From Mening to Syringe: Outbreak of Meningococcal Disease at a New Jersey University, 2013

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Ethics

No Financial Conflicts of Interest (COI)

Outline

- Background on Meningococcal Disease
- Timeline of Outbreak-Associated Cases and Response to Outbreak
  - Onsite investigation
  - Vaccination
- Successes and Challenges

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Meningococcal Disease

- Severe acute bacterial disease
- Caused by the bacterium *Neisseria meningitidis*
- Causes meningitis, sepsis, and focal infections
  - Meningococcal meningitis: acute inflammation of the lining of the brain and spinal cord
  - Meningococcal septicemia: dissemination of the bacterium into the blood stream

Neisseria meningitidis

- Aerobic, gram-negative diplococcus
- At least 13 serogroups based on characteristics of the polysaccharide capsule
- Most invasive disease caused by serogroups A, B, C, Y, and W-135
  - Licensed vaccine available in U.S. for all except serogroup B (MenB) (MPV licensed 1978, MCV4 licensed 2005)

Pathogenesis

- Organism colonizes nasopharynx
  - 5-10% of the general population are asymptomatic carriers
- In some persons the organism invades the body and causes infection at a distant site

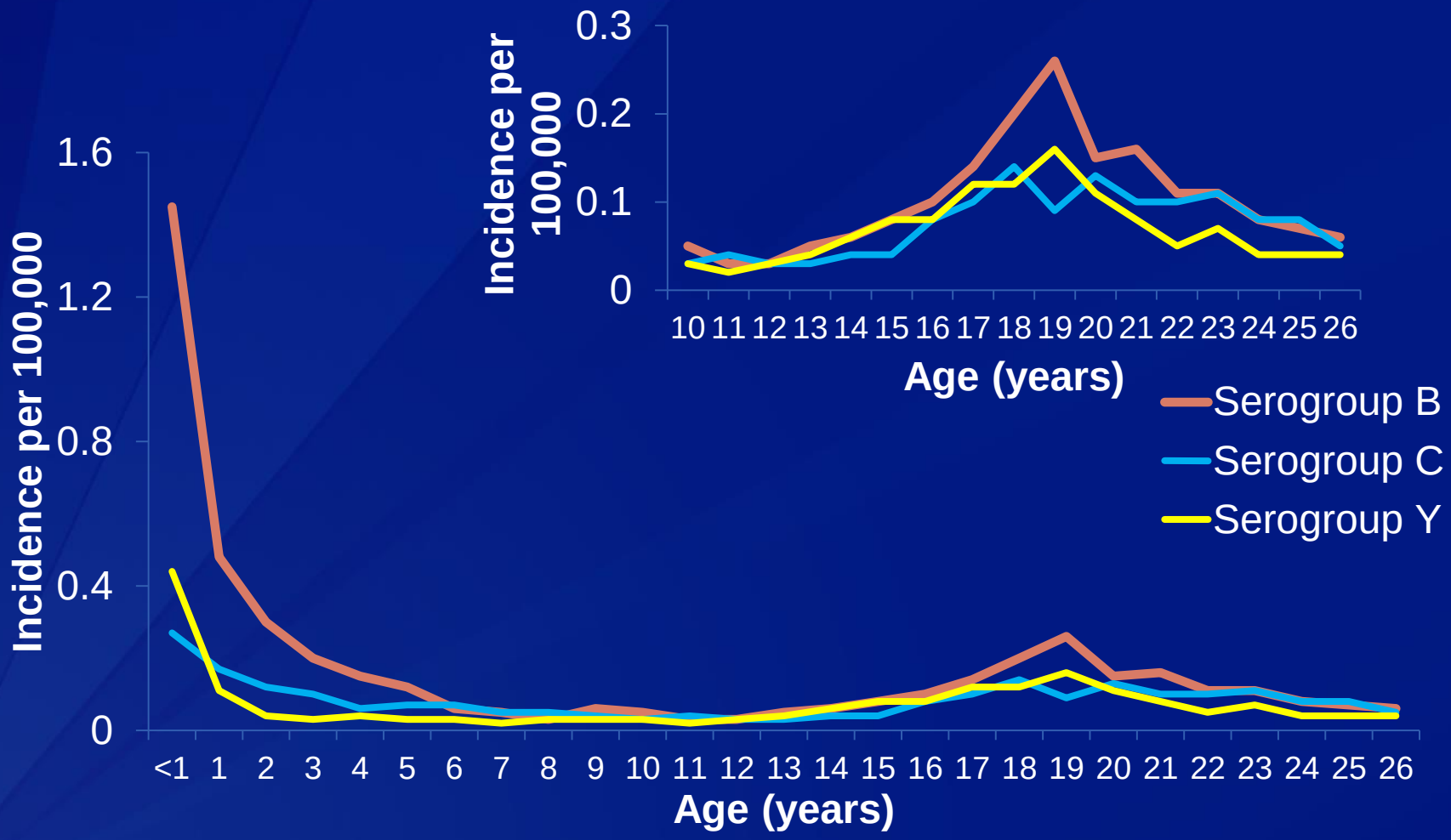
Clinical Features

- Transmission via:
  - Respiratory droplet spread, or
  - Direct contact with oral secretions
- Incubation period:
  - Commonly 3-4 days (range: 2 to 10)
- Infectious period:
  - From 10 days prior to disease onset through 24 hours after initiation of antibiotics
- Communicability limited

Neisseria meningitidis
Risk factors for invasive disease

- Host factors
  - Age
  - Certain medical conditions, i.e. not having a spleen
- Exposure factors
  - Community setting
  - Demographic and socioeconomic factors
  - Over crowding
  - Concurrent upper respiratory tract infection
  - Active and passive smoking

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



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Outbreak Overview

- Since March 2013, 9 cases of meningococcal disease- no common link
- All caused by serogroup B
- 1 fatality; 2 permanent sequelae

Timeline of Outbreak-Associated Cases

Princeton students

Related cases

 # Days hospitalized

- 18 year old female, PU student
- Became symptomatic returning from spring break
- Went directly to ER, admitted for 8 days
- NJPHEL confirms serogroup B

Timeline of Outbreak-Associated Cases

Princeton students

Related cases

 # Days hospitalized

- 17 year old male, HS student
- Prospective student visiting from another state - stayed 3 days in dormitory
- Developed symptoms 4 days after return home - confirmed serogroup B

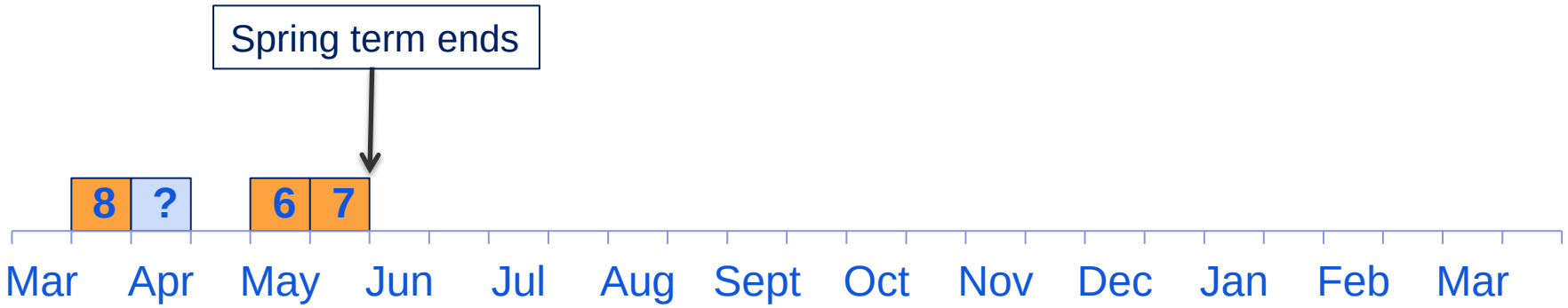
Timeline of Outbreak-Associated Cases

- 21 year old male, PU student
- Became symptomatic on campus, transported to ER
- Admitted for 6 days
- NJPHEL confirms serogroup B

Response

- NJDOH consults with CDC meningitis experts
- NJDOH declares a cluster of meningococcal disease
- Next steps
  - NJDOH to develop FAQ's and fact sheets
  - Messaging to Princeton University students (and parents), faculty, and staff
  - 3 isolates to CDC meningitis lab for genotyping

Timeline of Outbreak-Associated Cases



Princeton students

Related cases

 # Days hospitalized

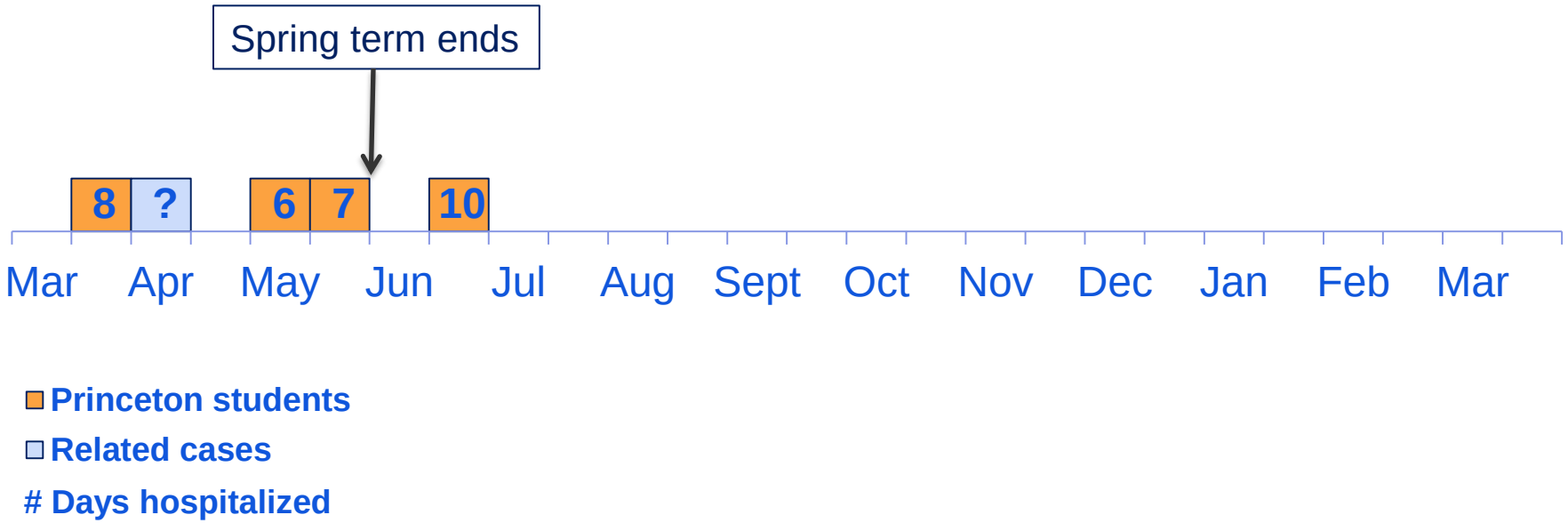
- 20 year old male, PU student
- Became symptomatic returning home from spring term
- Went directly to ER, admitted for 7 days
- Confirmed serogroup B

Outbreak Response

- NJDOH consults with CDC – genetic testing confirms cases caused by identical strain
- NJDOH declares an outbreak of meningococcal disease

- Next steps
  - NJDOH updates FAQ's and fact sheets
  - Messaging to Princeton University students (and parents), faculty, and staff- tone of message changes
  - NJDOH sends out an Epi-X notification
  - Princeton University develops education campaign
  - Princeton University conservative with patient assessment

Timeline of Outbreak-Associated Cases

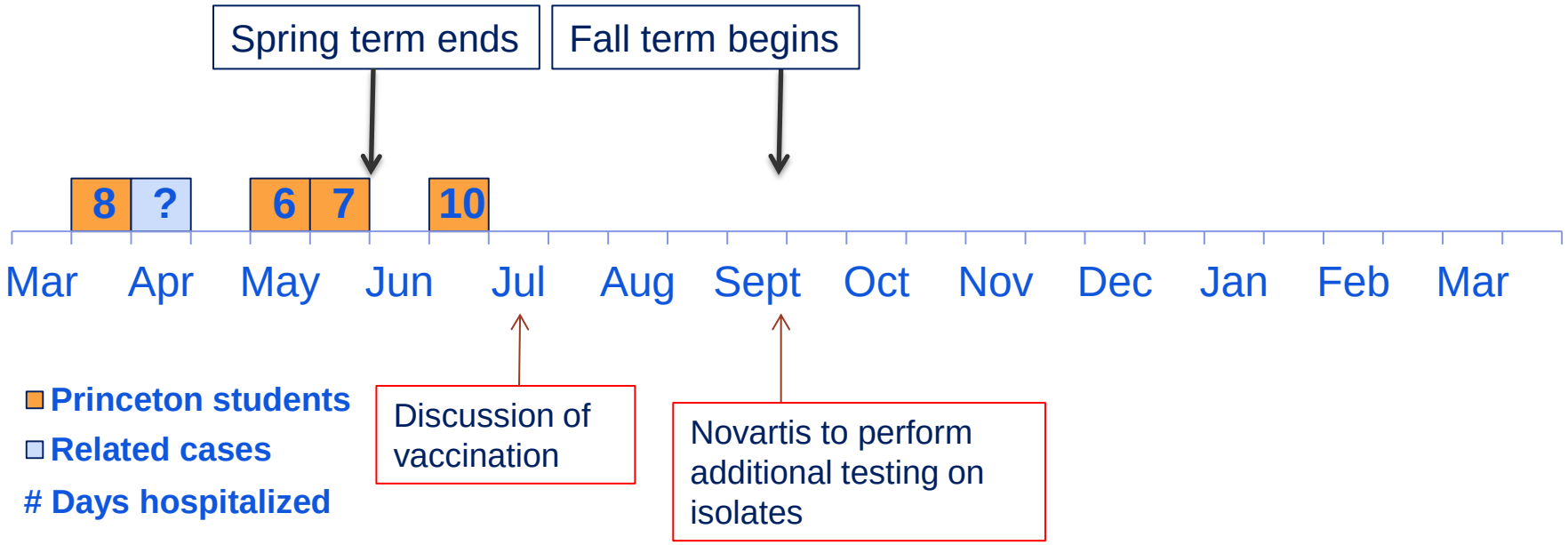


- 19 year old male, PU student
- Became symptomatic on Princeton study abroad trip in Greece
- Admitted for 10 days (Greece, France)
- Serogroup B by PCR, incomplete molecular characterization

Outbreak Response

- Consultation with CDC
- Outbreak is ongoing
- Next steps
  - Discussion of the possibility of vaccine

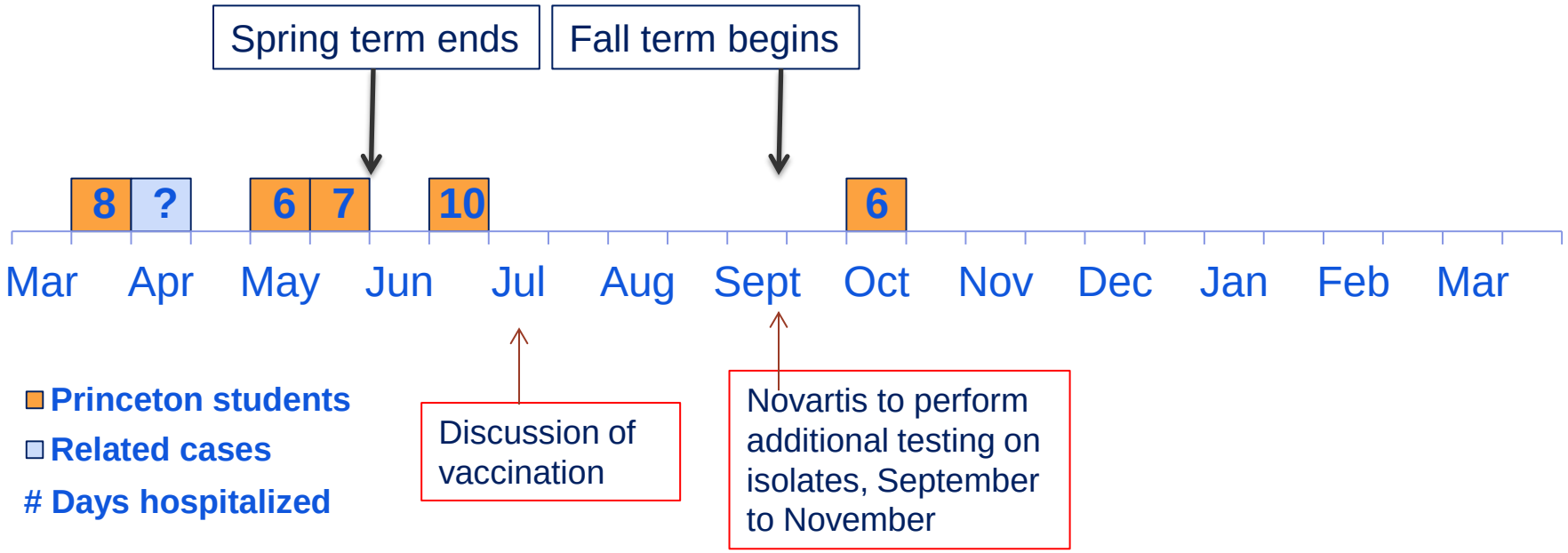
Timeline of Outbreak-Associated Cases



Investigational New Drug Protocol (IND)

- Expanded access for emergency use
- Bexsero: Recombinant MenB+OMV NZ (rMenB) Vaccine (Novartis; Siena, Italy)
  - Recently licensed in Europe, Australia, and Canada
- Need emphasized and high-risk groups well defined
- FDA to determine if benefits outweigh risks

Timeline of Outbreak-Associated Cases

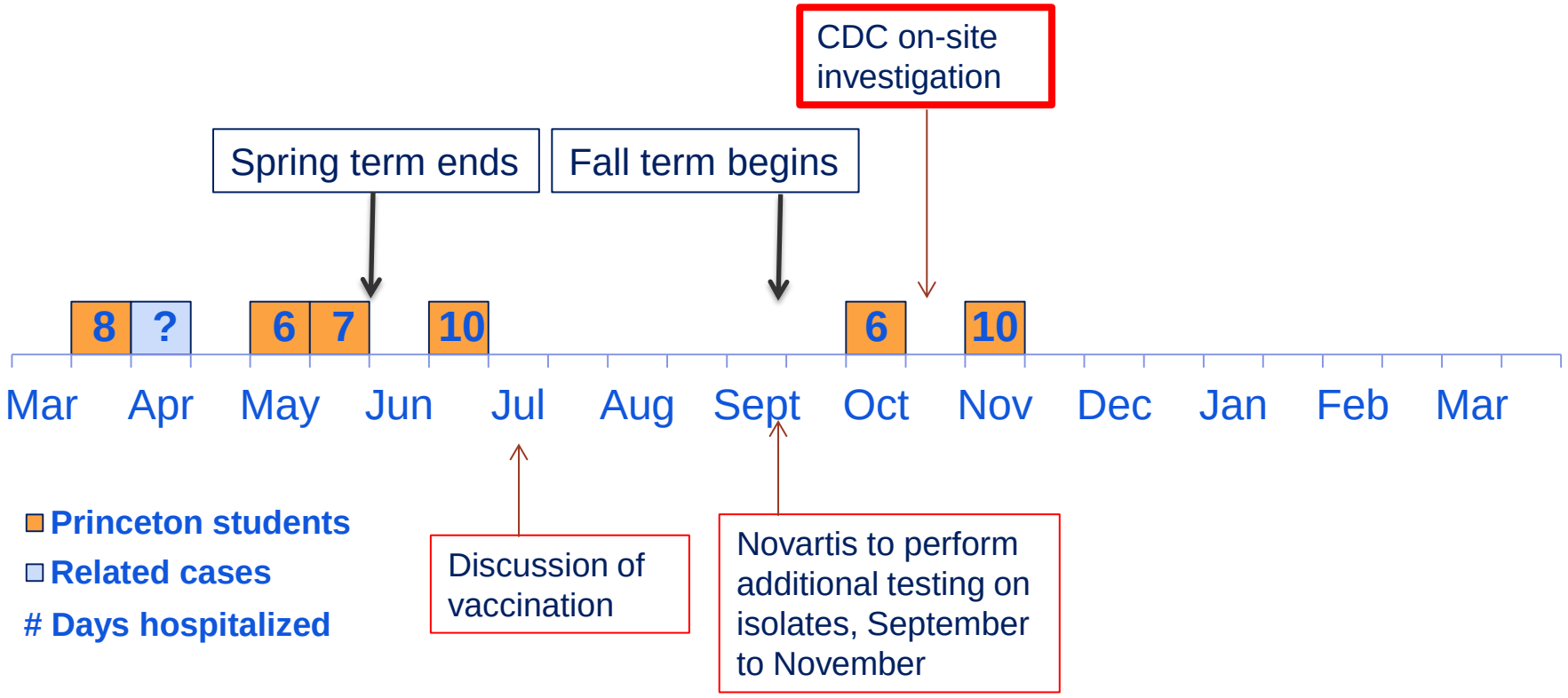


- 21 year old female, PU student
- Became symptomatic on campus, transported to ER
- Admitted for 6 days
- NJPHEL confirms serogroup B; CDC confirms same strain

Outbreak Response

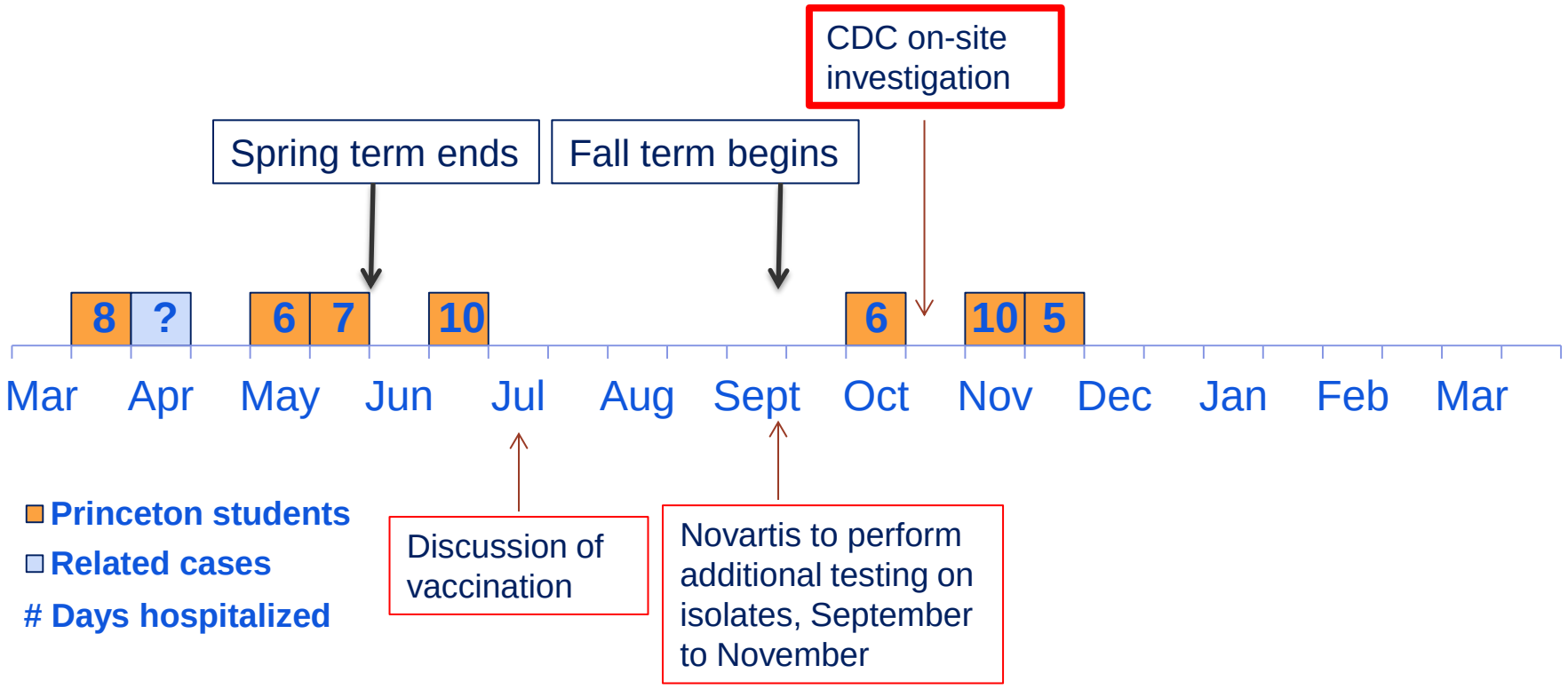
- Outbreak is ongoing
- Next steps
  - Continued conversations between CDC and FDA and Novartis
  - NJDOH requests CDC Epidemiologic Assistance (Epi-Aid)
  - CDC at Princeton University October 15 – 25, 2013

Timeline of Outbreak-Associated Cases



- 20 year old male, PU student
- Spent night in infirmary (strep positive)
- Developed rash, transferred to ER, admitted for 10 days
- NJPHEL confirms serogroup B; CDC confirms same strain

Timeline of Outbreak-Associated Cases

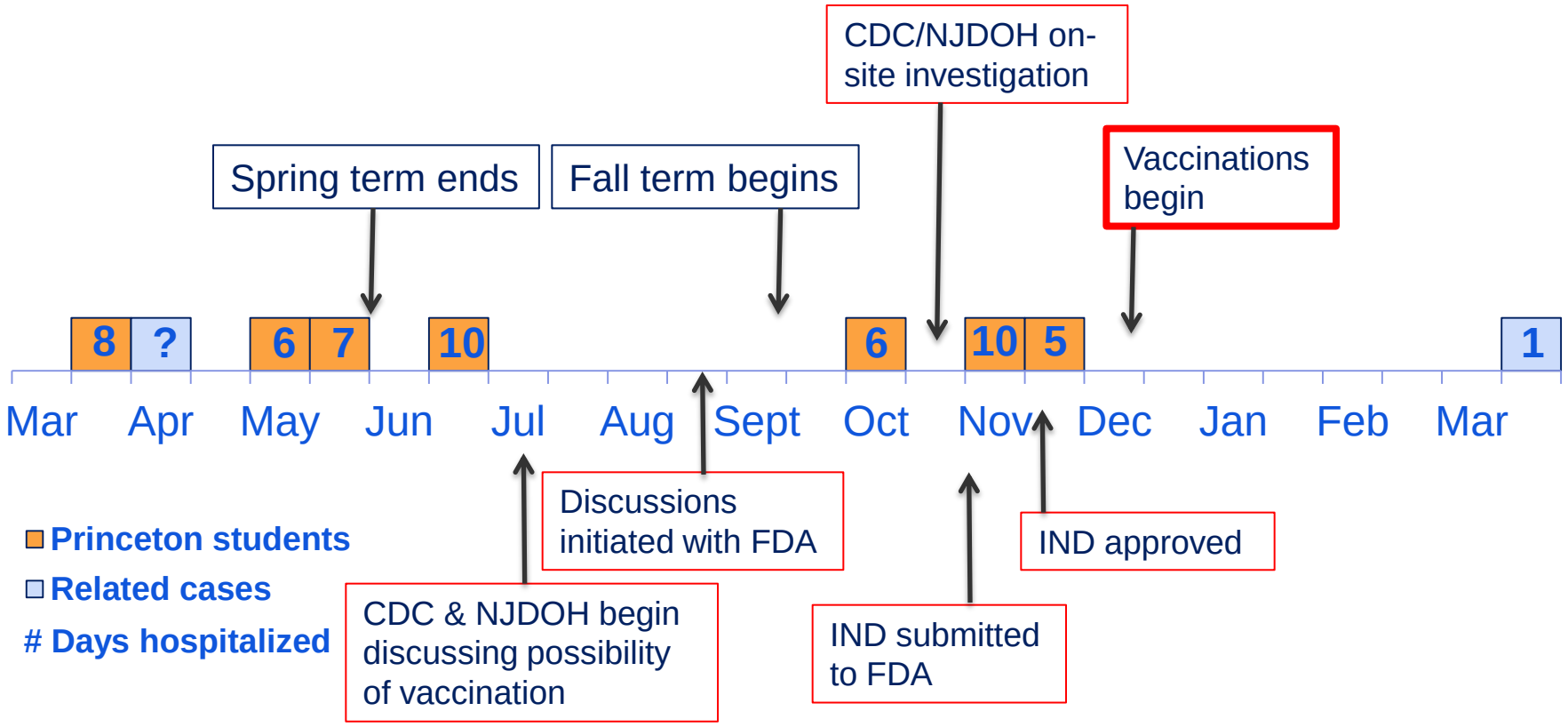


- 18 year old female, PU student
- Became symptomatic on campus, reported to infirmary
- Transferred to ER, admitted for 5 days
- NJPHEL confirms serogroup B; CDC confirms same strain

Outbreak Response

- Novartis confirms vaccine protects against outbreak strain
- CDC submits Investigational New Drug (IND) application
  - November 14, 2013 the FDA approves the IND protocol
- November 26, 2013, Princeton University officially announces the use of vaccine in eligible high-risk population
- Vaccine campaign began December 9, 2013

Timeline of Outbreak-Associated Cases



- 19 year old female from another Drexel University
- Incubation period included contact with students from Princeton, other schools
- Found unresponsive, transferred to ER and died
- PA confirms serogroup B; CDC confirms same strain

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- **Successes and Challenges**

CDC On-Site Investigation – Objectives & Methods

- **Characterize the outbreak**
  - Review literature on past MenB outbreaks
  - Review outbreak-associated cases
- **Define the population at risk**
  - Meet with representatives from the University
  - Tour the campus
  - Review and analyze data
- **Plan logistics for possible vaccination campaign**
  - Meet with representatives from the University

Characterize the Outbreak – A Review of the Literature

Meningococcal Disease Outbreaks

- **Only ~2% of US cases outbreak related**
  - Majority sporadic
- **>80% of cases in Men B outbreaks are <25 years of age[1]**
- **Of reported university cases, 97% undergraduates[2]**
- **College students living in dormitories at increased risk for meningococcal disease**
  - 3-23 fold increased risk[3]
- **Greek society membership, attending bars, alcohol consumption, >1 kissing partner, and smoking have been associated with meningococcal disease[4]**

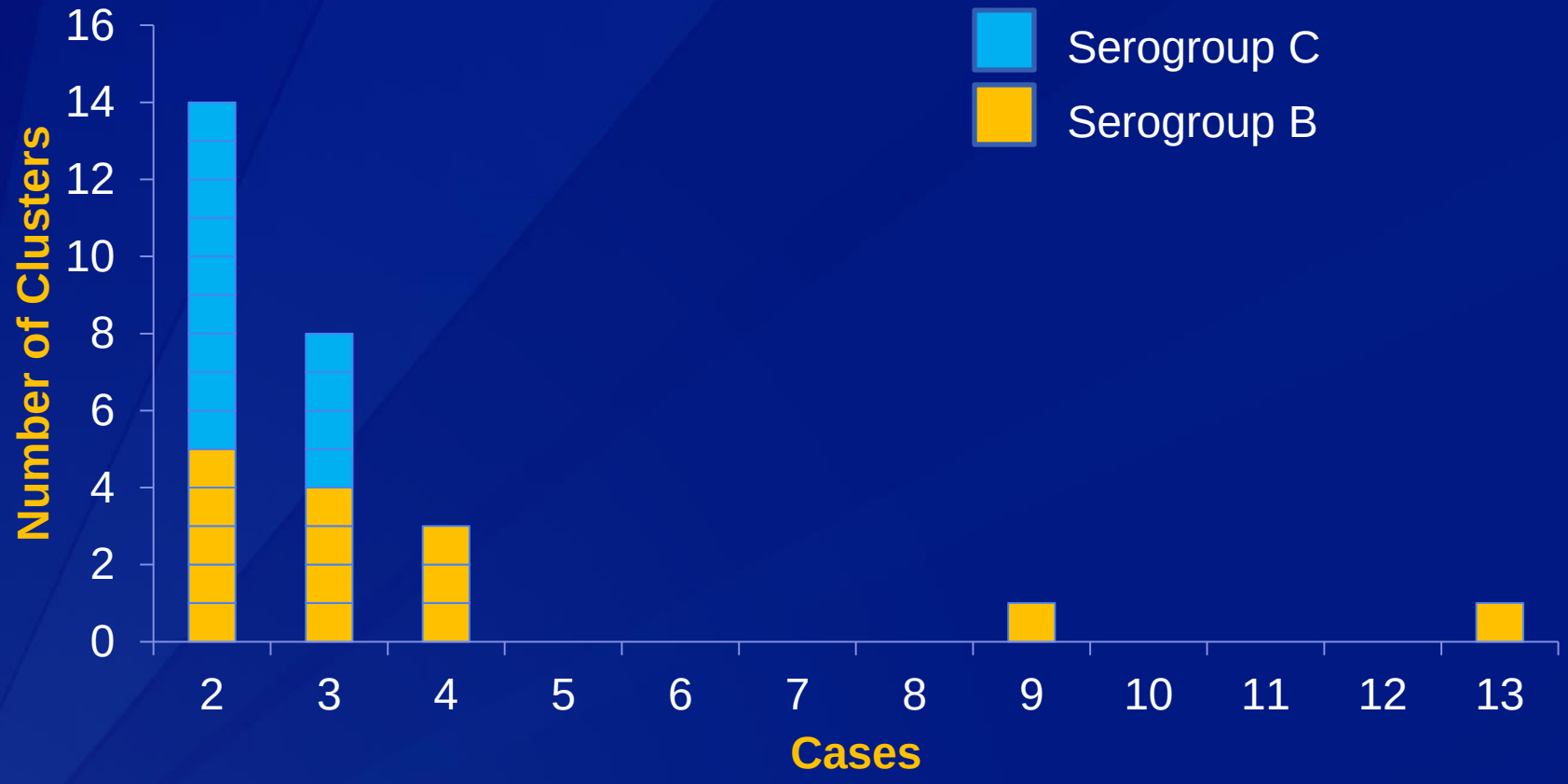
[1]CDC NNDSS data; [2]CDC.MMWR. 2000;49(RR07):11-20.; [3]Froeschle et al. CID 1999;29(1):215-6; Harrison et al. JAMA 1999;281(20):1906-10;[4]Mandal et al. CID 2013, Imrey et al Am J Epidemiol 1996;143:624-630, Cookson et al. JID 1998;178:266-269, Imrey et al. J Clin Microbiol 1995;33:3133-3137

Recent Serogroup B Clusters/Outbreaks*

- University of California, Santa Barbara – Nov 2013 – **4 cases (ST32)**
- Princeton University – Mar 2013 – Mar 2014 – **9 cases (ST409)**
- Lehigh University – Nov 2011 – **2 cases (ST1624)**
- Oregon – Jul 2009 – **4 cases (ST32)**
- Wisconsin – Mar 2009 – **3 cases**
- University of Pennsylvania – Feb 2009 – **3 cases**
- Ohio University – Jan 2008-Nov 2010 – **13 cases (ST269)**

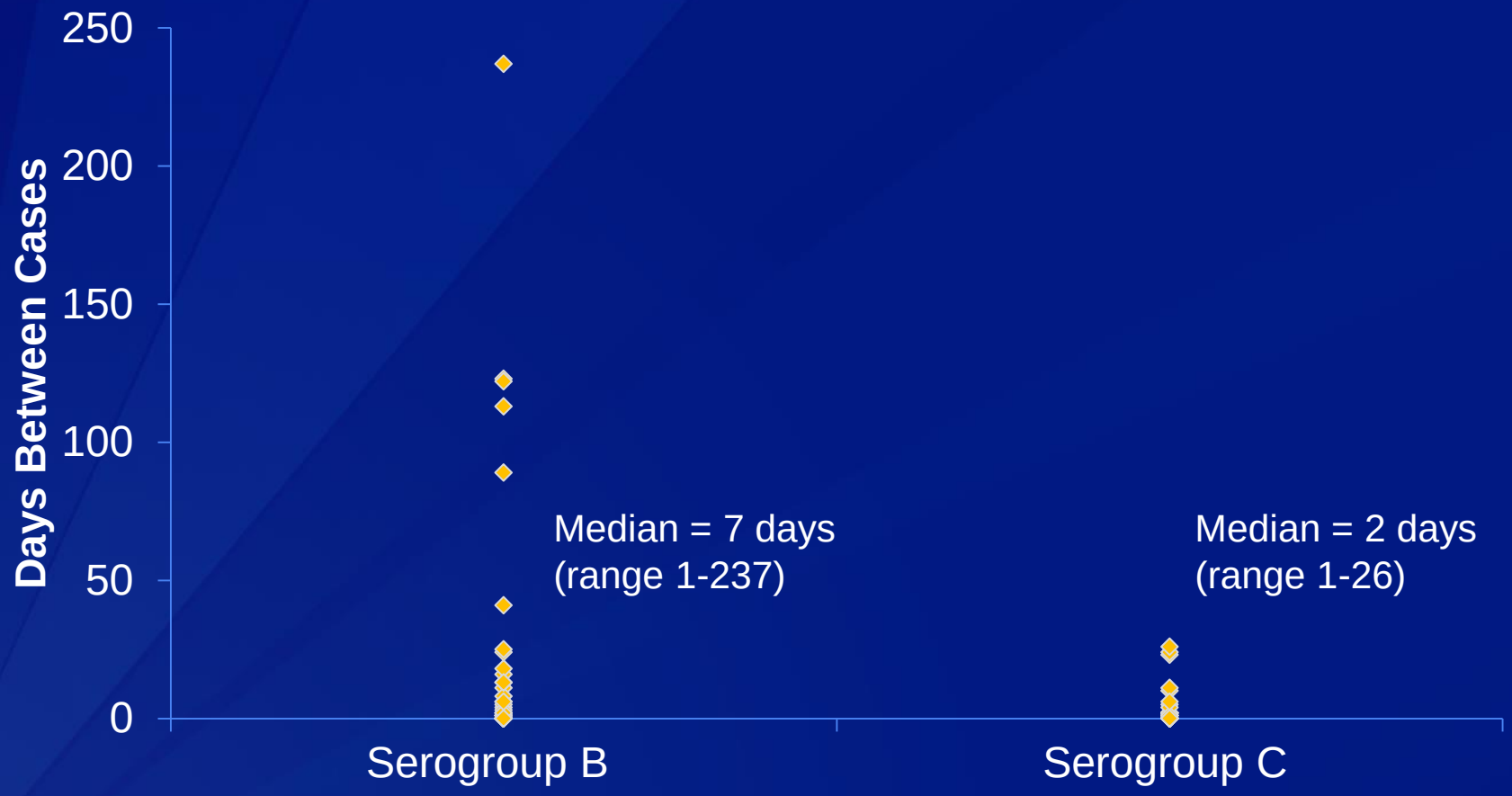
*Where CDC consulted

Frequency of Clusters/Outbreaks by Size, Serogroup B and C



Includes 22 school based clusters from 1989 – 1994 reported by Zangwill et. al and more recent serogroup B outbreaks where CDC was consulted (n=5)

Interval Between Reported Cases in Serogroup B or C Clusters/Outbreaks



Includes 22 school based clusters from 1989 – 1994 reported by Zangwell et. al and more recent serogroup B outbreaks where CDC was consulted (n=5)

Characterize the Outbreak – A Review of Outbreak-Associated Cases

Demographics of Outbreak-Associated Cases (N=9)

Variable	
Median Age (Range)	19 years old (17-21)
Sex	5 male, 4 female
Princeton Class Year	
Class of 2014	3
Class of 2015	1
Class of 2016	2
Class of 2017	1
Not PU student	2
Outcome	
Hospitalization	9
Sequelae	2
Death	1

Characteristics of Outbreak-Associated Cases

- **Undergraduate students + 1 high school visitor**
  - Four different class years
- **Associated with 7 different residence halls**
- **No sports or activities in common**
- **No direct epidemiologic links among cases**
- **No temporal overlap among cases**

Define the Population at Risk – A Review of University Data

Princeton Profile

- Population
  - ~ 5,200 undergraduates
  - 2,700 graduate students
  - 1,200 faculty
  - 11,500 staff (5,500 FTE)

Attack Rate, Princeton Outbreak

- Background attack rate serogroup B, 17-22 year olds in U.S.:

  0.09 per 100,000

- Attack rate in Princeton undergraduate population:

  134 per 100,000

Princeton Undergraduate Students: Living/Social Situations

- **98% undergraduates live on campus in dormitories**
  - Shared bathrooms, common areas
  - Freshmen, sophomores eat in dining halls
- **Eating clubs**
  - 75-85% of upperclassmen join one
  - Members eat meals there
  - Similar to fraternities or sororities at other schools
  - Bars, game rooms, common areas
  - Center of social life on campus


KEEP
HEALTHY
AND
CARRY
ON

Princeton Graduate Students: Living Arrangment

- **62% live in University-owned housing**
  - 60 (2%) are Resident Graduate Students in undergraduate dormitories
  - 18% live in dormitory-style grad housing
  - 42% live in University-owned apartments
- **38% live off-campus**

Age Distribution of Graduate Students at Princeton University by Housing

Housing	Number of Residents	Average Age (years)	SD	Age Range
Graduate dormitories	469	24.1*	2.42	20-39
Residential Graduate Students	60			
Graduate apartments	1,118	26.5*	3.52	19-53
Off-campus	1019			
Total	2666			

* p <0.00001 (t-test)

Recommended Population for Vaccination (Population at Risk in This Outbreak)

Group	Number of Persons
All undergraduate students	5,241
Graduate students who living in undergraduate or graduate dormitories	541
Any other students, faculty, and staff with medical condition putting them at increased risk for meningitis; others living in dormitories	17
Total	5,799

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Reasoning Behind Vaccination – A Quick Recap

- Outbreak had persisted through summer break and into the new school year
- Attack rate in undergraduate population significantly larger than background
- Vaccine licensed in European Union, Australia, and Canada
- Novartis confirmed vaccine covered Princeton strain

Decision to Vaccinate

- Princeton University
  - Consulted outside experts on risks and benefits
  - Extensive discussion with Novartis on safety of vaccine
  - Institutional Review Board (IRB) involvement
  - Review with Board of Trustees
  - Approval by President
- CDC IRB approval

Planning to Vaccinate

- Vaccine procurement, timing, storage and handling
- Medical professionals to administer vaccine
  - Use of Maxim Health Systems
- Vaccination logistics
  - Clinic layout and specifications
  - Crowd management inside and outside the clinic
  - Clinic security

Planning to Vaccinate, Continued…

- Vaccine/clinic advertising
  - Information to students and parents
  - Town hall meetings with CDC experts
  - Student health advisory board advertising
- Emphasis on education about vaccine, IND process
  - Safety record of vaccine
  - NOT research study/clinical trial
  - Only available to defined population at risk
  - Voluntary consent
- CDC and Princeton University Health Services safety monitoring plan

Vaccination Coverage* at Princeton University
(as of March 31, 2014)

	Number in Risk Group	Coverage With First Dose (%)	Coverage With Second Dose (%)
Undergraduate Students	5,241	5,060 (97)	4,772 (91)
Graduate Students Living in Dormitories	541	426 (79)	356 (66)
Others**	17	16 (94)	11 (65)
Total	**5,799**	**5,502 (95)**	**5,139 (89)**

*To date; clinics not yet complete

**Others include community members with medical condition putting them at increased risk, and others living in a dormitory

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Successes and Challenges

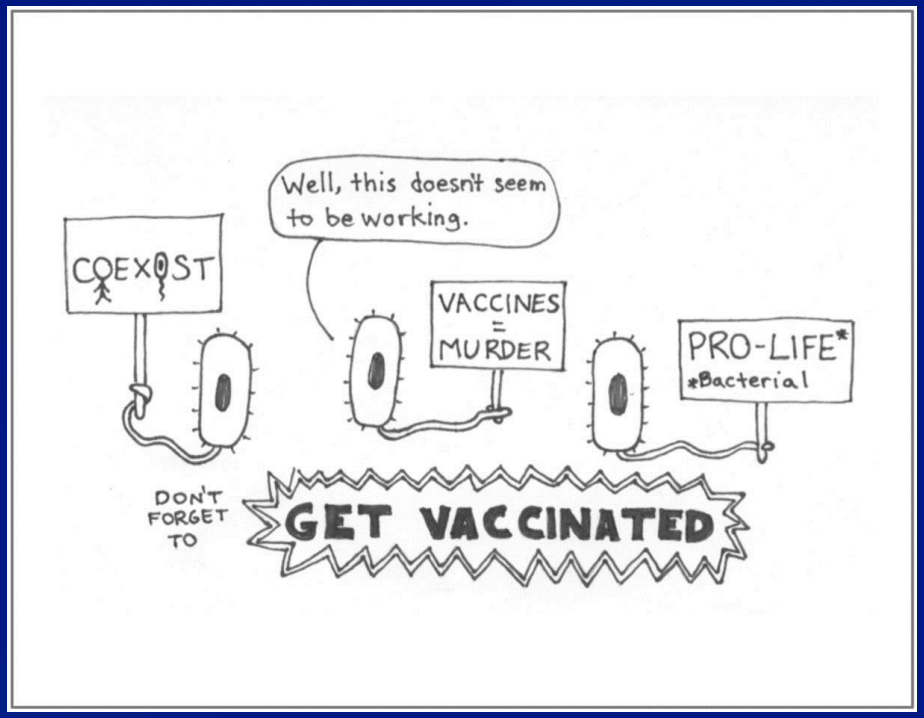
- Protecting community members
  - Role of University Health Services - rapid identification and treatment of cases
  - LHD investigation of cases and contact tracing

- CDC's efforts on the IND application – time and resource intensive

- Getting students vaccinated
  - Logistics of vaccine procurement and implementation
  - Safety follow-up requirements

Success – Getting Students Vaccinated

- Recent case
- Parental pressure
- Peer pressure
  - Meng arm
  - Tiger stamp
- Expedient clinic
- Media coverage



Success - Messaging

- Princeton's communication team meet almost weekly

- Developed Communications Plan/Timeline
  - Web
  - E-mails
  - Pamphlets
  - Videos
  - Text Messages
  - Forums and Meetings
  - The Daily Princetonian
  - Other media

18 comments

'Mine. Not Yours': Princeton University hands out red cups to curb meningitis, promote safe drinking

By Jon Offredo/The Times of Trenton
Follow on Twitter
on September 20, 2013 at 6:30 AM, updated September 20, 2013 at 6:42 AM

PRINCETON — In an effort to avoid a repeat of a bacterial meningitis outbreak that hit Princeton University's campus last spring, the university is distributing 5,000 red, 16-ounce cups emblazoned with a message for students to not share their beverages.

The cups read, "Mine. Not Yours." and include markings for the standard alcoholic drink size for liquor, wine and beer, along with the phone number for the university's department of public safety. They are intended to help curb the spread of meningitis and

Student Stuff

MENINGITIS B VACCINE CLINIC

FEBRUARY 17 - 20
12 - 8 PM

FRIST CAMPUS CENTER
B LEVEL

TWO DOSES ARE NEEDED FOR MAXIMUM PROTECTION

- FREE for all undergraduate students, and eligible graduate students and eligible employees
- Bring your PUID
- All eligible individuals must sign consent form
- Students under 18 years old must bring permission form signed by a parent/guardian
- First or second dose available
- For information about eligiblity visit: http://bit.ly/MqJ83l

MENINGITIS B VACCINE CLINIC

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Success and Challenges

- Message fatigue (>1 year)
- High vaccination rates
  - False sense of security?
- Effect of vaccine on carriage is unknown
- Protecting incoming freshmen

Success and Challenges

- Coordinated effort
- Delivery of one consistent message
  - Different stakeholders, concerns, pressures
- Partners included
  - CDC
  - NJDOH
  - Princeton Health Department
  - Princeton University
  - Maxim Health Systems
  - Novartis

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NJDOH Laboratory Staff

CDC Laboratory Staff

THANK YOU!!!

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