

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

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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 manufactures 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
 ≥ 65 yr-olds
(or ≥ 60 yr-olds)



Intervention

Vaccinating
 ≥ 65 yr-olds
(or ≥ 60 yr-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”?

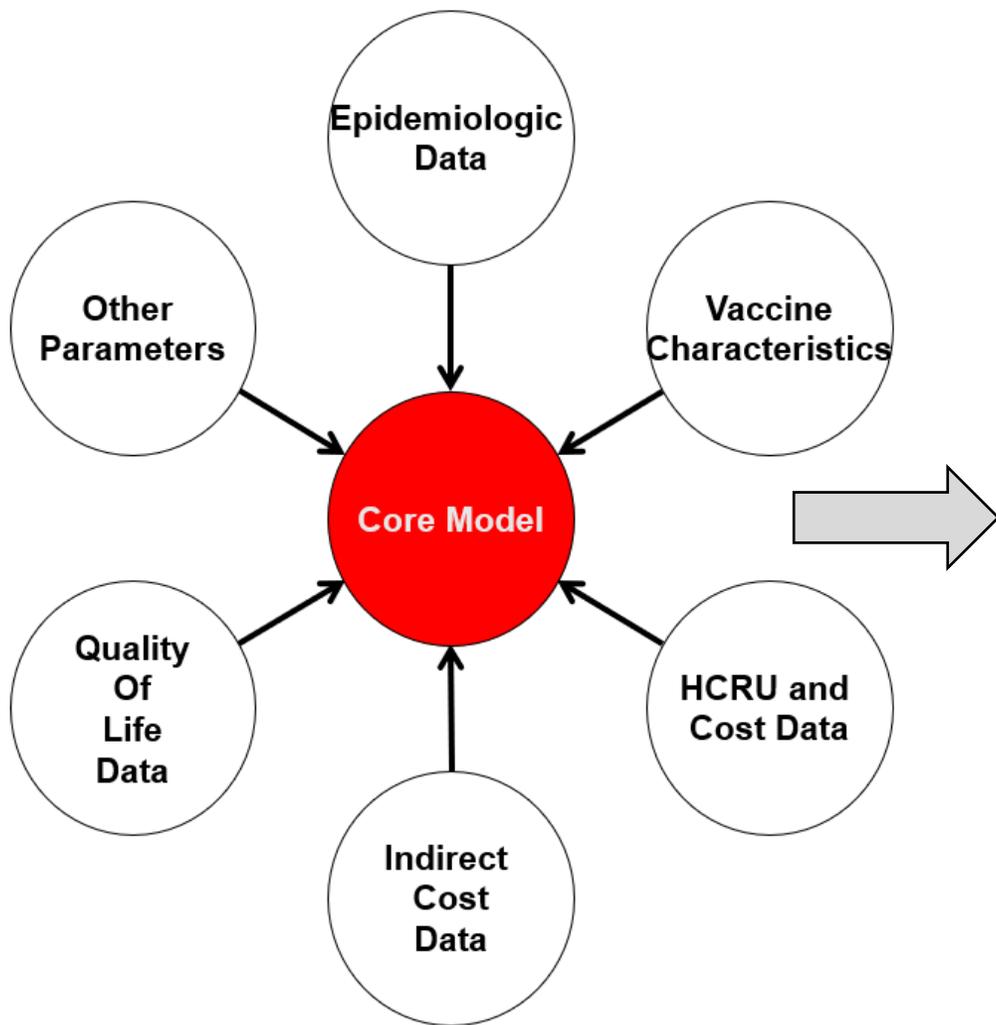
Focus on key features for model comparison

- 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
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✓	✓	✓
✓	✓	✓

