Economics of Potential Pentavalent Meningococcal Conjugate Vaccine (MenABCWY) versus the Current MenACWY and MenB vaccines for US Adolescents

A SUMMARY REPORT COMPARING MODELS FROM:

Pfizer* AND *CDC

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NCIRD/CDC

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Disclaimer*: The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.*

Conflict of interest

- ***Pfizer* model**: Shannon Sullivan et al., [complete authors list and affiliations, upon request]
  - *Pfizer* manufactures pentavalent (MenABCWY) vaccine
  - Evidera Inc. (France, USA, Hungary) was funded by *Pfizer*

- **CDC model**: ***Ismael R Ortega-Sanchez*** *et al.* from CDC [complete authors list and affiliations, upon request]
  - All authors: No conflicts of interest

3 Policy questions for economic modeling

- Should the pentavalent vaccine (MenABCWY) be considered as an option for MenACWY/MenB vaccination in people currently recommended to receive both vaccines? (PICO 1)

- Should the pentavalent vaccine (MenABCWY) be included as an option for people currently recommended to receive MenACWY only? (PICO 2)

- Should the pentavalent vaccine (MenABCWY) be included as an option for people currently recommended to receive MenB only? (PICO 3)

Economic analysis

Question: Is vaccinating adolescents 11-16 years old with Pentavalent (MenABCWY) vaccine series to prevent Invasive Meningococcal Disease in adolescents *cost-effective*?

Comparator

MenACWY vaccine: one dose at 11-12 years and one dose at 16 years. (**Q-Q**)
MenB vaccines: two doses at 16 years. (**B-B**)

Interventions

Use of Pentavalent MenABCWY vaccine combined either as
Q-P-B
P-P-N
or **Q-P-P**

Base-case scenario: What is the *incremental cost-effectiveness* of vaccinating healthy adolescents 11-12 and 16 years old with Pentavalent vaccine relative to *using* MenACWY and MenB vaccines ?

Description of Current and Hypothetical Vaccines and Vaccination Strategies

Standard of Care (SoC)		
First dose	**Second dose**	**Key Label**
At 11-12 yrs old with MenACWY	At 16 yrs old with MenACWY	**Q-Q**
At 16 yrs old with MenB	At 16.5 yrs old with MenB	B-B

Potential vaccination strategies			
First dose	**Second dose**	**Third dose**	**Key Label**
At 11-12 yrs old with MenACWY	At 16 yrs old with MenABCWY	At 16.5 yrs old with MenB	**Q-P-B**
At 11-12 yrs old with MenABCWY	At 16 yrs old with MenABCWY	None (N)	**P-P-N**
At 11-12 yrs old with MenACWY	At 16 yrs old with MenABCWY	At 16.5 yrs old with MenABCWY	**Q-P-P**

SoC= Standard of care (current vaccination programs: **Q-Q** and **B-B**)
MenABCWY = Potential pentavalent vaccine (**P**) with serogroups A, B, C W Y
MenACWY = currently recommended quadrivalent vaccine (**Q**) for serogroups A, C, W, Y,
MenB =currently recommended monovalent vaccine for serogroup **B**

Pfizer and CDC: incremental cost-effectiveness analyses of vaccination strategies with pentavalent

Policy question	Incremental analysis	*Pfizer*	CDC	Vaccine Price used for Pentavalent **
PICO #1	Q-P-B **vs** SoC	Included*	Included	$250 (private) / $187.5 (public)
PICO #2	P-P-N **vs** Q-Q	Included	Included	$210 (private) / $157.5 (public)
PICO #3	Q-P-P **vs** SoC	Included	Included	$210 (private) / $157.5 (public)

SoC = Standard of care (current vaccination programs: Q-Q and B-B)

* Included in *Pfizer* technical report updates until August 2023, not included in the *Pfizer* technical report update of October 2023

** The price of $250 (private) / $187.5 (public) is for strategies using a single dose of pentavalent and the price of $210 (private) / $157.5 (public) for strategies using ≥2 doses of pentavalent

