> **Immunization against HBV can prevent 95 percent of infections.** About 90 percent of U.S. children were fully immunized against HBV in 2013, but as of 2014, only about a quarter of adults over 19 were.
>
> – The National Academies of Sciences, Engineering, Medicine.
> *A National Strategy for the Elimination of Hepatitis B and C: Phase Two Report*[27]

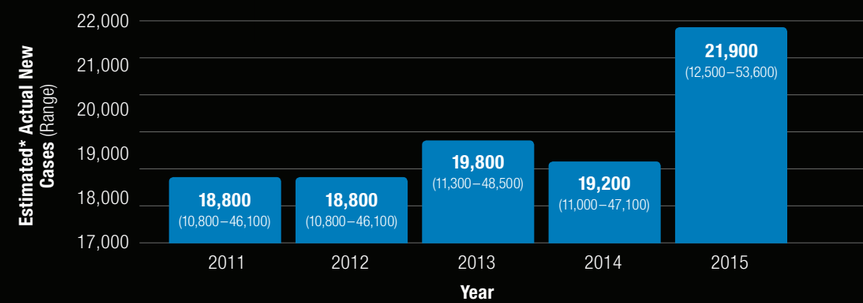
References

1. US Department of Health and Human Services. *National Viral Hepatitis Action Plan 2017–2020*. January 2017. Available at: https://www.cdc.gov/hepatitis/hhs-actionplan.htm. Accessed February 8, 2018.
2. Centers for Disease Control and Prevention. *Viral Hepatitis: Statistics and Surveillance. Disease Burden From Viral Hepatitis A, B, and C in the United States*. Available at: https://www.cdc.gov/hepatitis/statistics/index.htm. Accessed March 1, 2018.
3. Centers for Disease Control and Prevention. *Viral Hepatitis Surveillance: United States, 2015*. June 19, 2017. Available at: https://www.cdc.gov/hepatitis/statistics/2015surveillance/index.htm. Accessed February 8, 2018.
4. Centers for Disease Control and Prevention. *Viral Hepatitis and Young Persons Who Inject Prescription Opioids and Heroin*. Available at: http://www.cdc.gov/hepatitis/featuredtopics/youngpwid.htm. Accessed February 21, 2018.
5. Zibbell JE, et al. Increases in hepatitis C virus infection related to injection drug use among persons aged ≤30 years - Kentucky, Tennessee, Virginia, and West Virginia, 2006-2012. *MMWR Morb Mortal Wkly Rep*. 2015;64:453-8.
6. Harris AM, et al. Increases in acute hepatitis B virus infections – Kentucky, Tennessee, and West Virginia, 2006—2013. *MMWR Morb Mortal Wkly Rep*. 2016;65:47-50.
7. Maine Center for Disease Control and Prevention. Hepatitis. Available at: http://www.maine.gov/dhhs/mecdc/infectious-disease/epi/hepatitis/index.shtml. Accessed February 8, 2018.
8. Lawlor J. Hepatitis cases mount in wake of opioid epidemic. *Portland Press Herald*. December 11, 2017. Available at: https://www.pressherald.com/2017/12/11/maine-center-for-disease-control-prevention-reports-recent-increase-in-hepatitis-a-cases/. Accessed February 28, 2018.
9. North Carolina Health and Human Services. Hepatitis B, C on rise in N.C.; health officials encourage precaution, testing. May 30, 2017. Available at: https://www.ncdhhs.gov/news/press-releases/hepatitis-b-c-rise-nc-health-officials-encourage-precautions-testing. Accessed March 2, 2018.
10. Racho R, Moraras K. The rise in acute hepatitis B infection in the U.S. February 21, 2018. Available at: https://www.hhs.gov/hepatitis/blog/2018/02/21/the-rise-in-acute-hepatitis-b-infection-in-the-US.html. Accessed March 2, 2018.
11. Perry J. Regional rise of hepatitis B. *The Wanderer*. January 21, 2018. Available at: https://www.wanderer.com/features/regional-rise-of-hepatitis-b/. Accessed March 2, 2018.
