Cost-Effectiveness of Meningococcal Vaccination in HIV Infected People in the US

Preliminary

Ismael Ortega-Sanchez, PhD

NCIRD, CDC

ACIP Meeting, June 2016

Disclaimers

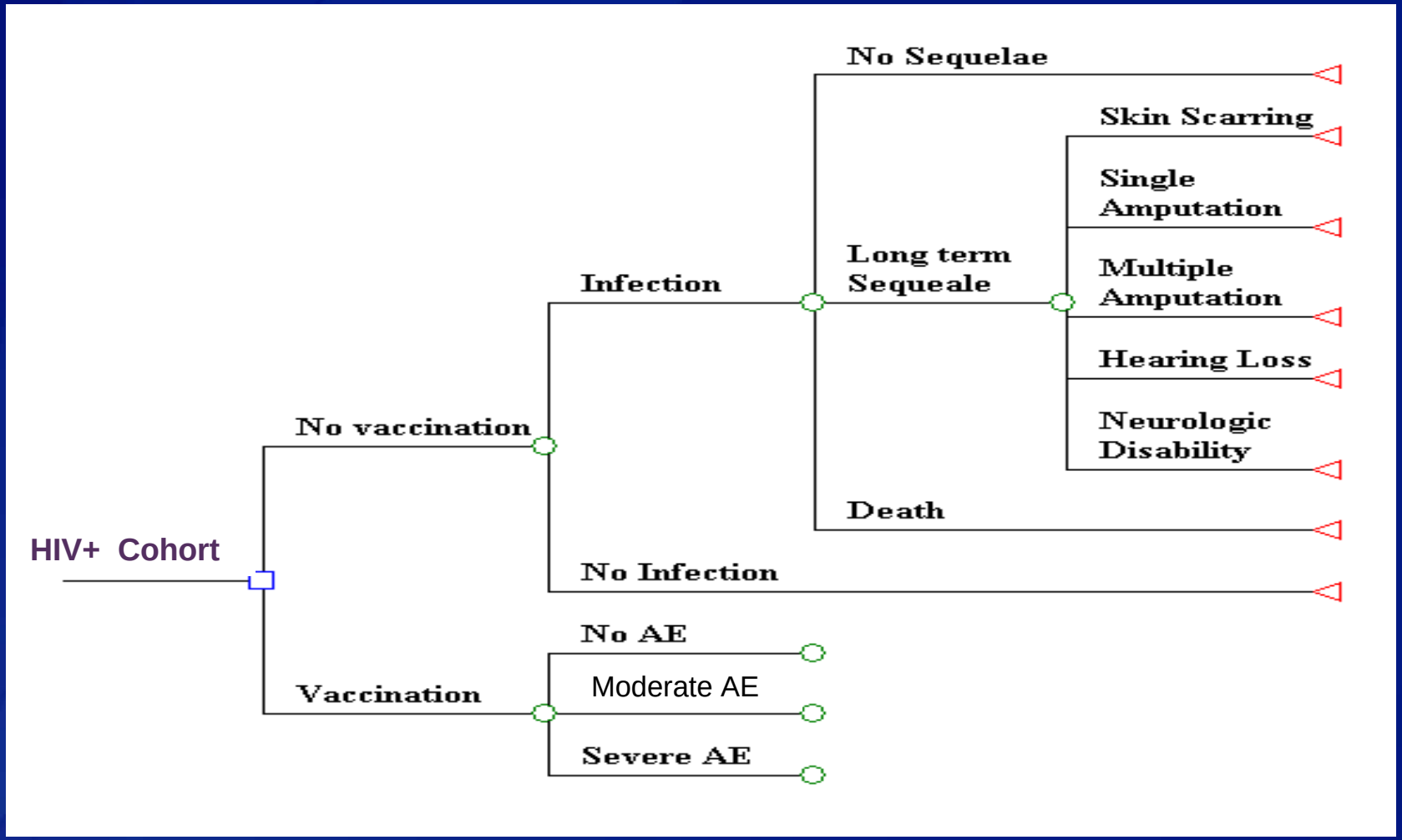
- Following the ACIP Guidance for Health Economics Studies this study has been reviewed at CDC. The review provided important observations that has been addressed for this presentation, explicit response to some comments are included at the end
- Acknowledgments: We thank:
  - The ACIP Meningococcal Working Group (2015-2016)
  - The NCIRD, Division of Bacterial Diseases
- Conflict of interest
  - Author has no conflict of interest
- The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Objective

- Analyze the effectiveness and cost-effectiveness of a potential vaccination program for persons living with HIV against meningococcal disease with primary series of MenACWY followed by lifelong one-dose boosters every 5 years*
- *Societal* perspective

