The Forgotten Trio

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Overview

- Disease presentation and vaccines for:
  - Hepatitis A
  - Human papillomavirus (HPV)
  - Meningococcal disease

Continuing education learning objectives

1. Recognize patient populations that will benefit from age-appropriate vaccination.
2. Recognize important concepts related to successful vaccine therapy and increasing immunization coverage rates.
3. Define strategies to prevent vaccine storage and handling errors.
4. Name three ways to utilize reports from within the WyIR to monitor data quality and manage vaccine inventories.
5. Recognize innovations in vaccine technology and trends and apply them in practice.
6. Describe different communication techniques that teams can use to achieve successful vaccine therapy in individuals and the community.

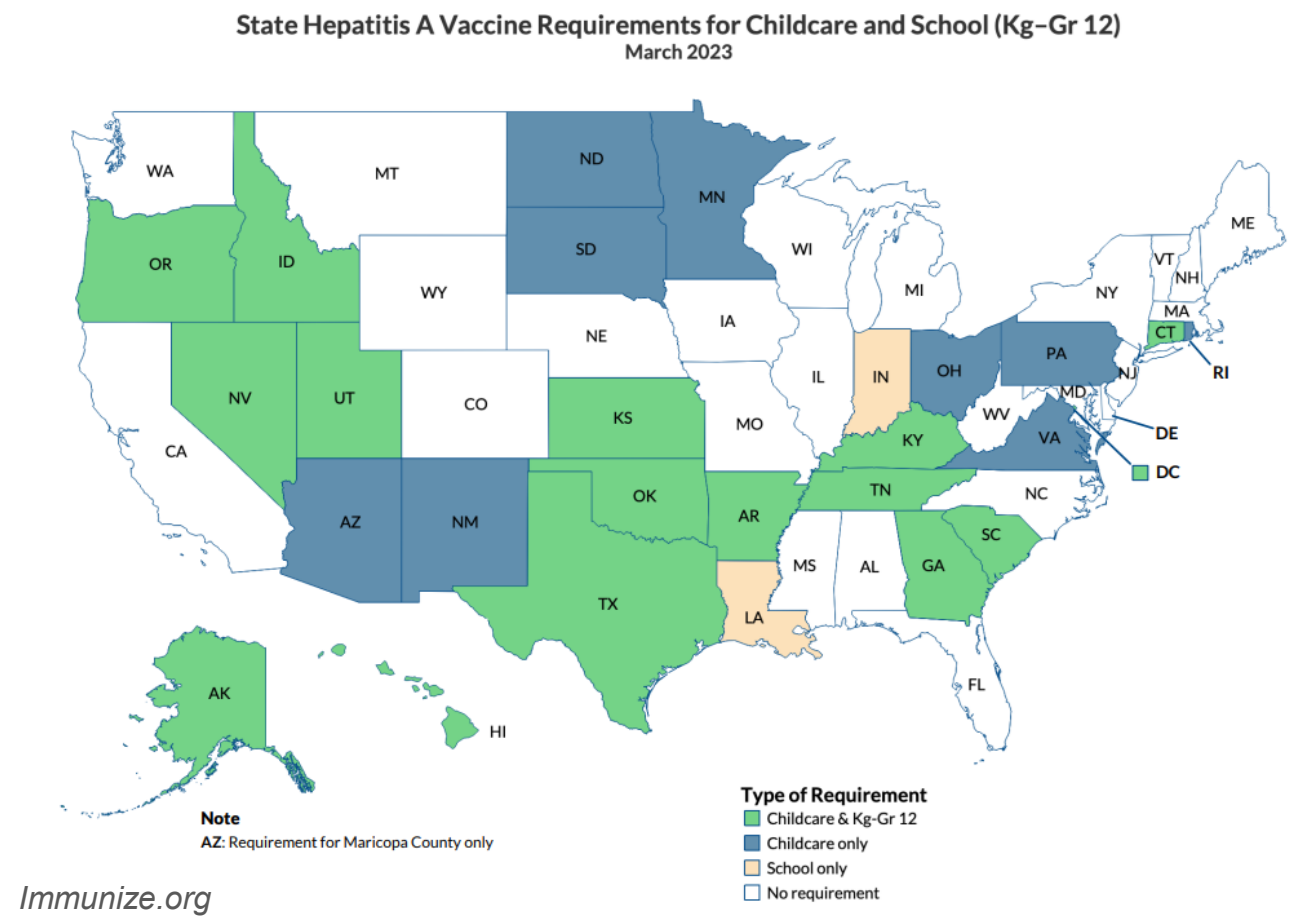
Recommended schedule vs. school mandates

- COVID-19
- Dengue Fever
- ***Haemophilus influenzae* type b (Hib)**
- Hepatitis A
- **Hepatitis B**
- Human papillomavirus (HPV)
- Influenza
- **Measles, mumps, rubella (MMR)**
- Meningococcal
- **Pneumococcal**
- **Polio**
- **Rotavirus**
- **Tetanus, diphtheria, pertussis (DTaP, Tdap, Td)**
- **Varicella**

- School mandated vaccines are not necessarily “more important” than other ACIP recommended vaccines
  - They are the *minimum* standard of immunizations a child should receive
- School mandates can be slow to adopt newer vaccines or ACIP recommendations

*__Bolded__ are required under administrative rule for children in child-care and K-12 education in Wyoming

Hepatitis A



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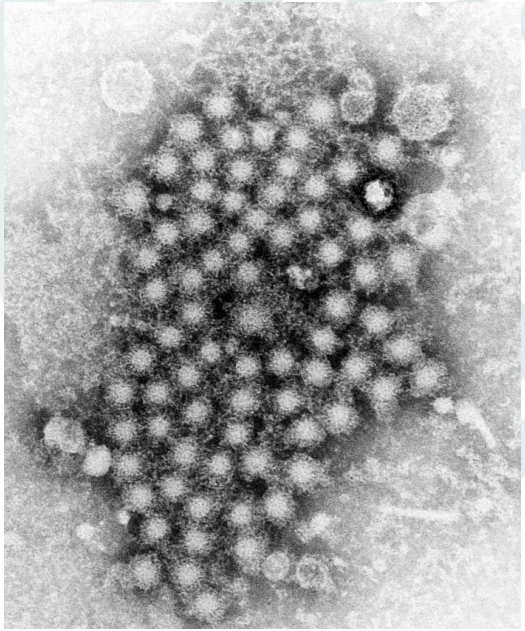
Hepatitis A

- Caused by the hepatitis A virus (HAV), an RNA picornavirus
- First isolated in 1979
- Humans are the only natural host
- Stable at low pH, moderate-to-frozen temperatures



CDC

Hepatitis A pathogenesis

- Fecal-oral transmission, typically through ingestion of contaminated food or water
- Replicates in the liver
- Virus present in blood and feces 10-12 days after infection
- Viral excretion may continue for up to 3 weeks after onset of symptoms

Hepatitis A clinical features

- Incubation period average 28 days (range 15-50 days)
- Clinical course is indistinguishable from that of other types of acute viral hepatitis
- Clinical illness usually does not last longer than 2 months
- Symptoms
  - Abrupt onset of fever, malaise, anorexia, nausea, abdominal discomfort, dark urine, and jaundice
- Likelihood of symptomatic illness is directly related to age
  - <6 years 70% of infections are asymptomatic
- Complications are rare
  - Immunologic, neurology, hematologic, pancreatic, and renal manifestations
  - Relapsing hepatitis, autoimmune hepatitis, subfulminant and fulminant hepatitis

Hepatitis A epidemiology

- Occurs throughout the world
  - Highly endemic in Central and South America, Africa, the Middle East, Asia, and the Western Pacific
- No seasonality
- Infected persons are contagious 1-2 weeks before onset of illness
- Risk factors
  - International travel, recent international adoptees from hep A endemic countries, men who have sex with men, people experiencing homelessness, persons with HIV, and people who use drugs

Hepatitis A epidemiology

- Recent outbreak in 2019
  - 18,846 U.S. cases
  - 12 in Wyoming
- 1,607 U.S. cases in 2023
  - 2 in Wyoming

