



Background – Hepatitis A among Persons Living with HIV

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Advisory Committee on Immunization Practices

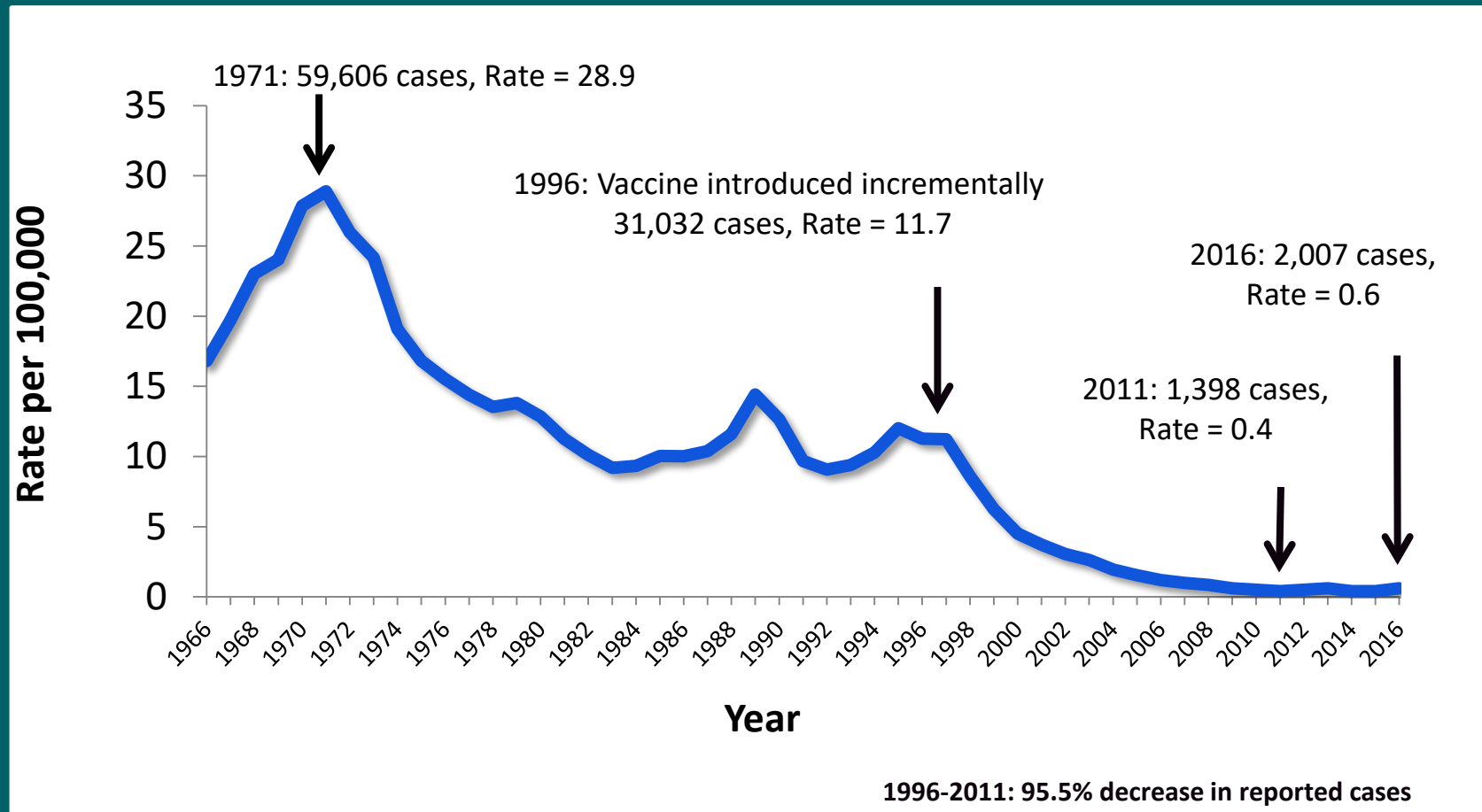
