

# **Meningococcal Disease and Meningococcal Vaccine**

## **Chapter 14**

**May 2019**

1

**Disease**

# *Neisseria meningitidis*

- Aerobic gram-negative bacteria
- At least 13 serogroups based polysaccharide capsule
- Most invasive disease caused by serogroups A, B, C, Y, and W
- Relative importance of serogroups depends on geographic location and other factors (e.g., age)

# Meningococcal Disease Pathogenesis

- Organism colonizes nasopharynx
- In some persons organism enters the bloodstream and causes infection at distant site
- Antecedent URI may be a contributing factor

# *Neisseria meningitidis*

## Clinical Features

- Incubation period 3-4 days (range 2-10 days)
- Abrupt onset of fever, meningeal symptoms, hypotension, and rash
- Fatality rate 10%-15%, up to 40% in meningococemia

# Meningococcal Meningitis

- Most common presentation of invasive disease
- Results from hematogenous dissemination
- Clinical findings
  - fever
  - headache
  - stiff neck

# Meningococcal Sepsis

- Meningococemia
- Bloodstream infection
- May occur with or without meningitis
- Clinical findings
  - fever
  - petechial or purpuric rash
  - hypotension
  - shock
  - acute adrenal hemorrhage
  - multi-organ failure

# Meningococcal Disease





# Meningococcal Disease



# *Neisseria meningitidis*

## Risk Factors for Invasive Disease

- Host Factors
  - Deficiencies in the terminal common complement pathways
  - Functional or anatomic asplenia
  - Chronic underlying disease
  - Certain genetic factors (altered genes: mannose-binding lectin and tumor necrosis factor)
- Environmental factors
  - Household crowding
  - Active and passive smoking
  - Antecedent viral infection
- Occupational (microbiologists)

# *Neisseria meningitidis*

## Risk Factors for Invasive Disease

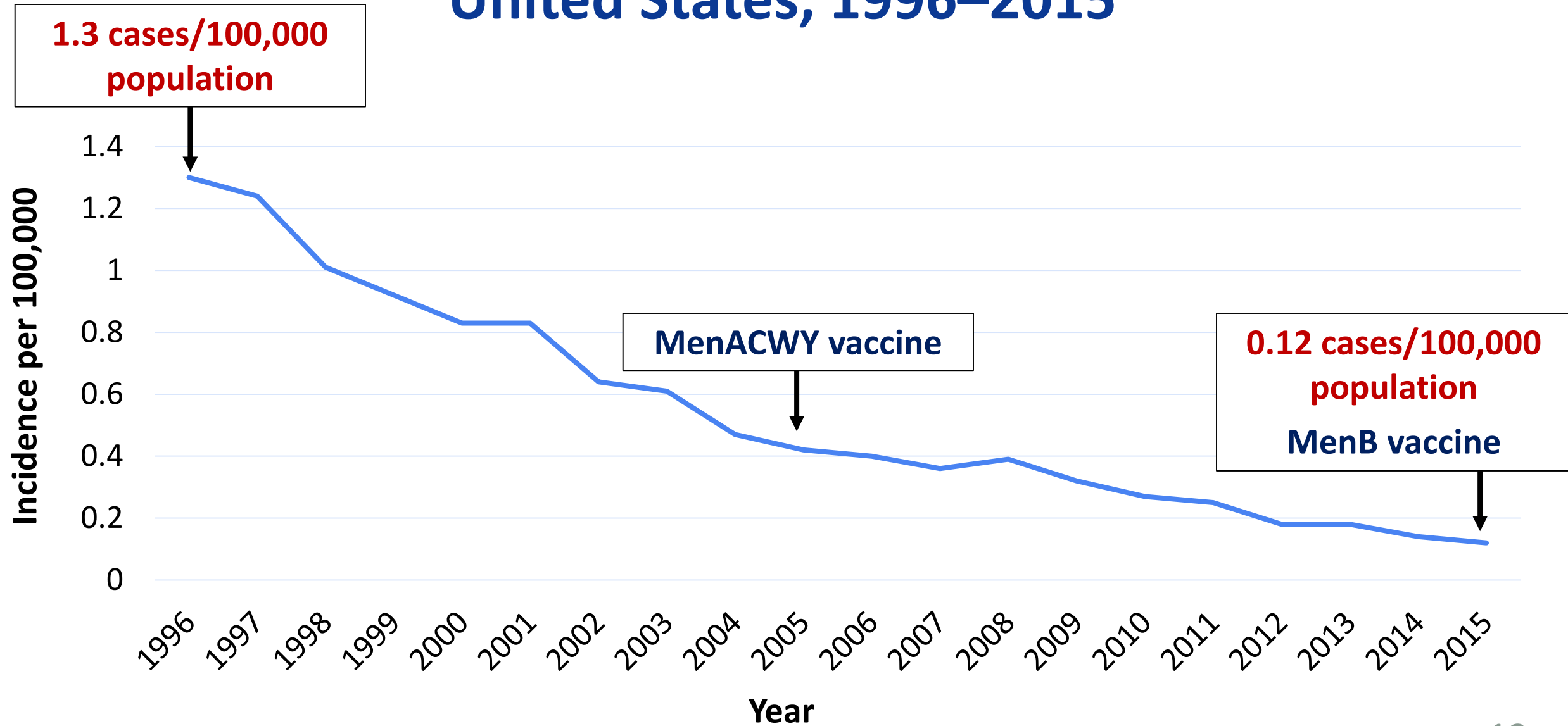
- College Students
  - Studies in 1990s – overall incidence similar to or lower than their counterparts in general population\*
  - Case control study of 50 cases and other studies in the 1990s#
    - First-year college students living in residence halls at higher risk