Rates* of reported cases† of Hepatitis A virus infection, by age group — United States, 2006–2021

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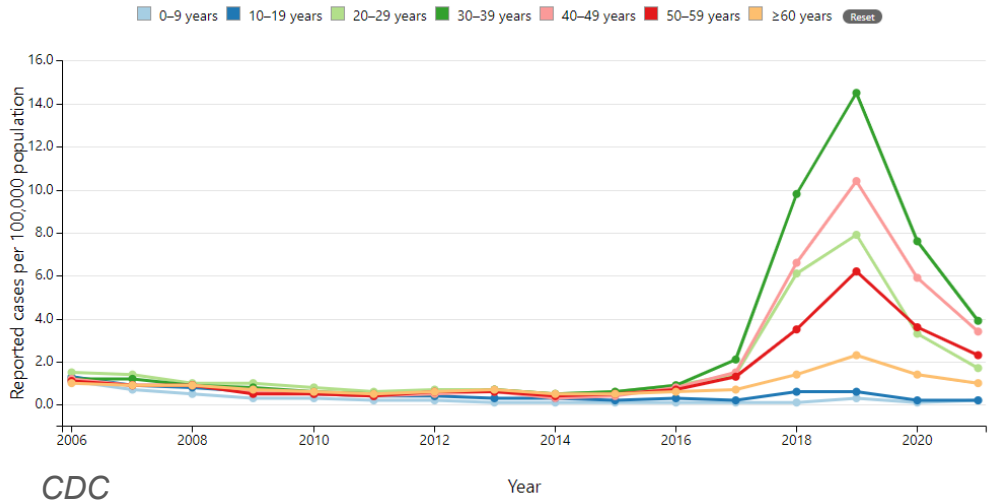


Hepatitis A vaccines

- First vaccine licensed in U.S. in 1995
- ACIP recommended universal routine vaccination of children beginning at 12 months of age in 2006
  - In 2020, ACIP recommended vaccination of all children and adolescents age 2-18 years who have not previously received hep A vaccine
- From 1996 to 2011, hep A cases decreased by over 95% largely thanks to vaccination
  - Re-emerged in widespread outbreaks beginning in 2016
    - Exception was for persons 20 years and younger, which is due to routine vaccination

Hepatitis A vaccines

- Administered by intramuscular (IM) injection
- Inactivated
- Single antigen vaccines
  - Available in pediatric (12 months-18 years) and adult formulations (19+ years)
  - Havrix (GSK)
    - Licensed in 1995
  - Vaqta (Merck)
    - Licensed in 1996
- Combination vaccine
  - Contains hep A and hep B
  - Twinrix (GSK)
    - Licensed in 2001
    - Approved for 18 years and older

Hepatitis A vaccination schedule

- All children age 12-23 months and all children and adolescents age 2-18 years who have not previously received hep A vaccine
  - 2-dose series
  - Minimum interval of 6 months between doses
- Adults age 19 years or older with risk factors or who desire immunity
  - Single antigen vaccine
    - 2-dose series with minimum interval of 6 months between doses
  - Twinrix
    - 3-dose series given at 0, 1, 6 month intervals
    - 3-dose accelerated series at 0, 7, 21-30 days, and booster 12 months after dose 1

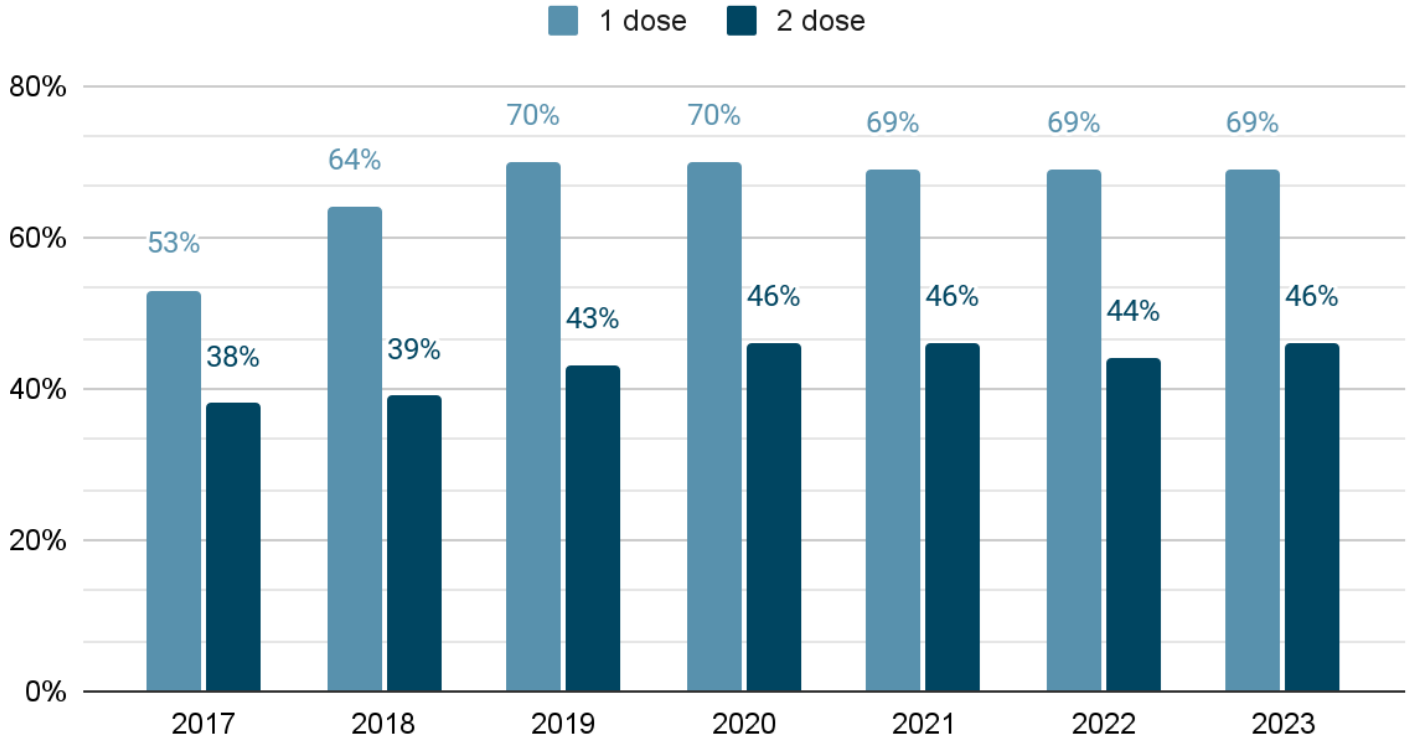
Hepatitis A vaccination schedule

- Children 6-11 months who are traveling outside of the U.S. when protection against hep A is recommended
  - 1 dose of vaccine
  - These children should still get 2 additional doses at the recommended ages

