

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

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

*Disclaimer: 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 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<sup>a</sup>: 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.

<sup>a</sup>-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**

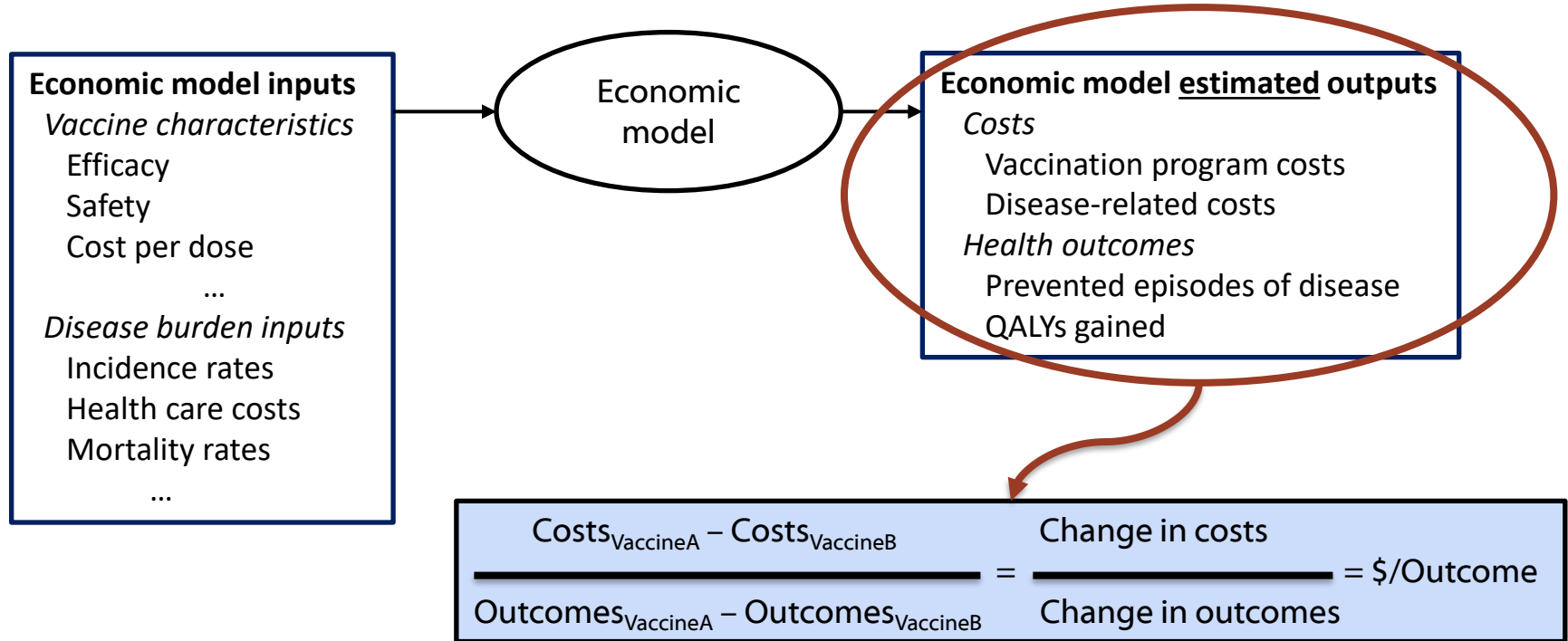
# What is cost-effectiveness analysis (CEA)?

- **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)

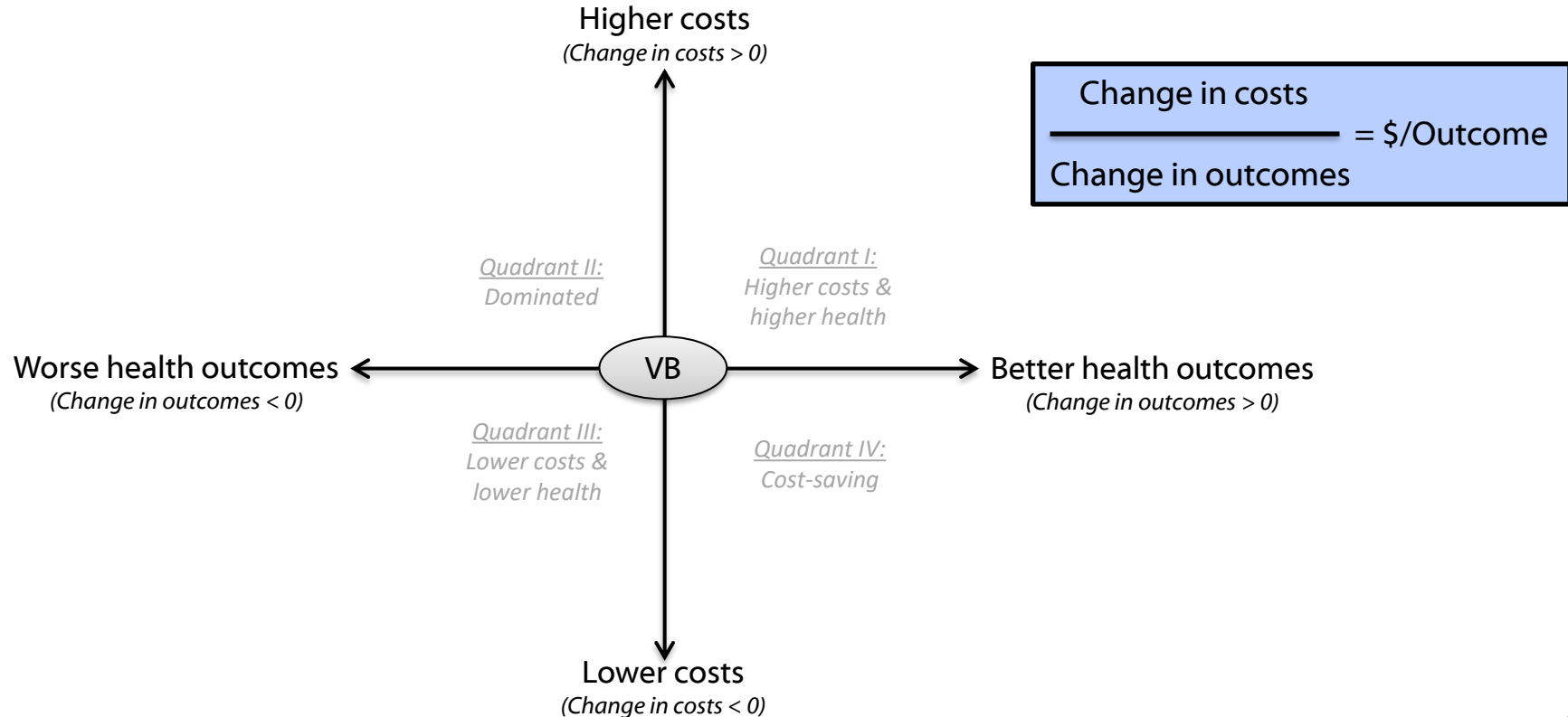
$$\frac{\text{Costs}_{\text{VaccineA}} - \text{Costs}_{\text{VaccineB}}}{\text{Outcomes}_{\text{VaccineA}} - \text{Outcomes}_{\text{VaccineB}}} = \frac{\text{Change in costs}}{\text{Change in outcomes}} = \$/\text{Outcome}$$

- 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





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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 <sup>a</sup>                |
| Vaccine cost  | PCV20: \$289<br>PCV21: \$319         | PCV20: \$261<br>PCV21: \$287         | PCV20: \$249<br>PCV21: \$333           |
| Other vaccine costs per dose                                      | Admin: \$30;<br>travel: \$36         | Admin: \$19                          | Admin: \$24;<br>adverse events: \$0.76 |
| How many years following a PCV dose until protections wanes to 0% | 15 years                             | 15 years                             | 15 years for NBP<br>20 years for IPD   |
| Circulating serotype protection ratio:<br>PCV21:PCV20             | 2.7 to 9.5<br>(vaccine-unique types) | 2.9 to 6.3<br>(vaccine-unique types) | 1.5 to 1.6<br>(all types)              |

<sup>a</sup>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 sequelae, post-IPD   | No <sup>a</sup>         | Yes                     | Yes                                      |
| Separately models disability sequelae, post-NBP   | No <sup>a</sup>         | 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 <sup>b</sup>     | 3 <sup>b</sup>          | 4 to 6 <sup>b</sup>                      |
| Productivity loss for disease-related deaths adjusted by employment status, varies by age | Yes                     | No                      | No                                       |

<sup>a</sup>In the Tulane-CDC model, inpatient disease burden assumptions includes a portion of the disease burden from disability sequelae, up to 1 year for QALY loss and up to 6 months for costs.

<sup>b</sup>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<br>(Cost-saving to \$18,599) <sup>a</sup>     | 5,090       | Cost-saving to 58,116 <sup>b,c</sup> |
| Risk-based vaccination with PCV21      | Risk-based vaccination with PCV20      | Cost-Saving<br>(Range was cost-saving) <sup>a</sup> | Cost-saving |                                      |

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

<sup>a</sup>This range was estimated using probabilistic sensitivity analyses, where all inputs were varied.

<sup>b</sup>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.

<sup>c</sup>These ICER values were calculated by the CDC ACIP economic review team from costs and effectiveness values reported in the Pittsburgh 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 <b>PCV21</b> | Age-based vaccination at 65 with <b>PCV21</b> <sup>b</sup>                        | 269,643<br>(\$198,098 to \$701,066) <sup>a</sup> | 105,303 to<br>256,318 <sup>b</sup> | 2,713 to<br>114,645 <sup>c</sup>  |
| Age-based vaccination at 50 and 65 with <b>PCV20</b> | Age-based vaccination at 65 and risk-based vaccination at 50-64 with <b>PCV20</b> | 628,473  | NA <sup>d</sup>                    | 36,854 to<br>149,269 <sup>c</sup> |

- **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**

<sup>a</sup>This range was estimated using probabilistic sensitivity analyses, where all inputs were varied.

<sup>b</sup>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.

<sup>c</sup>These ICER values were calculated by the CDC ACIP economic review team from costs and effectiveness values reported in the Pittsburgh model. High range value comes from healthcare sector perspective; low range value comes from societal perspective.

<sup>d</sup>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) <sup>b</sup> | Age-based vaccination at 50 with PCV21 (Tulane-CDC); or at 65 with PCV20 (Merck) <sup>b</sup> | Dominated<br>(Range was dominated) <sup>a</sup> | 647,569 <sup>b</sup> |

- 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.

<sup>a</sup>This range was estimated using probabilistic sensitivity analyses, where all inputs were varied.

<sup>b</sup>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 <sup>a</sup> | 274,844 to 512,266 <sup>b</sup> |

- **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.

<sup>a</sup>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.

<sup>b</sup>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.

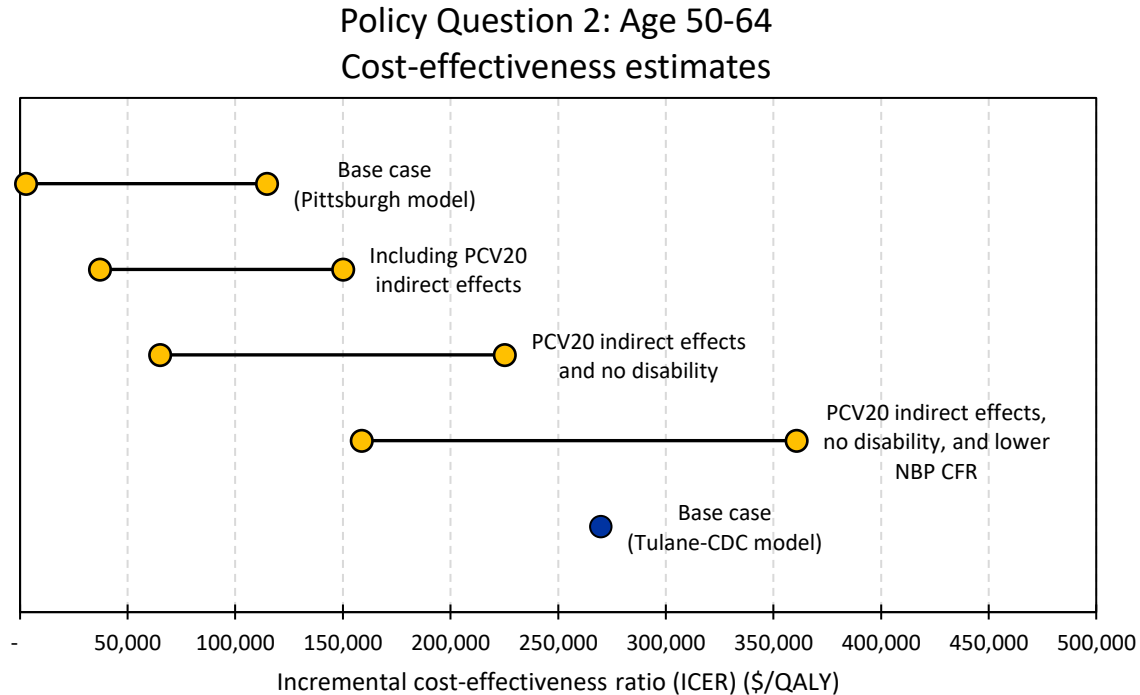
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# Sensitivity/scenario analyses

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



# Policy question 2: Age 50-64

## Base case estimates (\$/QALY)

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

- **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

<sup>a</sup>This range was estimated using probabilistic sensitivity analyses, where all inputs were varied.

<sup>b</sup>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.

<sup>c</sup>These ICER values were calculated by the CDC ACIP economic review team from costs and effectiveness values reported in the Pittsburgh model. High range value comes from healthcare sector perspective; low range value comes from societal perspective.

<sup>d</sup>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 sequelae
  - Vaccine price
    - Merck model base case input for PCV21 cost per dose was \$287, which has also been announced publicly as the list price<sup>a</sup>
- **Potential challenges to vaccination implementation due to changing the pneumococcal vaccine schedule were not included**

# 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

### **Tulane-CDC team**

Charles Stoecker (Tulane University)  
Yin Wang (Tulane University)  
Miwako Kobayashi (CDC)  
Andrew Leidner (CDC)  
Bo-Hyun Cho (CDC)  
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### **Merck team**

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