Overview of Meningococcal Disease, Available Meningococcal Vaccines and Recommendations from the Advisory Committee on Immunization Practices (ACIP) on Meningococcal Groups ACWY and B Vaccines

Maine Immunization Providers

Jim Palazzo, PharmD
Medical Science Liaison
GSK Vaccines Clinical and Medical Affairs

April 27, 2022

This presentation on an overview of meningococcal disease, available meningococcal vaccines and recommendations from the Advisory Committee on Immunization Practices (ACIP) on meningococcal groups ACWY and B vaccines was created at the request of Amanda Luciano.

It may contain off-label or pre-approval information. This is not a sales, marketing, or promotional presentation.

IMD is an Acute, Serious Illness that can be Easily Misdiagnosed and Requires Urgent Medical Attention[1,2]

Easily misdiagnosed

Rapid disease course

Can progress to **death** within **24–48 hrs**[1,2]

Acute serious illness

High mortality:[1]
Without treatment: **>50%**
With treatment: **~5–10%**

Up to 20% of survivors of IMD (all serogroups) may have sequelae

Organism and Transmission[3,4]:

Neisseria meningitidis

- Nasopharyngeal carriage is common
- Bacteria spread through close contact/ exchange of respiratory secretions

IMD, invasive meningococcal disease

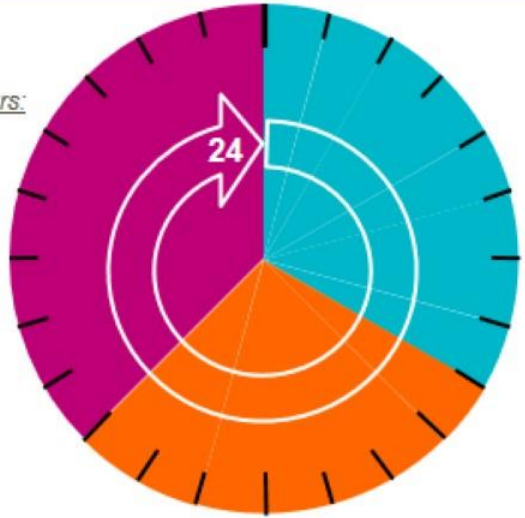
1. Thompson MJ *et al. Lancet* 2006;367:397–403; 2. WHO, 2015. Meningococcal meningitis fact sheet No.141. http://www.who.int/mediacentre/factsheets/fs141/en/# (accessed May 2017); 3. Yazdankhah SP, et al. J Med Microbiol. 2004;53(Pt 9):821-832. 4. National Foundation for Infectious Diseases. The changing epidemiology of meningococcal disease among U.S. children, adolescents and young adults.Schaffner W, Harrison LH, Kaplan SL, et al, eds. Bethesda, MD, 2004.

Invasive Meningococcal Disease: Progresses Rapidly and Can Be Fatal

~16–24 hours[a1,2]

May progress from non-specific symptoms to death within 24 hours:

- Unconsciousness
- Confusion/Delirium
- Seizure[b]
- Septic shock
- Multisystem failure
- Death



~0–8 hours[1]

Early signs and symptoms:
Non-specific and flu-like:

- Irritability
- Loss of appetite
- Fever
- Nausea/vomiting
- Sore throat, coryza
- General aches (Older children/adolescents)
- Leg pain (Infants/young children)
- Drowsiness
- Floppy muscle tone (Infants <1 year of age)

~9–15 hours[1]

Classic meningitis and septicemia symptoms:

- Cold hands/feet
- Hemorrhagic rash (May present as petechiae or purpura fulminans)
- Severe headache
- Headache, fever, & stiff neck (Infants <1 year of age: Bulging fontanelle)
- Neck stiffness
- Photophobia

[a]Hours expressed as median time of first consultation with family doctor for patients 15-16 years of age.
[b]Seizure was noted at a median of 26 hours.

1. Thompson MJ, et al. *Lancet*. 2006;367:397-403; 2. Brandtzaeg P. In: Frosch M, Martin C, Maiden J, eds. *Handbook of Meningococcal Disease: Infection Biology, Vaccination, Clinical Management*. Weinheim, Germany: Wiley-VCH Verlag GmbH & Co. KGaA; 2006:427-479

IMD Can Develop Rapidly, Outpacing Development of Natural Immune Responses

Innate immune responses are non-specific and can take several days to mount a defense, leaving individuals without adequate pre-existing circulating antibodies and vulnerable to severe outcomes[1]

The bacteria gain access to the bloodstream within hours and the **incubation period can be as short as 2 (average 4) days**[1,2]

Memory cell response after stimulation occurs no sooner than **2–7 days** after antigen exposure[1,3]

Generation of **antibody responses** to new pathogens takes **4–5 days**[3,4]

IMD, invasive meningococcal disease

1. Pichichero ME. *Pediatrics* 2009;124:1633–1641; 2. World Health Organization (WHO), 2018. Meningococcal meningitis. Fact sheet. https://www.who.int/news-room/fact-sheets/detail/meningococcal-meningitis; 3. Blanchard Rohner G *et al. J Immunol* 2008;180:2165–2173; 4. Janeway CA Jr *et al. Immunobiology: The Immune System in Health and Disease*. 5th edn. New York, NY: Garland Science, 2001. The course of the adaptive response to infection. https://www.ncbi.nlm.nih.gov/books/NBK27125/ (URLs accessed March 2021)