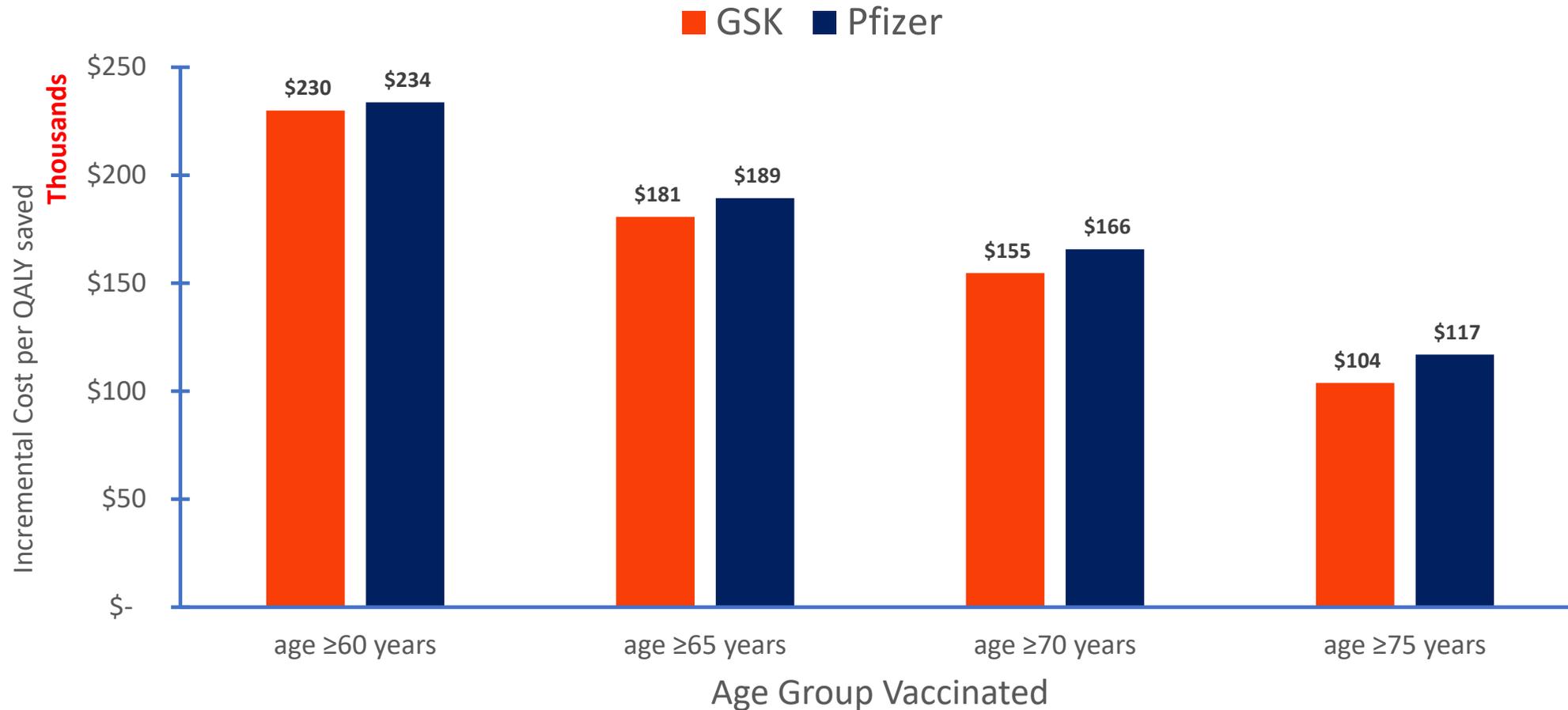
Number needed to vaccinate (NNV) to avert an:

- 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

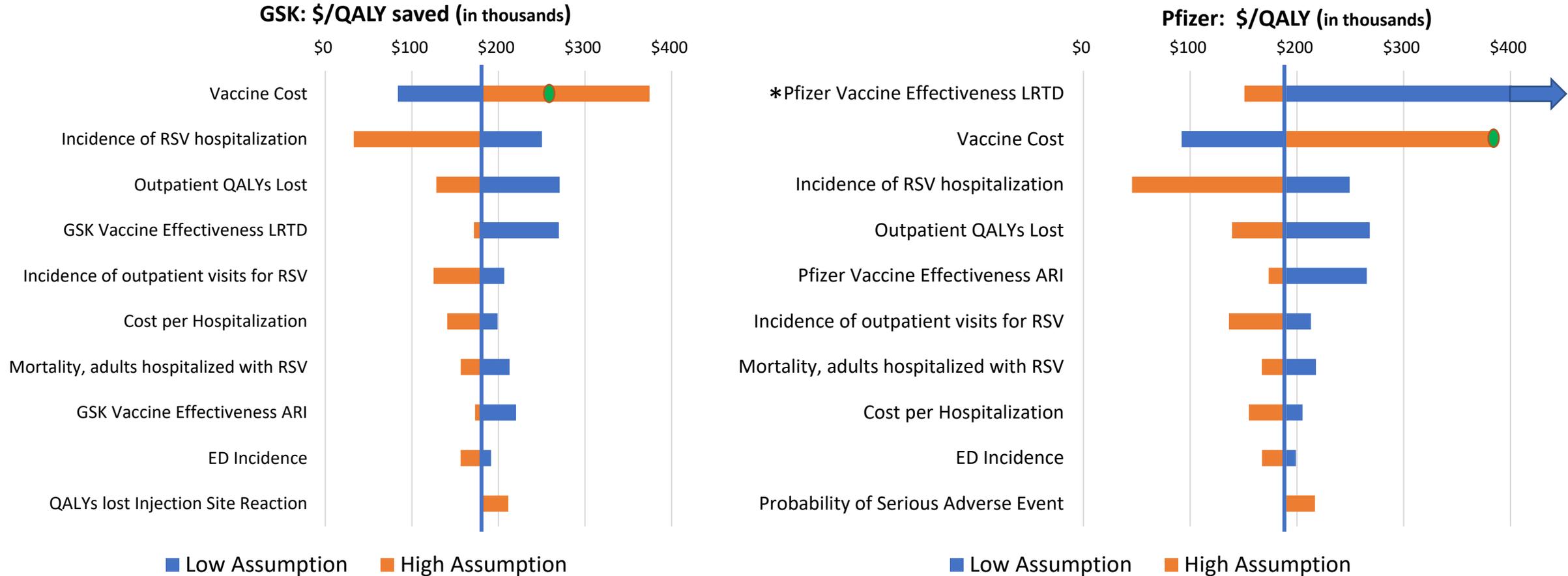
	UM-CDC model Vac Price \$100	GSK model Vac Price \$148
\$ / QALY gained		
Vaccinating adults ≥65 yrs.	180,720	68,489
Vaccinating adults ≥60 yrs.	229,895	78,971
\$ / hospitalization averted		
Vaccinating adults ≥65 yrs.	101,406	57,114
Vaccinating adults ≥60 yrs.	133,992	69,638

