Meningococcal Disease Epidemiology and Serogroup B Outbreaks

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GA EIP Day

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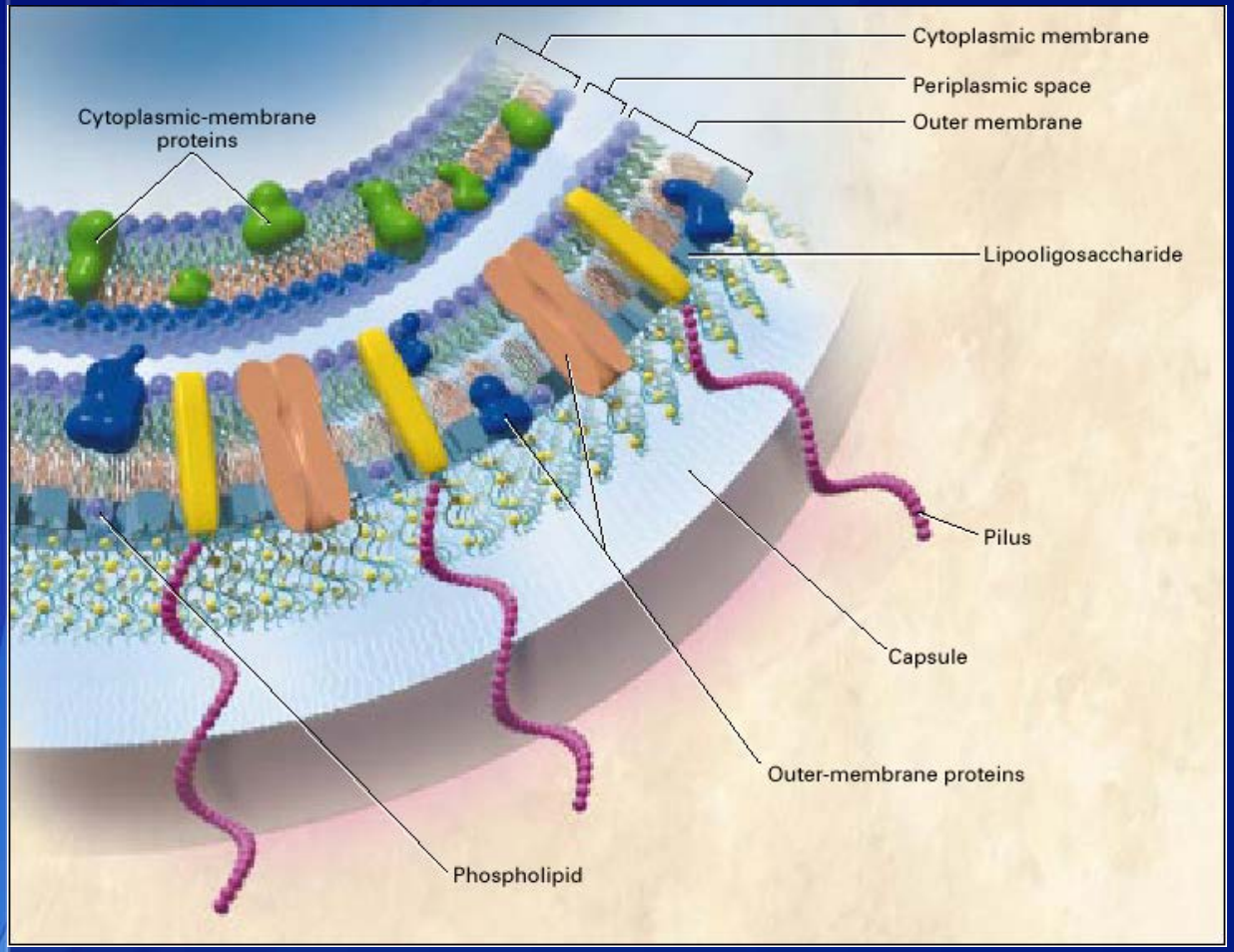
Overview

- Overview of meningococcal disease
- Epidemiology and burden of disease
- Recent outbreaks on college campuses
- Prevention and management

Meningococcal Disease

- **Three syndromes:**
  - Meningitis
  - Bloodstream infection
  - Pneumonia
- **“Flu-like” symptoms early**
- **Rapidly progressive**
- **High morbidity and mortality**
  - 10-15% die
  - 11-19% have long-term disability
- **Most disease occurs in healthy people**

Neisseria meningitidis bacteria



Capsule

- 13 types
- 6 cause most disease globally (A, B, C, W, X, and Y)
- Target for conjugate vaccines