Carriage and Risk Factors

Asymptomatic Carriage

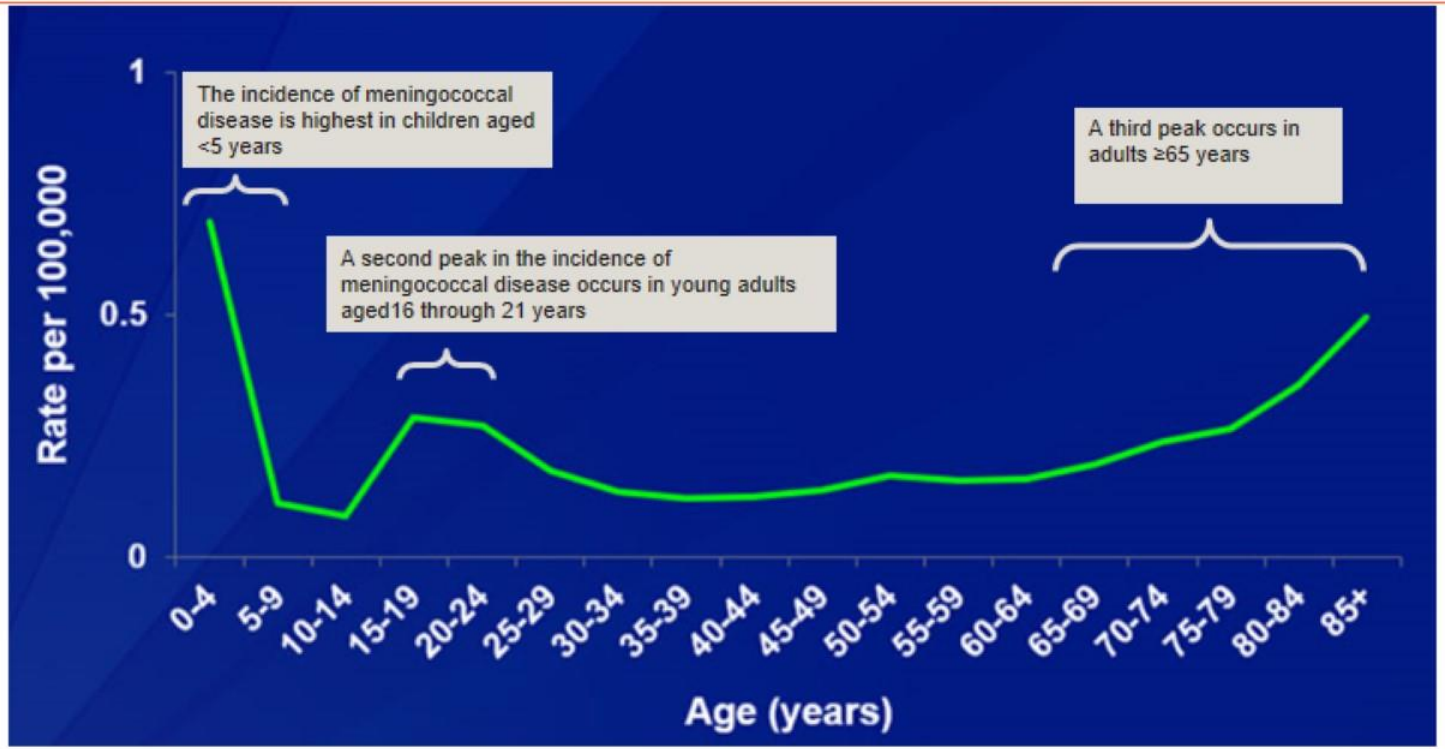
- Prevalence: 5% to 10% in adolescents and young adults[1]
- Incidence of carriage peaks in adolescence and young adulthood[1]
- Invasive disease is an infrequent consequence of nasopharyngeal carriage[1]

Risk Factors

- Impaired immune system[2]
- Social behaviors in adolescents and young adults, such as[1,3-6]:
  - Kissing
  - Coughing
  - Spending time in close quarters
  - Sharing food, drinks, and utensils
- Infancy[7]
- Other factors, such as[3,4]:
  - Smoking and second-hand smoke
  - Respiratory tract infection
  - Traveling to endemic areas

References: 1. McNamara LA, Blain A. Meningococcal Disease. In: Roush SW, Baldy LM, Hall MAK, eds. *Manual for the Surveillance of Vaccine-Preventable Diseases*. National Center for Immunization and Respiratory Diseases. https://www.cdc.gov/vaccines/pubs/surv-manual/chpt08-mening.html. Reviewed December 27, 2019. Accessed March 12, 2020. **2.** Cohn AC, MacNeil JR, Clark TA, et al. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR*. 2013;62(2):1-28. **3.** Meningococcal disease. In: Hamborsky J, Kroger A, Wolfe C, eds. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. 13th ed. Washington, DC: Public Health Foundation; 2015:231-245. www.cdc.gov/vaccines/pubs/pinkbook/mening.html. Accessed January 1, 2020. **4.** Cohn AC, MacNeil JR, Harrison LH, et al. Changes in *Neisseria meningitidis* disease epidemiology in the United States, 1998-2007: implications for prevention of meningococcal disease. *Clin Infect Dis*. 2010;50(2):184-191. **5.** Centers for Disease Control and Prevention. Causes and spread to others. https://www.cdc.gov/meningococcal/about/causes-transmission.html. Reviewed May 31, 2019. Accessed January 1, 2020. **6.** Meningitis. Mayo Clinic website. www.mayoclinic.org/diseases-conditions/meningitis/symptoms-causes/syc-20350508. Updated January 8, 2019. Accessed January 1, 2020. **7.** Rosenstein NE, Perkins BA, Stephens DS, Popovic T, Hughes JM. Meningococcal disease. *N Engl J Med*. 2001;344(18):1378-1388.