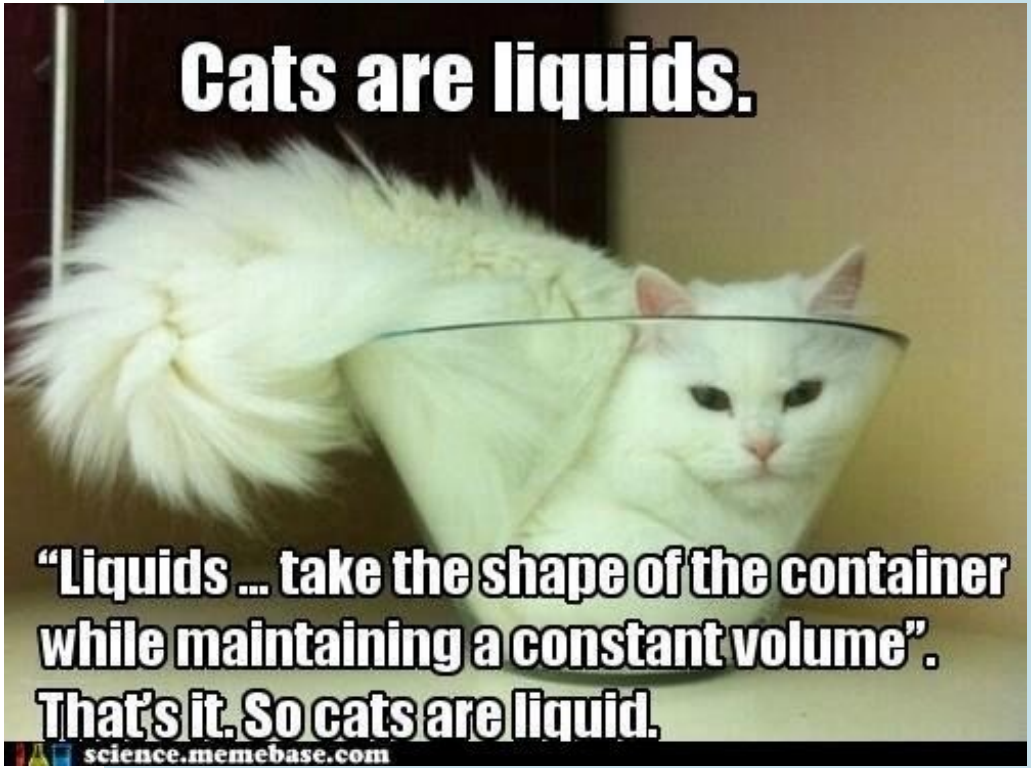
Hepatitis A vaccination coverage

- Of the Forgotten Trio, Wyoming doses the best with hep A vaccine
- However…
  - Second dose coverage lags behind and series are often not completed

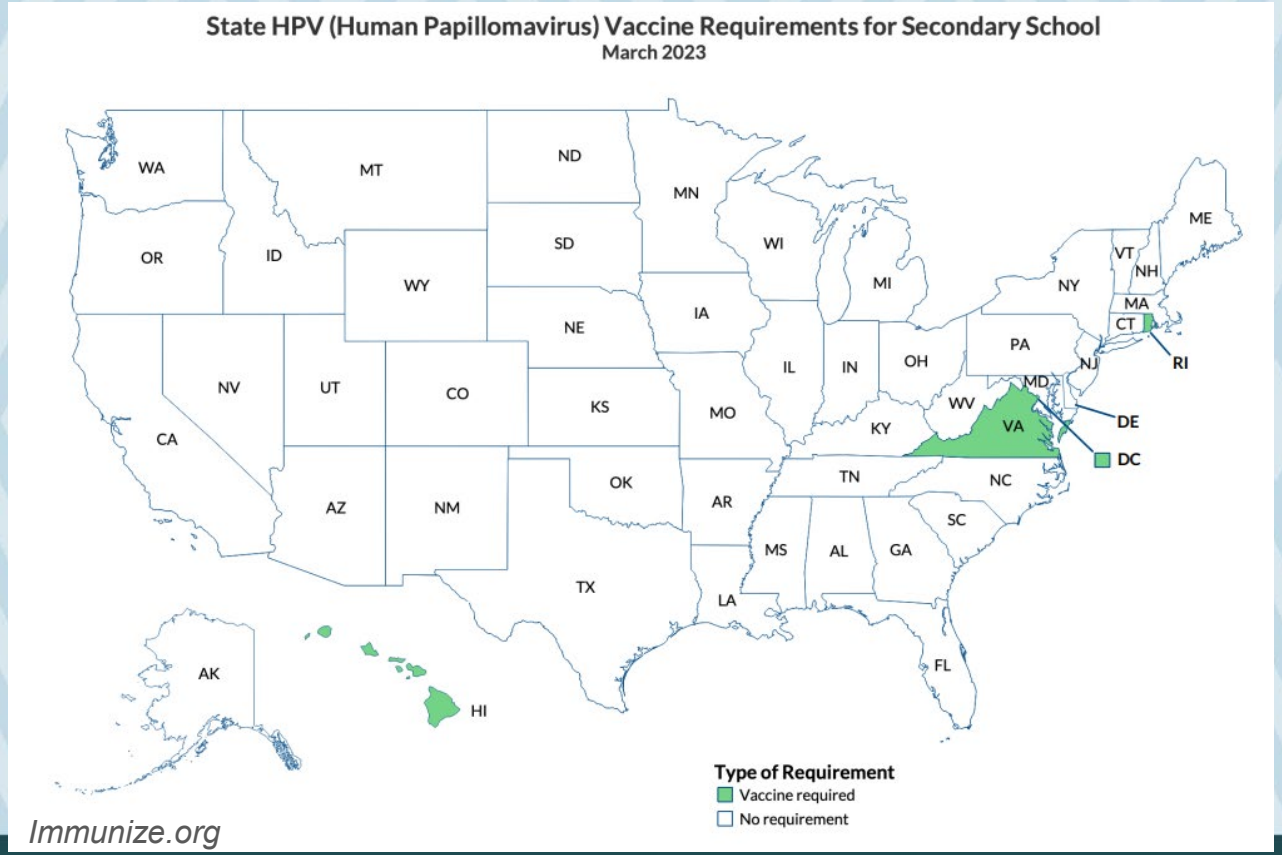
Hepatitis A 19-35 Months - WyIR



Questions?


Cats are liquids.
"Liquids ... take the shape of the container while maintaining a constant volume".
That's it. So cats are liquid.
science.memebase.com

Human papillomavirus (HPV)



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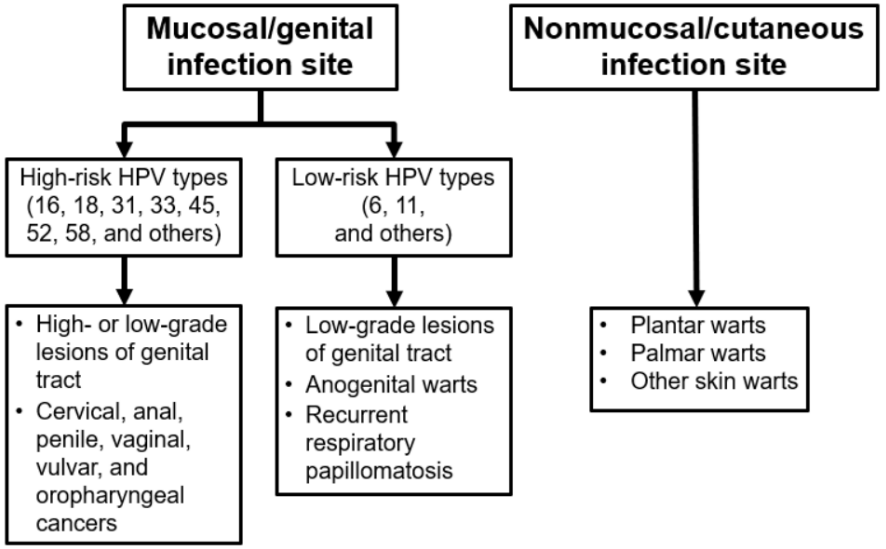
Human papillomavirus (HPV)

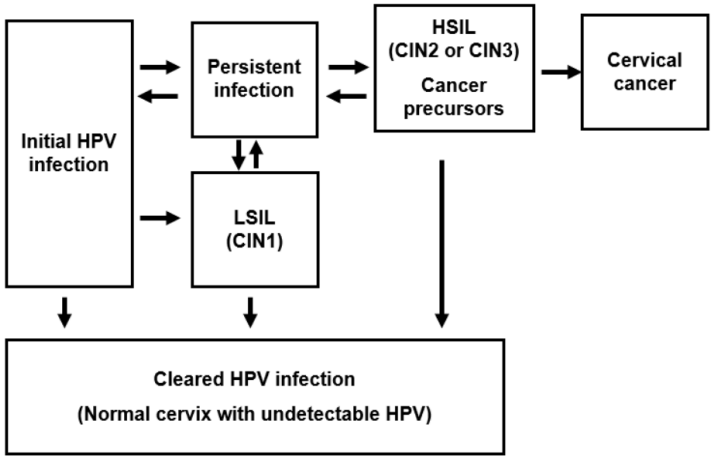
- Small DNA virus
- More than 200 types have been identified
- Most HPV types infect the cutaneous epithelium and can cause common skin warts
- 40 types infect the mucosal epithelium