12. National Immunization Program; Division of Viral Hepatitis, National Center for Infectious Diseases, Centers for Disease Control and Prevention. Achievements in public health: Hepatitis B vaccination–United States, 1982—2002. *MMWR Morb Mortal Wkly Rep*. 2002;51:549-52, 63.
13. Williams WW, et al. Surveillance of vaccination coverage among adult populations — United States, 2015. *MMWR Surveill Summ*. 2017;66:1-28.
14. Weiser J, et al. Low prevalence of hepatitis B vaccination among patients receiving medical care for HIV infection in the United States, 2009 to 2012. *Ann Intern Med*. 2018;168:245-54.
15. Centers for Disease Control and Prevention. Hepatitis B. In: Hamborsky J, Kroger A, Wolfe S, eds. *Epidemiology and Prevention of Vaccine-Preventable Diseases*, 13th ed. Washington, DC: Public Health Foundation; 2015:149-74.
16. Centers for Disease Control and Prevention. *HIV Surveillance Report: Diagnoses of HIV Infection in the United States and Dependent Areas, 2016*. November 2017;68. Available at: http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html. Accessed February 8, 2018.
17. Centers for Disease Control and Prevention. *Hepatitis B FAQs for the Public*. Available at: https://www.cdc.gov/hepatitis/hbv/bfaq.htm. May 23, 2016. Accessed February 8, 2018.
18. Burdick A, et al. Patterns of hepatitis B prevalence and seroconversion in hemodialysis units from three continents: The DOOPS. *Kidney Int*. 2003;63:2222-9.
19. Schillie S, et al. Prevention of hepatitis B virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. *MMWR Recomm Rep*. 2018;67(RR-1):1-31.
20. Nelson JC, et al. Compliance with multiple-dose vaccine schedules among older children, adolescents, and adults: Results from a Vaccine Safety Datalink study. *Am J Public Health*. 2009; 99(suppl 2):S389-97.
21. Harris JL, et al. Hepatitis B vaccination in six STD clinics in the United States committed to integrating viral hepatitis prevention services. *Public Health Rep*. 2007;122(suppl 2):42-7.
22. Bowman S, et al. Factors associated with hepatitis B vaccine series completion in a randomized trial for injection drug users reached through syringe exchange programs in three US cities. *BMC Public Health*. 2014;14:820.
23. Fan W, et al. Hepatitis B vaccine response in obesity: A meta-analysis. *Vaccine*. 2016;34:4836-41.
24. Douvin C, et al. Hepatitis B vaccination in diabetic patients. *Diabetes Care*. 1997;20:148-51.
25. Schillie SF, et al. Immune response of hepatitis B vaccine among persons with diabetes: A systematic review of the literature. *Diabetes Care*. 2012;35:2690-7.
26. Fabrizi F, et al. Meta-analysis: The impact of diabetes mellitus on the immunological response to hepatitis B virus vaccine in dialysis patients. *Aliment Pharmacol Ther*. 2011;33:815-21.
27. The National Academies of Sciences, Engineering, Medicine. *A National Strategy for the Elimination of Hepatitis B and C: Phase Two Report*. Buckley GJ, Strom BL, eds. Washington, DC: The National Academies of Sciences, Engineering, and Medicine; 2017. Available at: https://www.nap.edu/read/24731/chapter/1. Accessed January 30, 2018.