Annual Estimated Incidence of Meningococcal Disease by Age Group – United States, 2009-2018

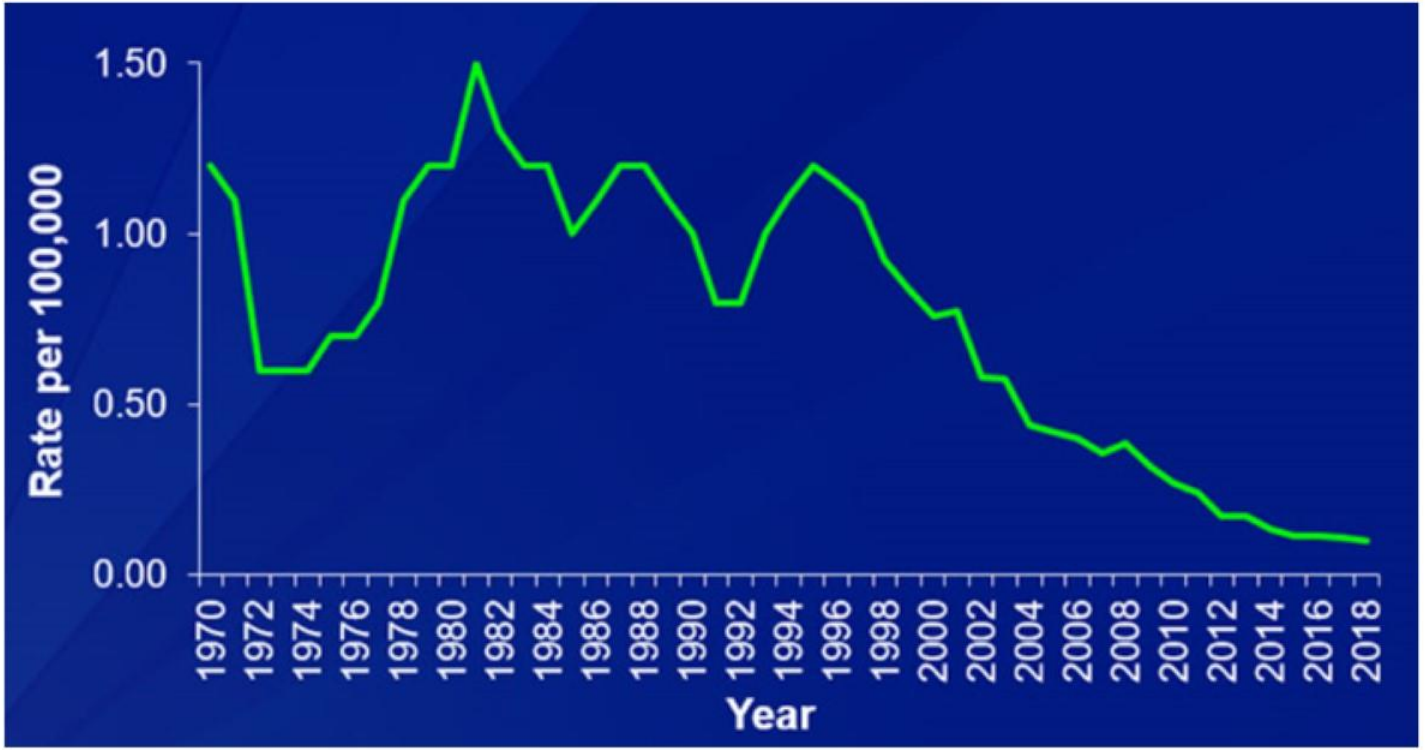


Source: CDC. National Notifiable Diseases Surveillance System

Adapted from CDC. Available at: https://www.cdc.gov/meningococcal/images/meningococcal-graph.jpg. Accessed October 16, 2020..

Historical Cases of Meningococcal Disease

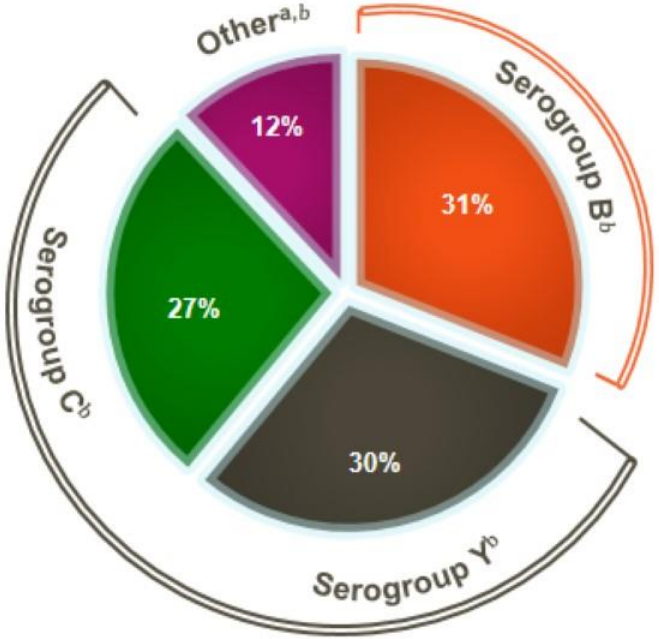
United States, 1970–2018



Source: CDC. National Notifiable Diseases Surveillance System

Available at: https://www.cdc.gov/meningococcal/images/meningococcal-disease-incidence.jpg. Accessed October 16, 2020.

