Economics of Vaccinating U.S. Adults ≥60 years-old against Respiratory Syncytial Virus

A SUMMARY REPORT COMPARING MODELS FROM:

GSK*, *Pfizer* AND *University of Michigan-CDC

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NCIRD/CDC

ACIP Meeting, February 23, 2023

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

Conflict of interest

- **GSK model**: Daniel Molnar et al., [complete list and affiliations, upon request]
  - GSK manufactures the adjuvanted RSVPreF3 vaccine
  - RTI Health Solutions was funded by GSK

- ***Pfizer* model**: Derek Weycker et al., [complete list and affiliations, upon request]
  - Pfizer manufacturers the bivalent RSVpreF vaccine
  - Policy Analysis Inc. was funded by Pfizer

- **UM-CDC model**: David W Hutton et al. from Univ Michigan, …, ***Ismael R Ortega-Sanchez*** *et al.* from CDC [complete author list and affiliations, upon request]
  - All authors: No conflicts of interest

Economic analysis

Policy questions: Should adults ≥60 years of age (or ≥65 years of age) receive one dose of Respiratory Syncytial Virus (RSV) vaccine (GSK or Pfizer product) for the prevention of RSV disease and its complications?

Question: Is vaccinating adults aged ≥65 years (or ≥60 years) against RSV *cost-effective*?

Comparator
Unvaccinated
≥65yr-olds
(or ≥60yr-olds)

Intervention
Vaccinating
≥65yr-olds
(or ≥60yr-olds)

Base-case scenario: What is the incremental *cost-effectiveness* of vaccinating adults aged ≥65 years (or ≥60 years) using RSV vaccine relative to "No vaccination"?

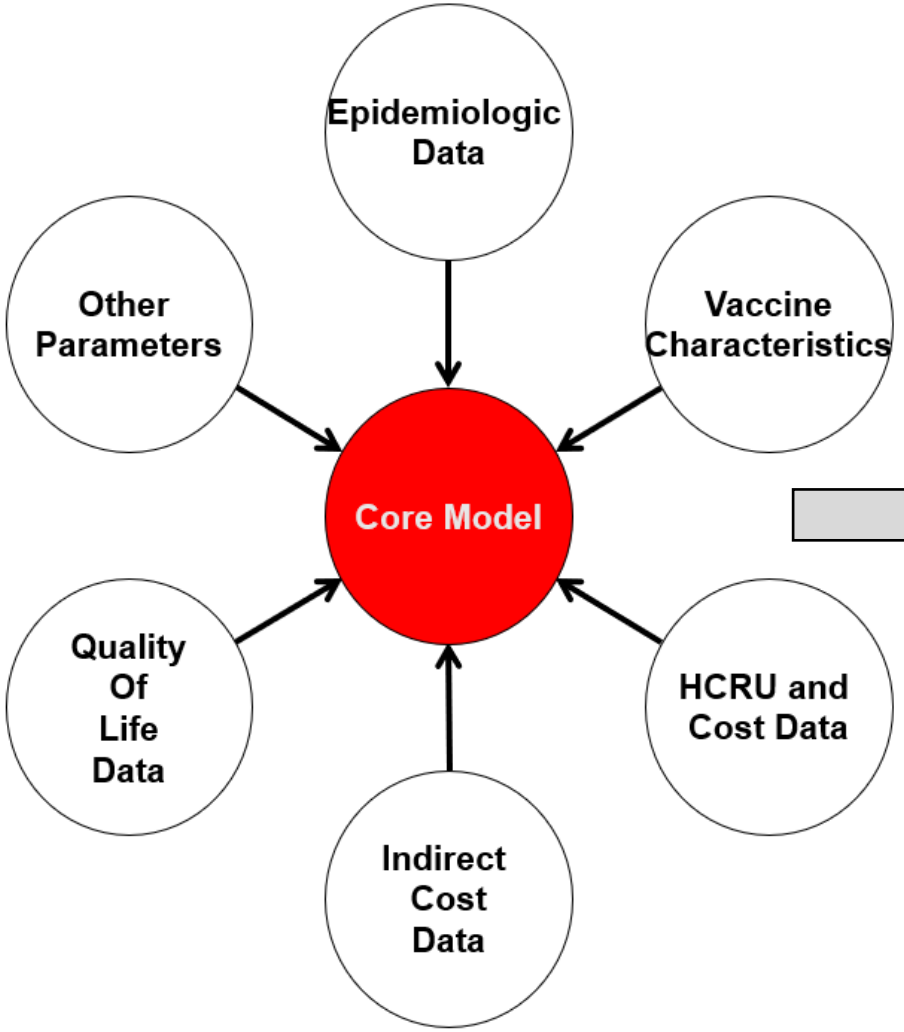
Focus on key features for model comparison

- Modeling approach
  - Targeted population(s)
  - Perspective (healthcare vs. societal)
  - Intervention strategy and comparator
- Inputs for RSV disease burden, vaccine efficacy, and costs
  - Incidence of RSV disease, rates of outcomes
  - Direct and Indirect costs of RSV disease
  - Intervention: Vaccine efficacy, duration of protection, safety and program costs
- Assumptions
  - Strong, influential assumptions

Modeling design and assumptions

	GSK	*Pfizer*	UM-CDC
Static analytical decision-making models	✓	✓	✓
Sensitivity analyses (and probabilistic simulation)	✓(✓)	✓(✓)	✓
Hypothetical population ≥65yrs-old (and ≥60-yrs-old)	✓(✓)	✓(✓)	✓(✓)
Time Frame: at least 1 yr. after a dose of RSV vaccine	✓	✓	✓
Analytic Horizon: Age-specific Life Expectancy	✓	✓	✓
Discount rate: 3%	✓	✓	✓
Year of economic outcomes measured: 2022	✓	✓	✓
Societal perspective (and healthcare perspective)	✓(✓)	✓(✓)	✓(✓)

Inputs and main outcomes



Prevention of:

- Outpatient visits for RSV
- RSV hospitalizations
- RSV-associated deaths

GSK	*Pfizer*	UM-CDC
✓	✓	✓
✓	✓	✓
✓	✓	✓

QALYs saved

$/QALY saved

✓	✓	✓
✓	✓	✓

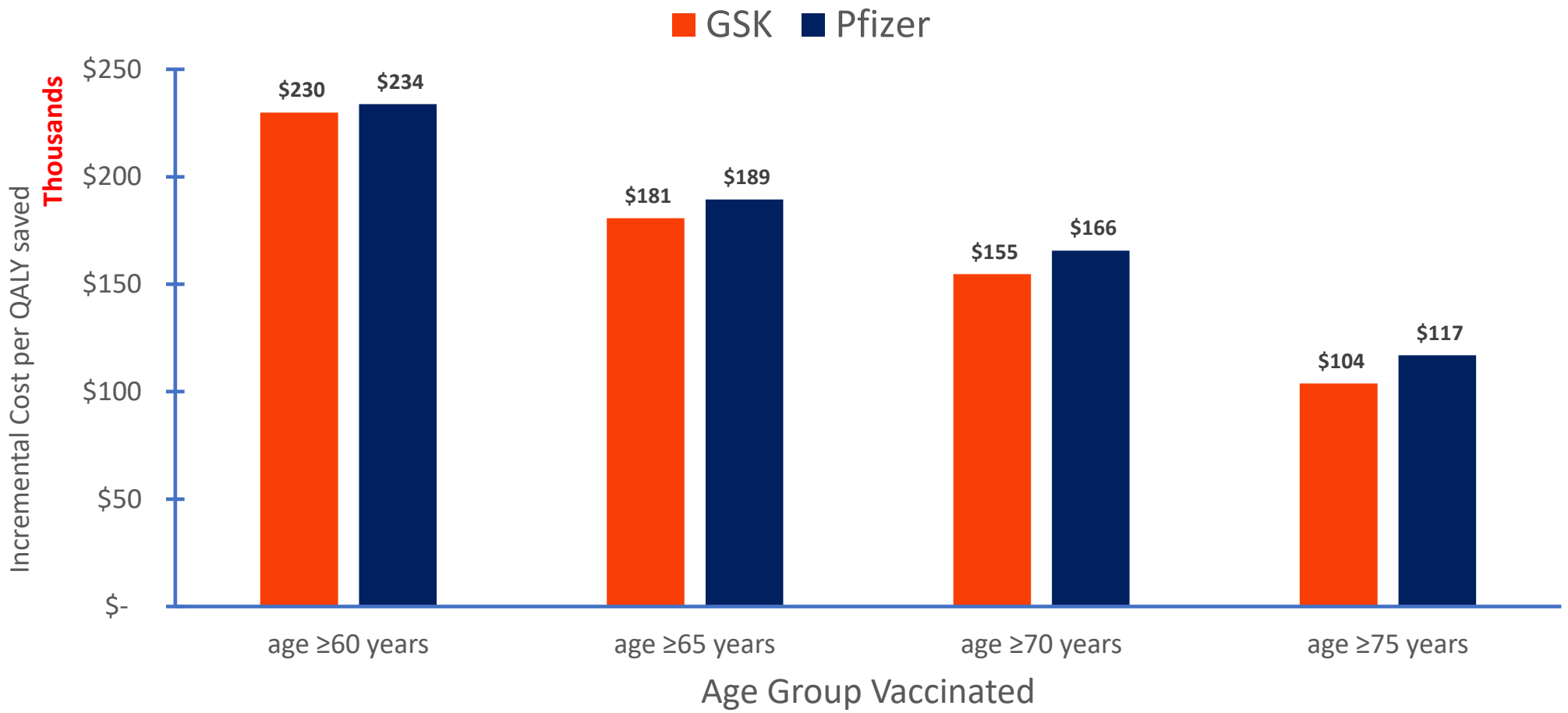
Number needed to vaccinate (NNV) to avert an:

- Outpatient visit for RSV
- RSV hospitalization
- RSV-associated death

✓	✓	✓
✓	✓	✓
✓	✓	✓

HCRU = health care resource use

UMich-CDC: Scenario analysis for age group, $100 vaccine cost and vaccine candidate



GSK, *Pfizer* and UM-CDC models comparison: Selected outcome ratios for RSV vaccines

GSK vaccine

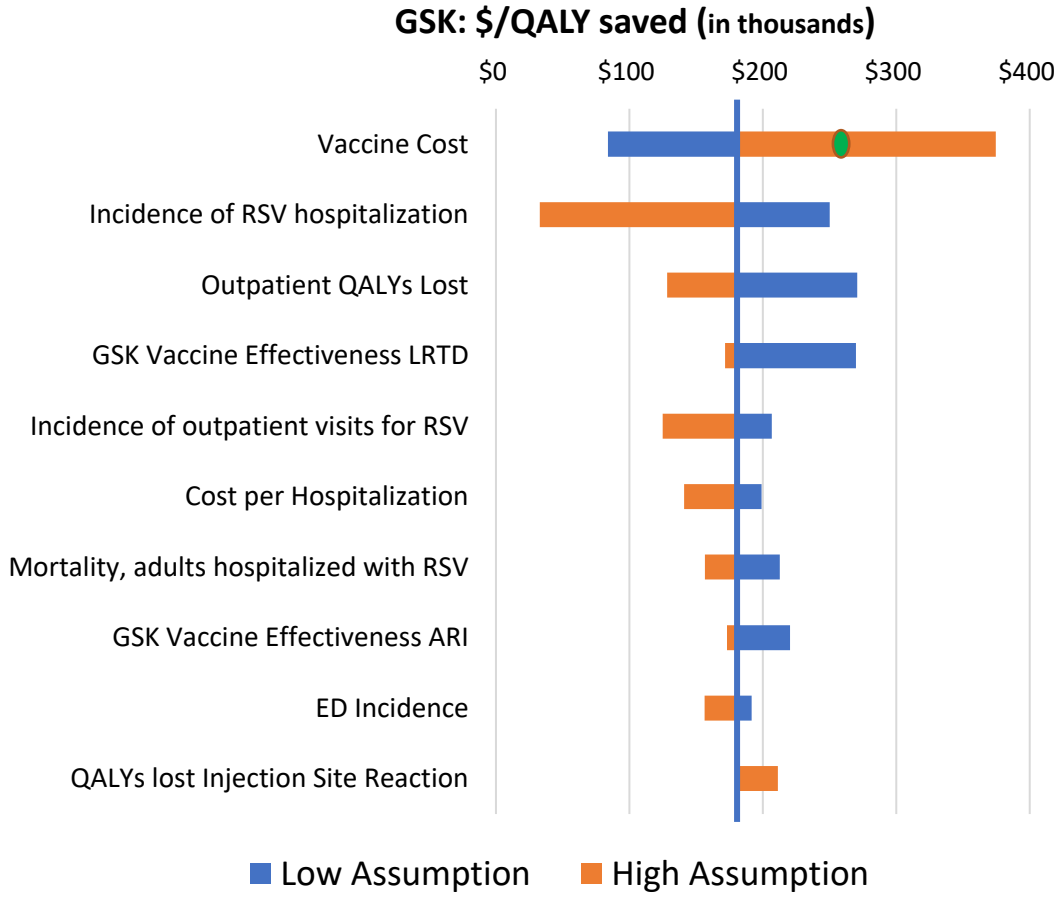
	UM-CDC model Vac Price $100	GSK model Vac Price $148
$ / QALY gained		
Vaccinating adults ≥65 yrs.	**180,720**	**68,489**
Vaccinating adults ≥60 yrs.	**229,895**	**78,971**
$ / hospitalization averted		
Vaccinating adults ≥65 yrs.	101,406	57,114
Vaccinating adults ≥60 yrs.	133,992	69,638