Pfizer vaccine

	UM-CDC model Vac Price \$100	<i>Pfizer</i> 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 ≥ 65 yrs \$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

Average annual incidence of first RSV ARI event

Percentage of RSV LRTD cases resulting in hospitalization

Efficacy against RSV LRTD: Waning rates first vaccination with RSVPreF3 vaccine <24 months

Probability of death given RSV LRTD

Proportion RSV LRTD within first RSV ARI event

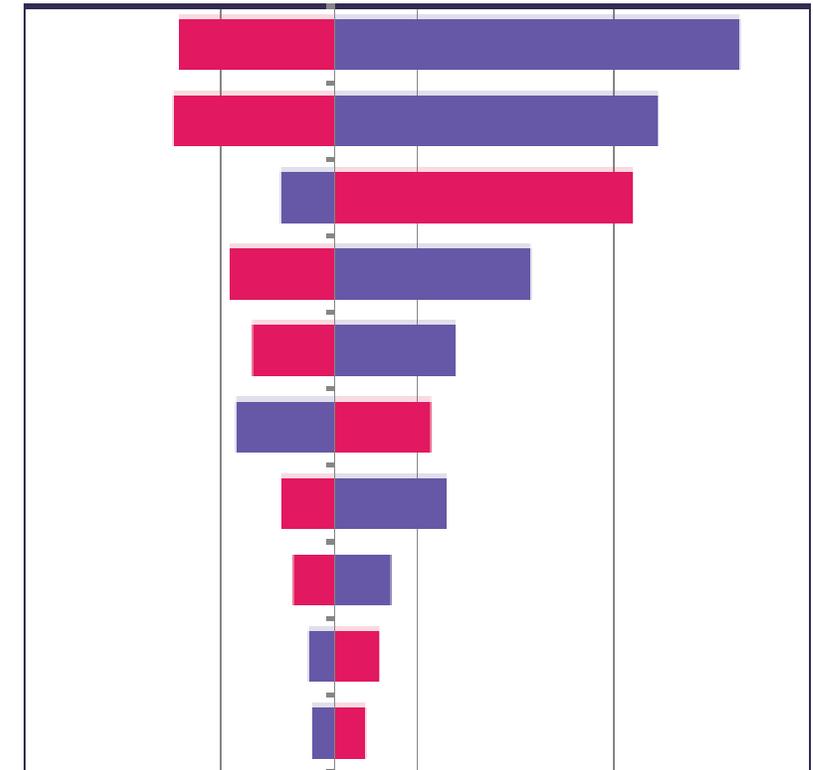
Vaccination costs per administered dose with RSVPreF3 vaccine - Purchase cost per dose – Cost

RSVPreF3 vaccine: Peak % efficacy after first vaccination against RSV LRTD caused by first RSV infection