CDC

HPV pathogenesis

- Infection occurs at the basal epithelium
- Most infections resolve spontaneously within a year or two
- Small proportion of infected persons become persistently infected
  - The most important risk factor of the development of cervical cancer
    - Low-grade squamous intraepithelial lesions (LSIL), or CIN1, often regress
    - High-grade squamous intraepithelial lesions (HSIL), or CIN2/CIN3, are considered cancer precursors
- Pathogenesis of other types of HPV-related cancers may follow a similar course
- Infection with one type of HPV does not prevent infection with another type



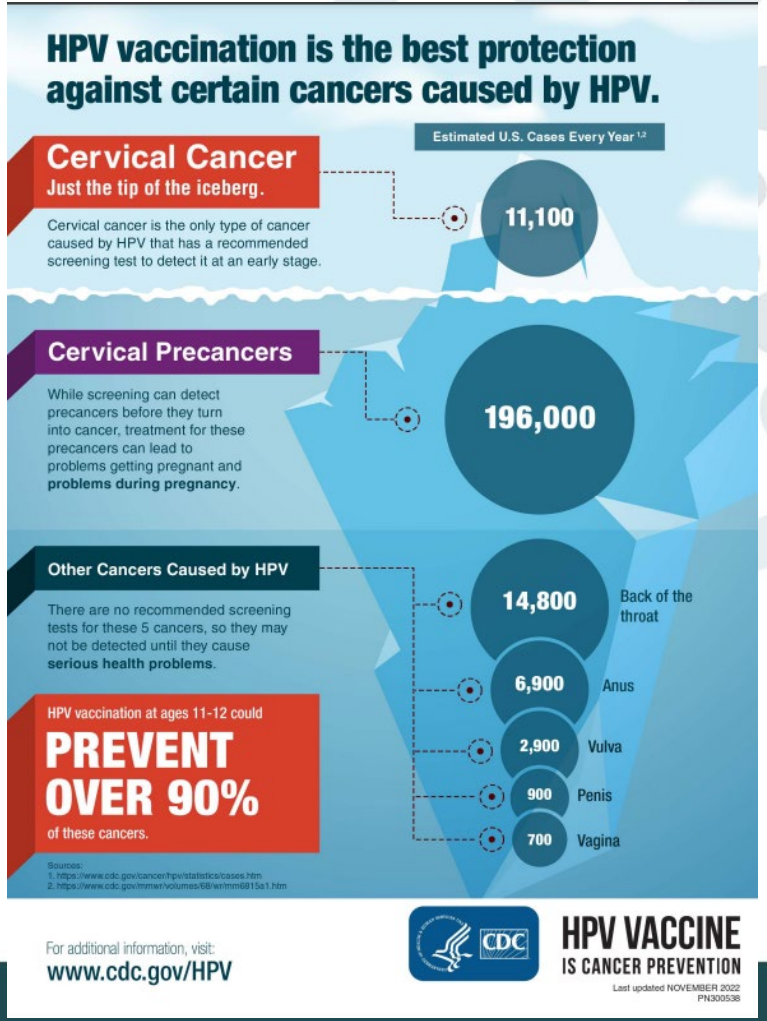
CDC

HPV clinical features

- Most infections are asymptomatic and result in no clinical disease
- Clinical manifestations include
  - Anogenital warts
  - Recurrent respiratory papillomatosis
  - Cancer precursors
  - Cancers
    - Cervical, anal, vaginal, vulvar, penile, and oropharyngeal

HPV epidemiology

- Extremely common throughout the world
- Humans are the only natural reservoir
- Transmitted through skin-to-skin contact
- Autoinoculation from one body site to another can occur
- Estimated 79 million persons infected in the U.S.
  - 14 million new infections per year
    - Half occurring in persons age 15-24 years
- On average, about 44,000 HPV-associated cancers are reported annually in the U.S.
  - 11,100 cervical cancer cases
    - 196,000 cervical precancers
  - 14,800 oropharyngeal cancer cases

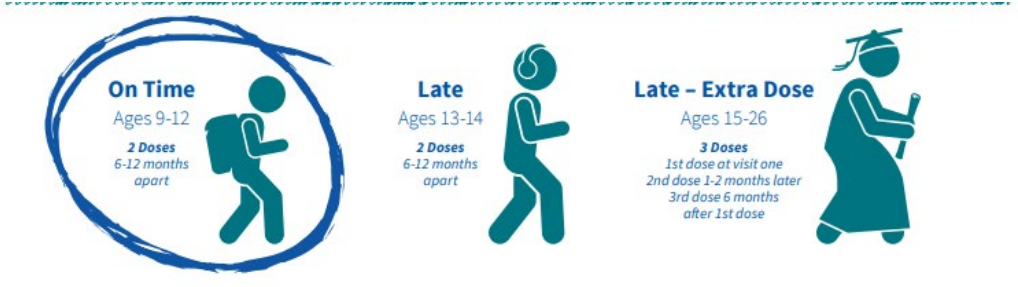


HPV vaccine

- First vaccine licensed in U.S. in 2006
- Inactivated
- Administered by IM injection
- Gardasil-9 (Merck)
  - Prevents HPV types 6, 11, 16, 18, 31, 33, 45, 52, 58
  - Licensed for ages 9-45 years
- Two other vaccines are licensed, but not currently distributed in the U.S.
  - No revaccination is recommended for those who received earlier versions of Gardasil or other licensed HPV vaccines

HPV vaccination schedule

- Routine vaccination with two-dose series recommended for everyone at age 11-12 years
  - Minimum valid age is 9 years
- Catch-up vaccination recommended for all persons not adequately vaccinated through age 26 years
- Catch-up vaccination not recommend for all adults over 26 years
  - Shared clinical decision making is recommended for some adults age 27-45 years
- Not licensed or recommended in adults over age 45