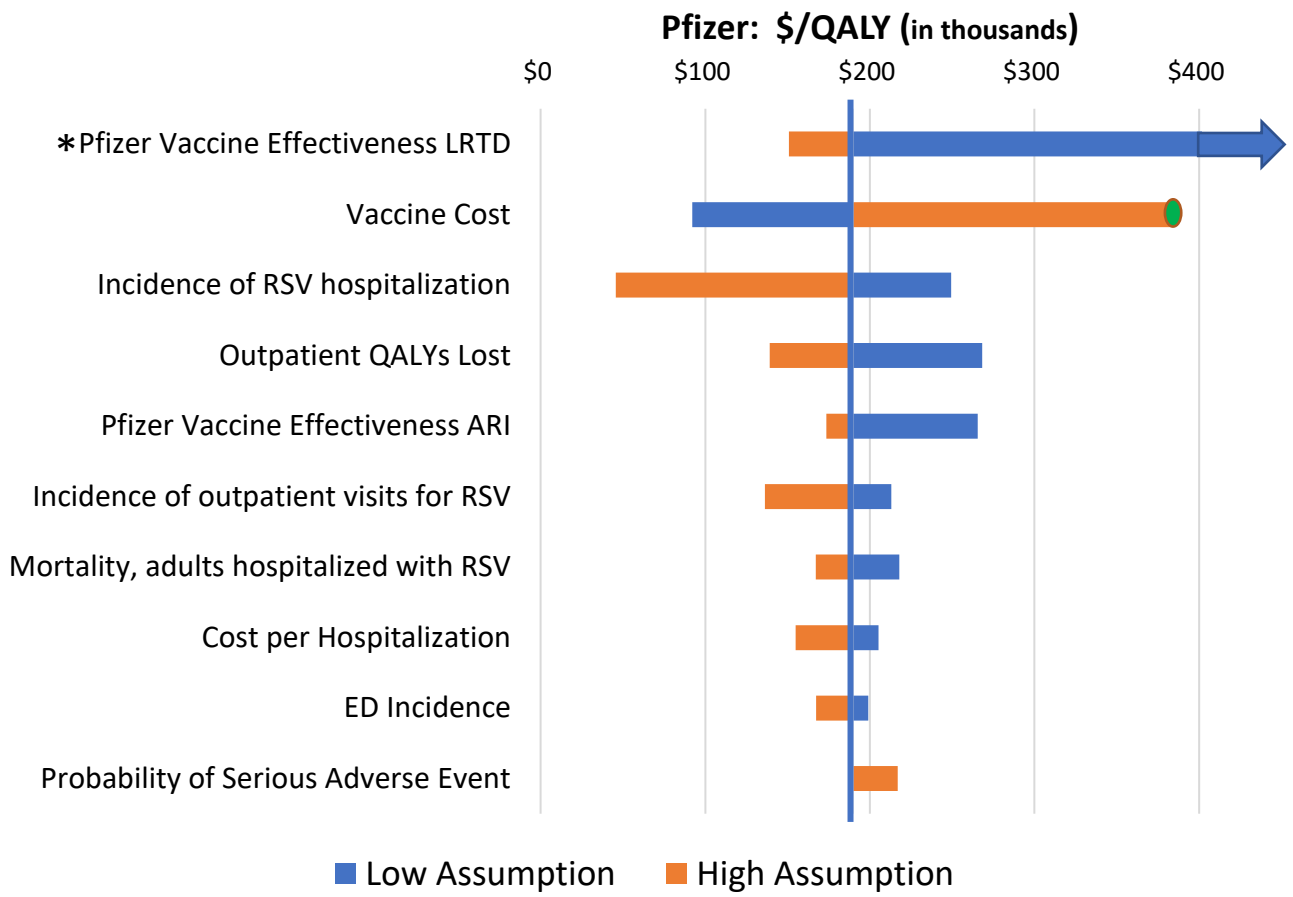
Pfizer vaccine

	UM-CDC model Vac Price $100	*Pfizer* model Vac Price $200
$ / QALY gained		
Vaccinating adults ≥65 yrs.	**189,407**	**43,749**
Vaccinating adults ≥60 yrs.	**233,779**	**50,197**
$ / hospitalization averted		
Vaccinating adults ≥65 yrs.	122,886	19,845
Vaccinating adults ≥60 yrs.	161,310	23,271

UM-CDC model: One-way Sensitivity Analyses

Base case: Age ≥65yrs $180,720/QALY (GSK), $189,407/QALY (Pfizer)



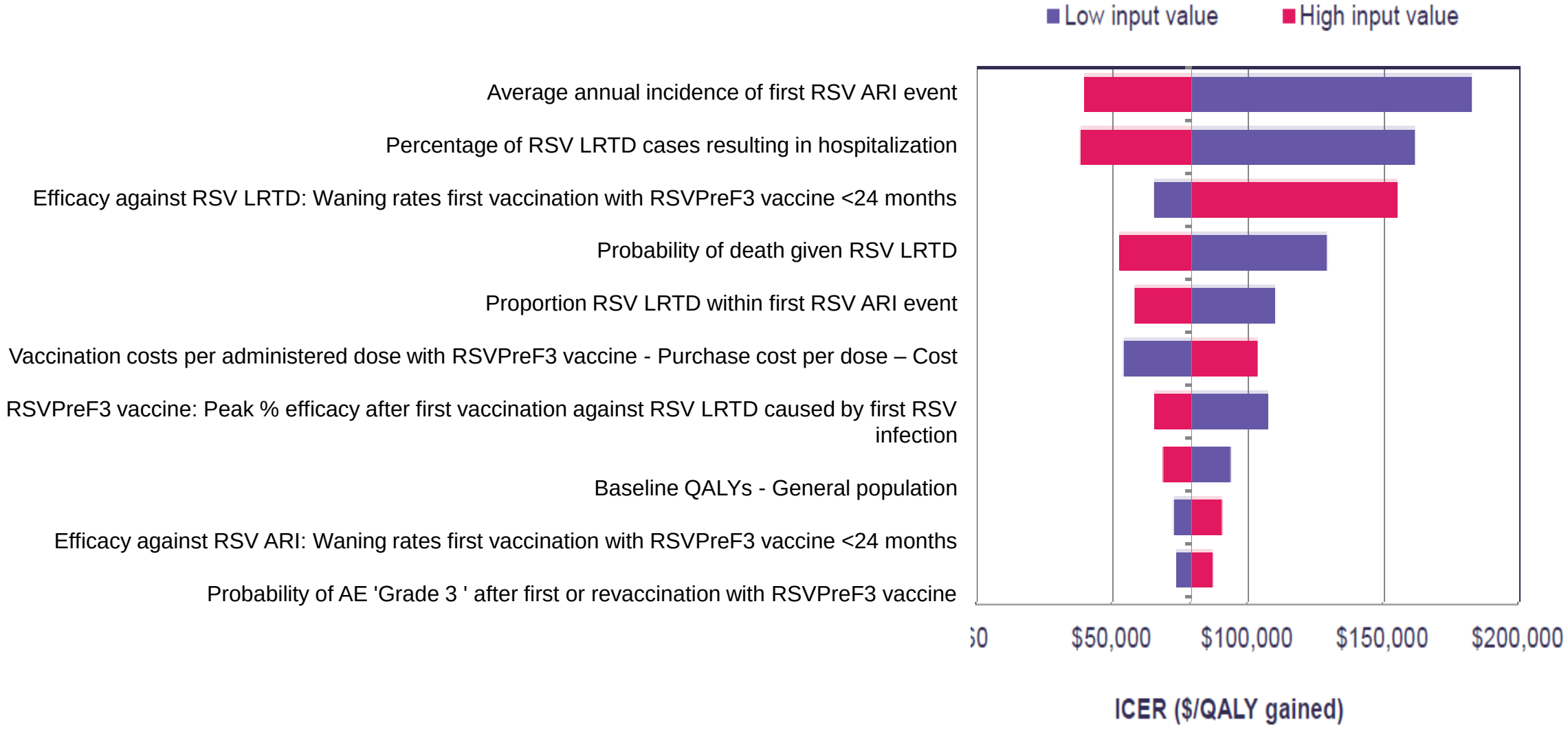


One Year Time Horizon

* At lower bound of Pfizer vaccine efficacy (VE =6.3%), the ICER rises to >$574 Thousand /QALY

