Summary of three economic analyses on the use of 21-valent pneumococcal conjugate vaccine (PCV21) among adults in the United States

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  - **Merck team**
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  - **Pittsburgh team**
    - Shoroq Altawalbeh, Angela Wateska, Mary Patricia Nowalk, Chyongchiou Lin, Lee Harrison, William Shaffner, Richard Zimmerman, Kenneth Smith

Conflicts of interest statement

- **Andrew Leidner: None**
- **Tulane-CDC team: None**
- **Merck team:**
  - Merck manufactures the PCV21, PCV15 and PPSV23 vaccines
- **Pittsburgh team:**
  - From the competing interest section of their article[a]: Dr. Wateska has had a research grant from NIAID in the past 3 years. Dr. Nowalk has had research grants from Merck & Co., Inc. and Sanofi Pasteur in the past 3 years. Dr. Schaffner has had a research grant from CDC in the past 3 years. Dr. Zimmerman has had research grants from NIH and Sanofi Pasteur in 3 years. Dr. Smith has had research grants from NIAID and Sanofi Pasteur in the past 3 years.

[a] Altawalbeh, Shoroq M., et al. "Cost-effectiveness of an in-development adult-formulated 21-valent pneumococcal conjugate vaccine in US adults aged 50 years or older." *Vaccine* 42.12 (2024): 3024-3032. Link.

Terminology

Abbreviation	Full term/Meaning
CER	Cost-effectiveness ratio
CFR	Case-fatality rate
CMC	Chronic medical conditions but not immunocompromised
IC	Immunocompromising conditions
ICER	Incremental cost-effectiveness ratio
IPD	Invasive pneumococcal disease
NBP	Non-bacteremic pneumonia
PCV15	15-valent pneumococcal conjugate vaccine
PCV20	20-valent pneumococcal conjugate vaccine
PCV21	21-valent pneumococcal conjugate vaccine
PPSV23	23-valent pneumococcal polysaccharide vaccine
QALYs	Quality-adjusted life-years

Outline

- Background on cost-effectiveness analysis
- Model overview
- Main results
- Model comparison
- Summary

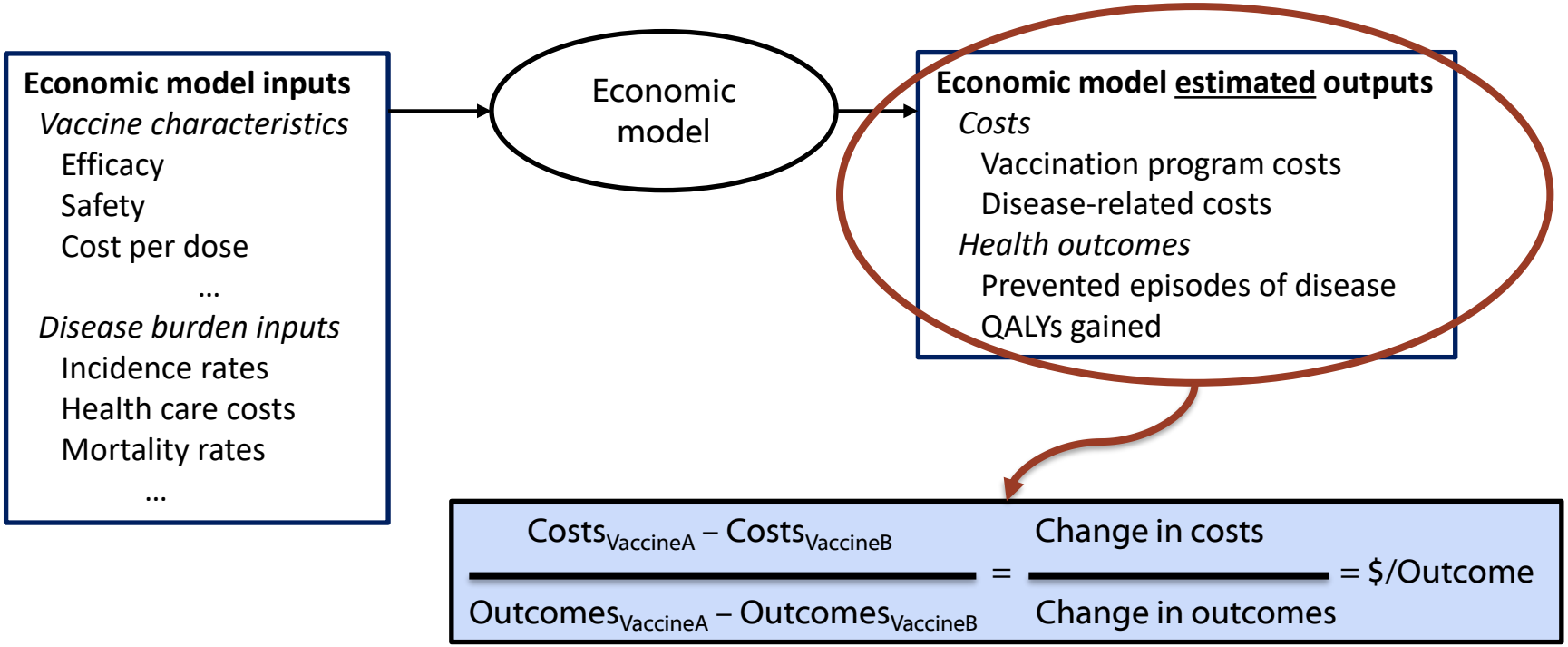
What is cost-effectiveness analysis (CEA)?

- **CEAs compare the costs and outcomes of two or more strategies by estimating a cost-effectiveness ratio (CER)**
  - CER is an estimated cost per unit of health outcome gained
    - Outcomes: averted cases, averted hospitalizations, quality-adjusted life years (QALYs)
    - Cost per QALY gained ($/QALY)

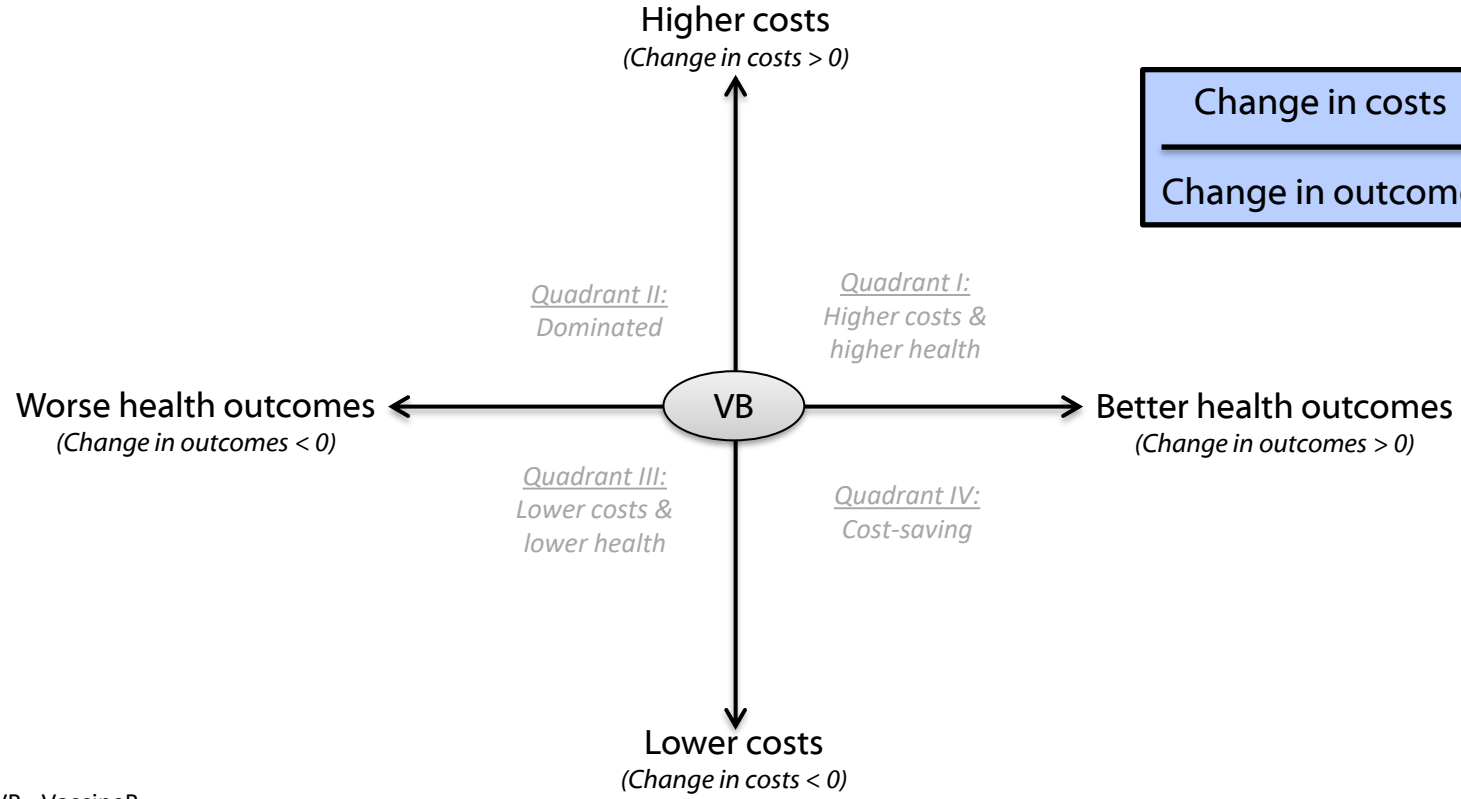
$$\frac{Costs_{VaccineA} - Costs_{VaccineB}}{Outcomes_{VaccineA} - Outcomes_{VaccineB}} = \frac{\text{Change in costs}}{\text{Change in outcomes}} = \$/\text{Outcome}$$

  - CERs always compare 2 potential strategies
    - E.g., vaccination vs. no vaccination, vaccine schedule A vs. vaccine schedule B, new vaccination vs. status quo

What is cost-effectiveness analysis (CEA)?



Interpreting a cost-effectiveness ratio



$$\frac{\text{Change in costs}}{\text{Change in outcomes}} = \$/\text{Outcome}$$

VB= VaccineB

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Model overview

Model characteristics	Tulane-CDC	Merck	Pittsburgh
Cohort type	Single cohort	Multi-cohort	Single cohort
Analytic model time frame	Lifetime	Lifetime	Lifetime
Base case perspective	Limited societal	Societal	Societal & healthcare sector
Currency year	2023 $ US	2023 $ US	2019 $ US[a]
Vaccine cost	PCV20: $289 PCV21: $319	PCV20: $261 PCV21: $287	PCV20: $249 PCV21: $333
Other vaccine costs per dose	Admin: $30; travel: $36	Admin: $19	Admin: $24; adverse events: $0.76
How many years following a PCV dose until protections wanes to 0%	15 years	15 years	15 years for NBP 20 years for IPD
Circulating serotype protection ratio: PCV21:PCV20	2.7 to 9.5 (vaccine-unique types)	2.9 to 6.3 (vaccine-unique types)	1.5 to 1.6 (all types)

[a]In this presentation, all cost-effectiveness ratios that were reported in the Pittsburgh model have been adjusted to US$2023 (from US$2019) for consistency with the other models.

Model overview, cont.

Model characteristics	Tulane-CDC	Merck	Pittsburgh
Include indirect effects from pediatric PCV20 use	Yes	In sensitivity analyses	In sensitivity analyses
Indirect effects magnitude, when included	84% reduction by year 6	33% reduction by year 5	50% reduction by year 1
Separately models disability sequalae, post-IPD	No[a]	Yes	Yes
Separately models disability sequalae, post-NBP	No[a]	No	Yes
Include age-adjusted incidence	Yes	Yes	Yes
Include risk-stratified incidence groups	General/CMC/IC	General/CMC/IC	Black/Non-black & General/Smoking/ CMC/IC
Case-fatality-rates (CFRs), inpatient pneumonia (NBP) (%, among 50-64 year olds)	3 to 4[b]	3[b]	4 to 6[b]
Productivity loss for disease-related deaths adjusted by employment status, varies by age	Yes	No	No

[a] In the Tulane-CDC model, inpatient disease burden assumptions includes a portion of the disease burden from disability sequalae, up to 1 year for QALY loss and up to 6 months for costs.
[b] For the Tulane-CDC and Merck model, NBP CFRs were based on National Inpatient Sample (i.e., hospital discharge) data, and in the Pittsburgh model NBP CFRs were assumed to be 50% of the rate of IPD CFRs.

Policy question 1: Currently recommended adults

Base case estimates ($/QALY)

Intervention	Comparator	Tulane-CDC	Merck	Pittsburgh
Age-based vaccination at 65 with PCV21	Age-based vaccination at 65 with PCV20	4,309 (Cost-saving to $18,599)[a]	5,090	Cost-saving to 58,116[b,c]
Risk-based vaccination with PCV21	Risk-based vaccination with PCV20	Cost-Saving (Range was cost-saving)[a]	Cost-saving	

- **PCV21 protection against circulating serotypes is greater, and PCV21 is modestly more expensive than PCV20**

[a] This range was estimated using probabilistic sensitivity analyses, where all inputs were varied.
[b] The Pittsburgh model assessed age-based and risk-based use in the same analysis, so strategies with age-based use at age 65 also included risk-based use from age 50 to 64.
[c] These ICER values were calculated by the CDC ACIP economic review team from costs and effectiveness values reported in the Pittsburg model. High range value comes from healthcare sector perspective; low range value comes from societal perspective.

Policy question 2: Age 50-64

Base case estimates ($/QALY)

Intervention	Comparator	Tulane-CDC	Merck	Pittsburgh
Age-based vaccination at 50 and 65 with **PCV21**	Age-based vaccination at 65 with **PCV21**[b]	269,643 ($198,098 to $701,066)[a]	105,303 to 256,318[b]	2,713 to 114,645[c]
Age-based vaccination at 50 and 65 with **PCV20**	Age-based vaccination at 65 and risk-based vaccination at 50-64 with **PCV20**	628,473	NA[d]	36,854 to 149,269[c]

- **Higher ICERs than for the currently recommended group because younger ages have lower disease burden**
- **PCV21 protection against circulating serotypes is greater**
- **PCV20 preventable disease burden is impacted by indirect effects**
- **Substantial variation in estimates within models, across models and across vaccines**

[a] This range was estimated using probabilistic sensitivity analyses, where all inputs were varied.

[b] The Merck model assessed PCV21 use at age 50 and 65 vs PCV21 use at age 65 among general risk (i.e., not CMC or IC) populations and PCV20 use among CMC/IC populations. High range value comes from a scenario with indirect effects and without productivity loss from disease-induced death; low range value comes from a scenario without indirect effects and with productivity loss from disease-induced death.

[c] These ICER values were calculated by the CDC ACIP economic review team from costs and effectiveness values reported in the Pittsburg model. High range value comes from healthcare sector perspective; low range value comes from societal perspective.

[d] The Merck model did not assess lowering the age-based recommendation to 50 for the use of PCV20.

Policy question 3: Age 19-49

Base case estimates ($/QALY)

Intervention	Comparator	Tulane-CDC	Merck
Age-based vaccination at 19 with PCV21 (Tulane-CDC); or at 19 and 65 with PCV21 (Merck)[b]	Age-based vaccination at 50 with PCV21 (Tulane-CDC); or at 65 with PCV20 (Merck)[b]	Dominated (Range was dominated)[a]	647,569[b]

- **Higher ICERs (or "dominated" interventions) than for currently recommended adult or age 50 strategies because younger ages have lower disease burden**

Notes: The Pittsburgh model did not assess strategies for individuals younger than 50 years. Across all models, the use of PCV20 was not directly assessed for 19-50-year-olds.

[a] This range was estimated using probabilistic sensitivity analyses, where all inputs were varied.

[b] The Merck model intervention strategy was PCV21 at age 19 and 65 and the comparator was PCV20 at age 65.

Supplemental dose

Base case estimates ($/QALY)

Intervention	Comparator	Tulane-CDC	Merck
Supplemental dose with PCV21 among individuals who have received PCV20	No supplemental dose with PCV21	206,191 to 442,010[a]	274,844 to 512,266[b]

- **Higher ICERs than for the currently recommended adult strategies because individuals previously vaccinated with PCV20 have lower disease burden due to PCV20 vaccine protection**
- **Variation in estimates due to duration between supplemental PCV21 dose and the previous dose of PCV20, and due to differences in disease burden by age and risk group**

Note: The Pittsburgh model did not assess supplemental PCV21 dose.

[a] Range depends on whether a person received PCV20 because of age-based or risk-based recommendation and the time since PCV20, where risk-based vaccinees with a longer duration since PCV20 had lower costs.

[b] Range depends on age and time since PCV20; high value assumed age 65 general population (i.e., no CMC or IC) and older and 2 years since PCV20; low value assumed age 50-64 CMC/IC population and 5 years since PCV20.

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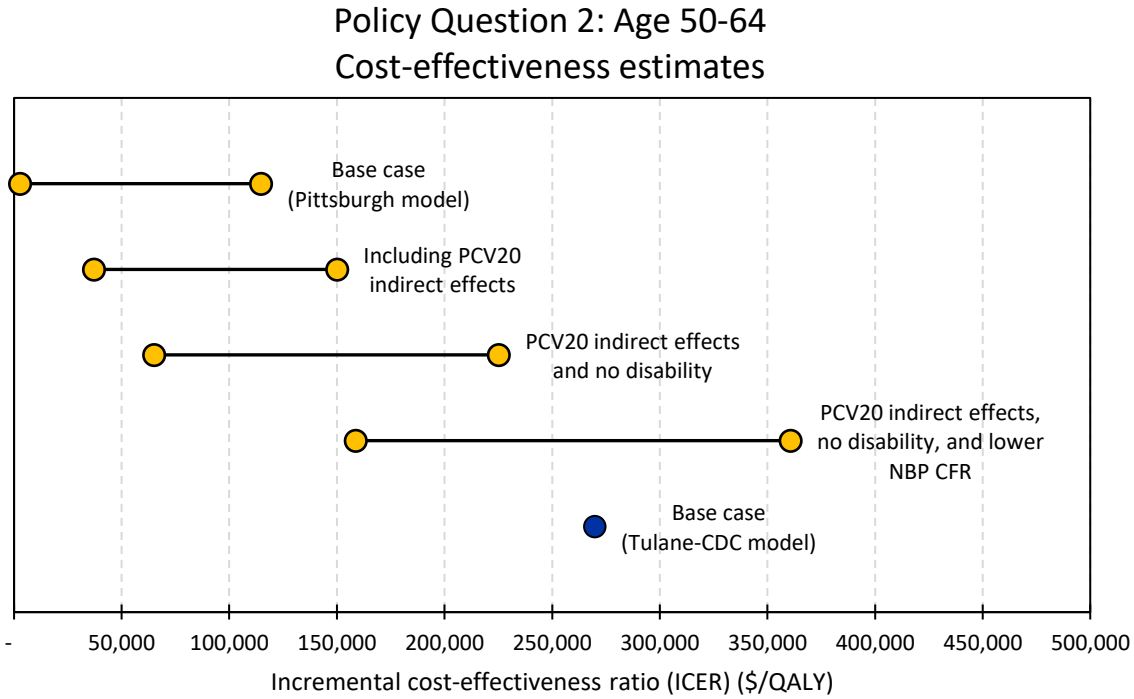
Sensitivity/scenario analyses

What if selected Pittsburgh model assumptions were more similar to the Tulane-CDC model?



In the Pittsburgh model results, lower ICERs are from the societal perspective, higher ICERs are from the health care sector perspective.

Policy question 2: Age 50-64

Base case estimates ($/QALY)

Intervention	Comparator	Tulane-CDC	Merck	Pittsburgh
Age-based vaccination at 50 and 65 with **PCV21**	Age-based vaccination at 65 with **PCV21**[b]	269,643 ($198,098 to $701,066)[a]	105,303 to 256,318[b]	2,713 to 114,645[c]
Age-based vaccination at 50 and 65 with **PCV20**	Age-based vaccination at 65 and risk-based vaccination at 50-64 with **PCV20**	628,473	NA[d]	36,854 to 149,269[c]

- **Comparison summary Tulane-CDC vs. Pittsburgh**
  - Not including PCV20 indirect effects, including long-term disability disease states, and higher pneumonia CFR assumptions yield more favorable (i.e., lower) CERs
  - Other factors include the magnitudes of indirect effect assumptions and productivity losses

[a] This range was estimated using probabilistic sensitivity analyses, where all inputs were varied.
[b] The Merck model assessed PCV21 use at age 50 and 65 vs PCV21 use at age 65 among general risk (i.e., no CMC or IC) populations and PCV20 use among CMC/IC populations. High range value comes from a scenario with indirect effects and without productivity loss from disease-induced death; low range value comes from a scenario without indirect effects and with productivity loss from disease-induced death.
[c] These ICER values were calculated by the CDC ACIP economic review team from costs and effectiveness values reported in the Pittsburg model. High range value comes from healthcare sector perspective; low range value comes from societal perspective.
[d] The Merck model did not assess lowering the age-based recommendation to 50 for the use of PCV20.

Limitations

- **Limited data available on vaccine efficacy and duration of protection**
- **Uncertainties about several model inputs and assumptions**
  - Future epidemiology of pneumococcal serotypes that are not included in PCV21 (e.g., serotype 4, 19F)
  - Indirect effects from pediatric PCV20 use
  - Prevalence and severity of disability sequalae
  - Vaccine price
    - Merck model base case input for PCV21 cost per dose was $287, which has also been announced publicly as the list price[a]
- **Potential challenges to vaccination implementation due to changing the pneumococcal vaccine schedule were not included**

[a] US FDA approves Merck's pneumococcal vaccine for adults | Reuters

Summary of model findings

Policy question populations	Strategy details	Summary across available models
1. Currently recommended adults	Age-based PCV21	Cost-saving to $58,000 per QALY gained
	Risk-based PCV21	Cost-saving in all three models
2. Ages 50-64	PCV21	$3,000 to $270,000 per QALY gained
	PCV20	$37,000 to $630,000 per QALY gained
3. Ages 19-49	PCV21	$650,000 per QALY gained to “Dominated”
Supplemental dose	Supplemental dose with PCV21	$210,000 to $510,000 per QALY gained

- **As modeled, most strategies improved health**
  - Age-based vaccination at 19 years instead of 50 years in the Tulane-CDC model did not improve health
- **Several strategies were cost-saving**
- **Variability in estimates across models for age 50 and supplemental dose strategies**

Thank you for your attention and thank you to those that contributed to this presentation

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