Baseline QALYs - General population

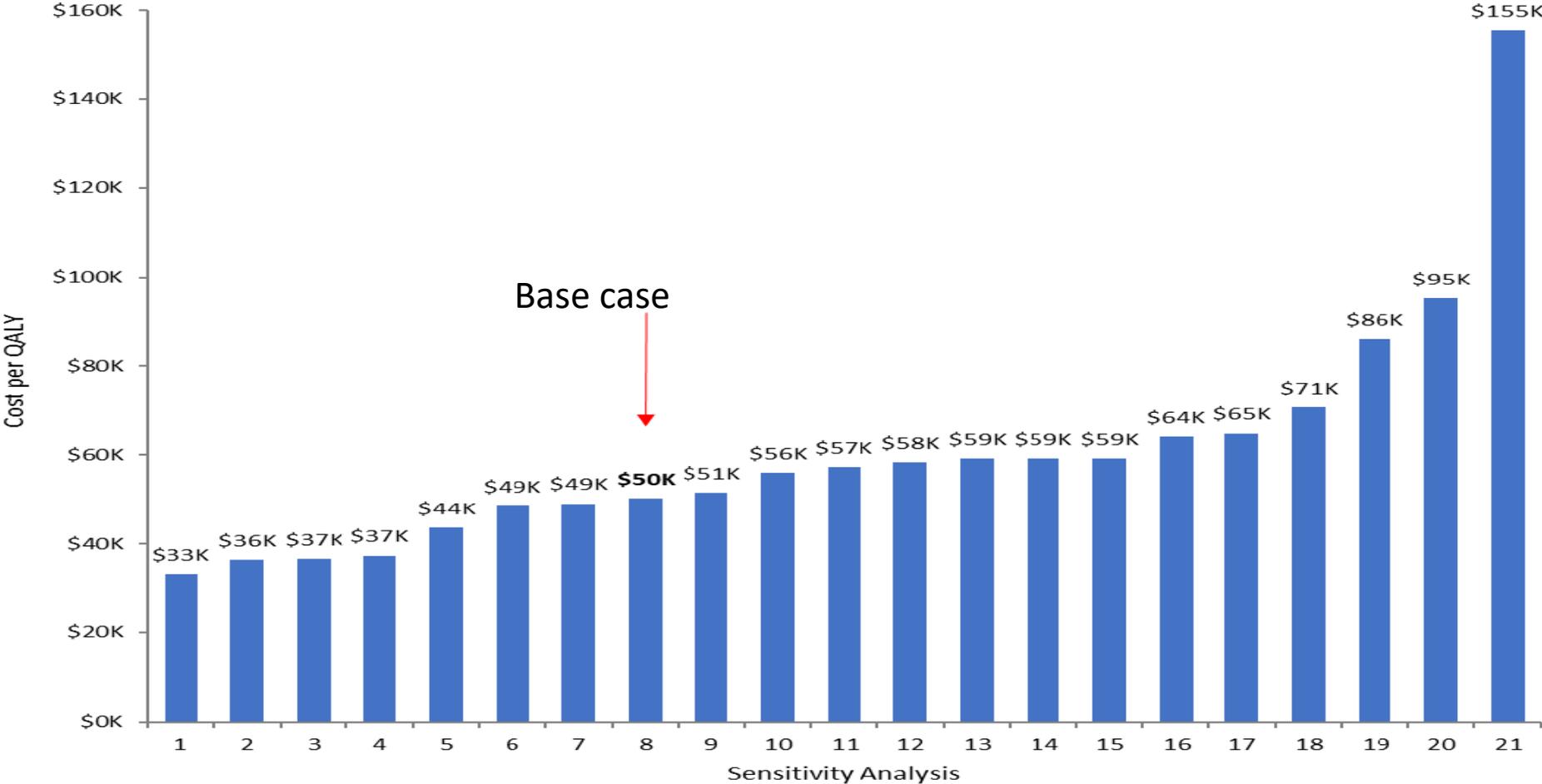
Efficacy against RSV ARI: Waning rates first vaccination with RSVPreF3 vaccine <24 months

Probability of AE 'Grade 3 ' after first or revaccination with RSVPreF3 vaccine



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%

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 (CAAE) 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);

