Summary of three economic models assessing pneumococcal vaccines in US adults

ACIP Meeting

9/29/2021

Andrew J. Leidner

Immunization Services Division

CDC / NCIRD

Disclaimers:
(1) 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.
(2) Three models described in this study are under review by the ACIP economics team.

Acknowledgements

- This presentation summarizes work conducted by three modeling groups
  - CDC Team
    - Charles Stoecker[a], Miwako Kobayashi[b], Bo-Hyun Cho[b], Tamara Pilishvili[b]
  - Merck Team
    - Kwame Owusu-Edusei[c], Arijita Deb[c], Kelly Johnson[c], Oluwaseun Sharomi[c], Elamin Elbasha[c], Thomas Weiss[c], Temi Folaranmi[c], Craig Roberts[c], Donald Yin[c], Richard Haupt[c], Tufail Malik[c]
  - Pfizer Team
    - Derek Weycker[d], Ahuva Averin[d], Mark Atwood[d], Melody Shaff[d], Reiko Sato[e], Erica Chilson[e], Vincenza Snow[e], Alejandro Cane[e], Raymond Farkouh[e]

[a.] Tulane University; [b.] CDC; [c.] Merck; [d.] Policy Analysis Inc (PAI); [e.] Pfizer;

Conflict of interest statements

- Andrew J. Leidner: None.
- CDC team: None.
- Pfizer team:
  - Pfizer manufacturers the PCV13 and PCV20 vaccines.
  - PAI team members are funded by Pfizer, other team members are employed by Pfizer.
- Merck team:
  - Merck manufacturers the PPSV23 and PCV15 vaccines.

Acronyms

Acronym	Description & notes
CR	Current recommendations for adult pneumococcal vaccines use
PCV	Pneumococcal conjugate vaccine, may be written as PCV13, PCV15, PCV20 to indicate the individual vaccines
PPSV	Pneumococcal polysaccharide vaccine, may be written as PPSV23
VE	Vaccine effectiveness
PCV13 VE ST3	Vaccine effectiveness of the PCV vaccines for serotype 3
IC	Immunocompromising conditions[a]
CMC	Chronic medical conditions[a]
IPD	Invasive pneumococcal disease
NBPP	Non-bacteremic pneumococcal pneumonia, may be stated as pneumonia
QALY	Quality-adjusted life-year
CER	Cost-effectiveness ratio

[a] These conditions are identified here: https://www.cdc.gov/vaccines/vpd/pneumo/hcp/who-when-to-vaccinate.html

Outline

- Cost-effectiveness background
- CDC model
  - Updates to VE assumptions
  - Updates to results
- Overview of available models
- Results
  - Age-based analyses
  - Risk-based analyses
  - Combined age- and risk-based analyses
- Discussion & summary

Cost-effectiveness modeling background

- Compares costs and outcomes of two strategies by calculating a cost-effectiveness ratio (CER):

