Serogroup B Meningococcal Outbreaks and Control

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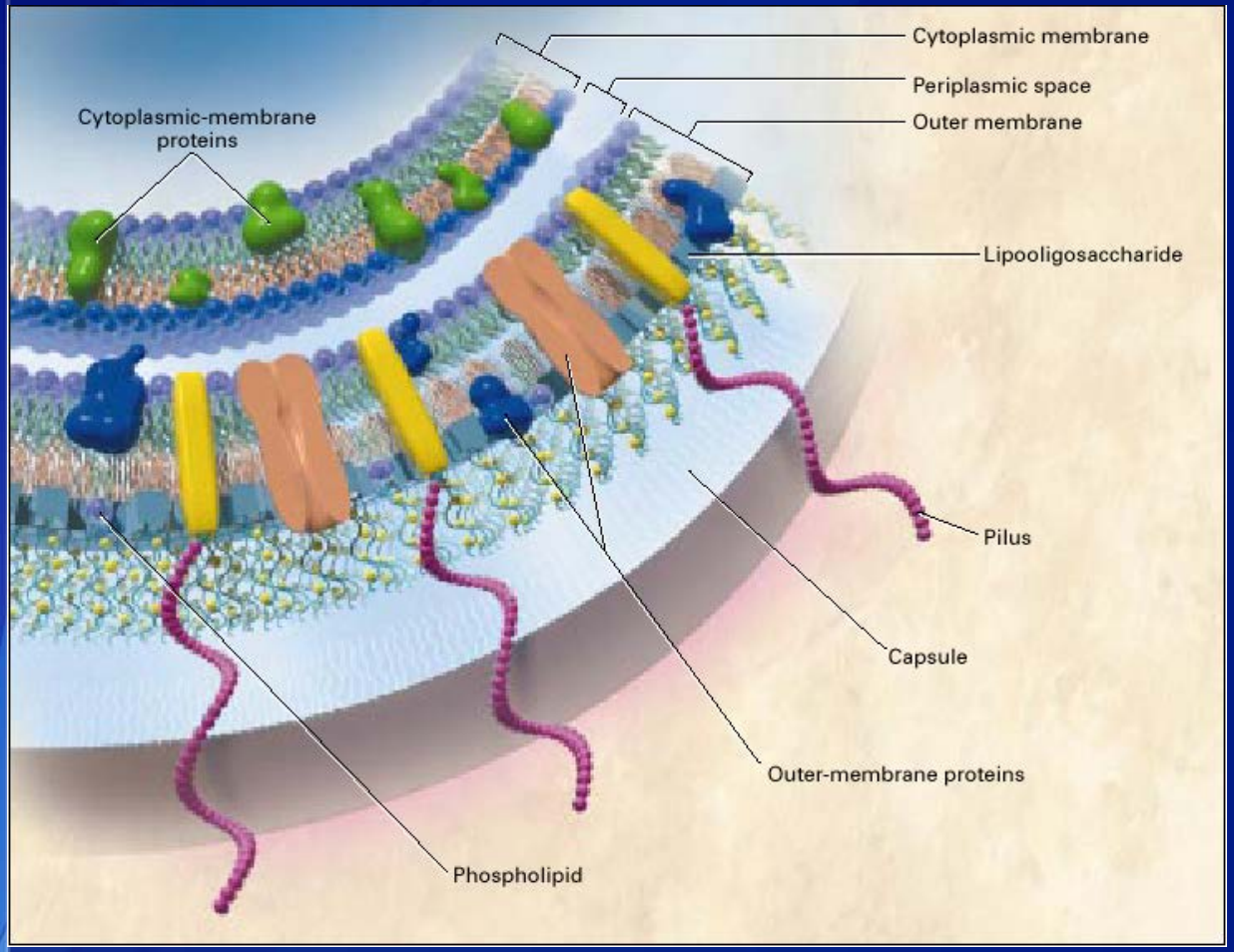
Meningococcal Disease

