



# Update on the Epidemiology of Meningococcal Disease and Guidance for the Control of Meningococcal Disease Outbreaks in the U.S.

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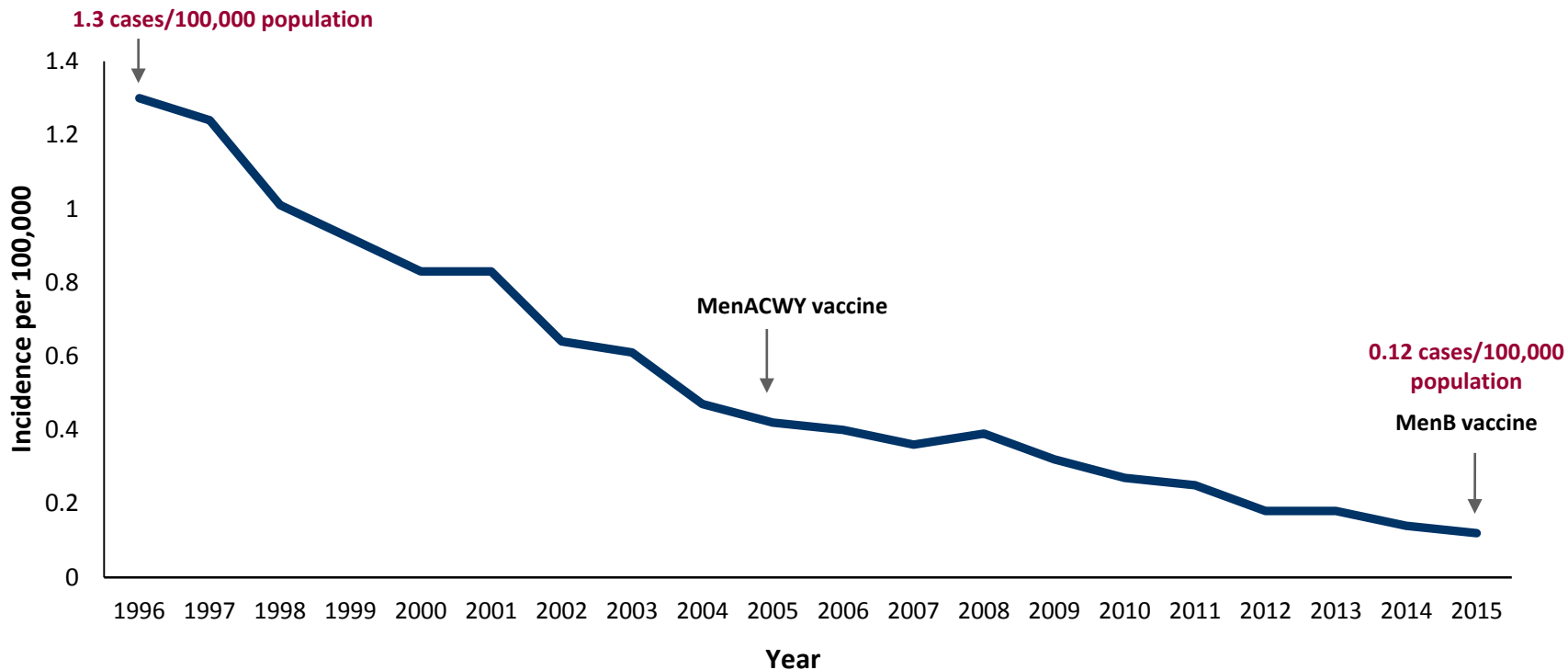
Advisory Committee on Immunization Practices Meeting