Thursday, February 28, 2019

Outline

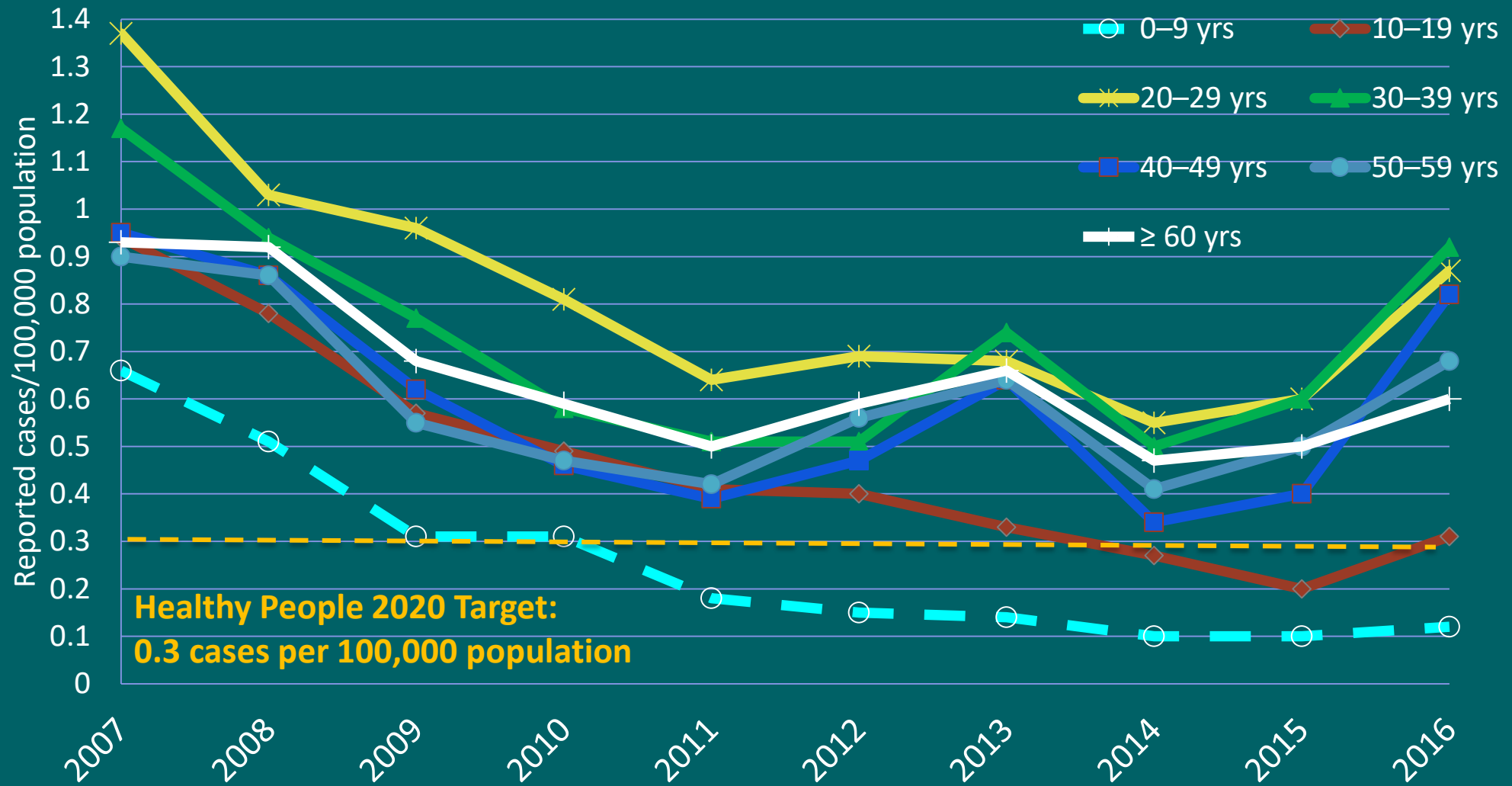
- **Epidemiology**
- **Hepatitis A Vaccines**
- **Hepatitis A Outbreaks**
- **HIV**

Epidemiology

Rates of Reported Acute Hepatitis A Cases United States, 1966-2016

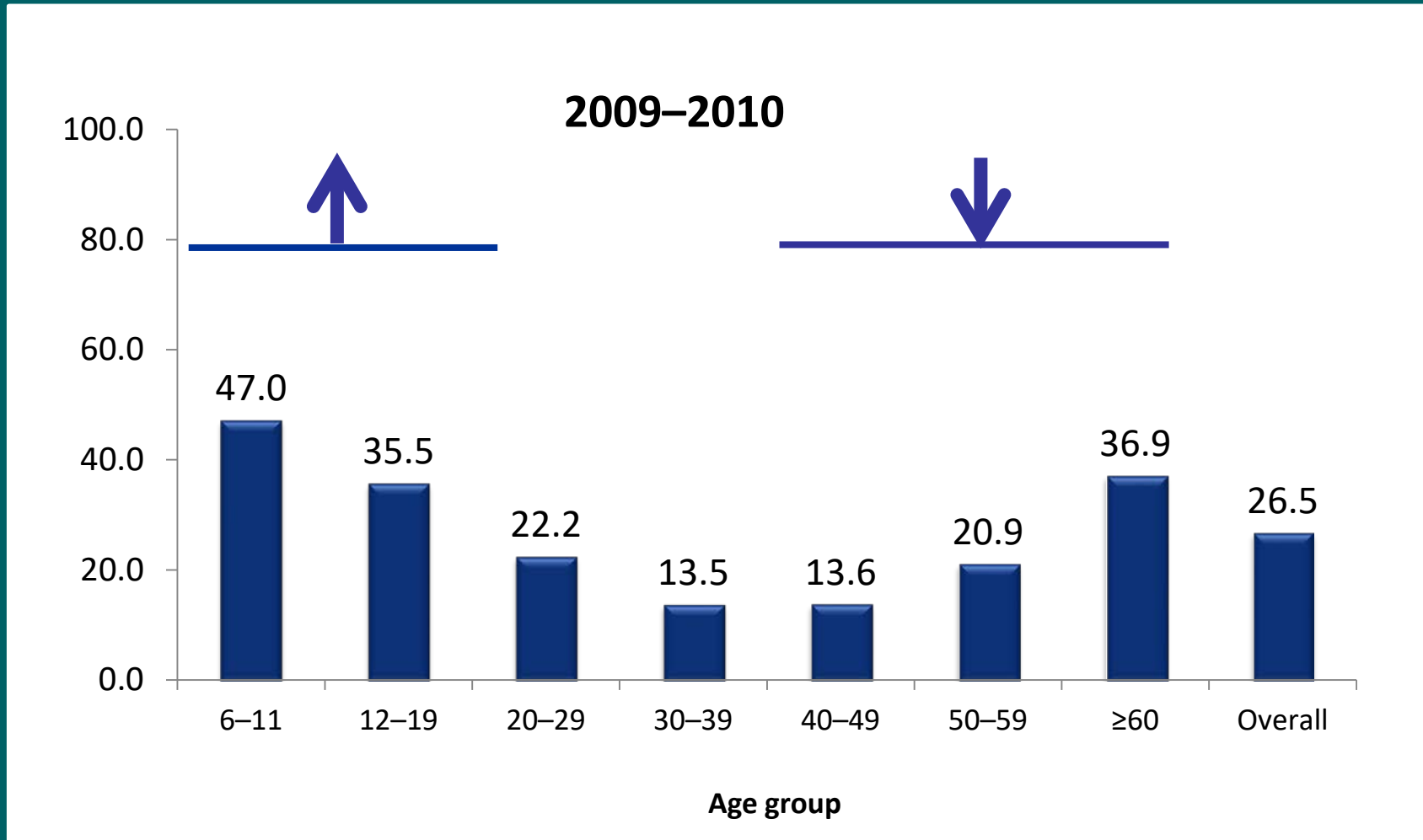


Rates of Reported Acute Hepatitis A United States, 2007-2016



Healthy People 2020 Target:
0.3 cases per 100,000 population

Prevalence of anti-HAV by age group, NHANES, United States 2009–2010



Hepatitis A Vaccines

ACIP Hepatitis A Vaccine Recommendations

Groups at increased risk of HAV or severe HAV disease

- Travelers (1996)
- Men who have sex with men (1996)
- Users of injection and non-injection drugs (1996)
- Persons with clotting-factor disorders (1996)
- Persons who work with nonhuman primates (1996)
- Persons with chronic liver disease (1996)
- Persons who anticipate close personal contact with an international adoptee (2009)
- Persons experiencing homelessness (2019)
- **Persons living with HIV (proposed)**

Immunogenicity of Hepatitis A Vaccines Among Adults

- All licensed vaccines are highly immunogenic in persons aged >18 years when administered according to the recommended schedules
- Protective antibody levels were identified in 94%–100% of immunocompetent adults one month after the first dose
- After the second dose, all persons had protective levels of antibody, with high geometric mean titers (GMTs)

Clemens R et al. J Infect Dis 1995;171(Suppl 1):S44–9.

Nalin DR. VAQTA™: hepatitis A vaccine, purified inactivated. Drugs of the Future 1995;20:24–9.

McMahon BJ, et al. Immunogenicity of an inactivated hepatitis A vaccine in Alaska Native children and Native and non-Native adults. J Infect Dis 1995;171:676–9.

Hepatitis A Vaccine Safety

- In pre-licensure trials, adverse reactions to HAVRIX, VAQTA and TWINRIX were mostly injection site reactions and mild systemic reactions
- **Postmarketing surveillance for adverse events following receipt of HepA vaccines has been performed primarily by two systems in the United States: the Vaccine Adverse Event Reporting System (VAERS) and the Vaccine Safety Datalink (VSD)**
 - No unusual or unexpected safety patterns were observed for any of the HepA vaccines licensed in the United States

Immunogenicity – Long-term Protection

- Anti-HAV has been shown to persist in vaccine recipients for at least 20 years in immunocompetent adults administered inactivated vaccine as children with a three-dose schedule.¹
- At least 20 year anti-HAV persistence was demonstrated among immunocompetent adults vaccinated with a two-dose schedule as adults.²
- Detectable antibodies are estimated to persist for 40 years or longer based on mathematical modeling and anti-HAV kinetic studies.^{2,3}
- Protection following natural infection is lifelong and may also be lifelong following vaccination.
- For persons with immunocompromising conditions or co-morbidities, protection may be less.

1. Plumb ID, et al. *J Viral Hepat.* 2017 Jul;24(7):608-612.

2. Theeten H, et al. *Vaccine.* 2015 Oct 13;33(42):5723-7.

3. Hens N, et al. *Vaccine.* 2014;32(13):1507-1513.

Hepatitis A Vaccine Coverage, United States, 2016

■ Children¹

- 60.6% for children age 19-35 months, ≥2 doses (59.7%, 2017)
- 86.1% for children age 19-35 months, ≥1 dose (86%, 2017)

■ Adolescents²

- 64.4% for adolescents age 13-17 years, ≥2 doses
- 73.9% for adolescents age 13-17 years, 1 dose

■ Adults³

- 9.5% for adults ≥19 years, ≥2 doses
- 13.4% for adults 19-49 years, ≥2 doses; Travelers, 19.3%; CLD, 23.7%
- 5.4% for adults ≥50 years, ≥2 doses

1. Hill HA, et al. MMWR 2017;66:1171–1177.

2. Nelson NP, et al. *Vaccine* 2018. Mar 14;36(12):1650-1659

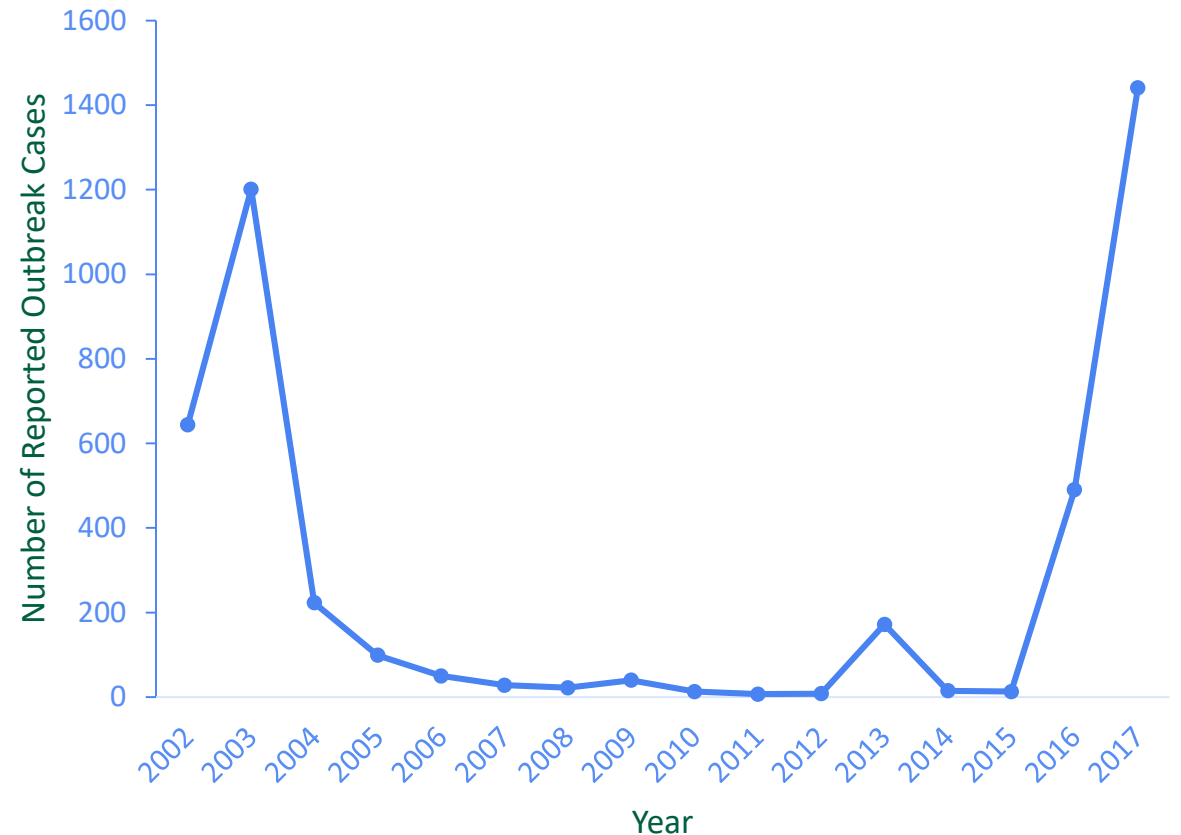
3. Vaccination Coverage Among Adults in the United States, National Health Interview Survey, 2016.

<https://www.cdc.gov/vaccines/imz-managers/coverage/adultvaxview/NHIS-2016.html#hepA>

Hepatitis A Virus Outbreaks

Shifting Hepatitis A Virus Epidemiology

- Past outbreaks were associated with asymptomatic children
- A large population of adults are not immune to hepatitis A virus
- Older people are more likely to experience severe disease and adverse outcomes
- Vaccination uptake among at-risk adults is low



Collier M, et al. *Hepatology* 2015.
Ly KN, Klevens RM. *J Infect Dis* 2015.
Epson E, et al. *Public Health*, 2015.
Murphy TV, et al. *MMWR Suppl* 2016.
Foster M, et al. *MMWR* 2018.

Hepatitis A Outbreaks in Multiple States Among Persons who Use Drugs and/or Persons Experiencing Homelessness

- Since these outbreaks were first identified in 2016, more than 13,000 cases and 7,400 (57%) hospitalizations have been reported
- Over 100 deaths have occurred nationwide because of these outbreaks
- Hospitalization rates have been higher than typically associated with hepatitis A infection
- Hepatitis A virus is highly transmissible from person-to-person
- Prolonged community outbreaks have been challenging to control

Division of Viral Hepatitis Outbreak Website Map: <https://www.cdc.gov/hepatitis/outbreaks/2017March-HepatitisA.htm>

State-Specific Hepatitis A Outbreak Information - click for state's website

The map displays the following states with blue highlights: CA, UT, NM, AR, MO, IL, IN, OH, WV, VA, NC, TN, KY, MI, WI, LA, FL, NH, MA, and ME. A legend on the right side of the map lists states in a vertical column: VT, NH, MA, RI, CT, NJ, DE, MD, and DC. The NH, MA, and ME entries in the legend are highlighted in blue. At the bottom left, there is a dropdown menu with 'Tennessee' selected and a 'Go' button. The CDC logo is located at the bottom right of the map area.

Tennessee

Go

Tennessee Person-to-Person Outbreak

- **In Tennessee, 14 PWHIV have been infected with hepatitis A virus (249 cases).**
 - 5 of 14 (36%) had been vaccinated with at least one dose of either combination or single-antigen hepatitis A vaccine at least 1 month prior to hepatitis exposure
 - 8 of 14 (57%) had no or unknown vaccination history
 - 13 of 14 (93%) had an indication for HepA vaccine prior to becoming ill with hepatitis A
- **Previously vaccinated HAV cases among PWHIV raise concern about HAV susceptibility among PWHIV and HepA vaccine long-term immunogenicity.**
 - Missed opportunities for vaccination
 - Potential waning immunity in persons vaccinated

Courtesy: Julia Brennan and TN Dept of Health

HIV

Definition of HIV Infection

- **The term refers to persons diagnosed with HIV infection, regardless of the stage of disease at diagnosis (i.e., HIV infection Stage 0, 1, 2, 3 [AIDS], or unknown), from all 50 states, the District of Columbia, and 6 U.S. dependent areas (American Samoa, Guam, the Northern Mariana Islands, Puerto Rico, the Republic of Palau, and the U.S. Virgin Islands).**

Centers for Disease Control and Prevention. HIV Surveillance Report, 2017; vol. 29.

<https://www.cdc.gov/hiv/library/reports/hiv-surveillance.html>. Published November 2018. Accessed 2.19.2019.

HIV Prevalence Estimate

- **An estimated prevalence of 1,122,900 persons aged ≥ 13 years were living with HIV infection, year-end 2015**
- **Includes 162,500 (14.5%) persons whose infection had not been diagnosed**

Diagnoses of HIV Infection, by Age, 2017, U.S. and 6 dependent areas

- In 2017, the number of new HIV diagnoses in the United States and 6 dependent areas was 38,739.

Age (Years)	Number of Diagnoses of HIV Infection, 2017
13-14	25
15-19	1,723
20-24	6,416
25-29	7,755
30-34	5,678
35-39	4,365
40-44	3,032
45-49	3,006
50-54	2,729
55-59	1,918
60-64	1,108
65 and older	885

Diagnoses of HIV Infection by Transmission Category

- CDC classifies HIV diagnoses into six transmission categories to which transmission may be attributed

Transmission Category	Adult and Adolescent Males	Adult and Adolescent Females	Total
Male-to-male sexual contact	25,748	NA	25,748
Injection drug use	1,373	1,016	2,389
Male-to-male sexual contact and injection drug use^a	1,252	NA	1,252
Heterosexual contact^b	2,829	6,341	9,170
Other^c	37	44	81

^a Includes infections attributed to male-to-male sexual contact *and* injection drug use (men who reported both risk factors).

^b Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.

^c Includes hemophilia, blood transfusion, perinatal exposure, and risk factor not reported or not identified.

What percentage of PWHIV do not have an existing risk factor for which HepA vaccine is recommended?



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Risk Factors for which HepA Vaccination is Recommended Among PWHIV, MMP, 2016

Risk Factor	Number	Weighted Percent	95% CI
MSM in past 12 months	1202	32.5	(30.3 - 34.6)
Non-injection drug use in past 12 months	1156	28.7	(26.0 - 31.5)
Injection drug use in past 12 months	114	2.4	(1.7 - 3.2)
Homeless in past 12 months	332	8.4	(7.3 - 9.5)
Chronic liver disease	601	15.0	(13.4 - 16.6)
Clotting factor disorder *	8	0.2*	(0.05 - 0.3)
Any of the above	2313	59.9	(57.3 - 62.4)
None of the above	1529	40.1	(37.6 - 42.7)

*CV>.3, estimate is unstable

Denominator is all records containing a diagnosis dataset

Summary

Summary - I

- **Hepatitis A vaccine is largely responsible for the marked reduction in hepatitis A cases**
- **Increasing proportion of adults in the United States are susceptible to hepatitis A**
 - Reduced exposure to HAV early in life
 - Significant decreases in anti-HAV seroprevalence in older adults (≥ 40 years)
 - Low two-dose vaccination coverage exists in adults, including high risk adults (e.g., travelers, chronic liver disease)

Summary - II

- **Outbreaks - Shifting epidemiology, person-to-person transmission among unvaccinated vulnerable populations**
- **About 1 million persons are living with HIV in the United States**
- **Up to 40% of PWHIV do not have a risk factor for which HepA vaccination is otherwise recommended**