Considerations for Use of Meningococcal Conjugate Vaccines in Infants

Amanda Cohn, MD

CDR, US Public Health Service

Advisory Committee on Immunization Practices

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Presentation Overview

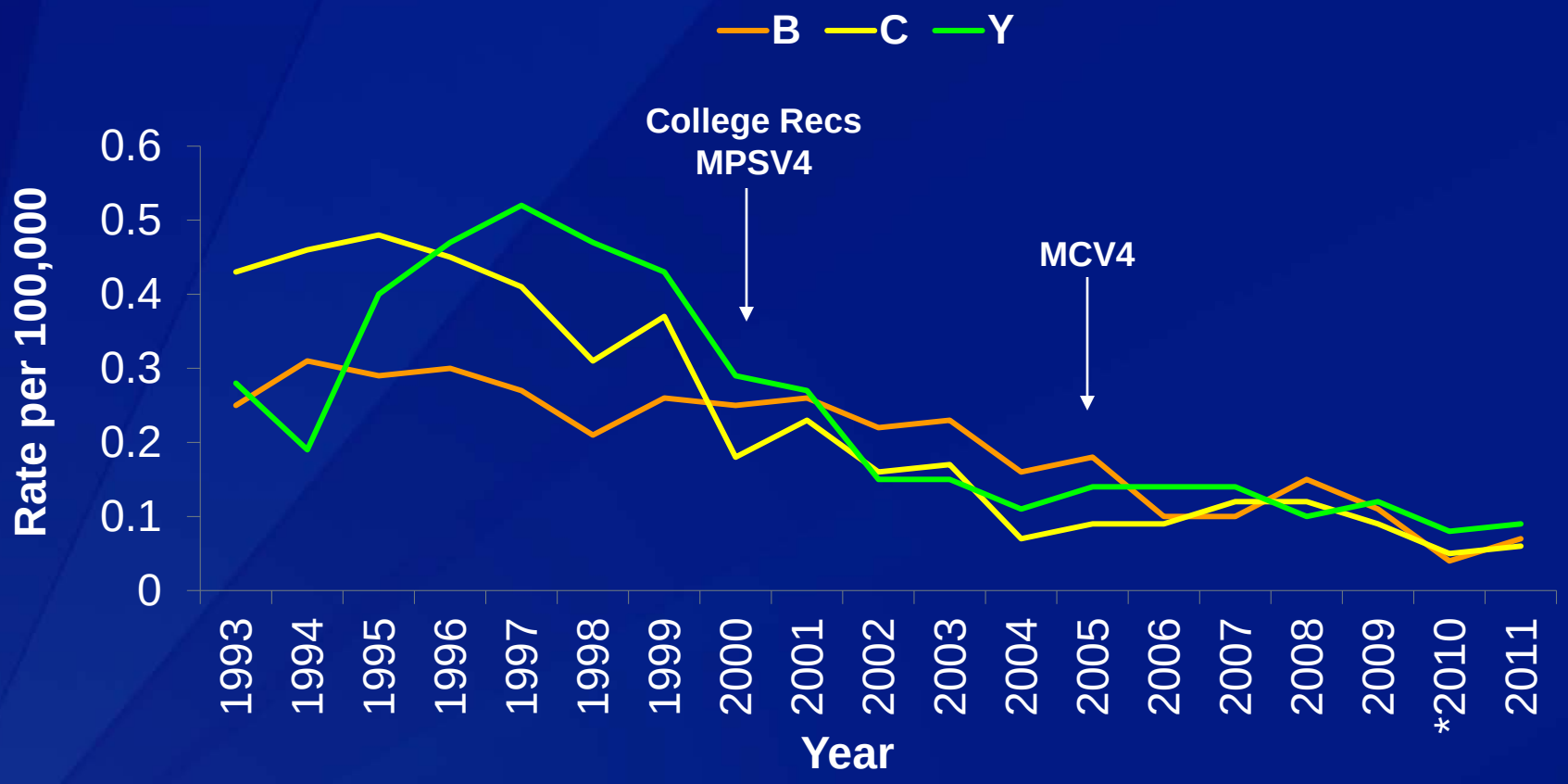
- Burden of meningococcal disease in infants
- Summary of cost-effectiveness analysis
- Work Group rationale for proposed use of HibMenCY
- Proposed recommendations and vote

BURDEN OF MENINGOCOCCAL DISEASE IN INFANTS

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

Incidence Declines in All Serogroups



ABCs cases from 1993-2011 estimated to the U.S. population with 18% correction for under reporting
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Incidence Declines in All Age Groups