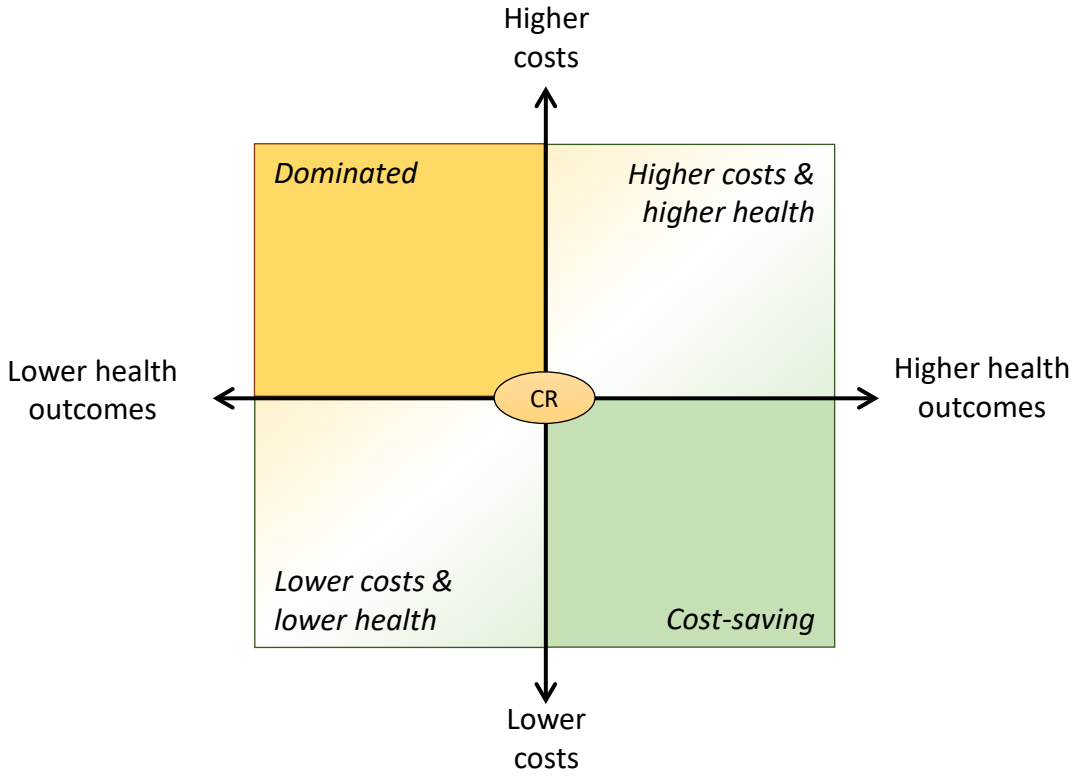
$$\frac{\text{Costs}_{\text{High valency PCV @ 65+}} - \text{Costs}_{\text{CR}}}{\text{Outcomes}_{\text{High valency PCV @ 65+}} - \text{Outcomes}_{\text{CR}}} = \frac{\text{Change in costs}}{\text{Change in outcomes}} = \$/\text{Outcome}$$

- An estimated cost per health outcome gained
  - Outcomes can be averted cases, averted deaths, quality-adjusted life-years (QALYs)
- $/Outcome can be considered a cost per unit of health gained
  - Cost per QALY gained ($/QALY)

Cost-effectiveness ratios

$$\frac{Costs_A - Costs_B}{Outcomes_A - Outcomes_B} = \frac{\text{Change in costs}}{\text{Change in outcomes}} = \$/\text{Outcome}$$

	Change in outcomes < 0 (lower health)	Change in outcomes > 0 (higher health)
Change in costs > 0 (higher costs)	Dominated	$/QALY (higher costs & higher health)
Change in costs < 0 (lower costs)	Lower costs & lower health ($/QALY, numeric estimate presented in parenthesis)	Cost-saving



Three analysis types: Age-based, risk-based, combined

Analysis type	Starting age of model population	Population to be vaccinated
Age-based	Either 50 or 65 years old	All adults
Risk-based	Between 19-49 or 19-64 years old	CMC/IC adults only
Combined age- and risk-based	19 years old (CDC model); 19 to 50 or 65 (Pfizer model)	CMC/IC only among younger adults, all adults among 50 or 65 year olds

Outline

- Cost-effectiveness background
- CDC model
  - Updated results
  - Changes to VE assumptions
- Overview of available models
- Results
  - Age-based analyses
  - Risk-based analyses
  - Combined age- and risk-based analyses
- Discussion & summary

Updates to CDC model

Updated VE/Waning Assumptions, September CDC model (base case)

	PCV	PPSV23
Duration of protection	**15 years**: no decline for 5 yrs[1], **linear decline to 0 over 10yrs**	15 years: linear decline to 0 over 15 years
Protection against VT-IPD	Healthy/CMC: 75 (41.4, 90.8)[1] IC: **25.0** (13.8, 30.3)[2]	Healthy/CMC: **59.7** (47.4, 69.1)[3] IC: **7.9** (0, 34.2)[3]
Protection against ST3-IPD	Healthy/CMC: 26 (0, 53.4)[1] IC: **8.7** (0, 17.8)[2]	
Protection against VT-pneumonia	Healthy: 66.7 (11.8. 89.3)[4] CMC: 40.3 (11.4, 60.2)[4] IC: **15.0** (4.7, 21.8)[2]	Healthy/CMC: 20 (0, 40)[5] IC: **6.7** (0, 13.3)[2]
Protection against ST3-pneumonia	Healthy/CMC: 15.6 (0, 32.0) IC: **5.2** (0, 10.7)[2]	

Key changes from June 2021 presentation:

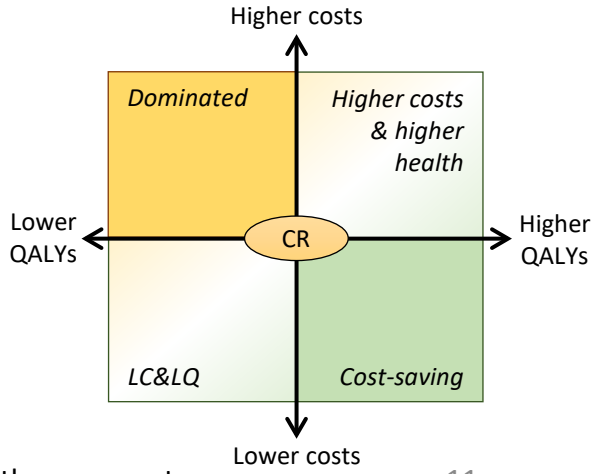
- **Duration of protection**: shorter for PCV
- **PPSV23 VE against VT-IPD**: higher for healthy/CMC, lower for IC adults
- **VE estimates for IC**: lowered for PCV and PPSV23

1. Bonten et al. NEJM 2015, 2. Assumed 1/3 of healthy/CMC adults, Cho et al. Vaccine 2013, 3. Meta-analysis of Andrews 2012, Rudnick 2013, and Djennad 2018, restricting to PPSV23 VE within 5 years of vaccination , 4. Suaya et al. Vaccine 2018, 5. Lawrence et al. PLoS Med 2020

Updates to CDC model

Results

Analysis	Strategy	CDC model June 2021	Updated CDC model September 2021
		$/QALY	$/QALY
Combined, age- and risk-based	PCV20 at CMC/IC and at age 50	Cost-saving[a]	Cost-saving[a]
	PCV20 at CMC/IC and at age 65	Cost-saving[a]	Cost-saving[a]
	PCV15+PPSV23 at CMC/IC and at age 65	389,000	338,000



[a] Cost-saving indicates an intervention strategy yielded higher health outcomes (more QALYs, fewer episodes of disease) and lower costs than the comparator.

Outline

- Cost-effectiveness background
- CDC model
  - Updated results
  - Changes to VE assumptions
- Overview of available models
- Results
  - Age-based analyses
  - Risk-based analyses
  - Combined age- and risk-based analyses
- Discussion & summary

Selected model characteristics

Model characteristics	CDC	Merck	Pfizer
Model type	Single cohort, lifetime	Multi-cohort, lifetime	Multi-cohort, lifetime
One base case or scenarios	One base case	4 scenarios	One base case
Societal perspective or healthcare sector	Societal	Societal	Both
Adverse events	No	No	No
Combined age- and risk-based estimates	Yes	No	Yes
Transitions from lower risk states to higher risk (e.g., healthy → CMC)	Yes	No	Yes

[a.] While the base case of the Pfizer model included possible indirect effects from a pediatric program, most Pfizer model results presented in this presentation will focus on scenarios without indirect effects. When the presented results include indirect effects, this will be noted in a footnote.