\*JAMA 1999;281:1906-10

#Abstracts of the 39th Meeting of the IDSA. Philadelphia, PA: IDSA; 1999:276

Epidemiol Infect 1999;122:351–7. Clin Infect Dis 1999;29:215–6.

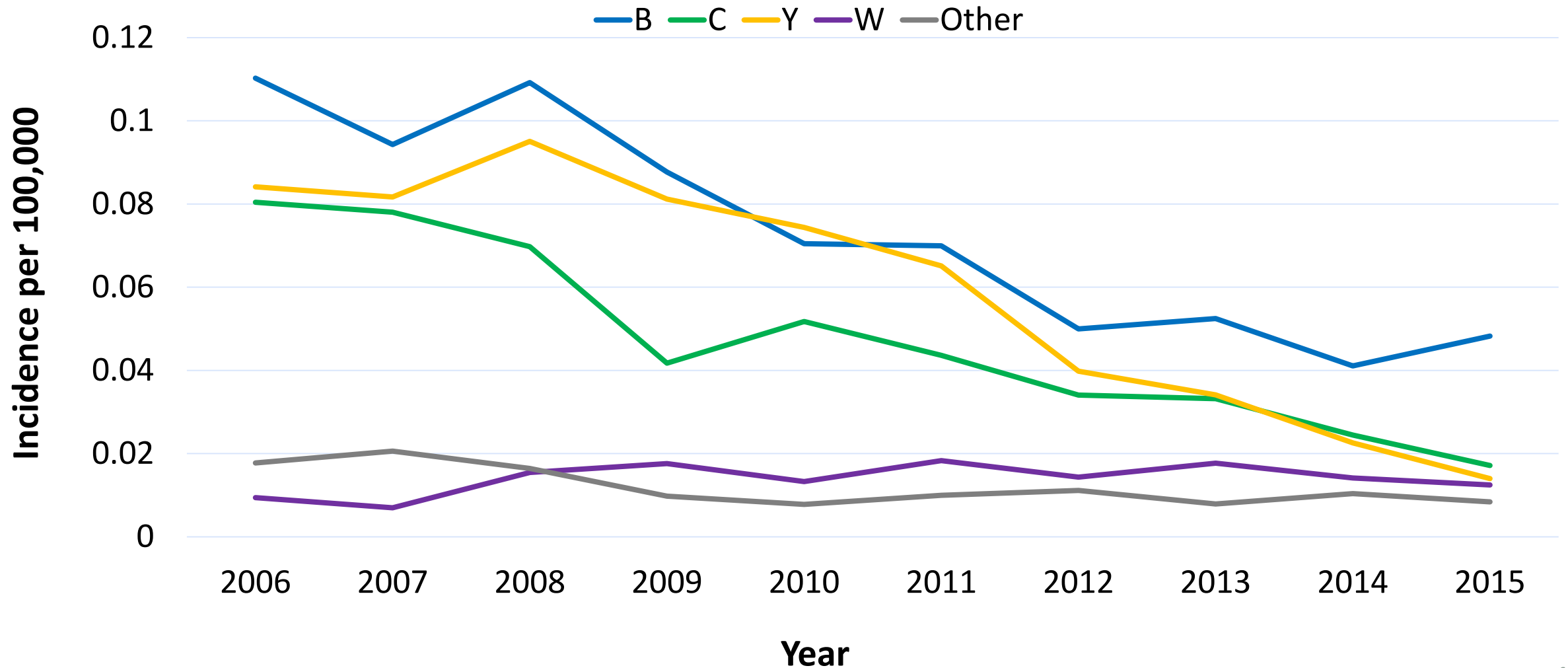
# Meningococcal Disease Incidence – United States, 1996–2015



