Epidemiology and Prevention of Meningococcal Disease in Adolescents

Jessica MacNeil, MPH

Epidemiologist

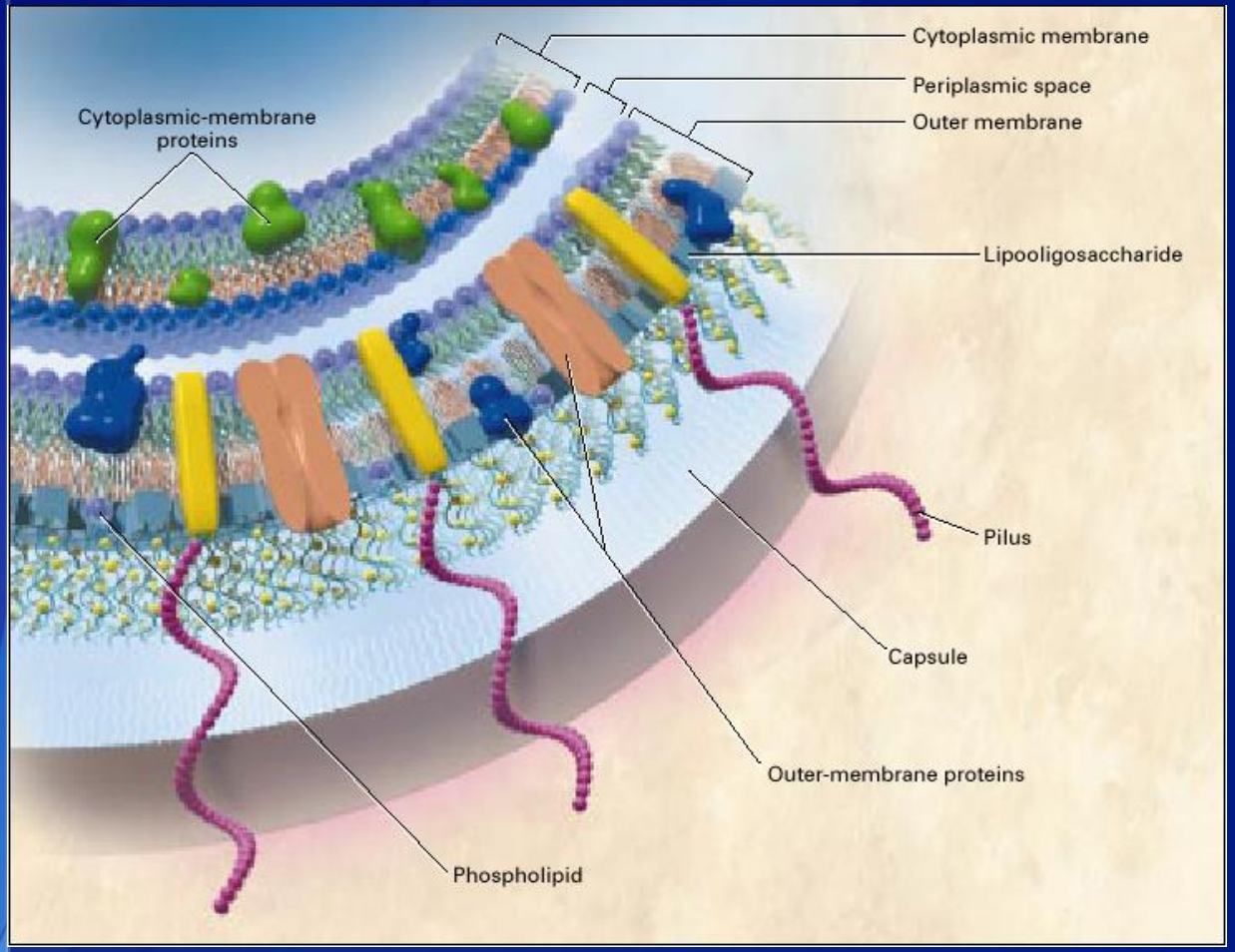
Centers for Disease Control and Prevention (CDC)

July 16, 2015

Meningococcal Disease

- **Three syndromes**
  - Meningitis
  - Bloodstream infection
  - Pneumonia
- **“Flu-like” symptoms early**
- **Rapidly progressive**
- **High morbidity and mortality**
  - 10-15% case-fatality
  - 11-19% with long-term sequelae
- **Most disease occurs in previously healthy persons**

Neisseria meningitidis bacteria



Capsule

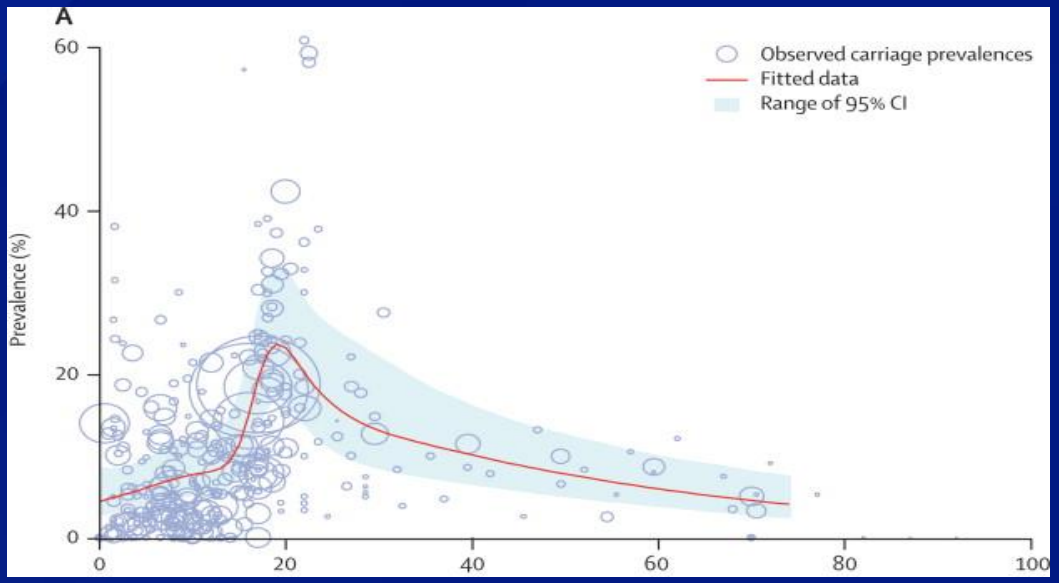
- 13 types
- 6 cause most disease globally (A, B, C, W, X, and Y)
- Target for conjugate vaccines

Outer-membrane proteins

- Targets for serogroup B vaccines

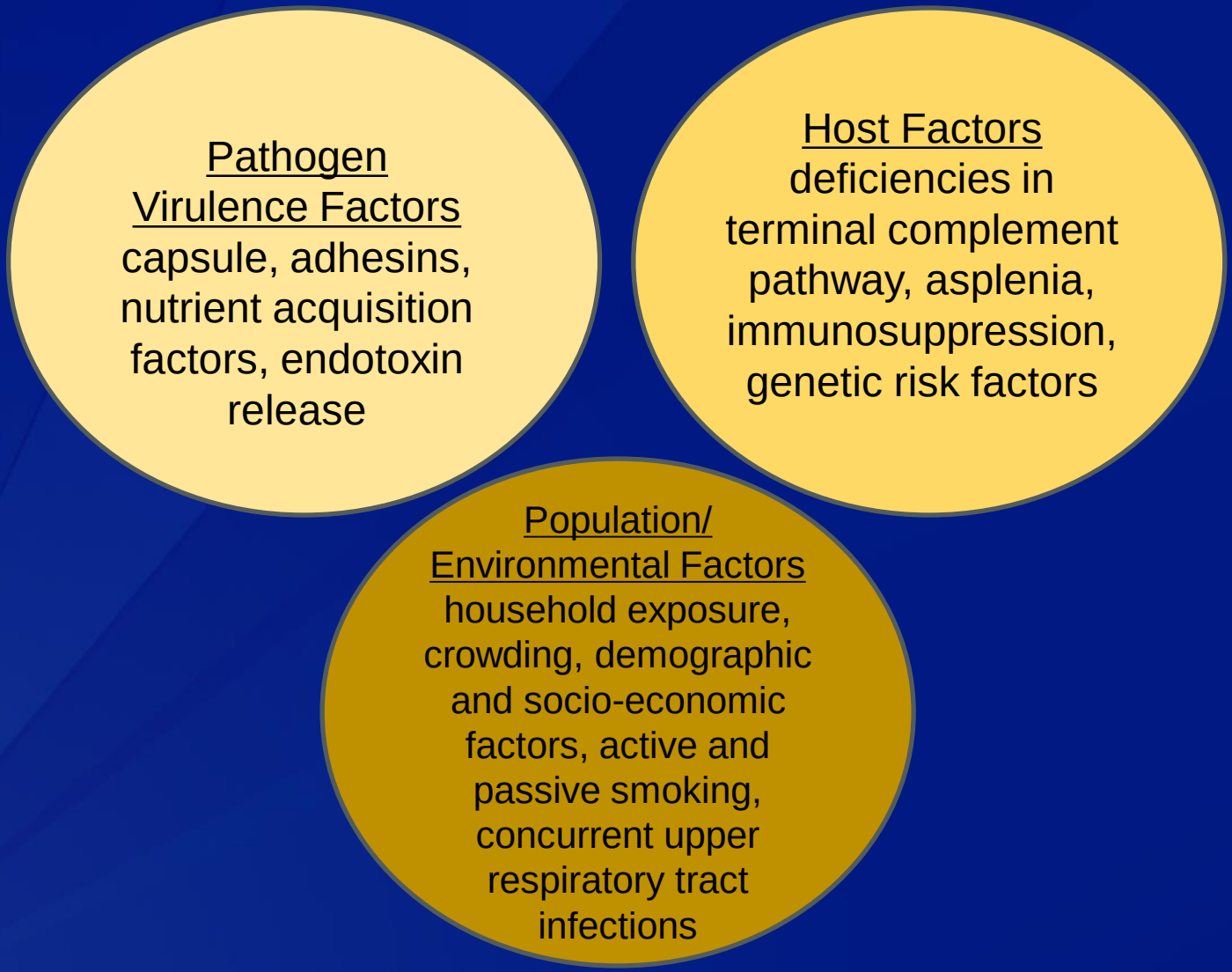
Nasopharyngeal Carriage

- **Approximately 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



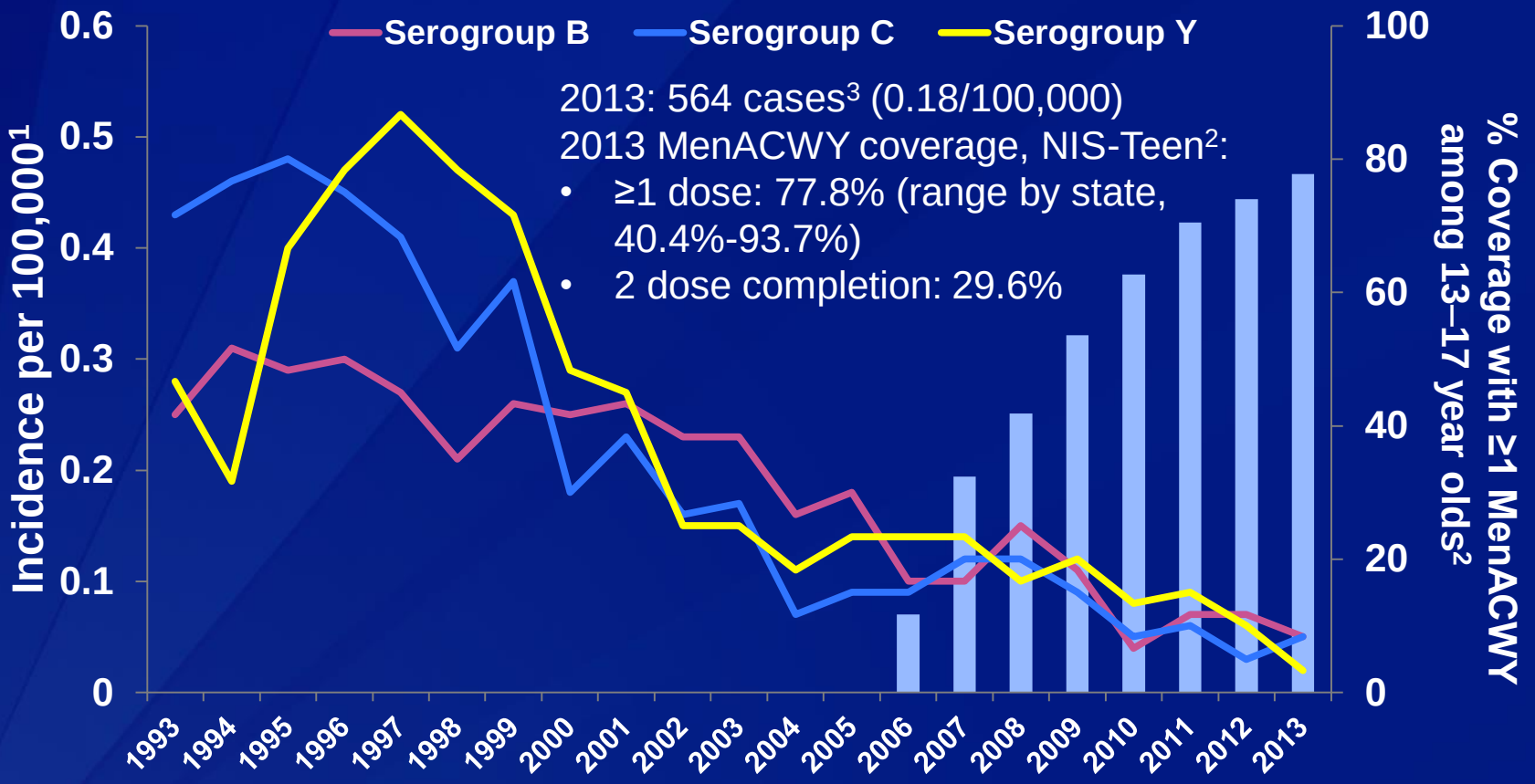
- **Carriage is asymptomatic and ranges from weeks to months**
  - Longer duration for strains that can establish long-term commensal relationships with the host

Meningococcal Disease Risk Factors



EPIDEMIOLOGY AND BURDEN OF MENINGOCOCCAL DISEASE

Meningococcal Incidence in All Ages by Serogroup and Adolescent MenACWY Vaccine Coverage, 1993–2013

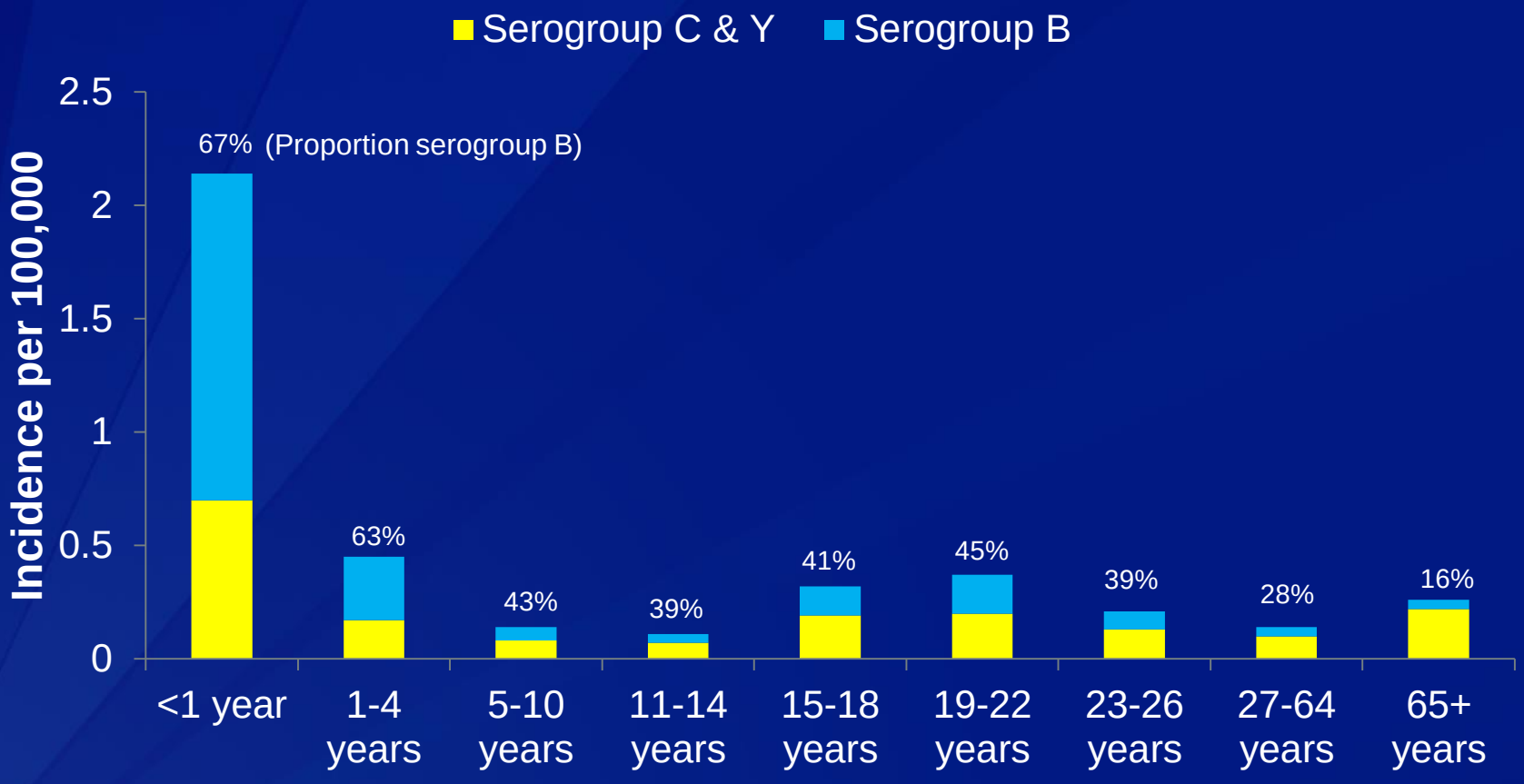


[1]Source: Active Bacterial Core surveillance (ABCs) cases from 1993-2013 estimated to the U.S. population with 18% correction for nonculture confirmed cases. In 2010, estimated case counts from ABCs were lower than cases reported to the National Notifiable Diseases Surveillance System (NNDSS) and might not be representative.

[2]National Immunization Survey-Teen; 2006-2013.

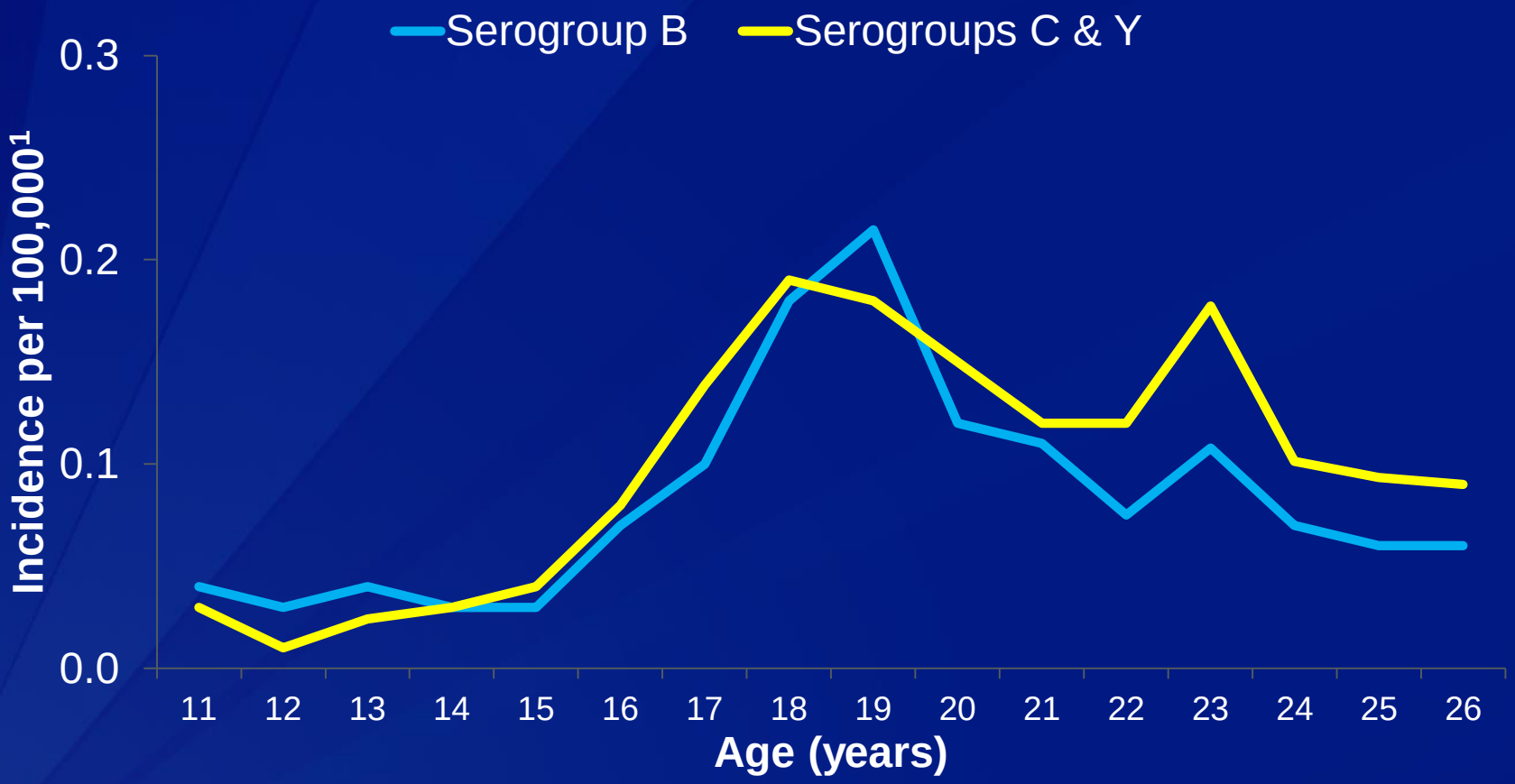
[3]NNDSS 2013 final case count

Meningococcal Incidence by Serogroup* and Age-Group, 2005-2012



*NNDSS data with additional serogroup data from ABCs and state health departments.
Unknown serogroup (23%) and other serogroups (8%) excluded

Meningococcal Incidence in Adolescents and Young Adults by Serogroup, 2009–2013



[1]Source: National Notifiable Diseases Surveillance System (NNDSS) data with additional serogroup data from Active Bacterial Core surveillance (ABCs) and state health departments
Unknown serogroup (19%) and other serogroups (8%) excluded

Estimated Average Annual Cases by Age Group and Serogroup, 2009–2013

	Age Group	Cases[1]
Serogroup B	<5 years	74–94
	11-24 years	54–67
	All ages	203–260
Serogroups C & Y	<5 years	34–43
	11-24 years	62–77
	All ages	307–393

- The majority (~80%) of serogroup B cases that occur in 11–24 year olds occur in older adolescents and young adults aged 16–24 years

[1]Range in estimated cases: Low=NNDSS data supplemented with additional serogroup data from ABCs and state health departments, High= NNDSS data supplemented with additional serogroup data from ABCs and state health departments + proportion serogroup B or serogroup C & Y applied to cases with unknown serogroup.

Average Annual Cases, Deaths, and Incidence from Serogroup B, 2009–2013

	Cases[1]	Deaths[1]	Incidence per 100,000[3]
All 18–23 year olds	36	5	0.14
Estimated cases:			
College students[2]	14	2	0.09
Non-college students[2]	22	3	0.21

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

[2]40% of serogroup B cases in 18–23 year olds from ABCs were in college students (excluding unknown or missing), 2005–2013

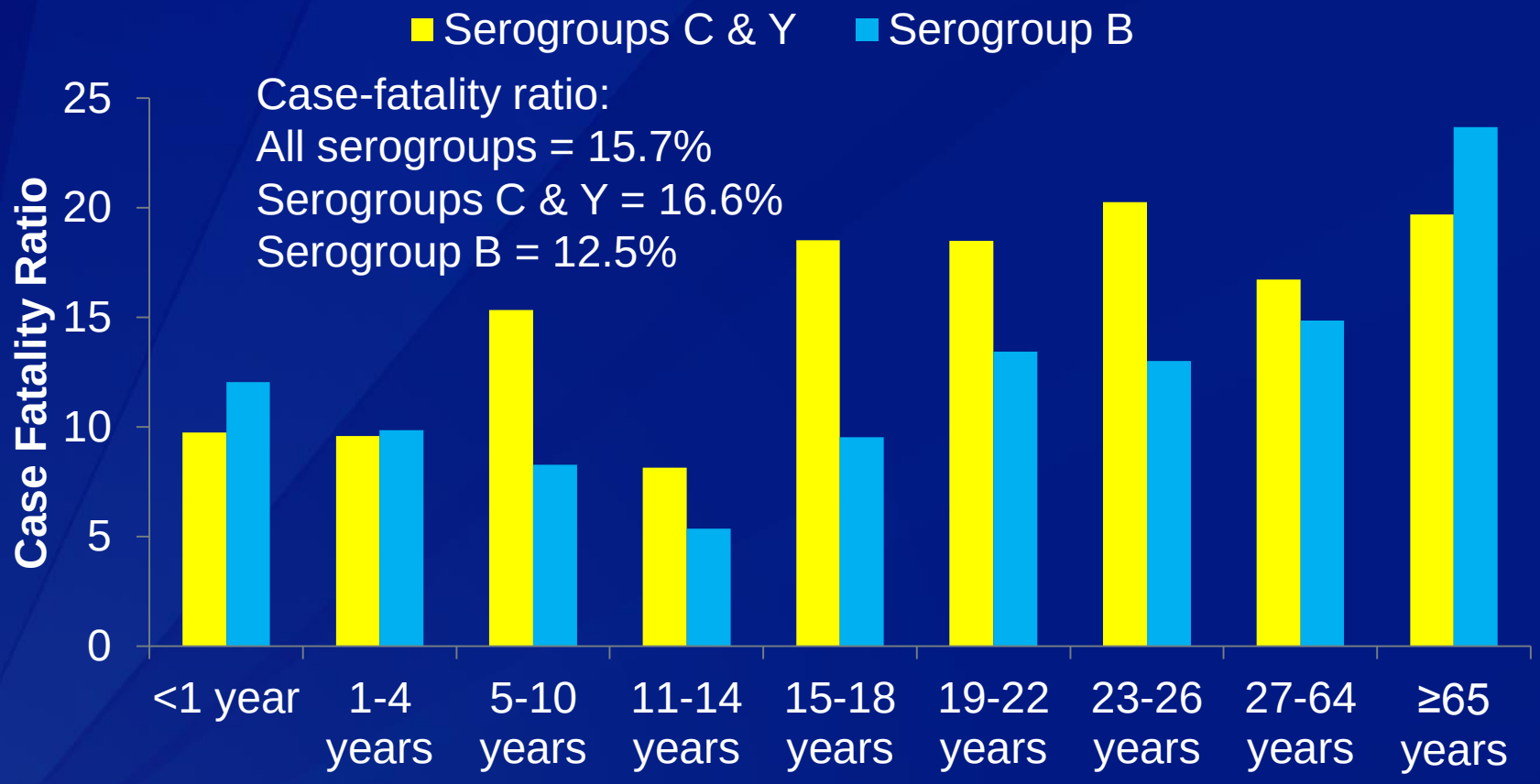
[3]Assume 61% of persons age 18–23 years enrolled in college

Recent University Based Serogroup B Clusters/Outbreaks†

University	Outbreak Period	Number of cases
University 1	Feb – Mar 2009	4
University 2	Nov 2011	2
University 3	Jan 2008 – Nov 2010	13
University 4	Mar 2013 – Mar 2014	9
University 5	Nov 2013	4*
University 6	Jan – Feb 2015	2
University 7	Jan – May 2015	7

†Where CDC consulted
*1 additional associated case identified after retrospective case review

Meningococcal Disease Case-Fatality Ratios by Serogroup and Age-group, 2005-2012



NNDSS data with additional outcome data from ABCs and state health departments. Unknown outcome excluded (18%)

MENINGOCOCCAL VACCINES

Licensed Meningococcal Vaccine Products, U.S.

Vaccine	Type	Manufacturer	Serogroups	Ages
Menactra®	Conjugate – Diphtheria 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
Trumenba®	Protein	Pfizer Vaccines	B	10—25 years
Bexsero®	Protein	Novartis Vaccines	B	10—25 years

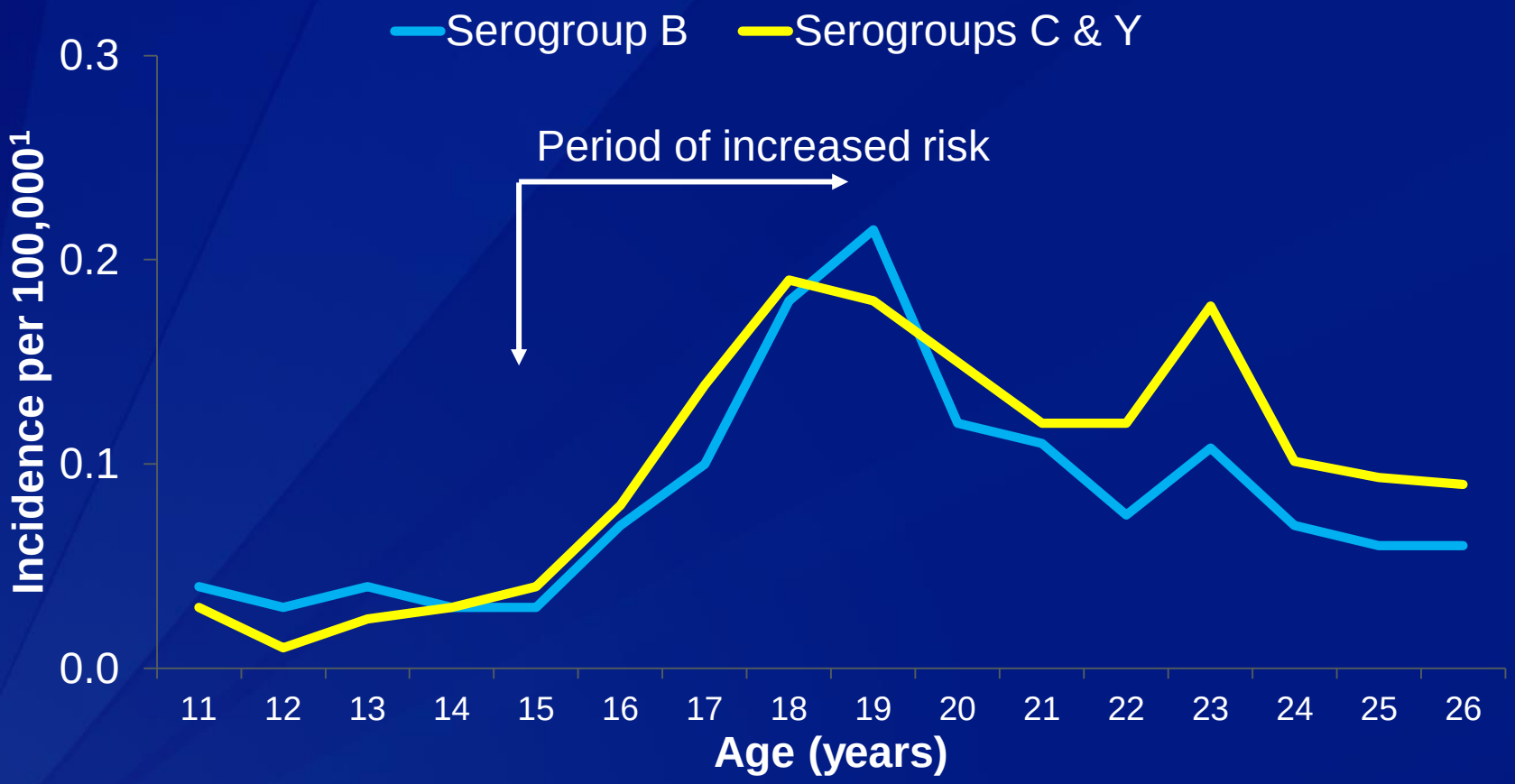
Meningococcal Conjugate Vaccines

- **Benefits compared to polysaccharide vaccines**
  - Immunogenic in infants and young children
  - Superior immunologic memory with boosting on re-exposure
  - Prevent nasopharyngeal carriage with potential for herd immunity
- **Recent conjugate vaccine successes**
  - PCV, Hib vaccination programs in the United States
  - MenC conjugate vaccines in the United Kingdom

Current ACIP Meningococcal Conjugate Vaccine Recommendations

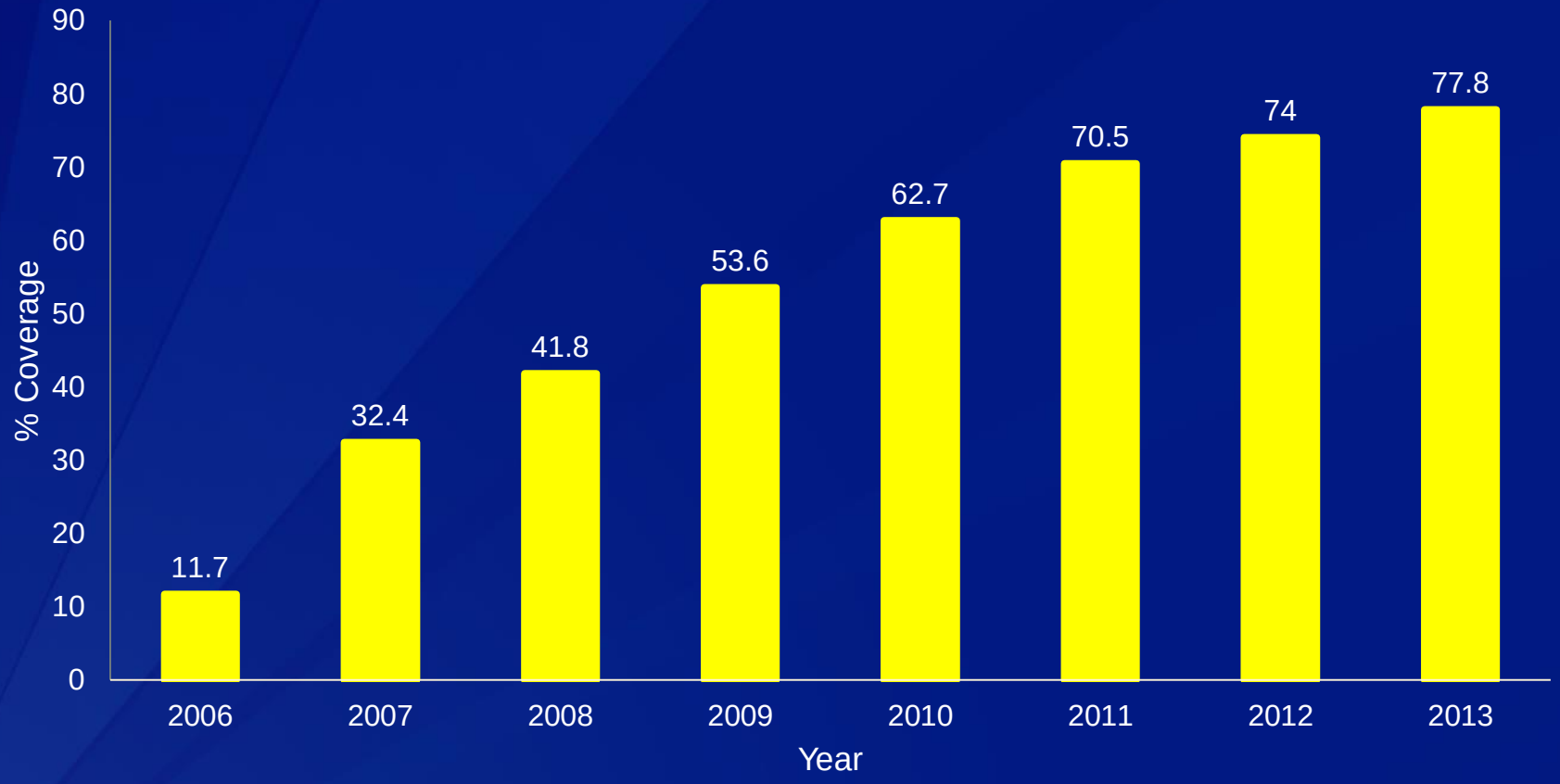
- **Routine vaccination of all adolescents aged 11-18 years**
  - 1st dose at age 11 or 12 years
  - Booster dose at age 16 years
- **Routine vaccination of persons aged ≥ 2 months at increased risk of meningococcal disease**
  - Vaccination of persons in at-risk groups to control outbreaks

Meningococcal Incidence in Adolescents and Young Adults by Serogroup, 2009–2013



[1]Source: National Notifiable Diseases Surveillance System (NNDSS) data with additional serogroup data from Active Bacterial Core surveillance (ABCs) and state health departments
Unknown serogroup (19%) and other serogroups (8%) excluded

Coverage with ≥1 dose of Meningococcal Conjugate (MenACWY) among 13-17 year olds, NIS-Teen, 2006-2013



National Immunization Survey-Teen; 2006-2013.

Decreasing Incidence of Serogroup C, W, Y Meningococcal Disease in 11–19 Year Olds

Year	Incidence per 100,000 (95% confidence intervals)[1]		
	<1 year	11–19 years	≥20 years
2004-2005	0.77 (0.33, 1.55)	0.27 (0.17, 0.39)	0.17 (0.14, 0.21)
2006-2007	1.20 (0.61, 2.11)	0.31 (0.21, 0.45)	0.23 (0.19, 0.28)
2008-2009	0.93 (0.48, 1.69)	0.15 (0.08, 0.26)	0.23 (0.19, 0.27)
2010-2011	1.37 (0.74, 2.33)	0.05 (0.02, 0.12)	0.14 (0.11, 0.18)
2012-2013	0.74 (0.39, 1.32)	0.05 (0.02, 0.10)	0.12 (0.10, 0.15)

- 80% decrease in serogroup C, W, Y meningococcal disease among 11–19 year olds

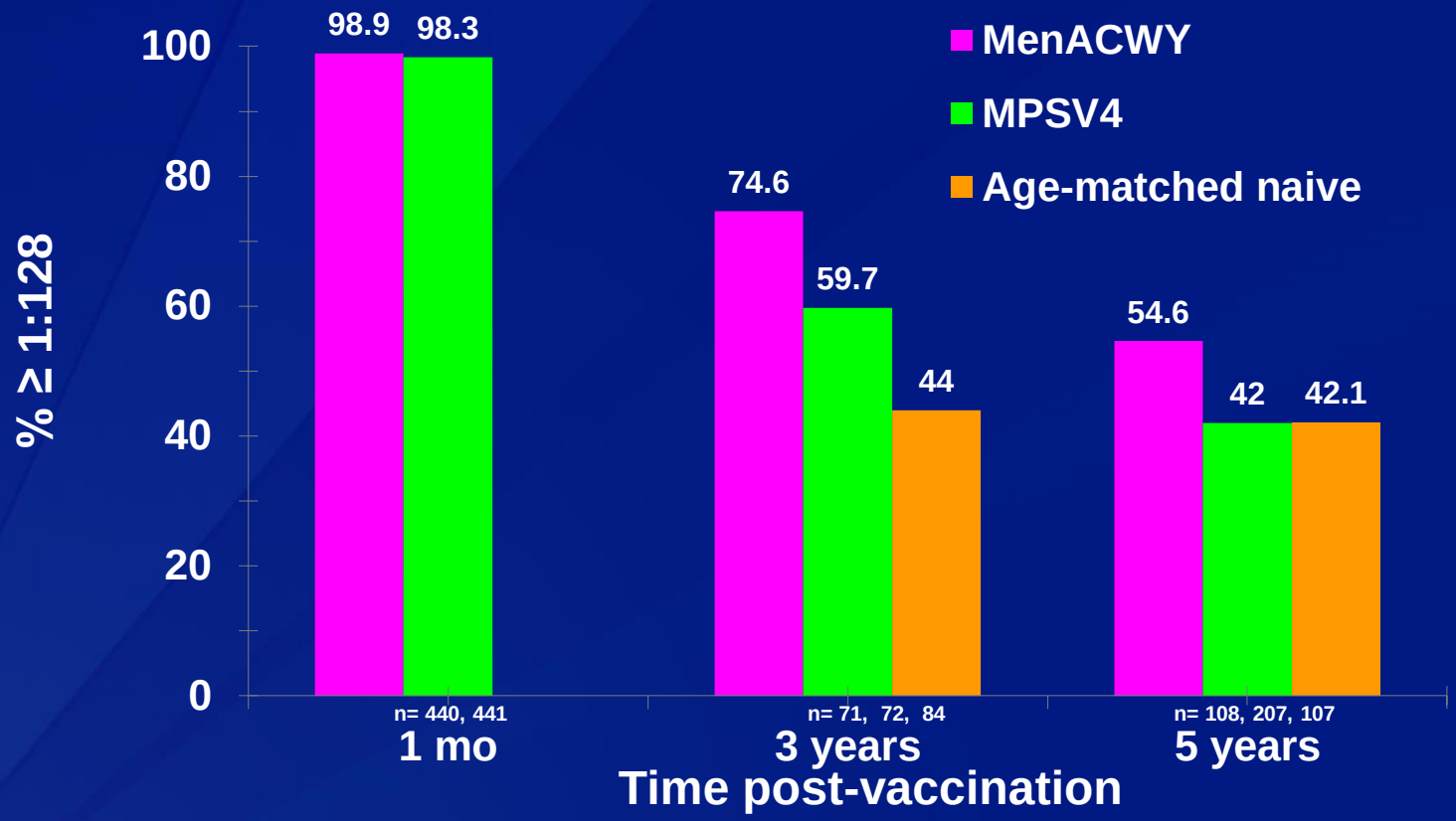
[1]Source: Active Bacterial Core surveillance (ABCs) cases from 2004-2013 estimated to the U.S. population with 18% correction for nonculture confirmed cases. In 2010, estimated case counts from ABCs were lower than cases reported to the National Notifiable Diseases Surveillance System (NNDSS) and might not be representative.

Menactra® Vaccine Effectiveness Estimates, Duration of Protection, GEE

	All Adolescents
	VE (95% CI)
Vaccinated	69% (51%, 80%)
Serogroup C	77% (57%, 88%)
Serogroup Y	51% (1%, 76%)
Vaccinated <1 year	79% (49%, 91%)
Vaccinated 1-<3 years	69% (44%, 83%)
Vaccinated 3-<7 years	61% (25%, 79%)

Controls for smoking, underlying condition status, and age

SBA-BR Seroresponse ≥1:128 Post-Vaccination, Menactra®, Serogroup C

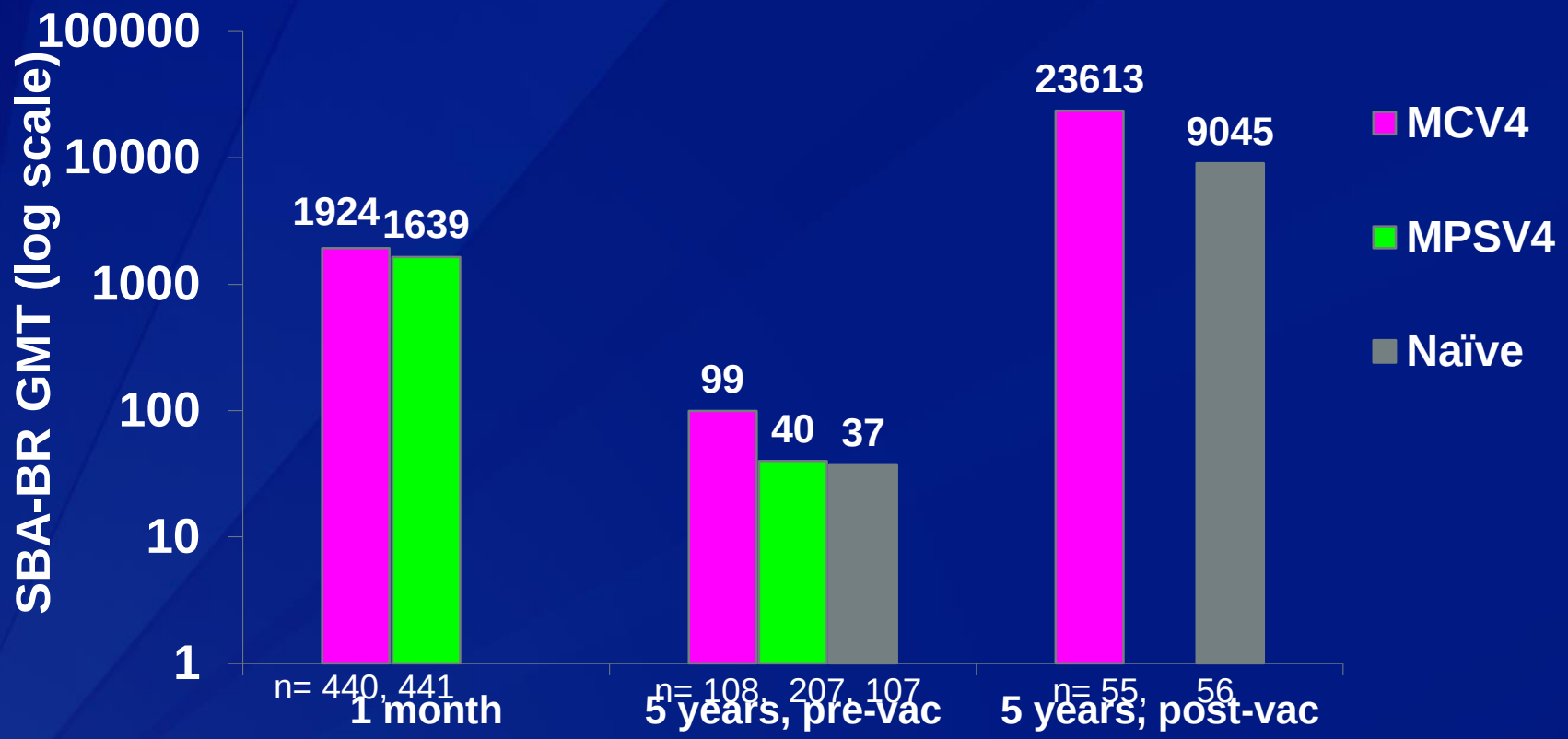


*Data courtesy of sanofi pasteur, 3 year follow-up of MTA02 (11-18 year-olds), 5 year follow-up of 603-02 (2-10 year-olds)

What's going on?

- **Immunologic memory not enough**
  - Boost response takes 5-7 days after exposure, incubation period of *N. meningitidis* is 1-4 days
  - Need circulating antibody at time of exposure
- **Circulating antibody wanes after conjugate vaccine**
  - Approximately 50-60% of persons vaccinated had titers above level required for licensure 5 years after vaccination
- **Unlikely getting the additional benefits of herd immunity with the current U.S. program**
  - Coverage increased slowly
  - Adolescent immunity at population level lower than 60%

SBA-BR Pre- and Post-booster, Menactra®, Serogroup C



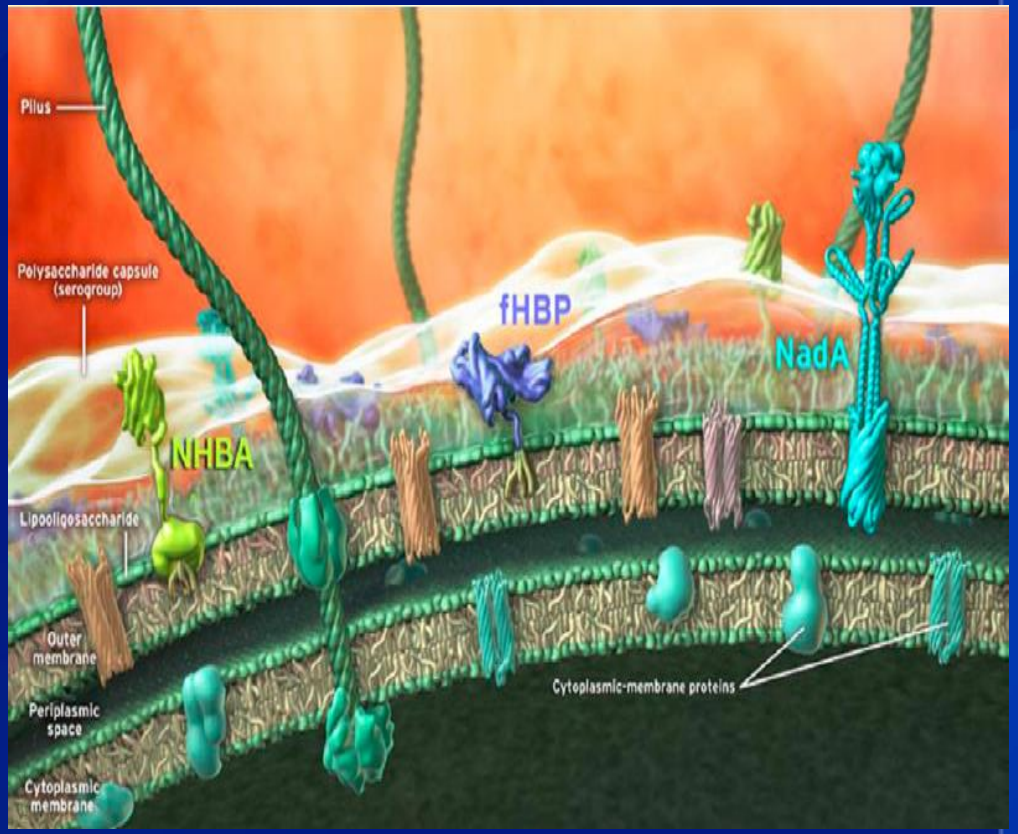
*Data courtesy of sanofi pasteur, 5 year follow-up of (11-18 year-olds at dose 1)

Rationale: 2011 Booster Dose Recommendations

- Optimize protection through late adolescence
- Expectation that antibody decline will not be as rapid after the booster dose
- Increase potential for herd immunity

Serogroup B Meningococcal (MenB) Vaccines

- Serogroup B capsular polysaccharide is poorly immunogenic
- Previously developed serogroup B vaccines are clone specific
- Alternative approaches for vaccine development needed



Vaccine 30S:B87,2012

Two MenB Vaccines For Persons Aged 10–25 Years in the United States

- **MenB-FHbp (Trumenba®, Pfizer)**
  - Components: fHbp subfamily A/v2,3; subfamily B/v1
  - 3 dose series, administered at 0, 2, 6 months
  - Licensed in the U.S. on October 29, 2014
- **MenB-4C (Bexsero®, Novartis/GSK)**
  - Components: fHbp subfamily B/v1, NhbA, NadA, Por A1.4
  - 2 dose series, administered at 0 and ≥1 month
  - Licensed in the U.S. on January 23, 2015
  - Licensed in >37 countries for persons ≥2 months of age

Licensure of MenB Vaccines

- **Following outbreaks of serogroup B meningococcal disease on two college campuses in 2013 licensure accelerated**
- **Both MenB vaccines were granted Breakthrough Therapy designations**
  - Expedites drug development and review by FDA
- **Both MenB vaccines were licensed based on accelerated approval regulations**

Options for Use of MenB vaccines

- **Recommendation for groups at increased risk**
  - Medical conditions
    - Persistent complement component deficiencies
    - Anatomic or functional asplenia
  - Microbiologists
  - Outbreak response
- **Routine recommendation for expanded groups**
  - Adolescent or college student recommendation

ACIP Recommendation for Use of MenB Vaccine in Persons at Increased Risk, Feb 2015

- **A serogroup B meningococcal (MenB) vaccine series should be administered to persons aged ≥10 years at increased risk for meningococcal disease. (Category A) This includes:**
  - Persons with persistent complement component deficiencies[1]
  - Persons with anatomic or functional asplenia[2]
  - Microbiologists routinely exposed to isolates of *Neisseria meningitidis*
  - Persons identified to be at increased risk because of a serogroup B meningococcal disease outbreak

[1]Including inherited or chronic deficiencies in C3, C5-9, properdin, factor D, factor H, or taking eculizumab (Soliris®)

[2]Including sickle cell disease

Use of Serogroup B Meningococcal Vaccines in Persons Aged ≥10 Years at Increased Risk for Serogroup B Meningococcal Disease: Recommendations of the Advisory Committee on Immunization Practices, 2015. MMWR. June 12, 2015 / 64(22);608-612

Challenges when Considering Routine Use of MenB Vaccines in Adolescents

- **Proportion of serogroup B cases that could be prevented with MenB vaccines is unknown**
  - Breadth of strain coverage estimated; actual breadth of strain coverage unclear
  - Available antibody persistence data suggests limited duration of protection
- **Effectiveness data are not available**
  - Licensure is based on bactericidal activity
  - Universal programs not implemented in any country to date
- **Impact on carriage unknown**
- **Potential impact of vaccine pressure on circulating strains unknown**

Potential Cases and Deaths Prevented per 4M Cohort

	Cases Prevented	Deaths Prevented	NNV* to prevent case	NNV to prevent death	Cost ($) per QALY
Series at 11 years	15	2	203,000	1,512,000	$8.700.000
Series at 16 years	28	5	107,000	788,000	$4,100,000
Series at 18 years	29	5	102,000	638,000	$3,700,000
College students	9	1	368,000	2,297,000	$9,400,000

*Number needed to vaccinate
Source: Ismael Ortega-Sanchez

Proposed Policy Option Language
June 2015 ACIP Meeting

- A serogroup B meningococcal (MenB) vaccine series may be administered to adolescents and young adults 16 through 23 years of age to provide short term protection against most strains of serogroup B meningococcal disease. The preferred age for MenB vaccination is 16 through 18 years of age. (Category B)

Guidance for Use

- MenB should be administered as either a 2-dose series of MenB-4C or a 3-dose series of MenB-FHbp
- The same vaccine product should be used for all doses
- Based on available data and expert opinion, 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

Summary

- **Meningococcal disease is a rare, but serious illness and each case is life-threatening**
- **Key data on MenB vaccines are not yet available**
- **Desire for access to MenB vaccines**
- **Additional work still needed to reinforce the second dose of MenACWY in the current adolescent program**
- **Risk for disease is low**
  - In the absence of vaccination there may be cases that are preventable
  - Even with a fully implemented vaccination program the MenB vaccines will not prevent all cases

Useful References

- "Prevention and Control of Meningococcal Disease" (2013 ACIP Recommendations), MMWR, March 22, 2013
- All ACIP recommendations for meningococcal vaccines: http://www.immunize.org/acip/acipvax_menin.asp
- "Meningococcal Disease" Rosenstein et al. New England Journal of Medicine, May 3, 2001, 344 (18): 1378-88
- "Meningococcal Disease" Red Book Chapter
- "Meningococcal Disease" Pink Book Chapter

Questions?

Thank you!

jmacneil@cdc.gov