Summary of three economic analyses on the use of PCVs among 50-64 year old adults in the United States

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ACIP Meeting

October 23, 2024

Acknowledgements

- This presentation summarizes work conducted by three modeling teams
  - **Tulane-CDC team**
    - Charles Stoecker (Tulane University), Yin Wang (Tulane University), Miwako Kobayashi (CDC), Andrew Leidner (CDC), Bo-Hyun Cho (CDC), Cheryl Ward (CDC)
  - **Merck team**
    - Kwame Owusu-Edusei, Zinan Yi , Muloongo Simuzingili, Elamin Elbasha, Elmira Flem, Thomas Weiss, Heather Platt, Kristen Feemster, Kelly Johnson, Ulrike Bushwald, Craig Roberts, Don Yin
  - **Pfizer team**
    - Ahuva Averin, Jeffrey Vietri, Mark Atwood, Dhwani Hariharan, Mark Rozenbaum, Alejandro Cane, Paul Balmer, Jelena Vojicic, Paula Peyrani, Ray Farkouh

Conflicts of interest statement

- **Andrew Leidner, Sofia Bletnitsky: None**
- **Tulane-CDC team: None**
- **Merck team:**
  - Merck manufactures the PCV21, PCV15 and PPSV23 vaccines
- **Pfizer team:**
  - Pfizer manufactures the PCV20 and PCV13 vaccines

Terminology

Abbreviation	Full term/Meaning
CER	Cost-effectiveness ratio
CFR	Case-fatality rate
CMC	Chronic medical conditions but not immunocompromised
CR	Current recommendations (Risk-based use of PCV at ages 50-64 and age-based use of PCV at age 65)
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
QALYs	Quality-adjusted life years
SA	Sensitivity analyses

Outline

- Background on cost-effectiveness analysis
- Model overview
- Main results
- Sensitivity analyses
- Discussion of other models
- Limitations
- Summary

What is cost-effectiveness analysis (CEA)?