* Every 3 years for <7 years of age

The Model of Meningococcal Vaccination

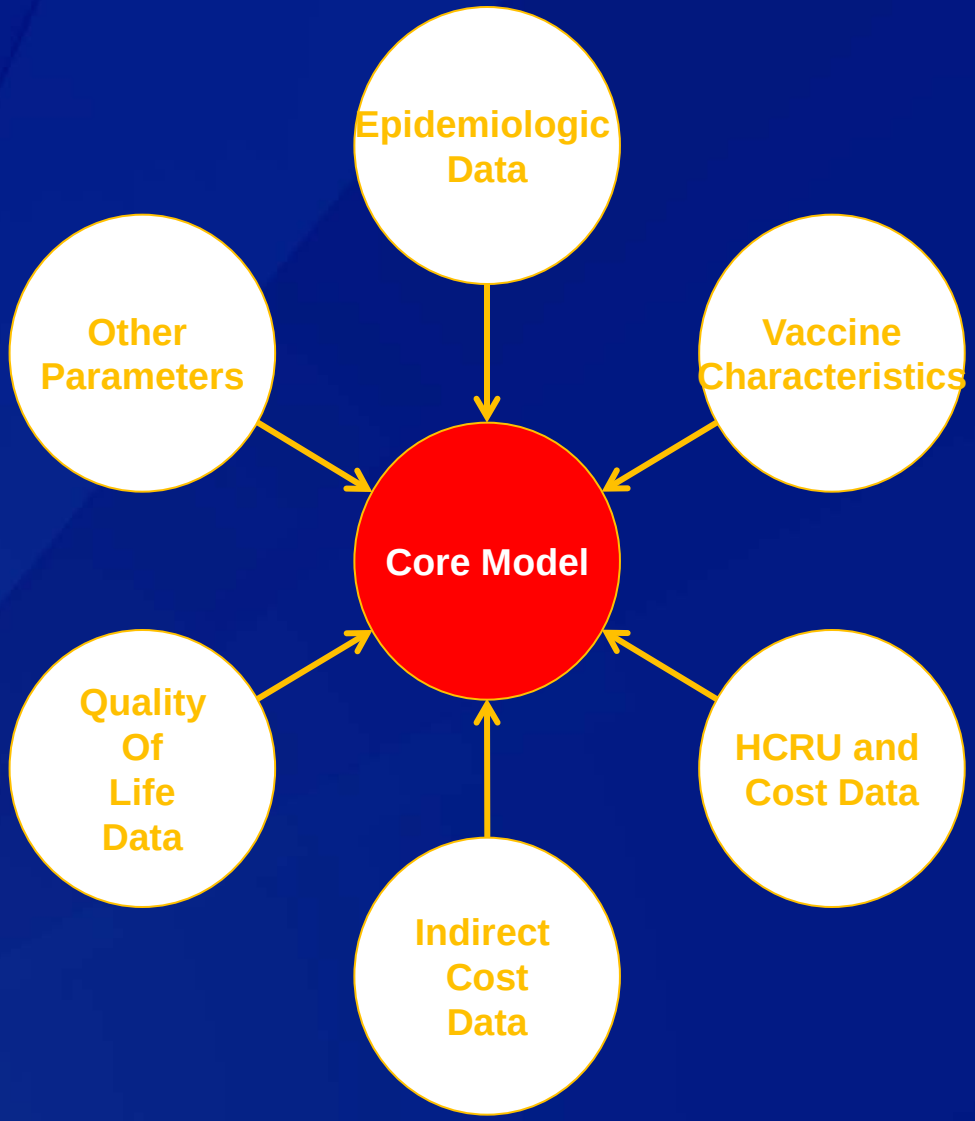


* Except for disease incidence rates which are lower in the "Vaccination" arm, nodes following these events are identical in structure to those that follow "No vaccination"

Design

- Monte Carlo simulation analysis
- Age-specific HIV+ population
  - ≈934,000 HIV+ distributed by age
- Time Frame: Age-specific Life Expectancy until age 70 years
- Analytic Horizon: Age-specific Life Expectancy
- Discount rate: 3% (0%-5%)

Core Model with Inputs



Epidemiologic Data

- Age-specific HIV+ population (2013)
- Age- year- and Mening ACWY serogroup-specific incidence rates (2005-2014)
- Age- and Mening ACWY serogroup-specific case fatality ratios (2005-2014)
- Proportion of survivors with sequelae by condition

Persons Living with HIV in the US
≈ 934,000 as of 2013*

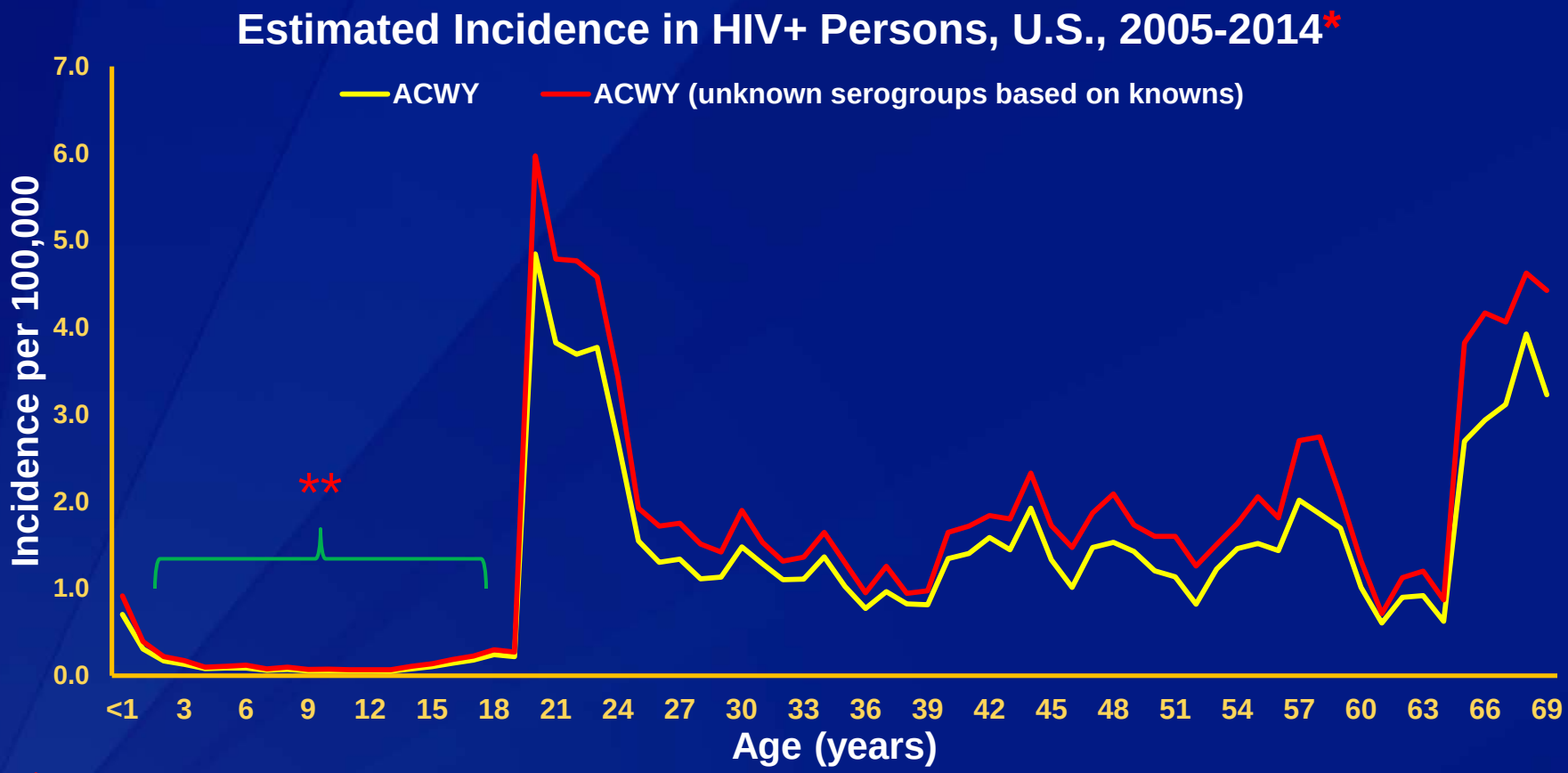
Age	Infections 2013*	% Stage III (AIDS)**	Life Expectancy***
< 13 years	2,415	4% - 17%	63.4 - 69.7
13-14 years	759	2.9% - 14%	59.3 - 65.7
15-19 years	5,778	3.9% - 14%	55.3 - 62.3
20-24 years	32,980	4.4% - 14%	50.6 - 57.4
25-29 years	58,652	4.3% - 14%	46.7 - 52.7
30-34 years	73,984	3.5% - 14%	41.8 - 47.9
35-39 years	85,193	3% - 14%	36.8 - 43.2
40-44 years	118,185	2.2% - 14%	32.6 - 38.5
45-49 years	160,327	1.8% - 14%	27.4 - 34.0
50-54 years	162,034	1.5% - 14%	23.7 - 29.6
55-59 years	114,306	1.5% - 14%	18.5 - 25.4
60-64 years	66,334	1.4% - 14%	14.3 - 21.3
65 + years	52,994	1.5% - 14%	9.7 - 15.6

* Based on HIV Surveillance Report 2014. Centers for Disease Control and Prevention. *HIV Surveillance Report, 2014*; vol. 26. http://www.cdc.gov/hiv/library/reports/surveillance/ Published November 2015.

** Lower bound based on proportion of new Stage 3 diagnoses for 2013 from HIV Surveillance Report 2014. Upper bound based on Revised Surveillance Case Definition for HIV Infection — United States, 2014. MMWR) April 11, 2014 / 63(RR03);1-10. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6303a1.htm?s_cid=rr6303a1_e

*** ***Assumption:*** average life expectancy similar to General Population (upper bound) and about 7 years reduction in people living with HIV (lower bound). Sources: (1) Wada et al. AIDS. 2014 January 14; 28(2): 257–265. (2) Samji et al. PLoS ONE 8(12): e81355.

Incidence of Meningococcal Serogroups ACWY in HIV+ Persons



* Source: Estimated incidence in HIV+ using proportion of cases who are HIV+ in Active Bacterial Core surveillance (ABCs) and incidence data from the National Notifiable Diseases Surveillance System (NNDSS) with additional serogroup data from ABCs and state health departments.

** Incidence data for 0 to 19 years is from NNDSS with additional serogroups data from ABC's and state health departments for the general population (regardless of HIV status)

Strategies of Vaccination with MenACWY Schedule by Age

- **≥2 years of age:**
  - Primary series: 0, 2 months
  - Boosters: life-long boosters required
    - Current booster recommendations: 3 years if age <7 years at previous dose and 5 years if age ≥7 years at previous dose
- **<1 year of age:**
  - Primary series: 2, 4, 6, 12 months
  - Boosters: same as above
- **1-2 years of age:**
  - Primary series: 0, 3 months
  - Boosters: same as above

Vaccine Characteristics: *Initial** Effectiveness & Coverage**

Assumptions ***

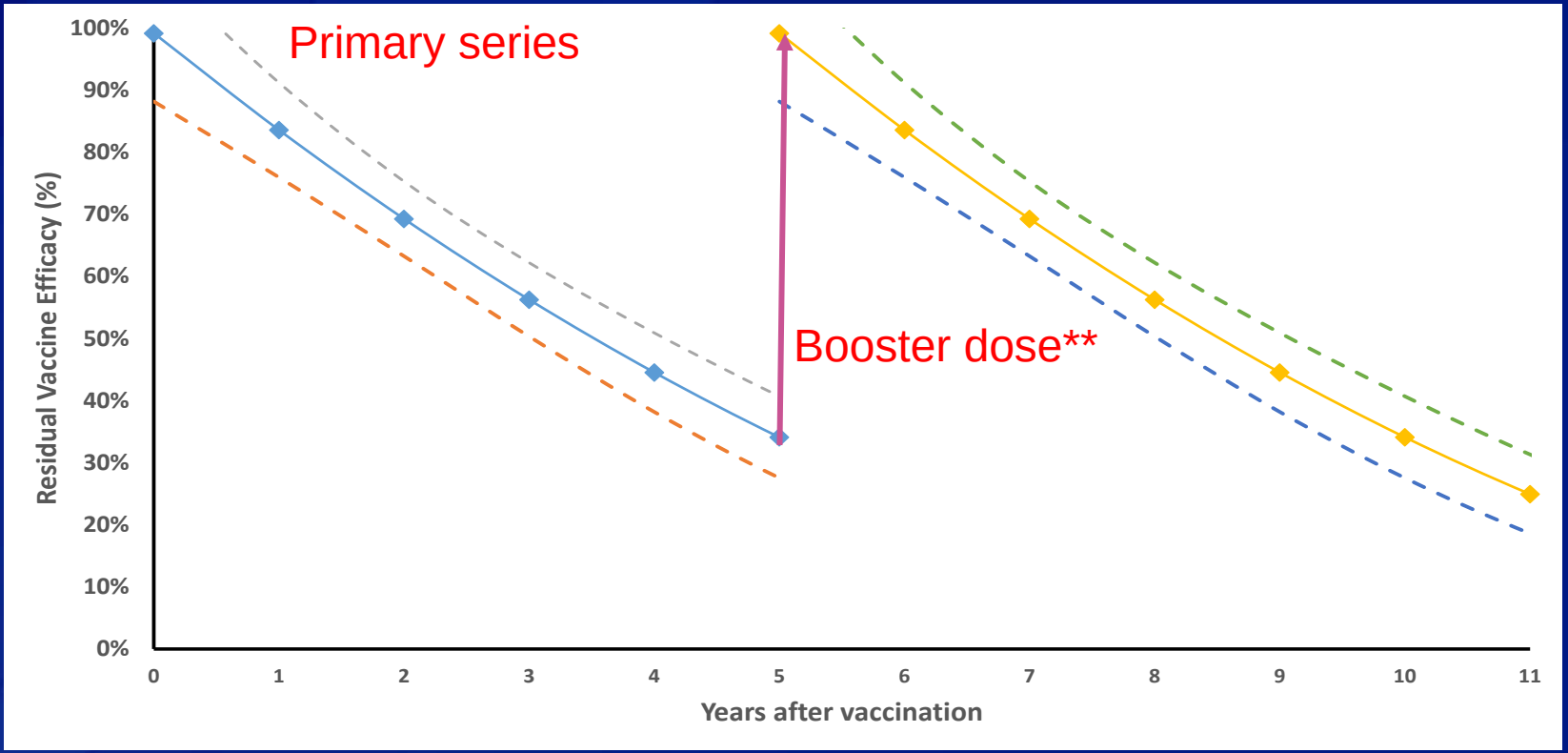
- Vaccinating age-specific HIV+ cohorts + booster doses
  - Initial Efficacy:
    - High CD4 count with 2 doses series 75% (37% - 91%)
    - Low CD4 count with 2 doses series 37% (24% - 60%)
  - Coverage:
    - Primary series (2 or 3 doses) 65% (40% -- 80%)
    - Booster dose (every 5 years) 45% (30% -- 65%)