Selected model characteristics

Model characteristics	CDC	Merck	Pfizer
Indirect effects from potential pediatric vaccinations with new vaccines	In scenarios	Not included	In base case[a]
PCV VE ST3 lower than other STs	In base case	In base case scenarios	In scenarios
PPSV VE NBPP > 0%	In base case	In base case scenarios	No
Vaccination coverage in the intervention (vs. current recommendations)	Varies in scenarios	PCV coverage higher	PCV coverage higher
Comparator in the risk-based analysis	Age-based use (incremental)	CR	CR
Important inputs and assumptions based on available sensitivity analyses	• Indirect effects • VE (initial, waning)	• VE (initial, waning)	• Indirect effects • VE (initial, waning) • NBP incidence

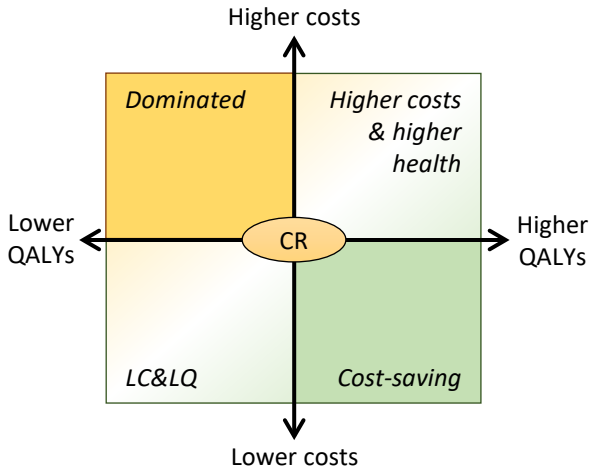
Outline

- Cost-effectiveness background
- CDC model
  - Updated results
  - Changes to VE assumptions
- Overview of available models
- Results
  - Age-based analyses
  - Risk-based analyses
  - Combined age- and risk-based analyses
- Discussion & summary

Age-based strategies, PCV20, all models

Compared to current recommendations

Analysis	Strategy	CDC	Merck	Pfizer
Age-based	PCV20 at age **65**	Cost-saving[a]	Cost-saving[a] to 39,000	Cost-saving[a]
Age-based	PCV20 at age **50**	LC&LQ[b] (5,300,000)	174,000 to 514,000	18,000



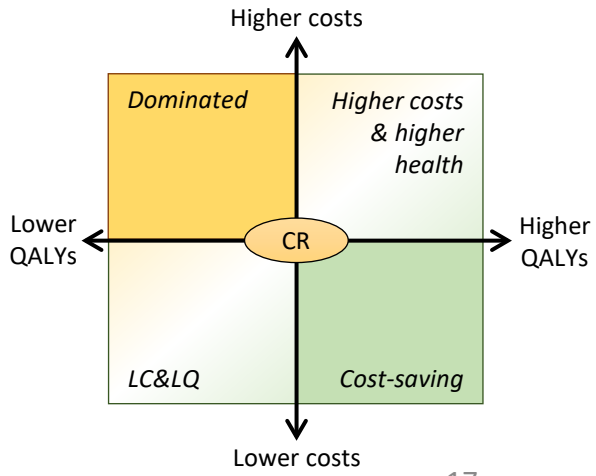
[a] Cost-saving indicates an intervention strategy yielded higher health outcomes (more QALYs, fewer episodes of disease) and lower costs than the comparator.

[b] LC&LQ indicates a strategy yielded lower health outcomes (fewer QALYs, more episodes of disease) and lower costs than the comparator.