ABCs cases from 1993-2011 estimated to the U.S. population with 18% correction for under reporting
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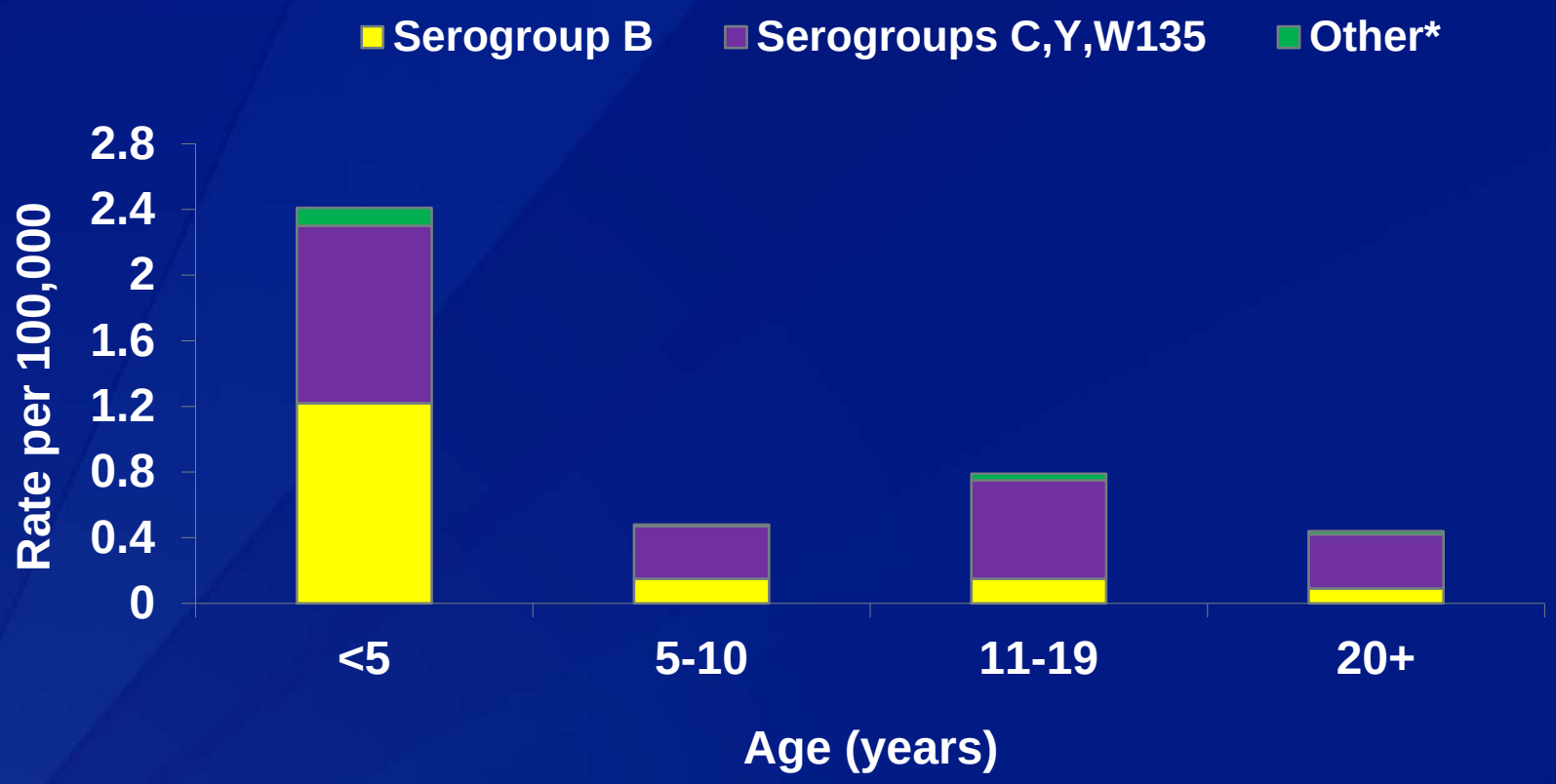
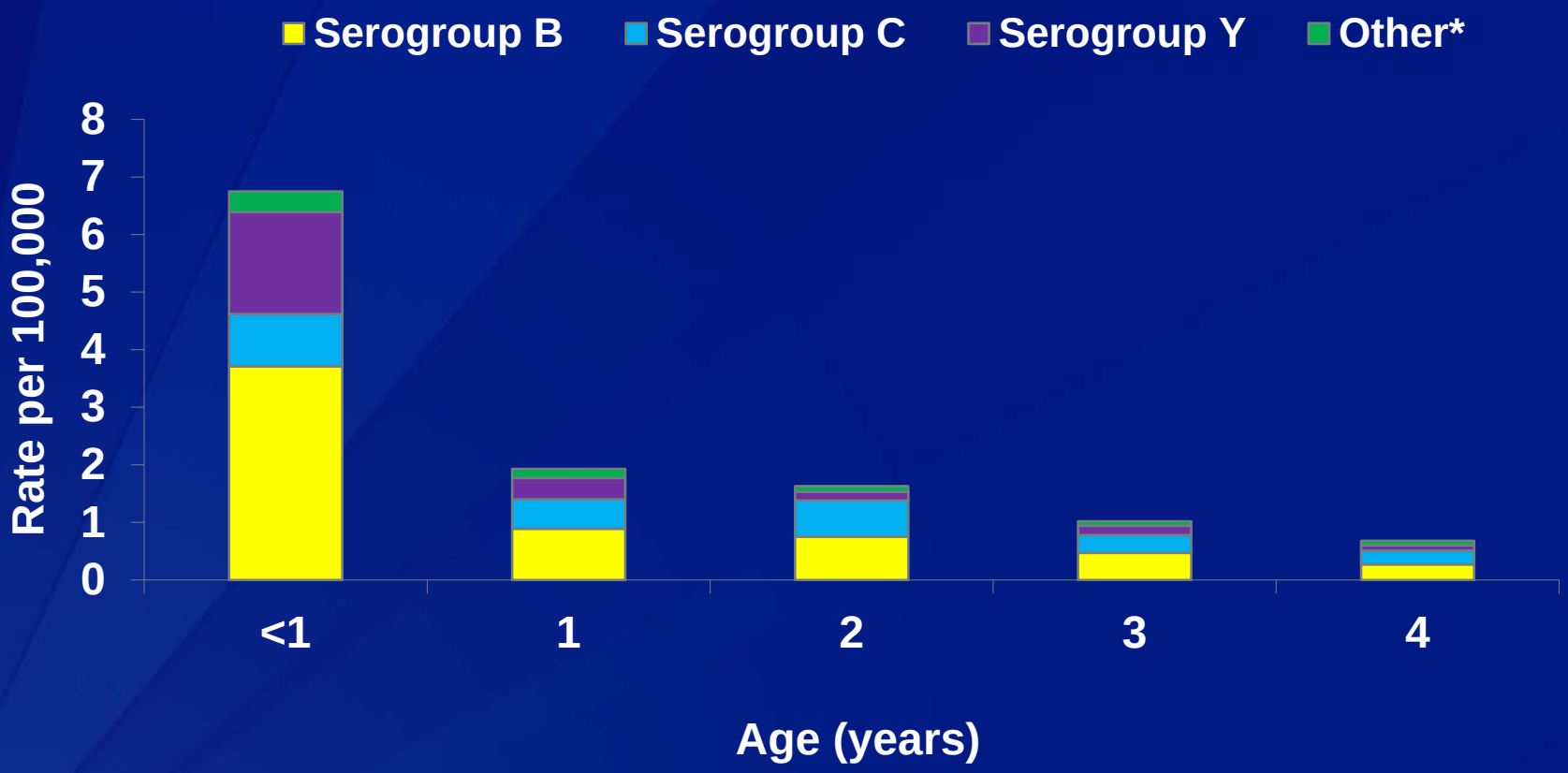
Lower Proportion of Vaccine Preventable Disease in Children <5 Years