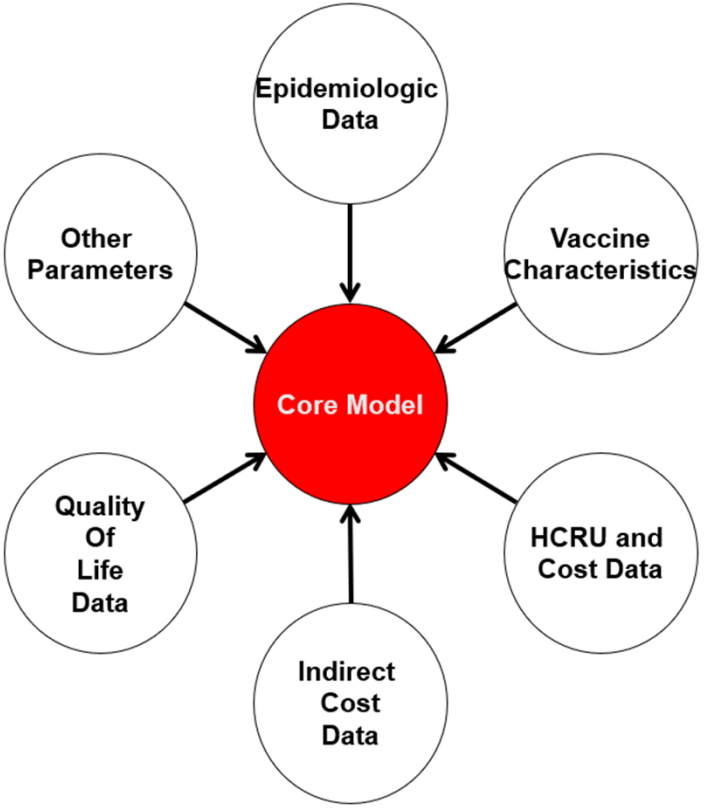
Focus on key features for model comparison

- Modeling approach
  - Targeted population(s)
  - Perspective (healthcare vs. societal)
  - Intervention strategies and comparators
- Inputs for IMD burden, vaccine efficacy, and costs
  - Incidence of IMD rates and sequelae outcomes
  - Direct and indirect costs of IMD
  - Intervention: efficacy, duration of protection, safety and program costs
- Assumptions
  - Strong, influential assumptions

Modeling design and assumptions

	Pfizer	CDC
Static analytical decision-making models	✓	✓
Sensitivity analyses (and probabilistic simulation)	✓(✓)	✓(✓)
Hypothetical population: US cohort of adolescents ≥11 years of age	✓	✓
Time Frame: 15 years (from 11-25 years)	✓	✓
Analytic Horizon: Temporary disability (acute without sequelae) and Life Expectancy (permanent sequalae or premature mortality)	✓ ✓	✓ ✓
Discount rate: 3%	✓	✓
Year of health and economic outcomes measured: 2022	✓	✓
Societal perspective (and healthcare perspective)	✓(✓)	✓(✓)

Inputs and main outcomes



	Pfizer	CDC
Prevention of:		
• IMD cases	✓	✓
• IMD-associated sequelae	✓	✓
• IMD-associated deaths	✓	✓
QALYs saved	✓	✓
$/QALY saved	✓	✓
Number needed to vaccinate (NNV) to avert an:		
• IMD case		✓
• IMD death		✓

IMD = invasive meningococcal disease
HCRU = healthcare resource utilization
QALY= quality-adjusted life year

Pfizer and CDC models comparison: Selected inputs

- Cost of vaccine and vaccine administration
- IMD incidence for pre vaccine and vaccine era
- Initial vaccine effectiveness and waning over time
- IMD associated permanent sequalae
- Age and serogroup specific Case Fatality Rate (CFR)
- Acute IMD: QALY scores and unitary direct costs

IMD = Invasive meningococcal disease
QALY= Quality-adjusted life years

Note: Starting this slide and forward, to specifically identify changes and updates from those presented last June 2023, the text will appear either highlighted, or with the word updated at the top of the slide or table.

Pfizer vaccine price for a dose of Pentavalent

Vaccination Strategies	March to June 2023*	August 2023**	October 2023***
With one dose			
Private	$240 ($230-$250)	$250.0	$250.0
Public	--	187.5	187.5
With ≥ 2 doses			
Private	$240 ($230-$250)	$250.0	$210.0
Public	--	187.5	$157.5