Age-based strategies, PCV20, CDC model

Scenario analyses, Compared to current recommendations

Analysis	Strategy	Base case	PCV waning 20 years	PCV coverage higher than in base case	Indirect effects	Lower PCV20 VE	**Health-improving scenarios**	**Cost-saving scenarios**
Age-based	PCV20 at age **65**	Cost-saving[a]	Cost-saving[a]	Cost-saving[a]	Cost-saving[a]	Cost-saving[a]	**5 of 5**	**5 of 5**
Age-based	PCV20 at age **50**	LC&LQ[b] (5,300,000)	Cost-saving[a]	7,000	Cost-saving[a]	LC&LQ[b] (944,000)	**3 of 5**	**2 of 5**



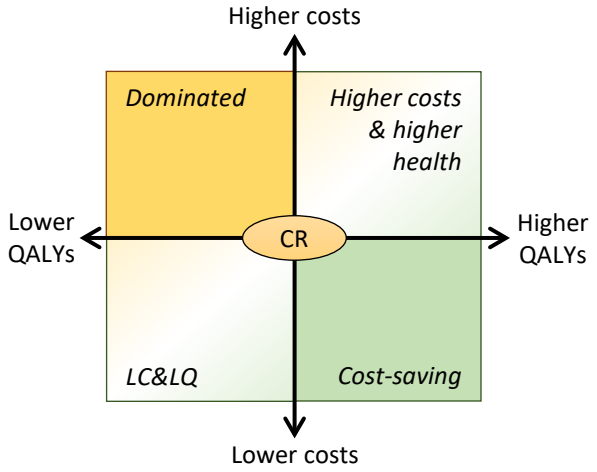
[a] Cost-saving indicates an intervention strategy yielded higher health outcomes (more QALYs, fewer episodes of disease) and lower costs than the comparator.

[b] LC&LQ indicates a strategy yielded lower health outcomes (fewer QALYs, more episodes of disease) and lower costs than the comparator.

Age-based strategy, PCV15+PPSV23, all models

Compared to current recommendations

Analysis	Strategy	CDC	Merck
Age-based	PCV15+PPSV23 at age **65**	Cost-saving[a]	237,000 to 282,000

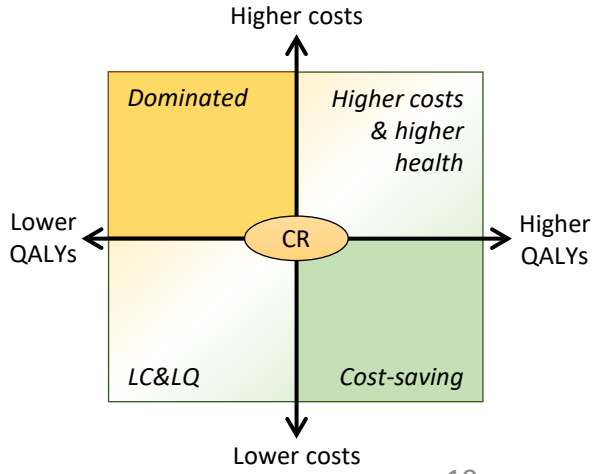


[a] Cost-saving indicates an intervention strategy yielded higher health outcomes (more QALYs, fewer episodes of disease) and lower costs than the comparator.

Age-based strategy, PCV15+PPSV23, CDC model

Scenario analyses, Compared to current recommendations

Analysis	Strategy	Base case	PCV waning 20 years	Indirect effects	Higher PCV15 ST3 VE	**Health-improving scenarios**	**Cost-saving scenarios**
Age-based	PCV15+PPSV23 at age **65**	Cost-saving[a]	Cost-saving[a,b]	Cost-saving[a]	Cost-saving[a]	**4 of 4**	**4 of 4**



[a] Cost-saving indicates an intervention strategy yielded higher health outcomes (more QALYs, fewer episodes of disease) and lower costs than the comparator.