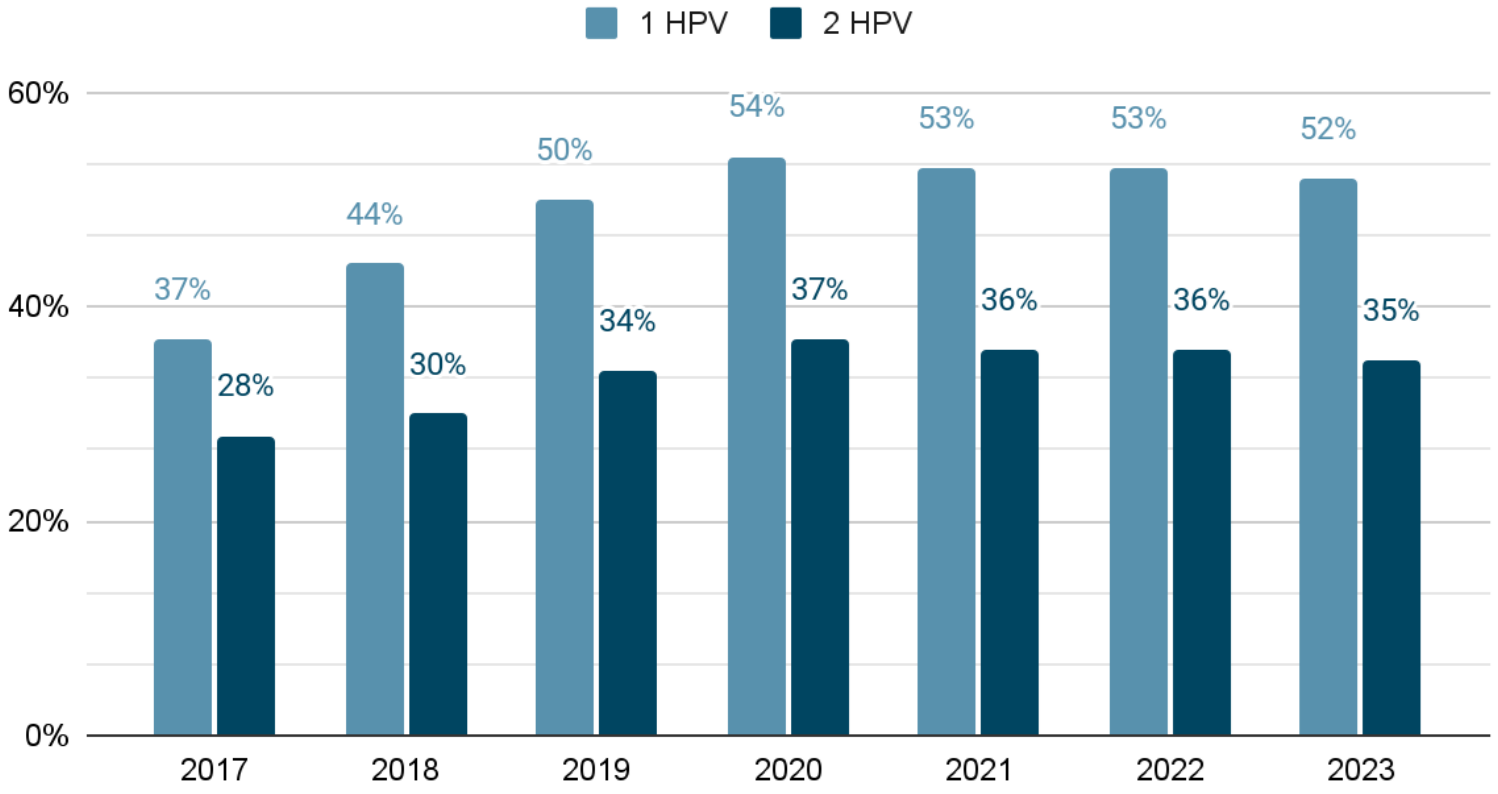
HPV vaccination schedule

- 2-dose series
  - For immunocompetent persons who receive first valid dose before 15th birthday
  - 0, 6-12 month schedule
  - Minimum interval for 5 months
- 3-dose series
  - For persons who receive first valid dose on or after 15th birthday
  - For persons with primary or secondary immunocompromising conditions
  - 0, 1-2, 6 month schedule
- Series does not need to be restarted if schedule is interrupted or delayed
- Pre-vaccination assessments not recommended, i.e. testing for HPV infection
- No therapeutic effect on existing HPV infection, anogenital warts, or HPV-related lesions

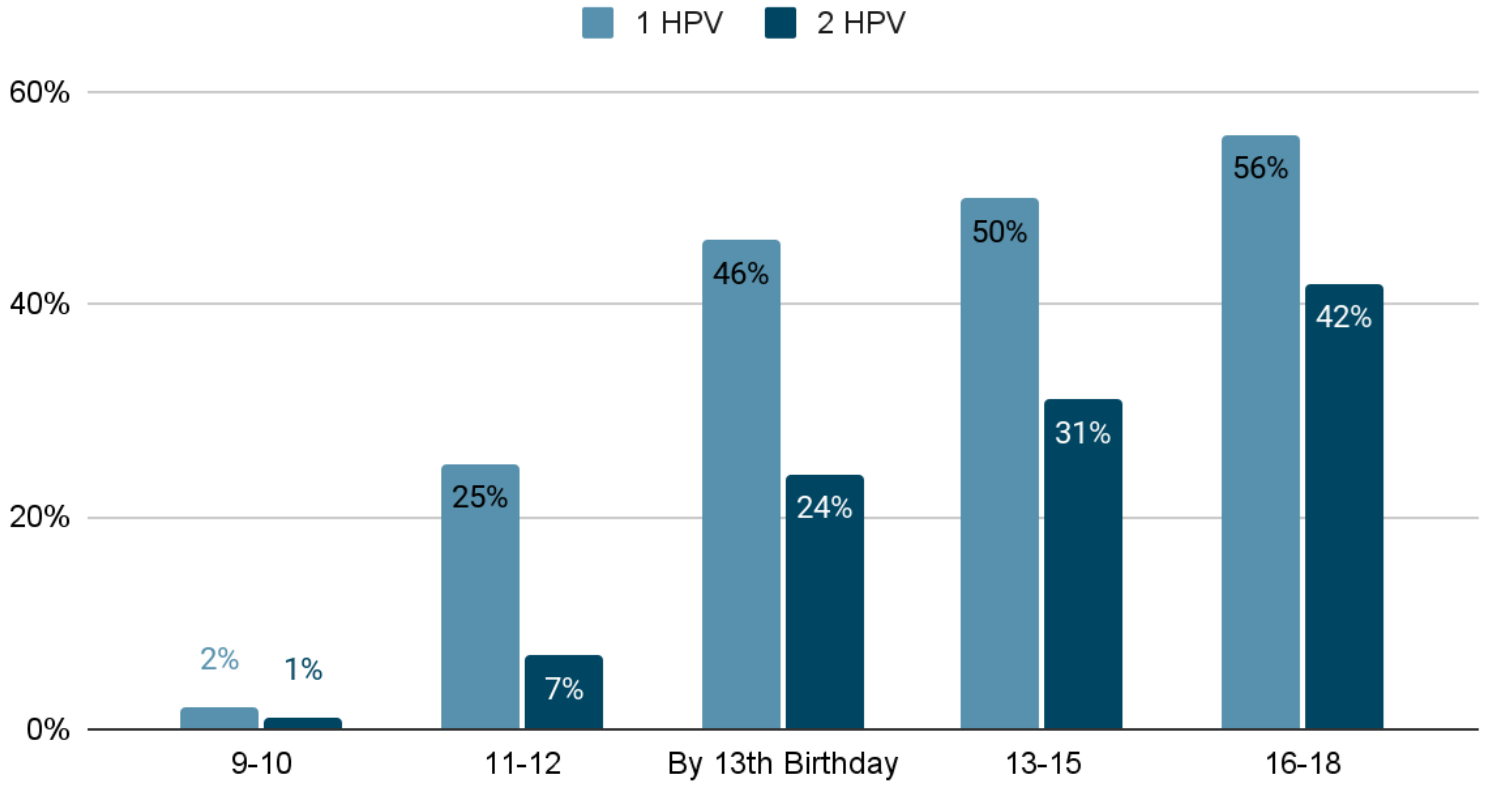
HPV vaccination impact

- Within 10 years following vaccine introduction, prevalence of HPV types 6, 11, 16, and 18 has decreased
  - 86% among females age 14-19 years
  - 71% among females age 20-24 years
- From 2008-2015, both CIN2 or worse rates have declined among women age 18-24, consistent with population-level impact of HPV vaccination
- Study published in January 2024 from Scotland found no cases of invasive cervical cancer in women vaccinated against HPV at ages 12 and 13 since the vaccination program started in 2008