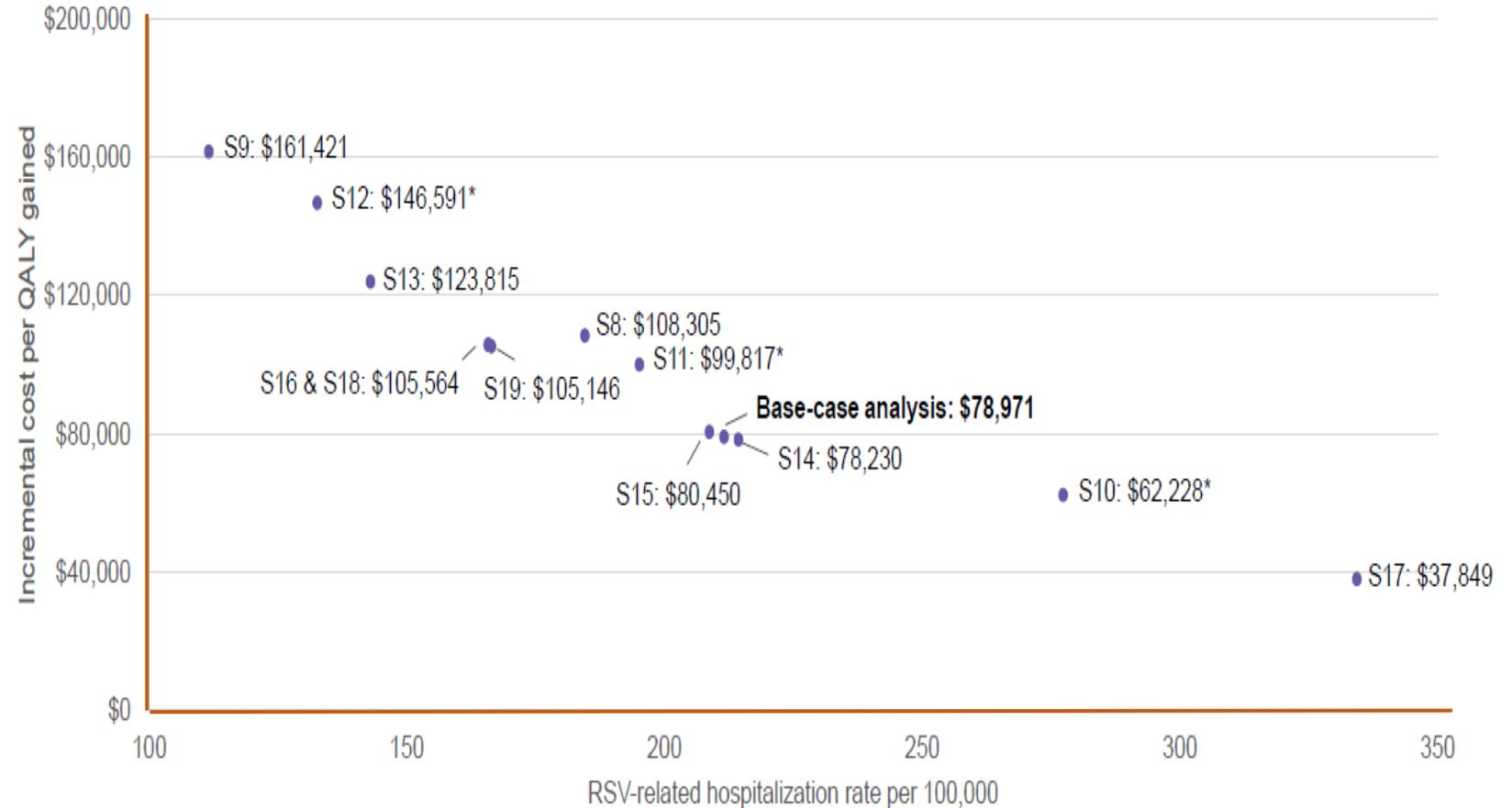
S15: Widmer et al. (2012);

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).