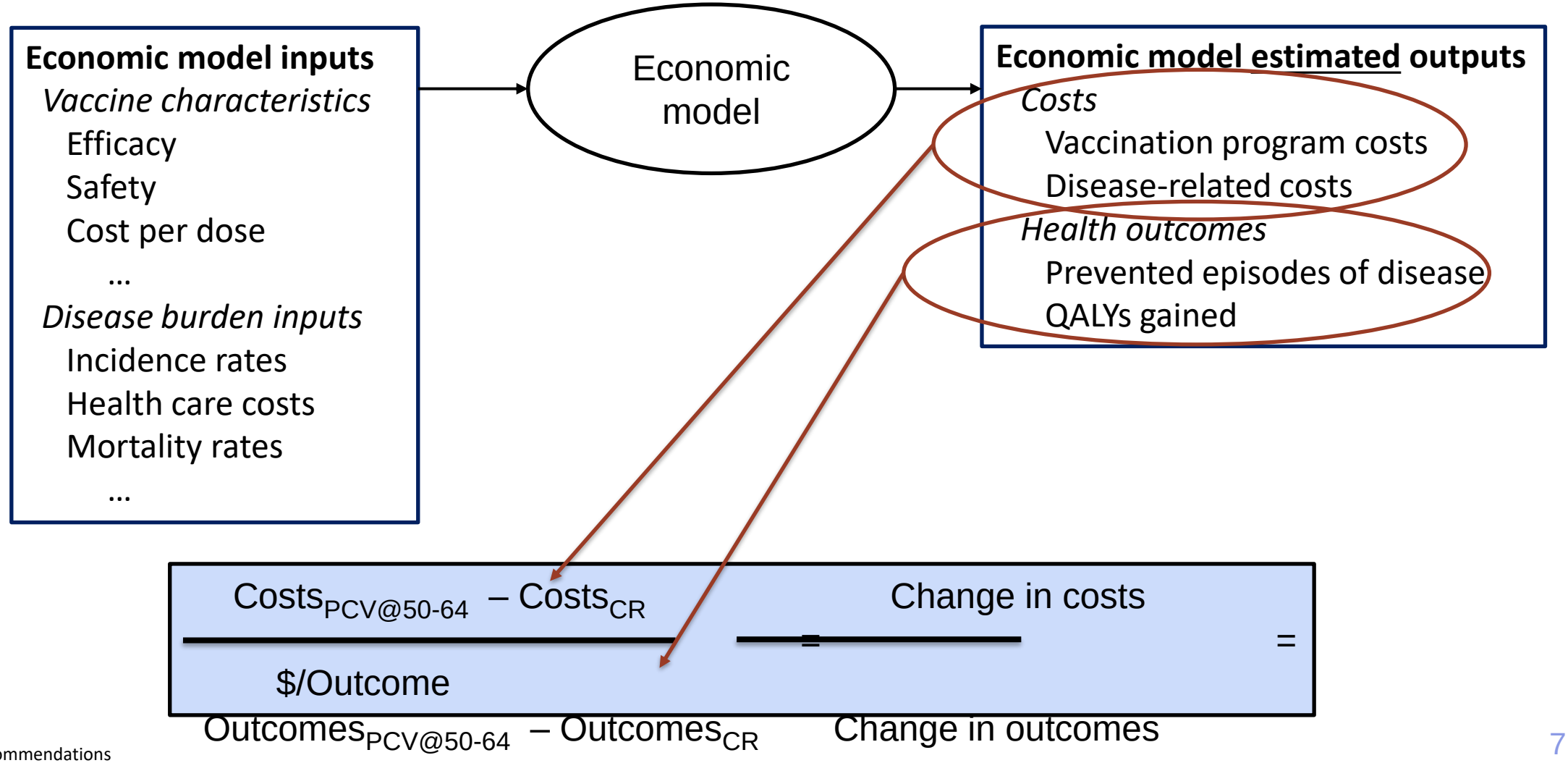
- **Cost-effectiveness analyses compare the costs and outcomes of two or more strategies by estimating an incremental cost-effectiveness ratio (ICER)**
  - An ICER is an estimated cost per unit of health outcome gained
    - Outcomes: averted cases, averted hospitalizations, quality-adjusted life years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

$$\frac{Costs_{PCV@50\text{-}64} - Costs_{CR}}{Outcomes_{PCV@50\text{-}64} - Outcomes_{CR}} = \frac{\text{Change in costs}}{\text{Change in outcomes}} = \$/\text{Outcome}$$

  - ICERs always compare 2 potential strategies
    - Strategies are referred to as the “intervention” and “comparator”
    - E.g., vaccination vs. no vaccination, vaccine schedule A vs. vaccine schedule B, new vaccination vs. status quo