It's Not Too Late
to Prevent **Hepatitis B** Infection Among US Adults Through Vaccination

> … progress in preventing new hepatitis B infections has stalled…
>
> *– National Viral Hepatitis Action Plan 2017–2020*[1]

Estimated Actual New Cases of Hepatitis B Virus[2,3]
United States 2011–2015



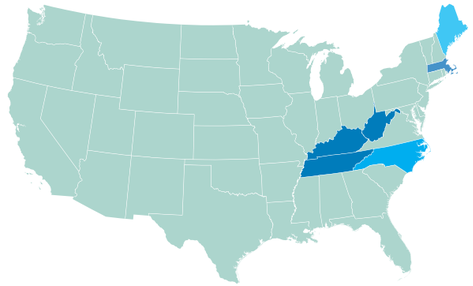
*Actual acute cases estimated to be 6.48 times the number of reported cases in any year. The 2011–2014 information is from: Centers for Disease Control and Prevention. *Viral Hepatitis: Statistics and Surveillance*.[2] The 2015 information is from: Centers for Disease Control and Prevention. *Viral Hepatitis Surveillance: United States, 2015*.[3]

> Increases in new viral hepatitis infections are being fueled by the opioid epidemic that is gripping parts of the United States.
>
> *– National Viral Hepatitis Action Plan 2017–2020*[1,4,5]

DYNAVAX
INNOVATING IMMUNOLOGY

It's Not Too Late to Prevent Hepatitis B Infection Among US Adults Through Vaccination

The opioid epidemic in the US is driving an increase in hepatitis B virus (HBV) cases, particularly in rural communities



56% increase in new HBV cases

In **North Carolina**, preliminary data show new cases of **hepatitis B increased by 56%** between 2014 and 2016, from 110 cases to 172 cases[9,10]

78% increase over annual average

In January 2018, the **Massachusetts** Department of Public Health issued an advisory about an increase in hepatitis B outbreaks in the southeastern region of the state: In 2017, there were 32 confirmed acute HBV cases, a **78% increase over the annual average**; 22 of the cases were in persons known to inject drugs and most were in adults[11]

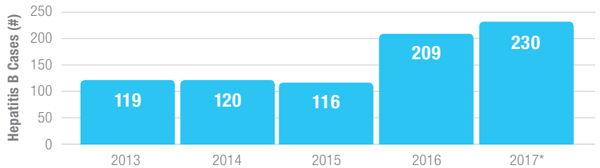
114% increase in new HBV cases

In 3 Appalachian states (**Kentucky, Tennessee, West Virginia**), 2006–2013 saw a **17% increase in prescription opioid abuse** in young adults accompanied by a **114% increase in new HBV cases** (mostly in injectable drug users)[6]

>400% increase in new HBV cases

Similarly, annual HBV cases in **Maine** increased from 8–12 per year in 2011–2015 to 53 cases in 2016, a **>400% increase**; **45% of new cases were in injectable drug users**[7]

Chronic and Acute Hepatitis B Cases in Maine 2013–2017[8]



*2017 cases through October 31, 2017.

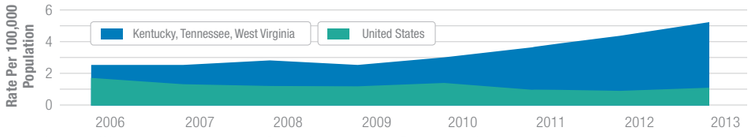
Lawlor J. Hepatitis cases mount in wake of opioid epidemic. *Portland Press Herald*. December 11, 2017.[8]

To illustrate the link between opioid use and HBV risk, consider the fact that **apart from the 3 Appalachian states, the overall rate of new HBV infections** per 100,000 persons in the US population **has actually declined slightly in recent years.**

> **The increase in incident HBV-infections has the potential to impede the nation's hepatitis B elimination strategy... [P]revention strategies, including increasing hepatitis B vaccination coverage...and implementing education campaigns that target persons who inject drugs are urgently needed."**
>
> – Harris et al; CDC and Kentucky, Tennessee, and West Virginia Departments of Health[6]

Incidence of Acute Hepatitis B Virus Infection, by Year

United States and Kentucky, Tennessee, and West Virginia, 2006–2013[6]



Adapted from Harris AM, et al. Increases in acute hepatitis B virus infections – Kentucky, Tennessee, and West Virginia, 2006—2013.[6]

In the US, universal vaccination in infants has **virtually eliminated** HBV infection in the very young, reducing its spread[3]