Serogroup Distribution of IMD Cases in the US (1 of 2) (2007-2016)

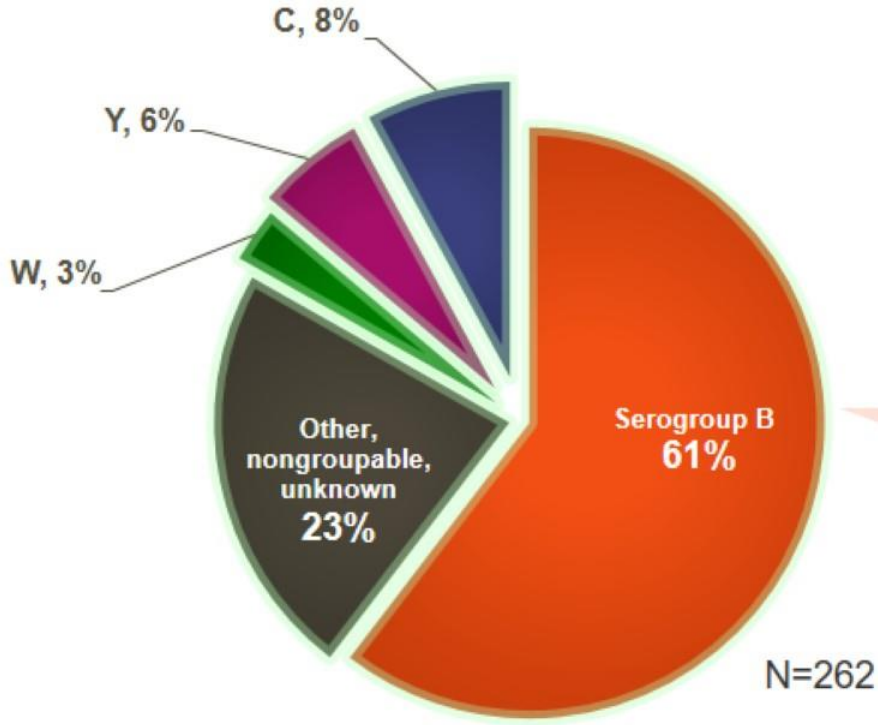


[a]Includes serogroup W and serogroups unable to be identified.

[b]In patients aged <1 to ≥65 years from 2007 to 2016; N=731.

Adapted from Centers for Disease Control and Prevention. *Active Bacterial Core surveillance (ABCs). Neisseria meningitidis*. Available at: http://www.cdc.gov/abcs/reports-findings/surv-reports.html. Accessed July 15, 2016.

Serogroup Distribution* of IMD Cases in the US (2 of 2) (2016-2019)

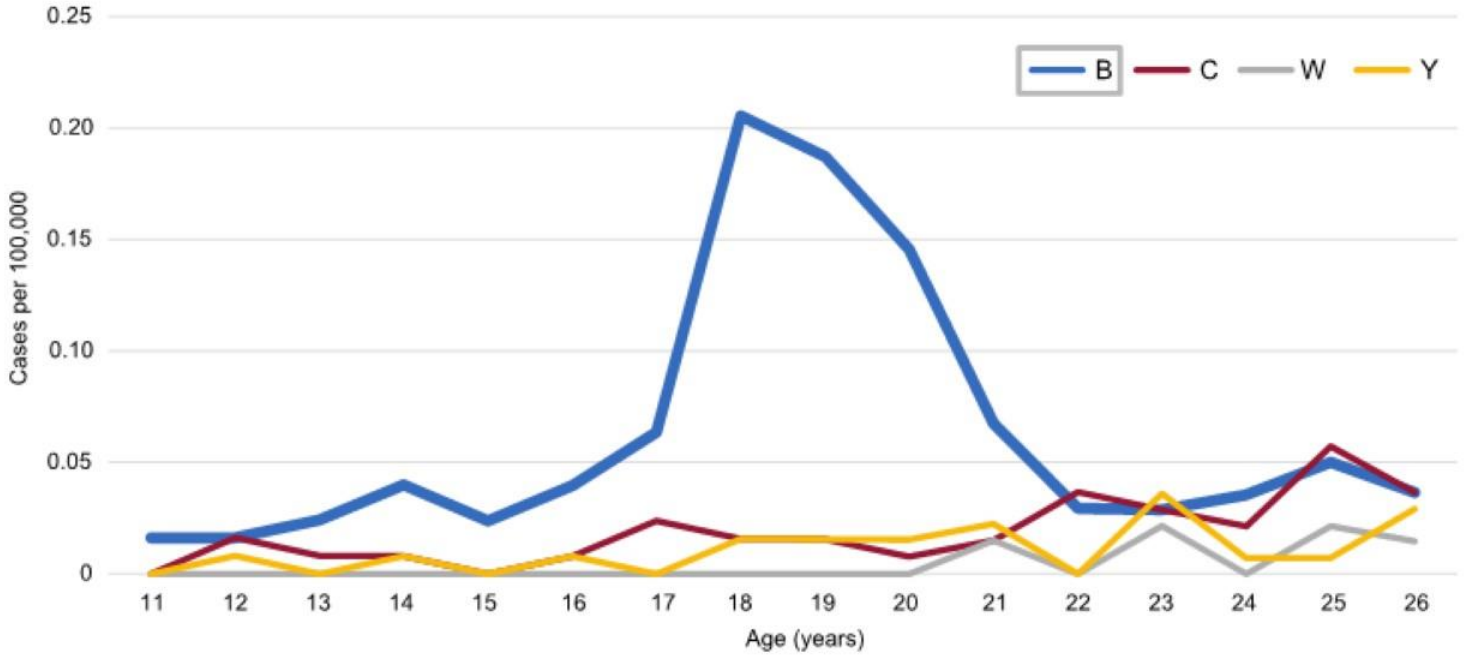


Among adolescents and young adults aged 16-23 years, **serogroup B caused over 60%** of all meningococcal disease cases from 2016 to 2019 (N=262)

*Values are rounded from decimal figures that total 100%.

Centers for Disease Control and Prevention website. Enhanced Meningococcal Disease Surveillance Reports, 2016-2019. www.cdc.gov/meningococcal/surveillance/index.html#enhanced-reports. Accessed December 1, 2021.

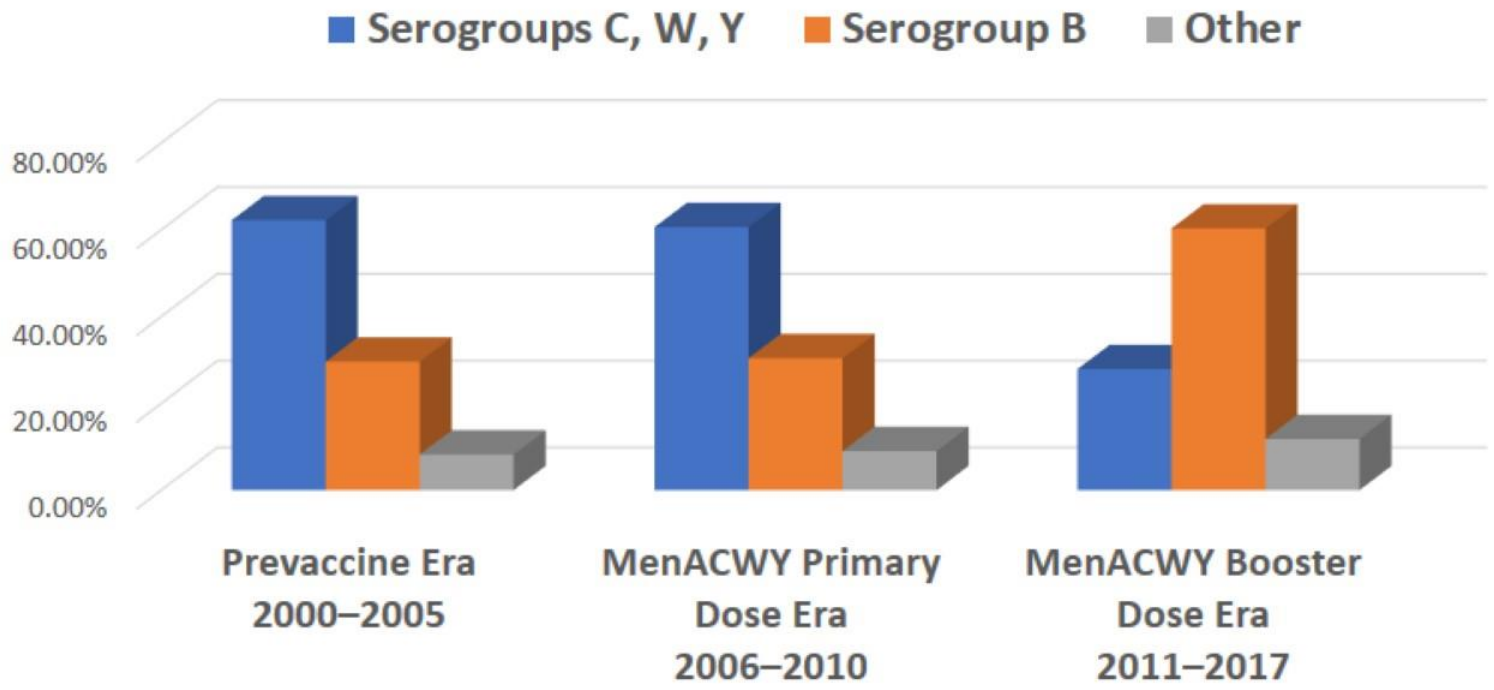
Incidence of Meningococcal Disease by Serogroup among US Adolescents and Young Adults, 2014-2016



Source: National Notifiable Diseases Surveillance System (NNDSS) data with additional serogroup data from Active Bacterial Core surveillance (ABCs) and state health departments.
Meyer S. Epidemiology of meningococcal disease among college students—United States, 2014-2016. https://stacks.cdc.gov/view/cdc/59918. Presented at the Advisory Committee on Immunization Practices; February 22, 2018.

