Overview of three economic analyses of pneumococcal vaccinations at age 65

Advisory Committee on Immunization Practices
February 28, 2019

Andrew J. Leidner PhD
Health Economist & ACIP Economics Lead

Berry Technology Solutions
Federal Contractor for CDC/NCIRD/ISD

Acknowledgements

- This presentation summarizes work conducted by three modeling teams
  - CDC team
    - Charles Stoecker (Tulane University), Miwako Kobayashi (CDC), Almea Matanock (CDC), Bo Hyun-Cho (CDC), Tamara Pilishvili (CDC)
  - Pfizer team
    - Derek Weycker (Policy Analysis Inc.), Ahuva Hanau (Policy Analysis Inc.), Mark Atwood (Policy Analysis Inc.), Reiko Sato (Pfizer Inc.)
  - Pittsburgh team
    - Kenneth J. Smith, Mary Patricia Nowalk, Angela R. Wateska, Chyongchiou Jeng Lin, Richard K. Zimmerman (all from University of Pittsburgh)

Views and opinions expressed in this presentation are the authors and do not necessarily represent the views and opinions of the Centers for Disease Control and Prevention.

Conflicts of Interest Statements

- Andrew Leidner: None.
- CDC team: None.
- Pfizer team:
  - Pfizer manufactures the PCV13 vaccine.
  - Derek Weycker, Ahuva Hanau, and Mark Atwood are employed by Policy Analysis Inc. (PAI), which received funding for this research from Pfizer Inc.
  - Reiko Sato is employed by Pfizer Inc.
- Pittsburgh team:
  - Mary Patricia Nowalk had research grants within 3 years from Merck & Co. and Pfizer on unrelated topics that are no longer active.
  - Chyongchiou Jeng Lin had research grants within 3 years from Pfizer, Merck & Co., and Sanofi Pasteur on unrelated topics that are no longer active.
  - Richard K. Zimmerman has no current conflicts but within 3 years had research grants from Sanofi Pasteur, Merck & Co., and Pfizer on unrelated topics.
  - Kenneth J. Smith and Angela R. Wateska: None.

Outline

- Introduction
- Overview of cost-effectiveness results
- Model assumptions
- Health outcomes and cost results
- Detailed cost-effectiveness results
  - Sensitivity analyses
- Conclusion
  - Discussion and Review Comments
  - Summary

Introduction

- This presentation describes three cost-effectiveness models developed by three different teams: CDC, Pfizer, and Pittsburgh
- A presentation and report for each model were given to the ACIP Pneumococcal Vaccines work group
- All three reports went through the CDC economic review following the ACIP Guidance for Health Economics Studies
  - *Completion of the economic review does not confer any explicit or implied approval of the model*

Study question

- Should PCV13 be administered routinely to all immunocompetent adults aged ≥65 years in the context of indirect effects from pediatric PCV use experienced to date?
  - Cost-effectiveness ratios from the three models will compare two scenarios:

    PCV+PPSV at age 65 years (current recommendation) vs. PPSV-only at age 65 years

$$\frac{\text{Costs}_{\text{PCV+PPSV}} - \text{Costs}_{\text{PPSV-only}}}{\text{Outcomes}_{\text{PCV+PPSV}} - \text{Outcomes}_{\text{PPSV-only}}} = \frac{\text{Change in costs}}{\text{Change in outcomes}} = \$/\text{Outcome}$$

Terminology

Abbreviation	Full term / description
CMC	Chronic Medical Conditions[1] but not immunocompromised
IC	Immunocompromising Conditions[2]
PCV	Pneumococcal conjugate vaccine, 13 serotypes
PPSV	Pneumococcal polysaccharide vaccine, 23 serotypes
IPD	Invasive pneumococcal disease
PCV-inP & PCV-outP	PCV-type inpatient pneumonia and PCV-type outpatient pneumonia
VE-PCV(ST3) [disease]	PCV effectiveness against serotype 3 disease
VE-PCV(non-ST3) [disease]	PCV effectiveness against all PCV13-type disease except for serotype 3 disease
CFR	Case-fatality ratio
CER	Cost-effectiveness ratio

1. Includes chronic heart, lung, and liver disease, diabetes, alcoholism, and those who smoke cigarettes
2. Includes chronic renal failure, nephrotic syndrome, immunodeficiency, iatrogenic immunosuppression, generalized malignancy, HIV, Hodgkin disease, leukemia, lymphoma, multiple myeloma, solid organ transplants, cochlear implants, CSF leaks, congenital or acquired asplenia, sickle cell disease, or other hemoglobinopathies (i.e. those who are covered by the 2012 ACIP recommendations)

Outline

- Introduction
- Overview of cost-effectiveness results
- Model assumptions
- Health outcomes and cost results
- Detailed cost-effectiveness results
  - Sensitivity analyses
- Conclusion
  - Discussion and Limitations
  - Summary

Overview of model results

Base case results: Comparing PCV+PPSV vs. PPSV-only

Model	Cost-effectiveness ratios ($/QALY)
CDC	$562,000 *$649,000, estimate from October 2018* $222,000, with higher VE-PCV(ST3)[1]
Pfizer	$199,000 *$186,000, including immunocompromised*[2]
Pittsburgh	$765,000 *$814,000, among black population*[3] *$761,000, among non-black population*[3]

[1] An alternate base case scenario from the CDC model assumes higher VE PCV (ST3).