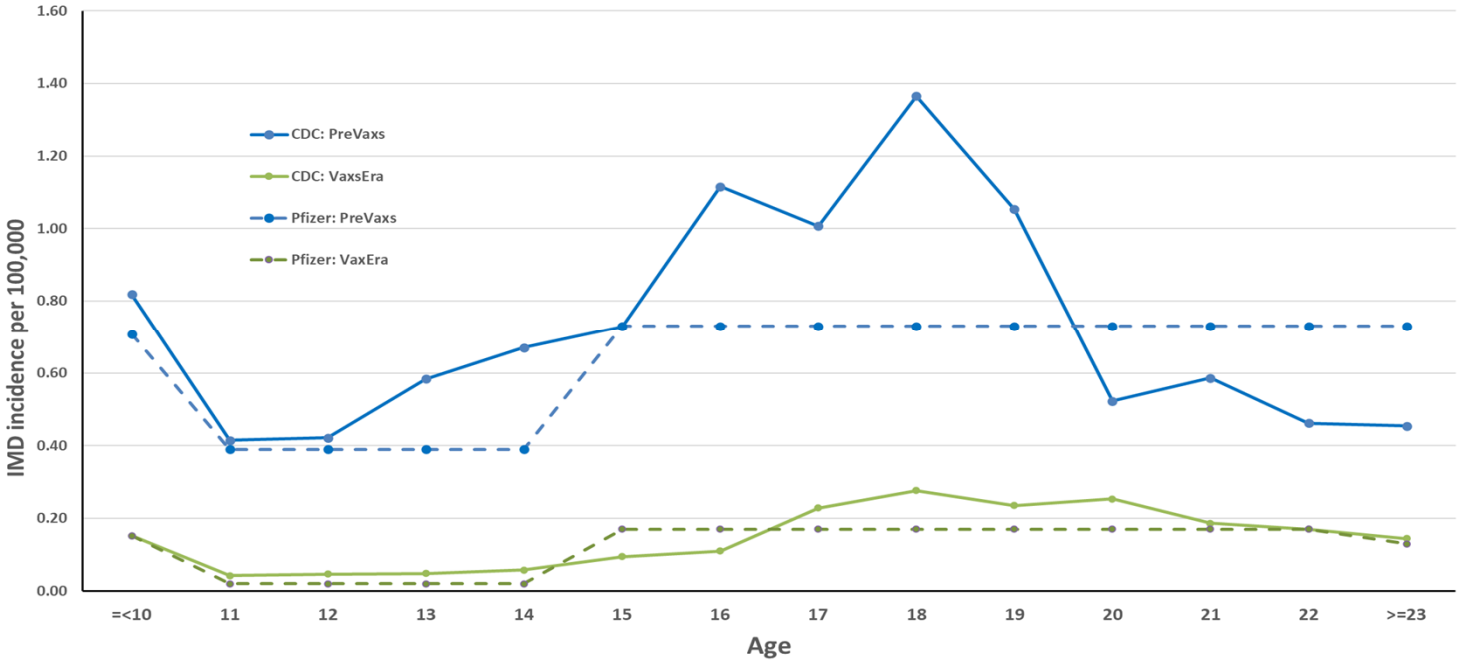
* From March to June 2023, ***Pfizer*** submitted various technical reports using the pentavalent vaccine prices of $240 (range $230 to $250) per dose
** In August 2023, ***Pfizer*** submitted a new technical report updating the pentavalent prices to $250 (private) / $187.5 (public) per dose
*** In October 2023, ***Pfizer*** submitted a newer technical report updating the pentavalent prices to $210 (private) / $157.5 (public) per dose for strategies using ≥2 doses of pentavalent

Pfizer and CDC: Vaccine cost per vaccine type, and vaccine administration costs

	Quadrivalent (Q)*	Men B (B)*	Pentavalent (P)	
			Q-P-B (single dose)	P-P-N & Q-P-P (≥2 doses)
public sector cost for vaccine	$105.6	$141.84	$187.5	$157.5
public sector admin cost	$15.0	$15.0	$15.0	$15.0
private sector cost for vaccine	$156.0	$211.32	$250.0	$210.0
private sector admin cost	$30.0	$30.0	$30.0	$30.0
% vaccine purchased at public sector price **	53.75%	53.75%	53.75%	53.75%
% vaccinations obtained from private sector providers **	78%	78%	78%	78%
***Pfizer*: weighted cost per dose + administration**	**$155.61**	**$ 200.67**	**$243.11*** **	**$208.48*** **
% vaccine waste¶	**4.5%**	**4.5%**	**4.5%**	**4.5%**
CDC: weighted cost per dose + administration	**$162.61 ($128 - $191)**	**$ 209.70 ($155 - $250)**	**$254.05*** ($205 - $290)**	**$217.86*** ($192 - $250)**

* 2023 public and private sector cost per dose; VFC Current CDC Vaccine Price List, CDC.
**2023 Proportions of vaccine purchased at private sector and procurement from either private or private providers were based on different sources (i.e., https://www.cdc.gov/nchs/data/nhis/earlyrelease/insur202305_1.pdf, Glazner et al., Pediatrics 2009)
*** Calculated using a hypothetical range of prices for public and private as reported by Pfizer Inc. for MenABCWY .
¶ Assumption considers wastage from either open vial, mishandling or outdated shelf life.
Note: **CDC model**: rates and associated costs of hypothetical vaccine associated adverse events, non shown here, were applied to all vaccines.
Trotter et al., *BMJ* 2002 https://pubmed.ncbi.nlm.nih.gov/11934772/ ; Ortega-Sanchez et al., *CID* 2008. https://pubmed.ncbi.nlm.nih.gov/18171206/

Pfizer and CDC: Average Annual Incidence in Vaccine Serogroups BCYW by Age per 100,000 used in the models



- Rates of IMD disease remain relatively higher in late adolescence, but in general rates have been declining for all age groups.
- Overall, IMD incidence rates are *one fifth* to *one sixth* of those from recent pre-vaccine era

Source: **CDC Model**: Age-by-year-specific data from ABC Core Surveillance and NNDSS for PreVaxs and Vax eras
***Pfizer* model**: **Pre Vax Era**: Mbaeyi et al. Incidence of Meningococcal Disease Before and After Implementation of Quadrivalent Meningococcal Conjugate Vaccine in the United States. JAMA Pediatr. 2020;174(9):843-851. doi:10.1001/jamapediatrics.2020
Vax Era: US CDC Enhanced Meningococcal Disease Surveillance Report, 2017. Enhanced Meningococcal Disease Surveillance Report, 2017 (cdc.gov)
Note: Trend and variability across years were used for range of uncertainties and sensitivity analyses