Outline

- Cost-effectiveness background
- CDC model
  - Updated results
  - Changes to VE assumptions
- Overview of available models
- Results
  - Age-based analyses
  - Risk-based analyses
  - Combined age- and risk-based analyses
- Discussion & summary

Risk-based strategies, PCV20, all models

Analysis	Strategy	CDC	Merck	Pfizer
Risk-based	PCV20 among CMC/IC at age **19-64**	292,000[a]	58,000 to 183,000	11,000[b]
Risk-based	PCV20 among CMC/IC at age **19-49**	483,000[a]	94,000 to 273,000	25,000[b]

- All risk-based vaccinations improve health
- Different comparators
  - Merck and Pfizer models compared risk-based use of PC20 to the CR for risk-based use
  - CDC model compared risk-based use to age-based use of PCV20 at age 65/50, an incremental analysis
- Pfizer model results on this slide include potential indirect effects
- Higher CERs for 19-49 than for 19-64

[a.] The CDC risk-based assessment compared the use of PCV20 among younger adults with CMC/IC to an age-based strategy where PCV20 was used among all older adults, either age 50 or age 65.
[b.] The Pfizer risk-based assessments presented here include potential pediatric indirect effects from new vaccines. When potential pediatric indirect effects were not included, the CER for 19-49 year olds was cost-saving.

Combined, age- and risk-based strategies, PCV20, all models

Analysis	Strategy	CDC	Pfizer
Combined, age- and risk-based	PCV20 among CMC/IC at age **19-64** and at age **65**	Cost-saving[a]	Cost-saving[a,b]
Combined, age- and risk-based	PCV20 among CMC/IC at age **19-49** and at age **50**	Cost-saving[a]	11,000[b]

- All assessments of combined strategies indicate vaccinations improve health
- All assessments with an age 65 threshold indicate cost-savings

[a.] Cost-saving indicates an intervention strategy yielded higher health outcomes (more QALYs, fewer episodes of disease) and lower costs than the comparator.

[b.] The Pfizer assessments presented here do not include potential pediatric indirect effects.

Age- and risk-based strategies, PCV15+PPSV23, all models

Analysis	Strategy	CDC	Merck
Age-based	PCV15+PPSV23 at age **65**	Cost-saving[a]	237,000 to 282,000
Risk-based	PCV15+PPSV23 among CMC/IC at ages **19-64**	656,000	250,000 to 312,000
Combined, age- & risk-based	PCV15+PPSV23 among CMC/IC at ages **19-64** & at age **65**	338,000	NA

- Risk-based vaccinations improve health at higher costs
- Different comparators
  - Merck model compared risk-based use of PCV15+PPSV23 to the CR for risk-based use
  - CDC model compared risk-based use to age-based use of PCV15+PPSV23 at age 65, an incremental analysis

[a] Cost-saving indicates an intervention strategy yielded higher health outcomes (more QALYs, fewer episodes of disease) and lower costs than the comparator.

Outline

- Cost-effectiveness background
- CDC model
  - Updated results
  - Changes to VE assumptions
- Overview of available models
- Results
  - Age-based analyses
  - Risk-based analyses
  - Combined age- and risk-based analyses
- Discussion & summary

Discussion, other studies

- Study by researchers at the University of Pittsburgh[a]

- This model used several assumptions that were less favorable than the models summarized earlier
  - No IC individuals (focused on healthy and CMC only)
  - No transitions to CMC
  - Slightly older data for vaccine serotype coverage and incidence inputs
  - Health care perspective
  - Included adverse events

- Results (vs. CR)
  - Age-based PCV20 at 65: $172,000 per QALY
  - Age-based PCV15+PPSV23 at 65: $438,000 per QALY

[a] This study was not reviewed by the ACIP economics review team but was peer-reviewed for publication in *American Journal of Preventive Medicine*. Citation: Smith, Kenneth J., et al. "Higher-Valency Pneumococcal Conjugate Vaccines: An Exploratory Cost-Effectiveness Analysis in US Seniors." *American Journal of Preventive Medicine* (2021).