[2] One Pfizer model base case scenario includes IC but does not allow vaccinations among IC. An alternate base case scenario in the Pfizer model excludes IC individuals, which is in closer alignment to the policy question under consideration and more similar to the structure of the CDC model.

[3] At the request of the ACIP work group, the Pittsburgh model was developed to investigate differences in cost-effectiveness across black and non-black populations.

Overview of model results

Selected assumptions compared to CDC model

Model	$/QALY
CDC	$562,000 $222,000, with higher VE-PCV(ST3)
Pfizer	$199,000
Pittsburgh	$765,000

Pfizer model

- Higher VE-PCV assumptions
  - Most importantly: VE-PCV(ST3) pneumonia
  - More severe case assumptions
- Lower indirect effects from childhood vaccination on older adults

Pittsburgh model

- Higher VE-PPSV assumptions
- No indirect effects
- More detailed modeling of black and non-black populations

Outline

- Introduction
- Overview of cost-effectiveness results
- Model assumptions
- Health outcomes and cost results
- Detailed cost-effectiveness results
  - Sensitivity analyses
- Conclusion
  - Discussion and Limitations
  - Summary

Model inputs

Selected base case assumptions[1]

Model inputs	CDC	Pfizer	Pittsburgh
Vaccine effectiveness	Varies (discussed later)	Varies (discussed later)	Varies
Indirect effects[2]	4.1% every year	4.1% for 3 years	None
Utility loss for IPD	0.0087	0.1300	0.0745[3]
Utility loss for inpatient pneumonia	0.0060	0.1300	0.0745[3]
Case-fatality ratios for inpatient pneumonia	3.7% to 7.2%	5.6% to 13.7%[4]	5.0%

[1.] From the review, these assumptions appear to be the most important in terms of determining differences between model results. Other assumptions and model characteristics across all three models include: static (non-dynamic) Markov models of age 65 year old cohort of 2.7 million individuals followed until the end of life, several risk groups (e.g., healthy, CMC), multiple disease states (e.g., IPD, inP, outP), vaccination and medical costs adjusted to US2017$, discount rate of 3%.

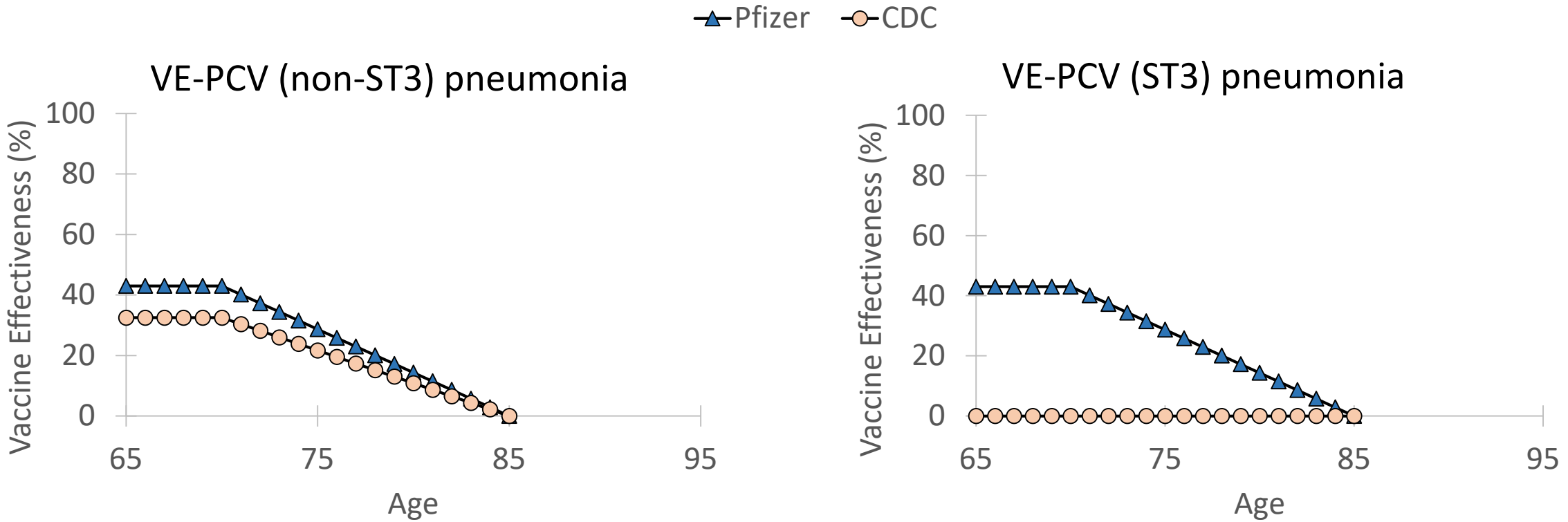
[2.] Reductions in PCV pneumonia and IPD (non-ST3, non-19F) from childhood vaccinations. Incidence of serotypes 3 and 19F disease have been observed to exhibit minimal or no reduction related to indirect protection from childhood vaccinations on older adults.

[3.] The Pittsburgh model IPD and pneumonia utility is based on 34 days with 0.2 utility per day. Not shown here, model assumptions also include a probability of lifelong disability following recovery from IPD, where disability was associated with 0.4 utility .

[4.] The Pfizer CFR ranges presented here do not include CFR among IC populations.

Model inputs[1]

PCV effectiveness against PCV-type pneumonia

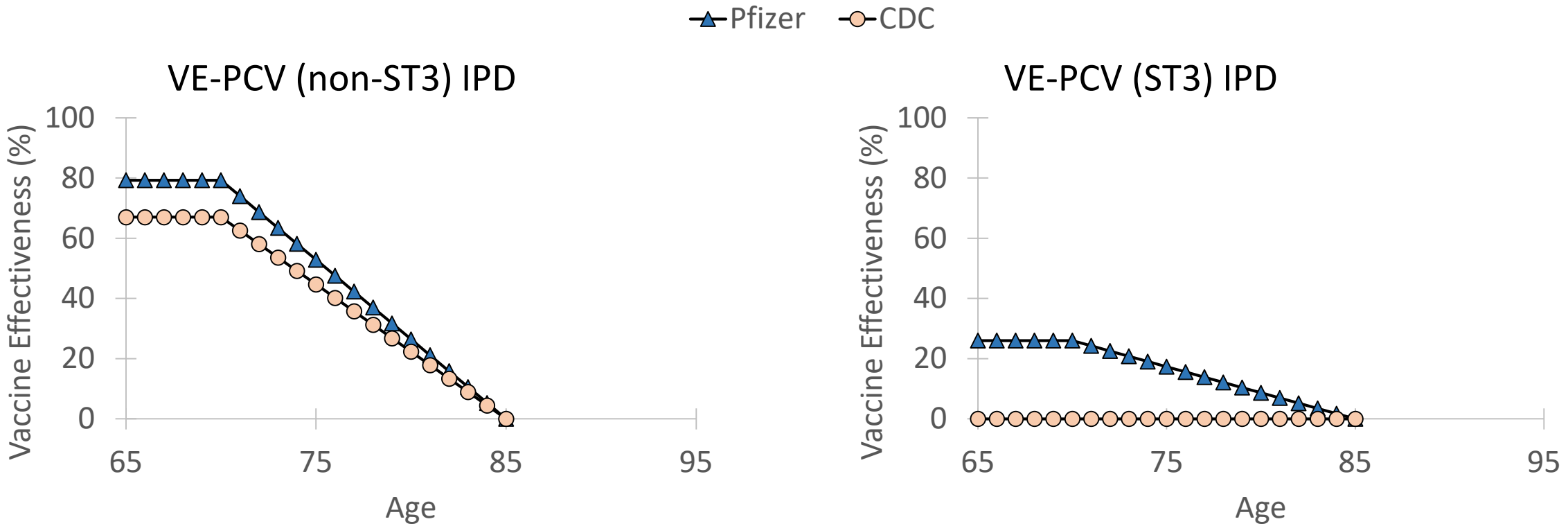


Sources: CDC model based VE-PCV (ST3) PCV-P on Suaya (2018) and VE-PCV (ST3) PCV-P = 0% based on no measured VE-PCV (ST3) IPD in Pilishvili (2018). Pfizer model VE PCV PCV-P assumptions were based on Bonten (2015), assumed VE-PCV (-ST3) PCV-P = VE-PCV (ST3) PCV-P. In the CDC model scenario with higher VE-PCV (ST3), VE-PCV (ST3) PCV-P starts at 45%

[1] Pittsburgh model assumptions on VE not presented here due to space and also because other assumptions make the Pittsburgh model less comparable, including no adjustments for VE-PCV ST3 diseases, no indirect effects, and higher VE-PPSV.

Model inputs[1]

PCV effectiveness against IPD



Sources: CDC model VE-PCV13 IPD based on Pilishvili (2018). Pfizer model VE-PCV (-ST3) IPD assumption based on Bonten (2015) with an age-based adjustment applied to Bonten (2015) estimates from the average age of 73 in Bonten (2015) to age 65 which is base case assumption in the model. Pfizer model VE-PCV (ST3) IPD based on Pilishvili (2018) point-estimate. In the CDC model scenario with higher VE-PCV (ST3), VE-PCV (ST3) IPD equals the Pfizer assumption.

[1] Pittsburgh model assumptions on VE not presented here due to space and also because other assumptions make the Pittsburgh model less comparable, including no adjustments for VE-PCV ST3 diseases, no indirect effects, and higher VE-PPSV.

Outline

- Introduction
- Overview of cost-effectiveness results
- Model assumptions
- Health outcomes and cost results
- Detailed cost-effectiveness results
  - Sensitivity analyses
- Conclusion
  - Discussion and Limitations
  - Summary

Health outcomes and cost results[1]

	Outcome and costs	CDC	Pfizer	Pittsburgh
Health Outcomes	(Inpatient) IPD cases prevented	76	175*	313
	Inpatient PCV-type pneumonia cases prevented	2,047	2,826*	NA
	Deaths due to IPD prevented	10	25*	46
	Deaths due to PCV-type pneumonia prevented	79	199*	69
	Total deaths prevented	89	224*	115
	QALYs gained	709	1,542	545
	Life-years gained	1,101	1,865	NA
Costs ($ millions)	Vaccine costs	423	357	405
	Medical costs	-25	-51	-27
	Total costs	398	306	378

[1] These are discounted total population values for the complete time horizon of the model for a cohort of about 2.7 million individuals aged 65 years at the start of the model. All the models also estimate prevented outpatient pneumonia cases, which are not presented here.

*Cases and deaths were not reported as discounted values in the Pfizer report. All other values were discounted at 3%.

Outline

- Introduction
- Overview of cost-effectiveness results
- Model assumptions
- Health outcomes and cost results
- Detailed cost-effectiveness results
  - Sensitivity analyses
- Conclusion
  - Discussion and Limitations
  - Summary

Review of cost-effectiveness results

Base case results: Comparing PCV+PPSV vs. PPSV-only

Model	$/QALY
CDC	$562,000 $222,000, with higher VE-PCV(ST3)
Pfizer	$199,000
Pittsburgh	$765,000

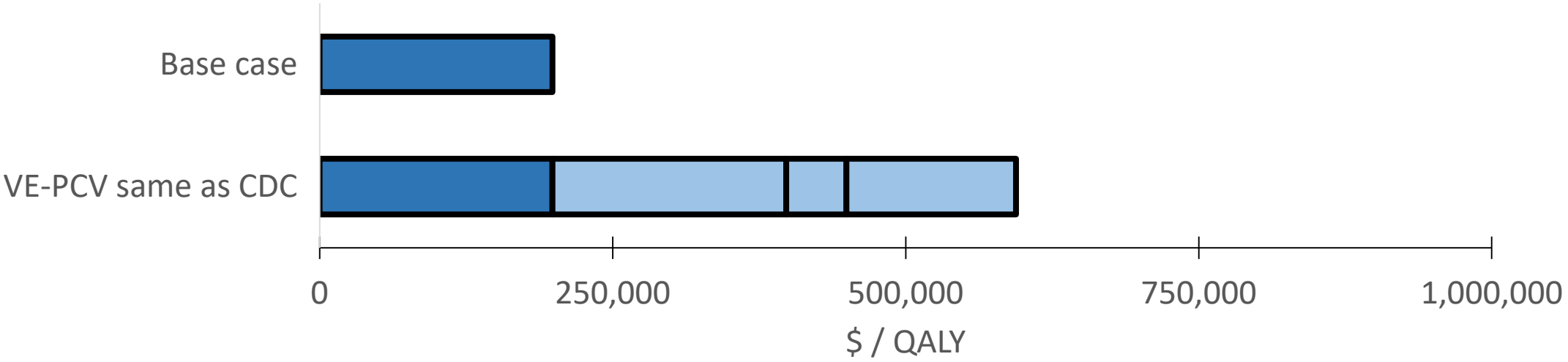
Important differences between CDC and Pfizer model assumptions

- VE-PCV assumptions
  - Most important: VE-PCV (ST3) pneumonia
- Other factors
  - Case-fatality ratios
  - Duration of indirect effects
  - Utility values

Cost-effectiveness results

PCV effectiveness sensitivity analyses

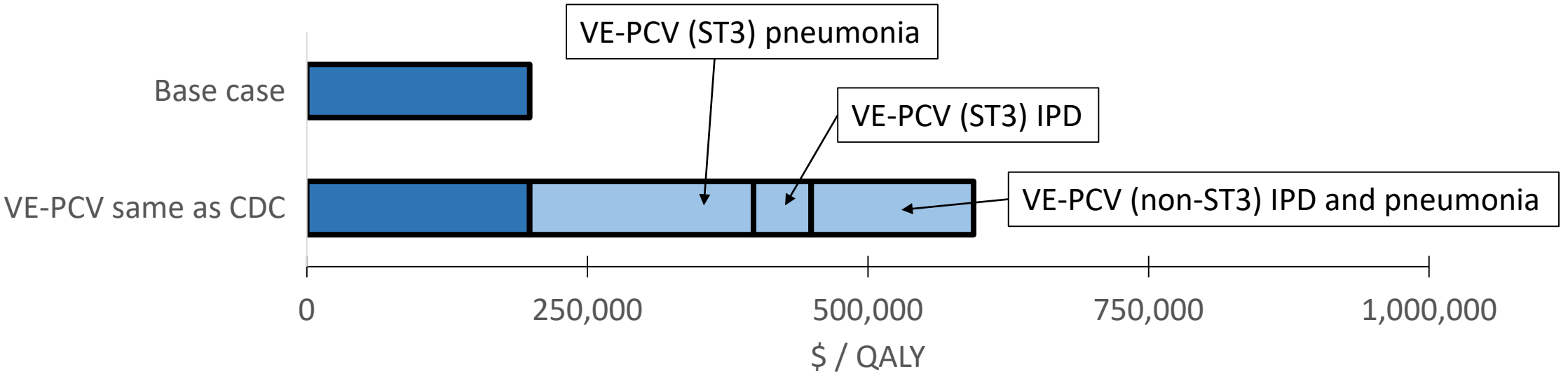
Pfizer model



Cost-effectiveness results

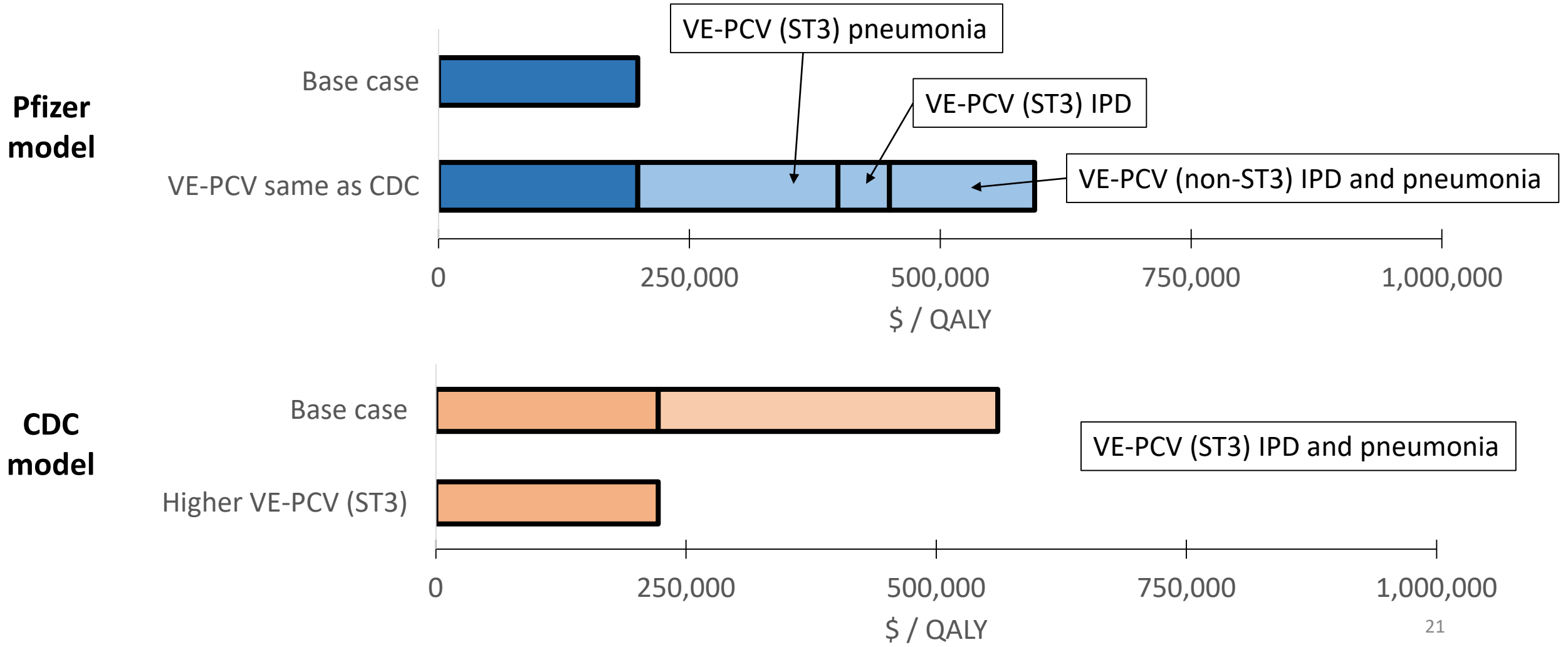
PCV effectiveness sensitivity analyses