*Other includes: 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

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
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Cases of Serogroup C and Y Meningococcal Disease in Children <5 Years

Age	Serogroup B	Serogroup C	Serogroup Y	Serogroup C + Y (Incidence)
0-2 months	52	8	19	27 (2.7)
3-5 months	43	13	26	39 (3.9)
6-8 months	33	7	15	22 (2.2)
9-11 months	19	9	11	20 (2.0)
1 year	35	20	15	35 (0.9)
2 years	30	25	6	31 (0.8)
3 years	19	12	6	18 (0.5)
4 years	11	10	4	14 (0.4)
Total	242	104	102	206 (1.0)

Average annual cases and incidence of meningococcal disease
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

Annual Serogroup C and Y Meningococcal Cases, Deaths, and Serious Sequelae in Children <5 Years

	1997-1999 "High Incidence Years"	1993-2011	2007-2009 "Low Incidence Years"
Cases	475	206	77
Incidence	2.50	1.04	0.37
Deaths *	24-48	10-21	4-8
Sequelae**	48-71	21-30	8-12

Average annual cases, incidence, deaths, and serious sequelae
*5-10% case-fatality ratio, **10-15% of survivors with serious sequelae
ABCs cases from 1993-2011 estimated to the U.S. population with 18% correction for under reporting
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Disease in 2011 and 2012, NNDSS*

- **139 cases reported in children <5 years in 2011**
  - 92/139 (66%) cases with serogroup available
    - 60 (65%) serogroup B
    - 10 (11%) serogroup C – 8 in children >6 months
    - 14 (15%) serogroup Y – 9 in children >6 months
- **72/139 (52%) cases with outcome available**
    - All deaths in serogroup B (n=7) or unknown serogroup (n=1)
    - Among children >6 months, all deaths from serogroup B (n=4)
- **Disease is tracking lower in 2012**
    - 407 (week 41, 2012) vs. 541 (week 41, 2011) total cases reported
    - 7 cases and 2 deaths from serogroup C & Y in children 6-59 months

*National Notifiable Diseases Surveillance System, suspect case status are excluded (n=2)
Proportions are out of cases with known serogroup result

Work Group Interpretation: Burden of Disease

- **Amount of potentially preventable disease in children aged <5 years is low**
  - Currently at a stable low in disease incidence
  - Most disease caused by serogroup B
  - Declining incidence after first 6-8 months of life
- **Dynamic epidemiology that will need to be monitored frequently**