Estimated Serogroup Distribution by Time Period in 11–15-year-olds

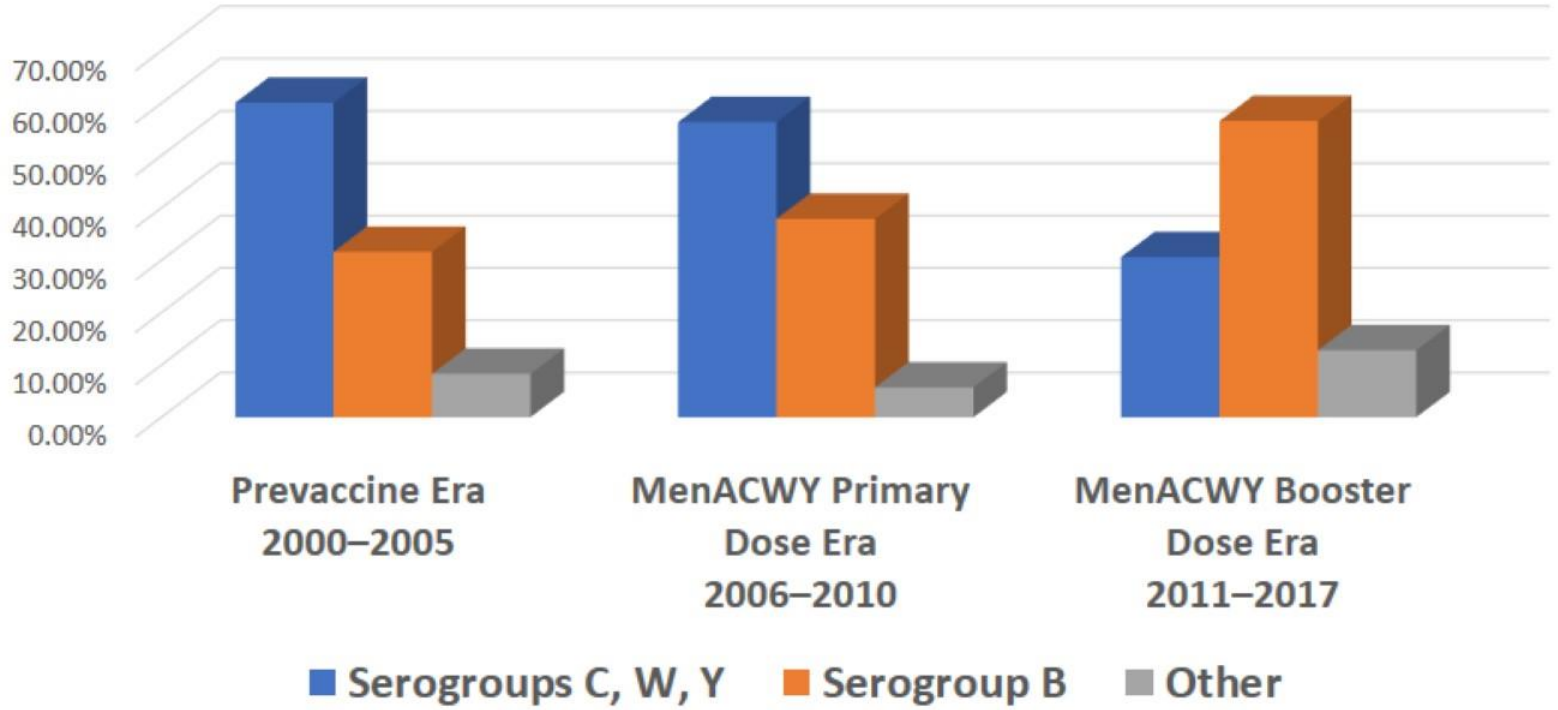
United States, 2000–2017



Mbaeyi S, Pondo T, Blain A, et al. Incidence of meningococcal disease before and after implementation of quadrivalent meningococcal conjugate vaccine in the United States. *JAMA Pediatr*. E-pub July 2020. https://doi.org/10.1001/jamapediatrics.2020.1990

Estimated Serogroup Distribution by Time Period in 16–22-year-olds

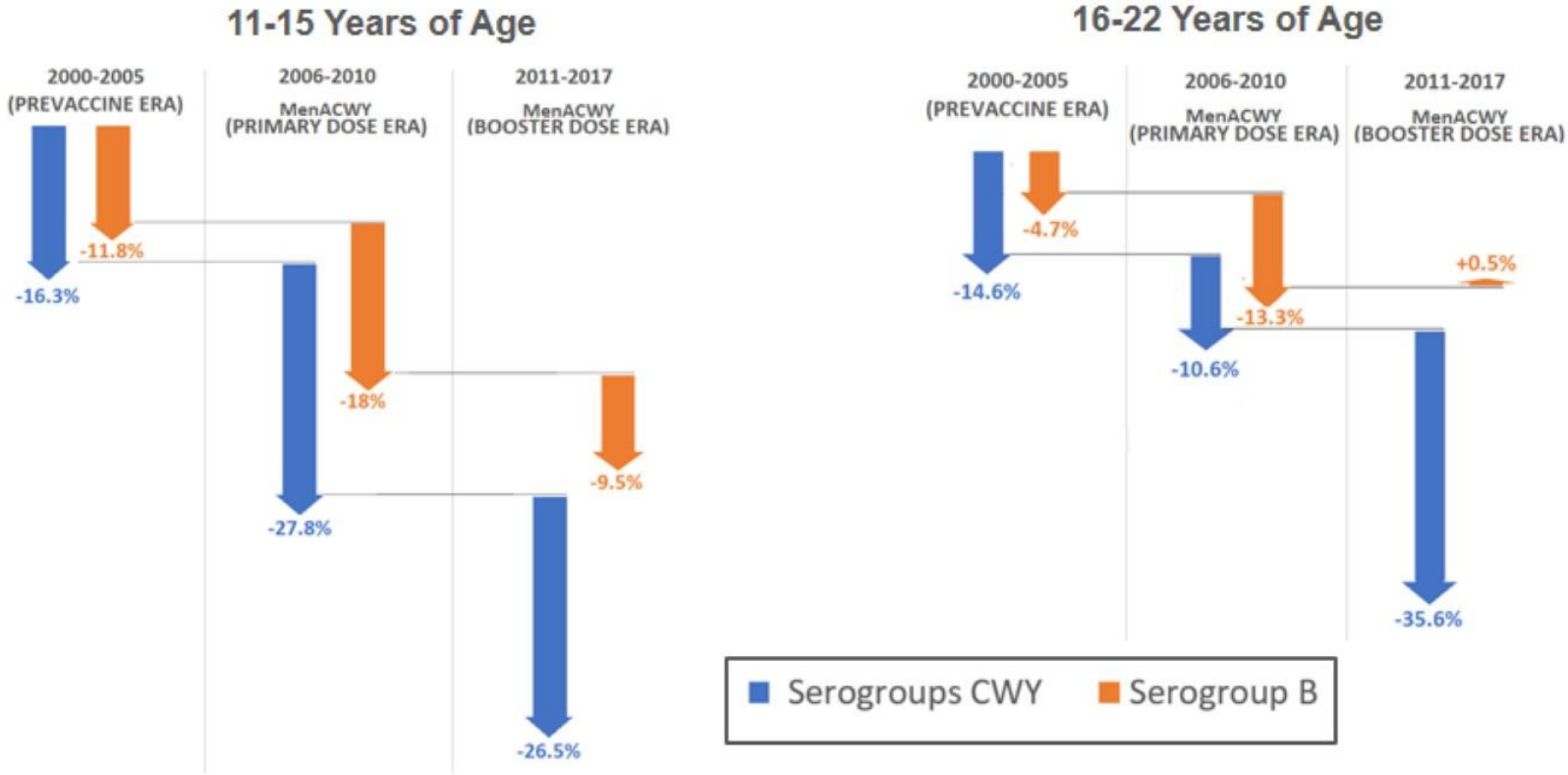
United States, 2000–2017



Mbaeyi S, Pondo T, Blain A, et al. Incidence of meningococcal disease before and after implementation of quadrivalent meningococcal conjugate vaccine in the United States. *JAMA Pediatr*. E-pub July 2020. https://doi.org/10.1001/jamapediatrics.2020.1990

Estimated Percentage Change in Meningococcal Disease Incidence Among Adolescents and Adults

United States, 2000–2017



Mbaeyi S, Pondo T, Blain A, et al. Incidence of meningococcal disease before and after implementation of quadrivalent meningococcal conjugate vaccine in the United States. *JAMA Pediatr*. E-pub July 2020. https://doi.org/10.1001/jamapediatrics.2020.1990

Available Meningococcal Vaccines in the U.S.

Two different types of meningococcal vaccines are needed for active immunization against the 5 most prevalent serogroups

Historically, 5 serogroups have caused a majority of cases of meningococcal disease: A, C, W, Y, and B

For active immunization against the 5 vaccine-preventable serogroups, adolescent or young adult patients need 2 different types of meningococcal vaccines: 1 for serogroups A, C, W, and Y, and 1 for serogroup B

Centers for Disease Control and Prevention. Meningococcal vaccination for adolescents: information for healthcare professionals. https://www.cdc.gov/vaccines/vpd/mening/hcp/adolescent-vaccine.html. Reviewed July 26, 2019. Accessed January 1, 2020.

Three meningococcal vaccines targeting serogroups ACWY are approved in the US: MENVEO, MENACTRA, and MenQUADFI*

	MENVEO[1]	MENACTRA[2]	MenQUADFI[3]
Number of Doses	Primary Series: 4 doses or 2 doses or 1 dose; Booster dose*	Primary Series: 2 doses or 1 dose; Booster dose*	Primary Series: 1 dose; Booster dose*
Dosing Schedules	Age-based	Age-based	Age-based
Administration	Intramuscular	Intramuscular	Intramuscular
Approved Ages	2 months to 55 years of age	9 months to 55 years of age	2 years and older
Description	Serogroups A (10 mcg), C, Y, W-135 (5 mcg ea.) oligosaccharides conjugated individually to *Corynebacterium diphtheriae* CRM_{197} protein	Serogroups A, C, Y, W-135 (4 mcg ea.) capsular polysaccharides individually conjugated to diphtheria toxoid protein	Serogroups A, C, Y, W-135 (10 mcg ea.) capsular polysaccharides individually conjugated to tetanus toxoid protein

*A single booster dose may be administered to individuals aged 15 through 55 years (Menveo and Menactra) and ≥15 years (MenQuadfi) who are at continued risk for meningococcal disease if at least 4 years have elapsed since a prior dose of a meningococcal (serogroups A, C, Y, W-135) conjugate vaccine.

*Please see Prescribing Information for complete product information

1. Prescribing Information for MENVEO. 2. Prescribing Information for MENACTRA. Prescribing Information for MenQUADFI.

Two meningococcal vaccines targeting serogroup B are approved in the US: BEXSERO and TRUMENBA*

	BEXSERO[1]	TRUMENBA[2]
Number of Doses	2 doses	2 or 3 doses
Dosing Schedule	≥1 month apart	At months 0 and 6 or 0, 1-2, 6
Administration	Intramuscular	Intramuscular
Approved Age	10 to 25 years of age	10 to 25 years of age
Antigens	NadA, fHbp (subfamily B), NHBA, PorA P1.4 (found in OMV)	fHbp (subfamilies A and B)

fHbp = Factor H binding protein, NadA = Neisserial adhesin A, NHBA = Neisserial Heparin Binding Antigen, PorA P1.4 = Porin A subtype P1.4), OMV= Outer Membrane Vesicle

*Please see Prescribing Information for complete product information

1. Prescribing Information for *Bexsero*. 2. Prescribing Information for *Trumenba*

Recommendations from the Advisory Committee on Immunization Practices (ACIP)

Overview of Meningococcal Vaccine Recommendations

Men ACWY Vaccines[1]

Age-based recommendation:

- At age 11-12 first dose
- At age 16 booster

Risk-based recommendation:

Persons ≥ 2 months of age deemed at high risk for IMD should receive a MenACWY vaccine series and booster doses accordingly based on persistent risk

Men B Vaccines[1]

Age-based recommendation based on shared clinical decision making:

- At age 16-23 years (preferred between 16-18) a series of Men B vaccine

Risk-based recommendation:

Persons ≥ 10 years of age deemed at high risk for IMD with serogroup B should receive a Men B vaccine series. Booster doses recommended accordingly based on persistent risk

1. Centers for Disease Control and Prevention. Meningococcal Vaccination: Recommendations of the Advisory Committee on Immunization Practices, United States, 2020. *MMWR*. 2020;69(9):1-42. Available at: https://www.cdc.gov/mmwr/volumes/69/rr/pdfs/rr6909a1-H.pdf.

Meningococcal ACWY Vaccine Recommendations[1]

Age-based recommendation:

✓ Healthy adolescents age 11 or 12 years **should** be routinely vaccinated with MenACWY and receive a booster dose at age 16 years. Adolescents who receive the first dose at age 13 through 15 years should receive a one-time booster dose, preferably at age 16 through 18 years. If the first dose is given at 16 years or older a second dose is not needed.