HPV 13-17 Years - WyIR

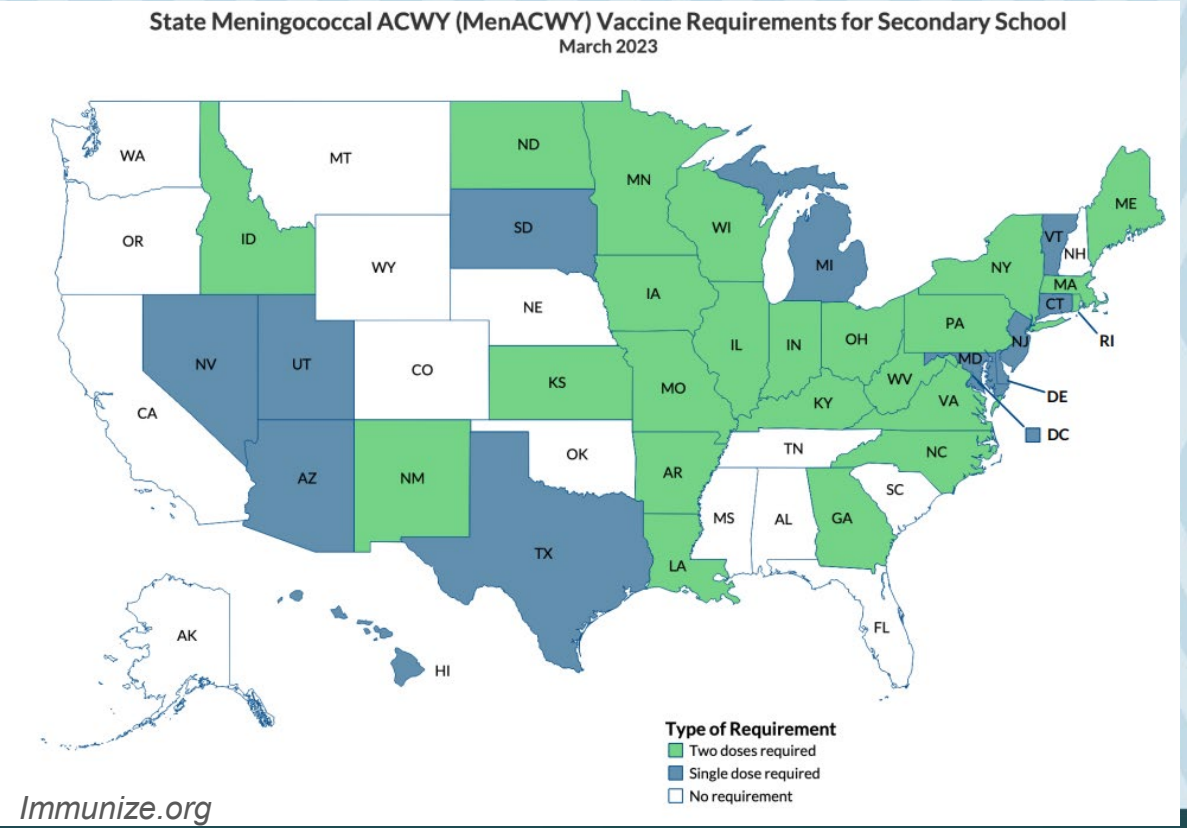


2023 HPV Coverage - WyIR



Questions?

Meningococcal



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Neisseria meningitidis

- Aerobic, gram-negative bacterium
- Polysaccharide capsule important for pathogenicity
  - 12 distinct capsules have been described and determine serogroup labeling
    - Almost all invasive disease caused by serogroups A, B, C, W-135, X, and Y
- Humans are only natural reservoir
  - 10% of adolescents and adults are asymptomatic nasopharyngeal carriers
- Transmission
  - Respiratory droplets or direct contact with respiratory secretions

CDC

Meningococcal pathogenesis

- Bacteria attach to and multiply in nasopharynx and oropharynx
- In <1% of persons, bacteria penetrate the mucosal cells and enter the bloodstream
  - Bacteria then spread through the blood to cause systemic disease and cross the blood-brain barrier into the cerebrospinal fluid (CSF) to cause meningitis

Meningococcal clinical features

- Incubation period 2-4 days (range 1-10 days)
- Presentations
  - Meningitis
    - Most common presentation of invasive disease, ~50% of U.S. cases
    - Sudden onset of fever, headache, stiff neck, nausea, vomiting, photophobia, altered mental status
    - Meningococci can be isolated from blood in up to 75% of persons with meningitis
  - Meningococcal septicemia (meningococcemia)
    - 30% of cases
    - Abrupt onset of fever, chills, cold hands and feet, severe aches or pain, vomiting, diarrhea, petechial or purpuric rash
    - Often associated with hypotension, shock, acute adrenal hemorrhage, and multi-organ failure

Meningococcal clinical features

- Purpuric rash

Meningococcal clinical features

- Presentations (continued)
  - Bacteremic pneumonia
    - 15% of cases
    - Most common presentation in adults over 65 years of age
  - Occasional non-invasive infections

Meningococcal clinical features

- Overall case-fatality ratio is 10-15%
- As many as 20% of survivors have permanent sequelae
  - Hearing loss, neurologic damage, loss of limb(s)
- In the U.S., the incidence is highest in
  - <4 years of age
  - 17-21 years of age
  - >85 years of age

Meningococcal epidemiology

- Communicability is generally limited
- Occurs worldwide
  - Geography impacts serology groups
- Incidence is highest in late winter and early spring
- Serogroups B and C responsible for majority of case in U.S.
  - 60% of cases among those <24 years of age are caused by serogroup B
- Outbreaks account for 5% of reported cases in U.S.
- In 2023, 384 U.S. cases
  - 168 cases were ACWY, 28 were B, 26 other serogroups, 162 unknown serogroup
- In Wyoming
  - 1 in 2024 (B), 1 in 2022 (B), 1 in 2021, 1 in 2020 (ACWY)

Meningococcal vaccines

- Inactivated
- Administered by IM injection
- Two types
  - Quadrivalent meningococcal conjugate vaccines
    - Serogroups A, C, W, and Y
  - Serogroup B vaccines

Quadrivalent meningococcal conjugate vaccines

- MenACWY-CRM / Menveo (GSK)
  - Licensed in 2010
  - Approved for ages 2 months through 55 years
- MenACWY-TT / MenQuadfi (Sanofi)
  - Licensed in 2020
  - Approved for 2 years and older
- Per ACIP recommendations, either of these vaccines can be used to vaccinate people 56 years or older who are recommended to receive quadrivalent meningococcal vaccine because of increased risk for meningococcal disease
- Waning immunity in 3-5 years following a single dose

MenACWY vaccination schedule

- Routine vaccination
  - 1 dose at 11-12 years
  - Booster dose at 16 years
  - Healthy persons who receive first dose at or after age 16 years do not need a booster dose unless they become at increased risk for meningococcal disease
  - Routine vaccination of healthy persons who are not at increased risk is not recommended after 21 years old
- Vaccination for those at increased risk for meningococcal disease
  - Varies by risk group
  - See footnotes in ACIP Recommended Immunization Schedule

Serogroup B meningococcal vaccines

- MenB-FHbp / Trumenba (Pfizer)
  - Licensed in 2014
  - Approved for ages 10-25 years
- MenB-4C / Bexsero (GSK)
  - Licensed in 2015
  - Approved for ages 10-25 years

Serogroup B meningococcal vaccination schedule

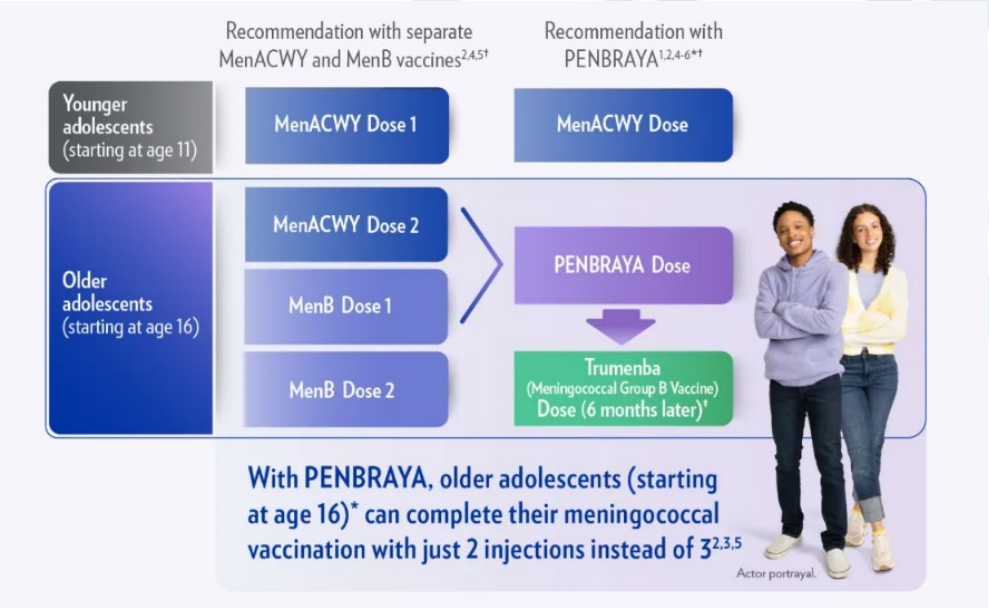
- Recommended for persons age 10 years and older who are at increased risk of MenB disease
  - See footnote in ACIP Recommended Immunization Schedule
  - 2-dose series of Bexsero at 0 and 1 month, or
  - 3-dose series of Trumenba at 0, 1-2, and 6 months
  - Booster dose:
    - See footnotes in ACIP Recommended Immunization Schedule
- Shared clinical decision making for health adolescents 16-23 years of age for short term protection
  - Preferred age for vaccination is 16-18 years
  - 2-dose series of Bexsero at 0 and 1 month, or
  - 2-dose series of Trumenba at 0 and 6 months