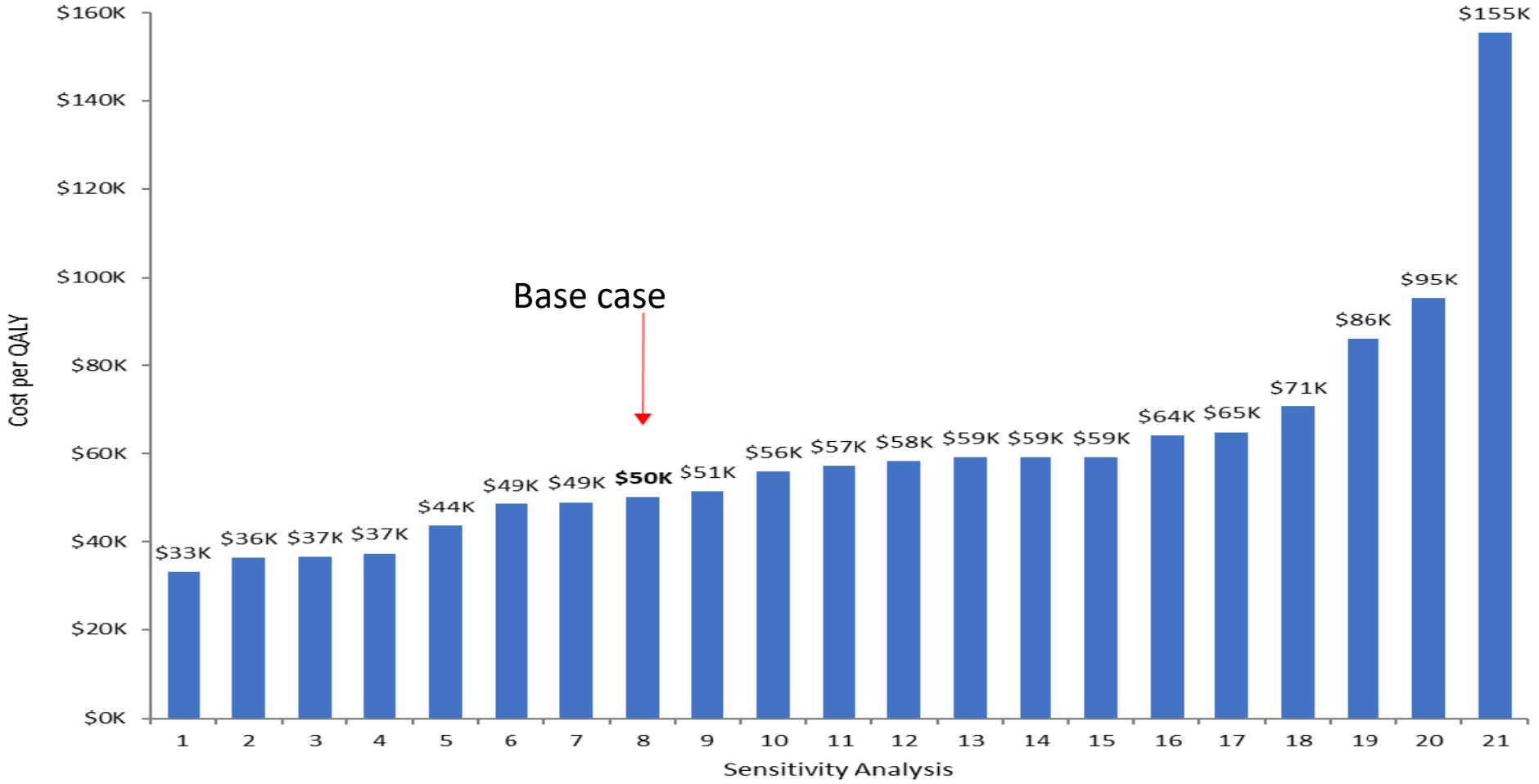
GSK model: One-way Sensitivity Analyses

Base case: Age ≥60 years; $ 78,971 /QALY saved



Pfizer model: One-way Sensitivity Analyses

Base case: Age≥60 years: $50,104/QALY saved



21. VE against RSV-Hospital lower bound
20. Vaccine price =270
19. RSV-Hospital CRF=5%
18. US healthcare system perspective
17. VE against RSV-PO/HO lower bound
16. Medical care cost lower bound

GSK, *Pfizer* and UM-CDC models comparison: Selected inputs

- RSV-hospitalization rate
  - GSK: Proportion of MA RSV hospitalized cases identified by PCR, differentiated by age (Belongia, 2018)
  - *Pfizer*: Differentiated by age and comorbidity profile (Pfizer data on file)
  - CDC: Differentiated by age (four RSV seasons in CDC RSV-NET data)
- Unitary medical cost of RSV outcomes
  - GSK: Age- & outcome specific cost for symptomatic RSV LRTD & URTI cases (MA and non-MA) (CMS)
  - *Pfizer:* Age-, outcome- & comorbidity-specific cost for MA RSV
  - CDC: Age- & outcome-specific cost for MA RSV
- Initial VE & waning over time
  - GSK: Phase 3, monthly waning: ARI (5.36%), LRTD (2.63%) until 12mos, then to 0%
  - *Pfizer:* Phase 3, flat 7mos, then linear decay to 0% at 24mos
  - CDC: GSK's & Pfizer's phase 3, flat 6mos, exponential decay until 12mos, then to 0%