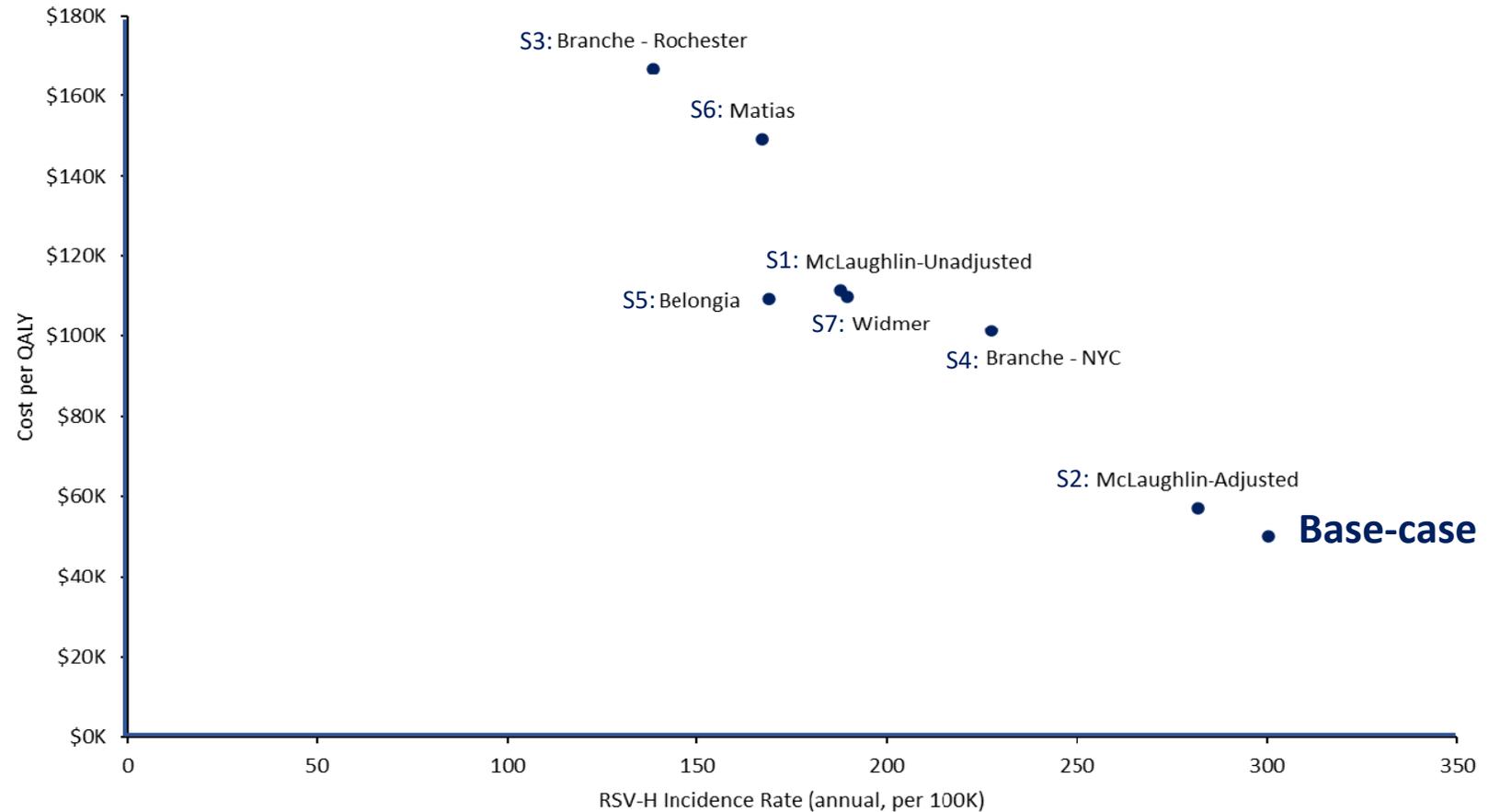
Note: BoD = burden of disease; SES = socioeconomic status.

* Derived from GSK modeling results.

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

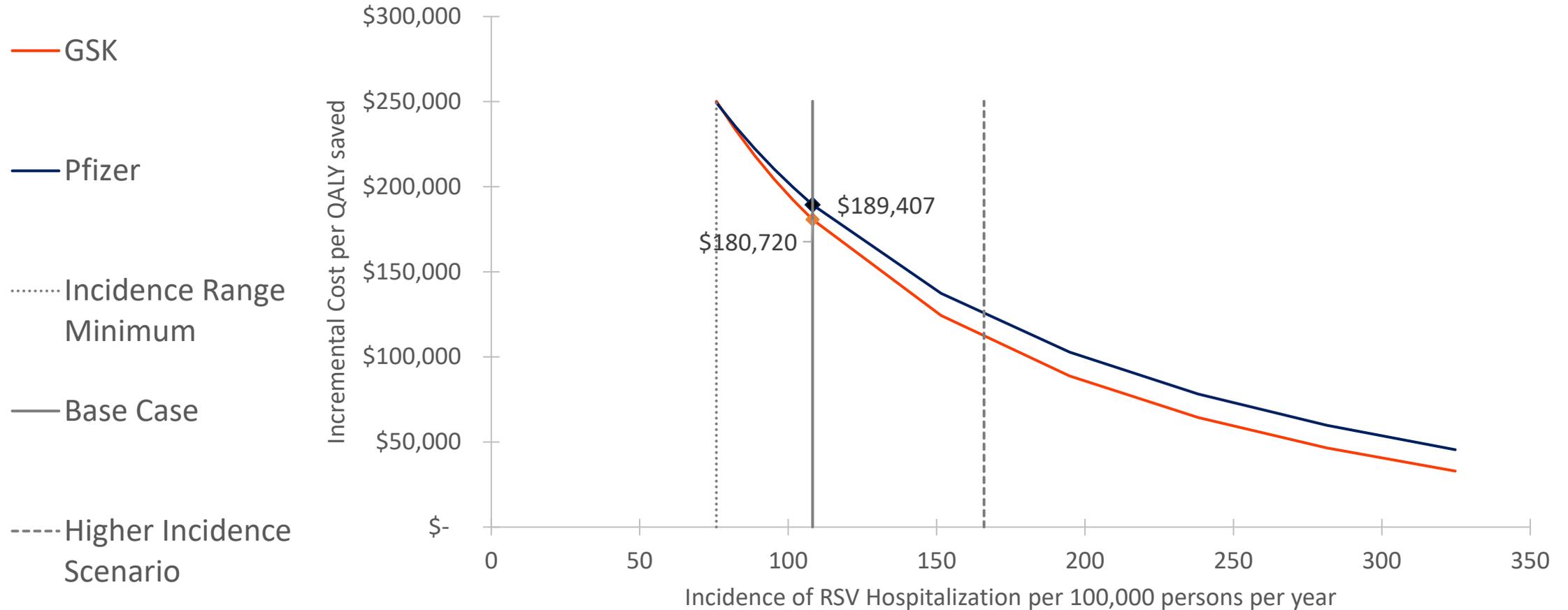
- **S1**: Pooled *unadjusted* rates from McLaughlin et al. (active prospective surveillance studies only)¹
- **S2**: Based on pooled *adjusted* rates from McLaughlin et al. 1.5-fold (active prospective surveillance studies only)¹
- **S3**: Rates in Rochester, NY, averaged across all study years, from 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