ICER= Incremental cost-effectiveness ratio; CR= Current recommendations

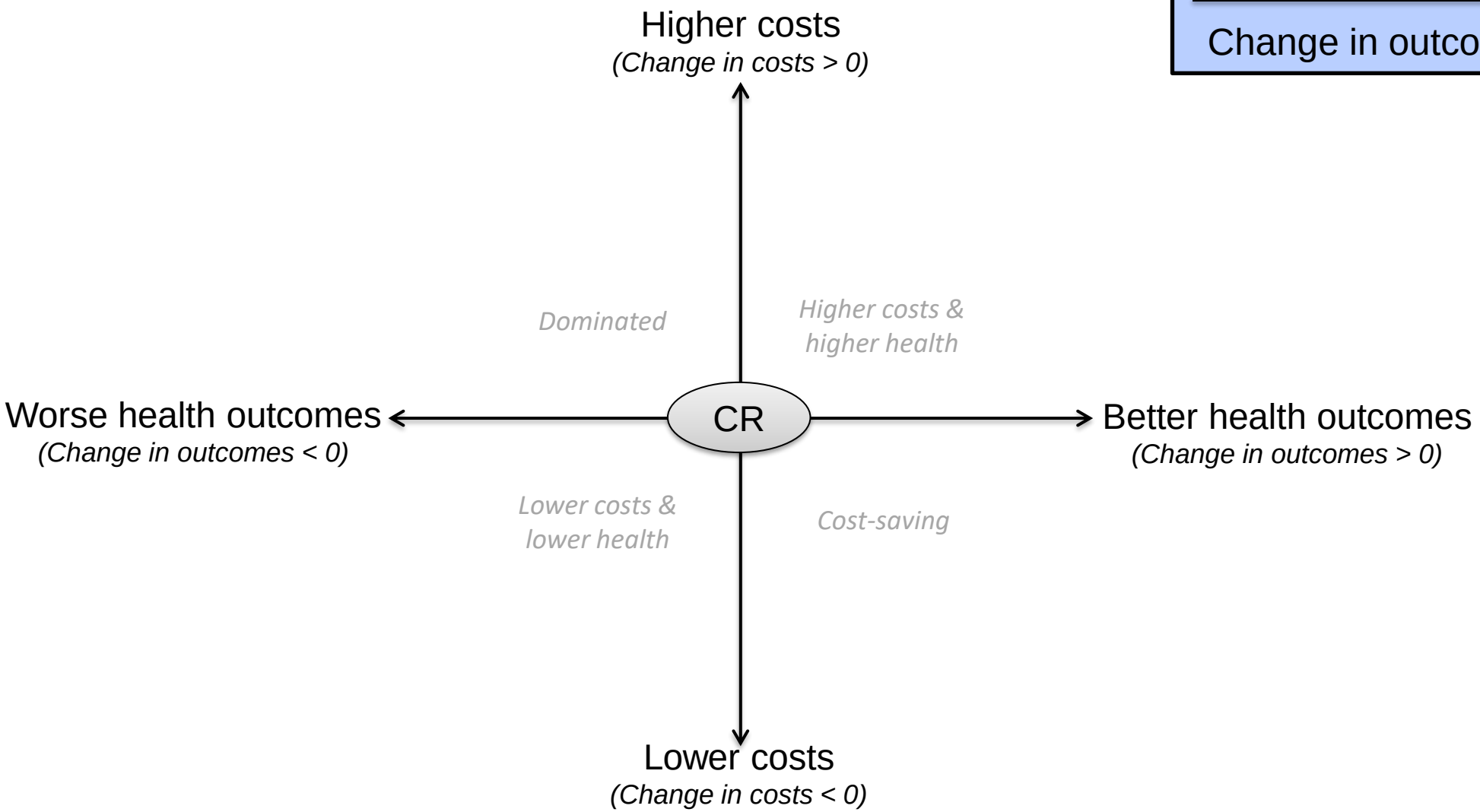
What is cost-effectiveness analysis (CEA)?



CR= Current recommendations

Interpreting an incremental cost-effectiveness ratio (ICER)

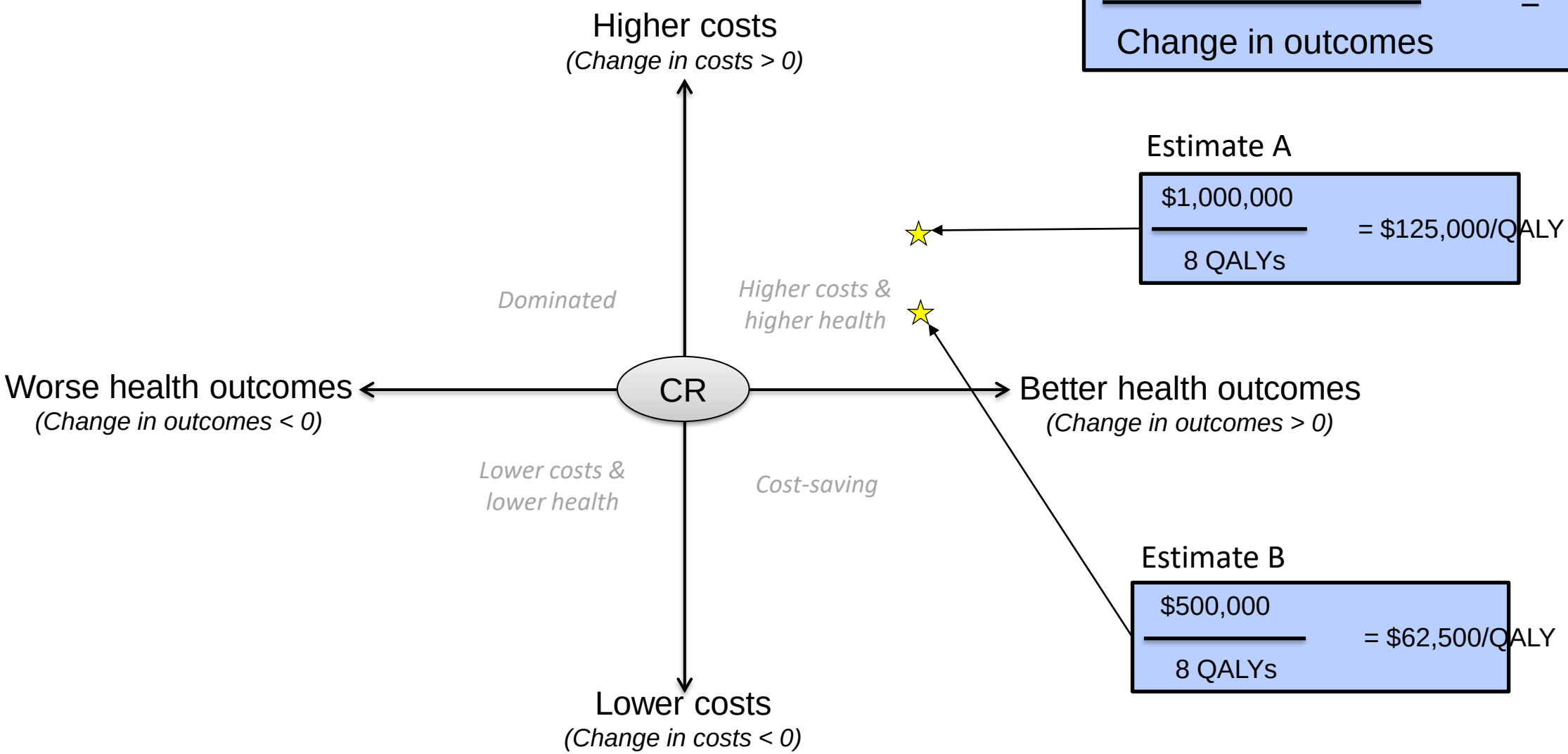
$$\frac{\text{Change in costs}}{\text{Change in outcomes}} = \$/\text{Outcome}$$



CR= Current recommendations

Interpreting an incremental cost-effectiveness ratio (ICER)

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



Estimate A

$$\frac{\$1{,}000{,}000}{8\ \text{QALYs}} = \$125{,}000/\text{QALY}$$

Estimate B

$$\frac{\$500{,}000}{8\ \text{QALYs}} = \$62{,}500/\text{QALY}$$

CR= Current recommendations

Policy question

- **Should a single dose of pneumococcal conjugate vaccine (PCV) be recommended for all PCV-naïve adults aged 50–64 years?**

“Moving” comparisons in the models

Alternate comparisons

- **Comparator (current recommendations):** Risk-based vaccination with PCV at ages 50-64 years and age-based vaccination with PCV at age 65 years[a]
- **Intervention (younger age-based vaccination):** Age-based vaccination with PCV at age 50 years

Age group	Risk group	PCV coverage by strategy[b]		Modeled impact of policy change
		Comparator	Intervention	
50-64	CMC/IC	38%	48%	PCV use increases by 10%
	General	0%	48%	PCV use increases by 48%
65+	General and CMC/IC	70%	0%	PCV use decreases by 70%

CMC = chronic medical conditions; IC = immunocompromised; PCV = pneumococcal conjugate vaccine.

[a] In the main results, all three models include some form of vaccination at age 65, but the coverage rates at age 65 varied across models and vary within specific scenarios. Some scenarios presented later did not include age-based vaccination at 65.

[b] This table shows coverage assumptions from the Tulane-CDC model. The other models have different vaccination coverage rate assumptions, and the coverage rate assumptions can vary across different scenarios within each of the models.

“Adding” comparisons in the models

Main comparisons

- **Comparator (current recommendations):** Risk-based vaccination with PCV at ages 50-64 years and age-based vaccination with PCV at age 65 years[a]
- **Intervention (younger age-based vaccination):** Age-based vaccination with PCV at age 50 years and age 65 years[a]

Age group	Risk group	PCV coverage by strategy[b]		Modeled impact of policy change
		Comparator	Intervention	
50-64	CMC/IC	38%	48%	PCV use increases by 10%
	General	0%	48%	PCV use increases by 48%
65+	General and CMC/IC	70%	70%	No change in PCV use

CMC = chronic medical conditions; IC = immunocompromised; PCV = pneumococcal conjugate vaccine.

[a] In the main results, all three models include some form of vaccination at age 65, but the coverage rates at age 65 varied across models and vary within specific scenarios. Some scenarios presented later did not include age-based vaccination at 65.

[b] This table shows coverage assumptions from the Tulane-CDC model. The other models have different vaccination coverage rate assumptions, and the coverage rate assumptions can vary across different scenarios within each of the models.

“Adding” comparisons in the models

Main comparisons

- **Comparator (current recommendations):** Risk-based vaccination with PCV at ages 50-64 years and age-based vaccination with PCV at age 65 years[a]
- **Intervention (younger age-based vaccination):** Age-based vaccination with PCV at age 50 years and age 65 years[a]
  - These comparisons can more directly estimate the impacts of expanding coverage among 50-64 year olds
  - Older adult groups (i.e., 65+) would receive some protection from disease during a time in life with high incidence, disease severity, and costs due to pneumococcal disease
    - Some vaccine-naïve individuals may not receive a PCV until age 65, even with an age-based recommendation at age 50+
    - Vaccine duration of protection assumed to last 10-20 years; there is limited available data on duration of protection after 5 years
    - In the future, new vaccines may be available for adults who have received PCV

[a] In the main results, all three models include some form of vaccination at age 65, but the coverage rates at age 65 varied across models and vary within specific scenarios. Some scenarios presented later did not include age-based vaccination at 65.

Model overview

Model characteristics	Tulane-CDC	Merck	Pfizer
Cohort type	Single cohort	Multi-cohort (Single-cohort in SA)	Multi-cohort (Single-cohort in SA)
Analytic model time frame	Lifetime	Lifetime	Lifetime
Base case perspective	Limited societal[a]	Societal	Societal (Healthcare in SA)
Currency year	2023 $ US	2023 $ US	2023 $ US
Vaccine cost per dose[b]	PCV20: $289 PCV21: $319	PCV20: $261 PCV21: $287	PCV20: $262
Other vaccine-associated costs per dose	Admin: $30 (50-64); $21 (65+) Travel: $44	Admin: $31 (50-64); $25 (65+) Travel: $45	Admin: $31
Vaccine coverage change in the intervention among 50-64 year olds	General: +48% CMC/IC: +10%	General: +39% CMC/IC: 0% (+8% in SA)	General: +21% CMC/IC: +15 to 17% (+20 to +32% in SA)
Serotype coverage ratio: PCV21:PCV20[c]	3.7 to 9.5 (vaccine-unique types)	4.3 to 6.3 (vaccine-unique types)	NA

SA=sensitivity analyses; CMC/IC= chronic medical conditions/immunocompromised.

[a.] The limited societal perspective does not include non-market production as part of productivity losses.

[b.] Private sector list prices were $262 for PCV20 and $288 for PCV21 on October 1, 2024. The Tulane-CDC model cost per dose includes an additional cost of reimbursement from health system payers, which is typically higher than the list price.

[c.] This is the ratio of PCV21-only type IPD disease to PCV20-only type IPD disease among 50+ year olds, the ranges come from different age stratifications used in the models.

Model overview, cont.

Model characteristics	Tulane-CDC	Merck	Pfizer
Years until PCV protection wanes to 0%	15 years[a] (20 years in SA)	15 years[a] (20 years, varied waning rates in SA)	16 years[a]
VE vs IPD in year 15, general population	0% (30% in SA)	0% (75% in SA)	36%
VE vs NBP based on all-cause pneumonia in alternative VE approach	No	No	Yes
Include indirect effects[b]	Yes (None in SA)	Yes (Higher and none in SA)	Yes (Reduced in SA)
Indirect effects magnitude (PCV20 non-PCV13 types), when included	81% reduction by year 5	33% reduction by year 4 (64% by year 5 in SA)	70% reduction by year 5
Include long-term post-IPD sequalae (e.g., disability)	No	Yes	No
Include age-adjusted and risk-stratified incidence	Yes	Yes	Yes
Productivity loss for disease-related deaths at age 60[c]	$331,732	$684,301	$330,654 to $333,623

SA=sensitivity analyses; VE= vaccine effectiveness; IPD= invasive pneumococcal disease; NBP= non-bacteremic pneumonia;

[a] The duration of protection assumptions were similar in the base case of Tulane-CDC and Merck, constant VE for the first 5 years followed by a linear decline to VE=0 at year 15. The Pfizer model assumed a slower decline in VE from years 5 to 15, resulting in about 30% more vaccine protection than the Tulane-CDC and Merck models.

[b] In these models, indirect effects refer to the reduced pneumococcal disease among adults from the use of PCVs in pediatric populations.

[c] Productivity losses for a death at age 60 for each model were calculated by the economics review team. These include lost productivity due to a premature death at age 60, assuming average life expectancy of 80 years, with total losses discounted to present values.

Main results

Cost-effectiveness estimates ($/QALY)

Intervention	Comparator	ICER ($/QALY)		
		Tulane-CDC[a]	Merck	Pfizer[d]
Age-based vaccination at 50 and 65 with **PCV21**	Current recommendations with **PCV21**	131,023 to 214,430	251,048 to 425,455[b]	NA
Age-based vaccination at 50 and 65 with **PCV20**	Current recommendations with **PCV20**	251,037 to 546,811	548,114 to 879,117[c]	56,376* to 133,524

- **Tulane-CDC model ICERs for PCV20 and PCV21 were lower than Merck, higher than Pfizer**
- **In the models that assessed both PCV20 and PCV21, PCV21 use had lower ICERs**

Current recommendations= Age-based vaccination at 65 and risk-based vaccination at 50-64; ICER= incremental cost-effectiveness ratio; QALY= quality-adjusted life year.

[a] Ranges are from different assumptions about indirect effects from PCV20 use in children. The lower value assumes no indirect effects, the higher value assumes base case inputs for indirect effects.

[b] The results are single-cohort estimates and the range is from scenarios that use different assumptions about vaccination coverage and indirect effects. The lower value assumes no indirect effects and CMC/IC individuals aged 50 experience an increase in vaccination coverage due to the age-based recommendation at age 50; higher value assumes higher indirect effects and that CMC/IC individuals are not affected by the age-based recommendation at age 50.

[c] The results are single-cohort estimates and the range is from scenarios that include different population groups. The lower values do not include indirect effects, the higher values have higher indirect effects. These scenarios did not include increase vaccination coverage among CMC/IC individuals aged 50-64.

[d] The range in the Pfizer estimates is from scenarios that use different assumptions about vaccine effectiveness and indirect effects. The lower value is based on vaccine effectiveness estimates from studies with all-cause pneumonia as the primary outcome and assumes higher indirect effects from PCV15-non-PCV13 type disease; the higher value is based on estimates that rely on quantifying the amount of circulating vaccine-type disease with base case indirect effect assumptions.

* The Pfizer model did not include vaccination at age 65+ in either the intervention or the comparator for this scenario.

Scenario results: Higher VE and duration of protection

Cost-effectiveness estimates ($/QALY)

Intervention	Comparator	ICER ($/QALY)		
		Tulane-CDC[a]	Merck[b]	Pfizer[c]
Age-based vaccination at 50 and 65 with **PCV21**	Current recommendations with **PCV21**	117,514 to 202,019	146,089	NA
Age-based vaccination at 50 and 65 with **PCV20**	Current recommendations with **PCV20**	231,438 to 422,657	342,263	62,264 to 99,632

- **Scenarios with higher VE and longer duration of protection (longer than 15 years) had lower ICERs**

Current recommendations= Age-based vaccination at 65 and risk-based vaccination at 50-64. ICER= incremental cost-effectiveness ratio; QALY= quality-adjusted life year.

[a] In this scenario in the Tulane-CDC model, the duration of protection waned to 0% at year 20. The ranges are from different assumptions about indirect effects from PCV20 use in children. The lower value assumes no indirect effects, the higher value assumes base case inputs for indirect effects.

[b] In this scenario in the Merck model, the duration of protection scenario assumed initial VE was constant (no waning) for 20 years and declined to 0% VE at year 21. The results in this table are from single-cohort estimates.

[c] In this scenario in the Pfizer model, the VE against NBP was set to the high value in the input range, VE against IPD and duration of protection remained at base case levels.

Scenario results: Reduced or no indirect effects[a]

Cost-effectiveness estimates ($/QALY)

Intervention	Comparator	ICER ($/QALY)		
		Tulane-CDC	Merck	Pfizer[b]
Age-based vaccination at 50 and 65 with **PCV21**	Current recommendations with **PCV21**	131,028	251,048 to 306,396[c]	NA
Age-based vaccination at 50 and 65 with **PCV20**	Current recommendations with **PCV20**	251,037	548,114	56,376 to 93,127*

- **Scenarios with reduced or lower indirect effects from pediatric PCV20 use yielded lower ICERs, particularly for PCV20 strategies**

Current recommendations= Age-based vaccination at 65 and risk-based vaccination at 50-64. ICER= incremental cost-effectiveness ratio; QALY= quality-adjusted life year.

[a] In these models, indirect effects refer to the reduced pneumococcal disease among adults from the use of PCV20 in pediatric populations.

[b] The range in the Pfizer estimates is from scenarios that use different assumptions about vaccine effectiveness. The lower value is based on vaccine effectiveness estimates from studies with all-cause pneumonia as the primary outcome, the higher value is based on estimates that rely on quantifying the amount of circulating vaccine-type disease.

[c] These results are single-cohort estimates and the range is from scenarios that use different assumptions about vaccination coverage. The lower value assumes CMC/IC individuals aged 50 experience an increase in vaccination coverage due to the age-based recommendation at age 50, the higher value assumes CMC/IC individuals are not affected by the age-based recommendation at age 50.

* The Pfizer model did not include vaccination at age 65+ in either the intervention or the comparator for these scenarios.

Discussion, other models

- **Merck health equity model**
  - The Merck model team submitted a separate report that estimated the impact of 50-64 year old PCV use on health equity
  - This report used the Atkinson index[a] to quantify the inequality with and without 50-64 year old PCV vaccination
  - Health inequality was found to be reduced with a lower age-based recommendation
- **Pittsburgh model[b]**
  - Summarized in the June 2024 ACIP meeting[c]
  - Estimated health equity benefits were associated with 50-64 year old PCV vaccination
  - Estimated lower ICERs than the other models presented today