SUMMARY OF COST EFFECTIVENESS ANALYSIS

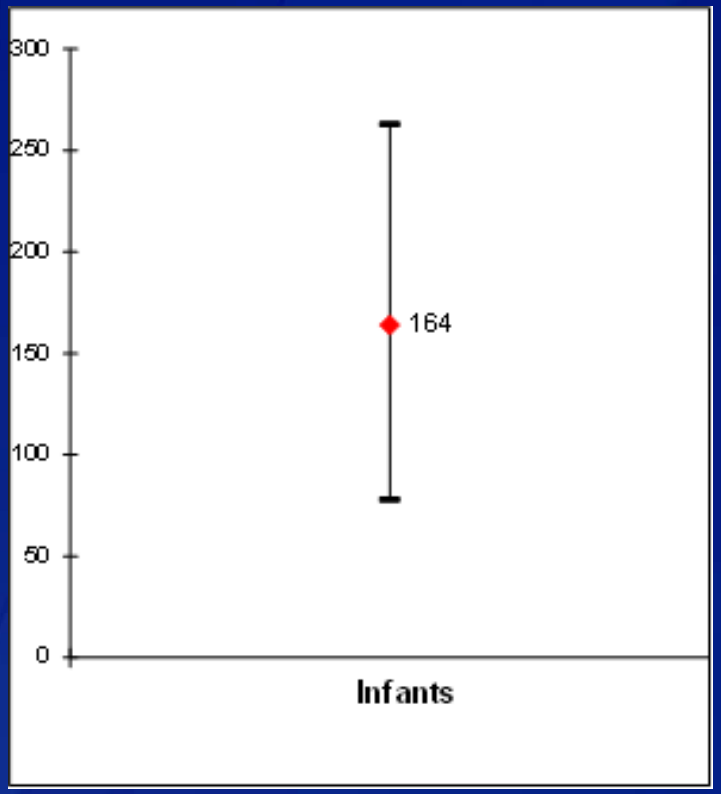
Methods

- **Full presentation during October 2011 meeting***
- **Monte Carlo simulation analysis**
  - Hypothetical 4 million birth cohort, 10 year time-frame
  - Analytic Horizon: Age-specific Life Expectancy
  - Discount rate: 3% (0%-5%)
  - Age and serogroup-specific average incidence rates from 1993-2009 for base analysis
- **Analysis updated to reflect 5 year duration of protection data and vaccine price of $30 a dose**
  - No administration costs because combined with Hib vaccine

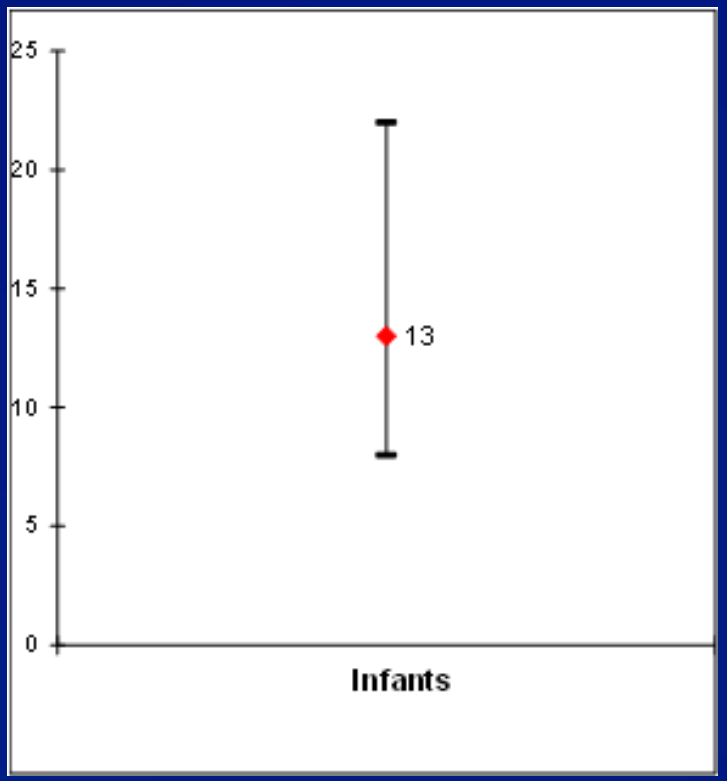
Cases and Deaths Prevented per 4M Cohort, HibMenCY (MenCY component)

1993-2009 incidence, Mean, 5th and 95th Percentiles*

- **Cases**



Deaths



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

Cases and Deaths Prevented per 4M Cohort HibMenCY (MenCY component)
2007-2009 Disease Incidence

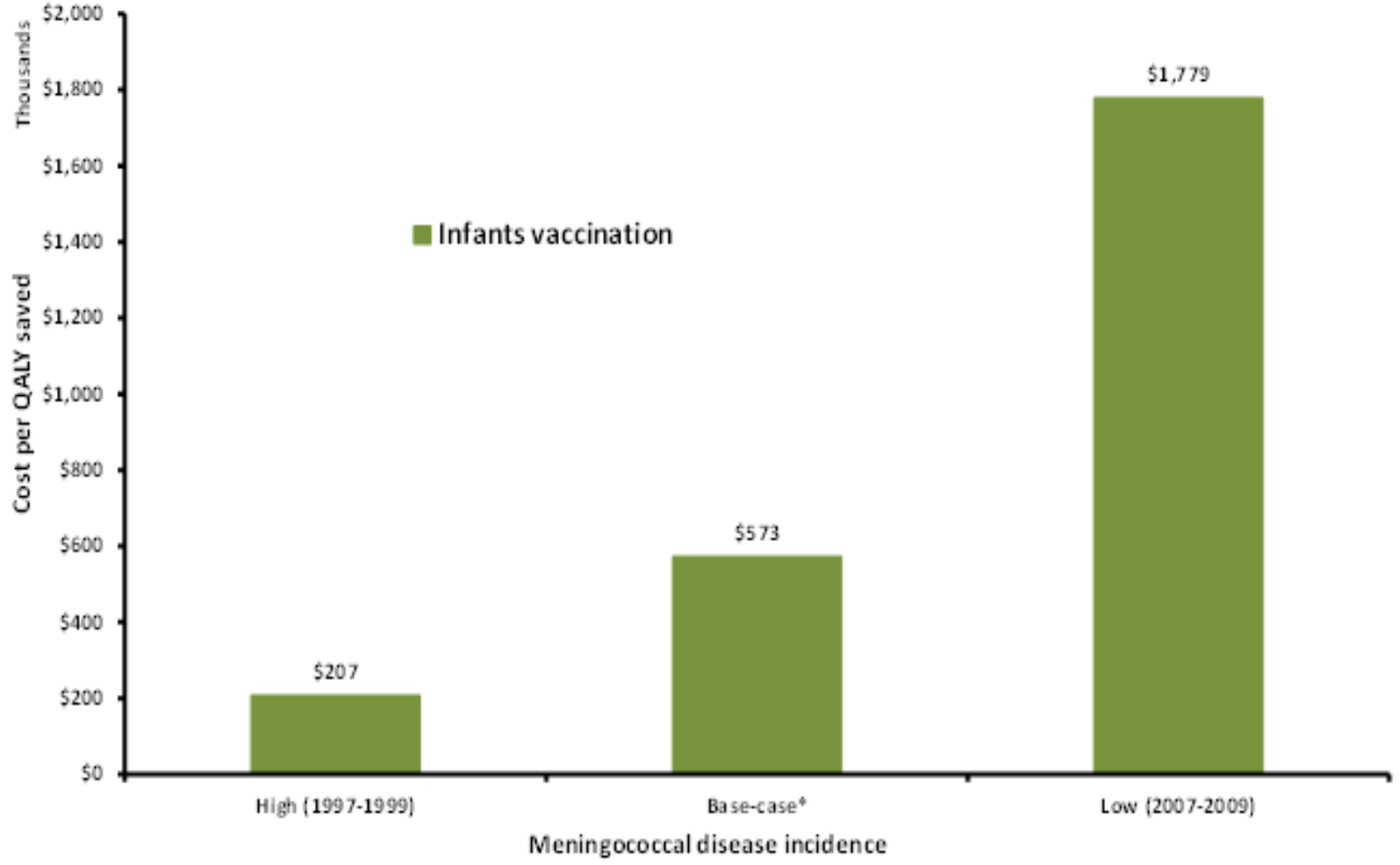
- An estimated 52 cases (44-62) and 4 deaths (3-5) prevented using current disease epidemiology