MA = medically attended, ARI = acute respiratory infection

GSK, *Pfizer* and UM-CDC models: Key differences in model inputs

	UM-CDC	GSK	*Pfizer*
Incidence of RSV outpatient illness (per 100,000 persons per year)	1,519 (base-case for adults ≥65 years)[a]	1,348 (for adults ≥65 years)[b]	2,430 (base case for adults ≥65 years)[c]
Incidence of RSV hospitalization (per 100,000 persons per year)	**108** (base-case for adults ≥65 years)[d]	**256** (for adults ≥65 years)[b,e]	**300** (base-case for adults ≥65 years)[c]
Direct medical costs per RSV hospitalization	$20,330 – $21,339 (age-dependent)[f]	$13,112 – $26,224 (age-dependent)[g,h]	$12,048 – $38,380 (age- and comorbidity-dependent)[h,i]

a McLaughlin et al. Open Forum Infect Dis (2022): https://doi.org/10.1093/ofid/ofac300; unadjusted for under-detection of RT-PCR testing
b Adapted from Belongia et al. Open Forum Infect Dis (2018): https://doi.org/10.1093/ofid/ofy316
c McLaughlin et al. Open Forum Infect Dis (2022): https://doi.org/10.1093/ofid/ofac300; Ramirez et al. (under review)
d RSV-NET, CDC unpublished data
e Adapted from Falsey et al. NEJM (2005): https://doi.org/10.1056/nejmoa043951; Herring et al. Vaccine (2022): https://doi.org/10.1016/j.vaccine.2021.12.002
f Ackerson et al. J Infect Dis (2020): https://doi.org/10.1093/infdis/jiaa183
g CMS Medicare Inpatient Hospitals (DRG Average Payments from 2019 dataset)
h Kaiser Family Foundation (How much more than Medicare do private insurers pay? 2020): https://www.kff.org/medicare/issue-brief/how-much-more-than-medicare-do-private-insurers-pay-a-review-of-the-literature/
i Merative MarketScan Commercial Claims and Encounters (CCAE) and Medicare Supplemental Coordination of Benefits (MDCR) Databases (2016-2019)

GSK model: Sensitivity of Cost per QALY saved to RSV-Related Hospitalization Rates among Adults ≥60 years

S8: Branche et al. (2022b; high BoD season [New York City, 2018-2019]);

S9: Branche et al. (2022b; low BoD season [Rochester, 2019-2020]);

S10: Zheng et al. (2022; low SES);

S11: Zheng et al. (2022; medium SES);

S12: Zheng et al. (2022; high SES);

S13: McLaughlin et al. (2022; unadjusted);

S14: **McLaughlin et al. (2022; adjusted);**

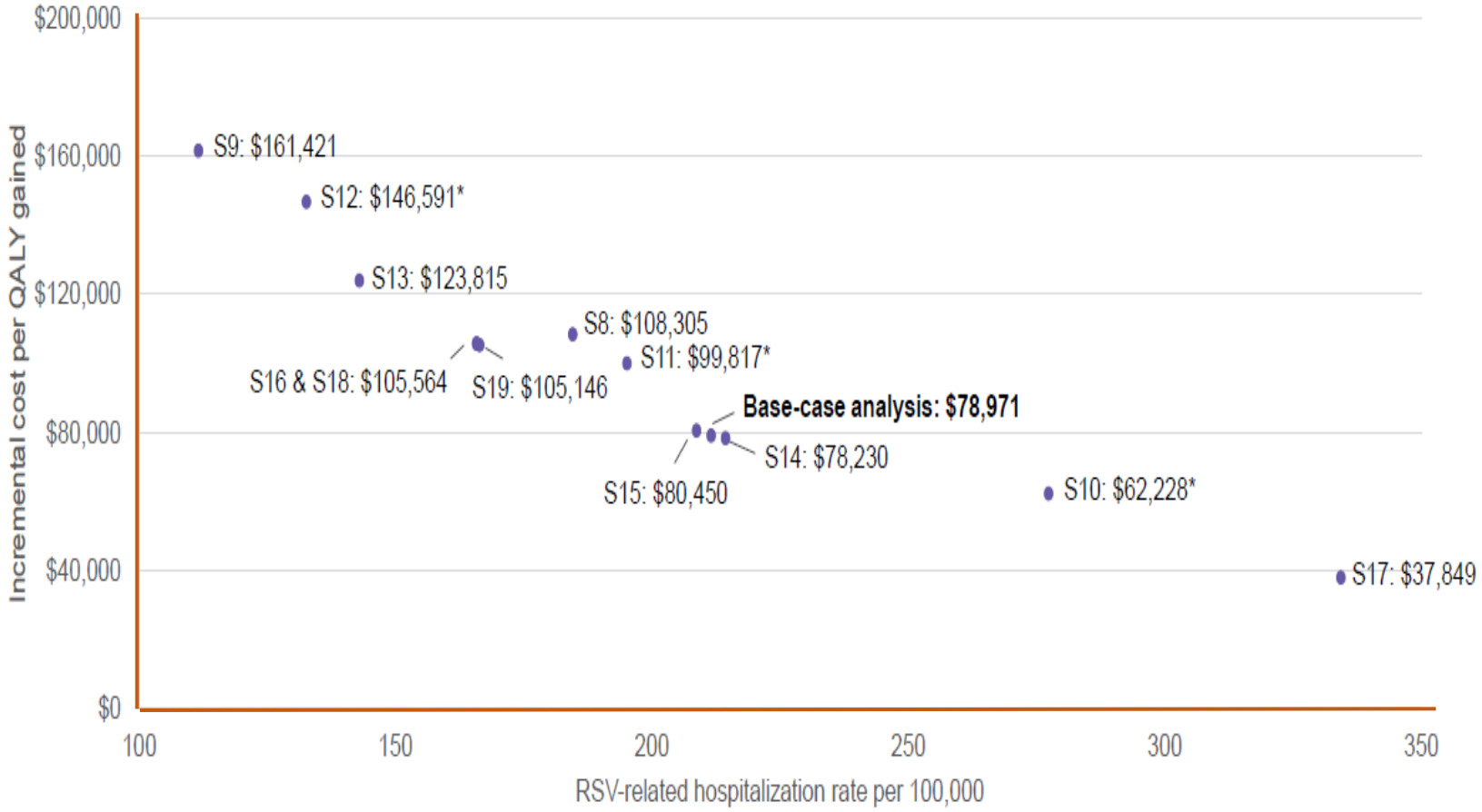
S15: **Widmer et al. (2012);**

S16: Herring et al. (2022; Belongia et al. [2018] estimate);

S17: Herring et al. (2022; Falsey et al. [2005] estimate);

S18: DeMartino et al. (2022);

S19: Fust et al. (2022a and 2022b).