Nonetheless, any reduction in HBV occurrence in portions of the adult population **falls short of the 60% reduction goal** set forth in the US Department of Health and Human Services' *National Viral Hepatitis Action Plan 2017–2020*,[1] and vaccination rates in adults born before the 1990s, when national vaccination recommendations for children and adolescents were instituted,[12] remain low[13]

Adults, by Group, That Are Unvaccinated

Only 9.6% HIV-positive patients had received HBV vaccination

In a nationally representative sample of HIV-positive patients (n=18,089), only **9.6% had received HBV vaccination, despite similar modes of transmission**[14]

- 7.5% had no documented vaccination but were either already HBV-infected or had acquired immunity
- 82.9% were candidates for vaccination but had not received one

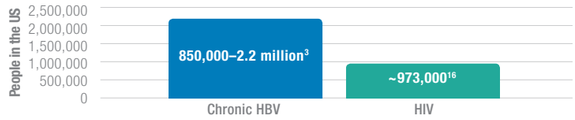
Hepatitis B remains unacceptably prevalent

~21% increase in new HBV cases vs 2014[3]

In 2015, an estimated 22,000 new cases of HBV developed in the US, an ~21% increase vs 2014[3]

- Approximately 5% of adults who develop an acute HBV infection will progress to chronic HBV[15]

As Many (or More) People in the US Are Living With Chronic HBV[3] Than Are Living With HIV[16]



25% die prematurely

of people with chronic HBV infection **die prematurely from cirrhosis or liver cancer**[15]

~3,000–4,000

persons die per year in the US from HBV-related cirrhosis[15]

50–100X more infectious than HIV

Hepatitis B is spread in most of the same ways as HIV but is **50–100 times more infectious**[17]

Hepatitis B is spread through[17,18]:

- birth (infected mother to her baby)
- sexual relations with an infected partner
- sharing of syringes and other drug paraphernalia
- sharing of personal items such as razors or toothbrushes
- direct contact with blood or open sores from an infected person
- sharing diabetes care products such as glucose monitors, insulin pens, or syringes
- dialysis treatment in facilities with suboptimal infection control practices

Once infected with hepatitis B, a person remains infected

(unless the immune system clears the virus on its own), unlike with certain types of hepatitis C, which can now be treated. There is no vaccine for hepatitis C.

- Acute hepatitis B infection can progress to chronic hepatitis B infection in which the infected person will always be a carrier capable of transmitting disease and may have a recurrence of illness

Hepatitis B vaccination coverage in adults is a challenge

Current US recommendations on hepatitis B vaccination are risk-based, not universal[19]

54% completed the standard 3-dose vaccination

Compliance

In a large managed care organization, only 54% of persons who received a first HBV vaccination dose completed the standard 3-dose vaccination[20]

~30% less compliance at STD clinics

Compliance has been lower for vaccines given in STD clinics (~30%)[21] and for injectable drug users (52.0% and 63.6% for standard and accelerated dose, respectively)[22]

Difficult-to-treat Populations

Age After age 40 years, the proportion of persons with a protective antibody response after a 3-dose vaccination regimen is approximately 90%, and after age 60 years, protective-antibody response only develops in 75%[15]

Obesity Obesity is strongly associated with nonresponse to HBV vaccination (odds ratio, 2.46 in a meta-analysis of 16 studies)[23]

Diabetes Adults with diabetes have shown slower and lower seroprotection rates after vaccination compared to their counterparts without diabetes,[24,25] particularly older persons[25] and those on dialysis[25,26]

Public Health Action Items for Preventing Hepatitis B

- ☑ **Raising awareness** about HBV and the critical importance of vaccination
- ☑ **Simplifying vaccination protocols** to improve compliance
- ☑ **Targeting high-risk populations** for vaccination
- ☑ **Improving vaccines** to promote immunity in difficult-to-treat groups

The best medicine for hepatitis B is prevention. Vaccination is prevention.