

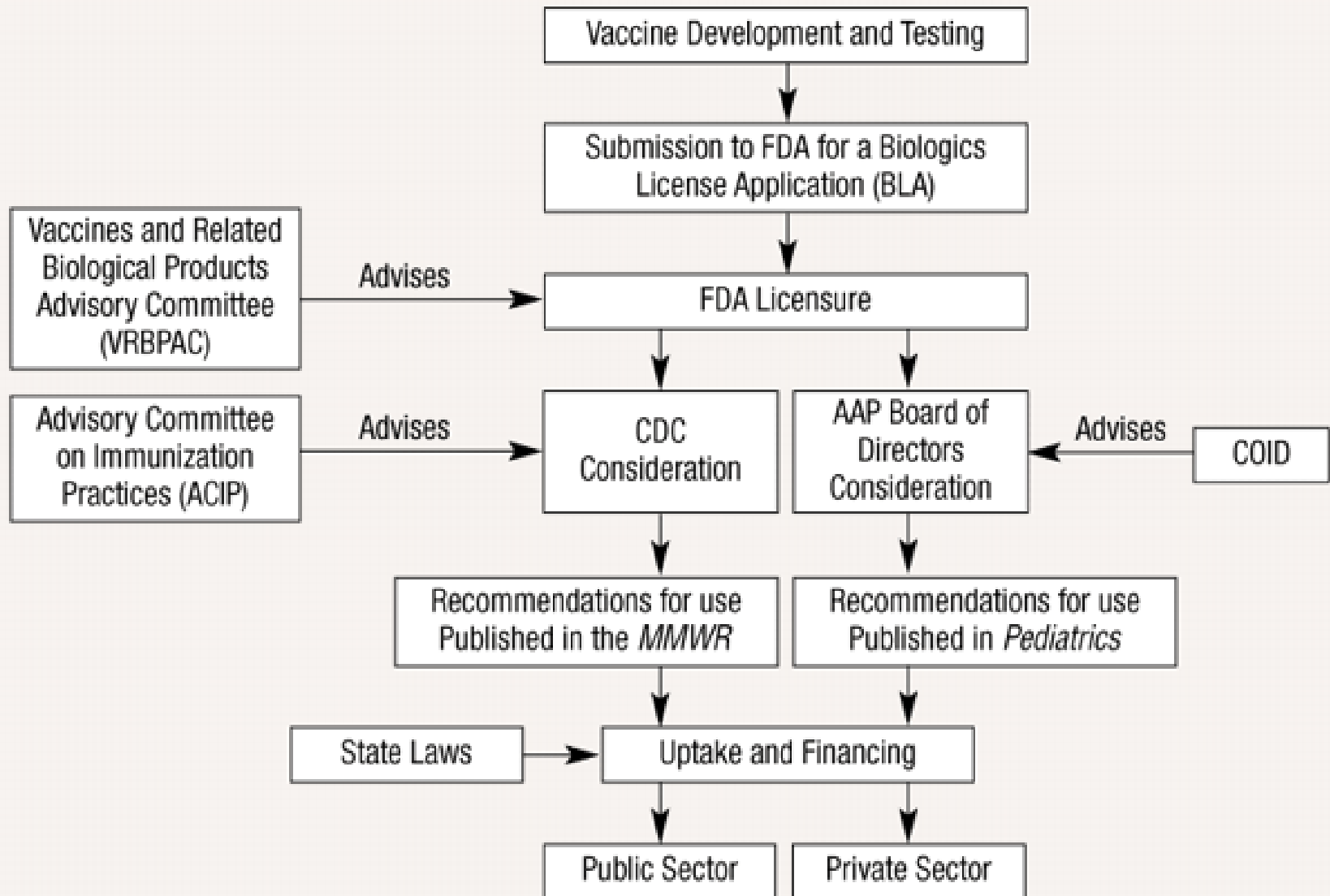
Experience with Quadrivalent Meningococcal Conjugate Vaccines in the United States

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U.S. Centers for Disease Control and Prevention