Serogroup B meningococcal vaccines

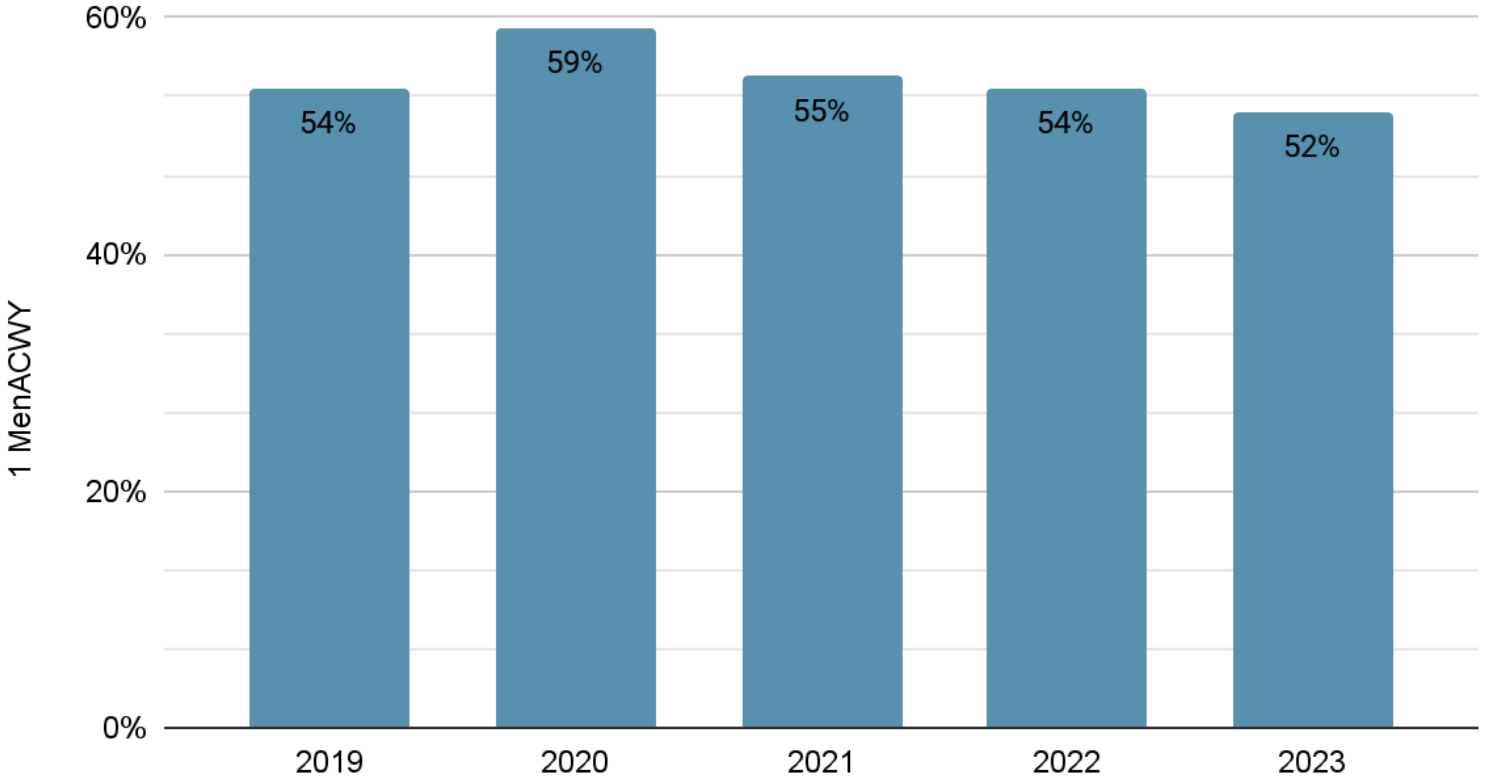
- Trumenba and Bexsero are not interchangeable
  - The same MenB vaccine must be used for all doses of the series
  - If doses of both brands have been administered, ensure the patient receives a complete series of either brand and “ignore” any doses of the other brand
    - The next dose of the selected brand should be given no sooner than the recommended interval after the previous dose of the same brand AND at least 4 weeks after the last (or only) doses of the other brand

Pentavalent meningococcal vaccine

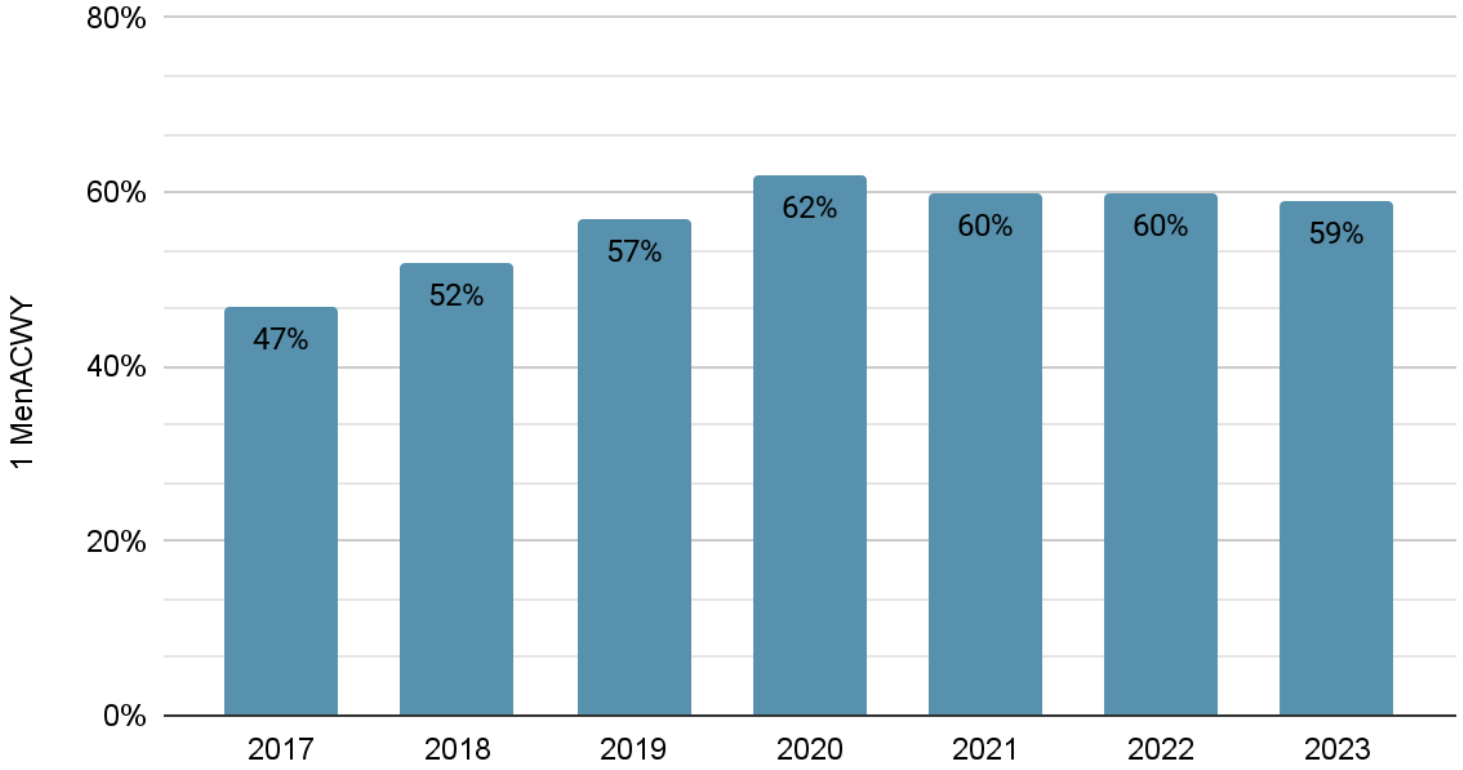
- MenACWY-TT/MenB-FHbp
  - Penbraya (Pfizer)
  - Licensed in 2023
  - Approved for ages 10-25 years
- Penbraya may be administered to persons aged 10 years old older when both a MenACWY and MenB vaccine are indicated at the same visit