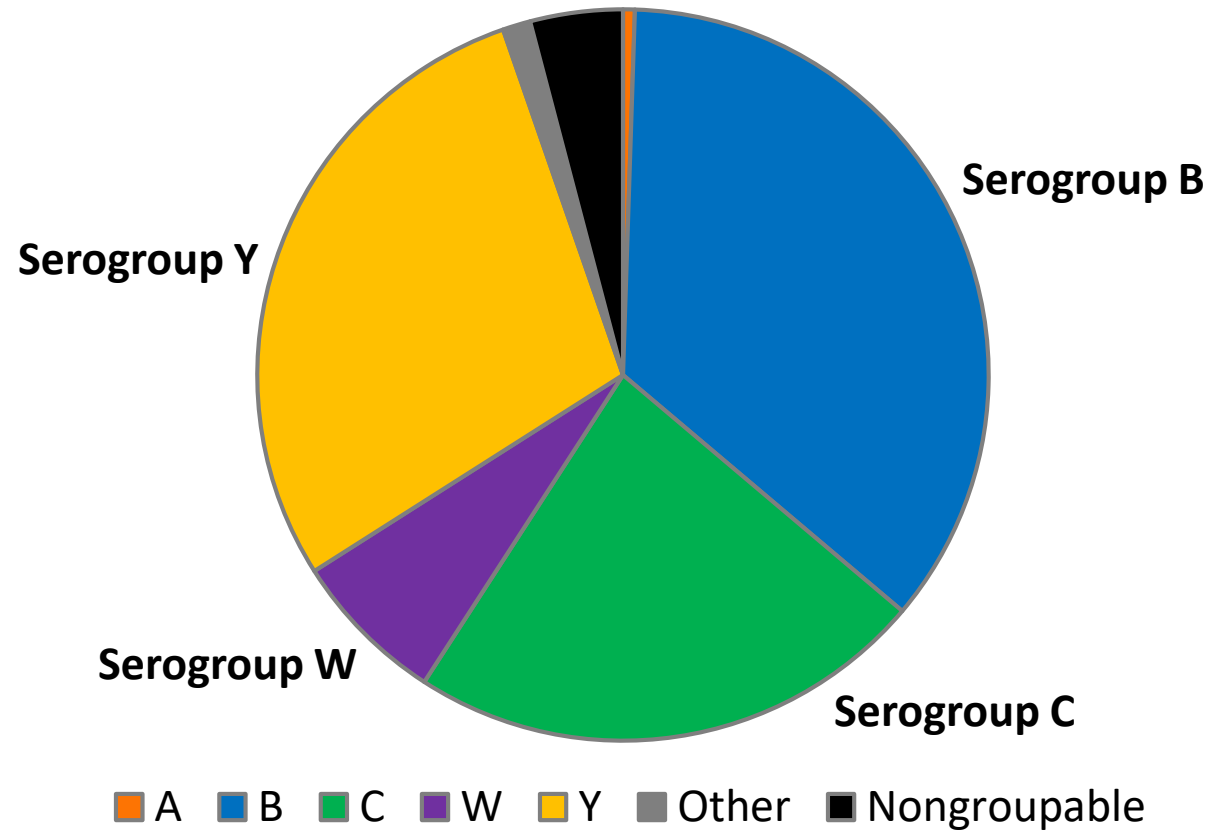
Abbreviations: MenACWY = quadrivalent meningococcal conjugate vaccine; MenB vaccine = serogroup B meningococcal vaccines

Source: 1996-2015 NNDSS Data

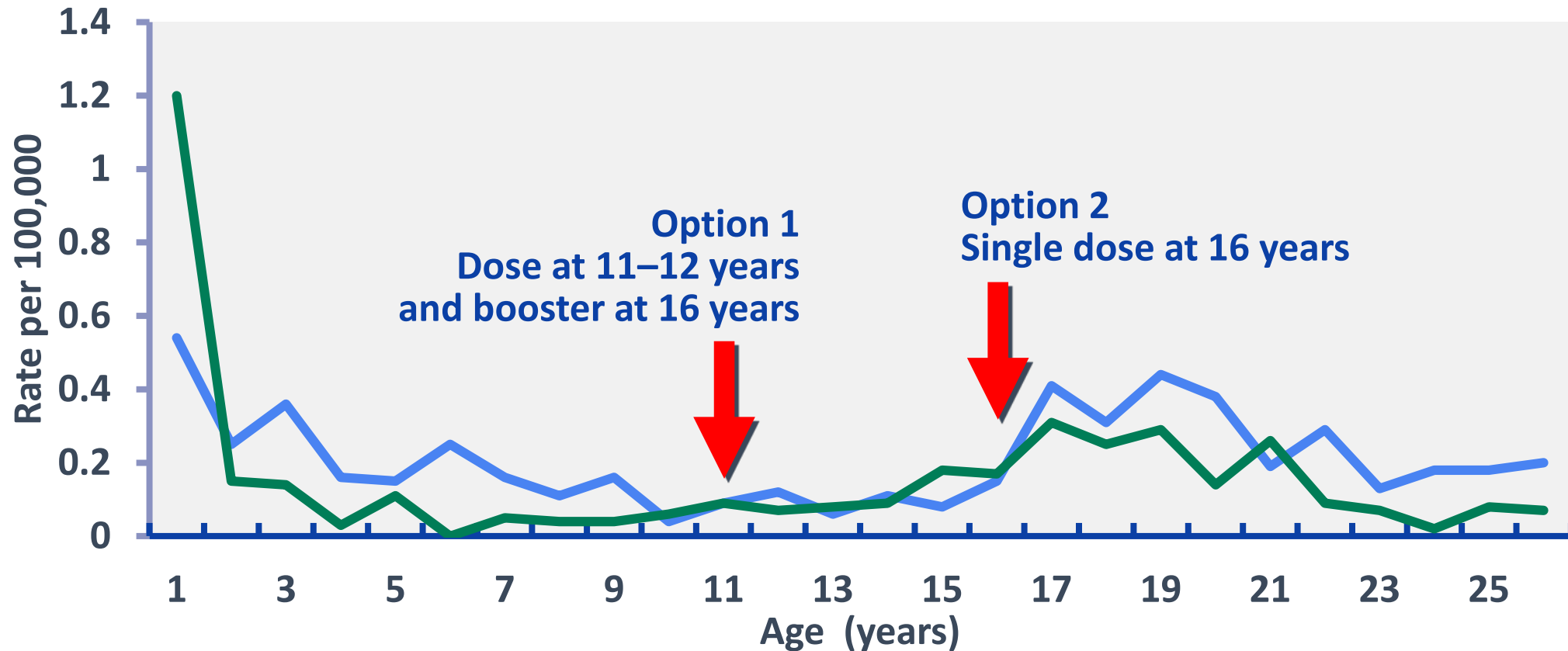
# Trends in Meningococcal Disease Incidence by Serogroup – United States, 2006-2015



# Meningococcal Disease by Serogroup, All Ages – United States, 2006-2015



# Rates of Meningococcal Disease (C and Y) by Age, 1999–2008



# Meningococcal Outbreaks in the United States

- Outbreaks account for 2%-3% of reported cases
- Most recent outbreaks caused by serogroup C and B



# Serogroup B meningococcal disease outbreaks on college campuses<sup>†</sup>, 2013–2018

State of University	Year started	Cases (deaths)	Undergraduate population
New Jersey	2013	9 (1)	5,000
California	2013	4*	19,000
Rhode Island	2015	2	4,000
Oregon	2015	7 (1)	20,000
California	2016	2**	5,000
New Jersey	2016	2	35,000
Wisconsin	2016	3	30,000
Oregon	2016	5	25,000
Massachusetts	2017	3	30,000
Pennsylvania	2017	2	3,600

During 2014–2016, 31.7% of serogroup B cases in college students were outbreak-related.

<sup>†</sup>Where CDC consulted; \* 1 additional associated case identified after retrospective case review; \*\* 1 additional patient with inconclusive laboratory results

2

**Vaccine**

Vaccine product	Age indications
MenACWY Vaccines	
Menactra	
MenACWY-D	9 months-55 years
Menveo	
MenACWY-CRM	2months–55 years
MenB Vaccines	
Trumemba	
MenB-FHbp	10-25 years
Bexsero	
Men B-4C	10-25 years

# Meningococcal Conjugate Vaccines

- Meningococcal polysaccharide conjugated to protein carrier
- Elicit both T- and B-cell immunity (T-cell dependent immunity)
- 2 brands currently licensed in the United States
  - Menactra = MenACWY-D (Sanofi Pasteur)
  - Menveo = MenACWY-CRM (Novartis)

# Menactra MenACWY Vaccine

- Licensed by FDA in January 2005
- Quadrivalent polysaccharide vaccine conjugated to diphtheria toxoid (MenACWY-D)
- Approved for persons 9 months through 55 years of age
- Intramuscular injection
- Single dose vials

# Menveo MenACWY Vaccine

- Licensed by FDA in February 2010
- Lyophilized serogroup A vaccine reconstituted with liquid containing serogroups C, Y, and W135 (MenACWY-CRM)
- May be used for any person 2 months through 55 years of age for whom MCV4 is indicated, including revaccination
- Intramuscular injection
- Single dose vials

# Interchangeability of Conjugate Vaccine Brands

- Limited data suggest that different conjugate vaccine products can be used interchangeably.
- Whenever feasible, the same brand of vaccine should be used for all doses of the vaccination series
- If vaccination providers do not know or have available the type of vaccine product previously administered, any product should be used to continue or complete the series

# 3

## **Clinical Considerations**



# MenACWY Recommendations

- Child and adolescent immunization schedule

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19-23 mos	2-3 yrs	4-6 yrs	7-10 yrs	11-12 yrs	13-15 yrs	16 yrs	17-18 yrs
Meningococcal (MenACWY-D ≥9 mos; MenACWY-CRM ≥2 mos)			See Notes											1 <sup>st</sup> dose		2 <sup>nd</sup> dose	

- Adult immunization schedule

Vaccine	19-21 years	22-26 years	27-49 years	50-64 years	≥65 years
Meningococcal A, C, W, Y (MenACWY)	1 or 2 doses depending on indication, then booster every 5 yrs if risk remains				

# MenACWY Recommendations

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19-23 mos	2-3 yrs	4-6 yrs	7-10 yrs	11-12 yrs	13-15 yrs	16 yrs	17-18 yrs
Meningococcal (MenACWY-D ≥9 mos; MenACWY-CRM ≥2 mos)			See Notes											1 <sup>st</sup> dose		2 <sup>nd</sup> dose	