Discussion, considerations

- Range of CER estimates in some strategies
  - Model structure differences
  - Input uncertainty
- Input and model structure uncertainty
  - Vaccine effectiveness
    - Serotype specific initial VE
    - Waning VE
  - Indirect effects from a possible pediatric vaccination program in the future
    - Analyses from three models (CDC, Pfizer, Pittsburgh) indicated that CERs would likely increase in the context of indirect effects
  - CDC model did not distinguish between serotype 15B/C
- Adverse events not included
- Comparisons across models are challenging because of the number of policy options considered, and multiple new vaccines being assessed by some models

Age-based strategies, PCV20

Summary of results

- PCV20 at age 65
  - Health improving across all age-based results
  - Most estimates were cost-saving[a]
    - 3 scenarios in Merck model were not cost-saving, and in those scenarios vaccination was estimated to cost $39,000/QALY or less
- PCV 20 at age 50
  - Health improving in many results
    - Pfizer and Merck base case indicated health improvements in main analyses
    - CDC model indicated health improvements in 3 of 5 scenarios
  - Some estimates were cost-saving[a]
    - Pfizer model and Merck did not indicate cost-savings[a], and estimated $18,000/QALY (Pfizer) and a range from $173,000 to $513,000 per QALY gained
    - CDC model indicated cost-savings in 2 of 5 scenarios

[a.] Cost-saving indicates an intervention strategy yielded higher health outcomes (more QALYs, fewer episodes of disease) and lower costs than the comparator.

Risk-based and combined strategies, PCV20

Summary of results

- Improved health indicated in all risk-based strategies and models
- PCV20 19-64
  - Risk-based assessments indicate a broad range of possible value
    - $11,000 to $292,000 per QALY gained
  - Combined age- and risk-based assessments indicate cost-savings[a] in 2 of 2 models
- PCV20 19-49
  - Risk-based assessments indicate a broad range of possible value
    - Cost-saving[a,b] to $483,000 per QALY gained
  - Combined age- and risk-based assessments indicate more favorable value
    - CDC model indicates cost-savings
    - Pfizer model indicates costs of $11,000 per QALY gained

[a.] Cost-saving indicates an intervention strategy yielded higher health outcomes (more QALYs, fewer episodes of disease) and lower costs than the comparator.

[b.] In the Pfizer model with no potential pediatric indirect effects, estimate for 19-49 risk-based use was cost-saving.

All strategies, PCV15+PPSV23

Summary of results

- Age-based analysis
  - Improved health indicated in all main results
  - Cost-savings[a] indicated by the CDC model (4 of 4 scenarios)
- Risk-based
  - Improved health and higher costs indicated in all main results
  - Risk-based only strategies yield a broad range of possible value
    - $250,000 to $656,000 per QALY gained
- Combined age- and risk-based assessments indicate values that were more favorable than risk-based alone, CDC model
    - $338,000 per QALY gained

[a.] Cost-saving indicates an intervention strategy yielded higher health outcomes (more QALYs, fewer episodes of disease) and lower costs than the comparator.

Acknowledgements

- This presentation summarizes work conducted by four modeling groups
  - CDC Team
    - Charles Stoecker[a], Miwako Kobayashi[b], Bo-Hyun Cho[b], Tamara Pilishvili[b]
  - Merck Team
    - Kwame Owusu-Edusei[c], Arijita Deb[c], Kelly Johnson[c], Oluwaseun Sharomi[c], Elamin Elbasha[c], Thomas Weiss[c], Temi Folaranmi[c], Craig Roberts[c], Donald Yin[c], Richard Haupt[c], Tufail Malik[c]
  - Pfizer Team
    - Derek Weycker[d], Ahuva Averin[d], Mark Atwood[d], Melody Shaff[d], Reiko Sato[e], Erica Chilson[e], Vincenza Snow[e], Alejandro Cane[e], Raymond Farkouh[e]

- Thank you to other CDC and ACIP contributors, reviewers, and colleagues
  - Fangjun Zhou, Bo-Hyun Cho, Kai Hong, Jamie Pike, Harrell Chesson, Yuping Tsai, Tom Clark, Shannon Stokley

[a.] Tulane University; [b.] CDC; [c.] Merck; [d.] Policy Analysis Inc (PAI); [e.] Pfizer;

Disclaimers:
(1) 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.
(2) Three models described in this study are under review by the ACIP economics team.