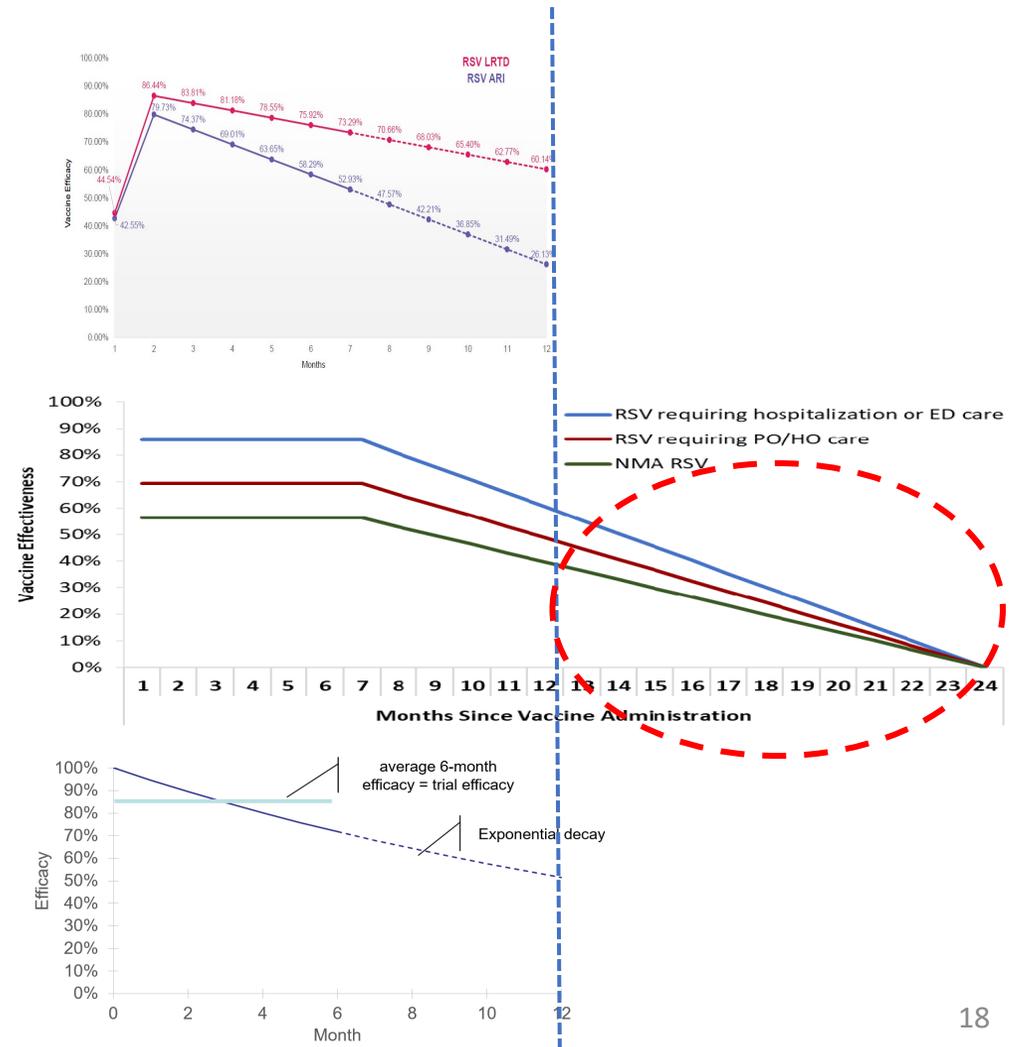
c GSK phase 3 trial data; [IDWeek abstract](#); VE against acute respiratory illness, regardless of whether medically attended