February 22, 2017

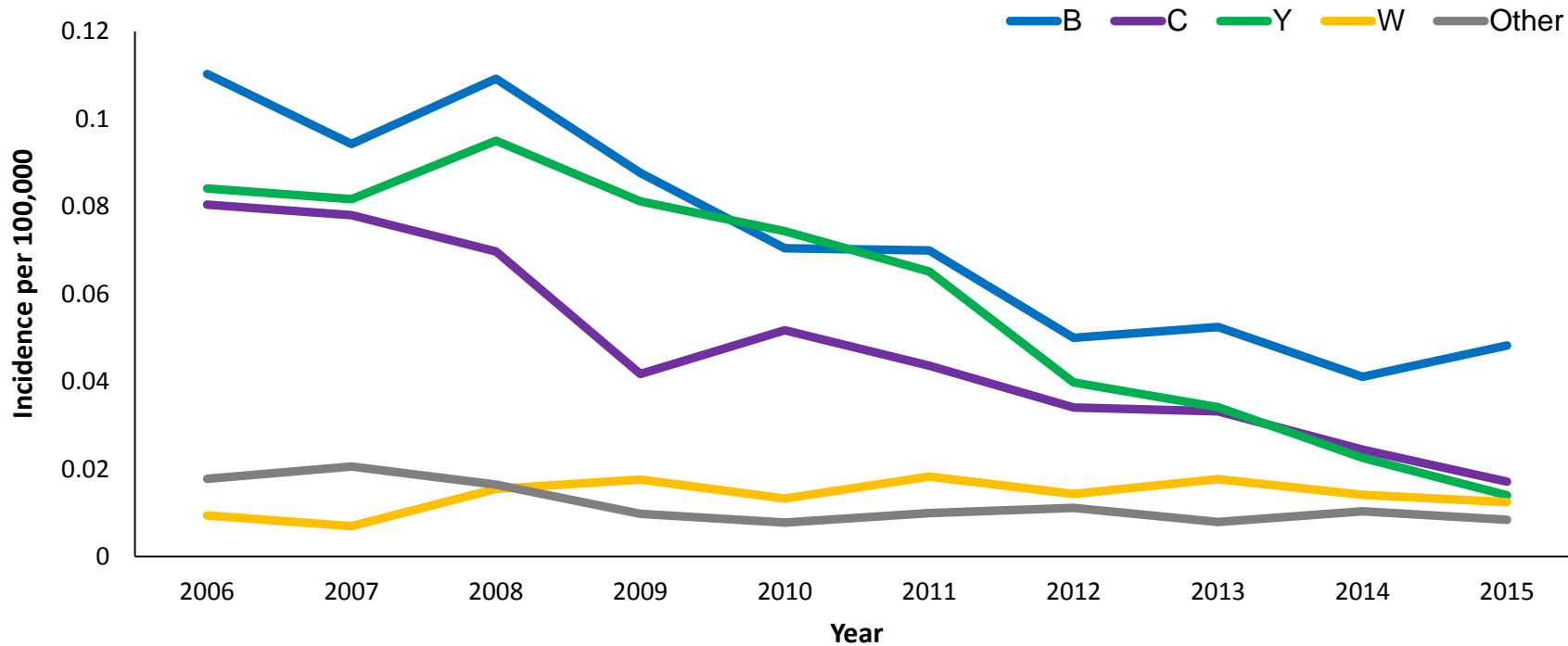
# Agenda

- Epidemiology of meningococcal disease and clusters/outbreaks in the United States
- Current guidance for the evaluation and management of meningococcal disease outbreaks
- Proposed updates to CDC meningococcal disease outbreak guidance
- Next steps