- 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

Cost per QALY saved with HibMenCY depends on incidence during period of time evaluated

Vaccine price= $30 a dose



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

Work Group Interpretation: Cost-Effectiveness Evaluation

- Cost per QALY saved is high for an infant vaccination program because of the limited impact on the number of cases and deaths prevented

- Cost considerations were not a major factor in ACIP Work Group deliberations

WORK GROUP RATIONALE FOR PROPOSED RECOMMENDATIONS

HibMenCY

- **Data support safety and immunogenicity of vaccine against Hib and *N. meningitidis* serogroups C and Y**
  - Supportive data of immune response after Dose 2
  - No evidence of immune interference with PCV7
  - Does not protect against serogroup B disease, or serogorup A and W135

- **HibMenCY vaccine price of $56.75 per dose**
  - $30 additive price for MenCY component

*GlaxoSmithKine Biologicals, personal communication

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 program

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**

Complement Deficiency: C3, properidin, factor D, and late component

- ***N. meningitidis*** **is primary pathogen with late component complement deficiency**
  - RR is 7,000-10,000 fold higher
  - 43%-57% will develop disease, half will have recurrent disease
- **Rarely diagnosed during infancy**
  - Most commonly diagnosed after first meningococcal infection, frequently occurring during adolescence
- **Infants will be recognized only in setting of family history of complement component deficiency**

Functional / Anatomic Asplenia

- ***N. meningitidis*** **is the 3rd most common cause of sepsis in persons with asplenia**

- **Difficult to determine true increased risk**
  - No incidence data
  - Evidence of increased mortality from all-cause sepsis compared to healthy population

- **HibMenCY offers alternative to using MenACWY-D with PCV13 during 2nd year of life**
  - Children with sickle cell disease detected on newborn screening could achieve protection prior to developing functional asplenia