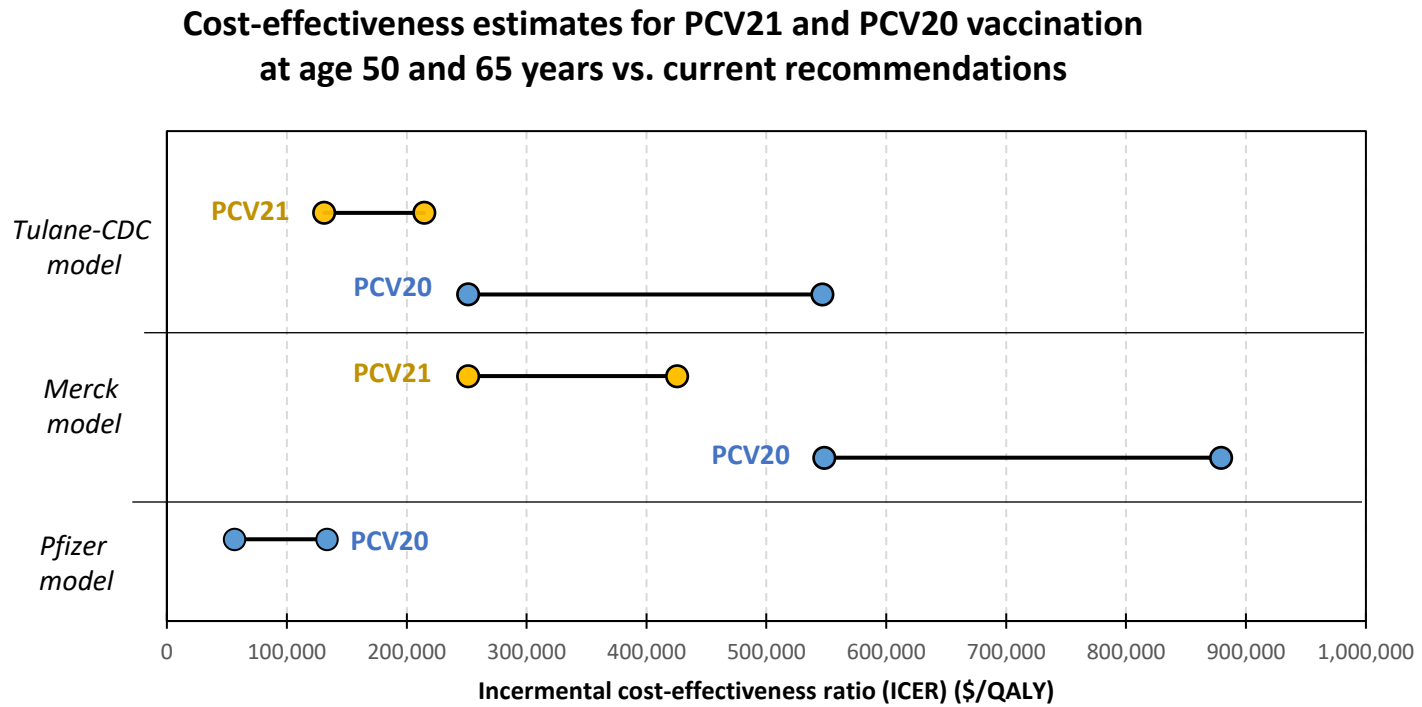
[a] Yang et al. 2020. Impact of Socioeconomic Differences on Distributional Cost-effectiveness Analysis. Atkinson 1970. On the measurement of inequality.
[b] Altawalbeh et al. 2024. Cost-effectiveness of an in-development adult-formulated 21-valent pneumococcal conjugate vaccine in US adults aged 50 years or older.
[c] Leidner et al. 2024. Summary of three economic analyses on the use of 21-valent pneumococcal conjugate vaccine (PCV21) among adults in the United States.

Limitations

- **Substantial uncertainty and limited data available for several key model inputs**
  - Vaccine effectiveness and duration of protection
  - Indirect effects from pediatric PCV20 use
  - Vaccination coverage impacts in a younger age-based recommendation policy

- **Additional uncertainties about several model assumptions**
  - Future epidemiology of pneumococcal serotypes that are not included in PCV21 (e.g., serotype 4, 19F)
  - Impact of supplemental doses with PCVs and new higher-valency vaccines
- **Impacts on vaccination implementation due to changing the pneumococcal vaccine schedule were not included**

Summary of model findings ($/QALY)



- From the "adding" comparisons, all strategies improved health, but none were cost-saving
- Cost per QALY gained estimates for PCV20 had a wider range, more uncertainty than PCV21
- In two of three models, PCV21 had lower costs per QALY gained than PCV20

Current recommendations= Age-based vaccination at 65 and risk-based vaccination at 50-64; QALY= quality adjusted life year.

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

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