- Administer MenACWY at age 11 or 12 years with a booster dose at 16 years of age
- Administer 1 dose at age 13 through 15 years if not previously vaccinated
- For persons vaccinated at age 13 through 15 years, administer a one-time booster dose, preferably at or after 16 through 18 years of age
  - The minimum interval between doses is 8 weeks

# MenACWY Adolescent Vaccination Recommendations

- A booster dose is not recommended for healthy persons if the first dose is administered at or after 16 years of age
- A booster dose is not recommended for healthy persons after 21 years of age who are not at increased risk of exposure
  - A booster dose is not recommended for healthy persons 22 years of age and older even if the first dose was administered at 11-15 years of age

# MenACWY Vaccine Recommendations for Persons at Increased Risk for Meningococcal Disease

# High-risk Groups: Functional or Anatomic Asplenia or HIV Infection\*

- Younger than 19 months
  - Infant series at 2, 4, 6, and 12-15 months with MenACWY-CRM
- 19-23 months who have not received a complete series
  - 2-dose primary series of MenACWY-CRM 12 weeks\*\*
- 24 months or older who have not received a complete series
  - 2-dose primary series of either MenACWY 8-12 weeks apart

\*Including sickle-cell disease

\*\* Doses valid if 8 weeks apart

# High-risk Groups: Persistent Complement Component Deficiency\*

- Children 2-18 months
  - Infant series at 2, 4, 6, and 12-15 months with MenACWY-CRM; OR
  - 2-dose primary series of MenACWY-D starting at 9 months at least 12 weeks apart\*\*
- 19-23 months without complete series of either MenACWY
  - 2-dose primary series of either MenACWY at least 12 weeks apart\*\*
- 24 months or older who have not received a complete series of either MenACWY
  - 2-dose primary series of either MenACWY at least 12 weeks apart\*\*

\* Including persons taking Soliris (eculizumab)

\*\* Doses valid if 8 weeks apart

# Meningococcal Vaccine Recommendations for Persons 2 through 55 years at High Risk

- Persons who:
  - Are first-year college students aged  $\leq 21$  years living in residential housing
  - Travel to, or are residents of, countries where meningococcal disease is hyperendemic or epidemic
  - Are microbiologists routinely exposed to isolates of *Neisseria meningitidis*
  - Military recruits
- Administer: 1 dose of MenACWY

# Meningococcal ACWY Vaccine Booster Doses

- Person who receive primary immunization and remain at increased risk should receive booster doses
  - If primary immunization complete **before** 7 years of age:
    - first booster should be 3 years after primary immunization and every 5 years thereafter if at continued risk
  - If primary immunization complete **on or after** 7 years of age
    - first booster should be 5 years after primary immunization and every 5 years thereafter if at continued risk



# MenACWY Revaccination Recommendations

- **Other high-risk persons recommended for boosters:**
  - Microbiologists with prolonged exposure to *Neisseria meningitidis*
  - Frequent travelers to or persons living in areas with high rates of meningococcal disease (see next slide)
- **Revaccinate every 5 years as long as the person remains at increased risk**
  - MenACWY for persons 2 through 55 years of age
  - MenACWY for persons 56 years and older also (off-label recommendation) if repeated vaccination anticipated

# International Travelers and Revaccination\*

- International travelers should receive a booster dose of MenACWY if the last dose was administered 5 or more years previously
  - Vaccination in the 3 years before the date of travel is required by the government of Saudi Arabia for all travelers to Mecca during the annual Hajj

# Updated Guidance for Use of Meningococcal Vaccines in Persons Aged $\geq 56$ Years

- Meningococcal vaccines that are licensed for use in person aged  $\geq 56$  year are not currently available in the United States
- Persons aged  $\geq 56$  years who are recommended meningococcal vaccination because they are at increased risk for meningococcal disease should receive MenACWY conjugate vaccine
  - This includes, meningococcal vaccine-naïve persons aged  $\geq 56$  years who anticipate requiring only a single dose of meningococcal vaccine (e.g. travelers and persons at risk as a risk of a community outbreak)
  - And persons who were vaccinated previously with MenACWY conjugate vaccine and are recommended for revaccination or for whom multiple doses are anticipated (e.g., person with asplenia, HIV, and microbiologists)

# Meningococcal ACWY Adverse Reactions

	MenACWY
Local reactions	11%-59%
Low-grade fever	5%-17%
Systemic reactions (headache, malaise, fatigue)	4%-54%

# MenB Vaccine Recommendations

# Meningococcal B Vaccines

Product Name (ACIP Abbreviation)	FDA Age Indications	Schedule/Dosage/Route
Trumenba® (MenB-FHbp)	10 through 25 years of age	<ul style="list-style-type: none"><li>• 3-dose series<ul style="list-style-type: none"><li>- 0, 1–2, and 6-month</li></ul></li></ul> <u>OR</u> <ul style="list-style-type: none"><li>• 2-dose series<ul style="list-style-type: none"><li>- 0, 6 month</li></ul></li><li>• 0.5 mL dose</li><li>• IM injection</li></ul>
Bexsero® (MenB-4C)	10 through 25 years of age	<ul style="list-style-type: none"><li>• 2-dose<ul style="list-style-type: none"><li>- 0, 1–6 month</li></ul></li><li>• 0.5 mL dose</li><li>• IM injection</li></ul>

# Meningococcal B Recommendations

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19-23 mos	2-3 yrs	4-6 yrs	7-10 yrs	11-12 yrs	13-15 yrs	16 yrs	17-18 yrs
Meningococcal B														See Notes			

Vaccine	19–21 years	22–26 years	27–49 years	50–64 years	≥65 years
Meningococcal B (MenB)	2 or 3 doses depending on vaccine and indication				

- Recommendation for use in individuals  $\geq 10$  years of age at increased risk of disease
- Recommendation for use in adolescents and young adults not at increased risk for disease

# ACIP MenB Recommendations

- Certain persons aged  $\geq 10$  years\* who are at increased risk for meningococcal disease ***should*** receive MenB vaccine. These persons include:
  - Persons with persistent complement component deficiencies
  - Persons with anatomic or functional asplenia\*\*
  - Microbiologists routinely exposed to isolates of *Neisseria meningitidis*
  - Persons identified as at increased risk because of a serogroup B meningococcal disease outbreak

\*ACIP off-label recommendation

\*\*Including sickle cell disease

[http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6422a3.htm?s\\_cid=mm6422a3\\_w](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6422a3.htm?s_cid=mm6422a3_w)



# ACIP MenB Recommendations

- Certain other groups included in MenACWY (MCV4) recommendations for persons at increased risk, are not in this recommendation
- MenB – **NOT currently recommended for:**
  - Children aged 2 months – 9 years of age
  - Persons who travel to or reside in countries where meningococcal disease is hyperendemic or epidemic because risk is generally not caused by serogroup B
  - Routine use in first-year college students living in residence halls, military recruits, or all adolescents

# Use of 2- and 3-Dose Schedules of MenB-FHbp (Trumenba) Meningococcal Serogroup B Vaccine

- For persons at increased risk for meningococcal disease and for use during serogroup B outbreaks, 3 doses of MenB-FHbp should be administered at 0, 1-2, 6 months
- When given to healthy adolescents who are not at increased risk for meningococcal disease, 2 doses of MenB-FHbp should be administered at 0 and 6 months

# Trumenba Timing and Spacing Errors

- If a patient is recommended for 3 doses of Trumenba, but the second dose is delayed beyond a 6-month interval, a third dose is NOT necessary
- If a patient is recommended for 2 doses of Trumenba, and the second dose is given less than 6 months after the first dose, then a repeat (3<sup>rd</sup>) dose must be administered 4 months after the second dose

# Meningococcal B Vaccine Booster Doses

- Voted upon at the June 2019 ACIP meeting
- Will become official policy when published in MMWR
- Sign-up for email alerts!

Recs Listed by Date

Comprehensive Recommendations and Guidelines +

Archived ACIP Recs

Vaccine Recommendations for Emergency Situations

Get Email Updates

To receive email updates about this page, enter your email address:

Email Address

[What's this?](#) Submit

Advisory Committee on Immunization Practices (ACIP)

Vaccine-Specific ACIP Recommendations

- [Anthrax](#)
- [BCG](#)
- [Cholera](#)
- [DTaP/Tdap/Td](#)
- [Hepatitis A](#)
- [Hepatitis B](#)
- [Hib](#)
- [HPV](#)
- [Influenza](#)
- [Japanese Encephalitis](#)
- [Measles, Mumps and Rubella](#)

- [MMRV](#)
- [Meningococcal](#)
- [Pneumococcal](#)
- [Polio](#)
- [Rabies](#)
- [Rotavirus](#)
- [Smallpox \(Vaccinia\)](#)
- [Typhoid](#)
- [Varicella \(Chickenpox\)](#)
- [Yellow Fever](#)
- [Zoster \(Shingles\)](#)

UPDATED Feb 2019

ACIP Abbreviations

These [abbreviations](#) provide a uniform approach to vaccine references used in ACIP Recommendations that are published in the *MMWR*, the *Pink Book*, and the AAP *Red Book*, and in the U.S. immunization schedules for children, adolescents, and adults.

Comprehensive ACIP Recommendations and Guidelines

- [General Best Practice Guidelines on Immunization](#)

# MenB for Adolescents and Young Adults

- A MenB vaccine series *may* be administered to adolescents and young adults aged 16–23 years to provide short-term protection against most strains of serogroup B meningococcal disease\*
- The preferred age for MenB vaccination is 16–18 years

\* Permissive recommendation (Category B)

# ACIP MenB Recommendations

- MenB should be administered as either a 2-dose series of MenB-4C or a 2-dose or 3-dose series of MenB-FHbp
- The same vaccine product should be used for all doses
- MenB-4C and MenB-FHbp may be administered concomitantly with other vaccines indicated for this age, but at a different anatomic site, if feasible
- No product preference to be stated

# MenB Vaccine Brand Error

- If a dose of MenB vaccine is administered and found to be a different brand from a dose previously administered:
  - Pick the brand with which you want to continue the series
  - Invalidate the dose of the other brand
  - Continue the series
  - Need a 4 week minimum interval from any invalid doses
  - Need to follow the minimum intervals between doses of the chosen brand

# Meningococcal B Adverse Reactions

	Adverse Reactions
Pain at injection site, injection site reactions, erythema	28%-85%
fatigue, headache, chills, nausea, arthralgia	13%-60%



# Meningococcal Vaccine

## Contraindications and Precautions

- Severe allergic reaction to vaccine component or following prior dose
- Moderate or severe acute illness

# Meningococcal Vaccine Use in Outbreaks

- MenACWY and MenB recommended for use in control of outbreaks caused by A, C, W, Y, or B
- Outbreak definition:
  - at least 3 confirmed or probable primary cases of the same serogroup
  - period of 3 months or less
  - primary attack rate of more than 10 cases per 100,000 population

4

**Resources**

# Meningococcal Resources

- ACIP's Meningococcal Recommendations web page

[www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/mening.html](http://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/mening.html)

- CDC's Meningococcal Infection web page

[www.cdc.gov/meningococcal/index.html](http://www.cdc.gov/meningococcal/index.html)

- CDC's Meningococcal Vaccination web page

[www.cdc.gov/vaccines/vpd-vac/mening/default.htm](http://www.cdc.gov/vaccines/vpd-vac/mening/default.htm)

- Immunization Action Coalition Meningococcal web page

[www.immunize.org/meningococcal/](http://www.immunize.org/meningococcal/)

- Children's Hospital of Philadelphia Vaccine Education Center Meningococcal web page

<http://www.chop.edu/centers-programs/vaccine-education-center/vaccine-details/meningococcal-vaccine>