Pfizer model



Cost-effectiveness results

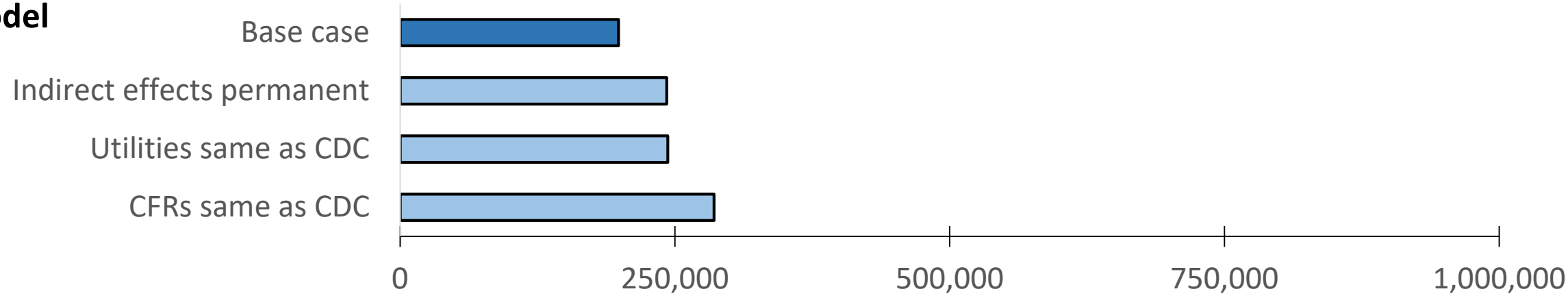
PCV effectiveness sensitivity analyses



Cost-effectiveness results

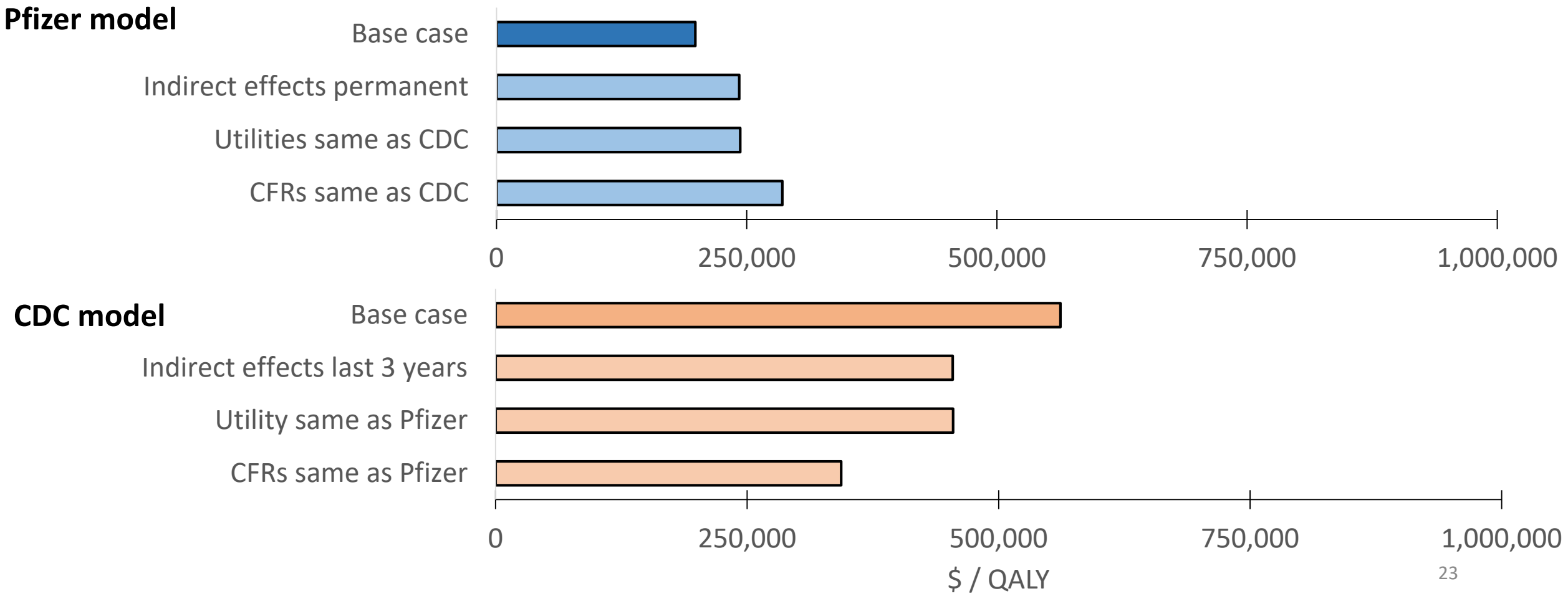
Other important factors sensitivity analyses

Pfizer model



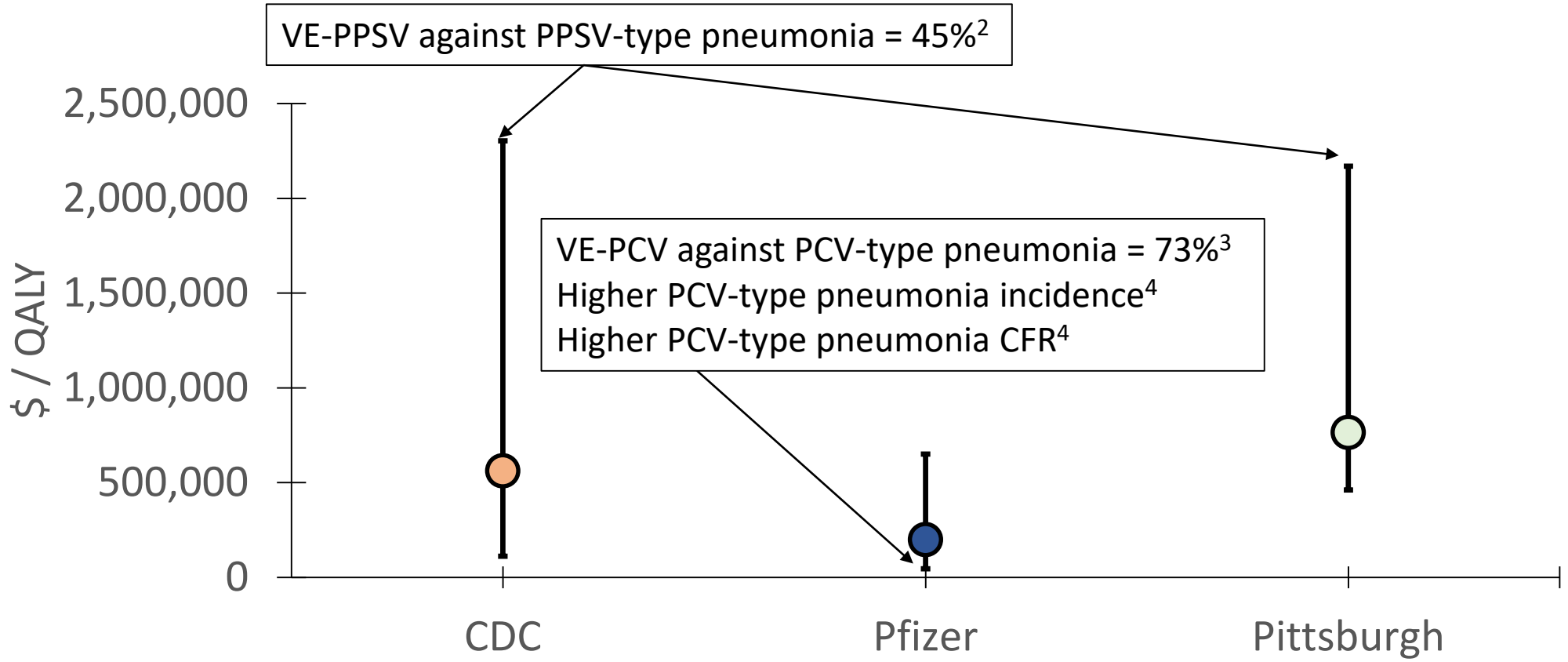
Cost-effectiveness results

Other important factors sensitivity analyses



Cost-effectiveness results

Ranges from one-way and multi-way sensitivity analyses[1]



Note: Axis has changed from previous graphs of CERs to accommodate wider range in estimated CERs.

[1]These do not include results from probabilistic sensitivity analyses. [2]Schiffner-Rohe (2016), Falkenhorst (2017), Tin Tin Htar (2017).[3]McLaughlin (2018). [4]Ramirez (2017) and Pfizer Inc. internal data.

Outline

- Introduction
- Overview of cost-effectiveness results
- Model assumptions
- Disease burden results
- Detailed cost-effectiveness results
  - Sensitivity analyses
- Conclusion
  - Discussion and Limitations
  - Summary

Discussion and Limitations

- Vaccine effectiveness appears to be the most important assumption
  - Especially VE of PCV against serotype 3 pneumonia
  - Varied assumptions on VE for PCV and PPSV across models
- Other important assumptions
  - Indirect effects
  - Utility loss for disease states
  - Case-fatality ratios
- Models assume different levels of uncertainty
  - Pfizer model assumes less uncertainty overall

Summary

- Cost-effectiveness of routine vaccination with PCV for 65 year olds

	Cost-effectiveness ratios ($/QALY)	
Model	**Base case**	**Range**
CDC	$562,000 $222,000, with higher VE-PCV(ST3)	$112,000 to $2.3 million
Pfizer	$199,000	$46,000 to $650,000
Pittsburgh	$765,000	$461,000 to $2.2 million

- Differences across models related to
  - Vaccine effectiveness assumptions, especially PCV VE against ST3 pneumonia
  - Other less important factors
    - Case-fatality ratios
    - Duration of indirect effects
    - Utility assumptions

References

Bonten MJM, Huijts SM, Bolkenbaas M, Webber C, Patterson S, Gault S, et al. Polysaccharide Conjugate Vaccine against Pneumococcal Pneumonia in Adults. N Engl J Med. 2015;372:1114-25.

Falkenhorst G, Remschmidt C, Harder T, Hummers-Pradier E, Wichmann O, Bogdan C. Effectiveness of the 23-valent Pneumococcal Polysaccharide Vaccine (PPV23) against Pneumococcal Disease in the Elderly: Systematic Review and Meta-analysis. PloS one. 2017;12:e0169368.

McLaughlin JM, Jiang Q, Isturiz RE, et al. Effectiveness of 13-valent pneumococcal conjugate vaccine against hospitalization for community-acquired pneumonia in older US adults:
a test-negative design. *Clin Infect Dis* 2018;67:1498-1506.

Pilishvili T, Almendares O, Nanduri S, Warnock R, Wu X, McKean S, et al. Case-Control Study to Evaluate Pneumococcal Vaccines Effectiveness against Invasive Pneumococcal Disease (IPD) Among U.S. Medicare Beneficiaries ≥65 Years Old. ISPPD Abstract 0682. 2018.

Ramirez JA, Wiemken TL, Peyrani P, et al. Adults hospitalized with pneumonia in the United States: incidence, epidemiology, and mortality. *Clin Infect Dis* 2017;65:1806-1812.

Schiffner-Rohe J, Witt A, Hemmerling J, Eiff Cv, Leverkus F-W. Efficacy of PPV23 in Preventing Pneumococcal Pneumonia in Adults at Increased Risk–A Systematic Review and Meta-analysis. PloS one. 2016;11:e0146338.

Suaya JA, Jiang Q, Scott DA, Gruber WC, Webber C, Schmoele-Thoma B, et al. Post Hoc Analysis of the Efficacy of the 13-Valent Pneumococcal Conjugate Vaccine against Vaccine-type Community-acquired Pneumonia in at-risk Older Adults. Vaccine. 2018;36:1477-83.

Tin Tin Htar M, Stuurman AL, Ferreira G, Alicino C, Bollaerts K, Paganino C, et al. Effectiveness of Pneumococcal Vaccines in Preventing Pneumonia in Adults, A Systematic Review and Meta-analyses of Observational Studies. PloS one. 2017;12:e0177985.

Acknowledgements

This presentation summarizes work conducted by three modeling teams

- CDC team
  - Charles Stoecker (Tulane University), Miwako Kobayashi (CDC), Almea Matanock (CDC), Bo Hyun-Cho (CDC), Tamara Pilishvili (CDC)
- Pfizer team
  - Derek Weycker (Policy Analysis Inc.), Ahuva Hanau (Policy Analysis Inc.), Mark Atwood (Policy Analysis Inc.), Reiko Sato (Pfizer Inc.)
- Pittsburgh team
  - Kenneth J. Smith, Mary Patricia Nowalk, Angela R. Wateska, Chyongchiou Jeng Lin, Richard K. Zimmerman (all from University of Pittsburgh)

Thank you to other CDC and ACIP contributors, reviewers, and colleagues

- Cindy Weinbaum, Yuping Tsai, Fangjun Zhou, Bo Hyun-Cho, Jamie Pike, Zana Somda, Megan Lindley, Adam Bjork, Harrell Chesson, and members of the ACIP Pneumococcal Vaccines Work Group

Views and opinions expressed in this presentation are the authors and do not necessarily represent the views and opinions of the Centers for Disease Control and Prevention.

Thank you