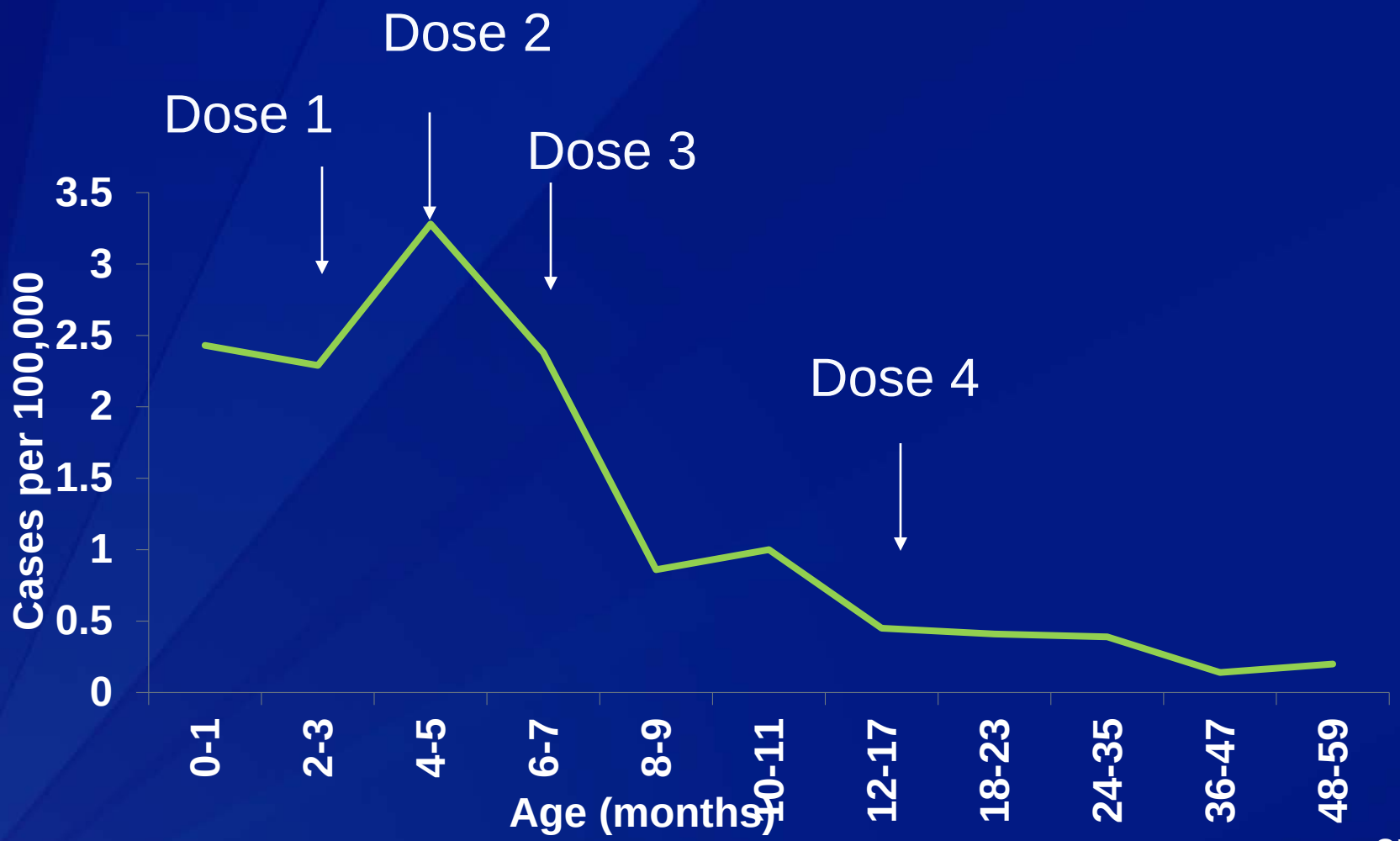
Community or organizational outbreak

- Vaccination may be recommended for target groups during outbreaks of meningococcal disease in communities and organizations
- Need for multiple doses limits benefit of HibMenCY in this setting
- However, availability of vaccine for infants useful if infants are targeted for vaccination in response to an outbreak

Primary Rationale for Work Group Recommendations

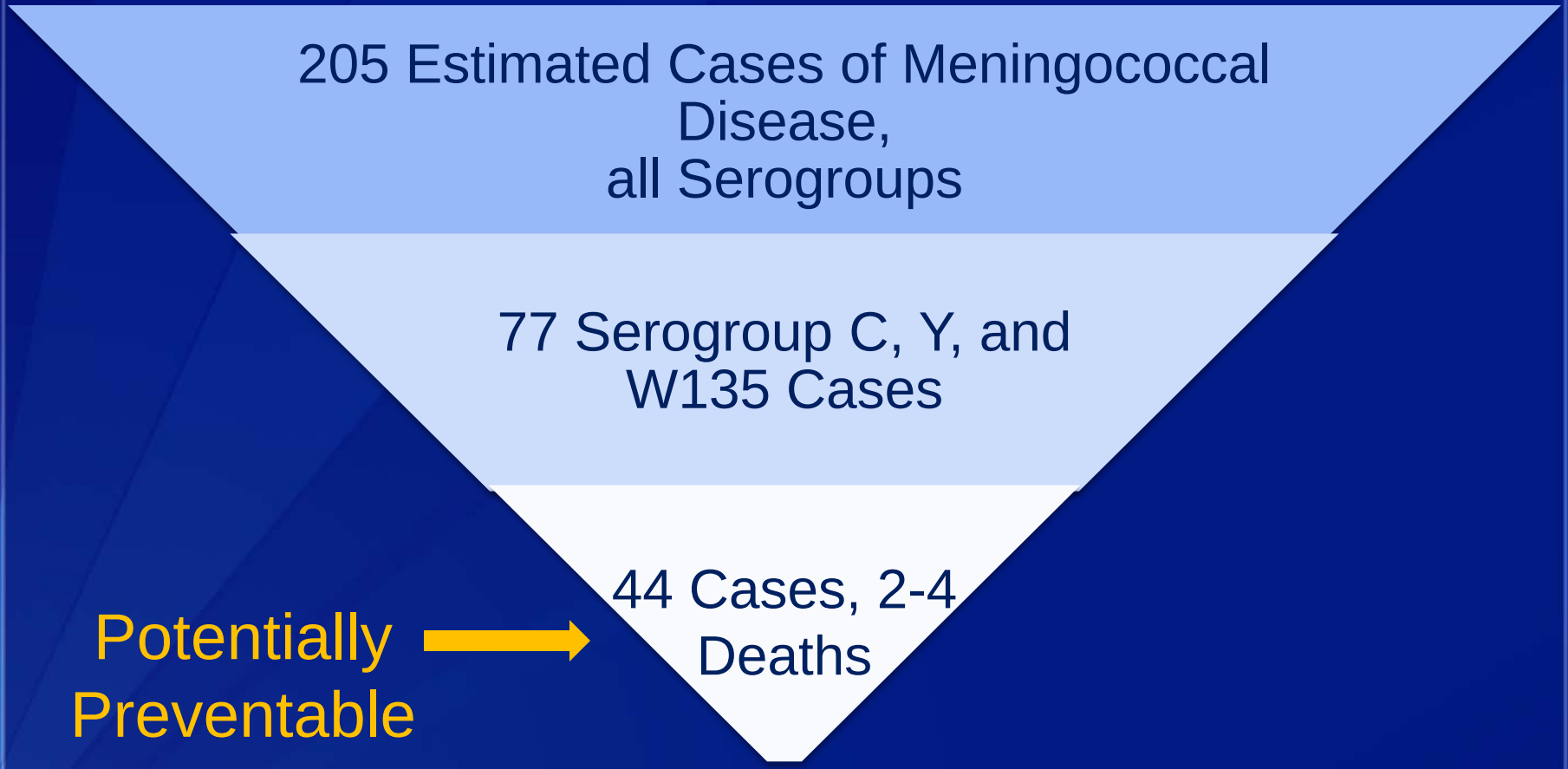
- Low burden of potentially preventable cases
- Low proportion of overall cases in infants prevented with this vaccine strategy

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

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



Supporting Evidence Considered by Work Group

- Duration of protection for meningococcal components of HibMenCY
- Potential for HibMenCY to reduce transmission of *N. meningitidis*
- Programmatic aspects of a routine infant meningococcal vaccination program

Long-term Protection Unlikely

- **Evidence of declining antibodies 5 years after the 12 month dose**
  - **Data on the proportion of infants who maintain protective levels of antibody against serogroups C and Y are reassuring**
  - **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

Vaccinating Infants Will Unlikely Protect Unvaccinated Age Groups*

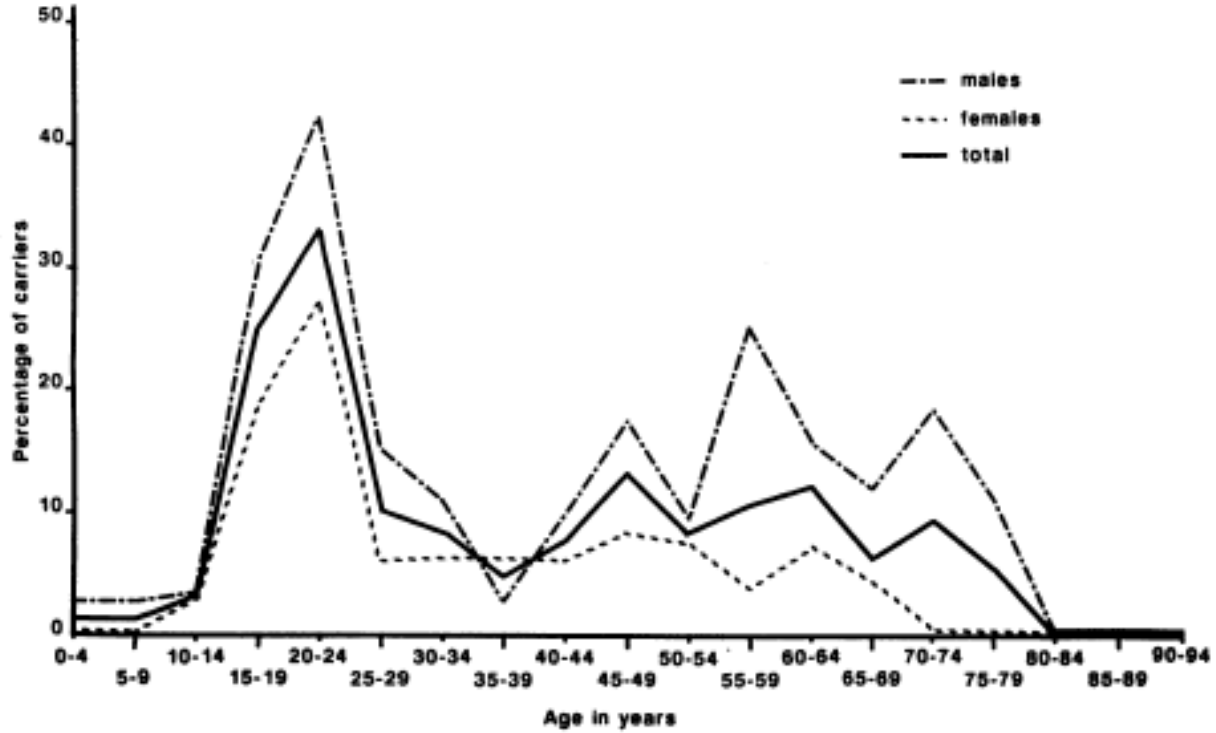
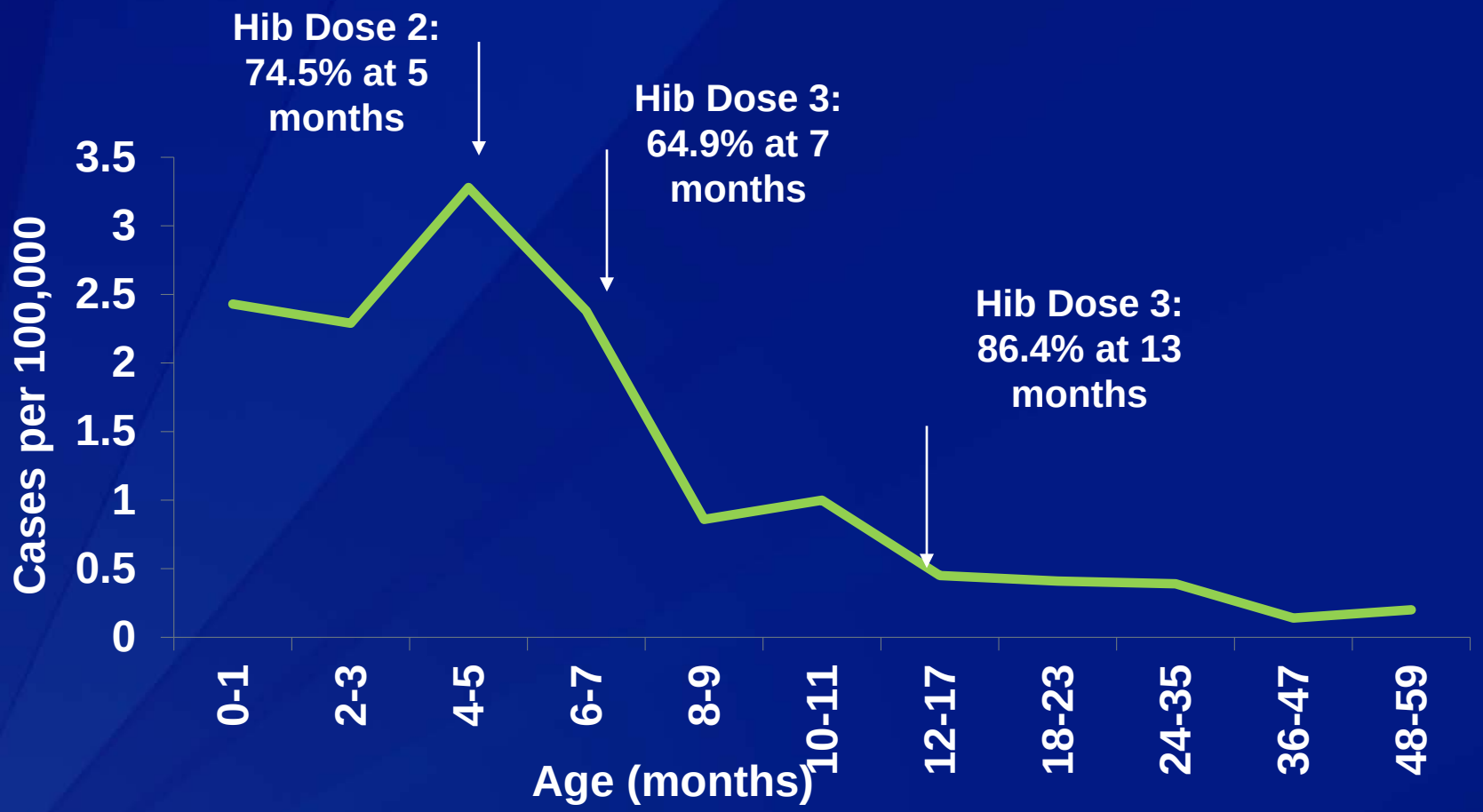