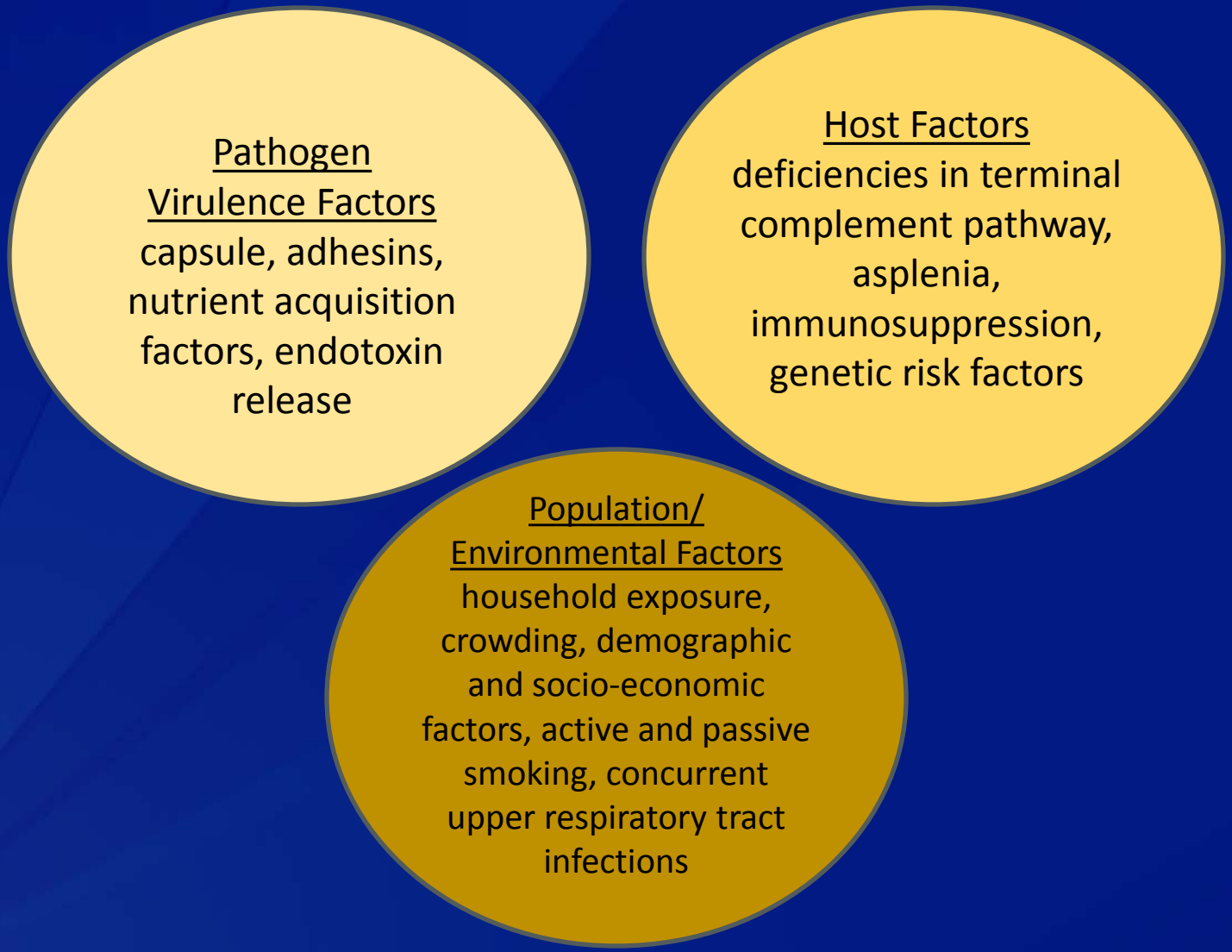
Outer-membrane proteins

- targets for serogroup B vaccines

Nasopharyngeal Carriage

- **Carried as part of the commensal microbiota in the upper respiratory tract of humans**
- **5-10% of the population are carriers**
  - Adolescents and young adults have highest carriage rates
- **<1% of persons exposed who become carriers develop invasive disease**
- **Carriage is asymptomatic and transient**
- **Level of carriage does not predict the course of the outbreak**

Meningococcal Disease Risk Factors



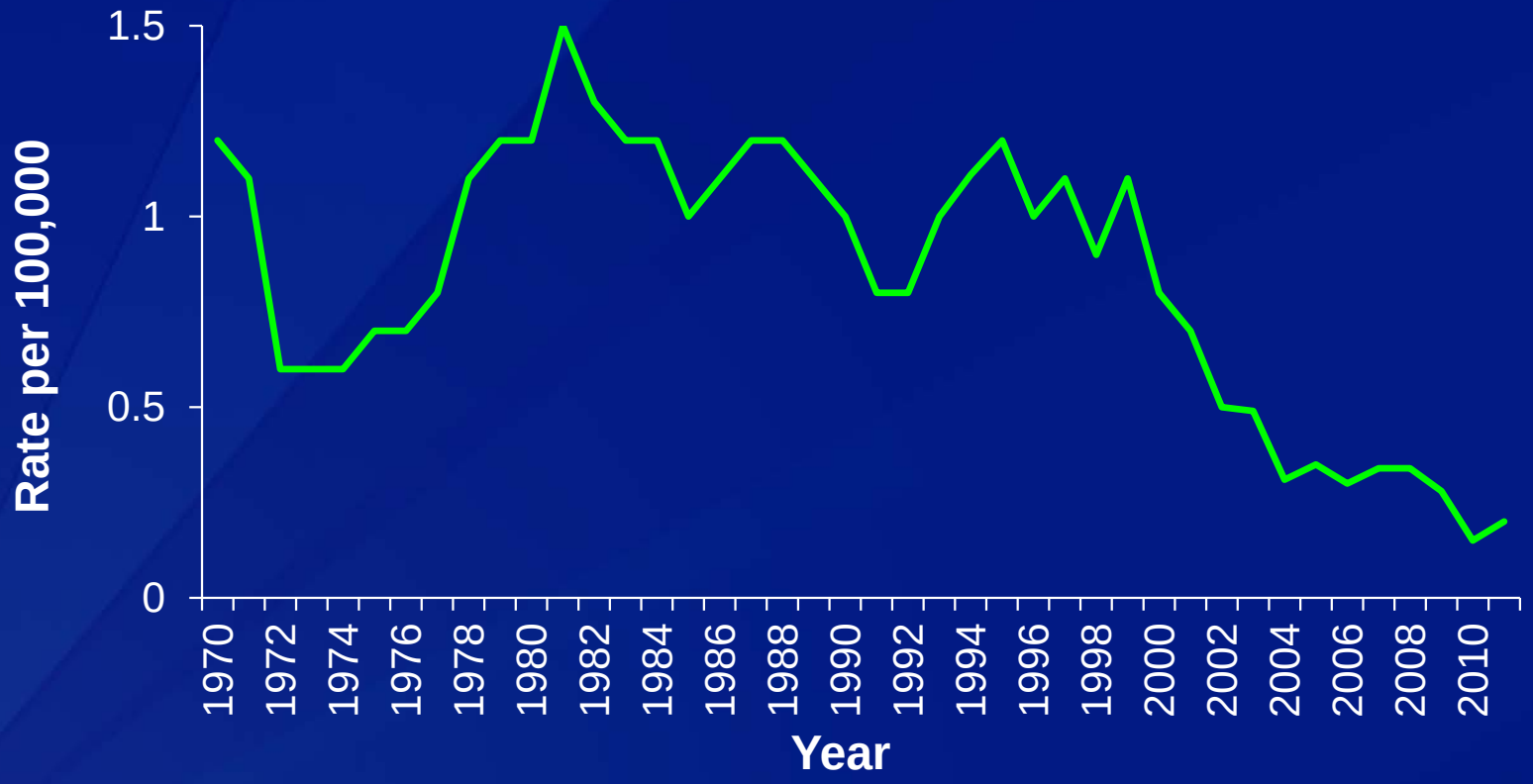
EPIDEMIOLOGY AND BURDEN OF MENINGOCOCCAL DISEASE

Meningococcal Disease Incidence by Country/Region

Country/Region	Incidence per 100,000	Predominant Serogroup(s)	Year
African meningitis belt	10-1,000 (during epidemics)	A	n/a
New Zealand	2.4	B	2010
Australia	1.2	B	2009
Europe	0.92	B, C	2009
Chile	0.5	B, C	2010
Argentina	0.6	B, W	2008
Canada	0.47	B, C	2008
United States	0.28	B, C, Y	2009

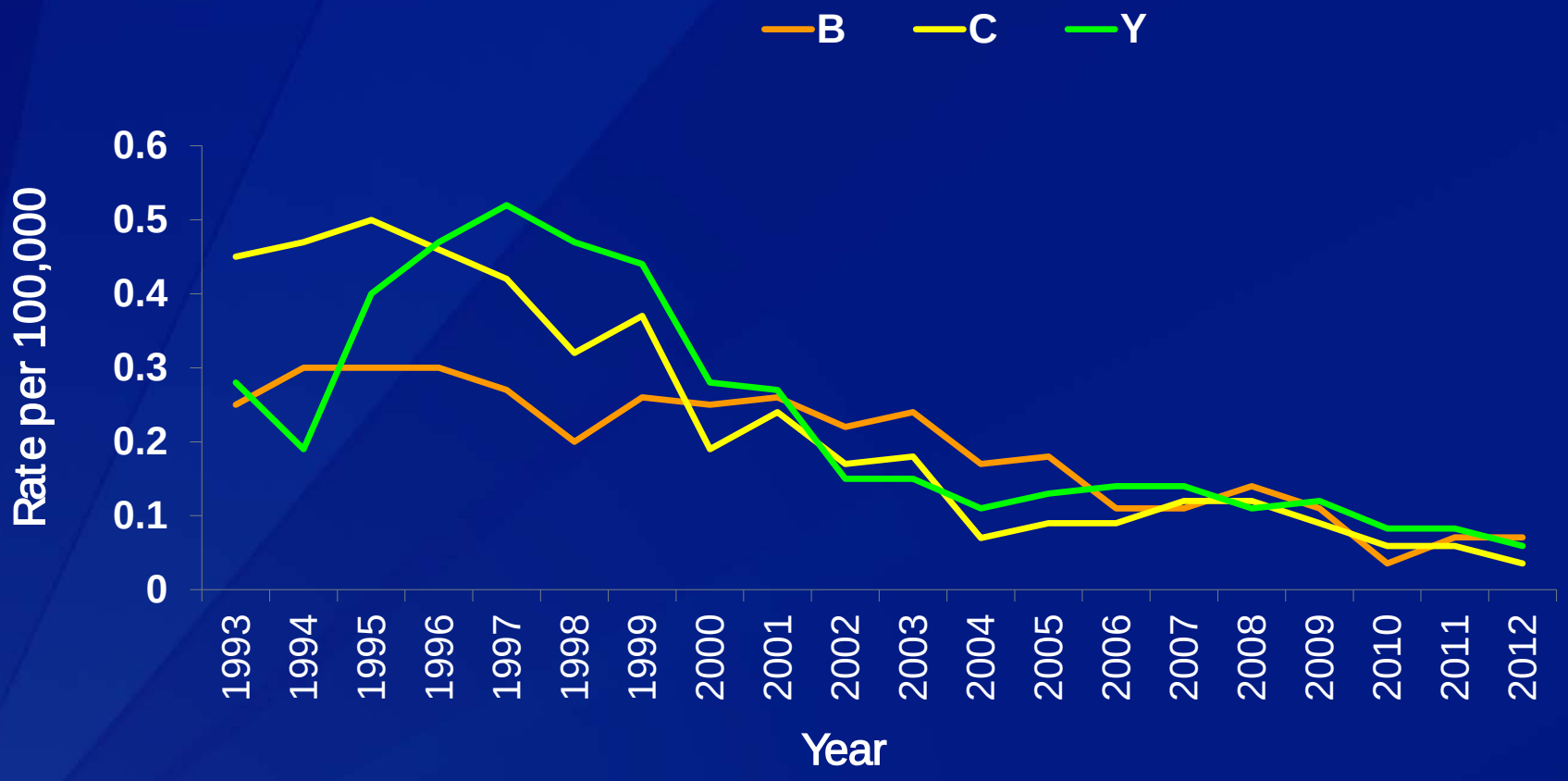
S.A. Halperin, et al. The changing and dynamic epidemiology of meningococcal disease. Vaccine 30S (2012): B26-B36.

Meningococcal Disease Incidence, United States, 1970-2011



1970-1996 NNDSS data, 1997-2011 ABCs data estimated to U.S. population

Meningococcal Disease Incidence by Serogroup, United States, 1993-2012*



*Source: ABCs cases from 1993-2012 estimated to the U.S. population with 18% correction for under reporting

Case-Fatality Ratio by Serogroup and Age-Group, United States, 1997-2011

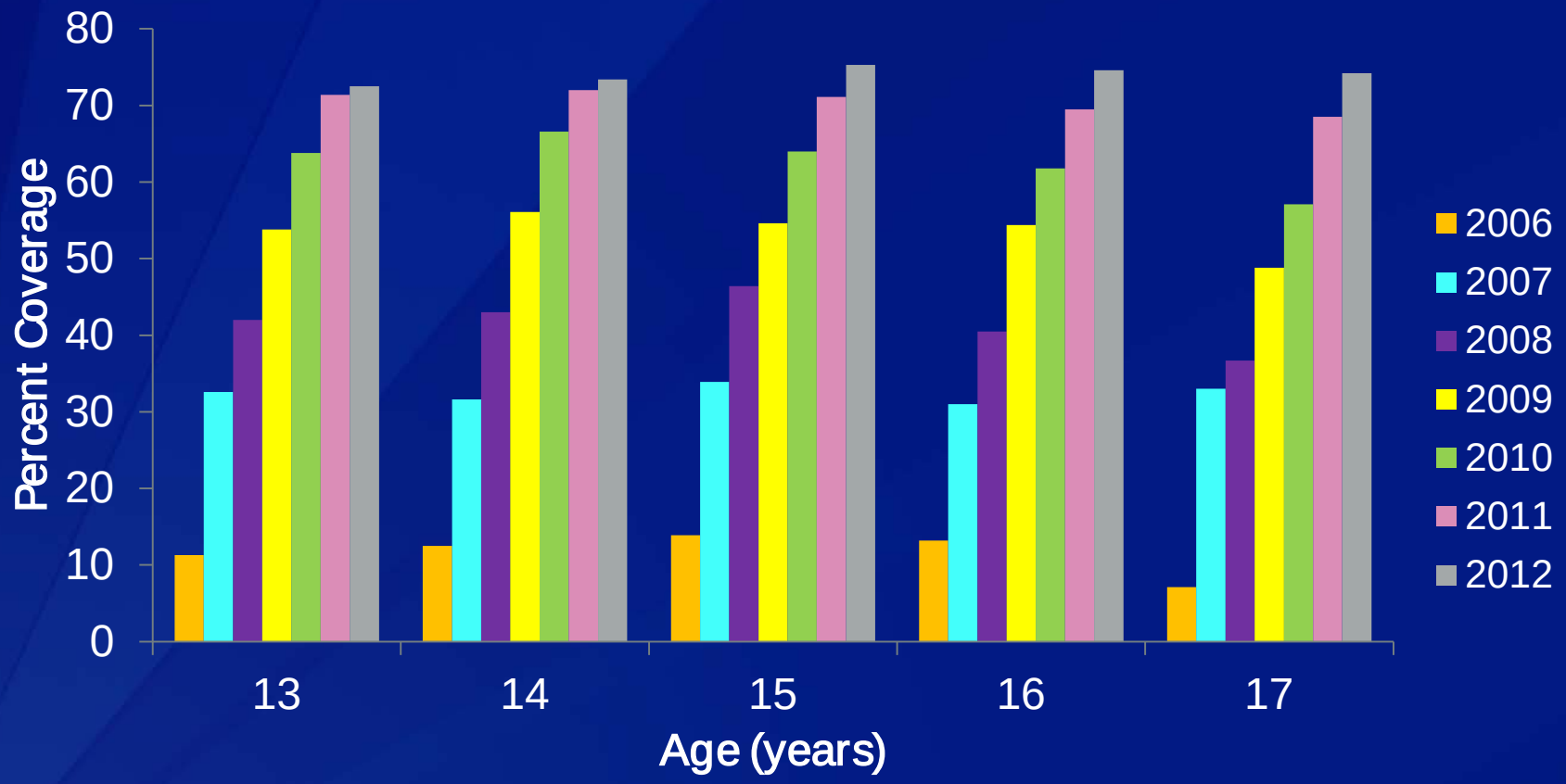
Serogroup	<5 years	5-10 years	11-19 years	20 years	Total
B	4%	22%	15%	23%	13%
C	13%	9%	12%	16%	13%
Y	0%	13%	13%	12%	10%
W135	<1%	0%	0%	10%	7%
Total	5%	12%	15%	15%	12%

ABCs cases from 1997-2011 estimated to the US population

Licensed Meningococcal Vaccine Products, U.S.

Vaccine	Type	Manufactur	Serogroups	Ages
Menactra®	Conjugate – Diptheria toxoid	Sanofi Pasteur	A, C, W, Y	9 months—55 years
Menveo®	Conjugate - CRM_{197}	Novartis Vaccines	A, C, W, Y	2 months—55 years
MenHibRix®	Conjugate – Tetanus toxoid	GSK Vaccines	C, Y	6 weeks—18 months
Menomune®	Polysaccharide	Sanofi Pasteur	A, C, W, Y	≥2 years

Coverage of 1-dose MenACWY among 13-17 year-olds, NIS-Teen, 2006-2012



*Coverage was 74% in 2012

National Immunization Survey – Teen
In 2012, MenACWY coverage varied from 37.5%-94.3% by state

Rates of Serogroup C,Y,W Meningococcal Disease*

Year	Rate per 100,000 (95% confidence intervals)	
	11-19 year-olds	≥20 year-olds
2004 and 2005	0.27 (0.17, 0.39)	0.17 (0.14, 0.21)
2006 and 2007	0.31 (0.21, 0.45)	0.23 (0.19, 0.28)
2008 and 2009	0.15 (0.08, 0.26)	0.23 (0.19-0.27)
2010 and 2011	0.05 (0.02, 0.12)	0.14 (0.11-0.28)

- Decreasing incidence in 11-19 y.o.

CDC. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2013; **62(RR02)**.

Meningococcal Vaccine Effectiveness: Enrolled Cases and Controls by Serogroup

	Serogroup C	Serogroup Y	Serogroup W	Total
Eligible Cases	151	140	25	316
Enrolled Cases	88 (58%)	79 (56%)	13 (52%)	180 (57%)
Number of Controls Matched to Each Enrolled Case:				
0	38	44	8	90 (50%)
1	15	16	4	35 (19%)
2	11	6	1	18 (10%)
3	7	3	0	10 (6%)
4 +	16	10	0	26 (14%)
Total Controls	127	79	6	

Time to Failure After 1 Dose of Menactra®

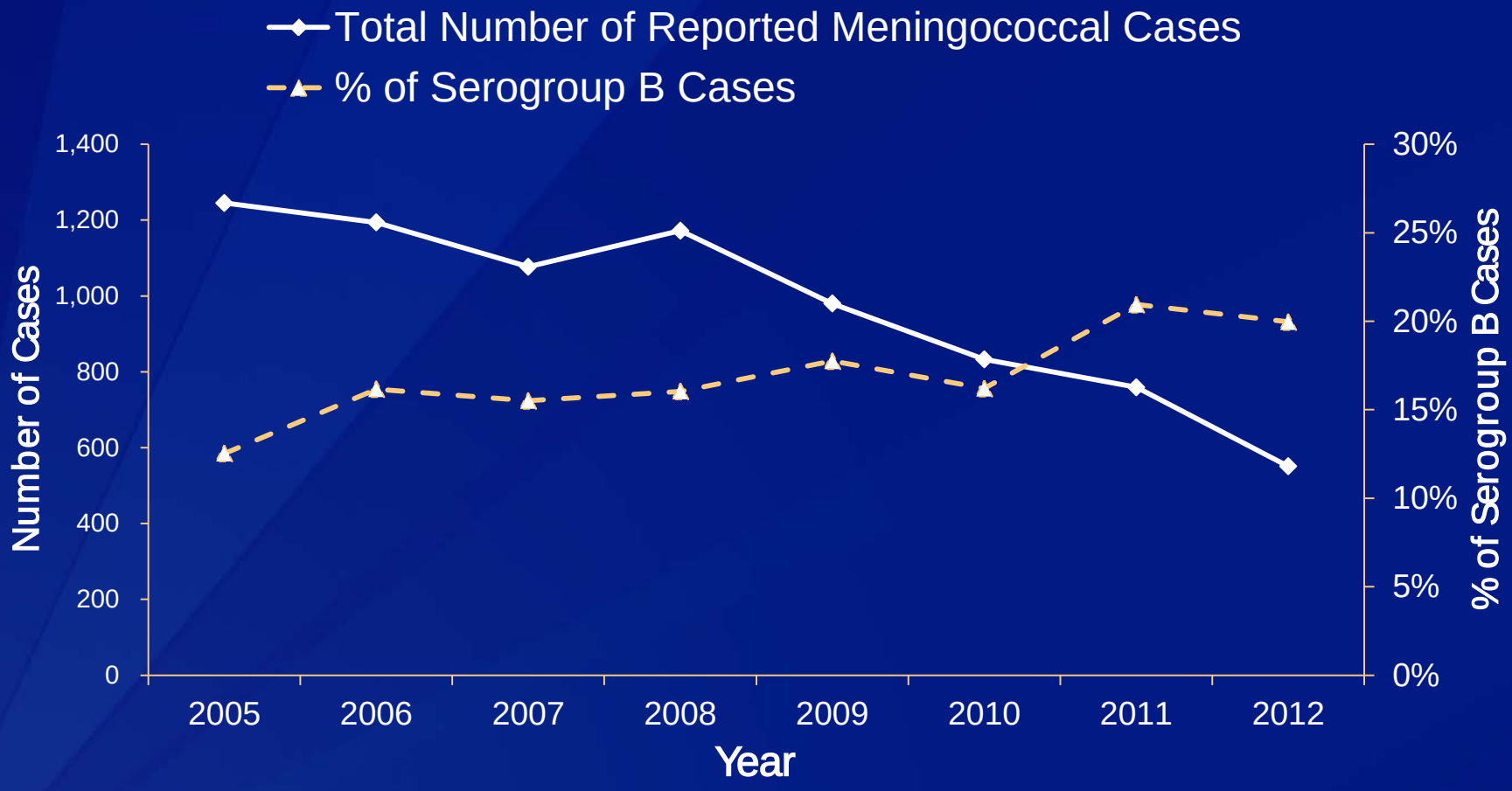
	Serogroup C	Serogroup Y	Serogroup W
Vaccinated <1 year	3	3	0
Vaccinated 1-<3 years	7	8	1
Vaccinated 3-<7 years	4	11	0

Menactra® VE Estimates, Duration of Protection, GEE

	All Adolescents
	VE (95% CI)
Vaccinated 0-7 years	67% (49%, 79%)
Serogroup C	75% (54%, 87%)
Serogroup Y	49% (0%, 74%)
Vaccinated <1 year (n=26)	76% (43%, 90%)
Vaccinated 1-<3 years (n=57)	70% (46%, 84%)
Vaccinated 3-<7 years (n=48)	61% (25%, 80%)

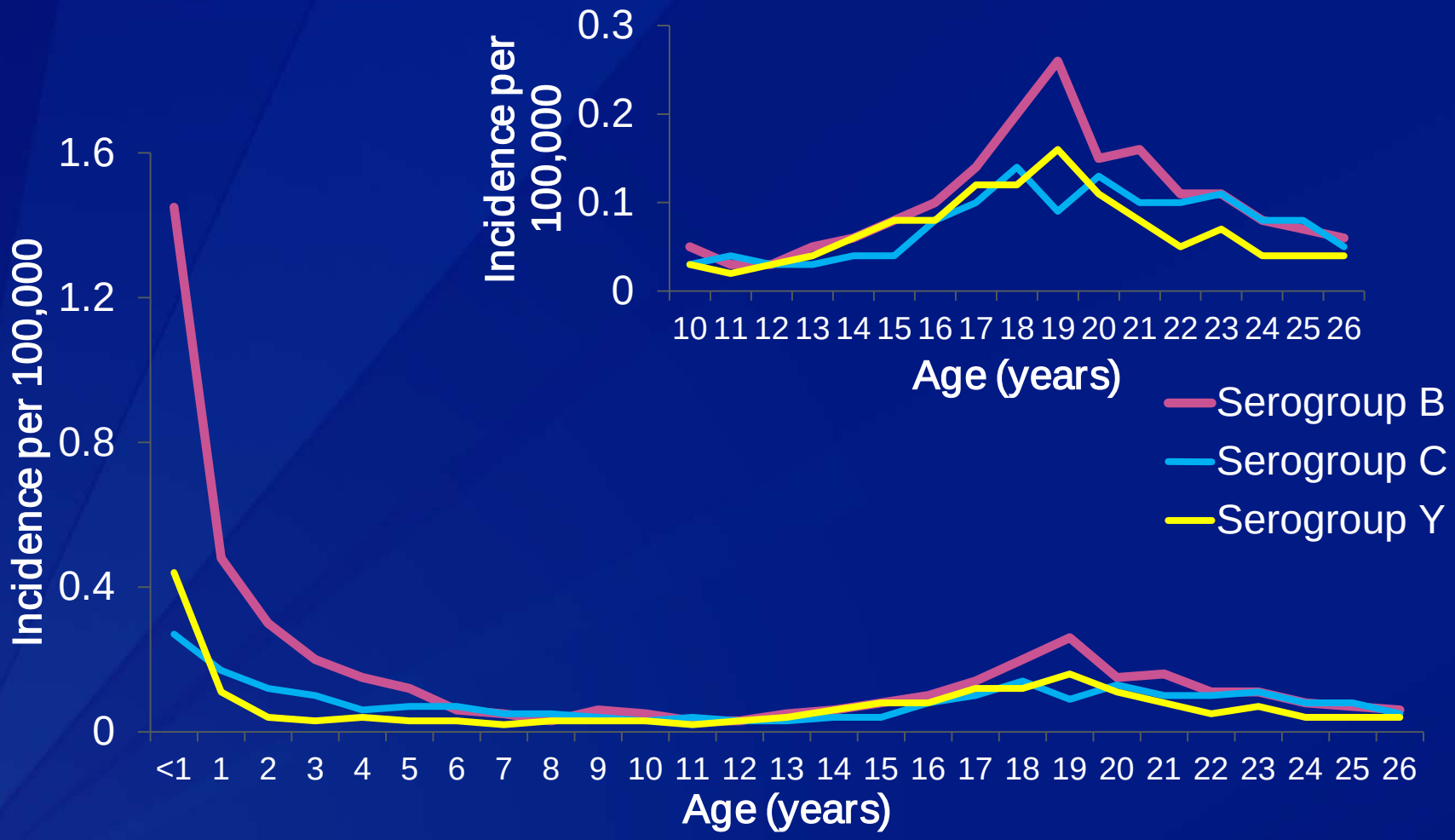
Controls for smoking, underlying condition status, and age

Epidemiology of Serogroup B Meningococcal Disease - United States 2005-2012



*Source: National Notifiable Diseases Surveillance System (NNDSS) with additional serogroup data provided by state and local health departments

Incidence of Meningococcal Disease by Age and Serogroup, United States, 2005-2012



RECENT OUTBREAKS ON COLLEGE CAMPUSES

Meningococcal Disease Outbreaks

- **Only ~2% of US cases are outbreak related**
- **Definition**
  - Organization-based
    - Common affiliations but no close contact
    - Schools, universities, prisons
    - 2-3 cases of the same serogroup in <3 mos; attack rate of 10/100,000
  - Community-based
    - Same area but not close contact or affiliations
    - Towns, cities, counties
    - 3 cases of the same serogroup in <3 mos; attack rate of 10/100,000

Cases of Serogroup B Meningococcal Disease, ABCs, 2003-2012

ABCs Site	Serogroup B cases in college students	Serogroup B cases in 17-22 year olds
CA	3	5
CO	1	1
CT	0	2
GA	2	7
MD	4	10
MN	5	13
NM	0	0
NY	1	4
OR	6	27
TN	1	1
Total	23	70