# Meningococcal Disease Incidence – United States, 1996-2015

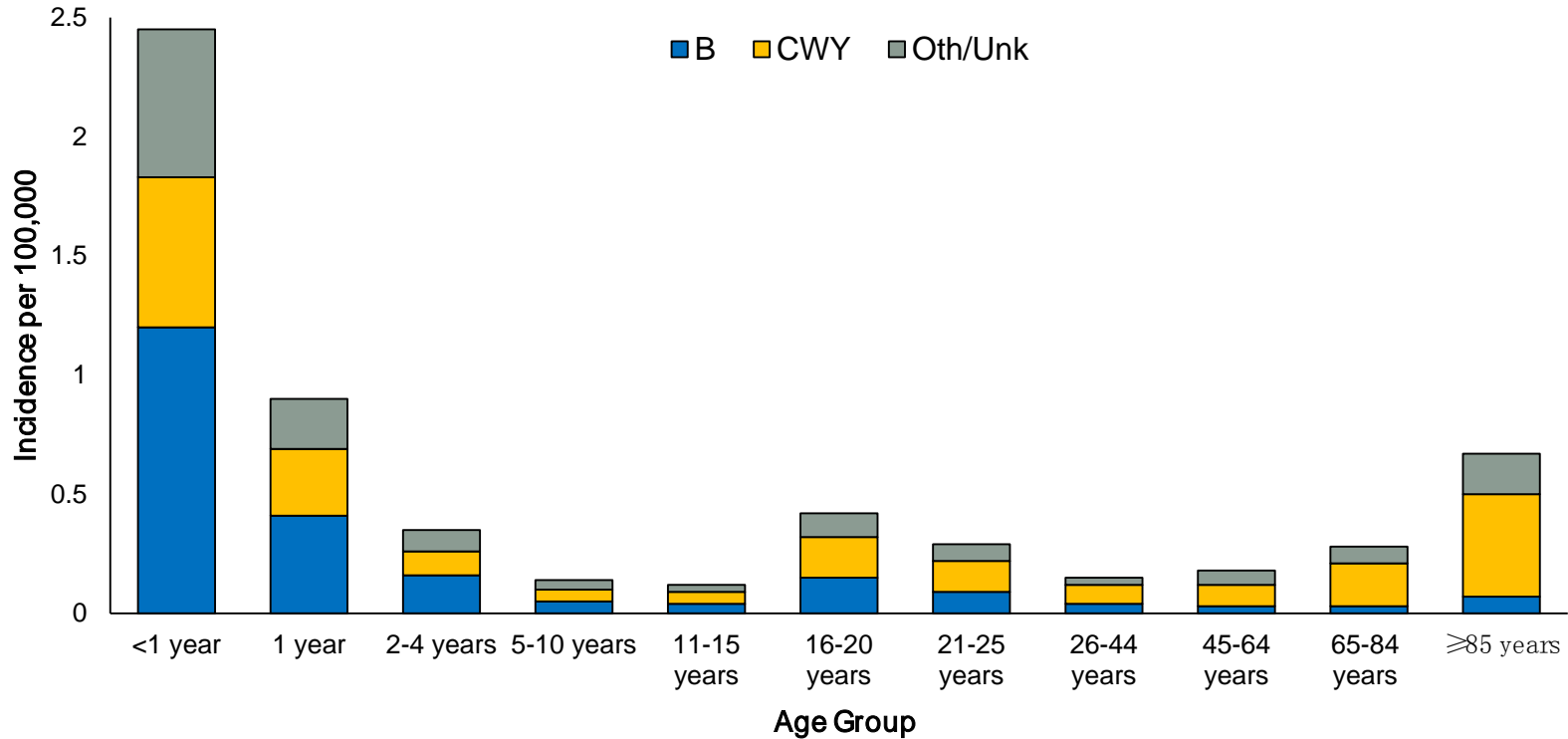


# Trends in Meningococcal Disease Incidence by Serogroup – United States, 2006-2015



Source: National Notifiable Diseases Surveillance System (NNDSS) data with additional serogroup data from Active Bacterial Core surveillance (ABCs) and state health departments

# Average Annual Incidence by Age-Group and Serogroup—United States, 2006-2015



# Clusters/Outbreaks of Meningococcal Disease in the U.S.

- Information on outbreak associated cases is collected through the National Notifiable Diseases Surveillance System (NNDSS), but reporting is likely incomplete.
- CDC conducted a retrospective review of all meningococcal disease cases from 2009-2013 to identify and characterize clusters/outbreaks.
  - Cluster: 2 cases of the same serogroup within 3 months
  - Outbreak:  $\geq 3$  cases of the same serogroup and attack rate (AR) of  $>10$  cases/100,000 population within 3 months
  - Classified as organization (common affiliation other than shared geography) or community-based (no other affiliations besides shared geography)
- From 2009-2013, of the 3,683 cases reported to NNDSS, 195 (5.3%) were primary cases associated with 41 clusters.