- **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



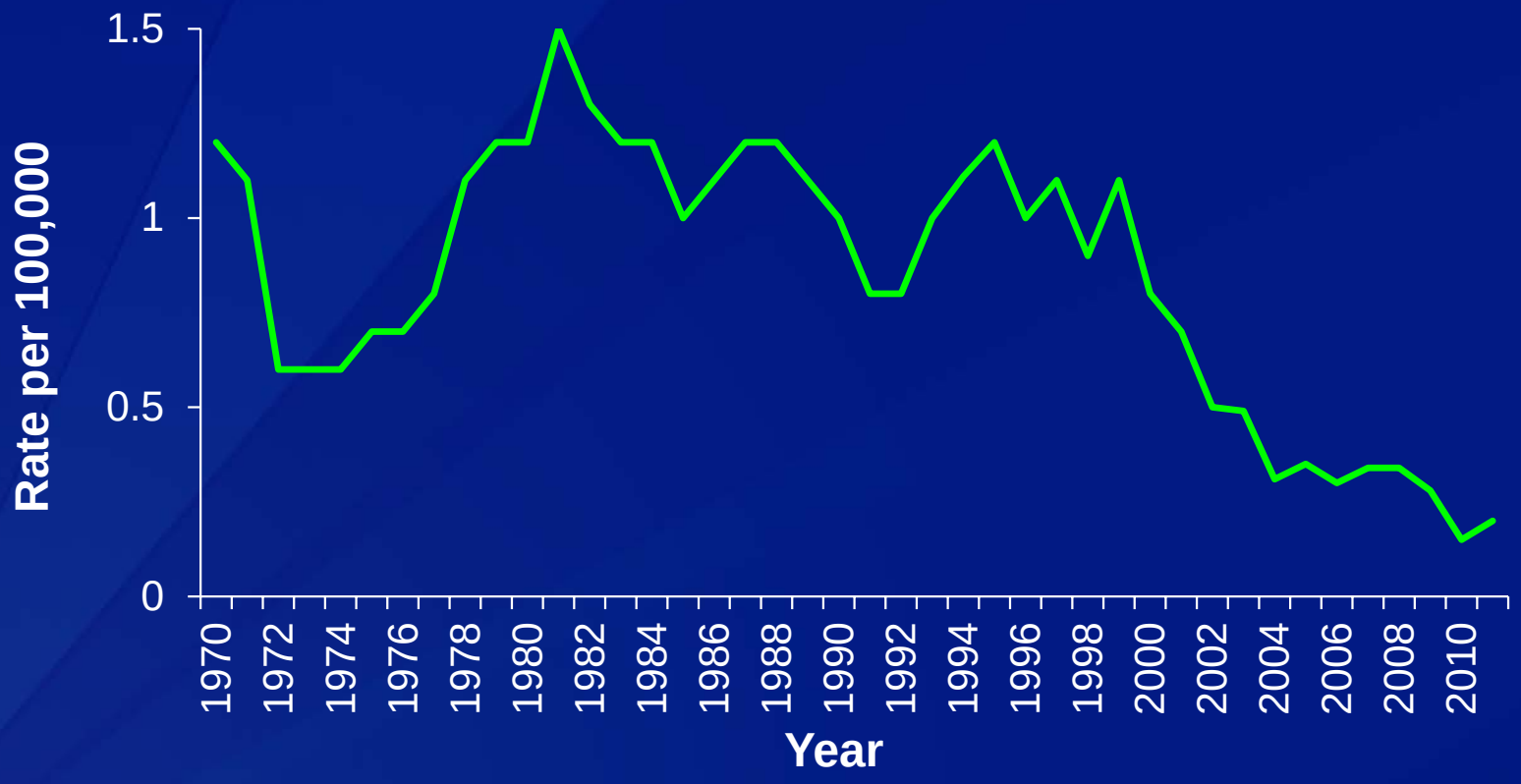
Capsule

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

Outer-membrane proteins

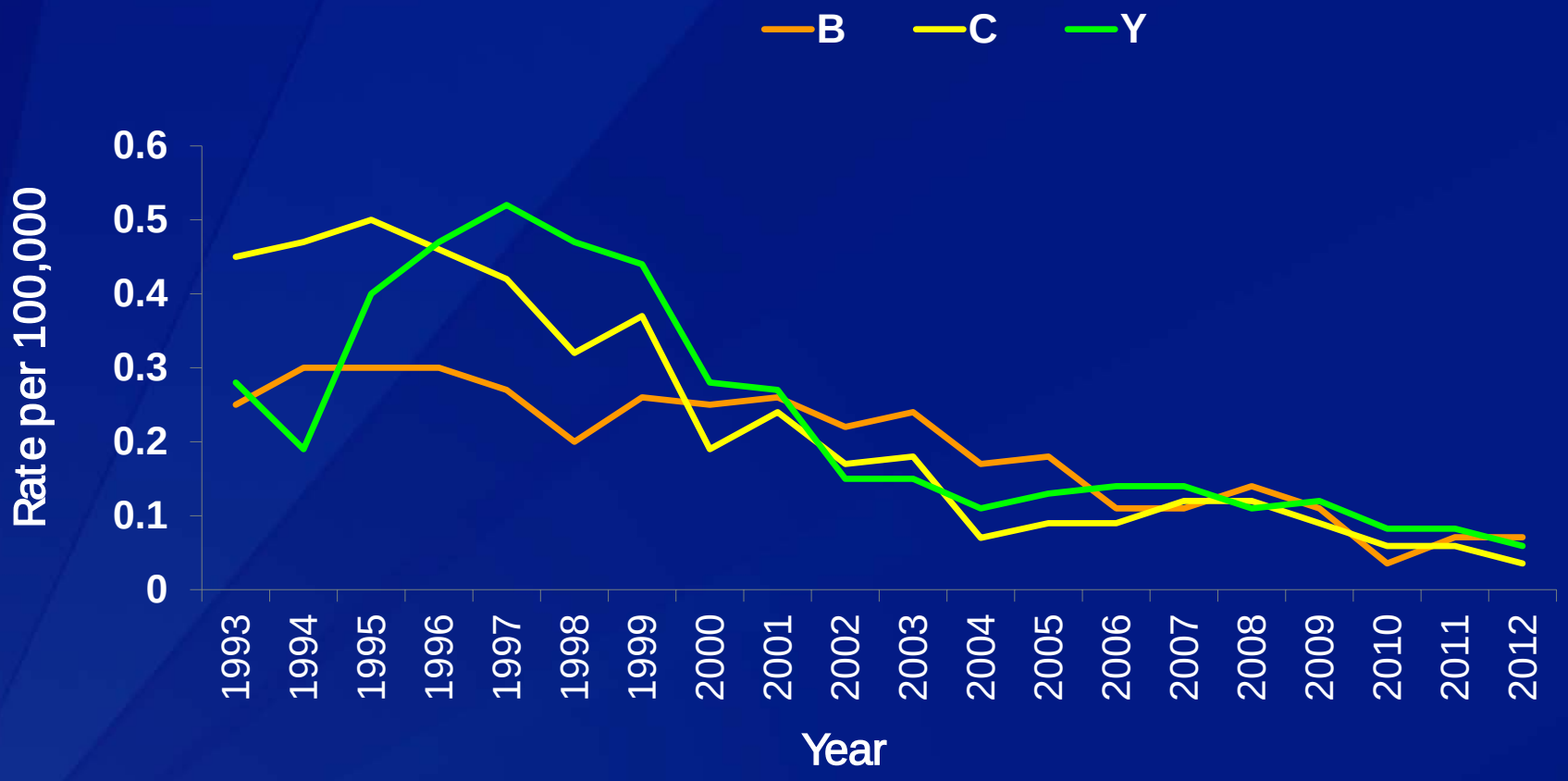
- targets for serogroup B vaccines

Meningococcal Disease Incidence, United States, 1970-2011



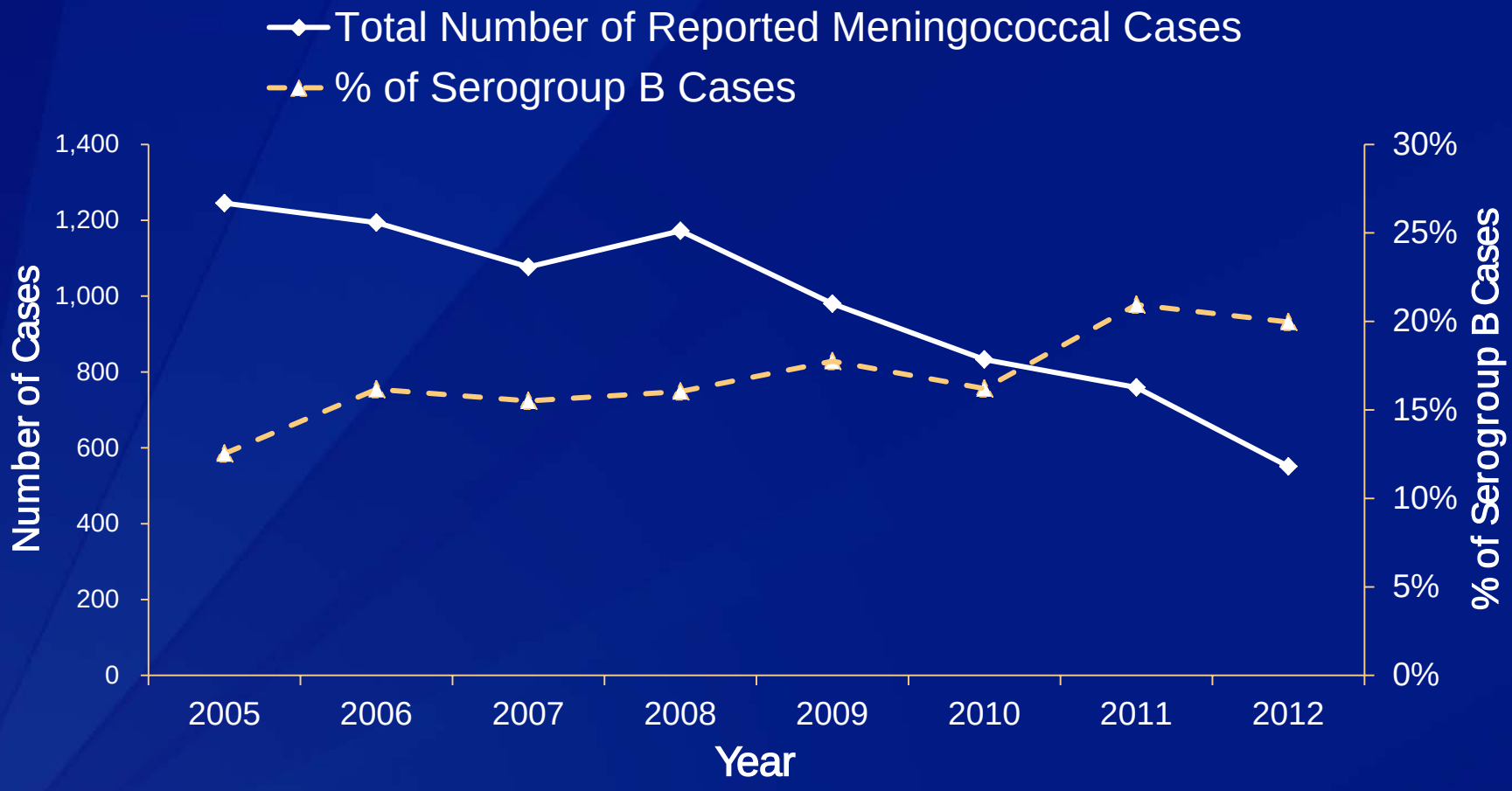
1970 1996 NNDSS data, 1997 2011 ABCs data estimated to U.S. population

