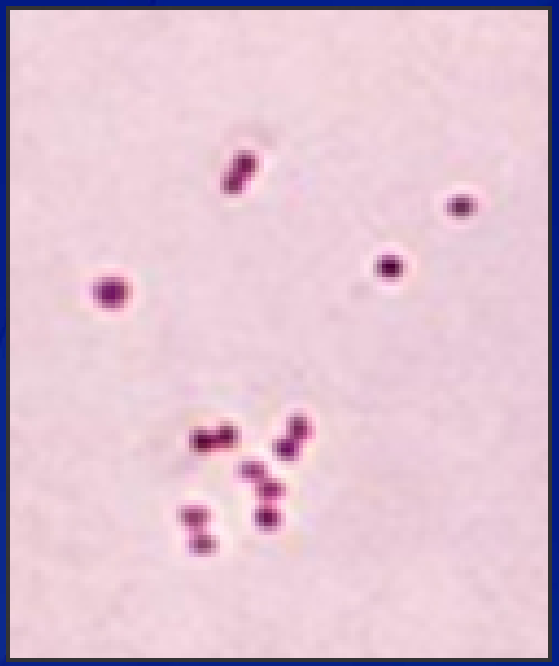
Universal Immunization Against Rare Diseases

- How much is a child's life worth?
- The individual vs society

Meningococcal Meningitis

- **THE SYMPTOMS INCLUDE SUDDEN ONSET OF FEVER, HEADACHE, AND STIFF NECK. IT IS OFTEN ACCOMPANIED BY OTHER SYMPTOMS, SUCH AS**
  - NAUSEA
  - VOMITING
  - PHOTOPHOBIA (INCREASED SENSITIVITY TO LIGHT)
  - ALTERED MENTAL STATUS (CONFUSION)
  - SEPSIS
    - RASH



After Effects

U.S. Multicenter Study: Sequelae in 146 Surviving Children at Hospitalization (Aged 0-19 Years)

Sequelae	N (%)
Amputation	2 (1.4)
Skin necrosis	14 (9.6)
Skin graft	4 (2.7)
Seizures after admission	9 (6.2)
Unilateral hearing loss*	6 (4.1)
Bilateral hearing loss*	8 (5.5)
Ataxia	4 (2.7)
Hemiplegia	3 (2.1)

*All among patients with meningitis

Kaplan et al., Pediatrics 2006, 118(4):e979-84.

Available Vaccines

TABLE 1. Licensed meningococcal vaccines — United States, 1981–2012

Formulation	Type	Trade name	Manufacturer	Licensed (yr)	Age group	Dose(s)	Serogroups
MPSV4*	Polysaccharide	Menomune	Sanofi Pasteur	1981	≥2 yrs	Single dose	A, C, W, and Y
MenACWY-D†	Conjugate	Menactra	Sanofi Pasteur	2005	11–55 yrs	Single dose	A, C, W, and Y
MenACWY-D†	Conjugate	Menactra	Sanofi Pasteur	2007	2–10 yrs	Single dose	A, C, W, and Y
MenACWY-D†	Conjugate	Menactra	Sanofi Pasteur	2011	9–23 mos	2-dose series	A, C, W, and Y
MenACWY-CRM§	Conjugate	Menveo	Novartis	2010	11–55 yrs	Single dose	A, C, W, and Y
MenACWY-CRM§	Conjugate	Menveo	Novartis	2011	2–10 yrs	Single dose	A, C, W, and Y
Hib-MenCY-TT¶	Conjugate	MenHibrix	GlaxoSmithKline	2012	6 wks–18 mos	4-dose series	C and Y

Meningococcal Vaccines for Infants and Toddlers

- **MenACWY-D (Menactra, sanofi pasteur)**
  - 2 dose series at 9 -23 months
  - Licensed in September 2010
- **HibMenCY-TT (MenHibRix, GlaxoSmithKline)**
  - 4 dose series at 2, 4, 6 and 12-15 months
  - Licensed in June 2012
- **MenACWY-CRM (Menveo, Novartis)**
  - 4 dose series at 2, 4, 6 and 12 months
  - Licensed in August 2013