* Initial vaccine effectiveness with first series is based on combined efficacy from Open-Label Trial of Safety and Immunogenicity of Meningococcal (Groups A, C, Y, and W)

** Rates of coverage for primary series and booster assumptions based on various sources

*** Preliminary assumptions

Vaccine Characteristics:
Residual Vaccine Efficacy*



* Preliminary assumptions: Linear and exponential fitting to antibody waning through available SBA data. Waning is adjusted for low and high CD4 counts and for 1st and 2nd dose in the series

** Efficacy of each booster dose is assumed to follow similar waning protection pattern

Disease Incidence Under Vaccination

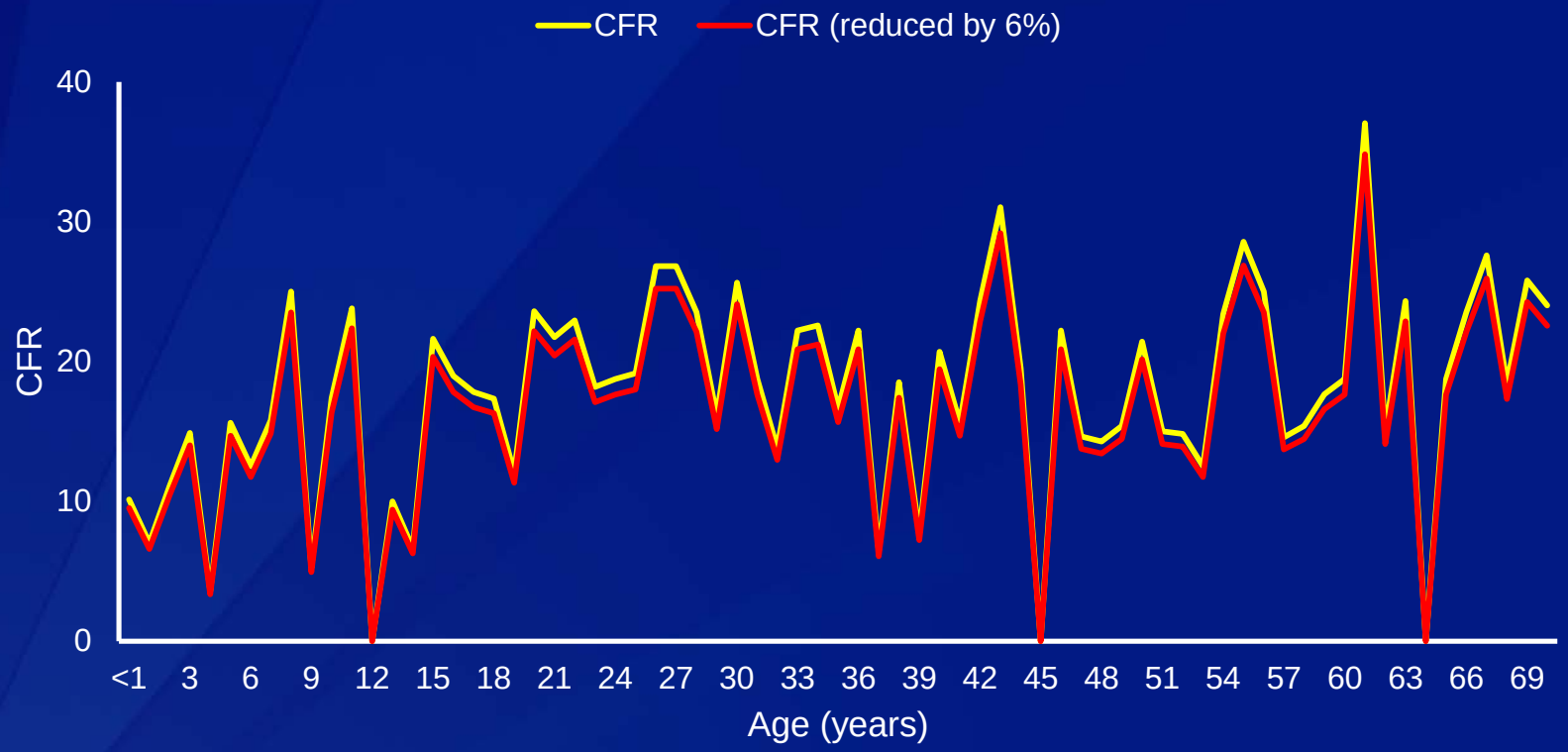
For each age group and for each strategy

$$MDI_{vacc} = MDI_{no\ vacc} * [1-(Vcov * IntVEff * Residual_t)]$$

Where:

- MDI_{vacc} = Meningococcal disease incidence under vaccination
- $MDI_{no\ vacc}$ = Meningococcal disease incidence without vaccination
- *Vcov* = Vaccination coverage
- *Int VEff* = Initial vaccine efficacy
- $Residual_t$ = Residual vaccine efficacy (0-100%) ***t*** years after vaccination $t = 0,\ldots,T$

Meningococcal Case-Fatality Ratio Among Persons Living with HIV*



* Estimated CFR for serogroups ACWY in HIV+ Persons based on NNDSS meningococcal cases with and without reduction as observed in ABCs data for HIV+ cases for the U.S., 2005-2014

Proportion of Survivor Cases with Sequelae by Type of Condition

Skin scarring	7.6	(0 - 19)
Single amputation	1.9	(0.5 - 10)
Multiple amputations	1.2	(0.02 - 6)
Hearing loss*	8.8	(2 - 20)
Significant long term neurologic disability**	2.1	(0.02 - 11)

* Edwards *et al*. Complications and sequelae of meningococcal infections in children. J Pediatrics 1981; 99:540-5

** Baraff *et al*. Outcomes of Bacterial meningitis in children: a meta-analysis PIDJ 1993;12:389-94

Quality of Life in HIV+ Persons Baseline Age-specific Scores for Modeling

AGE (in years)	Health Utility Index General Population*	Marginal Effect in Utility Score from HIV**	Health Utility Index People Living with HIV
<24	92.2%	-11.0%	**81.2%**
25-34	92.2%	-11.0%	**81.2%**
35-44	92.3%	-13.0%	**79.3%**
45-54	91.5%	-13.0%	**78.5%**
55-64	88.1%	-14.0%	**74.1%**
65-74	86.4%	-14.0%	**72.4%**
75-84	83.9%	-14.0%	**69.9%**
85+	78.5%	-14.0%	**64.5%**

* Health Utilities Index, Mark 3, (HUI-3) combined for males and females. Sources: (1) http://www.healthutilities.com/HUINormsKeyTable.htm (2) http://www.chepa.org/Files/Working%20Papers/01-02.pdf

** Adjusted for Age, Sexuality, CD4 counts (AIDS) and Date of diagnosis. Source: Miners et al. "Health-related quality-of-life of people with HIV in the era of combination antiretroviral treatment: a cross-sectional comparison with the general population. The Lancet V1, (1), October 2014, e32–e40

Health-related Quality of Life QALY Scores from Meningococcal Complications*

	Base case	High	Low
Death	0		
Skin scarring	0.95	1.00	0.80
Single amputation	0.70	0.80	0.31
Multiple amputations	0.61	0.71	0.31
Hearing loss/cochlear implants	0.72	0.82	0.64
Neurologic disability	0.06	0.39	0.00

* Several sources cited in: Shepard *et al*., *Pediatrics* 2005
Ortega-Sanchez et al., *CID* 2008

Components of Cost of Disease Calculation

	Acute phase			Lifetime	
Outcome	Med care (mening)	Caregivers' Work-Loss	Med care sequelae	Lifetime care (rehab, long term care)	Productivity Loss
No Sequelae	√	√			
Death	√	√			√
Skin scarring	√	√	√		
Single amput	√	√	√	√	
Multi amput	√	√	√	√	√
Hearing loss	√	√		√	√
Neuro seq	√	√		√	√

Vaccine Characteristics: Cost of Vaccination

- Cost components of vaccination program
  - Public and private sector prices
  - Using price of meningococcal conjugate vaccine
  - Wastage 10.7% (range 0-25%)
  - Administration fees (public and private)
  - Adverse events from UK experience with MCC
- Cost of per dose
  - **$138 (**$121 - $153**)** (costs a dose + Adm + AE+ waste)

Results*

** Preliminary*

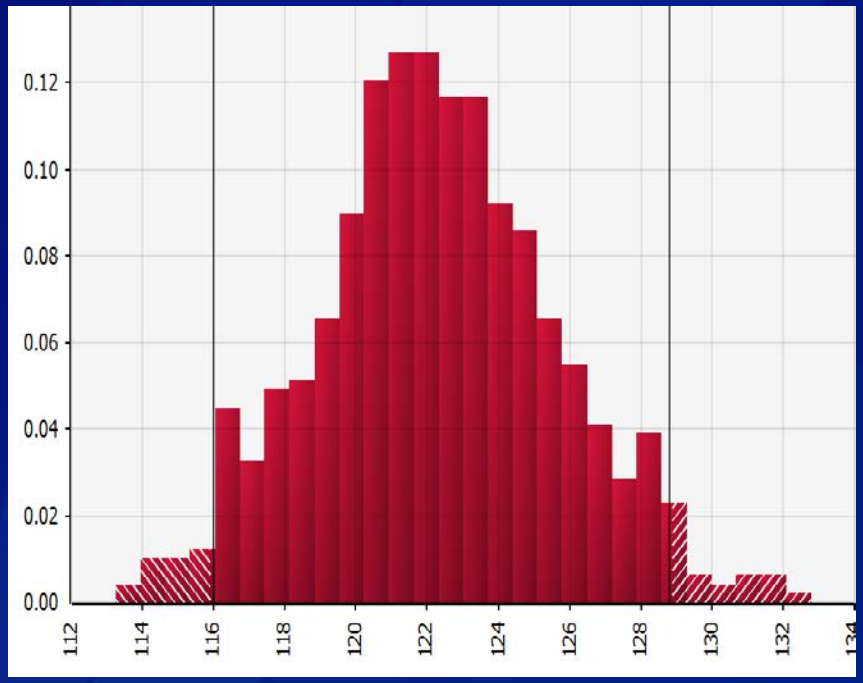
Baseline per Age Group of HIV+ No Vaccination, Mean Estimates*

	Cases	Deaths	QALYs lost**	Disease Costs**
<13 years	2.0	0.4	5.8	$ 466,000
13-14 years	0.6	0.1	2.5	$ 176,000
15-19 years	4.6	0.9	21.2	$ 1,566,000
20-24 years	23.4	4.4	101.2	$ 8,524,000
25-29 years	34.2	6.3	118.1	$ 12,080,000
30-34 years	38.6	7.0	119.1	$ 13,763,000
35-39 years	40.2	7.3	118.7	$ 9,074,000
40-44 years	49.9	9.3	156.5	$ 11,557,000
45-49 years	56.7	10.6	162.4	$ 13,143,000
50-54 years	44.4	8.8	134.7	$ 10,168,000
55-59 years	27.0	5.2	76.2	$ 6,288,000
60-64 years	11.5	2.3	33.8	$ 2,646,000
65 + years	5.4	1.2	16.9	$ 1,278,000
All HIV+	**338**	**64**	**1067**	**$ 90,728,000**

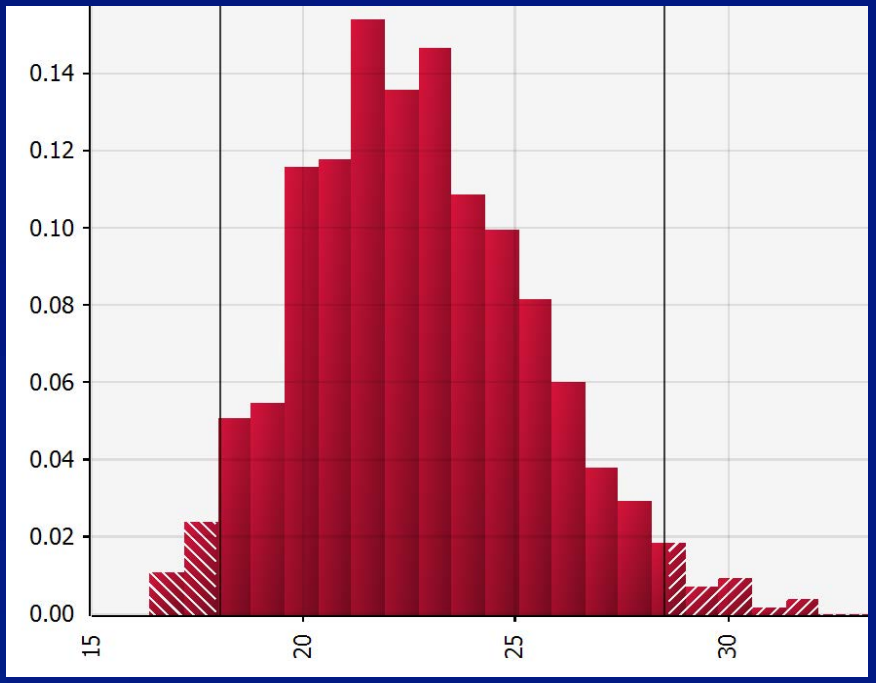
* Mean values from Monte Carlo simulation

** Discounted at 3% rate, disease costs rounded to the nearest thousand

Total Cases* and Deaths* Averted in People Living with HIV



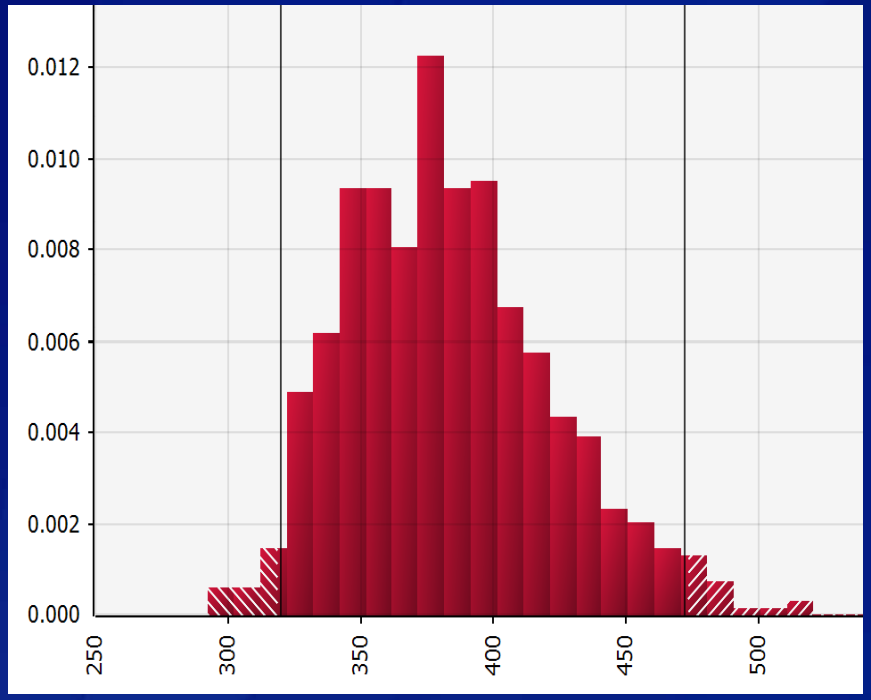
Cases averted:
Mean 122 (95% CI, 116-129)



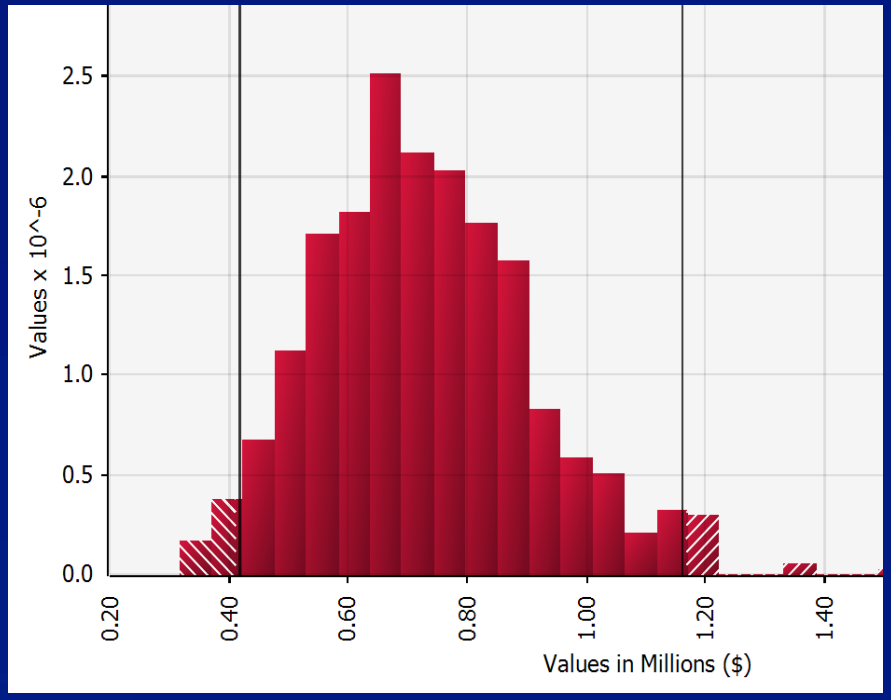
Deaths averted:
Mean 23 (95% CI, 18 – 29)

* Estimated distributions from Monte Carlo Simulation

Total QALYs saved and Cost per QALY* saved in People Living with HIV



QALYs Saved:
Mean 385 (95 % CI, 320 - 473)



Cost per QALY saved:
Mean $731K (95% CI, 420K – 1.16 Mil)

* $/QALY excludes indirect cost from deaths
Estimated distributions from Monte Carlo Simulation

Cases, Deaths Prevented & QALYs Saved Baseline Estimates* by Age Group

Age	Cases saved (5th - 95th)		Lives saved (5th - 95th)		QALYs saved (5th - 95th)**	
<13 years	**0.8**	(0.8 - 0.9)	**0.1**	(0.1 - 0.2)	**2.1**	(1.8 - 2.5)
13-14 years	**0.2**	(0.2 - 0.2)	**0.0**	(0.0 - 0.1)	**0.9**	(0.7 - 1.0)
15-19 years	**1.6**	(1.5 - 1.70	**0.3**	(0.3 - 0.4)	**7.3**	(6.1 - 8.6)
20-24 years	**8.5**	(8.2 - 9.0)	**1.6**	(1.4 - 1.8)	**37.8**	(32.0 - 45.2)
25-29 years	**12.2**	(11.8 - 12.6)	**2.2**	(1.9 - 2.6)	**42.4**	(41.2 - 58.1)
30-34 years	**13.8**	(13.2 - 14.4)	**2.5**	(2.1 - 3.0)	**42.5**	(34.3 - 53.2)
35-39 years	**14.4**	(13.8 - 15.0)	**2.6**	(2.1 - 3.1)	**42.4**	(33.8 - 54.0)
40-44 years	**18.0**	(17.1 - 18.8)	**3.3**	(2.7 - 4.1)	**57.5**	(44.7 - 74.9)
45-49 years	**20.5**	(19.5 - 21.5)	**3.7**	(3.0 - 4.7)	**57.2**	(45.1 - 73.2)
50-54 years	**15.9**	(15.0 - 16.9)	**3.1**	(2.4 - 3.9)	**46.3**	(37.0 - 57.6)
55-59 years	**10.0**	(9.3 - 10.7)	**1.9**	(1.4 - 2.5)	**28.0**	(20.7 - 36.3)
60-64 years	**4.2**	(3.8 - 4.6)	**0.9**	(0.6 - 1.2)	**12.4**	(8.6 - 17.6)
65 + years	**2.2**	(2.0 - 2.5)	**0.5**	(0.3 - 0.8)	**7.1**	(4.2 - 11.3)
All HIV+	**122**	**(116 - 129)**	**26**	**(18 - 29)**	**385**	**(320 - 458)**

* Mean, 5th and 95th percentiles from Monte Carlo simulation

** Discounted at 3% rate

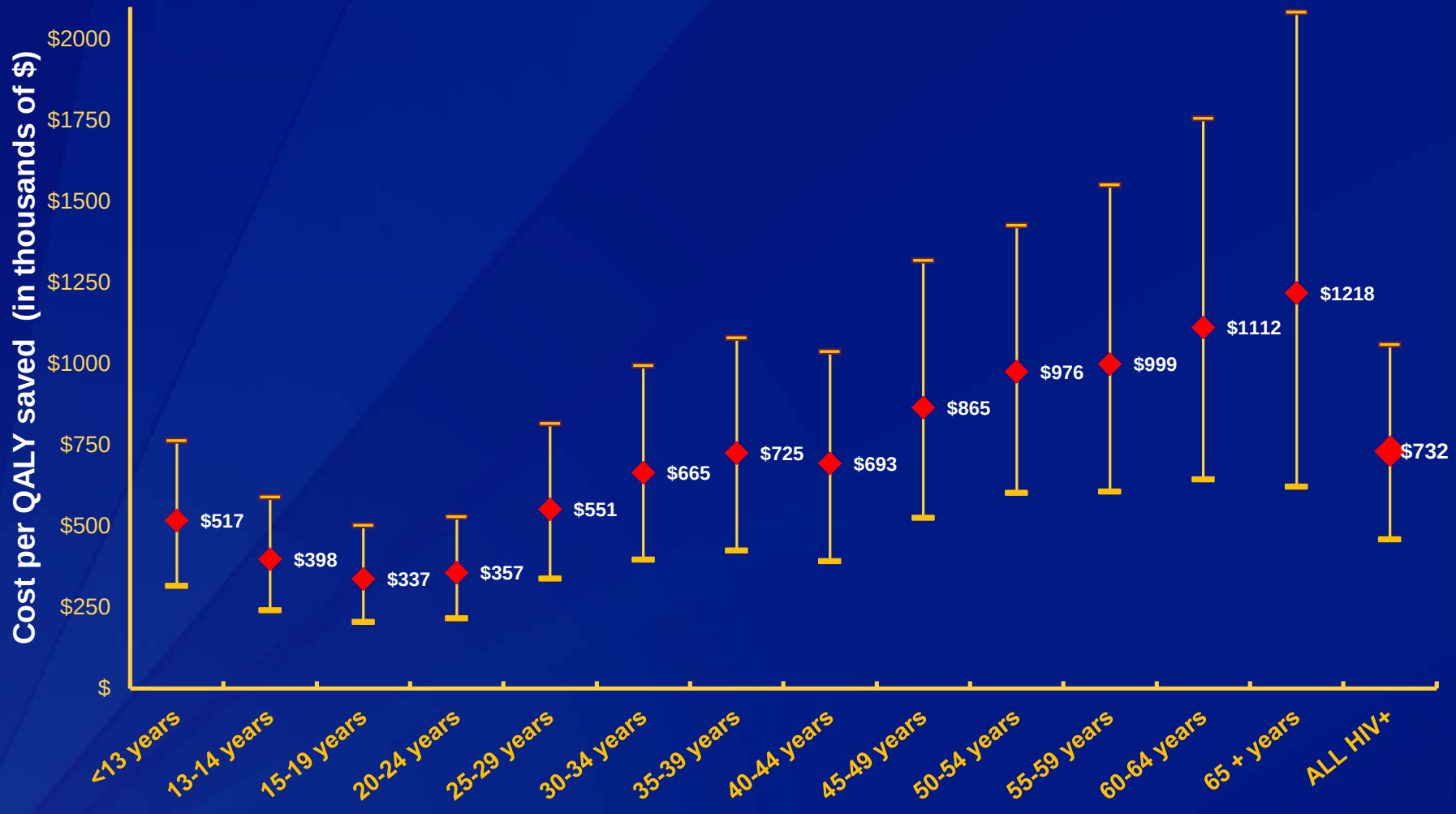
Disease, Vaccination and Net Costs Baseline Estimates* by Age Group

Age	Disease Cost with Vax	Vaccine Cost	Net Cost **
<13 years	$ 297,000	$ 1,156,000	$ 1,081,000
13-14 years	$ 115,000	$ 353,000	$ 330,000
15-19 years	$ 1,024,000	$ 2,615,000	$ 2,417,000
20-24 years	$ 5,397,000	$ 14,437,000	$ 13,314,000
25-29 years	$ 7,767,000	$ 24,677,000	$ 23,115,000
30-34 years	$ 8,836,000	$ 29,675,000	$ 27,787,000
35-39 years	$ 9,285,000	$ 32,248,000	$ 30,141,000
40-44 years	$ 11,605,000	$ 41,692,000	$ 38,856,000
45-49 years	$ 12,591,000	$ 51,903,000	$ 48,465,000
50-54 years	$ 9,506,000	$ 47,168,000	$ 44,353,000
55-59 years	$ 5,288,000	$ 29,039,000	$ 27,121,000
60-64 years	$ 2,117,000	$ 14,007,000	$ 13,170,000
65 + years	$ 896,000	$ 8,505,000	$ 8,022,000
All HIV+	**$ 74,766,000**	**$ 298,373,000**	**$ 279,050,000**

* Values from Monte Carlo simulation, discounted at 3% and rounded

** Net costs exclude all indirect or productivity costs

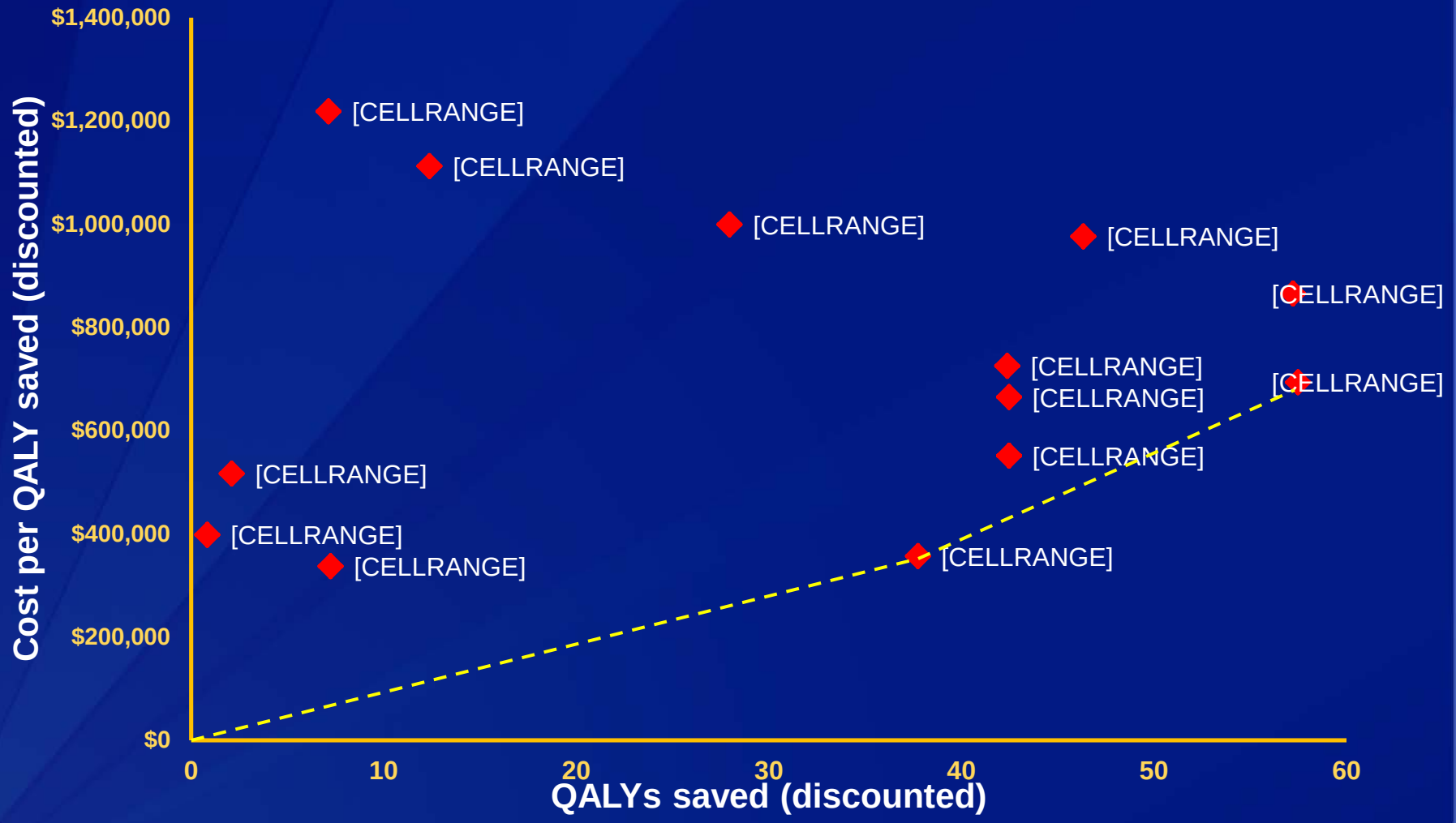
Cost per QALY saved per Age Group
Mean, 5th and 95th percentiles (in thousands of $)*



* $/QALY excludes indirect cost from deaths

Estimates from Monte Carlo Simulation

Incremental Cost Effectiveness Meningococcal Vaccination by Age group



Cost-Effectiveness Selected Scenario Analyses*

	QALYs saved	Cost-per-QALY saved
Base-case	**385**	**$732,000**
Life Expectancy in people living with HIV -- 7 year lower than GP	327	$819,000
Proportion of HIV people in Stage 3 – 14% based in CD4 counts	321	$841,000
Waning of vaccine efficacy -- lower 5th percentile	296	$901,000
Initial vaccine efficacy -- 37% as for low CD4 count	231	$1,119,000
Baseline health-related quality of life similar to general population	447	$595,000

* Preliminary estimates from Monte Carlo simulation

$/QALY of Selective Vaccines in the US Base-case Comparisons

Vaccine	Target group	Cost per QALY gained (compared to no vaccination)
Hepatitis B	College freshmen	<$0 (cost-saving) to ≈ $10,000
Hepatitis A	College freshmen	<$0 (cost-saving) to ≈ $15,000
Pneumococcal (PCV13)	Adult persons with HIV/AIDS	≈ $4,000
Meningococcal (MCV4)	All 11- to 17-year-olds (with herd immunity)	≈ $94,000
Meningococcal (MCV4)	MSM in New York City (with, without herd immunity)	≈ $66,000 to >$177,000
Meningococcal (MCV4)	2-dose, all 11 & 16-year-olds	$212,000
Meningococcal (Hib MenCY)	4 doses, all Infants at 2, 4 , 6 and 12-15 mons	≈215,000 ($90,000 to >$450,000)
Meningococcal ACWY	**All persons living with HIV in the US**	**$732,000 ($337,000 to $1,218,000)**
Meningococcal (MenB)	Series @16 years	≈$4.1 Million
Meningococcal (MenB)	Series, all freshman college in 4yr and 2yr programs	≈$9.4 Million

Sources: Ortega-Sanchez et al. *Pediatrics* 2008 Jan;121 Suppl 1:S63-78
Cohn et al., *MMWR*, 2013 Mar 22;62(RR-2):1-28.
Simon et al. *J Acquir Immune Defic Syndr*. 2016 Feb 1;71(2):146-54.
Cho et al. Vaccine 2013 Dec 5; 31 (50): 6011-6021

Strengths and Limitations

Strengths

- Complex modeling
- Explicit use of incidence and CFR surveillance data for Meningococcal serogroups ACWY

Limitations

- Data on incidence and mortality among people with HIV is limited
- Data on *initial* vaccine effectiveness are from serology and immunogenicity
- Data on duration of vaccine efficacy is limited

CDC One-side-Blinded Review
ACIP: Guidance for Health Economics Studies

- **Part I**
  - Comment 1. “[C]oncerns about the numbers presented for the number of people living with AIDS
    - Using the “Revised Surveillance Case Definition for HIV Infection - United States, 2014” we re-estimated the percentage range of people living with HIV in stage 3, along with a scenario analysis
  - Comment 2. The reduction in cases of disease as a result of vaccination does not seem to line up with the assumptions about vaccine efficacy, vaccine coverage, and waning of protection
    - We reviewed the model calculations for formulas and parameter values. Health outcomes and costs were re-estimated
- **Part II**
  - In Comments 3 to 9. Reviewer provided “minor” or “editorial” comments which were addressed in these slides and in the technical report

Conclusions

- Routine vaccination of people living with HIV with a primary series + periodic boosters against Meningococcal ACWY disease is relatively costly
- Disease cases, deaths (both with relatively low numbers) and vaccine costs of lifelong booster doses drive the analyses
- Although costly, additional cases could be prevented by all vaccination strategies