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



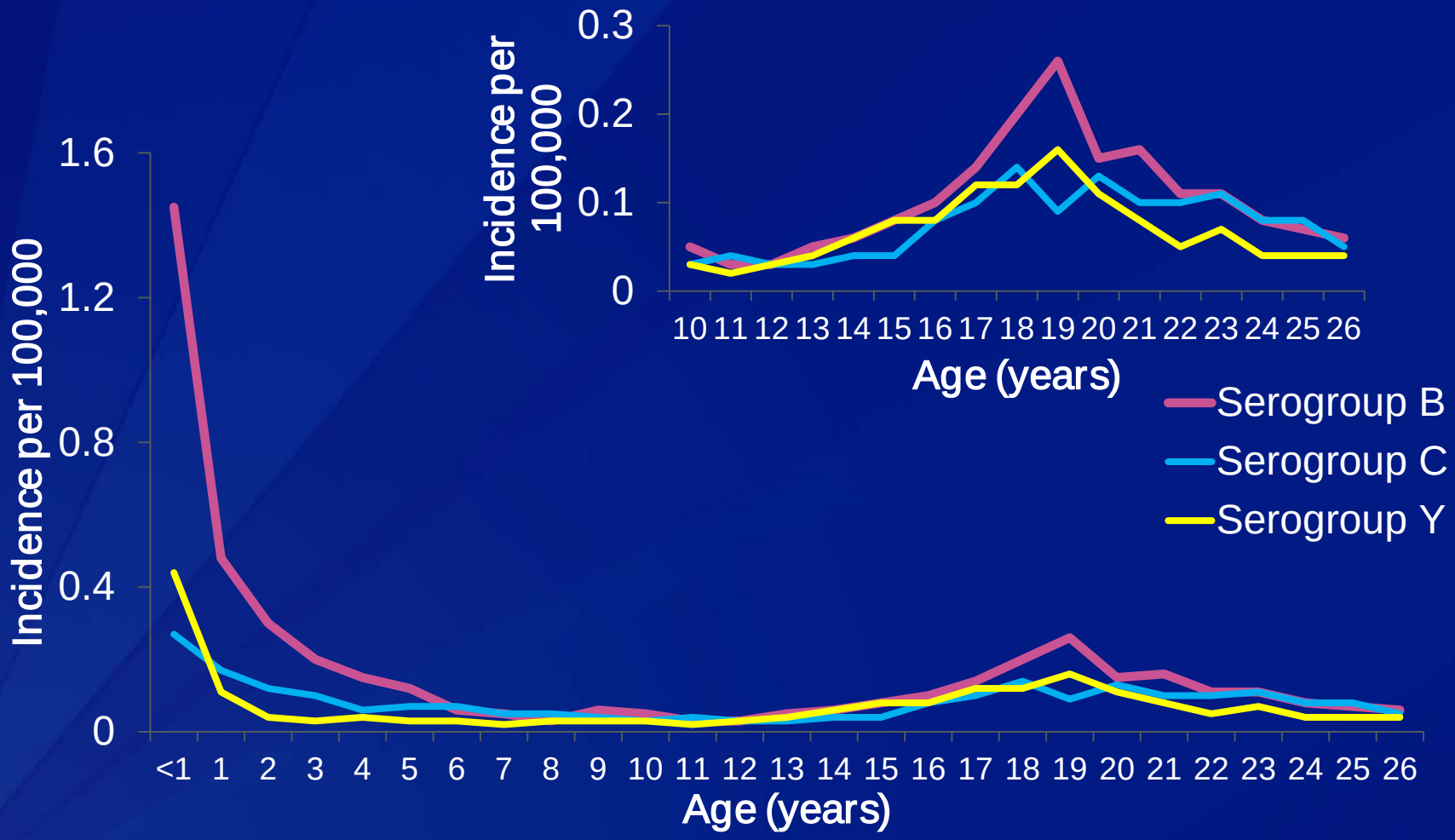
*Source: ABCs cases from 1993 2012 estimated to the U.S. population with 18% correction for under reporting

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



Average Annual Cases in Three Time Frames: Base Case, High and Low

	Age Group	1997-1999 "High Incidence Years"	1993-2012 "Base Case"	2010-2012 "Low Incidence Years"
All Serogroups	<5 years	820	515	159
	11-24 years	778	446	105
	All ages	3099	1821	618
Serogroup B	<5 years	304	216	92
	11-24 years	138	81	28
	All ages	660	432	186

Average annual cases of meningococcal disease
1993 2012 ABCs data estimated to U.S. population with 18% correction for under reporting

Meningococcal Disease Outbreaks

- Only ~2% of US cases are outbreak related
- Definition
  - 2-3 cases of the same serogroup in <3 months; attack rate of 10/100,000
- >80% cases are <25 years of age[1]
  - In University outbreaks, 97% are undergraduates
- College students living in dorms at 3 to 23 fold increased risk[1]
- Other risk factors: Greek society membership, attending bars, alcohol consumption, >1 kissing partner and smoking[2]

1Froeschle et al. CID 1999;29(1):215-6; Harrison et al. JAMA 1999;281(20):1906-10;[2]Mandal et al. CID 2013, Imrey et al Am J Epidemiol 1996;143:624-630, Cookson et al. JID 1998;178:266-269, Imrey et al. J Clin Microbiol 1995;33:3133-3137

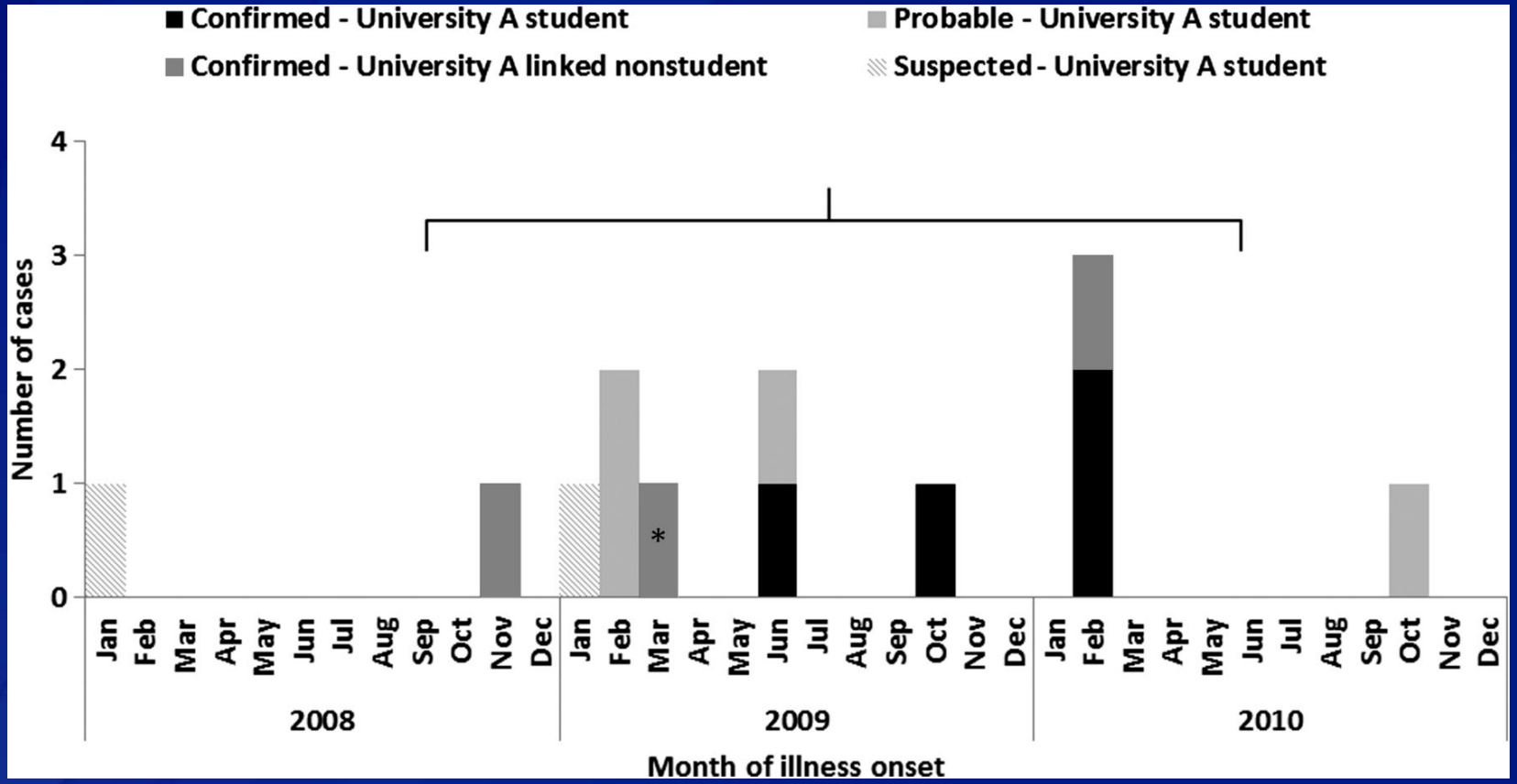
Recent School Based Serogroup B Clusters/Outbreaks*

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

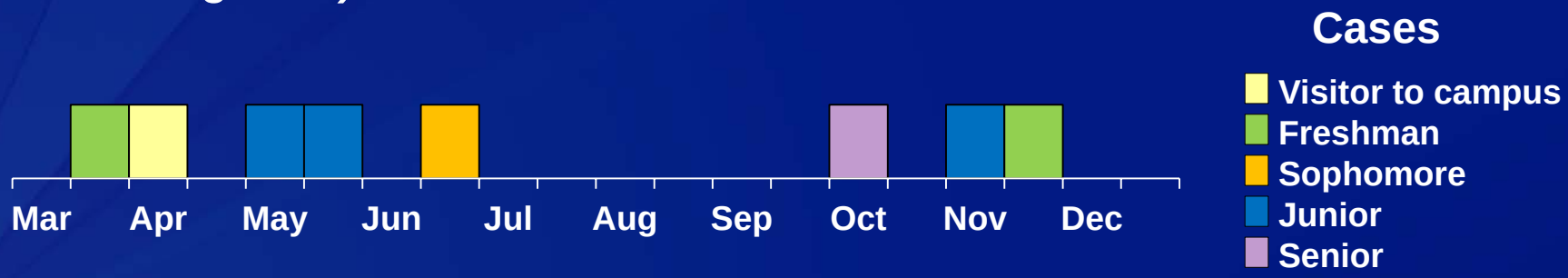
Epidemic curve of 13 meningococcal cases associated with University A, January 2008–December 2010.



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

Princeton University, NJ

- Eight cases of MenB among Princeton University students or persons with links to Princeton University from March – November 2013
  - Attack rate 134/100,000 among undergraduates
  - No fatalities; 2 cases with sequelae (neurocognitive deficit, unilateral hearing loss)
- Laboratory testing
  - All 7 isolates identical: ST 409 (CC41/44/lineage3), PFGE 429, PorA (P1.5-1,2.2) , FHbp (1.276), NhbA (p0002) and *NadA* (PCR negative)

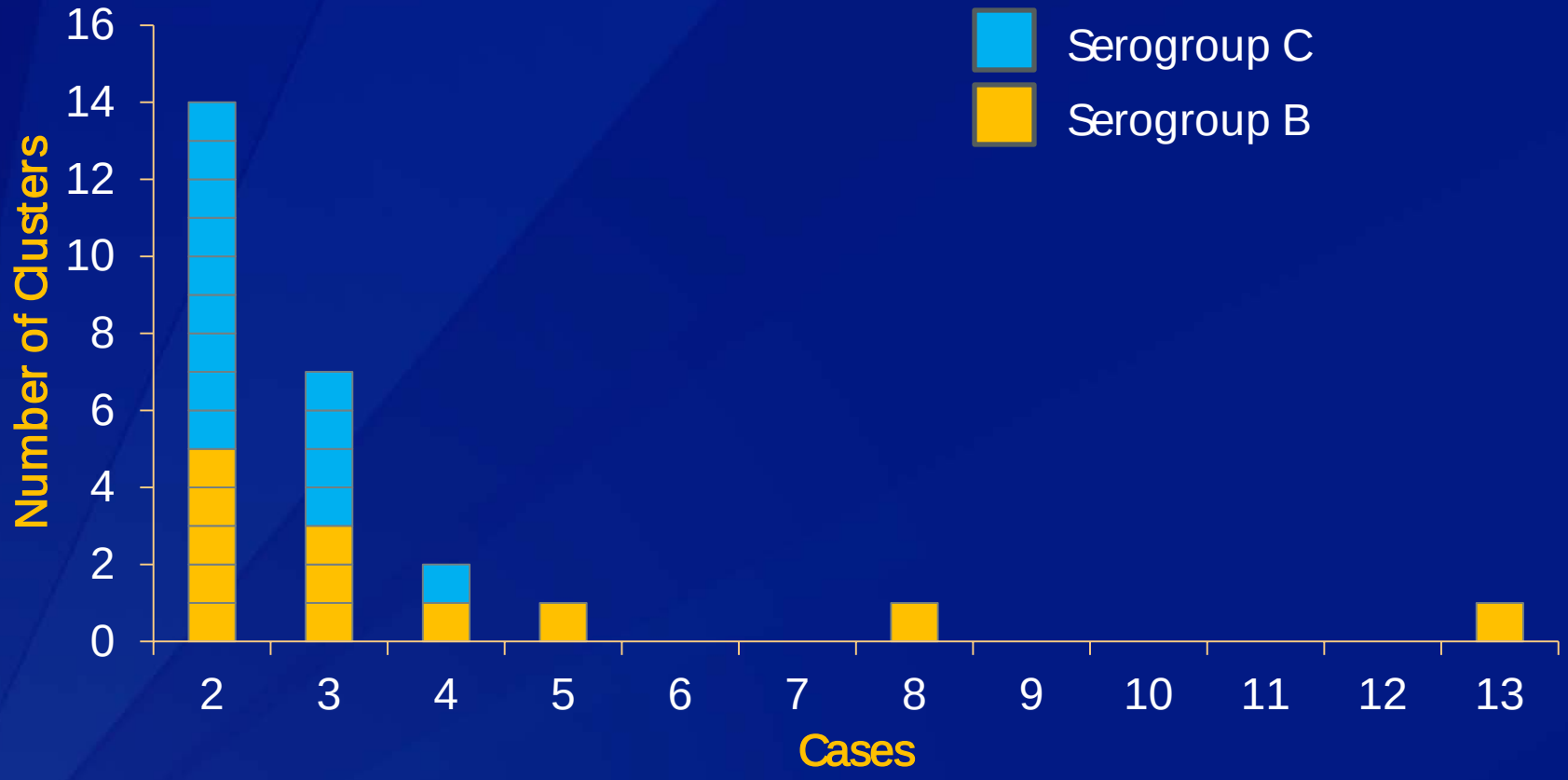


Serogroup B Meningococcal Disease in University of California- Santa Barbara (UCSB) Undergraduate Students (N=4*)

*Additional associated case identified on review of serogroup B cases with connections to UCSB during 2011-2013

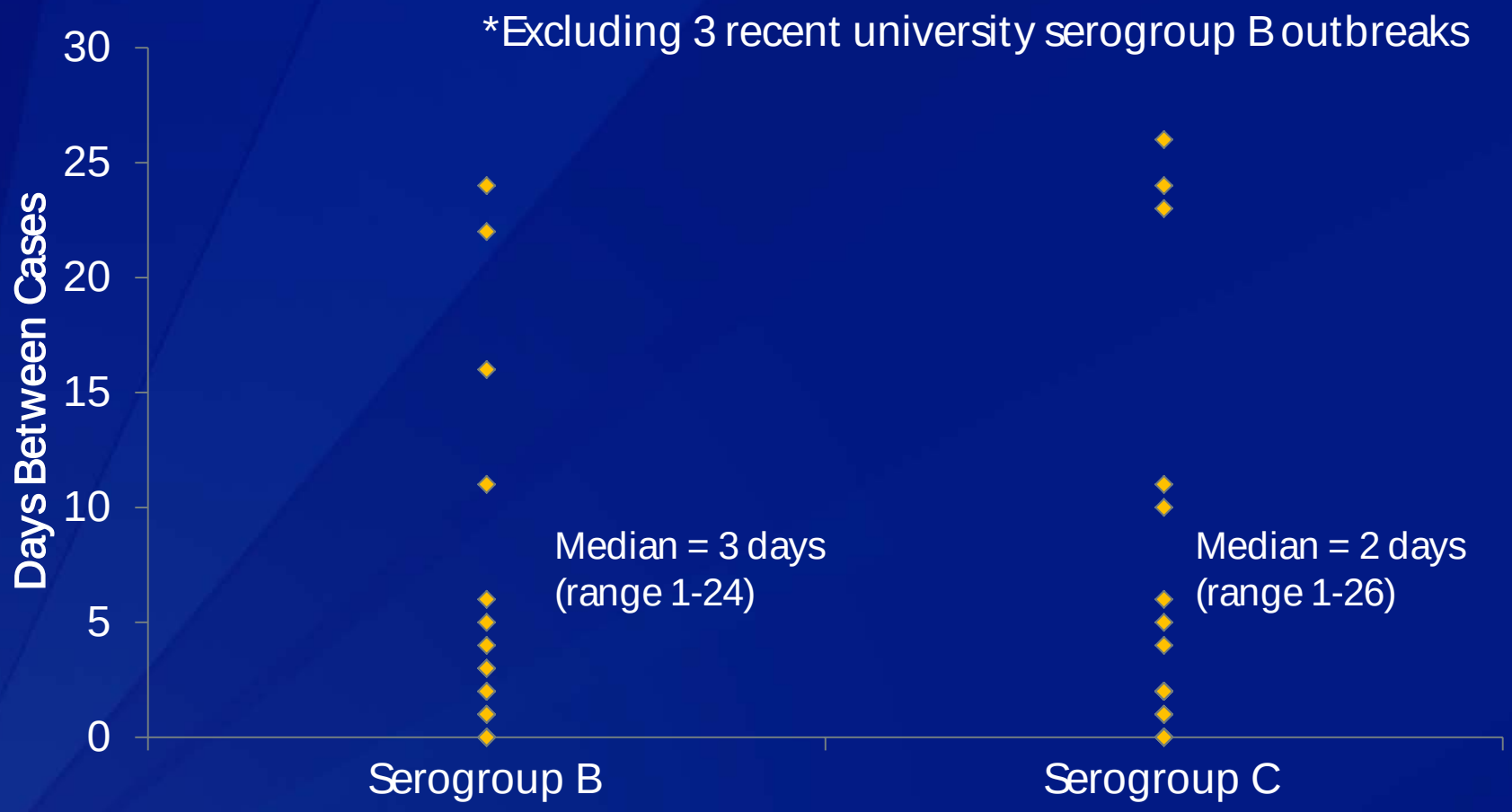
- All cases in undergraduates (aged 18-22 years); no epi-links
  - 4 recovered, 1 case with sequelae (bilateral foot amputation)
- Attack rate of 21.1/100,000 (among UCSB 17-22 year olds)
  - 234-fold higher than incidence rate for 17-22 year olds in general US population
- All 5 isolates ST-32 (CC32/ET-5); PorA (P1.7,16-20), FHbp (1.1), NhbA (p0005), *NadA* (1.1); PFGE 467 (n=3) and 468 (n=2)
  - Different strain compared to Princeton

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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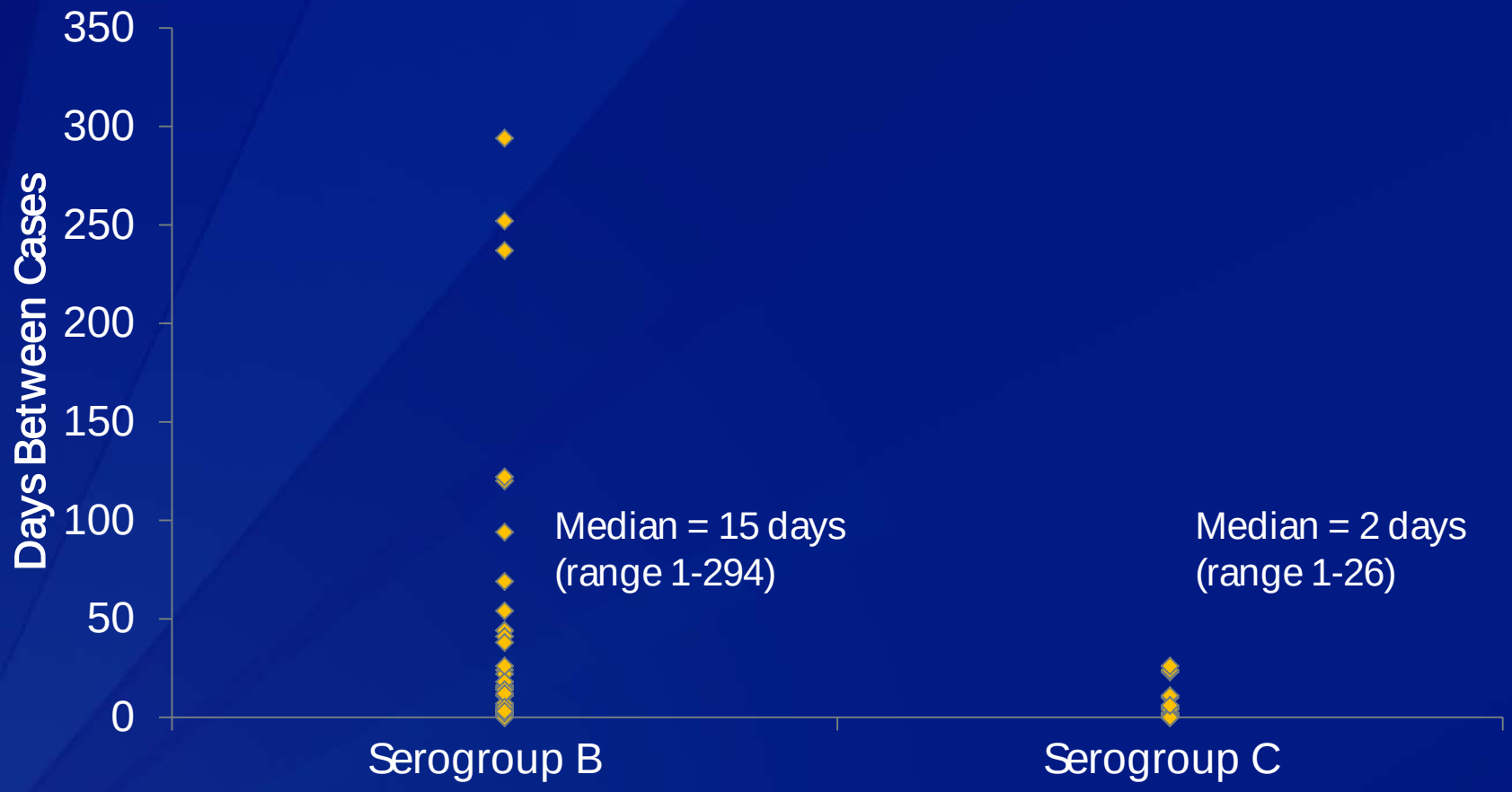

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PREVENTION AND MANAGEMENT

No MenB Vaccine Licensed in the US

- **Novartis: Bexsero®, Recombinant MenB+OMV NZ (rMenB) Vaccine licensed in Europe, Australia and Canada in 2013**
  - 2 dose series in adolescents
  - Contains 4 antigenic components (fHBP, NHBA, *NadA*, PorA)
  - Provides broad protection against multiple MenB strains
- **Pfizer: MenB vaccine currently in development**
  - 3 dose series in adolescents
  - Contains 2 fHPB antigens to achieve broad protection against multiple MenB strains

Use of rMenB under under an Investigational New Drug Application

- **CDC Institutional Review Board approval and FDA Safe-to-Proceed letter issued – November 2013**
  - Safety monitoring plan
  - Consents (minors, pregnant women), vaccine information sheets, data collection instruments
- **Contractual agreements finalized between CDC, Novartis, and Princeton University – December 2013**
  - Vaccine Injury Compensation Program
  - Safety reporting to Novartis
  - Vaccine handling and storage
    - Vaccines could not be returned to central storage after removal

Getting Students Vaccinated

- Emphasis on education about vaccine, Investigational New Drug (IND) process
  - Safety record of vaccine
  - NOT research study/clinical trial
  - Only available to defined population at risk
  - Voluntary
- Communication to inform, encourage
  - Information to students and parents
  - Town hall meetings with CDC experts
  - Student Health Advisory Board advertising
- Clinic modeled after flu vaccine clinic each fall
- University took on vaccine storage, security, maintaining cold chain

Vaccination Coverage, Princeton University

Eligible Groups
Entire undergraduate student
Graduate students who live in undergraduate or graduate dormitories
Students, faculty, and staff with medical conditions at increased risk for meningococcal disease and spouses/parents living with undergraduates in dorms

	Dose 1 N (%)	Dose 2 N (%)
Undergraduate Students	5060 (97)	4772 (91)
Graduate Students	426 (79)	356 (66)
Faculty/Staff/Other	16 (94)	11 (65)
TOTAL	5502 (95)	5139 (89)

UCSB Vaccination Campaign

- CDC-sponsored expanded access IND approved by FDA for use in UCSB outbreak
- Target populations: All undergraduates, graduate students/faculty living in dormitories, and others with high-risk conditions (asplenia, complement component deficiency)
  - Estimate ~20,000 persons eligible for vaccination
- First dose campaign: February 24-March 7, 2014
  - Coverage with first dose close to 50%
- Safety surveillance plan in collaboration with UCSB and CDC

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
- MenB vaccines may protect vaccinated individuals but not prevent transmission



Other control measures

- Chemoprophylaxis for close contacts of cases
- 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 critical for early detection of cases

Summary

- Recent serogroup B outbreaks on college campuses in the setting of very low disease incidence
- 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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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.