FIG. 1. Percentages of carriers of *N. meningitidis* according to age among males, females, and all participants in a random sample of the Norwegian population.

*Caugant et al, 1994

High 3 dose coverage needed early to prevent maximum number of cases



*ABCs, 1998-2007 average annual estimated rates to the U.S. population, NIS 2011 survey

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 reevaluate disease trends

Additional Considerations for HibMenCY

- **HibMenCY is a Hib vaccine**
  - Guidance for use as a Hib vaccine
- **HibMenCY not a travel vaccine**
  - Does not contain serogroups A and W135
  - MenACWY vaccination required to for infants traveling to the Hajj or Meningitis Belt

PROPOSED GUIDANCE AND RECOMMENDATIONS

Extending Meningococcal Vaccine Recommendation to Infants at Increased Risk

- **No preference for licensed vaccine formulations with exceptions:**
  - HibMenCY not recommended in infants who are traveling to meningitis belt or Hajj
  - MenACWY-D not recommended for infants 9 through 23 months with functional or anatomic asplenia to avoid potential interference with PCV13
- **Guidance for use of HibMenCY in high-risk infants will be integrated with guidance for MenACWY-D in 9 through 23 month-olds**

Proposed Recommendation for Vote

- Infants at increased risk for meningococcal disease should be vaccinated with 4 doses of HibMenCY at 2, 4, 6, and 12 through 15 months.

- These include infants with recognized persistent complement pathway deficiencies and infants who have anatomic or functional asplenia including sickle cell disease.

- HibMenCY can be used in infants ages 2 through 18 months who are in communities with serogroup C and Y meningococcal disease outbreaks.

Guidance for Use

- At this time, ACIP does not recommend routine meningococcal vaccination for infants.
- HibMenCY is safe and immunogenic. HibMenCY may be administered to infants to complete the routine Hib vaccination series.
- If HibMenCY is used to achieve protection against serogroups C and Y, HibMenCY should be used for all four doses of Hib vaccine.

Discussion

For more information please contact Centers for Disease Control and Prevention
1600 Clifton Road NE, Atlanta, GA 30333
Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov Web: www.cdc.gov

Thank you

- ACIP Meningococcal Vaccines Work Group
- Lorry Rubin
- Nancy Messonnier
- Thomas Clark
- Jessica MacNeil
- Ismael Ortega-Sanchez
- Amy Blain