# Summary of Clusters/Outbreaks\* in the United States, 2009-2013

Type	Number	Max Cases	Median Cumulative Attack Rate‡
Community			
MSM#	2	22	12.4
Non-MSM#	20	14	1.0
Organization			
University	9	10	47.6
Other†	10	8	44.4
<b>Total</b>	<b>41</b>	<b>22</b>	<b>8.3</b>

\* Excludes clusters from Texas as different criteria for defining clusters was used.

# MSM = Men who have sex with men

‡ Among clusters with known population size

† Includes correctional facility, health-care facility, high-school, sports camp, etc.

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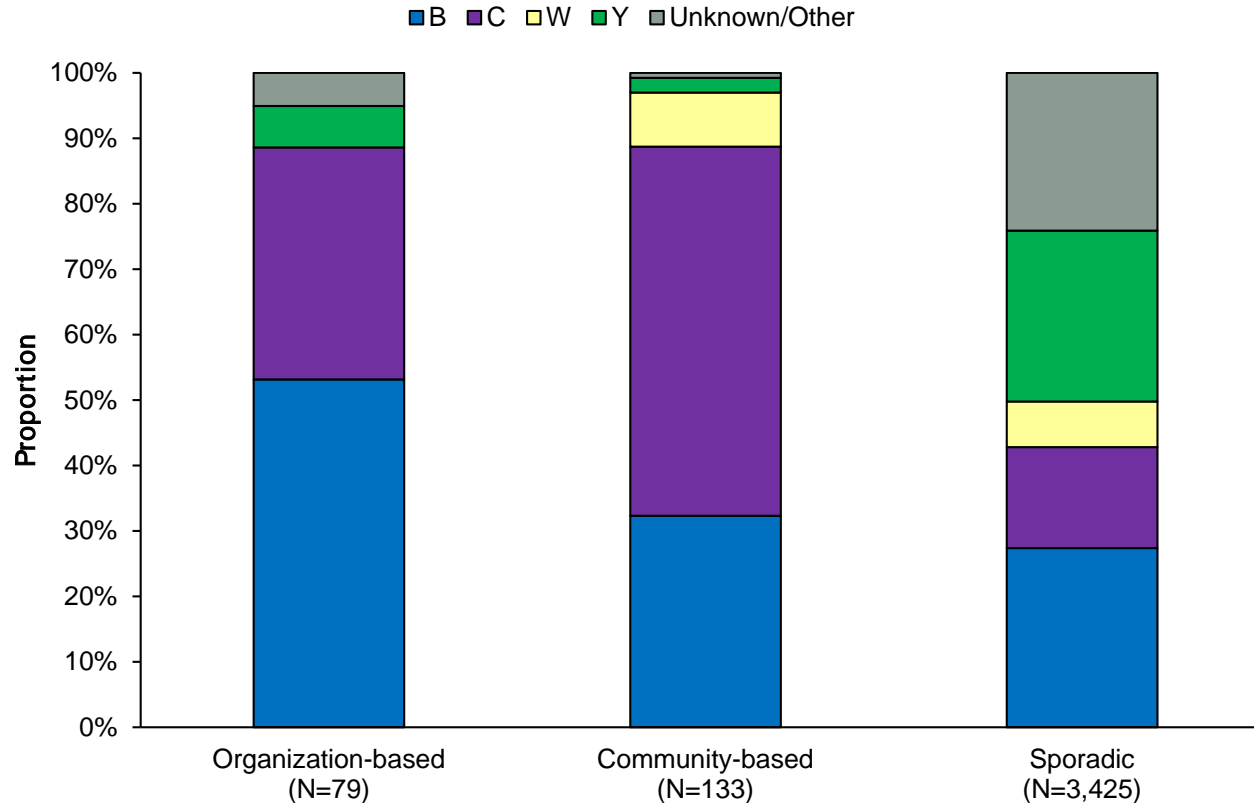
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# Serogroup Distribution of Organization-Based Cluster/Outbreak-Associated vs. Sporadic Meningococcal Disease Cases, 2009-2013