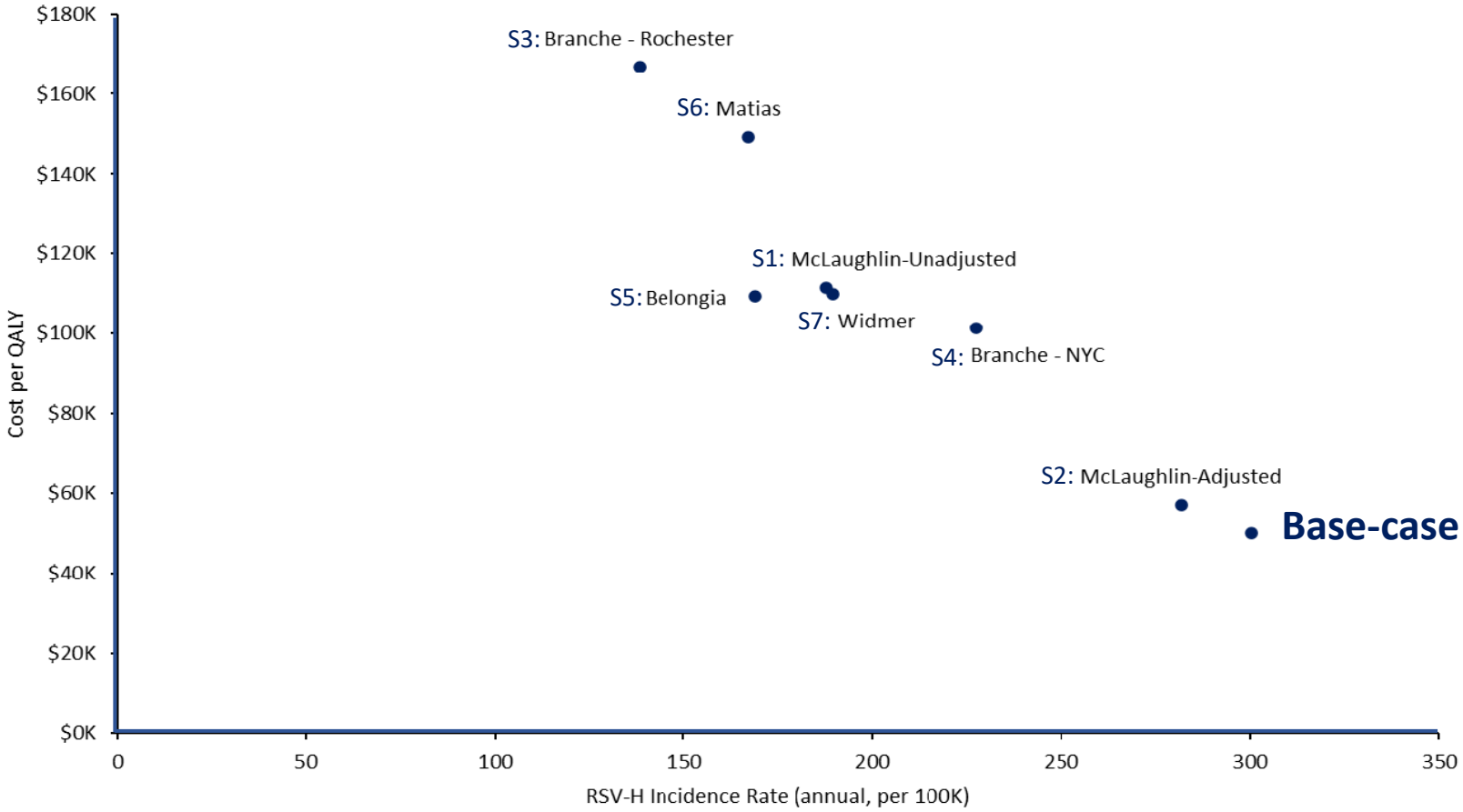


Note: BoD = burden of disease; SES = socioeconomic status.
* Derived from GSK modeling results.

Pfizer model: Sensitivity of Cost per QALY saved to RSV-Related Hospitalization Rates among Adults ≥60 years

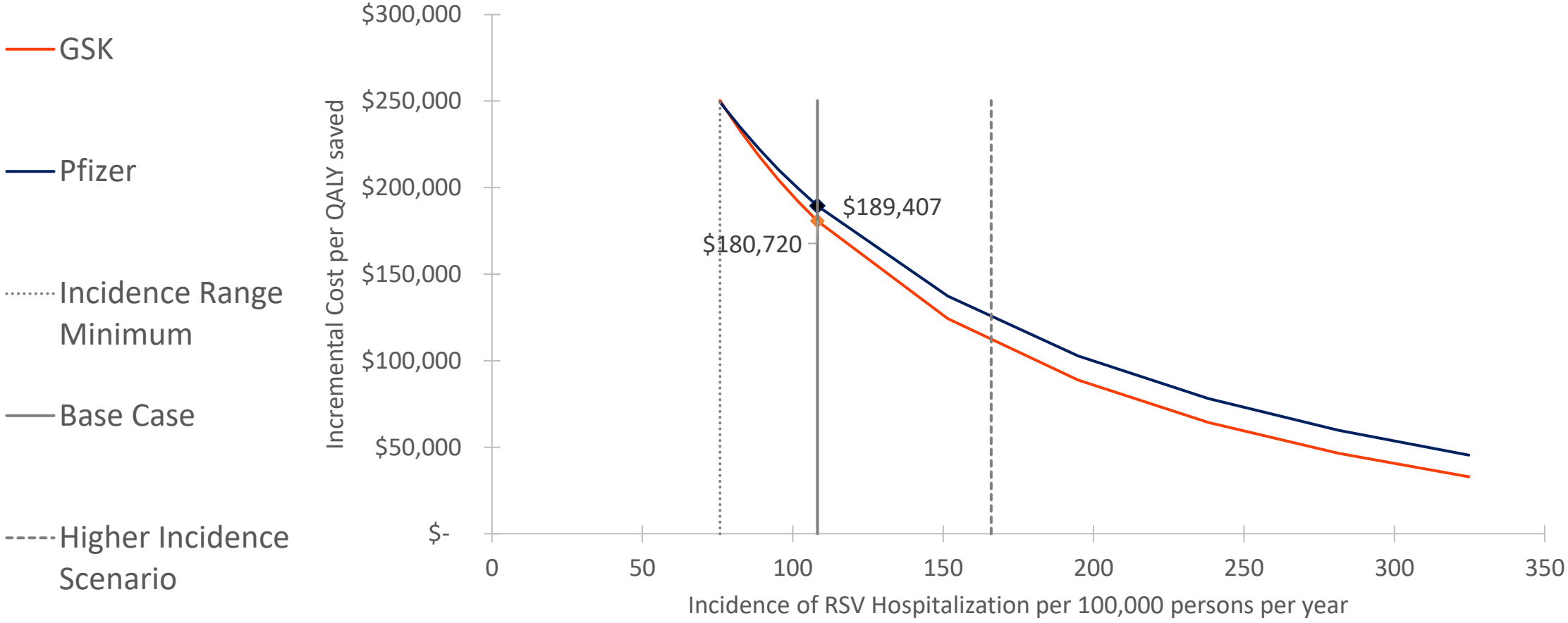
- **S1**: Pooled ***unadjusted*** rates from McLaughlin et al. (active prospective surveillance studies only)[1]
- **S2**: Based on pooled ***adjusted*** rates from McLaughlin et al. 1.5-fold (active prospective surveillance studies only)[1]
- **S3**: Rates in Rochester, NY, averaged across all study years, from Branche et al.[2]
- **S4**: Rates in New York, NY, averaged across all study years, from Branche et al.[2]
- **S5**: Rates averaged across all study years and accounting for the ***proportion of RSV-confirmed cases*** treated in hospital from Belongia et al.[3]
- **S6**: Rates based on Matias et al.[4]
- **S7**: Rates based on Widmer et al.[5]

Base Case: **Ongoing unvetted prospective study with adjusted RSV detection rates of** 1.6- to 1.7-fold. **Pfizer Inc. data on file**



1. McLaughlin JM, et al. *Open Forum Infectious Diseases*. 9(7), 2022
2. Branche AR et al. *Clinical Infectious Diseases*. 2021;74(6):1004-1011.
3. Belongia et al. *Open Forum Infect Dis*. 2018;5(12):ofy316.
4. Matias et al. *BMC Public Health*. 2017;17(1):271.
5. Widmer et al. *Influenza and Other Respiratory Viruses*. 2014;8(3):347-352.

UM-CDC model: Sensitivity of Cost per QALY saved to RSV-Related Hospitalization Rates among Adults ≥65 years



Base case: mean value of the burden adjusted rate over RSV seasons: 2015-16, 2016-17, 2017-18, and 2018-19. Adjusted rate for 95% sensitivity of PCR testing. CDC RSVnet
Lower bound: mean of lower confidence limit estimates across all 4 seasons assuming 95% sensitivity of PCR testing.
Upper bound: mean of upper confidence limit estimates across all 4 seasons assuming 71% sensitivity of PCR testing.

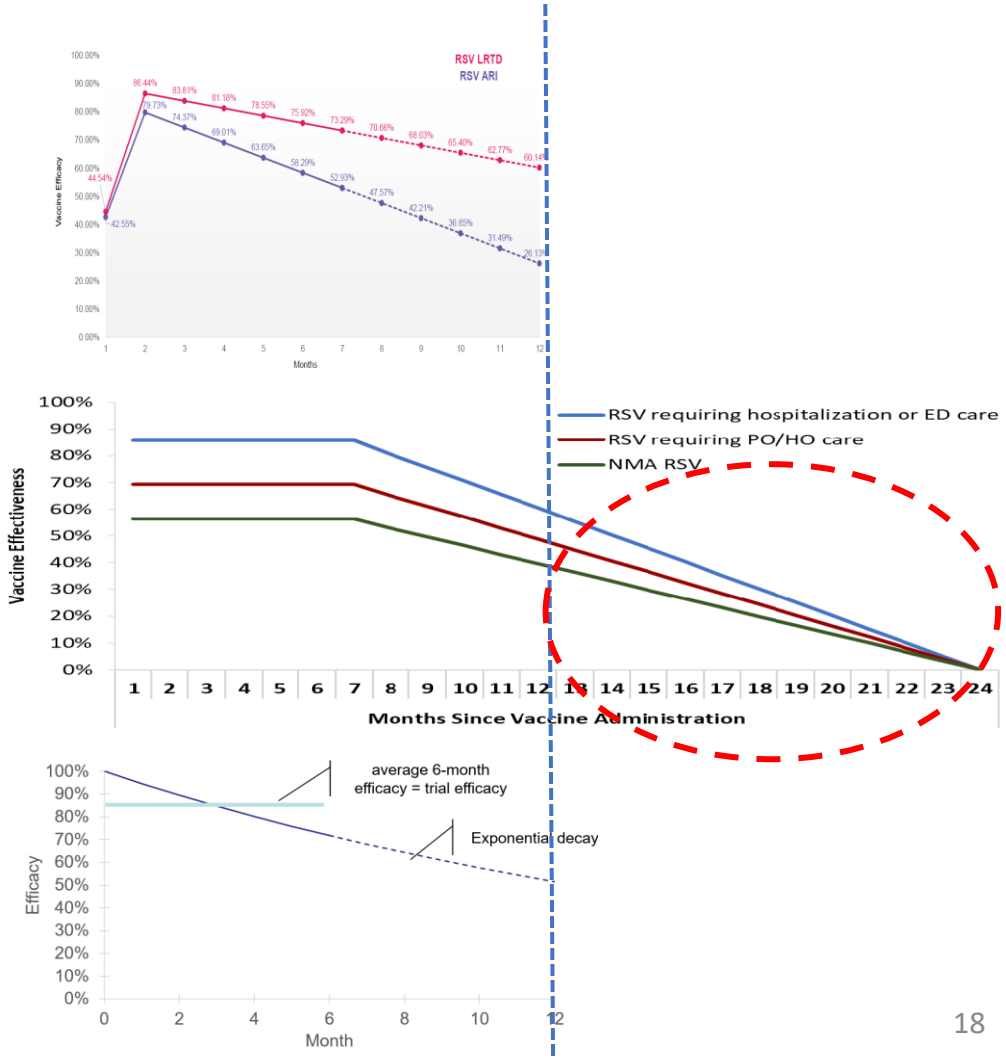
GSK, *Pfizer* and UM-CDC: Initial or Early Peak of Vaccine Efficacy

	UM-CDC		GSK	*Pfizer*
	GSK vaccine	**Pfizer vaccine**		
Vaccine efficacy (VE) against RSV outpatient illness[a]	79.0 (54.3–91.5)[b]	69.2 (30.0–88.0)[b]	71.7 (56.7–82.3)[c]	69.2 (30.0–88.0)[b]
VE against RSV hospitalization and emergency department visit[a]	87.5 (58.4–96.2)[d]	80.0 (6.3–97.9)[d]	82.6 (57.9–94.1)[e]	85.7 (37.9–98.4)[e]

a VE over mean 6–7 months of follow up in phase 3 clinical trials
b Manufacturer phase 3 trial data; VE against medically attended acute respiratory illness
c GSK phase 3 trial data; IDWeek abstract; VE against acute respiratory illness, regardless of whether medically attended
d Manufacturer phase 3 trial data; GSK: VE against medically attended lower respiratory tract disease; Pfizer: VE against medically attended lower respiratory tract illness with ≥3 lower respiratory symptoms
e Manufacturer phase 3 trial data; GSK: IDWeek abstract VE against lower respiratory tract disease, regardless of whether medically attended; Pfizer: IDWeek abstract VE against lower respiratory tract illness with ≥3 lower respiratory symptoms, regardless of whether medically attended (95% CI applied)

GSK, *Pfizer* and UM-CDC: Assumption on waning of vaccine efficacy (VE) per outcome

GSK	VE peaks at 2 months then wanes per month RSV-ARI = 5.36% points per month (range: 0.00-13.37%) RSV-LRTD = 2.63% points per month (range: 0.00-10.95%) No residual protection after 12 months
Pfizer	Initial VE assumed to persist for 7 months, Then to decline linearly to 0% effectiveness at 24 months Residual though declining protection up to 24 months
UM-CDC	Vaccine and outcome-specific For both vaccines: Exponential decay up to 12 months and then 0% afterwards; calibrated such that the first 6 months VE equals the trial estimate



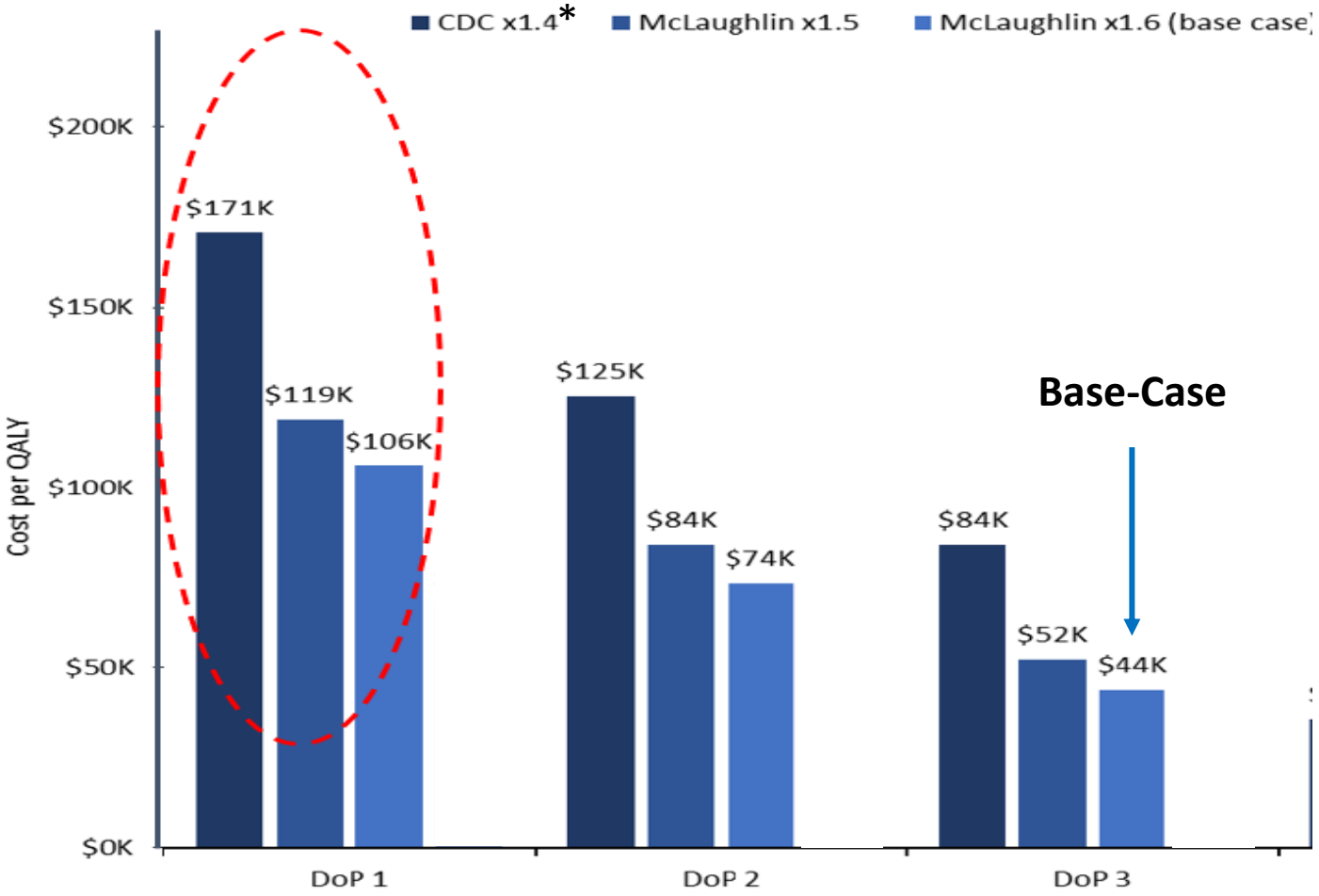
Pfizer: Impact of vaccine's duration of protection (DoP) assumption on ≥65yrs Cost per QALY saved

DoP 1: 7 months durable protection, followed by linear waning to 0% at 12 months

DoP 2: 7 months durable protection, followed by linear waning to 0% at 18 months

DoP 3: 7 months durable protection, followed by linear waning to 0% at 24 months

Base-Case



* RSV hospitalization incidence labelled "CDC x1.4" used data presented by CDC at IDWeek 2022 (Havers et al. https://doi.org/10.1093/ofid/ofac492.1828), upwardly adjusted by a factor of 1.4 (based on Zhang et al. https://doi.org/10.1128/jcm.01701-16).

Comparison of GSK and *Pfizer* vaccines: base case & scenario $/QALY results using UM-CDC model

Scenario	GSK	*Pfizer*
Vaccine cost $200 per dose (one year time frame)	$374,530	$384,267
Vaccinating adults aged ≥60 years	$229,895	$233,779
Medical cost for hospitalization (lower bound)	$199,018	$205,236
Base case [a] (Vaccine Price $100, 1 year time frame)	**$180,720**	**$189,407**
Higher incidence of RSV [b]	$91,028	$104,160
Vaccine cost $50 per dose (one year time frame)	$85,815	$91,977

a Recommendation = vaccination at age ≥65 years; vaccine unit cost = $100; incidence rates of RSV outcomes unadjusted for increased diagnostic yield from testing in addition to RT-PCR on a respiratory specimen; vaccine efficacy only considered for one year post-vaccination

b Base case incidence rates adjusted upward for increased diagnostic yield from testing in addition to RT-PCR on a respiratory specimen (1.5x for outpatient illness [McLaughlin et al; Open Forum Infect Dis (2022)], 1.4x for inpatient illness [Zhang et al; J Clin Microbiol(2016)])

Limitations

- **Factors not considered that may result in overestimating the ICER (underestimating the cost-effectiveness) of RSV vaccination**
  - None of the 3 models included RSV-related medical costs incurred after discharge from an RSV-associated hospitalization or emergency department visit:
    - Stay in long-term care or rehabilitation facility
    - Assisted living at home
    - Productivity losses incurred by caregivers whose support is needed post-discharge
  - All of the 3 models assumed no indirect effects of vaccination (i.e., no protection against RSV transmission)

- **Vaccine efficacy beyond clinical trial follow-up time (6–7 months) is <u>unknown</u>**
  - All 3 models assumed non-zero <u>declining</u> efficacy beyond 6–7 months (UM-CDC: 12 months, **GSK**: 12 months, ***Pfizer***: 24 months).

Conclusion

- **Differences in key inputs among GSK, *Pfizer* and UM-CDC models explain differences in results:**
  - Incidence of hospitalization
  - Duration of vaccine efficacy
  - Medical costs
  - Vaccine costs
- **Assumptions and selection of input data were crucial in differences in ICERs**
  - Adjustment approach of incidence rates of Hospitalization, ER and Outpatient
  - Selection of medical costs sources and data extraction approach
- **Base-case in the 3 models:**
  - Vaccination would significantly reduce RSV disease burden in older adults
    - VE clinical trials data and assumptions support impact on disease reduction
  - Economic value of RSV vaccines appear to be ***costly*** and could be *cost-effective*
    - RSV incidence, related healthcare costs, initial VE and duration combined with reasonable vaccine price would determine the ***cost-effectiveness*** value of RSV vaccination

Acknowledgements

From NCIRD/CDC

- Michael Melgar
- Jamison Pike
- Fiona Havers
- Meredith McMorrow

Also:

- Adult RSV working group members
- Econ Team members at ISD/NCIRD

End of Summary

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov