www.cdc.gov/tobacco/basic_information/e-cigarettes/assets/2019-Lung-Injury-Surveillance-Case-Definition-508.pdf).

† [https://www.cdc.gov/tobacco/basic\\_information/e-cigarettes/severe-lung-disease/healthcare-providers/pdfs/National-Case-Report-Form-v01.pdf](https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease/healthcare-providers/pdfs/National-Case-Report-Form-v01.pdf).

§ NSSP records free-text comments about the reason for ED visit, discharge diagnosis codes, and patient demographic characteristics from approximately 70% of ED visits nationwide.

**TABLE. Demographic and product use characteristics among hospitalized patients with e-cigarette, or vaping, product use–associated lung injury (EVALI) reported to CDC — United States, August 2019–January 2020\***

Characteristic (no. with available information)	No. (%) <sup>†</sup> (N = 2,668)
<b>Sex (2,606)</b>	
Male	1,731 (66)
Female	875 (34)
<b>Median age, yrs (range)</b>	24 (13–85)
<b>Age group (yrs) (2,619)</b>	
13–17	404 (15)
18–24	979 (37)
25–34	631 (24)
35–44	335 (13)
45–64	223 (9)
≥65	47 (2)
<b>Race/Ethnicity<sup>‡</sup> (1,856)</b>	
White	1,360 (73)
Black	64 (3)
American Indian/Alaska Native	12 (1)
Asian/Native Hawaiian/Other Pacific Islander	38 (2)
Other	97 (5)
Hispanic	285 (15)
<b>Case status (2,668)</b>	
Confirmed	1,401 (53)
Probable	1,267 (47)
<b>Substances used in e-cigarette, or vaping, products (2,022)<sup>¶,**</sup></b>	
Any THC-containing product	1,650 (82)
Any nicotine-containing product	1,162 (57)
Both THC- and nicotine-containing product use	834 (41)
Exclusive THC-containing product use	669 (33)
Exclusive nicotine-containing product use	274 (14)
No THC- or nicotine-containing product use reported	44 (2)

**Abbreviation:** THC = tetrahydrocannabinol.

\* For cases reported to CDC as of January 14, 2020.

† Percentages might not sum to 100% because of rounding.

‡ These were mutually exclusive groups. Whites, blacks, American Indians/Alaska Natives, Asians/Native Hawaiians/Other Pacific Islanders, and Others were non-Hispanic. Hispanic persons could be of any race.

¶ Limited to persons who reported vaping or dabbing at least one substance in the past 3 months.

\*\* In the 3 months preceding symptom onset.

that reported previously (1,5,6). Most patients reported THC-containing product use. However, 14% reported exclusive use of nicotine-containing products.

Vitamin E acetate is strongly linked to THC-containing products used by EVALI patients (2). However, a minority of EVALI patients consistently report exclusive use of nicotine-containing products, which might be due to several factors. First, some patients might not accurately report, or know the content of, THC or other compounds in the products they have used (2,7). Second, some cases might be misclassified; for example, the high sensitivity of the EVALI case definition likely lowered specificity, leading to inclusion of some patients who do not have EVALI. Third, these patients might be accurately reporting exclusive use of nicotine-containing products (7). A previous report found a relatively low, but longstanding, background rate of ED visits associated with e-cigarette, or vaping, products predating the current outbreak,

which could in part reflect one or more chemicals of concern in nicotine-containing products; however, this background rate could also reflect sporadic cases from the same products or substances that later contributed to the wider EVALI outbreak when they became more commonly used (4). The contributing cause or causes of EVALI for persons reporting exclusive use of nicotine-only products warrants further investigation.

Declines in the number of EVALI cases reported each week since mid-September 2019, and ED visits associated with e-cigarette, or vaping, products reported to NSSP, indicate that the outbreak peaked in September. Reasons for the decline might be multifactorial, including rapid public health action to increase public awareness of the risk associated with THC-containing e-cigarette, or vaping, product use, as well as actions by users to reduce this risk. Identification of the strong link between EVALI and vitamin E acetate, a diluent in THC-containing products, might have resulted in removal of vitamin E acetate from these products<sup>¶,\*\*</sup> (2,8,9). Further, actions by enforcement agencies might have affected the supply of informally sourced THC-containing products (8,10). However, clinicians, public health practitioners, and the public should remain vigilant by taking steps to reduce risk, including efforts by clinicians to identify and treat EVALI patients.

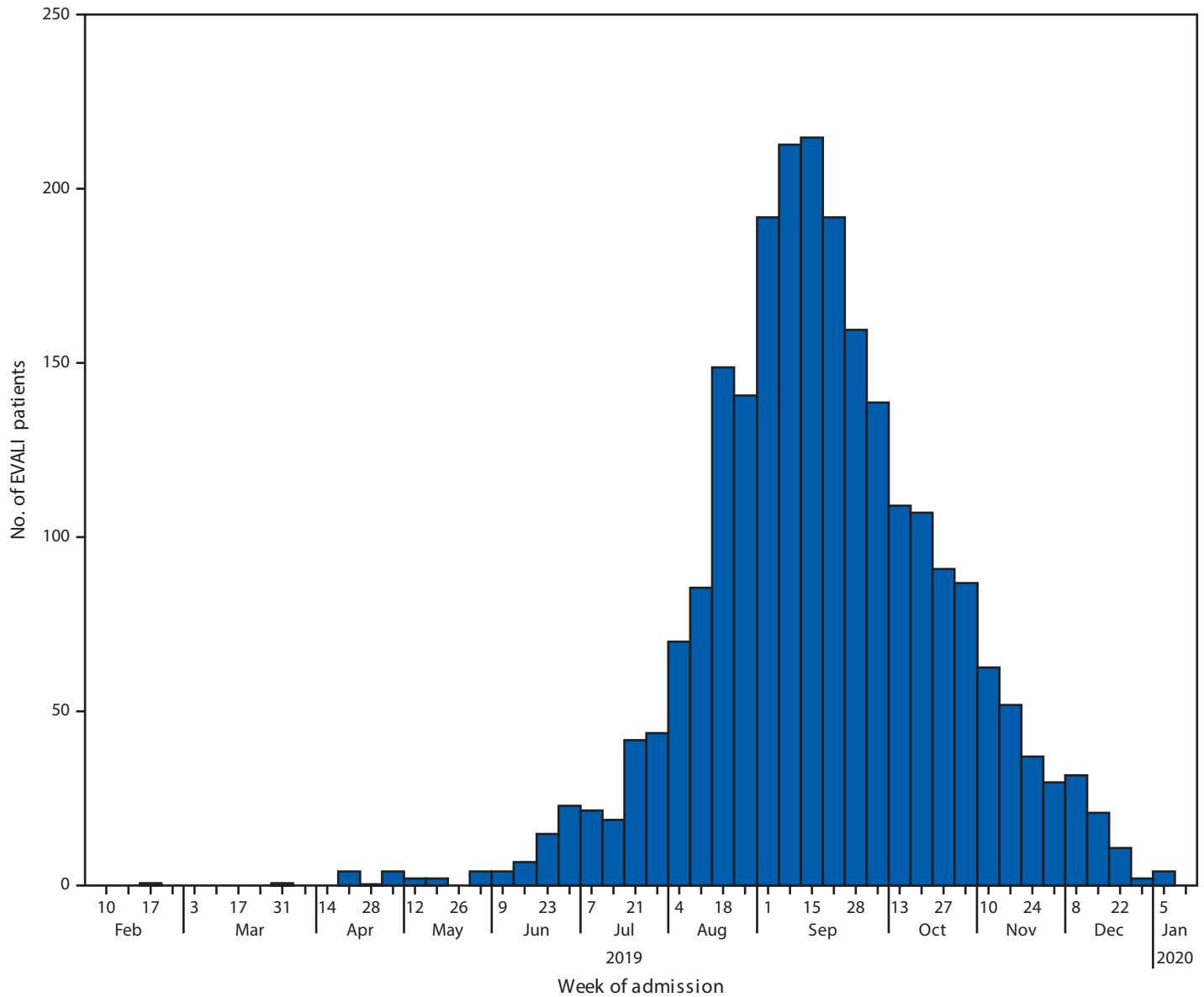
The identification of EVALI as a new clinical syndrome highlights a need for further studies. Understanding the long-term health consequences of EVALI will require long-term patient follow-up. It is not known whether additives other than vitamin E acetate in e-cigarette, or vaping, products might cause similar lung injury. In addition, ongoing surveillance for lung injury associated with e-cigarette, or vaping, product use needs to continue to detect possible increases in lung injury if new additives (e.g., a harmful diluent other than vitamin E acetate) are added to these products in the future. Syndromic surveillance helped demonstrate that EVALI was a new clinical syndrome, with ED visits sharply increasing in August 2019 and declining after peaking in September 2019 (4).

The findings in this report are subject to at least three limitations in addition to those already discussed related to ascertainment of the product type used. First, data related to product use were missing for 24% of patients, and many EVALI patients were not interviewed because of loss to follow-up, refusal to be interviewed, or lack of resources to conduct interviews. Any of these factors might limit the generalizability of these findings to other EVALI patients. Second, the exposure query in NSSP might have been affected by public and clinical awareness of the outbreak, which increased the likelihood that e-cigarette, or vaping, products would be mentioned in stated reasons for ED visits. Finally, NSSP

¶ <https://www.detroitnews.com/story/news/local/michigan/2019/12/17/michigan-recalls-marijuana-vaping-products-vitamin-e-acetate/2679157001/>.

\*\* <https://www.cnn.com/2019/12/24/health/black-market-vapes/index.html>.

FIGURE 1. Number of patients (N = 2,398) with e-cigarette, or vaping, product use–associated lung injury (EVALI) by week of hospital admission — United States, February 10, 2019–January 14, 2020



coverage is not uniform across or within states, and health care facilities contributing data change over time as new facilities are added to the system or removed when they close.

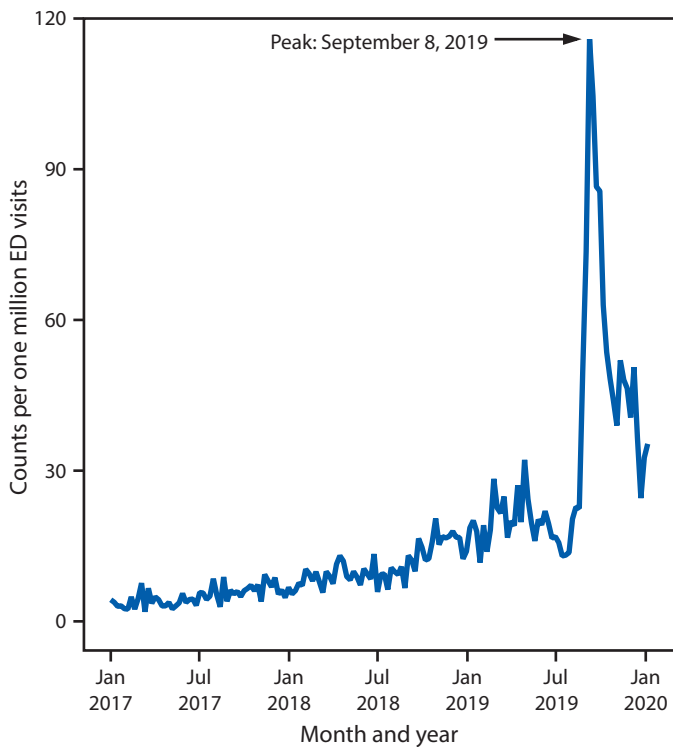
Based on data obtained in the investigation of EVALI since August 2019, CDC recommends that persons not use THC-containing e-cigarette, or vaping, products, particularly those from informal sources such as friends, family members, or from in-person or online dealers.<sup>††</sup> Vitamin E acetate is strongly linked to the EVALI outbreak; it has been detected in product samples tested by FDA and state laboratories and in lung

<sup>††</sup> [https://www.cdc.gov/tobacco/basic\\_information/e-cigarettes/severe-lung-disease.html](https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html).

fluid samples from patients tested by CDC from geographically diverse states (2,8,9). Vitamin E acetate should not be added to any e-cigarette, or vaping, products. In addition, any substances not intended by the manufacturer should not be added to e-cigarette, or vaping, products, including to products purchased through retail establishments. However, evidence is not sufficient to rule out the contribution of other chemicals of concern, including chemicals in either THC- or non-THC-containing products, in some reported EVALI cases. Adults using e-cigarette, or vaping, products as an alternative to cigarettes should not go back to smoking; they should weigh all available information and consider using FDA-approved



**FIGURE 2. Emergency department (ED) visits with e-cigarette, or vaping, product use in the reason for visit (chief complaint)\* — National Syndromic Surveillance Program, United States, January 1, 2017–January 11, 2020**



\* Excludes injuries unrelated to e-cigarette, or vaping, product use–associated lung injury (e.g., device explosions and accidental ingestion of e-liquid) but does not exclude potentially related syndromes such as acute intoxication from tetrahydrocannabinol or nicotine poisoning.

cessation medications.<sup>§§</sup> They should contact their health care provider if they need help quitting tobacco products, including e-cigarettes, and if they have concerns about EVALI. Adults who do not currently use tobacco products should not start using e-cigarette, or vaping, products. Finally, e-cigarette, or vaping, products should never be used by youths, young adults, or pregnant women.

### Lung Injury Response Epidemiology/Surveillance Task Force

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<sup>§§</sup> [https://www.cdc.gov/tobacco/campaign/tips/quit-smoking/index.html?s\\_cid](https://www.cdc.gov/tobacco/campaign/tips/quit-smoking/index.html?s_cid).

### Summary

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

Nationwide, 82% of patients hospitalized with e-cigarette or vaping, product use–associated lung injury (EVALI) reported tetrahydrocannabinol (THC)-containing product use. Vitamin E acetate, an additive to THC-containing e-cigarette, or vaping, products, is strongly linked to the EVALI outbreak.

#### What is added by this report?

The number of EVALI cases reported to CDC peaked during the week of September 15, 2019; the weekly number of hospitalized patients has since steadily declined.

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

Clinicians and public health practitioners should remain vigilant for EVALI cases. CDC recommends that persons not use THC-containing e-cigarette, or vaping, products, particularly from informal sources. Evidence is not sufficient to rule out the contribution of other chemicals of concern, including chemicals in either THC- or non-THC-containing products, in some reported EVALI cases.

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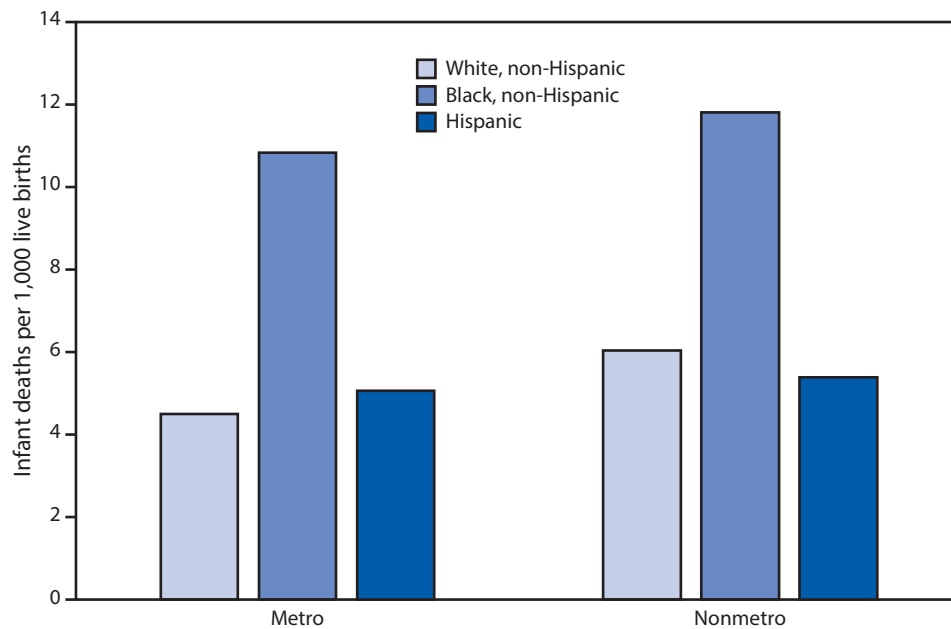
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## QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

## Infant Mortality Rates for Metro and Nonmetro Counties,\* by Race and Hispanic Origin — National Vital Statistics System, United States, 2017



\* Urbanization level is based on maternal county of residence. Counties were classified according to their metropolitan status using the National Center for Health Statistics Urban–Rural Classification Scheme ([https://www.cdc.gov/nchs/data\\_access/urban\\_rural.htm](https://www.cdc.gov/nchs/data_access/urban_rural.htm)).

In metropolitan counties, infant mortality rates were lowest for infants of non-Hispanic white mothers (4.50 infant deaths per 1,000 live births), followed by rates for infants of Hispanic mothers (5.08) and highest for infants of non-Hispanic black mothers (10.84). In nonmetropolitan counties, the mortality rate was lowest for infants of Hispanic mothers (5.38) followed by infants of non-Hispanic white mothers (6.05) and highest for infants of non-Hispanic black mothers (11.81). The infant mortality rate was significantly lower for infants of non-Hispanic white women in metro counties compared with nonmetro counties; differences in rates between metro and nonmetro counties for the two other groups were not significant.

**Source:** National Vital Statistics System, Linked birth/infant death period file, 2017.

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