# University Based Serogroup B Clusters/Outbreaks<sup>†</sup>, 2008–2016

State of University Location	Outbreak Period	Cases (deaths)	# Undergraduates
Ohio	Jan 2008 – Nov 2010	13 (1)	24,000
Pennsylvania	Feb – Mar 2009	4	10,000
Pennsylvania	Nov 2011	2	5,000
New Jersey	Mar 2013 – Mar 2014	9 (1)	5,000
California	Nov 2013	4*	18,000
Rhode Island	Jan – Feb 2015	2	4,000
Oregon	Jan – May 2015	7 (1)	20,000
California	Jan – Feb 2016	2**	5,000
New Jersey	Mar – Apr 2016	2	35,000
Wisconsin	Oct 2016	3	30,000
Oregon	Nov 2016	2	25,000

MenB Vaccination

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

# Serogroup C Meningococcal Disease Clusters/Outbreaks<sup>†</sup> Among Men Who Have Sex With Men, 2010-2017

Jurisdiction	Outbreak Period	Number of cases (deaths) among MSM	
New York City	Aug 2010 – Feb 2013	22 (7)	} MenACWY vaccination
Los Angeles	Oct 2012 – Sep 2014	10 (4)	
Chicago*	June 2015 – Sep 2016	11 (1)*	
Southern California	Mar – Sep 2016	21 (2)	
Miami	Sep 2016 – Jan 2017	3 (1)	

<sup>†</sup>Where CDC consulted; \*Includes one case identified among a resident of a different state who had epi-links to Chicago

## Summary: Epidemiology of Meningococcal Disease

- Rates of disease have declined from approximately 1 to 0.1 cases/100,000 population in the past 20 years.
  - Decline seen in all serogroups, including serogroup B.
- Each cluster/outbreak is unique with wide range in number of cases, population size and characteristics, and duration.
  - Creates challenges in applying guidance for the control of meningococcal disease outbreaks.
- In recent years, several serogroup B outbreaks in universities and serogroup C outbreaks among MSM populations have been reported.

# **Guidance for the Evaluation and Management of Meningococcal Disease Outbreaks:**

## **Current Guidance and Proposed Updates**

# Guidance for Evaluation and Management of Meningococcal Disease Outbreaks in the U.S.

- **Published guidance:** Originally developed in 1997 and updated in 2013 in Appendix B of the ACIP “Prevention and Control of Meningococcal Disease” statement.
- **Interim guidance:** Developed in 2014 for the control of serogroup B outbreaks in organizational settings prior to licensure of MenB vaccines in the U.S.

<sup>1</sup> Centers for Disease Control and Prevention. Prevention and Control of Meningococcal Disease; Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2013;62(No. RR-#2): 1-28.

<sup>2</sup>[www.cdc.gov/meningococcal/downloads/interim-guidance.pdf](http://www.cdc.gov/meningococcal/downloads/interim-guidance.pdf)



# Key Components of Meningococcal Disease Outbreak Guidance

- Cases to be included in the case count for vaccine decision-making
- Population: organization- and community-based outbreaks
- Outbreak thresholds and the decision to vaccinate
- Defining the vaccination group
- Role of molecular genotyping
- Other control measures (e.g., mass chemoprophylaxis)

# Updated Guidance for the Evaluation and Management of Meningococcal Disease Outbreaks

- Current guidance developed under different epidemiologic context and prior to the availability of conjugate MenACWY or MenB vaccines.
- Several recent outbreaks have identified challenges in managing outbreaks using the current guidance.
- State and local health departments expressed a need for updated guidance better adapted to the current situation.

# Updated Guidance for the Evaluation and Management of Meningococcal Disease Outbreaks

- Objective: Update and harmonize guidance for the investigation and public health management of meningococcal disease outbreaks due to all serogroups.
- Activities:
  - Experts consulted from September 2015-March 2016 to review current guidance, available data, and challenges in managing outbreaks using current guidance.
  - Review of the literature to describe the use and impact of meningococcal vaccines in outbreak settings.

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- Population: organization- and community-based outbreaks
- Outbreak thresholds and the decision to vaccinate
- Defining the vaccination group
- Role of molecular genotyping
- Other control measures (e.g., mass chemoprophylaxis)
- Serogroup B vaccine selection based on expected vaccine coverage against an outbreak strain
- Re-evaluation of outbreak status

# **Cases to Include for Vaccine Decision-Making and the Role of Molecular Genotyping**



# Current Guidance: Cases to Include for Vaccine Decision-Making and the Role of Genotyping

- Only primary cases of the same serogroup should be included in case count for vaccine decision-making, as primary cases indicate ongoing transmission:
  - Primary case: case that occurs in the absence of previous known close contact with another patient.
  - Co-primary or secondary case: case that occurs among close contacts of a primary case, with onset  $\leq 24$  hours (co-primary) or  $> 24$  hours (secondary) of the primary case.



# Challenges: Cases to Include for Vaccine Decision-Making

- Determining whether cases had close contact may be challenging in some populations.
- Community versus public health perception of an outbreak: may create confusion and communication challenges when some cases “don’t count.”

# Challenges: Role of Molecular Genotyping

- Serogroup alone may not be sufficient to determine whether cases are related.
- New tools for molecular typing: whole genome sequencing (WGS) provides highest resolution.
  - Role of WGS in confirming outbreaks becoming increasingly important, particularly with the availability of serogroup B vaccines.
  - However, there will continue to be cases in whom an isolate is not available.

# Proposed Guidance: Cases to Include for Vaccine Decision-Making

- Removal of classification of cases as primary, co-primary, or secondary.
- Evidence of related/identical strains by WGS not required for inclusion of cases in the case count.
  - However, if sequencing demonstrates that a case is unrelated to others in the outbreak, this case should not be included.
- **Proposed guidance:** All cases of meningococcal disease of the same serogroup are included in the case count unless there is evidence of genetically distinct strains by whole genome sequencing.

# Outbreak Thresholds and the Decision to Vaccinate

# Current Guidance: Outbreak Thresholds and the Decision to Vaccinate

Guidance	Outbreak Threshold
Published	3 cases with attack rate > 10 cases/100,000 population in 3 months
Interim	2 cases in pop <5,000 and $\geq 3$ cases in pop $\geq 5,000$ in 6 months ( <i>serogroup B organization-based outbreaks only</i> )

# Challenges: Outbreak Thresholds and the Decision to Vaccinate

- Meningococcal outbreaks are not “one size fits all”; there is a need for flexibility to evaluate each outbreak on a case-by-case basis.
- The threshold of 10 cases/100,000 is ~100 times higher than U.S. national incidence; however, in the absence of data, difficult to define a more appropriate threshold.
  - Situations occur in which outbreak threshold not reached despite a clear need for intervention (i.e., 2016 serogroup C outbreak among MSM in California, with 21 cases and attack rate of ~6 cases/100,000.)
- Little tolerance for additional cases viewed as preventable.
- Attack rates are challenging to calculate in community outbreaks and outbreaks among special populations due to difficulty in defining the denominator.

# Proposed Guidance: Outbreak Thresholds

- **Proposed guidance:** Each outbreak should be evaluated on a case-by-case basis to determine threshold for vaccination. In general:
  - Organization-based: 2-3 cases of meningococcal disease of the same serogroup within 3 months.
  - Community-based: Incidence of meningococcal disease of the same serogroup that is above expected in the affected community during a 3-month period.

# Proposed Guidance: Decision to Vaccinate

- **Considerations for vaccine decision-making:**
  - Size of population
  - Ability to define a target group for vaccination
  - Whether ongoing transmission is likely or if cases likely represent a single transmission event (i.e., household contacts, roommate, boyfriend/girlfriend)
  - Feasibility of a vaccination campaign
  - Timing of potential vaccination in relation to cases



# Serogroup B Vaccine Selection and Coverage of Outbreak Strain

# Current guidance: MenB Vaccine Selection

- Current guidance: None (no MenB vaccines available at time of writing.)

# Challenges: MenB Vaccine Selection

- Unlike conjugate MenACWY vaccines, MenB vaccines induce an immune response to subcapsular proteins, which vary by strain.
- While WGS can identify the presence of MenB vaccine antigens in the outbreak strain, it cannot determine expression of the antigens or expected coverage by MenB vaccines against a particular outbreak strain.
- There are challenges to conducting additional testing to determine coverage against the outbreak strain in real-time during an outbreak.

# Proposed Guidance: MenB Vaccine Selection

- **Proposed guidance:**
  - Identification of MenB vaccine antigens by molecular characterization should not drive the choice of MenB vaccine (MenB-FHbp or MenB-4C) during an outbreak of meningococcal disease at this time.
  - No vaccine preference for outbreak control:
    - MenB-4C: 2-dose schedule
    - MenB-FHbp: 3-dose schedule

# Re-evaluation of Outbreak Status

# Current Guidance: Re-evaluation of Outbreak Status

- No current guidance on when to declare an outbreak as being “over.”

# Challenges: Re-evaluation of Outbreak Status

- Meningococcal disease epidemiology is dynamic and unpredictable, with outbreak-associated cases sometimes reported months after the last known case.
- Public health officials need guidance on how long to continue vaccination and other public health interventions.
  - i.e., after vaccinating undergraduates at a university with MenB vaccine, do incoming freshman the following year need to be vaccinated?
- Prematurely declaring an outbreak as being “over” can erode public trust if further cases are identified.

# Proposed Guidance: Re-evaluation of Outbreak Status

- Because of the unique epidemiology of meningococcal disease outbreaks, it is difficult to declare an outbreak as being “over.”
- **Proposed guidance:** For public health decision-making, after one year without any new reported cases, the risk of meningococcal disease likely returns to baseline.



# Summary of Updated Guidance

- **Case count for vaccine decision-making:** All cases of meningococcal disease of the same serogroup are included unless there is evidence of genetically distinct strains by whole genome sequencing.
- **Outbreak threshold for vaccine decision-making:** Each outbreak should be assessed on a case-by-case basis, though in general:
  - Organization-based: 2-3 cases of the same serogroup within 3 months.
  - Community-based: Incidence of the same serogroup above expected in the affected community during a 3-month period.
- **MenB vaccine selection:** No preference between MenB vaccines during outbreaks.
- **Re-evaluation of outbreak status:** After one year without any new reported cases, the risk of meningococcal disease likely returns to baseline.

## Next Steps

- Finalization of CDC guidance document for control of meningococcal disease outbreaks.
- Publication of updated guidance document on CDC website, to replace current guidance in Appendix B of ACIP's "Prevention and Control of Meningococcal Disease" and the interim guidance for MenB outbreaks.
- Continued efforts to improve reporting and collection of epidemiologic data of meningococcal disease outbreaks.

# Acknowledgements

## State and local health departments

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Cody Meissner

Barbara Montana

Jeffry Moore

Paul Offit

Georges Peter

Anuja Rastogi

Lorry Rubin

William Schaffner

David Stephens

Tina Tan

Don Weiss

Margaret Yacovone

Jane Zucker

Alison Albert

Amy Blain

Virginia Bowen

Elizabeth Briere

Amanda Cohn

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# Thank You

For more information, contact CDC  
1-800-CDC-INFO (232-4636)  
TTY: 1-888-232-6348 [www.cdc.gov](http://www.cdc.gov)

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