Risk-based recommendations:

✓ Individuals ≥ 2mo old who are at increased risk for meningococcal disease **should** be vaccinated with MenACWY and boosted accordingly based on persistent risk status.

- Anatomic or functional asplenia (including sickle cell disease)
- HIV infection
- Persistent complement component deficiency
- Eculizumab or ravulizumab use
- Travel to or live in countries where Meningococcal disease is hyperendemic or epidemic
- Microbiologists routinely exposed to *N. meningitidis*
- Military recruits
- First year college students who live in residential housing
- Outbreaks

1. Centers for Disease Control and Prevention. Meningococcal Vaccination: Recommendations of the Advisory Committee on Immunization Practices, United States, 2020. *MMWR*. 2020;69(9):1-42. Available at: https://www.cdc.gov/mmwr/volumes/69/rr/pdfs/rr6909a1-H.pdf.

Meningococcal B Vaccine Recommendations[1,2,3]

Age-based recommendation:

- ✓ Healthy adolescents/young adults aged 16-23 years (preferred age:16-18 years) based upon shared clinical decision making.[1] The discussion and decision regarding vaccination should be documented in the medical record.[2]

Risk-based recommendation:

- ✓ Individuals ≥10 years of age who are at increased risk for meningococcal disease **should** be vaccinated with a Men B series
  - Anatomic or functional asplenia (including sickle cell disease)
  - Persistent complement component deficiency
  - Eculizumab or ravulizumab use
  - Microbiologists routinely exposed to *N. meningitidis*
  - Outbreaks

1. Centers for Disease Control and Prevention. Meningococcal Vaccination: Recommendations of the Advisory Committee on Immunization Practices, United States, 2020. *MMWR*. 2020;69(9):1-42. Available at: https://www.cdc.gov/mmwr/volumes/69/rr/pdfs/rr6909a1-H.pdf.
2. Byington CL, et al. Pediatrics. 2016;138:1-7. https://doi.org/10.1542/peds.2016-1890.

‘Shared Clinical Decision Making’ Recommendations for the Use of Meningococcal Group B Vaccines[1]

“Shared clinical decision-making refers to an individually based vaccine recommendation informed by a decision-making process between the health care provider and the patient or parent/guardian. Considerations for shared clinical decision-making for vaccine administration and timing of administration might include:

- the serious nature of meningococcal infections, with high rates of death and permanent sequelae in those who develop invasive disease;
- the low number of serogroup B meningococcal disease cases (average of 34 serogroup B cases annually among persons aged 16–23 years in the United States during 2015–2018);
- the increased risk among college students, especially those who are freshmen, attend a 4-year university, live in on-campus housing, or participate in sororities and fraternities;
- the protection provided by MenB vaccines against most strains of serogroup B *N. meningitidis;*
- the estimated relatively short duration of MenB protection (antibody waning within 1–2 years postcompletion of the primary series); and
- the evidence to date suggesting that MenB vaccination has no effect on meningococcal carriage (i.e., MenB vaccines might provide individual protection against serogroup B disease but herd protection is unlikely).”

1. Centers for Disease Control and Prevention. Meningococcal Vaccination: Recommendations of the Advisory Committee on Immunization Practices, United States, 2020. *MMWR.* 2020;69(9):1-42. Available at: https://www.cdc.gov/mmwr/volumes/69/rr/pdfs/rr6909a1-H.pdf.

Booster Recommendations for the Use of Meningococcal Group B Vaccines by Persons at Increased Risk

"ACIP recommends MenB booster doses for previously vaccinated persons who become or remain at increased risk."[1]

- For persons aged ≥10 years with complement deficiency, complement inhibitor use, asplenia, or who are microbiologists:
  - ACIP recommends a MenB booster dose 1 year following completion of a MenB primary series followed by MenB booster doses every 2-3 years thereafter, for as long as increased risk remains.

- For persons aged ≥10 years determined by public health officials to be at increased risk during an outbreak:
  - ACIP recommends a one-time booster dose if it has been ≥1 year since completion of a MenB primary series.
  - A booster dose interval of ≥6 months may be considered by public health officials depending on the specific outbreak, vaccination strategy, and projected duration of elevated risk.

- BEXSERO is approved as a 2-dose series (0.5-mL each) administered at least 1 month apart. BEXSERO is not approved for administration as a booster dose.[2]

1. Centers for Disease Control and Prevention. Meningococcal Vaccination: Recommendations of the Advisory Committee on Immunization Practices, United States, 2020. *MMWR*. 2020;69(9):1-42. Available at: https://www.cdc.gov/mmwr/volumes/69/rr/pdfs/rr6909a1-H.pdf.
2. Prescribing Information for BEXSERO.

Indications for MENVEO and BEXSERO

MENVEO is a vaccine indicated for active immunization to prevent invasive meningococcal disease caused by Neisseria meningitidis serogroups A, C, Y, and W-135. MENVEO is approved for use in persons aged 2 months through 55 years. MENVEO does not prevent N. meningitidis serogroup B infections.

BEXSERO is a vaccine indicated for active immunization to prevent invasive disease caused by *Neisseria meningitidis* serogroup B. BEXSERO is approved for use in individuals 10 through 25 years of age.
Approval of BEXSERO is based on demonstration of immune response, as measured by serum bactericidal activity against 3 serogroup B strains representative of prevalent strains in the United States. The effectiveness of BEXSERO against diverse serogroup B strains has not been confirmed.

Important safety information is found in the Prescribing Information for MENVEO and BEXSERO.

Questions