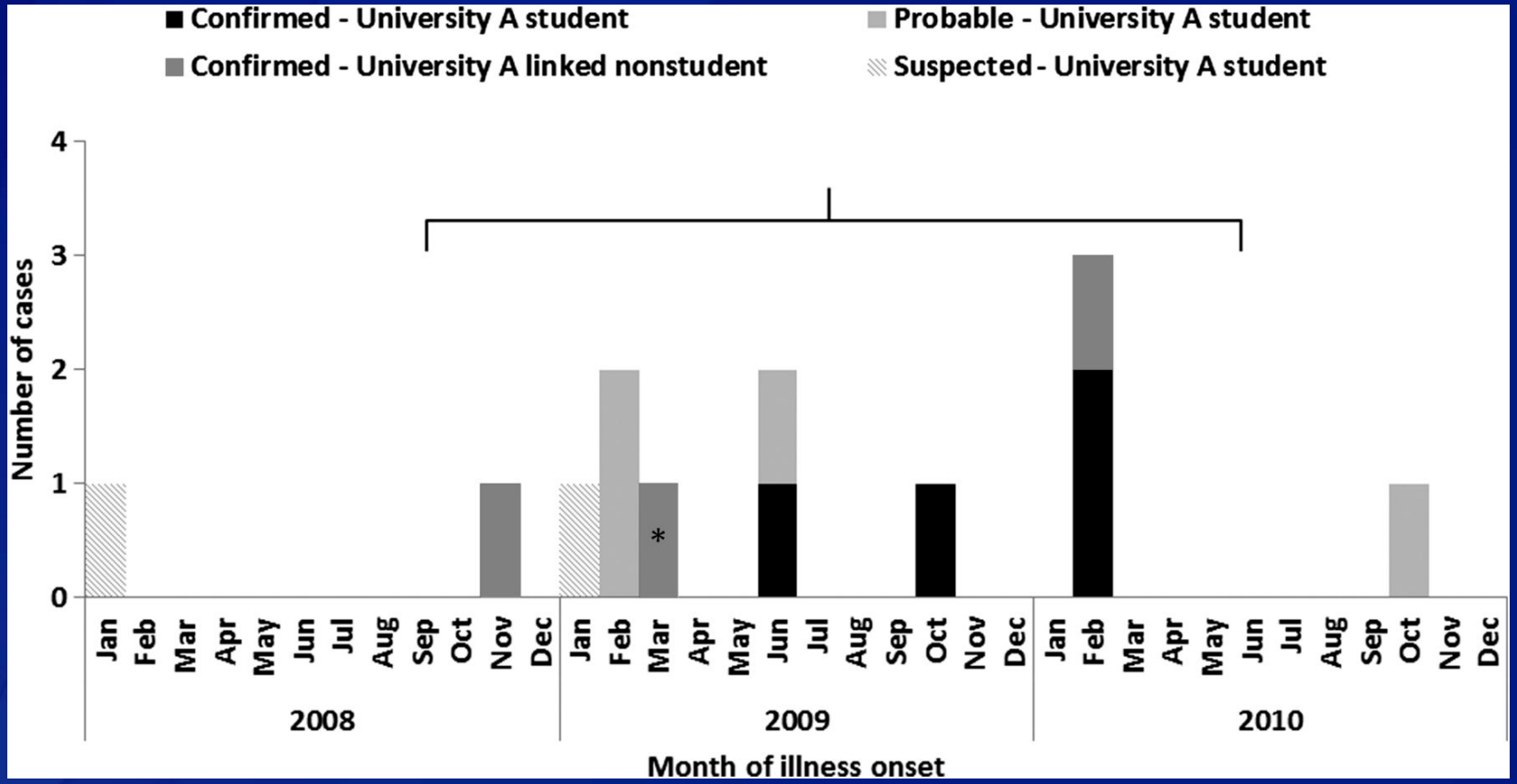
Recent School Based Serogroup B Clusters/Outbreaks*

University	Outbreak Period	Number of cases
University 1	Feb – March 2009	4
University 2	Nov 2011	2
University 3	Jan 2008 – Nov 2010	13
Princeton University	March – Nov 2013	8
University of California—Santa Barbara	Nov 2013	4

CDC defines institutional meningococcal outbreaks as 3 cases (sometimes 2 cases) in a 3 month period comprising an attack rate of ≥10/100,000

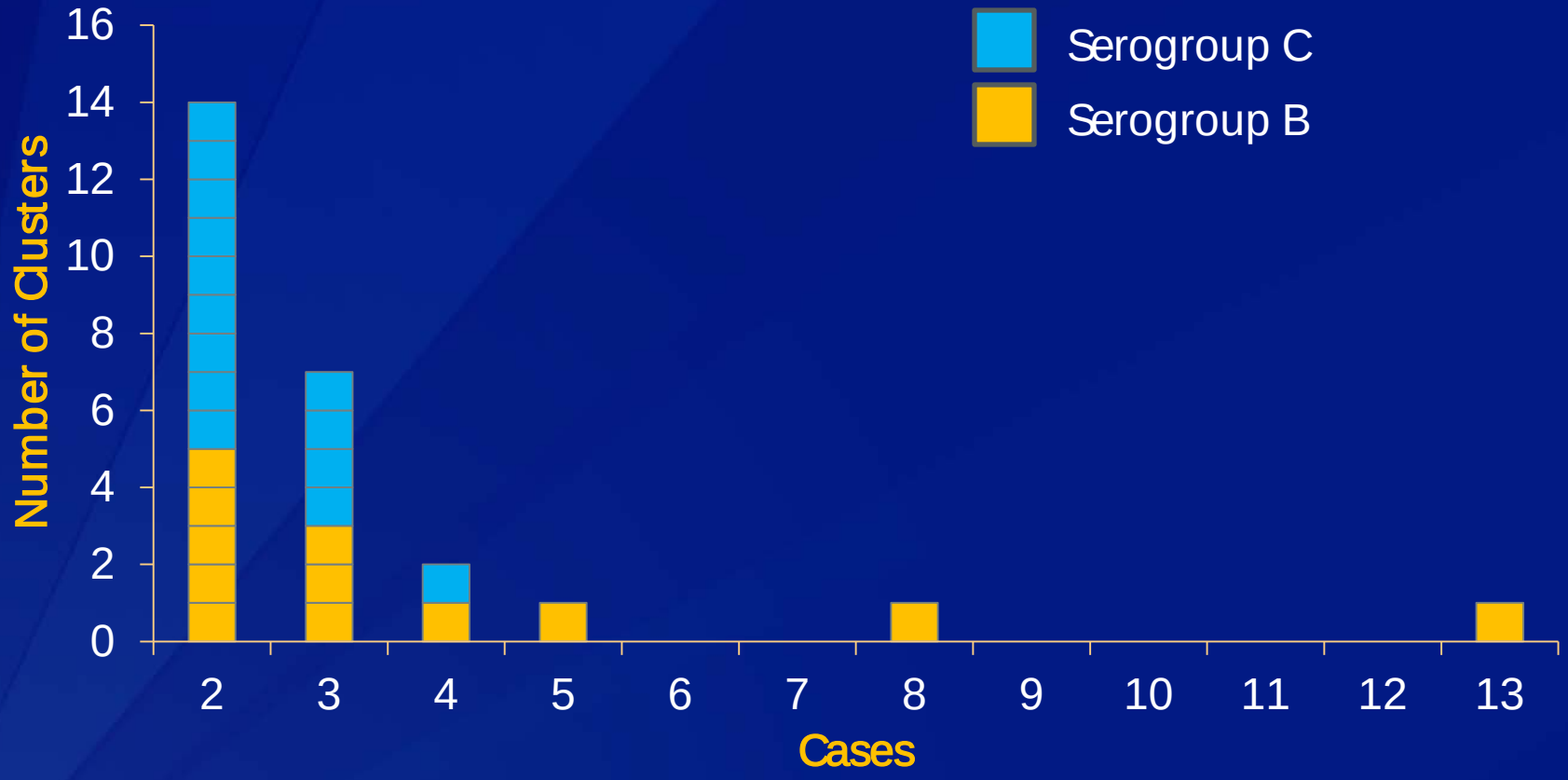
*Where CDC consulted

Epidemic curve of 13 meningococcal cases associated with University A, January 2008–December 2010.



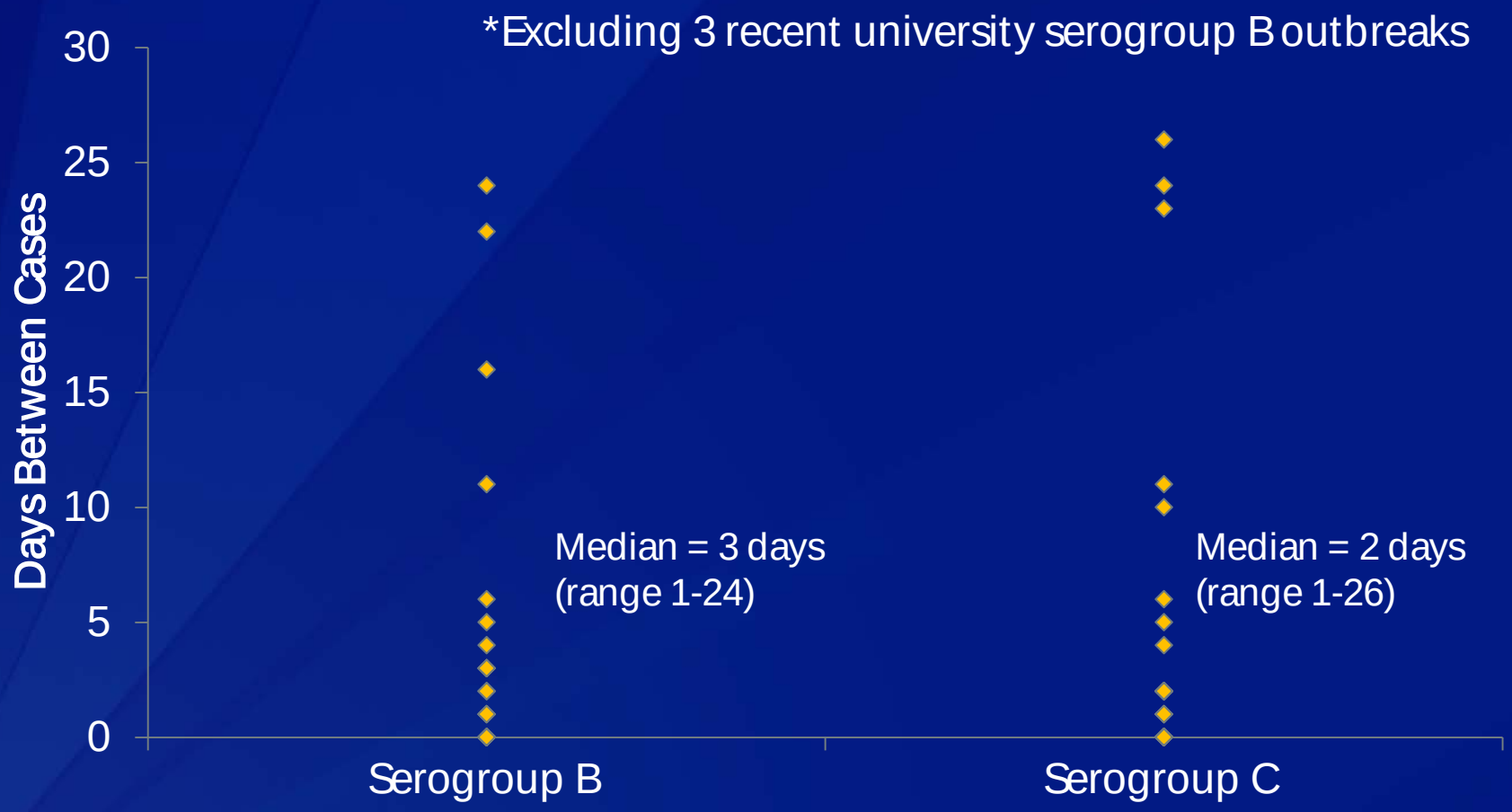
Mandal S et al. Clin Infect Dis. 2013;57:344-348

Frequency of School-Based Outbreaks by Size, Serogroup B and C



Includes 22 school based clusters reported by Zangwell et. al (serogroup B, n=7; serogroup C, n=14, serogroup Y, n=1) and recent serogroup B school-based outbreaks where CDC was consulted (n=5)

Interval Between Reported Cases in School-Based Serogroup B or C Outbreaks



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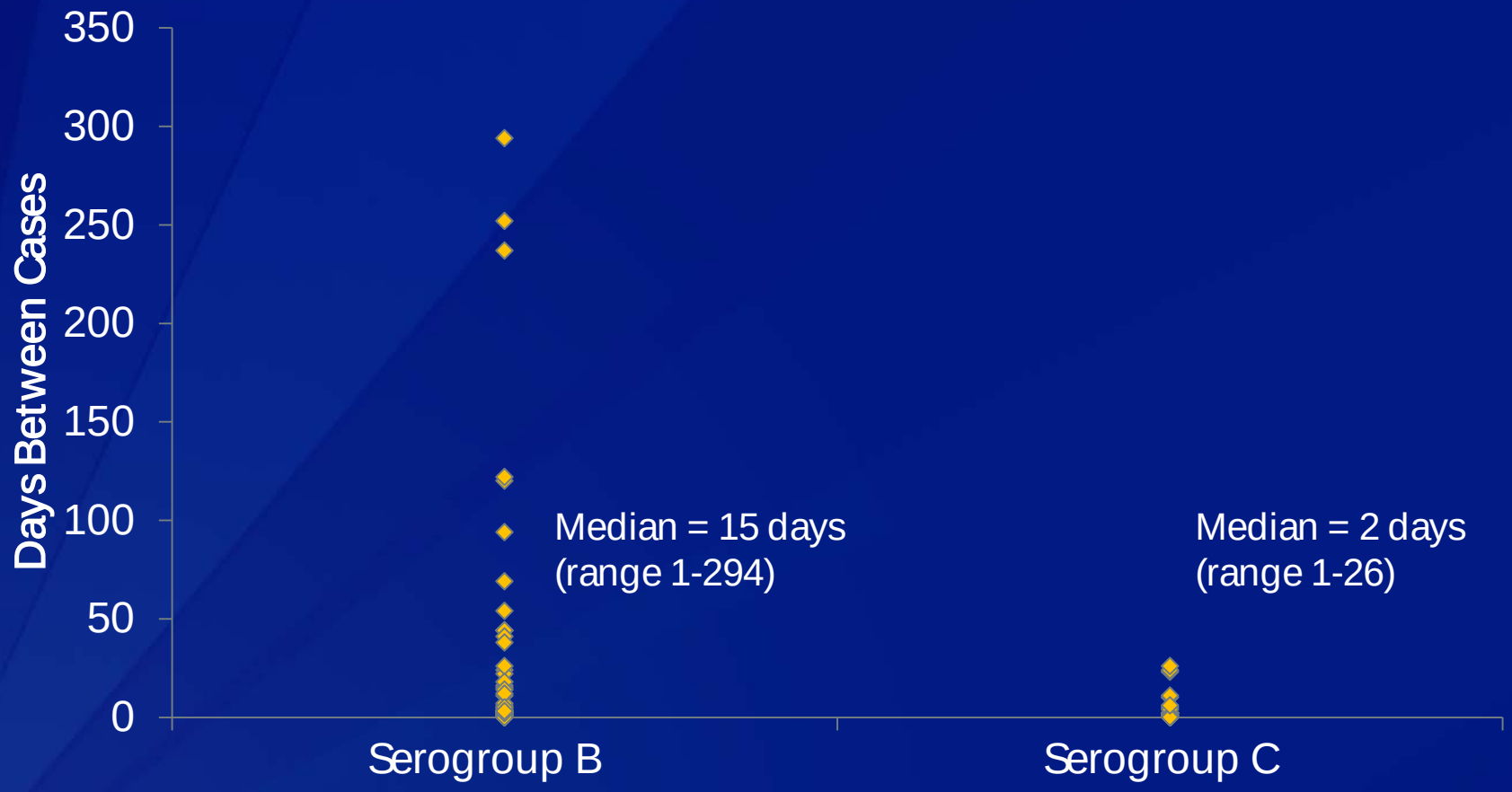

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PREVENTION AND MANAGEMENT

No licensed MenB vaccine in US

- Pfizer: MenB vaccine currently in development
- Novartis: Bexsero®, Recombinant MenB+OMV NZ (rMenB) Vaccine
  - Recently licensed in Europe, Australia and Canada
    - Effectiveness inferred from immunogenicity
      - 2 dose series, with immune response after 1 dose
    - Safety in adolescents and adults (n=1584)
      - Headache, nausea, severe injection site pain, swelling erythema, malaise, myalgia and arthralgia reported in ≥10%
      - No reports of serious adverse events related to rMenB
    - Contains 4 antigenic components (fHBP, NHBA, *NadA*, PorA)

Other control measures

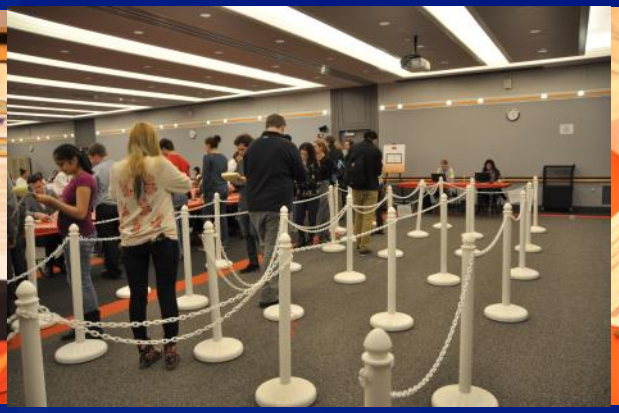
- Mass chemoprophylaxis not recommended to control large outbreaks, as often impractical and unlikely to succeed
  - May be considered in some cases, such as outbreaks involving limited populations, particularly serogroup B outbreaks
- If mass chemoprophylaxis is undertaken, should be administered to all targeted persons at same time
- Interventions not recommended: restricting travel to outbreak areas, closing schools, canceling events
- Educating communities, physicians, and other health-care personnel is important and should be initiated as soon as an outbreak is suspected

Procurement of rMenB

- Initial proposal to FDA to explore the use of rMenB in outbreak settings under an expanded access Investigational New Drug (IND) Protocol – August 2013
- Testing of isolates by Novartis for vaccine antigen matching – September – November 2013
- Epidemiologic investigation – October 2013
- Submission of IND protocol – November 2013
  - Safety monitoring plan
  - Consents, vaccine information sheets, data collection instruments
- CDC Institutional Review Board approval and FDA Safe-to-Proceed letter issued – November 2013
- Contractual agreements finalized between CDC, Novartis and Princeton University – December 2013

Challenges

- IND preparation process and vaccine procurement process takes time
- Unable to determine when additional cases may occur
- Need for clear guidance about when to initiate process


Summary

- Low meningococcal disease incidence requires a broad, high quality approach to surveillance
  - Clear impact of 2 dose adolescent MenACWY recommendations
- Although outbreaks are uncommon, the disease can be devastating with serious impact on organizations
- Vaccination now possible in response to MenB outbreaks
  - Implementation of an unlicensed vaccine requires coordinated efforts between the institution, state and local health departments, manufacturer, FDA, and CDC
  - Guidance for use of MenB vaccines for outbreak control under development

Thank you

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For more information please contact Centers for Disease Control and Prevention

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Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
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