November 12, 2009

Development of pediatric vaccine recommendations and policies

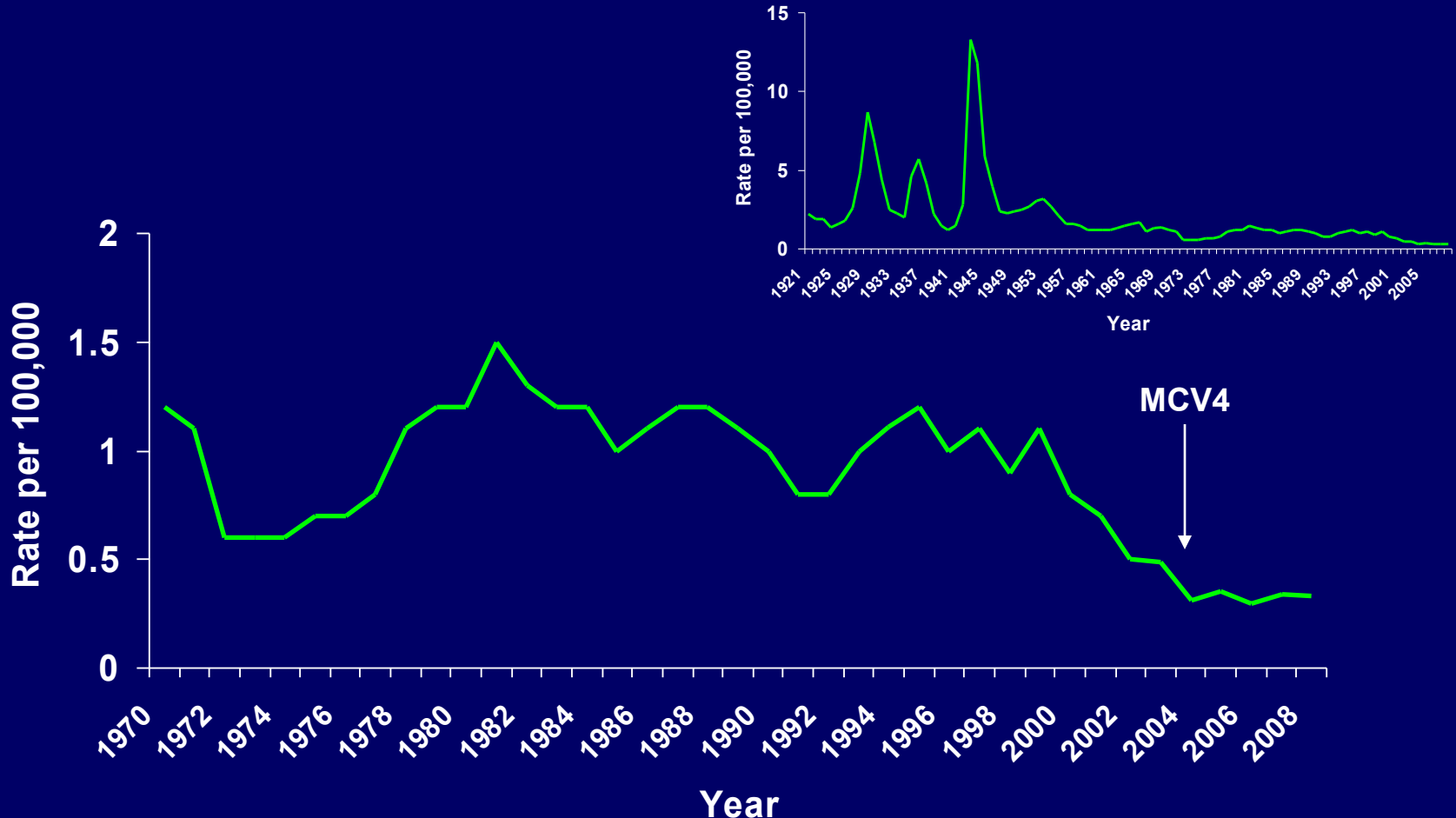


Modified from Pickering LK, Orenstein WA. Development of pediatric vaccine recommendation and policies. *Semin Pediatr Infect Dis.* 2002;13:148-154. Reprinted with permission.

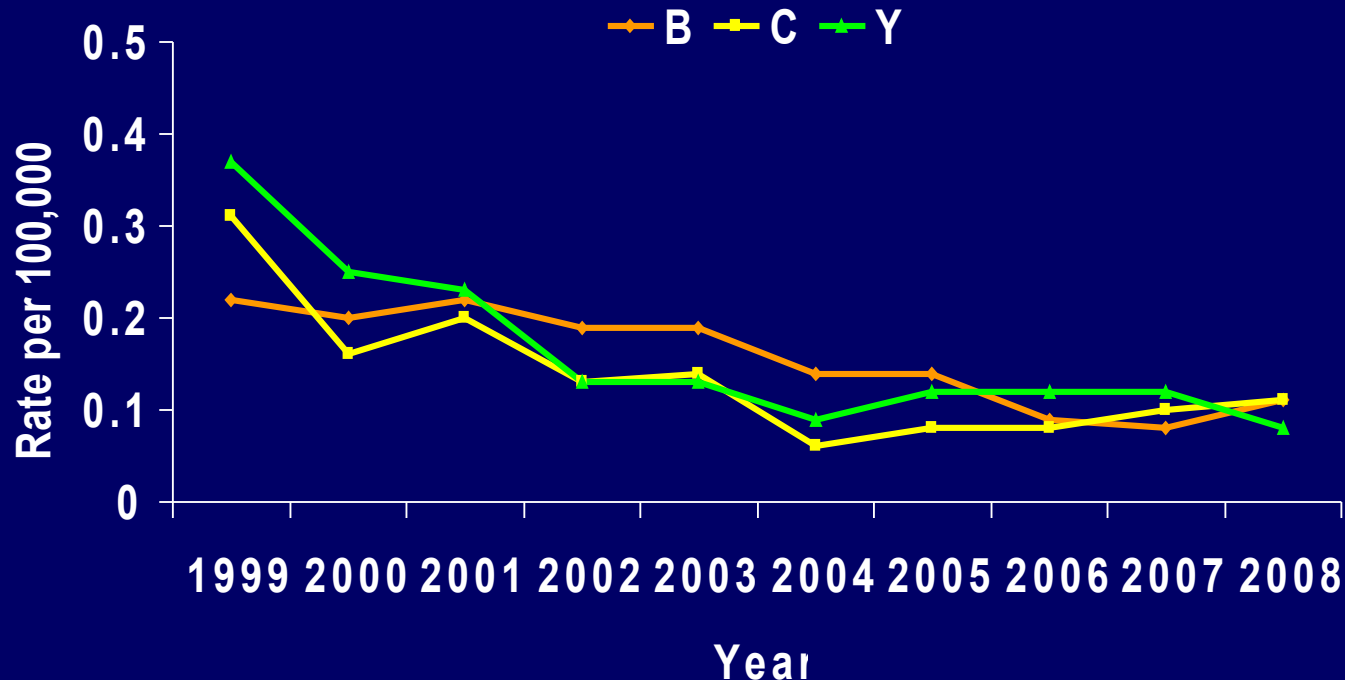
Outline

- Epidemiology of meningococcal disease in the U.S.
- Quadrivalent Meningococcal vaccines in adolescents
- Meningococcal vaccines in infants

Meningococcal Disease Incidence, United States



Meningococcal Disease Incidence by Year and Serogroup, 1999-2008



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ABCs cases from 1999-2008 are projected to the U.S. population

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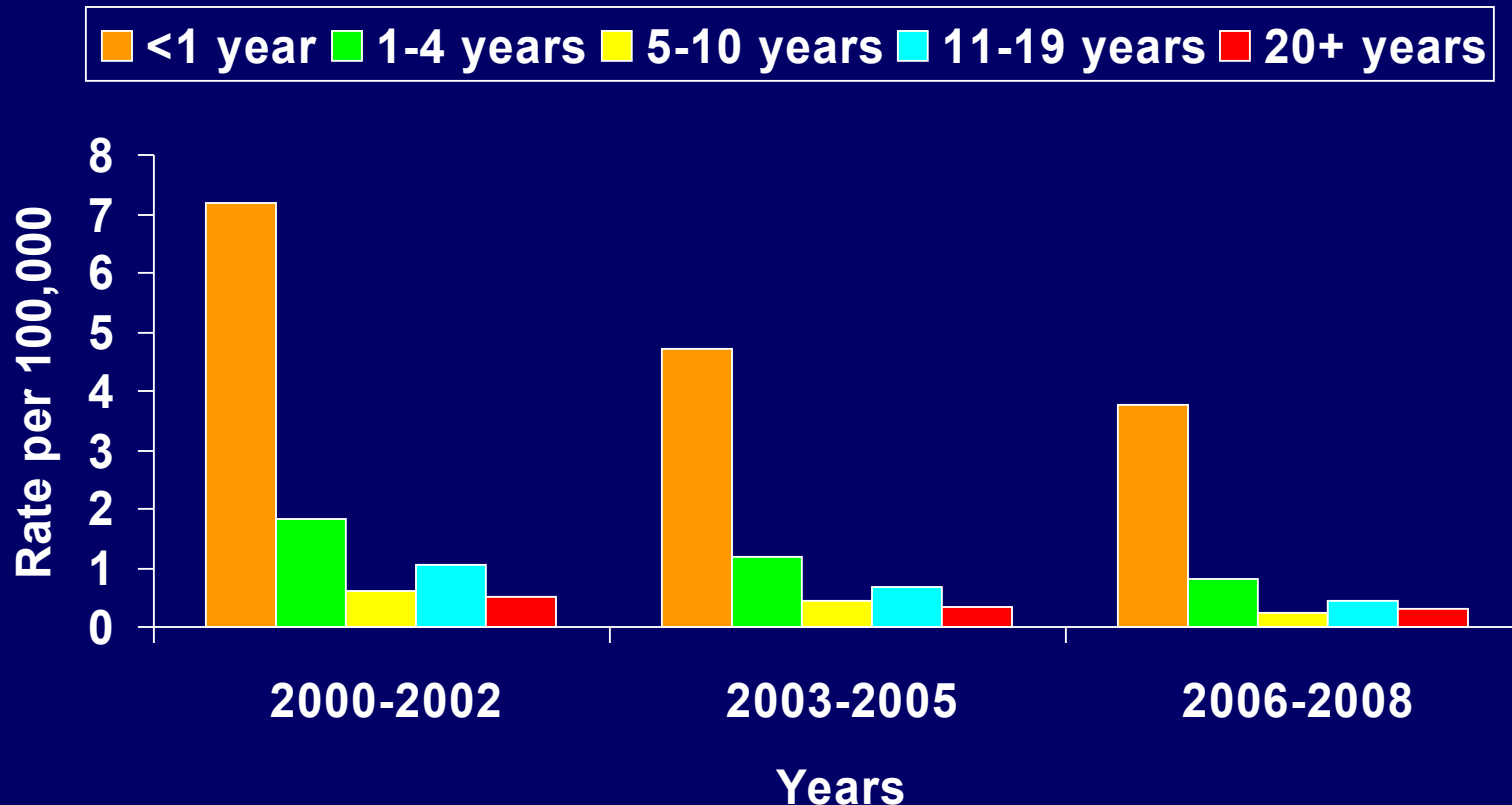


Carriage Among Adolescents in 2 Highschools, 2006

State	Group	Sample size	B		C		Y		NG		Total	
			N	%	N	%	N	%	N	%	N	%
All	Vaccinated	1731	6	0.35	0	0	6	0.35	49	2.83	61	3.52
	Control	1543	3	0.19	0	0	3	0.19	39	2.53	45	2.92
	Total	3274	9	0.27	0	0	9	0.27	88	2.69	106	3.24

Clark et al, IPNC 2008

Meningococcal Disease Incidence by Year and Age, 2000-2008

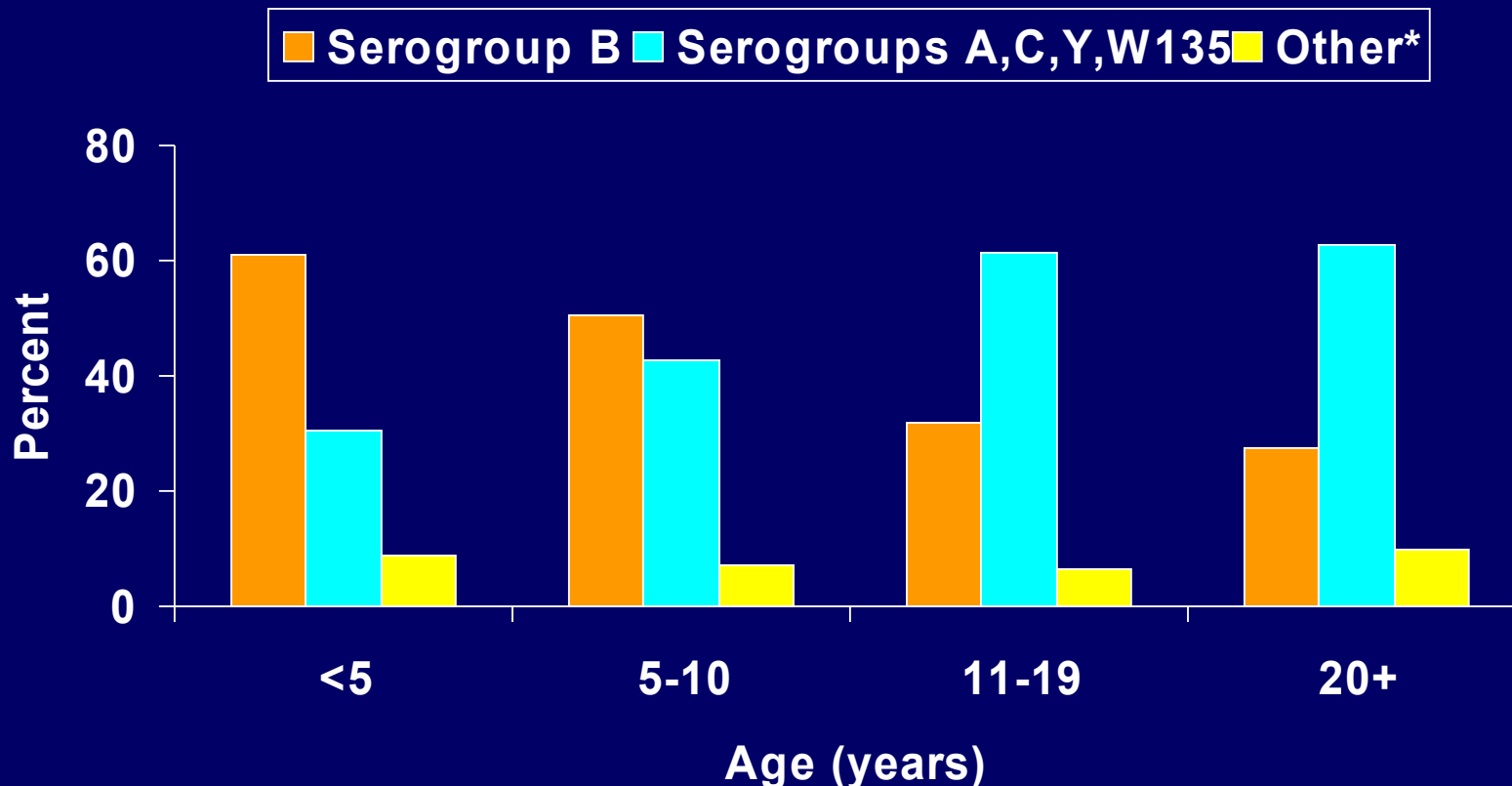


2000-2008 NNDSS reports, includes probable and confirmed cases

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Proportion of Meningococcal Cases by Age and Serogroup, ABCs, 1999-2008



*Other includes: nongroupables, other, and unknown

Average Annual Cases of Meningococcal Disease in Children <5 years, 1999-2008

Age	Serogroup B	Serogroup C	Serogroup Y	Serogroup C + Y (Incidence)
0-2 months	52	6	18	24 (2.3)
3-5 months	36	8	19	27 (2.5)
6-8 months	35	7	14	21 (2.0)
9-11 months	17	5	2	7 (0.7)
1 year	33	11	7	18 (0.4)
2 years	23	16	6	22 (0.5)
3 years	17	7	1	8 (0.2)
4 years	8	7	5	12 (0.3)
Total	231	78	72	150 (0.6)

Average Annual Cases of Meningococcal Disease in Children ≤ 5 years, United States, 1999-2008

Age	ABCs Total	NNDSS Total	2000 NNDSS	2008 NNDSS
0-3 months	80	56	95	45
4-7 months	84	53	70	32
8-11 months	40	32	31	26
1 year	48	74	115	52
2 years	43	54	72	37
3 years	23	43	70	18
4 years	18	30	35	14
5 years	19	23	64	12

Average Annual Deaths and Case-Fatality Ratios by Serogroup and Age, 1999-2008

Serogroup

	B	C	Y	Overall
<1 year	11 (8.3)	3 (11.4)	1 (1.7)	15 (6.7)
1-4 years	2 (2.7)	3 (7.1)	1 (4.8)	6 (3.9)
5-10 years	4 (12.4)	3 (7.3)	3 (20.0)	10 (10.9)
11-19 years	5 (8.7)	15 (15.8)	5 (6.0)	25 (10.5)
20+ years	26 (12.6)	40 (16.9)	47 (14.2)	122 (14.7)

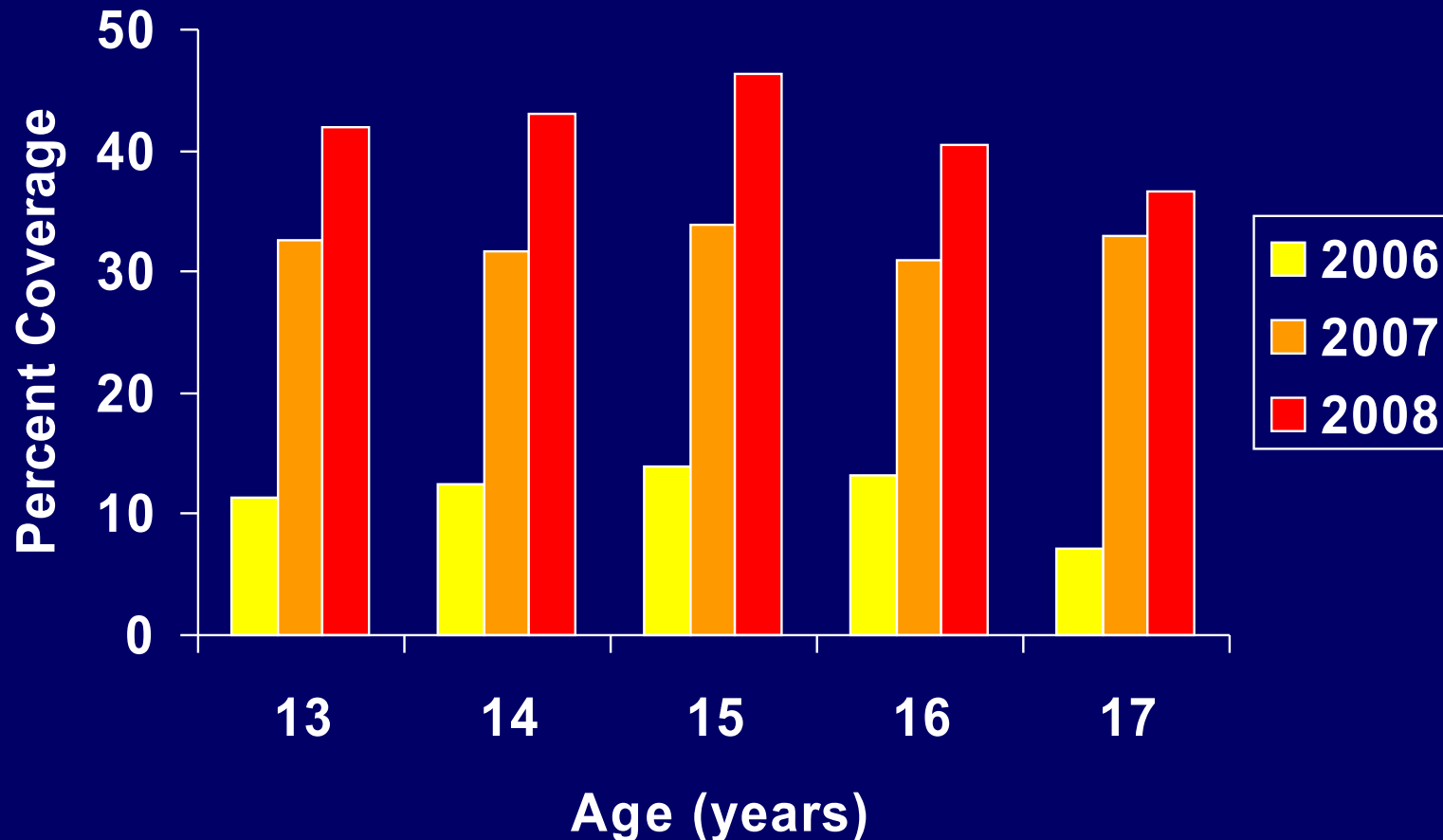
Burden of Meningococcal Disease in the US

- Disease burden currently lower than any other time period
 - Unclear reasons for disease decreases
- Disease incidence is highest in the first 6 months of life
- Proportion of preventable disease is lower among 0-5 year-olds compared to adolescents

Quadrivalent Meningococcal Conjugate Vaccines for Adolescents

- MCV4 (Menactra) licensed for 2-54 year-olds
 - Conjugated to diphtheria toxoid
- Recommended for adolescents 11-12 years, high school entry, college freshmen living in dorms
- Expanded recommendation to 11-19 year-olds in 2007
- Revaccination for high-risk persons every 5 years

Meningococcal Vaccination Coverage among 13-17 year-olds, 2006-07

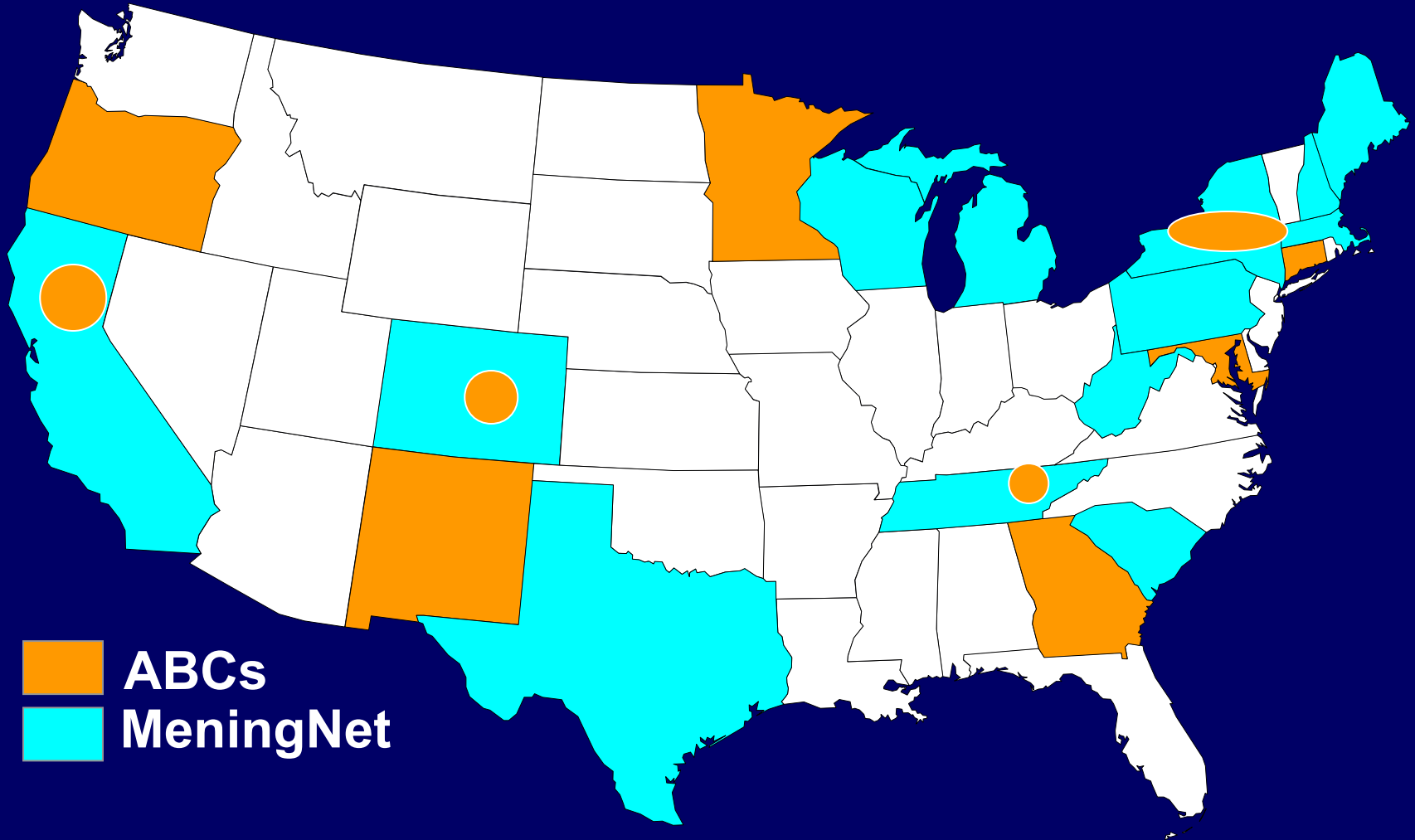


Trends in Meningococcal Disease: Any Detectable MCV4 Impact?

	Serogroup C, Y, W135 cases per 100,000 population (95% credible intervals)		Serogroup B cases per 100,000 population (95% credible intervals)	
	<i>11-18 year olds</i>	<i>All other ages</i>	<i>11-18 year olds</i>	<i>All other ages</i>
1998-1999	1.02 (0.78-1.29)	0.65 (0.58-0.72)	0.16 (0.09-0.27)	0.22 (0.18-0.26)
2000-2001	0.55 (0.39-0.75)	0.40 (0.34-0.45)	0.20 (0.09-0.32)	0.23 (0.19-0.27)
2002-2003	0.41 (0.28-0.59)	0.24 (0.20-0.29)	0.15 (0.08-0.25)	0.19 (0.15-0.23)
2004-2005	0.26 (0.16-0.40)	0.15 (0.12-0.19)	0.07 (0.03-0.14)	0.15 (0.12-0.18)
2006-2007	0.25 (0.15-0.39)	0.20 (0.16-0.24)	0.03 (0.01-0.09)	0.11 (0.08-0.14)

*ABCs cases from 1998-2007 and projected to the U.S. population

ABCs and MeningNet Sites



- ABCs and MeningNet cover 54% of US population

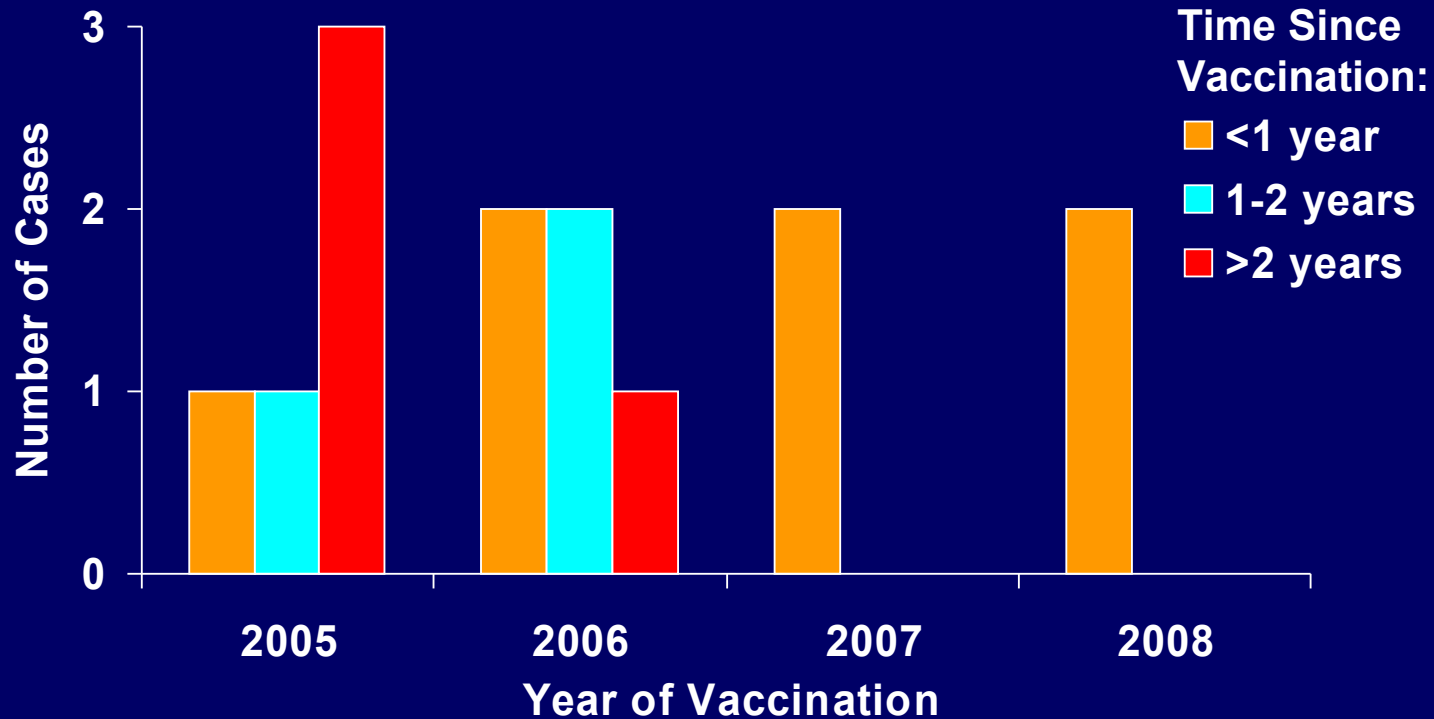
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Meningococcal Disease in Vaccinated Persons, 2005-2008

- 14 confirmed cases*
 - 13 (93%) cases culture confirmed, 1 PCR+ with clinically compatible illness
 - 8 (57%) serogroup C and 6 (43%) serogroup Y
- All received MCV4; no common lot
- Cases identified in 6 of 20 sites

Time from Vaccination to Disease Onset, n=14



- MCV4 coverage was low in 2005 and 2006, most people have been vaccinated <2 years ago

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*Cases identified January 1, 2005 - December 31, 2008

How Many Cases Would We Expect To See Among Vaccinated Persons?

Vaccine Effectiveness	Median Number of Cases (Range)	Probability of Observing ≥ 14 Cases
90%	7 (0-17)	2.9%
85%	11 (2-30)	29.3%
80%	15 (5-28)	66.1%
75%	18 (7-32)	83.0%

Adolescent Meningococcal Vaccines

- Impact blunted by low disease incidence at time of vaccine introduction
- Early estimate of VE lower than 90%, potential implications for duration of protection
 - Vaccine Type
 - Program
- Program not ideal for inducing herd immunity

Potential Options to Address Waning Immunity

- Revaccinate adolescents at 18 years-old, prior to college entry
- Shift first dose into later adolescence
 - 11-12 years → 14-15 years

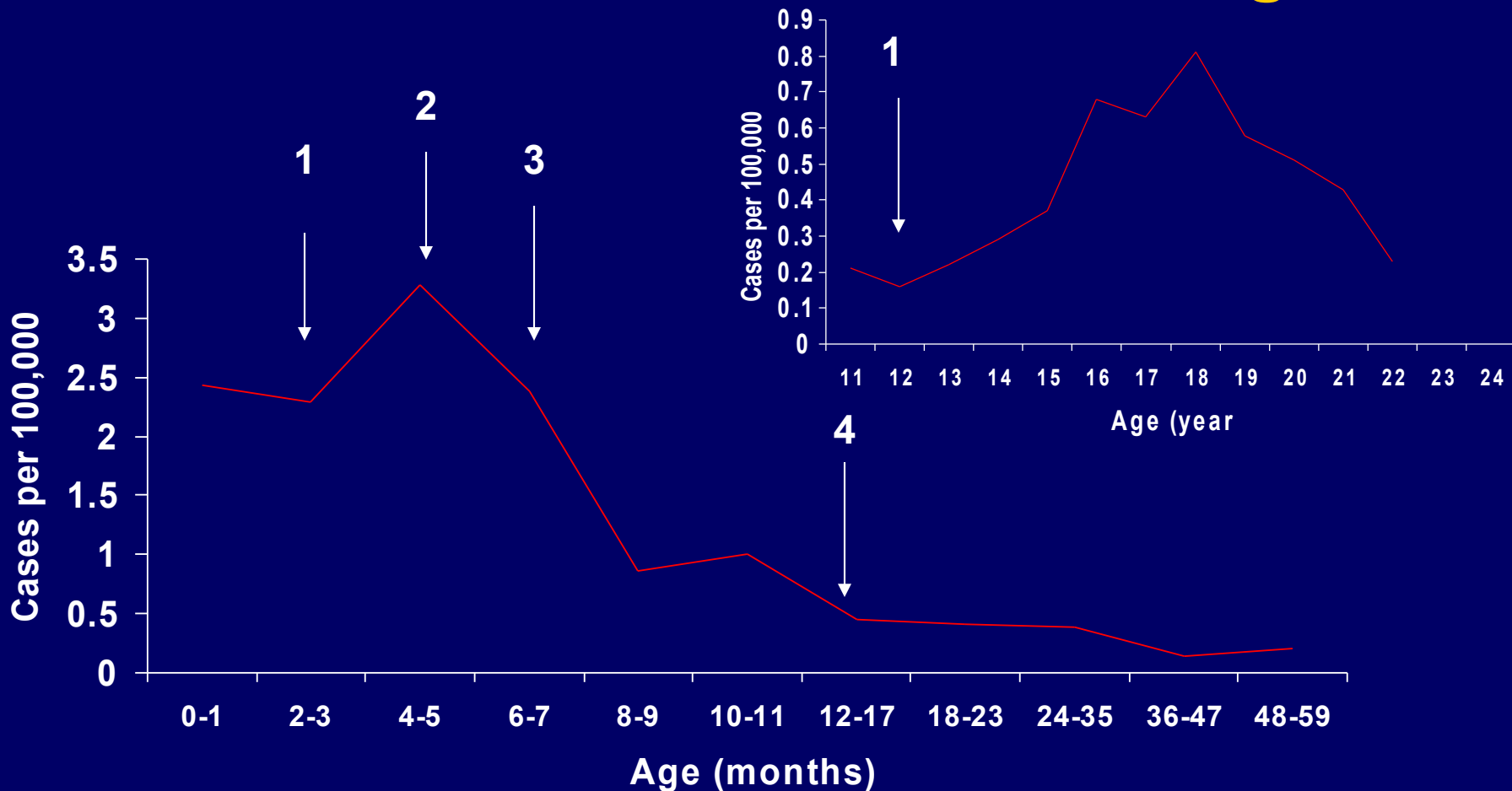
Meningococcal Vaccines for Infants and Toddlers

- Hib-MenCY (GSK)
 - 3 dose priming (2,4,6m) + 12-15 mo booster
- MCV4 (Sanofi)– 9, 12-15 mo 2 dose series
- MenACYW (Novartis)
 - 3 dose priming (2,4,6m) + 12-15 month booster

Use of Multivalent Meningococcal Conjugate Vaccines in the US

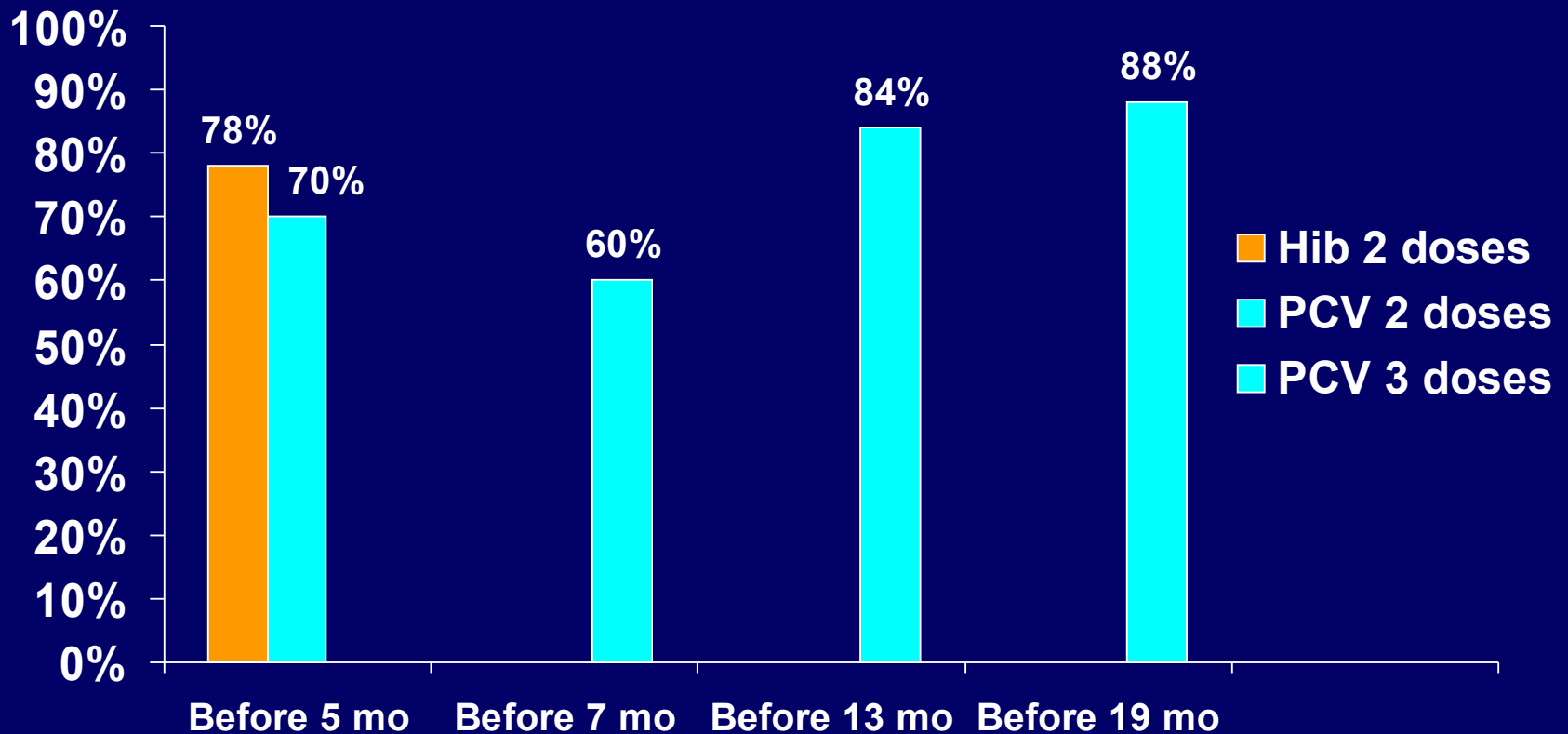
- Immunogenicity and safety
- Burden of disease
- Population impact
- Programmatic considerations
- Cost effectiveness

Serogroups C, Y Meningococcal Disease: Ideal Vaccination Timing



ABCs, 1998-2007 average annual estimated rates to the U.S. population

Attaining High Coverage Early: National Immunization Survey, 2007, Hib and PCV7 coverage



Average Annual Cases of Meningococcal Disease Potentially Prevented, United States, 1999-2008

	Total cases expected	Serogroup C and Y Cases expected	Estimated Preventable Cases	Estimated Preventable Deaths
4 dose series <i>(0-59 month-olds; assumes 80% effectiveness at 4 mo, 70% coverage; 100% effectiveness at 6 mo, 60% coverage; 80% coverage at 9 months; 100% effectiveness at 12 mo, 90% coverage;)</i>	360	139	84	4-6
2 dose series <i>(0-59 month-olds; assumes 100% effectiveness at 12 mo, 90% coverage)</i>	360	139	54	3-4
Adolescent vaccination <i>(11-19 year-olds; assumes 85% effectiveness, 70% coverage)</i>	225	170	101	11-19

Active Bacterial Core Surveillance Data

Programmatic Considerations

- Differences between HibMenCY and other meningococcal vaccines
 - MCV4
 - MenACWY-Crm
- Practical aspects of adding meningococcal vaccines into infant schedule
- Cost-effectiveness

Recommended Immunization Schedule for Persons Aged 0 Through 6 Years—United States • 2009

For those who fall behind or start late, see the catch-up schedule

Vaccine ▼	Age ►	Birth	1 month	2 months	4 months	6 months	12 months	15 months	18 months	19–23 months	2–3 years	4–6 years		
Hepatitis B ¹	HepB		HepB		<i>see footnote 1</i>		HepB							Range of recommended ages
Rotavirus ²				RV	RV	<i>RV</i> ²								
Diphtheria, Tetanus, Pertussis ³				DTaP	DTaP	DTaP	<i>see footnote 3</i>	DTaP				DTaP		Certain high-risk groups
<i>Haemophilus influenzae</i> type b ⁴				Hib	Hib	<i>Hib</i> ⁴	Hib							
Pneumococcal ⁵				PCV	PCV	PCV	PCV				PPSV			
Inactivated Poliovirus				IPV	IPV	IPV						IPV		
Influenza ⁶						Influenza (Yearly)								
Measles, Mumps, Rubella ⁷							MMR			<i>see footnote 7</i>		MMR		
Varicella ⁸							Varicella			<i>see footnote 8</i>		Varicella		
Hepatitis A ⁹							HepA (2 doses)				HepA Series			
Meningococcal ¹⁰											MCV			

Three combination vaccines for first 6 months of life: DTaP-HepB-IPV, DTaP-Hib-IPV, Hib-HepB

Infant Meningococcal Vaccines: A Difficult Balance

- Desire to prevent morbidity and mortality
 - Availability of a safe and effective vaccine that would prevent disease
- Public health “costs” of vaccination program
 - Impact of additional vaccine on overall coverage
 - Rare adverse events in setting of low disease occurrence
 - Long-term implications of adding a vaccine with potentially limited impact on burden of disease

Questions Remaining

- Will disease incidence cycle back up again or remain low?
- Will higher adolescent MCV4 coverage provide indirect protection in other age groups?
- What is the duration of protection of meningococcal conjugate vaccines?

Looking Forward

- Continue to monitor disease rates, impact of adolescent program, need for policy changes
- Alternative immunization options?
 - Reduced dose schedules
 - Maternal immunization
 - Vaccination at birth
- Implications for future use of serogroup B vaccines in the U.S.

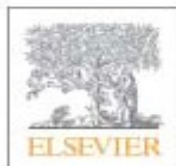
Conclusions

- Quadrivalent meningococcal conjugate vaccines have potential to prevent disease and death in the U.S.
 - Disease rates declining for all serogroups
- Duration of protection important consideration for adolescent program
 - Unable to rely on herd immunity
 - Program adjustments may be needed
- Low disease burden may limit use of conjugate vaccines in infants

Thank you!

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The Leading Independent



The instigation for his vaccine cost analysis was "just looking at our nursing staff. They were going crazy," said Dr. Andrew Racine.

Plethora of Shots Burdens Providers

BY BETSY BATES
Los Angeles Bureau

HONOLULU — A complex regimen of 21 vaccines added to the routine child immunization schedule since 2000 has left many health care providers shaking their heads.

Dr. Andrew D. Racine, chief of clinical pediatrics at Albert Einstein College of Medicine, New York, took his frustration one step further and took out his calculator.

By his calculations, administration of the new vaccines recommended for pediatric patients from infancy through adoles-

mended in 1983. That number now stands at a mean 27 vaccines per healthy child, depending on their gender and risk profiles.

Added to the schedule since 2000 are pneumococcal 7-valent conjugate vaccine (PCV7) at 2, 4, 6, and 12 months; influenza vaccine at 6 and 7 months, then annually to all patients up to 5 years and to 50% of 6- to 21-year-olds; meningococcal polysaccharide conjugate (MCV4) vaccine and tetanus/diphtheria toxoid/acellular pertussis (Tdap) vaccine at 11 years; hepatitis A vaccine at 18 and 24 months; rotavirus vaccine at 2, 4, and 6 months; 3 human

See Plethora page 4