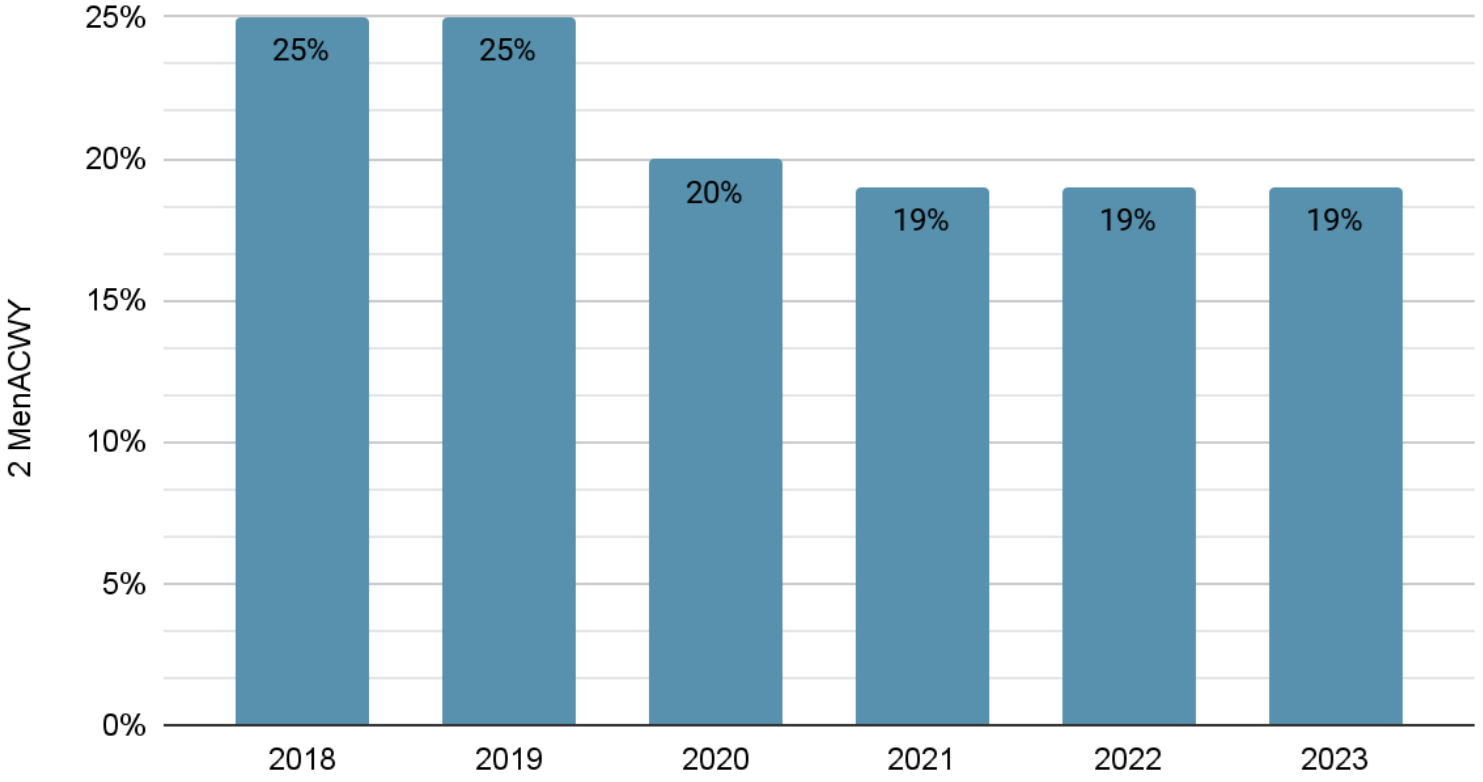
1-dose MenACWY 13 Year Olds - WyIR



1-dose MenACWY 13-17 Years - WyIR



2-doses MenACWY 16-18 Years - WyIR



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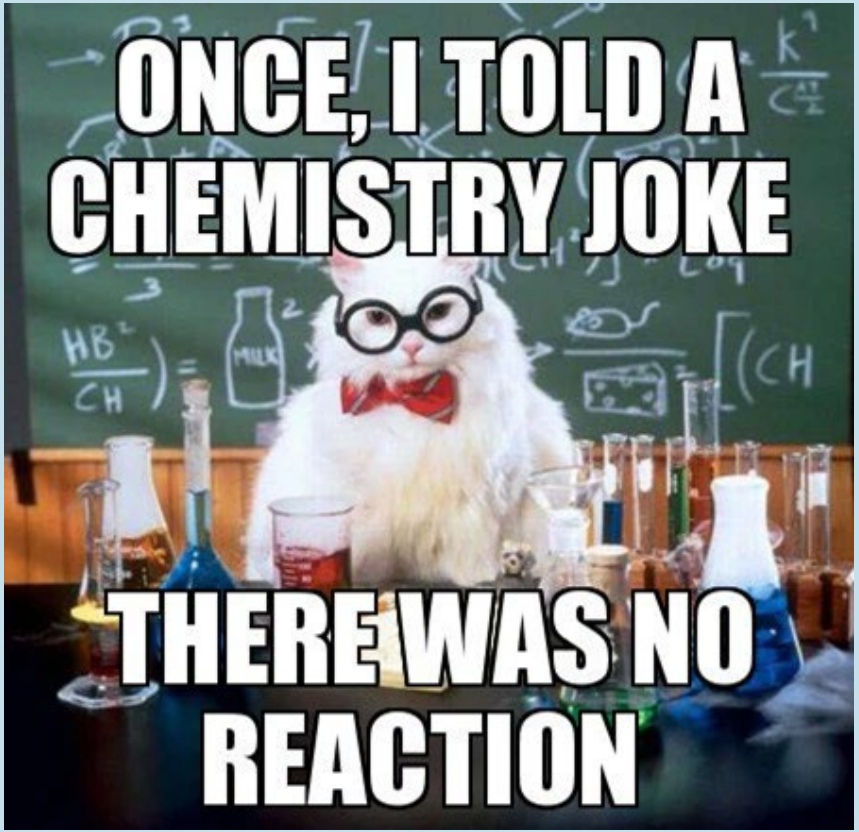

Best Practices

Strong recommendation

- A strong recommendation by a healthcare provider is the number one reason parents decide to vaccinate
  - A parent who receives a recommendation from their child's provider is 4 to 5 times more likely to get the HPV vaccine for their child
- Presumptive announcement recommendation
  - "Your child needs HPV, Tdap, and meningococcal shots today"
    - Contrasted to participatory approach
      - "Have you thought about the HPV shot for your child?," or
      - "Are we doing shots today?"
    - It is not recommended to distinguish vaccines not required for school as "optional"

Facilitating return for vaccination

- Scheduling the next appointment before parent/patient leaves the office
- Reminder recall systems
- Reminder systems for providers and staff

Other best practices

- Standing orders
- Vaccinate at every visit
- Utilizing forecasting
- Maintain a culture of immunization in the clinic

Thank you!

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