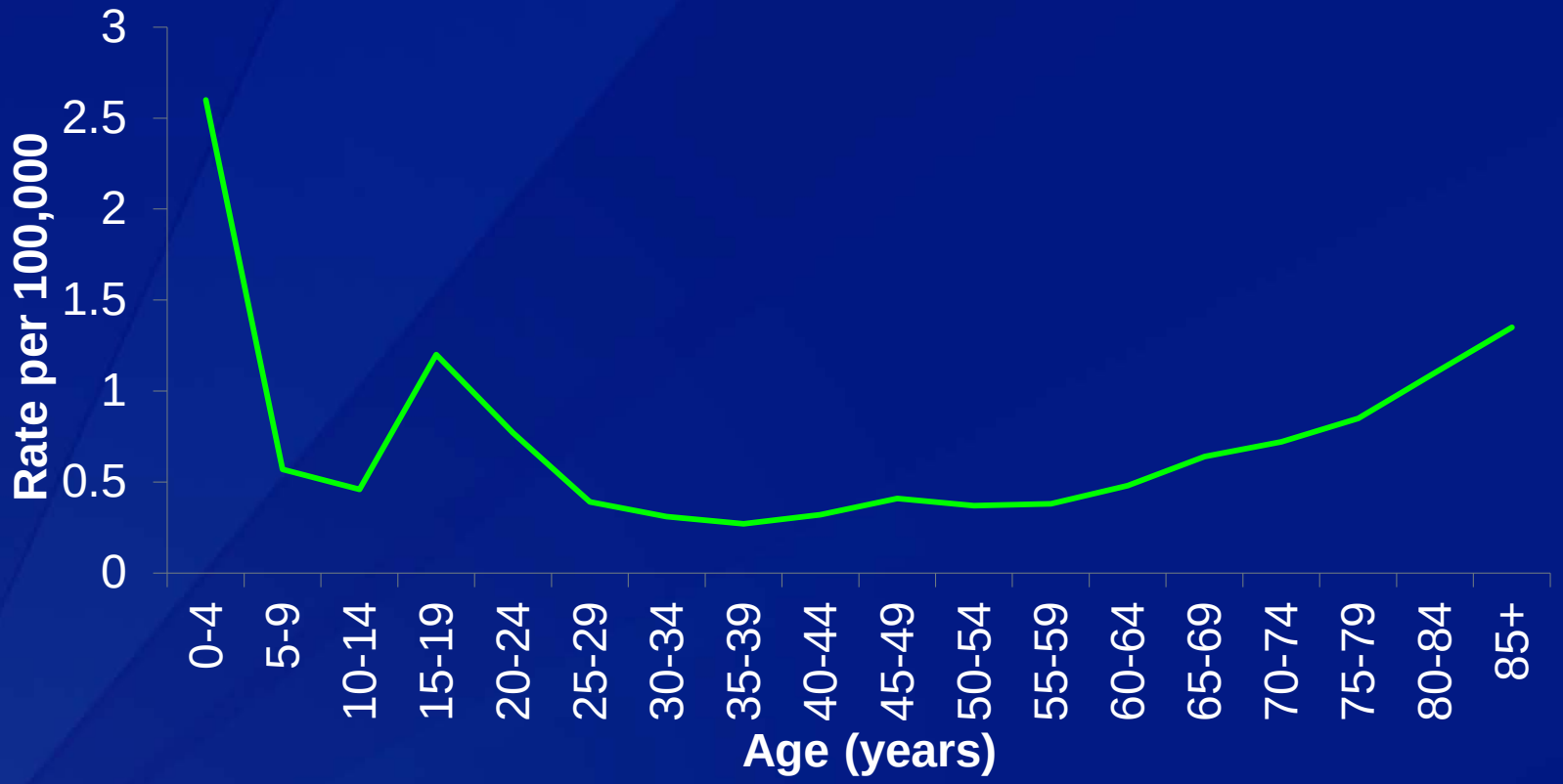
TABLE 6. Recommended meningococcal vaccines for use in children and adults — Advisory Committee on Immunization Practices (ACIP), United States, 2012

Age group	Vaccine	Status
2 mos–10 yrs	MenACWY-D (Menactra, Sanofi)*	Not routinely recommended; see Table 7 for persons at increased risk
	MenACWY-CRM (Menveo, Novartis)†	Not routinely recommended; see Table 7 for persons at increased risk
	HibMenCY-TT (MenHibrix, GSK)§	Not routinely recommended; see Table 7 for persons at increased risk
11–21 yrs	MenACWY-D or MenACWY-CRM	Primary: • Age 11–12 yrs, 1 dose • Age 13–18 yrs, 1 dose if not vaccinated previously • Age 19–21 yrs, not routinely recommended but may be administered as catch-up vaccination for those who have not received a dose after their 16th birthday Booster: • 1 dose recommended if first dose administered before 16th birthday
22–55 yrs	MenACWY-D or MenACWY-CRM	Not routinely recommended; see Table 7 for persons at increased risk
≥56 yrs	MPSV4, MenACWY-D, or MenACWY-CRM	Not routinely recommended; see Table 7 for persons at increased risk

Meningococcal Disease Incidence, United States, 1970-2011

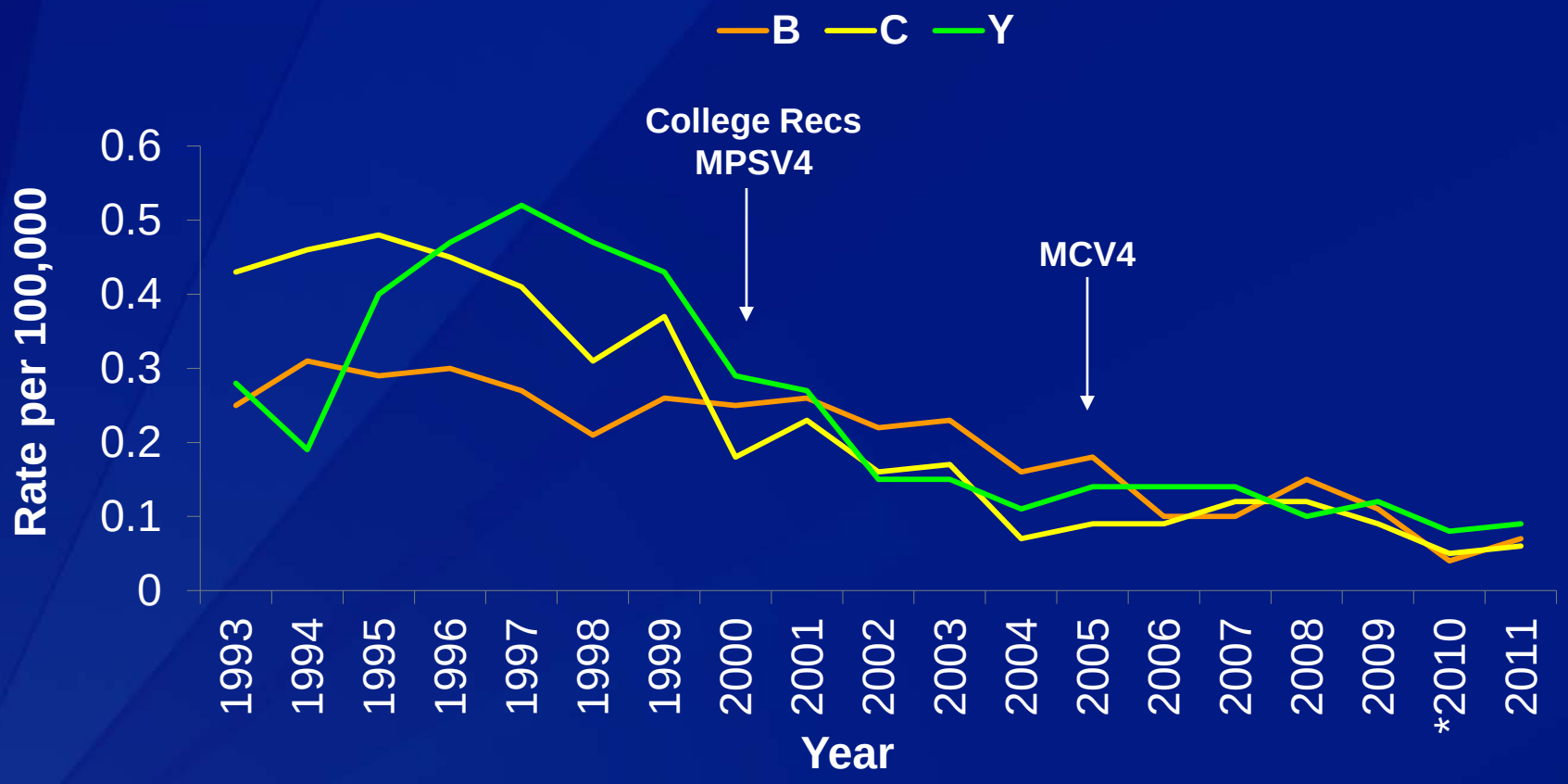
1970-1996 NNDSS data, 1997-2011 ABCs data estimated to U.S. population with 18% correction for under reporting
*In 2010, estimated case counts from ABCs were lower than cases reported to NNDSS and may not be representative

Three Age Peaks in Meningococcal Disease Incidence



ABCs cases from 1993-2009 and projected to the U.S. population with 18% correction for under reporting

Incidence Declines in All Serogroups



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Incidence Declines in All Age Groups

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Three Incidence Time Frames: Base Case, High and Low

Age Group	1997-1999 "High Incidence Years"	1993-2009* "Base Case"	2007-2009 "Low Incidence Years"
<5 years	2.60	1.17	0.40
All ages*	0.85	0.47	0.24

Average annual incidence of serogroup C, Y, and W135 meningococcal disease
1993-2009 ABCs data estimated to U.S. population with 18% correction for under reporting
*1993-2005 for adolescents 11-22 years

High Frequency of Hospitalization but Low Case-Fatality in Children <5 Years

- **86% of all cases were hospitalized**
  - Median length of hospitalization*: 7 days (0-373)
  - Does not vary by month of age, serogroup or syndrome
- **Case-fatality Ratio is 6%**
  - Serogroup B: 5%
  - Serogroup C: 10%
  - Serogroup Y: 1%

*Limited to hospitalized patients
1993-2009 ABCs data

Annual Cases, Deaths, and Serious Sequelae in Children <5 Years

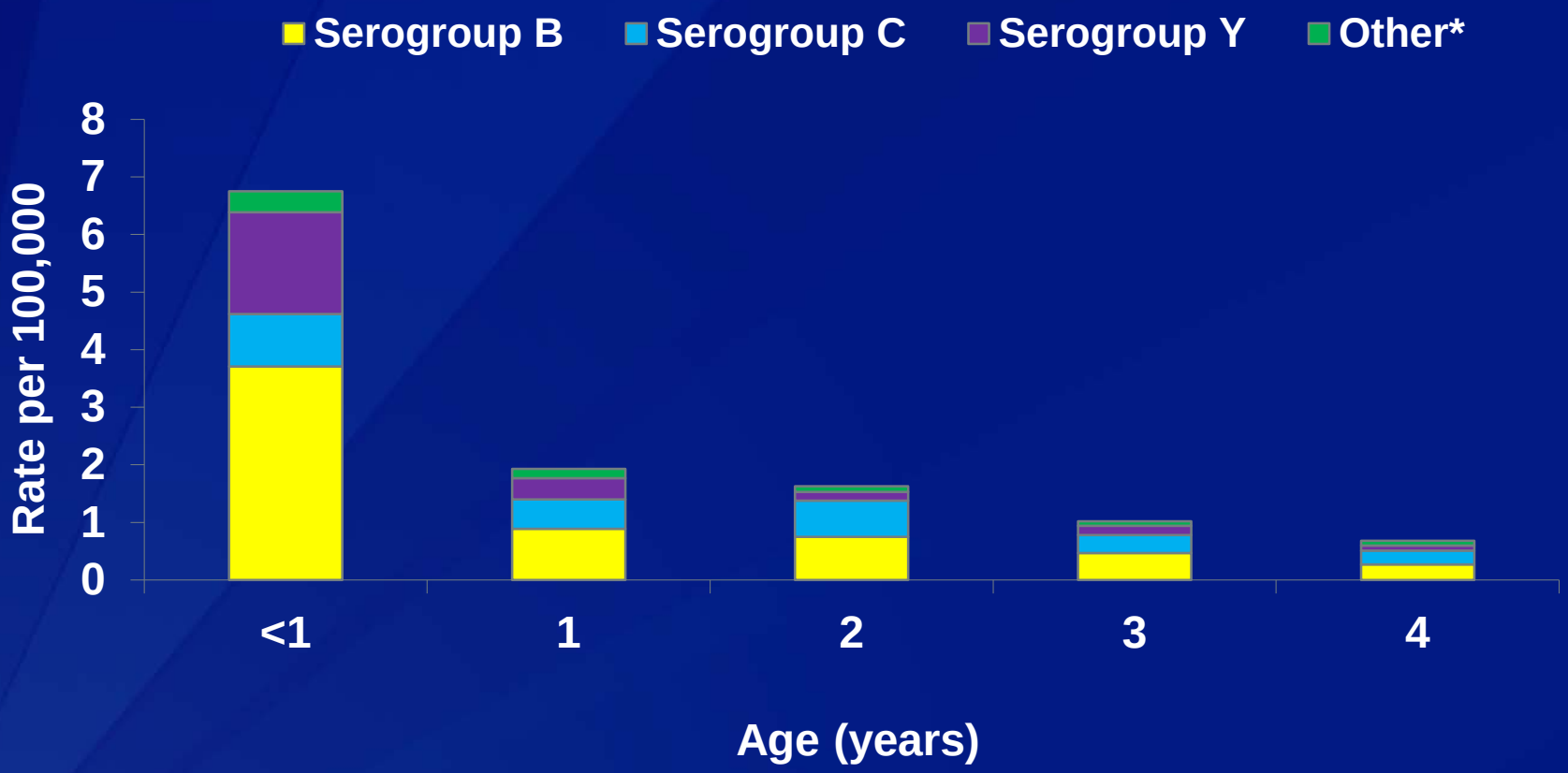
	1997-1999 "High Incidence Years"	1993-2009*	2007-2009 "Low Incidence Years"
Cases	475	222	77
Incidence	2.50	1.32	0.37
Deaths **	24-48	11-22	4-8
Sequelae***	48-71	22-33	8-12

Average annual cases, incidence, deaths, and serious sequelae
*1993-2005 for adolescents 11-17 years
**5-10% case-fatality ratio, ***10-15% of survivors with serious sequelae
1993-2009 ABCs data estimated to U.S. population with 18% correction for under reporting

Summary: Morbidity and Mortality

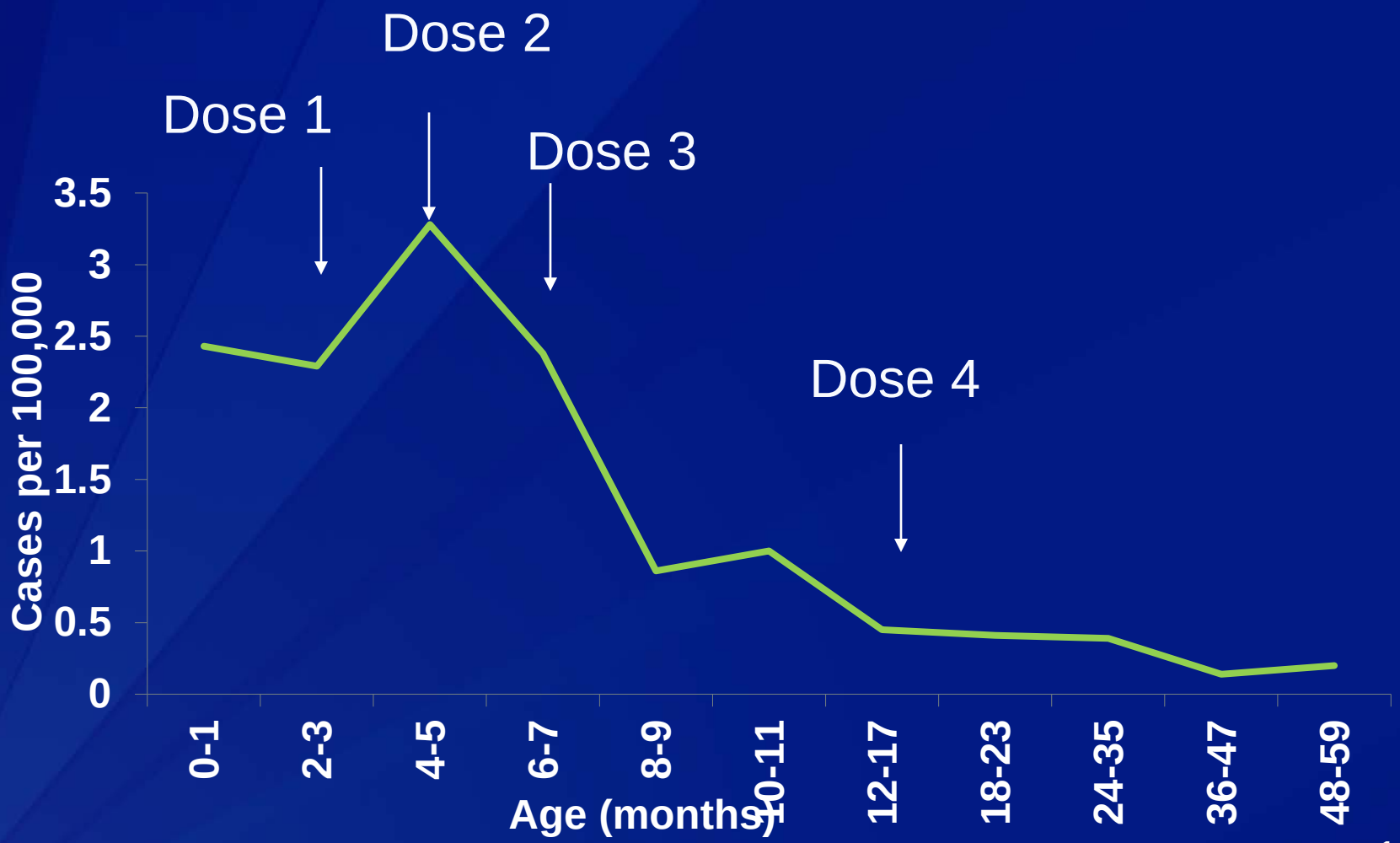
- **75-80% of children <5 years with meningococcal disease survive and fully recover from their illness**
  - Major complications are less frequent in infants than adolescents
- **Case-fatality ratio is lower in infants**

50-60% of Disease in Children <5 Years is Due to Serogroup B



*Other includes: serogroup W-135, nongroupables, and other serogroups
ABCs cases from 1993-2011 estimated to the U.S. population with 18% correction for under reporting
In 2010, estimated case counts from ABCs were lower than cases reported to NNDSS and may not be representative

Short Period of Risk for Infants Not at Increased Risk for Meningococcal Disease



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

Long-term Protection Unlikely

- **Evidence of declining antibodies 5 years after the 12 month dose**
  - **Persistence of antibodies better with 4 doses of HibMenCY compared to 2 doses of MenACWY-D**
  - **Lower evidence GRADE compared to short-term immunogenicity data**

- **A vaccinated infant is unlikely to be protected until the 11-12 year-old vaccination**
  - Adolescent vaccine effectiveness
  - Infant vaccination in United Kingdom

Work Group Interpretation: Burden of Disease

- **Amount of potentially preventable disease in infants is low at this time**
  - Currently at a stable low in disease incidence
  - Low proportion of serogroup C+Y disease
  - Declining incidence after first 6-8 months of life
- **Dynamic epidemiology that will need to be monitored frequently**

Cases and Deaths Prevented per 4M Cohort 2007-2009 Disease Incidence

- An estimated 52 cases (44-62) and 4 deaths (3-5) prevented using current disease epidemiology

- Number Needed to Vaccinate: 63,882 per case
  826,465 per death

Ismael Ortega-Sanchez, October 2011 ACIP Meeting, updated with 5 year persistence data

WORK GROUP RATIONALE FOR PROPOSED RECOMMENDATIONS

Should Meningococcal Vaccines be Routinely Recommended for the 4 Million Infants Born Each Year?

Data

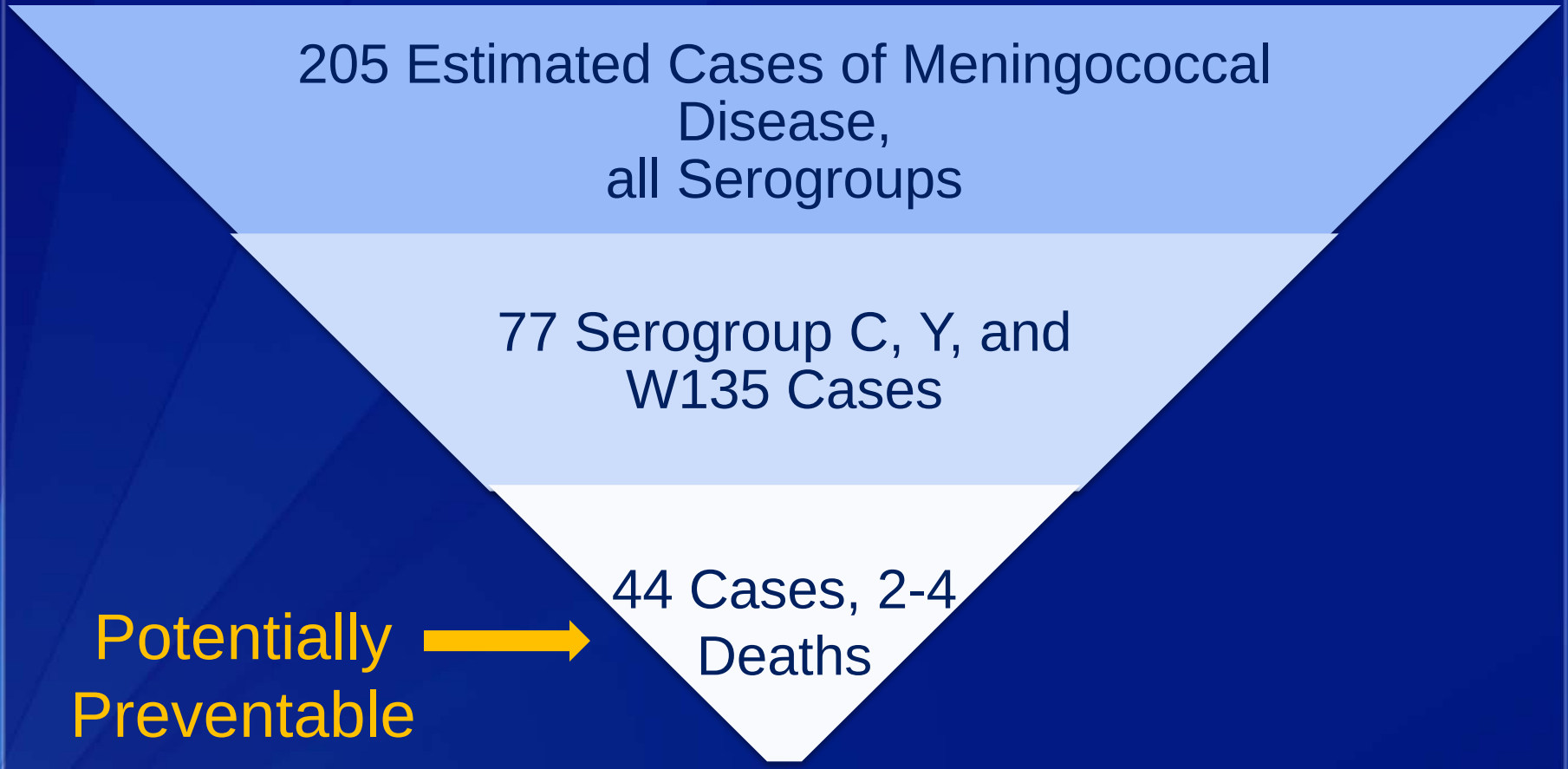
Is the public health impact based on amount of potentially preventable disease alone sufficient?

Values

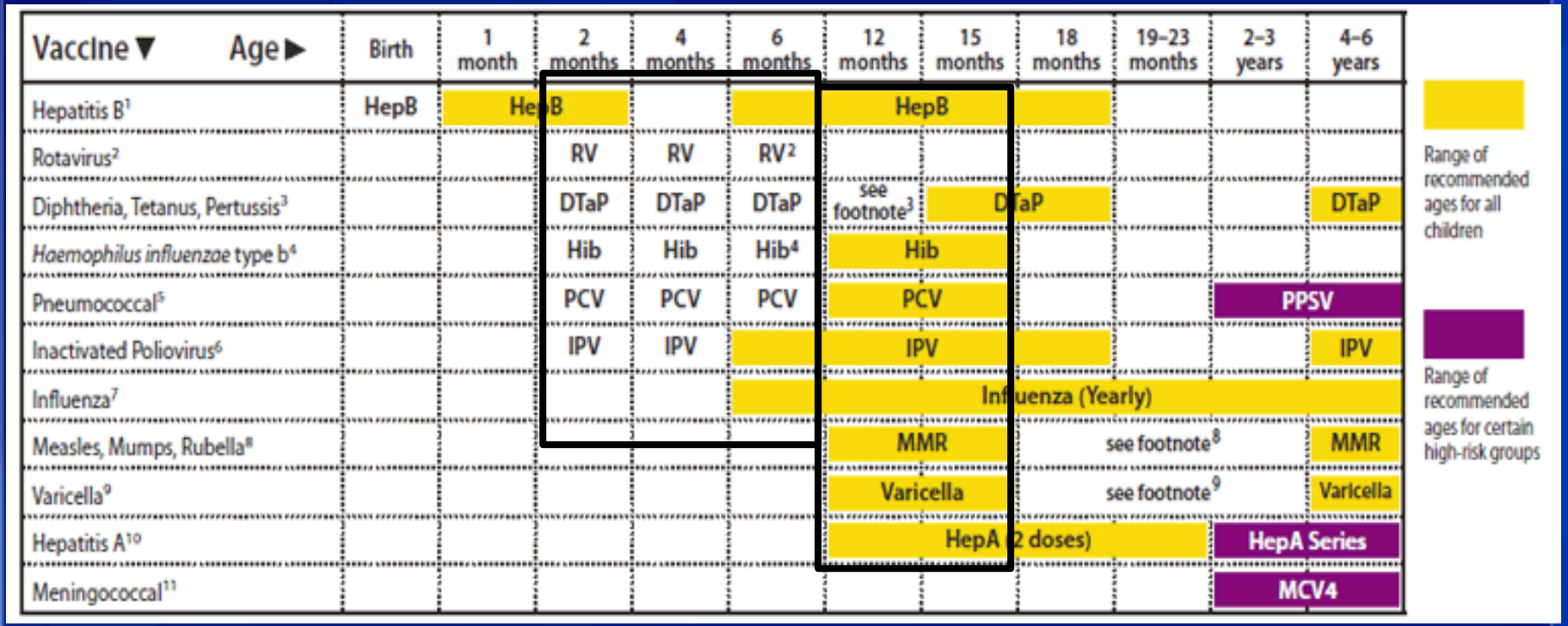
Do the potential programmatic aspects (challenges or ease) impact your conclusion about the public health impact?

Does the cost (either total costs or cost-effectiveness) impact your conclusion about the public health impact?

Proportion of Annual Preventable Cases in Children <5 Years is 20-25%, 2007-2009



2011 Childhood Immunization Schedule



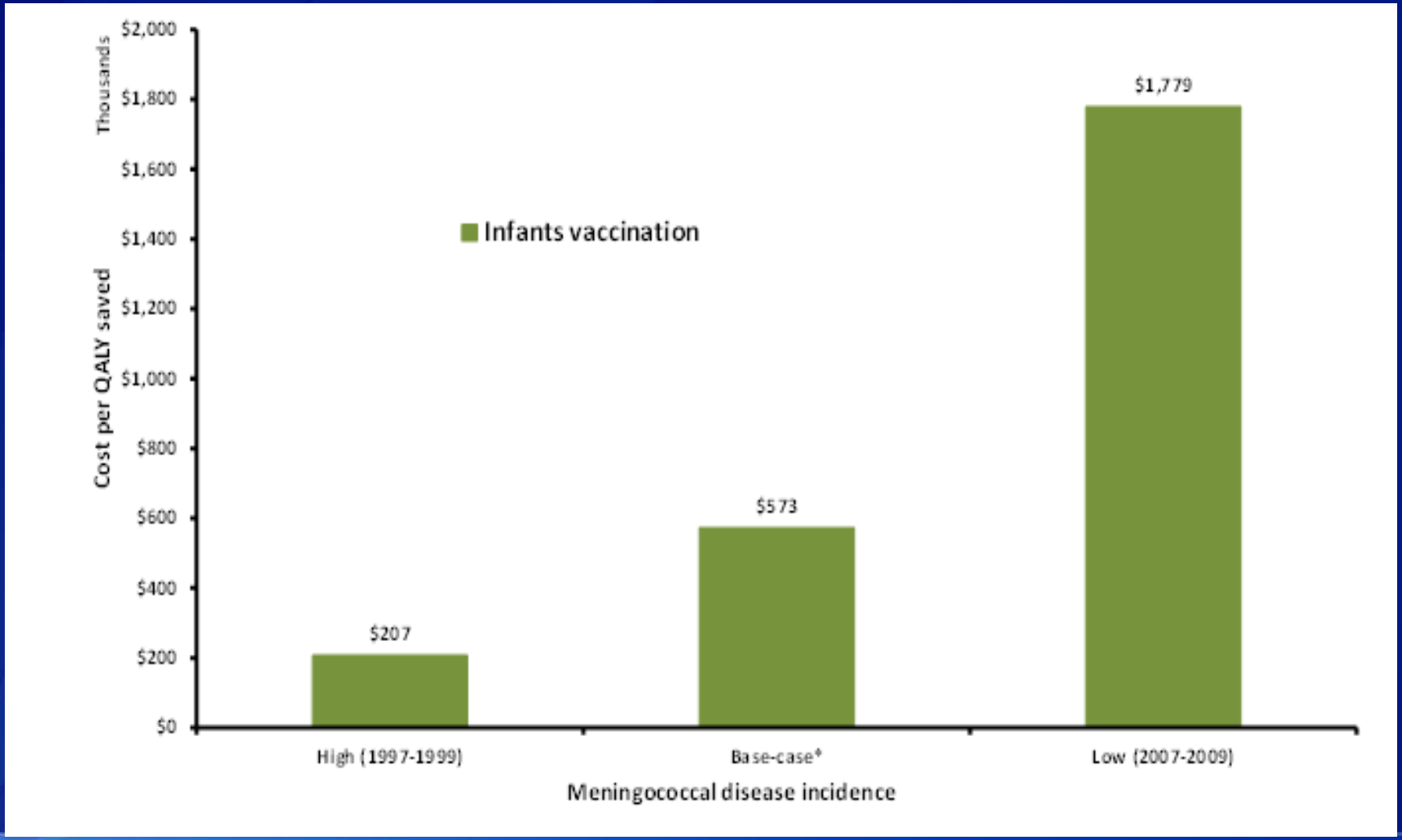
Vaccine ▼ Age ▶	Birth	1 month	2 months	4 months	6 months	12 months	15 months	18 months	19–23 months	2–3 years	4–6 years
Hepatitis B[1]	HepB	HepB				HepB					
Rotavirus[2]			RV	RV	RV[2]						
Diphtheria, Tetanus, Pertussis[3]			DTaP	DTaP	DTaP	see footnote[3]	DTaP				DTaP
Haemophilus influenzae type b[4]			Hib	Hib	Hib[4]	Hib					
Pneumococcal[5]			PCV	PCV	PCV	PCV				PPSV	
Inactivated Poliovirus[6]			IPV	IPV		IPV					IPV
Influenza[7]						Influenza (Yearly)					
Measles, Mumps, Rubella[8]						MMR		see footnote[8]			MMR
Varicella[9]						Varicella		see footnote[9]			Varicella
Hepatitis A[10]						HepA (2 doses)				HepA Series	
Meningococcal[11]										MCV4	

Range of recommended ages for all children

Range of recommended ages for certain high-risk groups

Cost per QALY depends on incidence during period of time evaluated

Vaccine price= $30 a dose



Options Considered By Work Group

1. Recommend HibMenCY for infants at increased risk for meningococcal disease

2. Recommend HibMenCY for all infants

- **Work Group used current landscape and data available to inform decision-making**
  - Recent disease epidemiology
  - Current understanding of vaccine durability
  - 2012 infant immunization schedule

Work Group Preference for High-Risk Infant Recommendation

- **Risk groups small, but feasible target for vaccination (est. 5000 infants/year at risk)**
  - Infants born with or having a family history of complement component deficiency
  - Infants with known asplenia, or those with sickle cell disease detected on newborn screening
  - Infants who are at increased risk due to a community outbreak of serogroup C or Y disease
- **Mirrors meningococcal recommendations for 9 month through 10 year-olds**

Primary Rationale for Work Group Recommendations

- Low burden of potentially preventable cases
- Low proportion of overall cases in infants prevented with this vaccine strategy

Working Group Conclusions

- **Data do not support routine infant meningococcal vaccination at this time**
- **Targeting high-risk infants is a feasible approach consistent with current recommendations for other age groups**
- **Working Group in agreement**
  - Difficult to accept that there will be cases that are preventable
  - Nevertheless, risk for serogroup C and Y disease is very low in the absence of vaccination
  - Frequently evaluate disease trends

Public Testimony

- Parents of children who died from meningoccal disease
- Adults with sequelae from meningococcal disease
- Parents and children with sequelae

- All stating that statistics and cost/benefits are not as important as …….

Preventing This

And… Asking the question:

- If we can prevent the death of even one child, why would we not do it?