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	<p>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</p>
Pfizer	<p>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</p>
UM-CDC	<p>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</p>



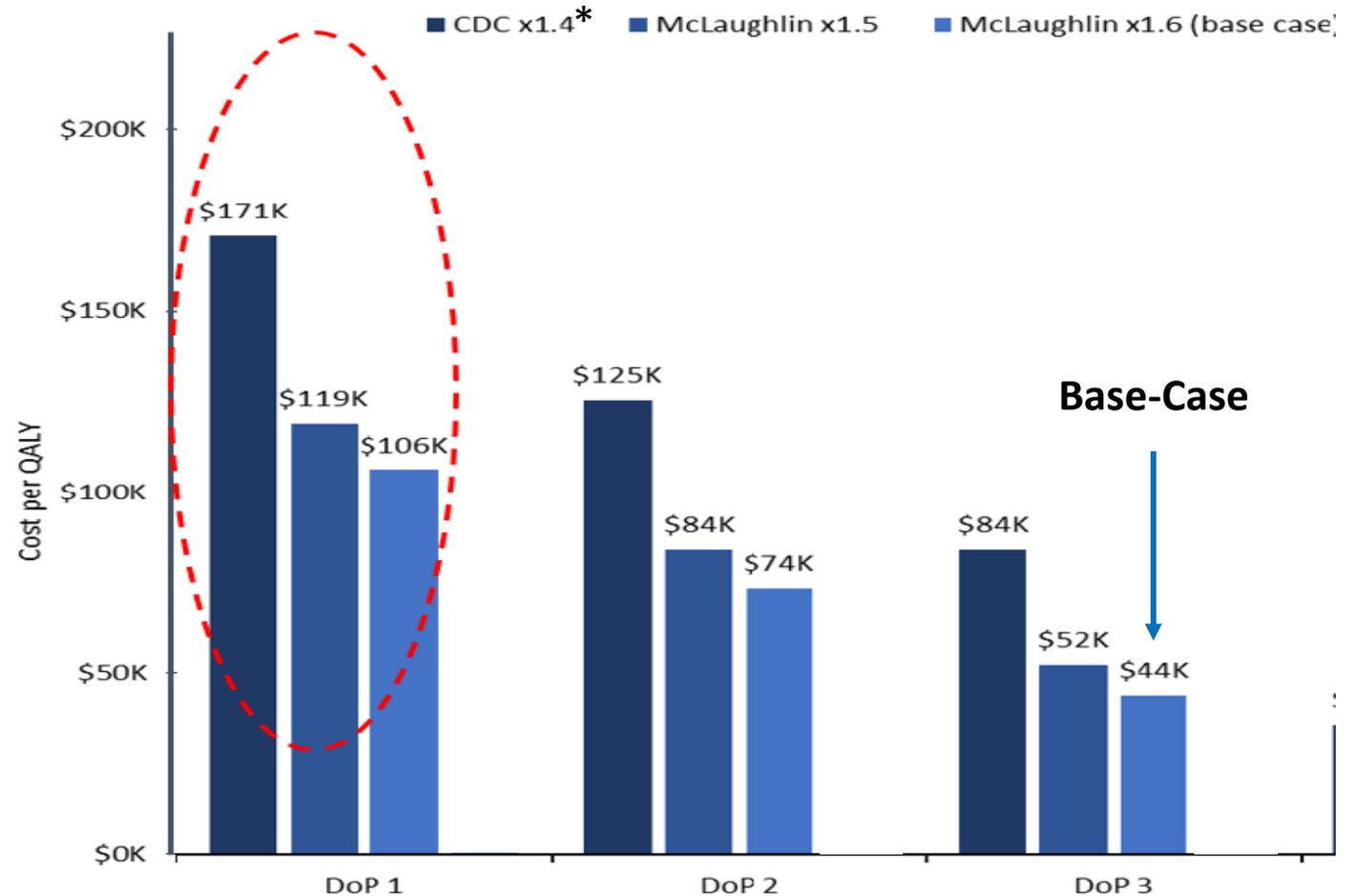
Pfizer. Impact of vaccine's duration of protection (DoP) assumption on ≥ 65 yrs Cost per QALY saved

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	<i>Pfizer</i>
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 unknown**
 - All 3 models assumed non-zero declining 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

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From NCIRD/CDC

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- Meredith McMorro

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

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