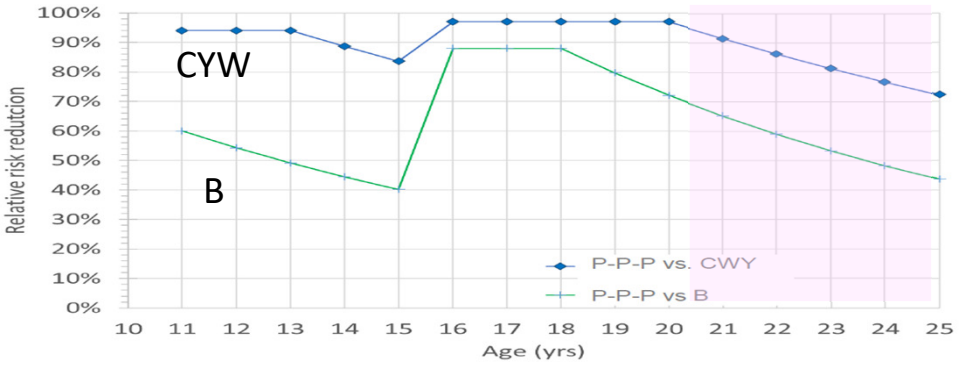
Pfizer and CDC: Initial vaccine effectiveness by vaccine and serogroup

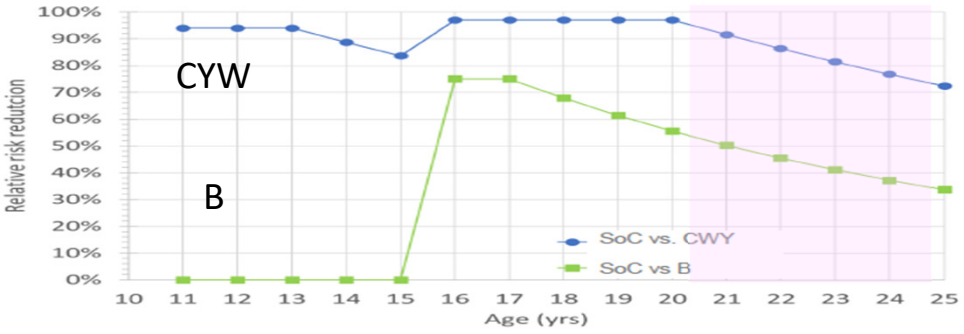
	QUADRIVALENT			MEN B			PENTAVALENT		
	Base-case	**Low**	**High**	**Base-case**	**Low**	**High**	**Base-case**	**Low**	**High**
First DOSE MenACWY	**93%**	73%	98%				**93%**	73%	98%
2nd + DOSE MenACWY	**97%**	73%	98%				**97%**	73%	98%
First DOSE MenB*				**60%**	18%	74%	**60%**	18%	74%
2nd + DOSE MenB				**85%**	50%	99%	**85%**	50%	99%

Values and assumptions on initial protection are based on various sources:
Phase 3 noninferiority initial vaccine efficacy by single dose (at 11-12yrs) and second-dose (16yrs) of pentavalent (Men ABCWY) vaccine as reported by Pfizer (data on file).
Updated Pfizer Technical reports on Cost-effectiveness of the Pentavalent Meningococcal Vaccine (MenABCWY) in the US
Cohn AC, MacNeil JR, Harrison LH, et al. Active Bacterial Core Surveillance (ABCs) Team and MeningNet Surveillance Partners. Effectiveness and Duration of Protection of One Dose of a Meningococcal Conjugate Vaccine. Pediatrics. 2017 Feb;139(2):e20162193. doi: 10.1542/peds.2016-2193. PMID: 28100689; PMCID: PMC8353579.
*The range for VE efficacy for first dose of MenB is from Castilla et al. *NEJM* 2023 https://www.nejm.org/doi/full/10.1056/nejmoa2206433

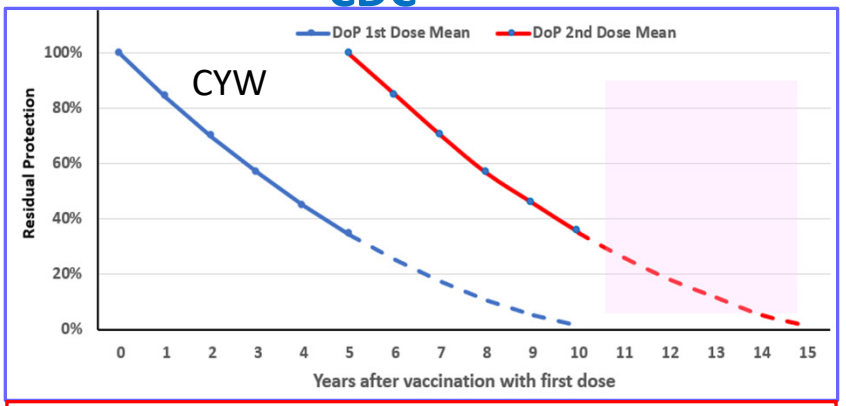
Pfizer and CDC: Assumption about residual protection by vaccine and serogroup

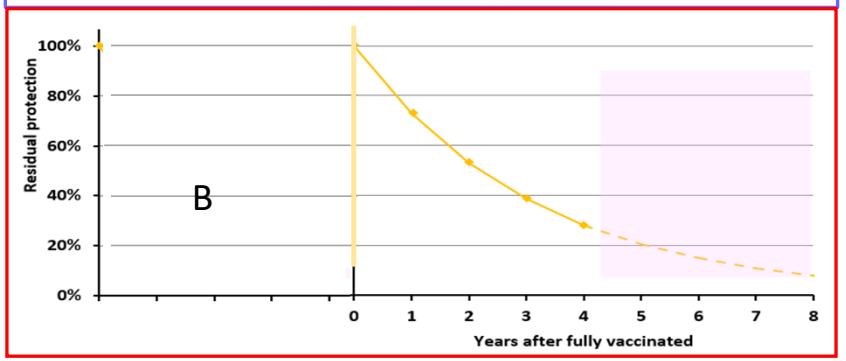
Pfizer





CDC





Assumptions on residual protection are based on various sources:

- Sero-protection is assumed to persist 4-5 years for a single dose of MenACWY and MenABCWY (based on hSBA sero bactericidal assay from Pfizer's clinical trials report)
- Pfizer Technical report on Cost-effectiveness of the Pentavalent Meningococcal Vaccine (MenABCWY) in the US.
- The pink-shaded areas denote a higher level of uncertainty of the waning assumption beyond available surveillance or Phase 3 data

Pfizer and CDC: Long-term sequalae and CFR included in the models

Pfizer

Long-Term Sequelae	Probability of Sequelae
Amputation	3.6%
Anxiety	2.7%
Arthritis	7.5%
Cognitive Impairment	0.0%
Depression	0.3%
Hearing Loss	6.3%
Migraine	0.6%
Motor Deficits	0.0%
Neurological Disability	3.1%
Renal Failure	0.3%
Seizure	2.6%
Skin Scarring	2.6%
Speech Problems	4.2%
Visual Impairment	0.4%
	28.5% (24.2 - 34.3)*

Case Fatality Rate (CFR)	For serogroups BCWY
CFR in 11-25 years **	12.5% (10 to <15yrs) 8% (15 to <25yrs)

* Range is a +/- 20% of base-case
** In addition to CFR, it is assumed an increased risk of excess mortality of 1.21 (1.06-1.37); i.e., reduced life expectancy among survivors with sequalae

CDC

Long-term sequelae	Probability (range for SA)
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)
	21.6%

Case Fatality Rate (CFR)	For serogroups BCWY
CFR in 11-25 years***	12.3% (8.9 – 15.5)

*** Weighted average by age and serogroup proportions (Lower value in range is from serogroup B, high value is from serogroups CWY).
SA=Sensitivity analysis

Pfizer and CDC: Direct costs and QALY scores used in modeling acute phase of IMD

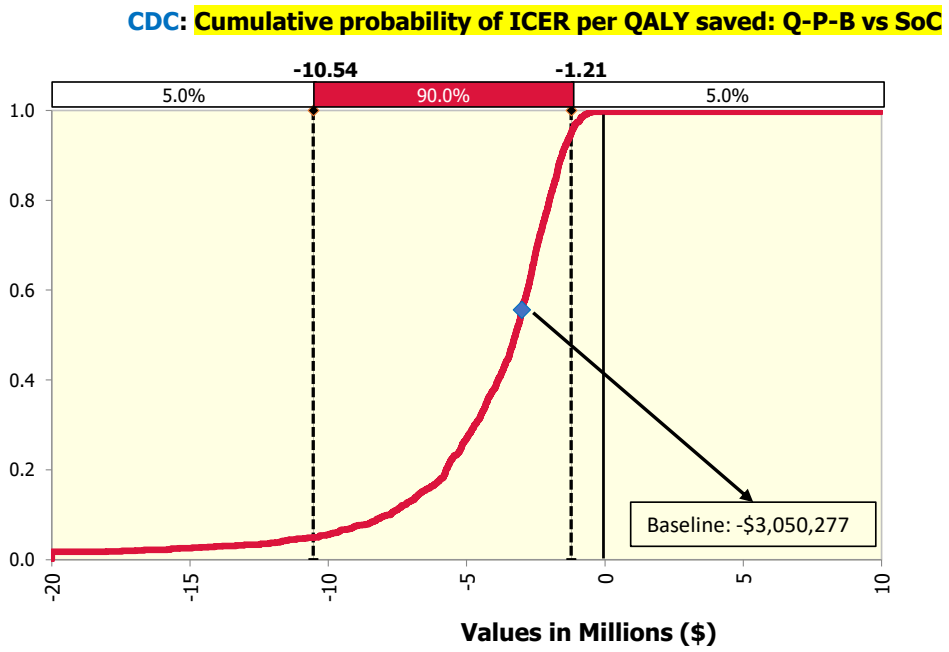
	CDC	*Pfizer*
Direct cost: Medical unitary costs Public health response	Medical cost for an IMD acute phase only $48,983 [a] Public response per isolated case $13,547	Medical cost of IMD acute phase by type [d] Meningitis $81,782 Septicemia $115,899 Unspecified $101, 320
IMD cases without permanent sequelae ***during*** acute phase	Disutility: 0.12 for a year [b] Equivalent QALDs: 46.24 days	Disutility: 0.4 to 0.51 for a year [e] Equivalent QALDs: 146 to 186 days
IMD cases without permanent sequelae ***after*** acute phase	Disutility: 0.083 for a year [c] Equivalent QALDs: 14.8 days	Disutility: 0.03 (range +/- 20%) [f] Duration: 9 years Equivalent QALDs: 100 days

a. Medical costs were adjusted to 2022 using the GDP implicit deflator index. Public response costs were based per hour wage of public health worker, hours of work per case, cost of chemoprophylaxis, average number of contacts per case.
b. QALD = quality-adjusted life days lost
c. Assumption after acute phase based on 2/3 of disutility during acute phase for patients without permanent sequelae
d. Unitary cost per type of IMD based on Davis et al https://pubmed.ncbi.nlm.nih.gov/21278486/
e. Derived from Lecocq et al. Vaccine 2016 https://pubmed.ncbi.nlm.nih.gov/27002504/
f. Koomen et al. Qual Life Res. 2005 https://pubmed.ncbi.nlm.nih.gov/16110936/ and Schmand et al J Infect. 2010 https://pubmed.ncbi.nlm.nih.gov/20659499/

Policy question 1: *Pfizer* and CDC*: Pentavalent vaccine price $250 (private)/$187.5 (public)**

What is the incremental effectiveness and cost-effectiveness of vaccinating healthy adolescents ***11-12 and 16 years old*** with Pentavalent vaccine ***relative*** to using MenACWY and MenB vaccines ?

	Pfizer Q-P-B vs SoC	CDC Q-P-B vs SoC
IMD cases saved	0	<0 – 5
IMD deaths saved	0	0 – 3
LY saved	0	<0 – 28
QALYs saved	0	<0 – 42
Total Net Costs (millions)	($426)**	($564)**
$/QALY saved	Cost savings ($/QALY <0)	Cost savings ($/QALY <0)



*Updated from Monte Carlo Simulation using a sample of 1000 iterations. Preliminary estimates.

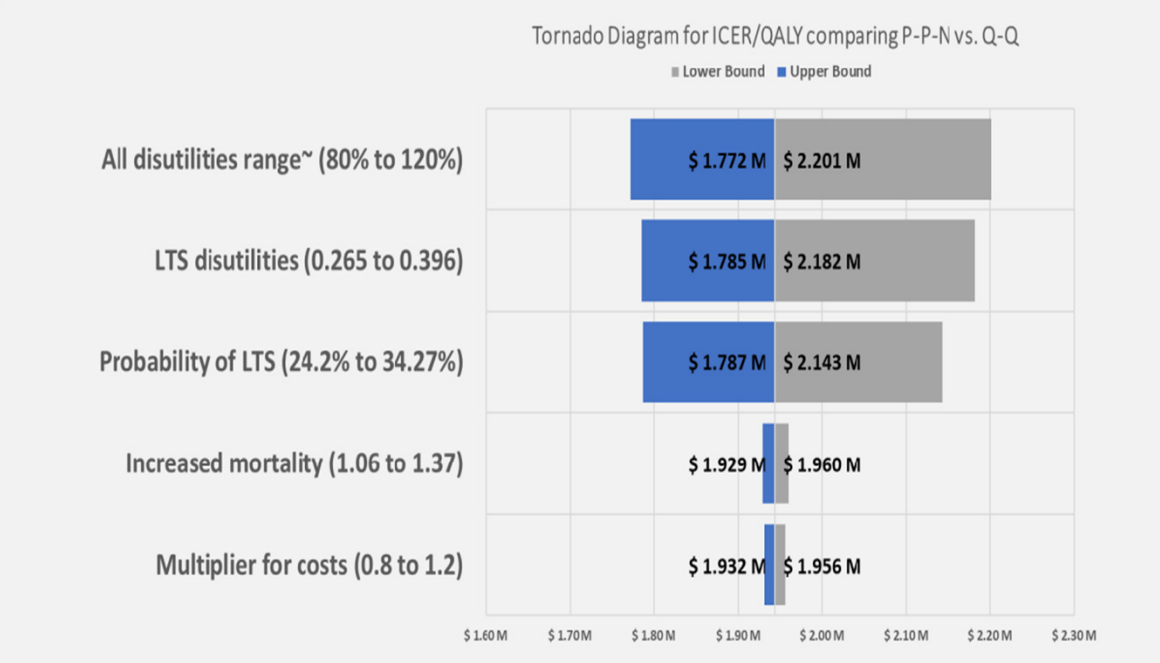
** Both total net costs estimates relied on $250 (private)/$187.5 (public) cost per dose of pentavalent vaccine

ICER = Incremental cost-effectiveness ratio

Policy question 2: *Pfizer:* Pentavalent vaccine price $210 (private)/$157.5 (public)*

What is the incremental effectiveness and cost-effectiveness of vaccinating healthy adolescents ***11-12 and 16 years old*** with Pentavalent vaccine ***relative*** to using MenACWY only?

	P-P-N vs Q-Q
IMD cases saved	41
IMD deaths saved	4
LY saved	86
QALYs saved	164
Total Net Costs (millions)	$319
$/QALY saved	$1.94 Million



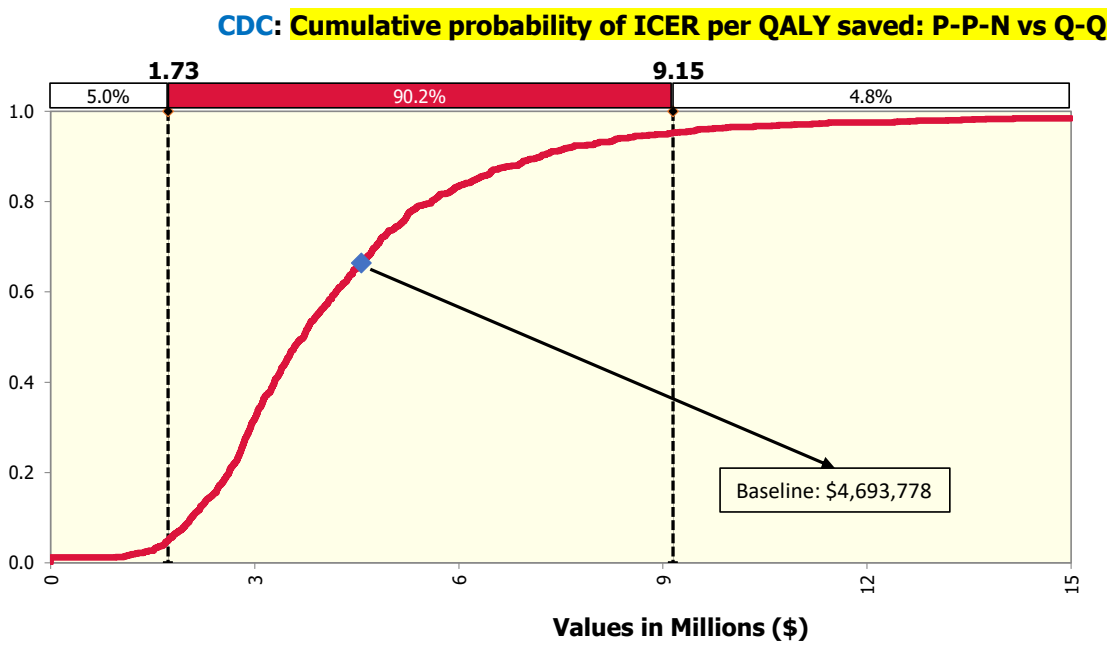
* Updated Pfizer estimates with pentavalent vaccine price $210 (private)/ $157.5 (Public) and tornado figure

ICER = incremental cost-effectiveness ratio
LTS = Long-term sequelae

Policy question 2: CDC*: Pentavalent vaccine price $210 (private)/$157.5 (public) **

What is the incremental effectiveness and cost-effectiveness of vaccinating healthy adolescents ***11-12 and 16 years old*** with Pentavalent vaccine ***relative*** to using MenACWY only?

	P-P-N vs Q-Q
IMD cases saved	12
IMD deaths saved	1
LY saved	27
QALYs saved	58
Total Net Costs (millions)	$270
$/QALY saved	$4.7 Million



*Updated from Monte Carlo Simulation using a sample of 1000 iterations. Preliminary estimates

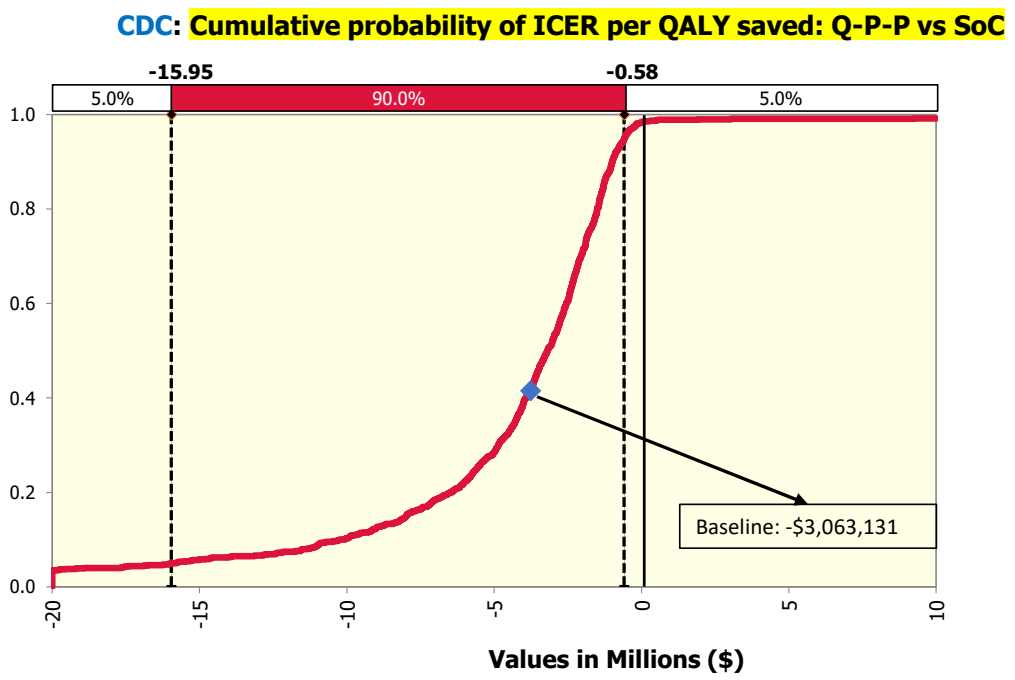
** Updated Pfizer estimates with pentavalent vaccine price $210 (private)/ $157.5 (Public)

ICER = Incremental cost-effectiveness ratio

Policy question 3: *Pfizer* and CDC: Pentavalent vaccine price $210 (private)/$157.5 (public)*

What is the incremental effectiveness and cost-effectiveness of vaccinating healthy adolescents ***≥16 years old*** with Pentavalent vaccine ***relative*** to using MenB vaccine only ?

	Pfizer **Q-P-P vs SoC**	**CDC**** **Q-P-P vs SoC**
IMD cases saved	4	5
IMD deaths saved	0	0 - 2
LY saved	9	26
QALYs saved	17	39
Total Net Costs (millions)	($528)	($639)
$/QALY saved	Cost savings ($/QALY <0)	Cost savings ($/QALY <0)



* Updated Pfizer estimates using $210 (private)/$157.5 (public) cost per dose of pentavalent vaccine

** Updated from Monte Carlo Simulation using a sample of 1000 iterations. Preliminary estimates

ICER = Incremental cost-effectiveness ratio

Limitations

- **Factors not considered in *Pfizer* and CDC models that may result in overestimating the ICER (underestimating the cost-effectiveness) of MenABCWY**
  - In base-case: both models assumed
    - No protection against non-IMD
    - No indirect protection against IMD of unvaccinated individuals
  - Productivity losses incurred by caregivers for long-term specific sequelae are based on assumptions and partially included
- **Differences in key inputs among *Pfizer* and CDC models and the uncertainty in inputs data may explain some differences in results:**
  - Duration of vaccine protection
  - Medical costs
  - Variability in IMD incidence and CFR data
  - Inclusion of different sequalae
  - QALY score for IMD cases without permanent sequelae
- **Pentavalent price for Q-P-B is uncertain: price used here is the minimum expected. Higher prices will increase total net cost & ICERs**

Conclusion

- In both ***Pfizer*** **and** **CDC** models**,** MenABCWY vaccine would reduce the IMD burden in adolescents
  - In both models, strategies with one or more doses of the MenABCWY vaccine would save ***more*** or ***equal*** number of IMD cases.
- **PICO #1**: Q-P-B ***could be*** incrementally cost-saving (ICER QALY saved <0) relative to SoC
  - Q-P-B includes one dose of MenABCWY in substitution of the second dose of MenACWY and first dose of MenB
- **PICO #2:** P-P-N is incrementally ***costly*** (not cost saving) relative to Q-Q.
  - P-P-N included two doses of MenABCWY in substitution of the two doses of MenACWY,
- **PICO #3:** Q-P-P ***is likely cost saving*** (ICER QALY saved <0) relative to SoC
  - About 96% percent of iterations in the **CDC** model simulations have an ICER<0
  - Q-P-P included two doses of MenABCWY in substitution of the second dose of MenACWY and the first and second dose of MenB
- Reasonable pentavalent price and duration of protection combined with careful design of vaccination interventions with MenABCWY would determine the ***cost*** or ***cost-saving*** value of the pentavalent vaccine among adolescents ≥11 year of age

Acknowledgements

From NCIRD/CDC

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- Andrew Leidner

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- ACIP Meningococcal working group members

End of Summary

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov