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

UPDATED SUMMARY 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 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 list and affiliations, upon request]
  - All authors: No conflicts of interest

Economic analysis

Policy questions: Should adults ≥65 years of age (or ≥60 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

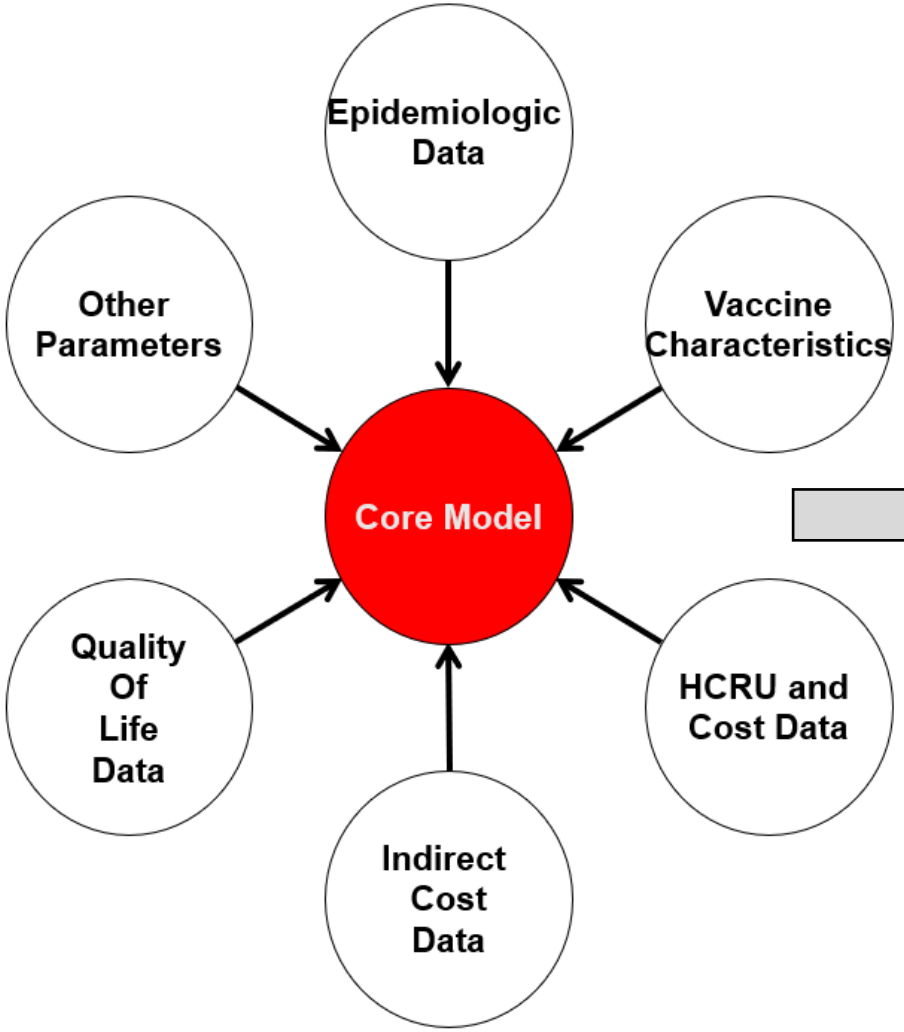
- Modeling approach
  - Targeted population(s)
  - Perspective (healthcare vs. societal)
  - Intervention strategy and comparator
- Inputs for RSV disease burden, vaccine efficacy, and costs
  - Incidence of RSV disease, rates of outcomes
  - Direct and indirect costs of RSV disease
  - Intervention: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

Note: For this and all slides, to specifically identify changes and updates from those presented last February 2023, the text will appear either highlighted, marked in red or with the word updated at the top of the slide or table.

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 2 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

QALYs saved

$/QALY saved

Number needed to vaccinate (NNV) to avert an:

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

GSK Updated	*Pfizer* Updated	UM-CDC Updated
✓	✓	✓
✓	✓	✓
✓	✓	✓
✓	✓	✓
✓	✓	✓
✓	✓	✓
✓	✓	✓
✓	✓	✓
✓	✓	✓

HCRU = health care resource use

GSK, *Pfizer* and UM-CDC models comparison: Selected outcome ratios for RSV vaccines (Feb 2023)

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

GSK, *Pfizer* and UM-CDC models comparison: Selected outcome ratios for RSV vaccines (June 2023)

GSK vaccine

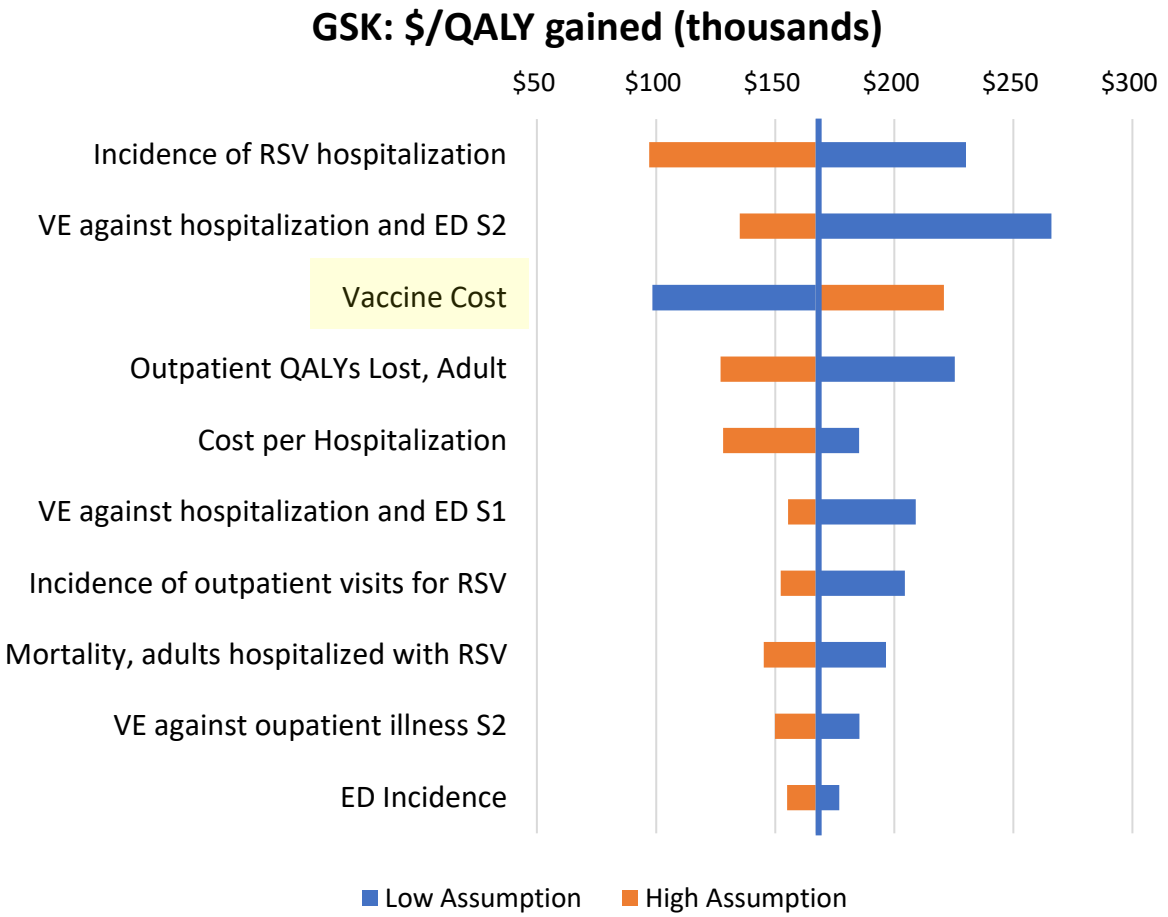
	UM-CDC model Vac Price $270	GSK model Vac Price $270
$ / QALY gained		
Vaccinating adults ≥65 yrs.	**167,301**	**55,088**
Vaccinating adults ≥60 yrs.	**205,638**	**64,348**
$ / hospitalization averted		
Vaccinating adults ≥65 yrs.	94,375	43,456
Vaccinating adults ≥60 yrs.	120,056	53,644

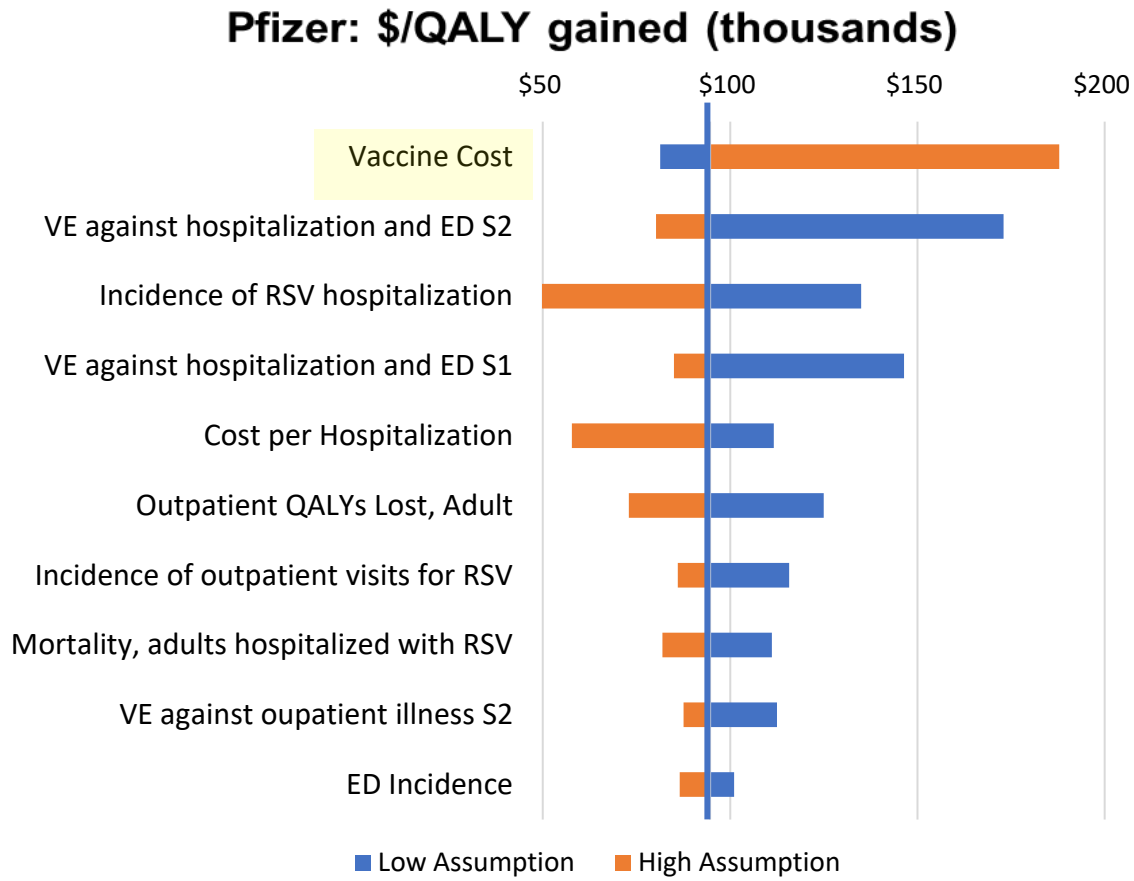
Pfizer vaccine

	UM-CDC model Vac Price $200	*Pfizer* model Vac Price $200
$ / QALY gained		
Vaccinating adults ≥65 yrs.	**94,673**	**19,585**
Vaccinating adults ≥60 yrs.	**118,735**	**23,921**
$ / hospitalization averted		
Vaccinating adults ≥65 yrs.	56,571	8,797
Vaccinating adults ≥60 yrs.	75,382	10,982

UM-CDC model: Updated One-way Sensitivity Analyses

Base case: Age ≥65yrs; $167,301/QALY (GSK), $94,673/QALY (Pfizer)





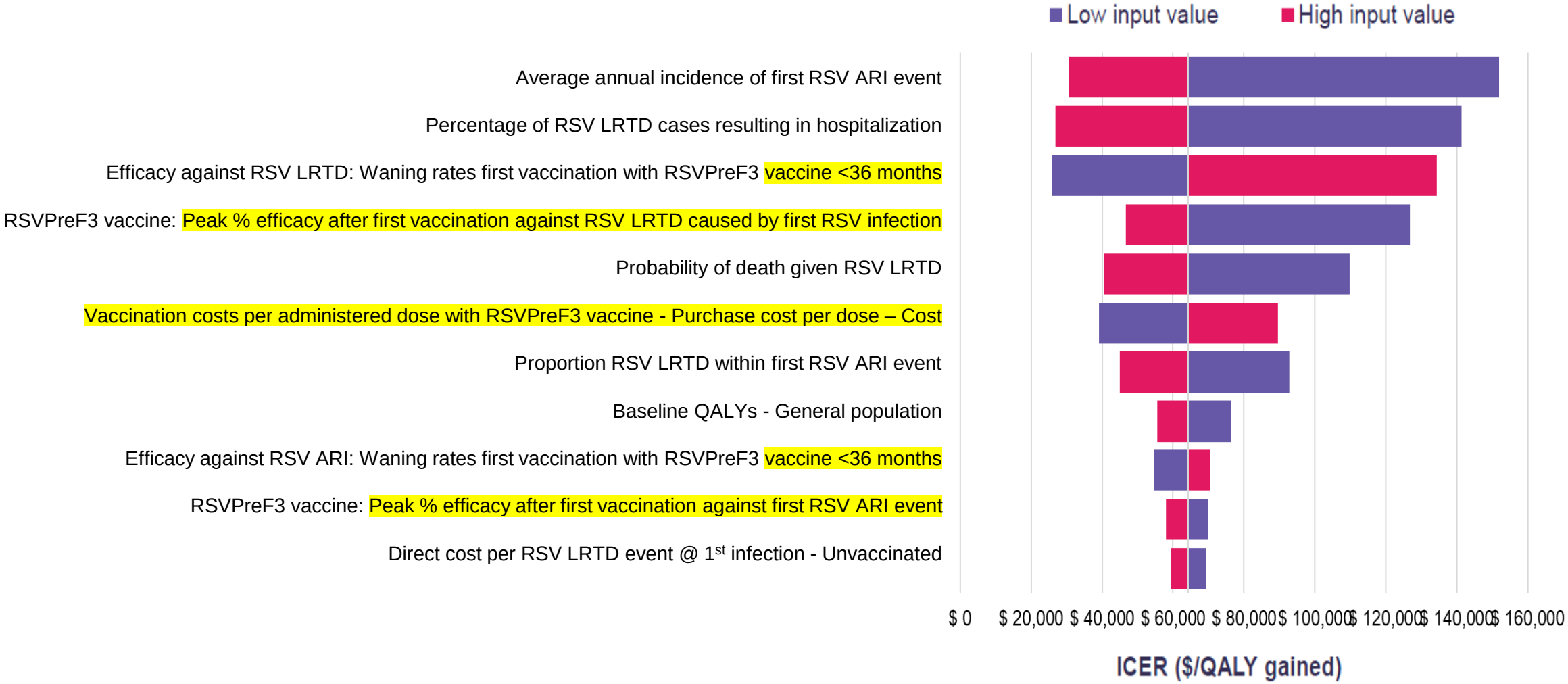
Vaccine cost per dose $270/dose (GSK), $200/dose (Pfizer)

Two-year time frame

Age-based vaccination recommendation: ≥65 years, VE=Vaccine Efficacy LRTD= Lower Respiratory Tract Disease, S1=Season 1, S2=Season 2.

GSK model: Updated One-way Sensitivity Analyses

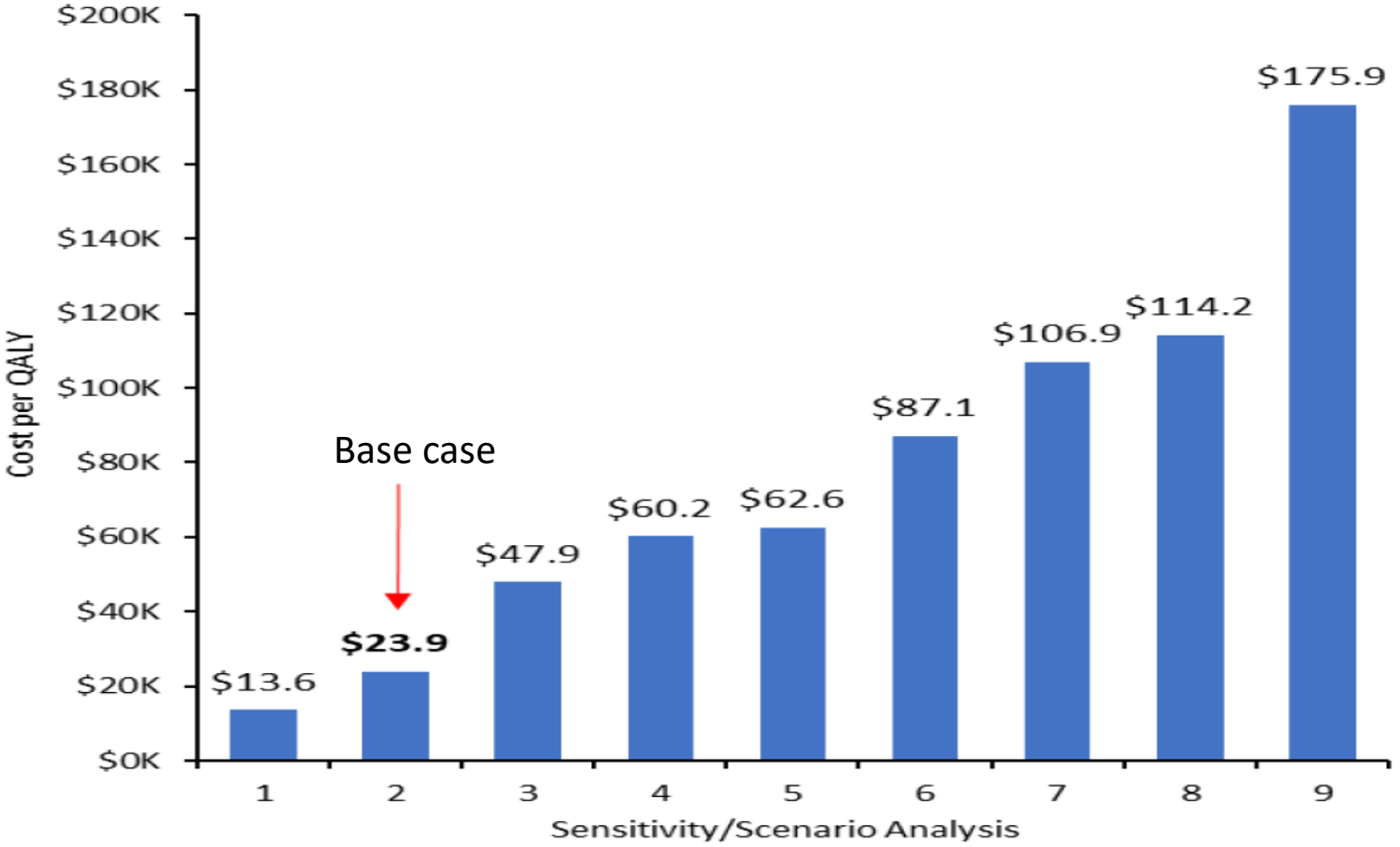
Base case: Age ≥60 years; $ 64,348 /QALY saved*



* GSK base-case vaccine price = $270/dose, three-year time frame

Pfizer model: Updated One-way Sensitivity Analyses

Base case: Age≥60 years: $23,921/QALY saved*



1.) RSVpreF price = $180
2.) Updated Base Case
3.) RSVpreF price = $180 and CDC RSV-H incidence x1.4
4.) RSVpreF price = $270
5.) RSVpreF price = $200 and CDC RSV-H incidence x1.4
6.) RSVpreF price = $180 and CDC RSV-H incidence
7.) RSVpreF price = $200 and CDC RSV-H incidence
8.) RSVpreF price = $270 and CDC RSV-H incidence x1.4
9.) RSVpreF price = $270 and CDC RSV-H incidence

* Pfizer base-case vaccine price = $200/dose, RSV-H= RSV-associated hospitalization

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

- RSV-hospitalization rate
  - GSK: Proportion of medically attended 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)
- Initial VE & waning over time: (updated data from GSK's & Pfizer's phase 3)
  - GSK: VE peaks in month 2, wanes linearly, reaching 0% at 34 or 43mos (depending on outcome)
  - *Pfizer:* VE is flat 7mos, wanes linearly thereafter, reaches 0% at 24mos
  - CDC: Step-wise: VE flat 7mos, partial drop & flat 7-14mos (Pfizer), 7-18mos (GSK), reaches 0% at 24mos
- Unitary medical cost of RSV outcomes
  - GSK: Age- & outcome specific cost for symptomatic RSV LRTD & URTI cases (medically attended and non-medically attended) (data from Centers for Medicare and Medicaid Services)
  - *Pfizer:* Age-, outcome- & comorbidity-specific cost for medically attended RSV illness
  - CDC: Age- & outcome-specific cost for medically attended RSV illness

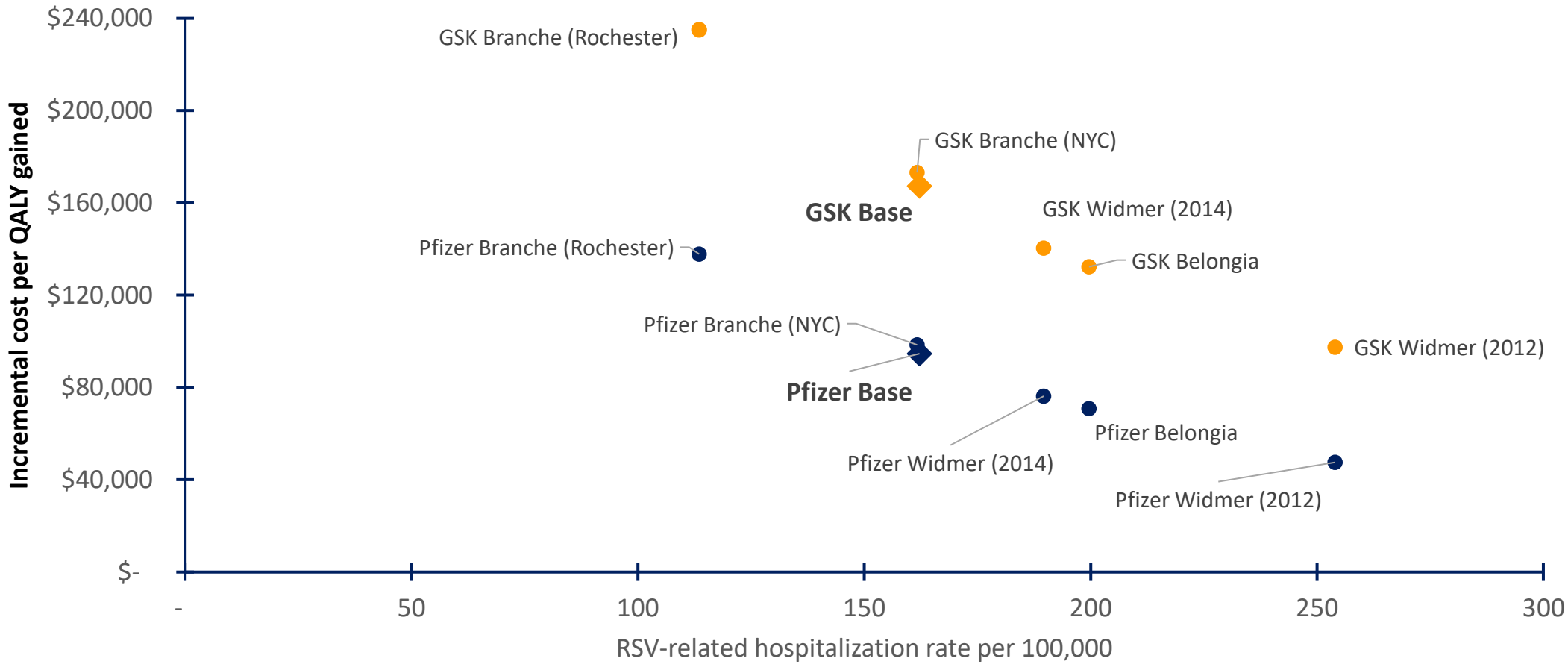
ARI = acute respiratory infection
LRTD = lower respiratory tract disease
URTI = upper respiratory tract illness

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)	2,278 (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)	**162** (base-case for adults ≥65 years)[d]	**256.3** (for adults ≥65 years)[b,e]	**300** (base-case for adults ≥65 years)[c]
Direct medical costs per RSV hospitalization	$21,417 – $22,425 (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
b Adapted from Belongia et al. Open Forum Infect Dis (2018): https://doi.org/10.1093/ofid/ofy316
c Adapted from McLaughlin et al. Open Forum Infect Dis (2022): https://doi.org/10.1093/ofid/ofac300; Ramirez et al. Infect Dis Ther (2023): https://doi.org/10.1007/s40121-023-00805-1
d RSV-NET, CDC unpublished data. Age-specific hospitalization rate per 100,000: 65.5 (60 to <65yrs), 93.8 (65 to <70yrs), 118.7 (70 to <75yrs) and 302.9 (75+yrs). Crude surveillance rates were upwardly adjusted 1.5x due to incomplete case detection from reliance on upper respiratory RT-PCR (McLaughlin et al. Open Forum Infect Dis (2022): https://doi.org/10.1093/ofid/ofac300
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). Updated to Q3 2022$ using GDP Deflator: https://doi.org/10.1093/infdis/jiaa183; Branche et al. Clin Infect Dis (2022): https://doi.org/10.1093/cid/ciab595
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)

UM-CDC model: Sensitivity of Cost per QALY saved to RSV-Related Hospitalization Rates among Adults ≥65 years: 2-year timeframe



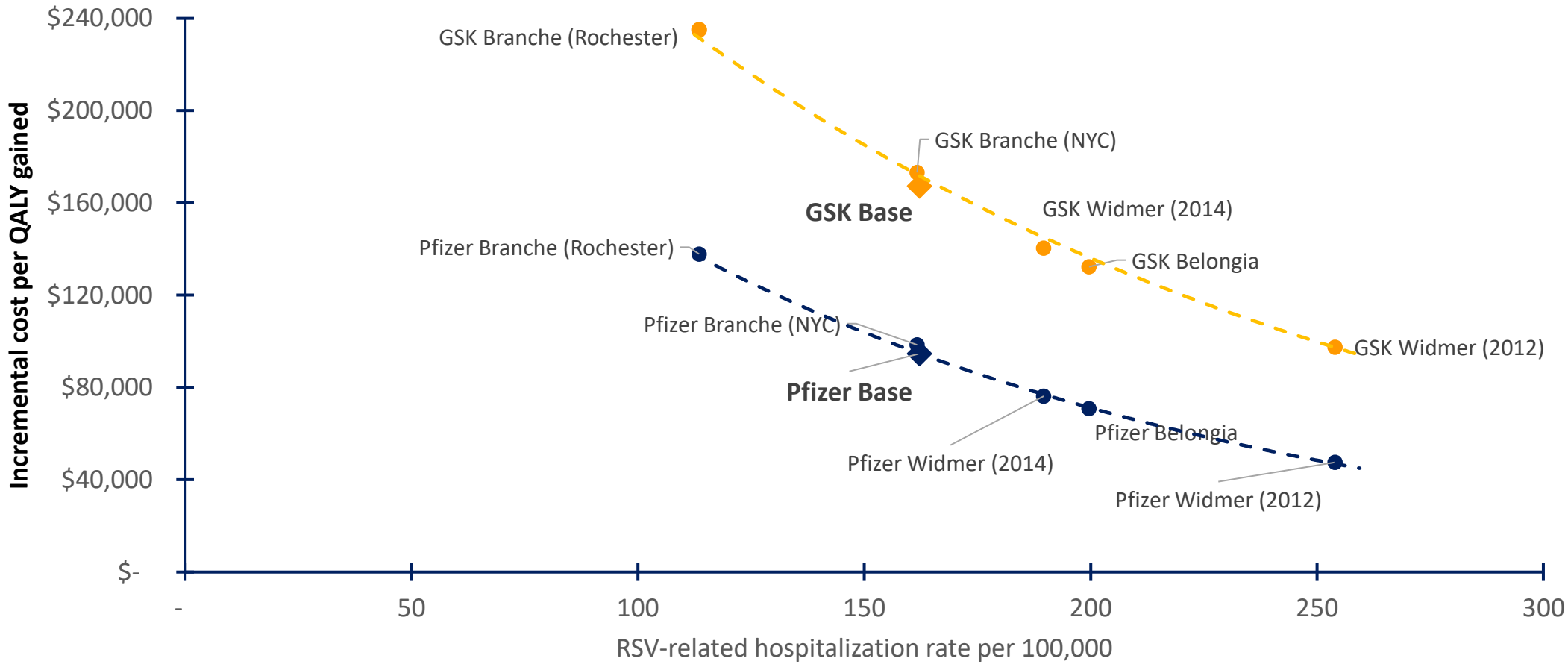
Base case for Pfizer and GSK are shown with blue and orange solid filled diamond markers, respectively: Estimated using the adjusted mean RSV-related hospitalization rate over RSV seasons: 2015-16, 2016-17, 2017-18, and 2018-19. Adjusted rate for lower sensitivity of PCR testing. CDC RSVnet

Blue ball markers: Estimated using Pfizer vaccine VE and price input data for the specific hospitalization rate as reported by the reference.

Orange ball markers: Estimated using GSK vaccine VE and price input data for the specific hospitalization rate as reported by the reference.

Labels in markers: They refer to the specific source of the RSV-associated hospitalization rate used in the estimation of either vaccine cost per QALY saved. Parentheses include either the year of the publication or the place where the data for the study was collected.

UM-CDC model: Sensitivity of Cost per QALY saved to RSV-Related Hospitalization Rates among Adults ≥65 years: 2-year timeframe



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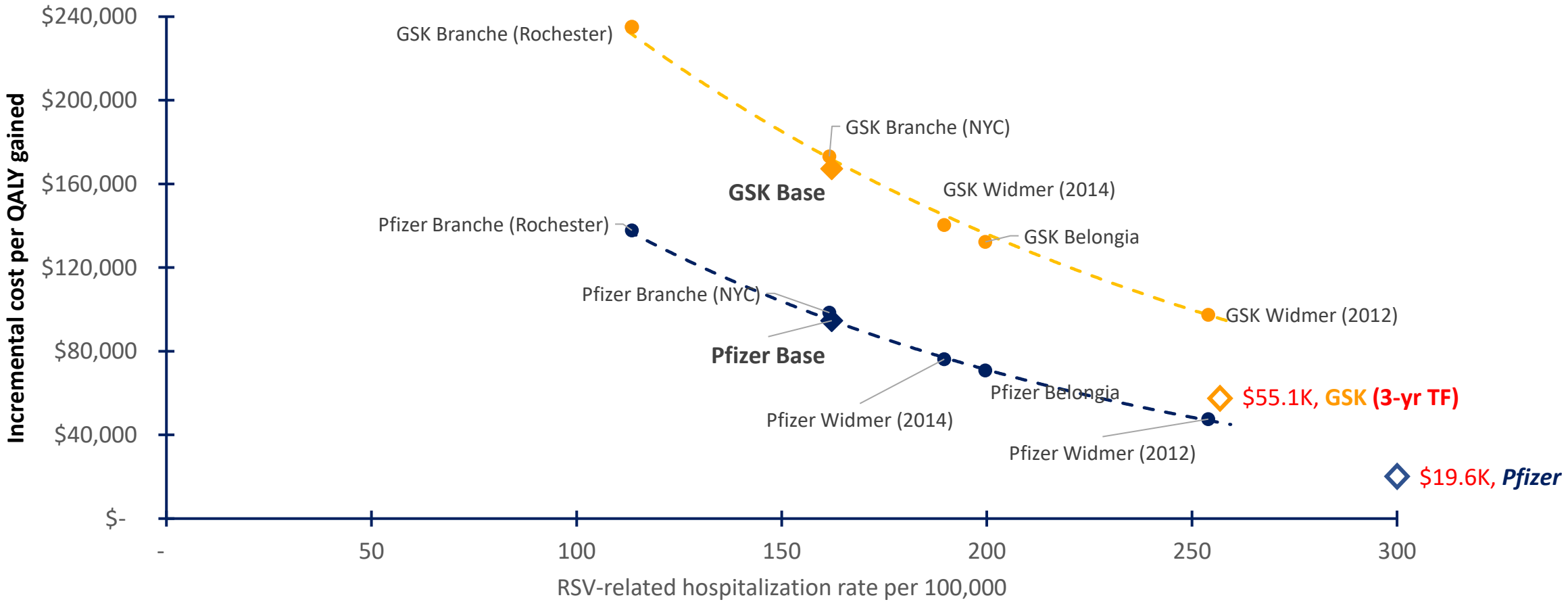
UM-CDC model: Sensitivity of Cost per QALY saved to RSV-Related Hospitalization Rates among Adults ≥65 years: 2-year timeframe



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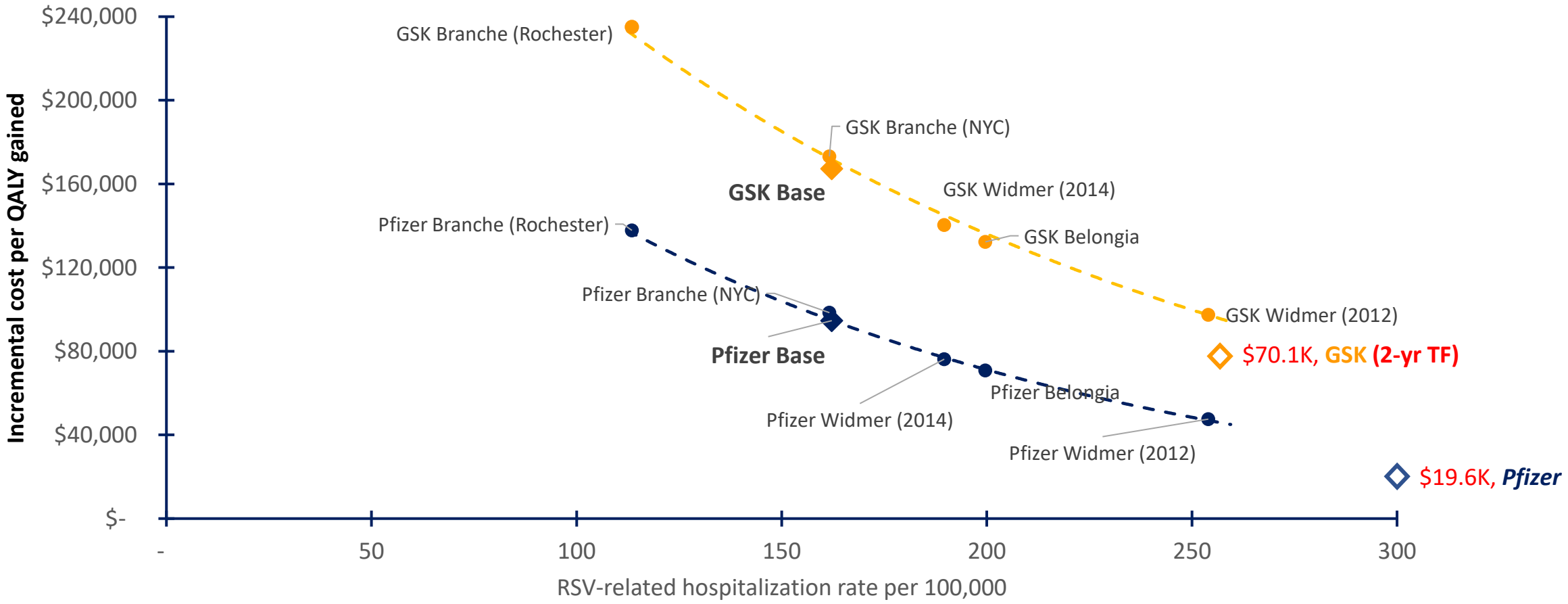
UM-CDC model: Sensitivity of Cost per QALY saved to RSV-Related Hospitalization Rates among Adults ≥65 years: 2-year timeframe



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Labels in markers: They refer to the specific source of the RSV-associated hospitalization rate used in the estimation of either vaccine cost per QALY saved. Parentheses include either the year of the publication or the place where the data for the study was collected.

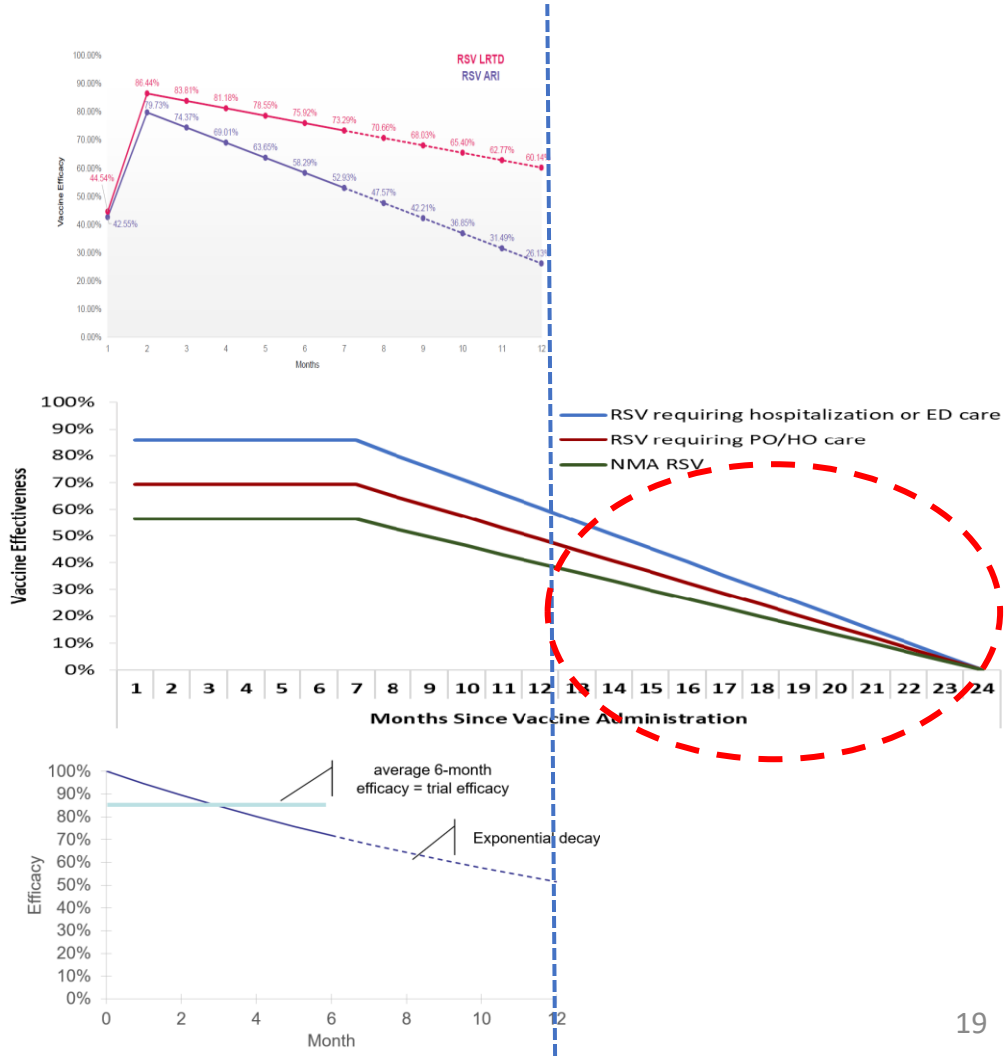
GSK, *Pfizer* and UM-CDC: Initial or Early Peak of Vaccine Efficacy & Decline in Season 2 (updated)

		UM-CDC Model		GSK Model	*Pfizer* Model
		GSK vaccine	**Pfizer vaccine**	**GSK vaccine**	**Pfizer vaccine**
Vaccine efficacy (VE) against RSV outpatient illness[a]	Season 1	79.0 (54.3–91.5)[b]	65.2 (36.0–82.0)[b]	Season 1 Peak: 74.2 (56.4–94.0) Weighted linear regression over time of estimated efficacy from clinical trial[c]	65.1 (35.9–82.0)[b]
	Season 2	27.8 (0 – 60.4)[b]	55.0 (0 – 82.0)[b]		55.0 (95% CI: -3.4–82.0)[b]
VE against RSV hospitalization and emergency department visit[a]	Season 1	87.5 (58.9–97.6)[d]	84.6 (32.0–98.3)[e]	Season 1 Peak: 88.0 (65.8–99.2) Weighted linear regression over time of estimated efficacy from clinical trial[f]	84.6 (32.0–98.3)[e]
	Season 2	52.9 (0 – 81.2)[d]	75.0 (0 – 97.4)[e]		75.0 (95% CI: -25.3–97.4)[e]

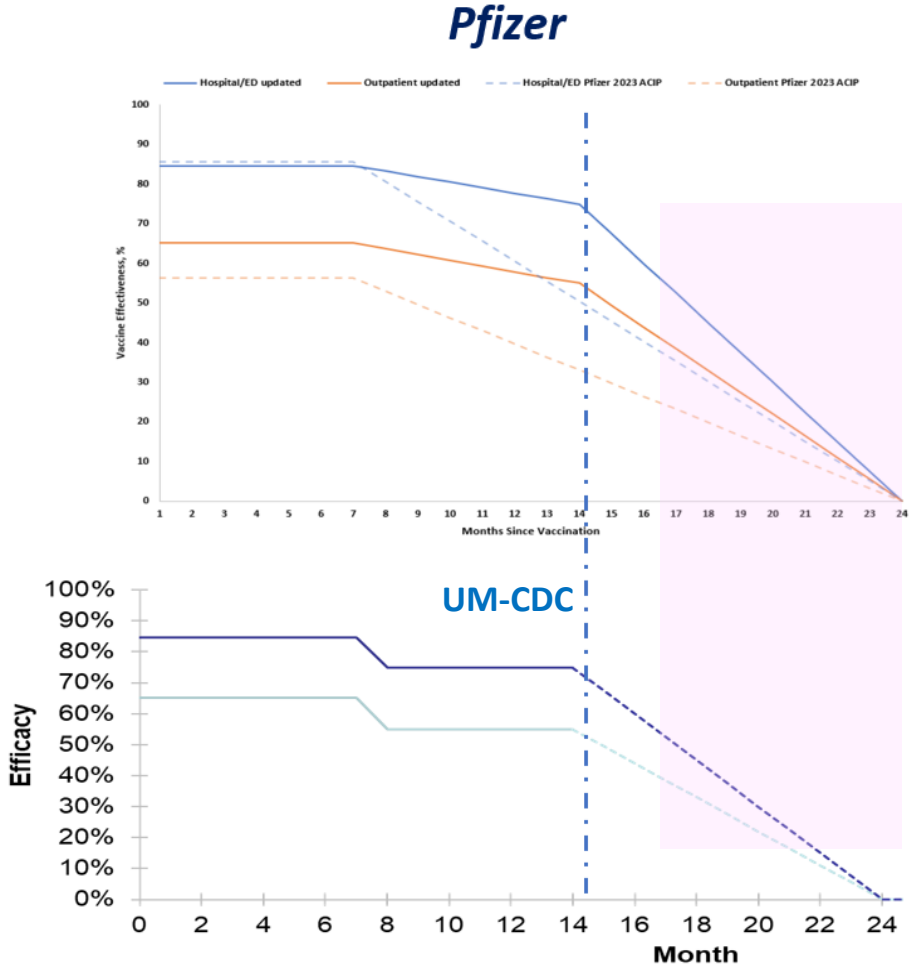
a VE over median (GSK) or mean (Pfizer) 7 months for season 1, VE through a median 18 months (GSK) or 14 months (Pfizer) for season 2 as reported in the follow up in phase 3 clinical trials
b Manufacturer phase 3 trial data; VE against medically attended acute respiratory illness
c GSK phase 3 trial data; VE against acute respiratory illness, regardless of whether medically attended. Reported peak value at month 2.
d GSK phase 3 trial data; VE against medically attended lower respiratory tract disease
e Pfizer phase 3 trial data; VE against medically attended lower respiratory tract illness with ≥3 lower respiratory symptoms
f GSK phase 3 trial data; VE against lower respiratory tract disease, regardless of whether medically attended. Reported peak value at month 2.

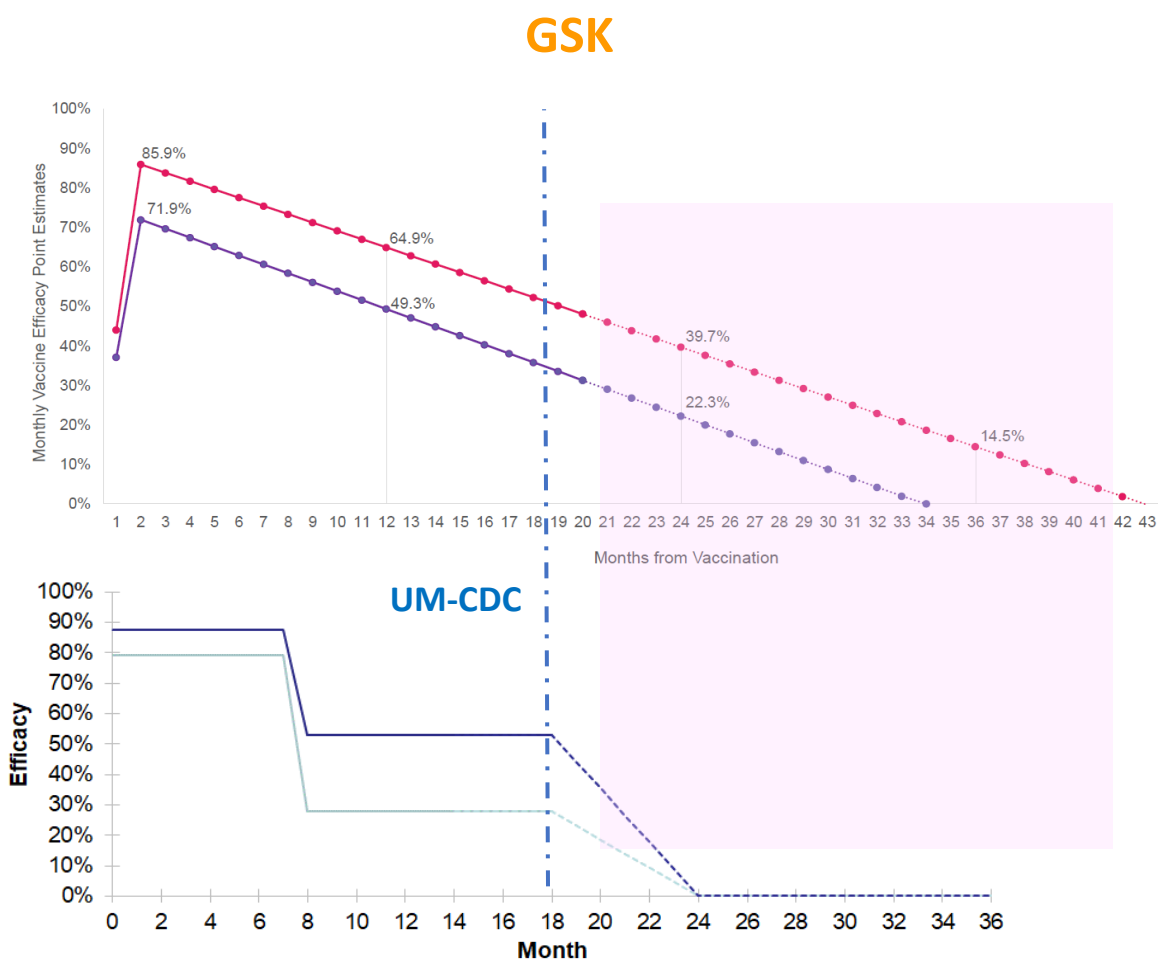
GSK, *Pfizer* and UM-CDC: Assumption on waning of vaccine efficacy (VE) per outcome (**Feb 2023**)

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



GSK, *Pfizer* and UM-CDC: Assumption on waning of vaccine efficacy (VE) per vaccine & outcome (June 2023)



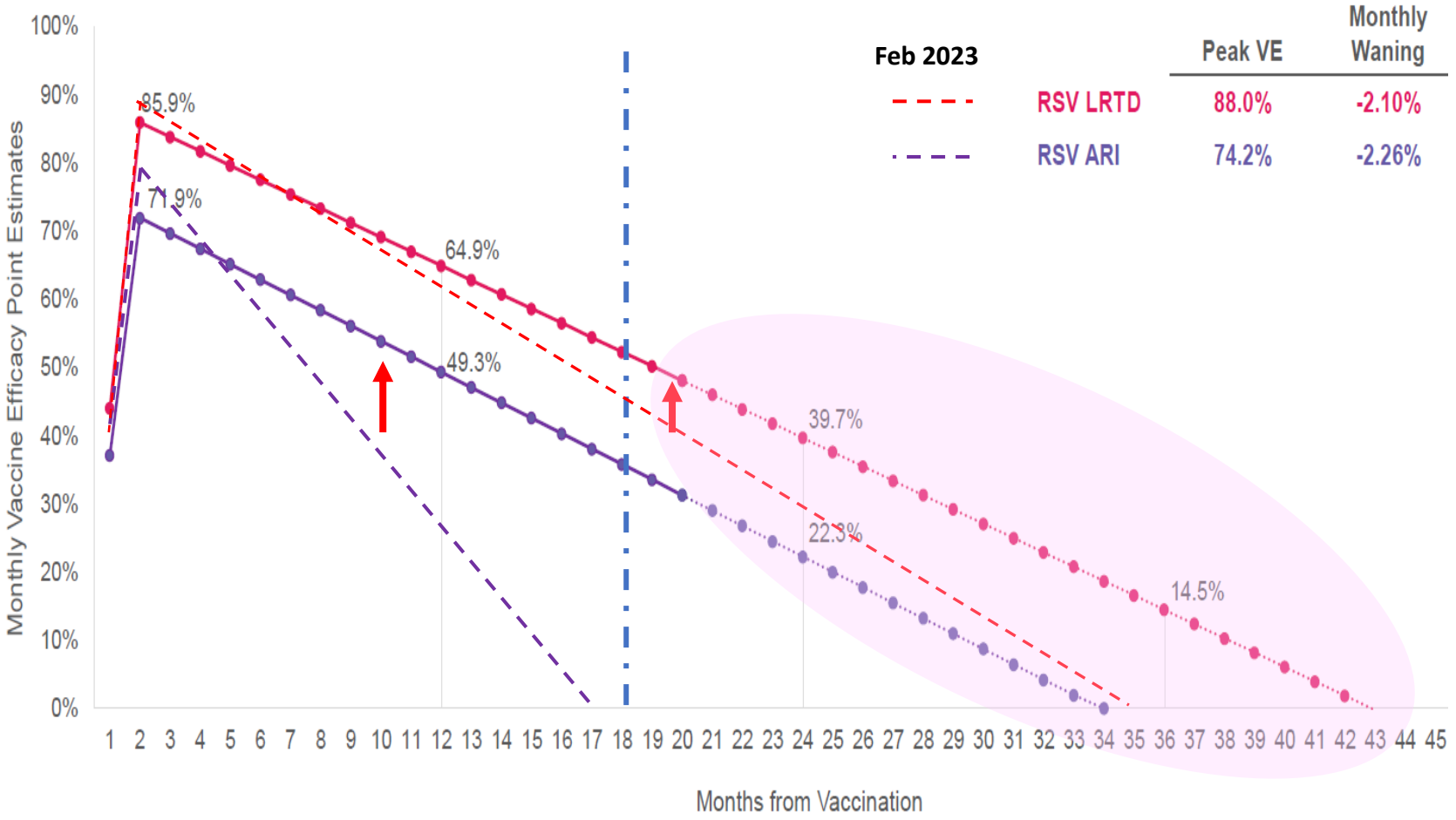


The pink-shaded areas denote a higher level of uncertainty of the waning assumption beyond available phase 3 data

GSK: Residual Vaccine Effectiveness (Feb 2023 ACIP) and *updated* analyses (June 2023)

RSV LRTD: 50% of peak VE (88%) assumed in month 1, peak VE declines by 2.10% (2.63% in Feb) monthly rate beginning in month 2 though 20-month maximum follow up of trial. Assumed to follow linear decline trend afterwards. Reaches 0% in month 43

RSV ARI: 50% of peak VE (74%) assumed in month 1, peak VE declines by 2.26% (5.36% in Feb) monthly rate beginning in month 2 though 20-month maximum follow up of trial. Assumed to follow linear decline trend afterwards. Reaches 0% in month 34

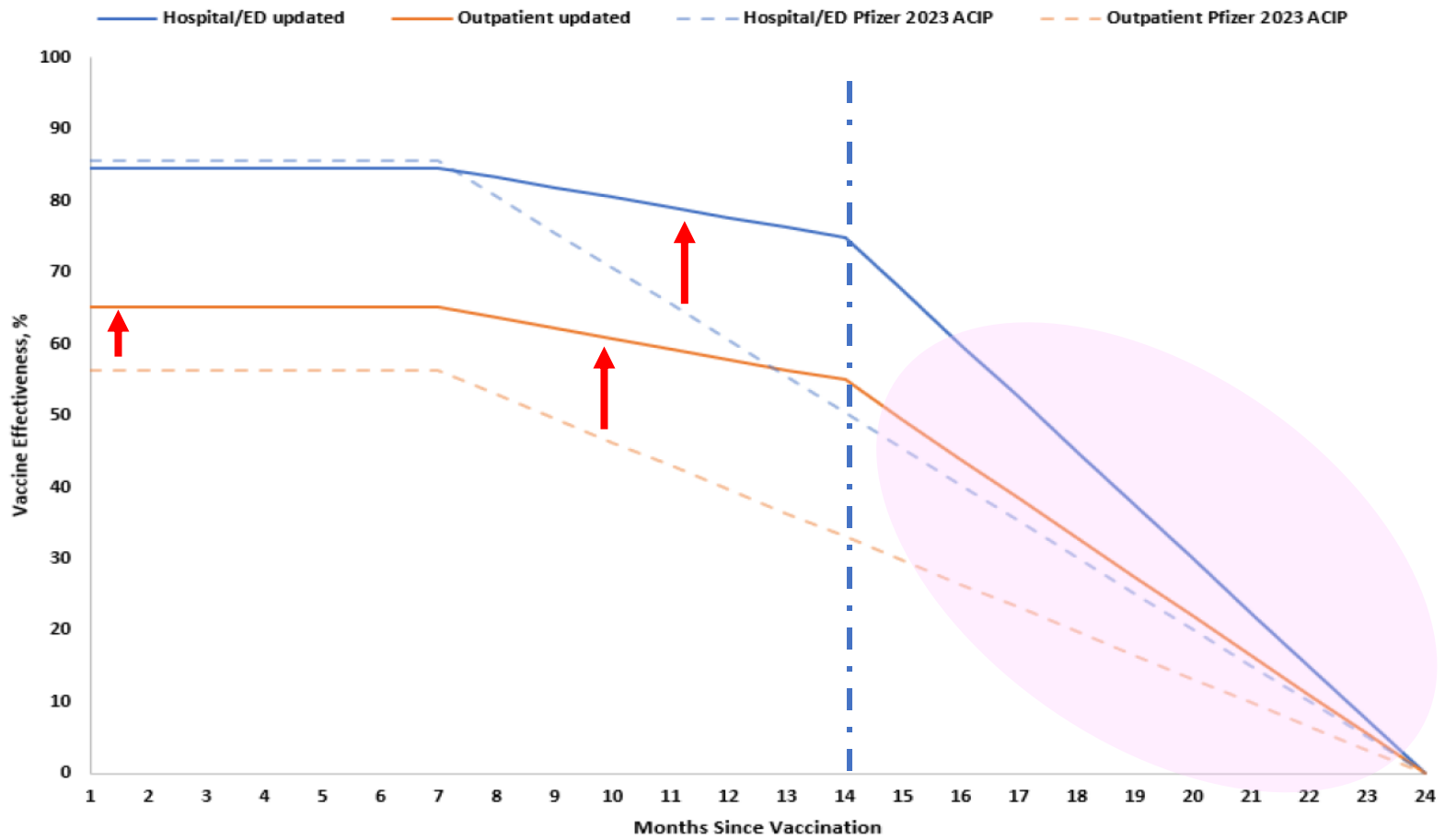


The pink-shaded area denotes a higher level of uncertainty of the waning assumption beyond available phase 3 data

Pfizer: Residual Vaccine Effectiveness (Feb 2023 ACIP) and *updated* analyses (June 2023)

Hospitalization or ED: Initial VE (84.6%) assumed to persist for 7 months, to decline to 75% at 14 months, and then decline to 0% at 24th month

Outpatient: Initial VE (**65.1%**) assumed to persist for 7 months, to decline to 55% at 14 months, and then decline to 0% at 24th month

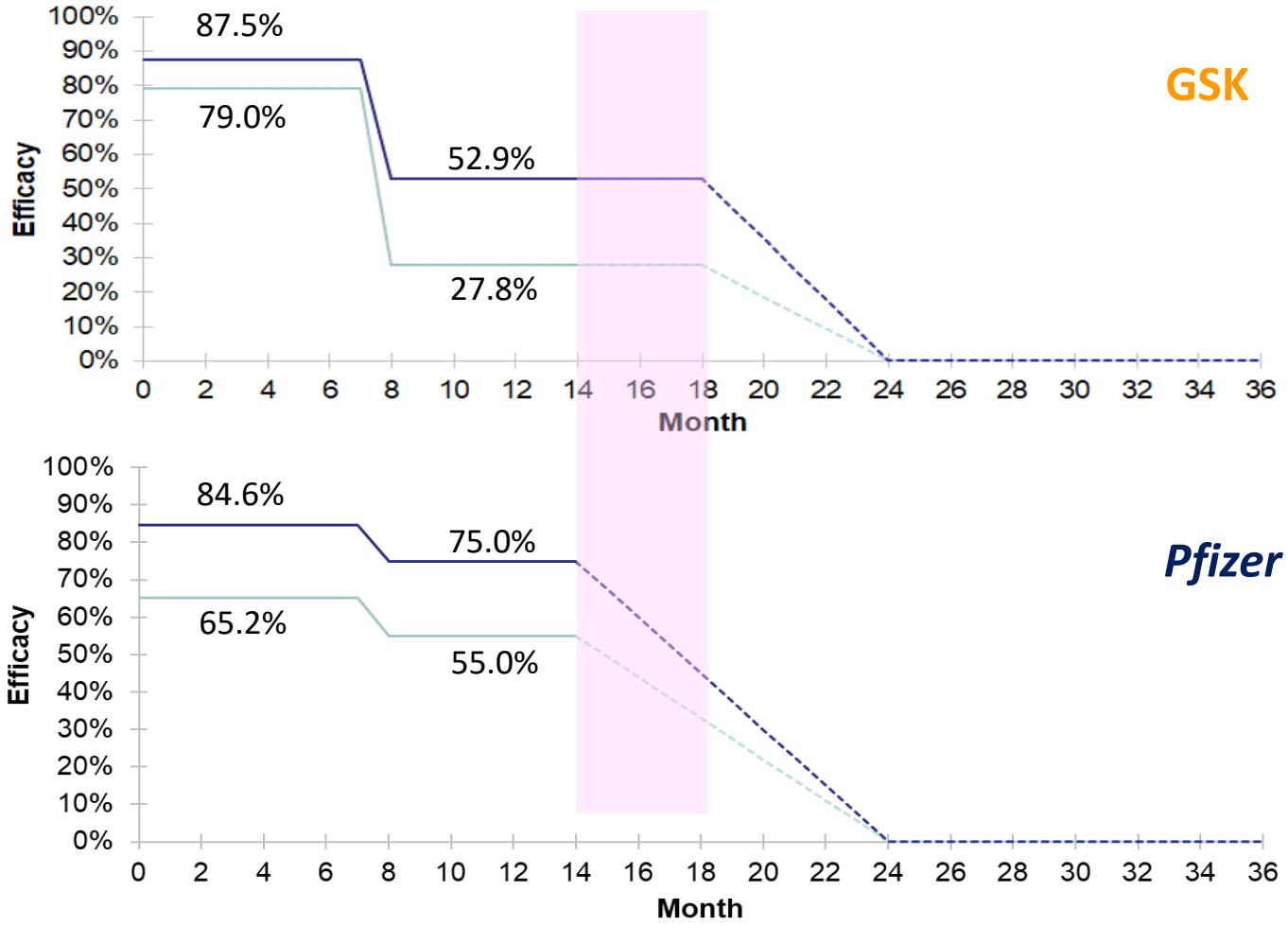


The pink-shaded area denotes a higher level of uncertainty of the waning assumption beyond available phase 3 data

UM-CDC: *Updated* assumption on waning of vaccine efficacy per vaccine and outcome

Hospitalization or ED: Initial VE (87.5% GSK; 84.6% *Pfizer*) assumed to persist for 7 months, to drop to 52.9% (GSK), 75%(*Pfizer)* and remain flat from month 8 to month 18 (GSK) or month 14 (*Pfizer*), and then decline linearly to 0% at month 24.

Medically attended (Outpatient): Initial VE (79% GSK; 65.2% *Pfizer*) assumed to persist for 7 months, to drop to 27.8% (GSK), 55%(*Pfizer*) and remain flat from month 8 to month 18 (GSK), month 14 (*Pfizer*), and then decline linearly to 0% at month 24



The pink rectangle highlights the difference in duration of protection assumption between vaccines

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

Scenario	GSK	*Pfizer*
Vaccinating adults aged 60 to <65 years only	$372,656	$218,250
Lower incidence of RSV[a] in adults ≥65 years	$276,393	$161,487
Vaccine cost $340 per dose	$220,864	$187,865
Vaccinating adults ≥60 years,	$205,638	$118,735
Residual vaccine protection = 0% at 18 (GSK) or 14 (Pfizer) months	$170,022	$135,886
Base case[b] (Vacc price $270 GSK, $200 *Pfizer*, adults ≥65yrs)	**$167,301**	**$94,673**
Vaccine cost $180 per dose	$98,485	$81,358
Higher incidence of RSV[b] in adults ≥65 years	$84,736	$40,467

a Incidence rates: Lower incidence assumes 95% RT-PCR test sensitivity, Higher rate incorporates the upper limit of the 95% CI around the base case incidence rate estimate.

b Recommendation = vaccination at age ≥65 years; incidence rates of RSV outcomes upwardly adjust 1.5x to account for incomplete RT-PCR sensitivity on a respiratory specimen (McLaughlin et al; Open Forum Infect Dis 2022); vaccine efficacy only considered for two years post-vaccination

Limitations

- **Factors not considered that may result in overestimating the ICER (underestimating the cost-effectiveness) of RSV vaccination**
  - All of the 3 models assumed no indirect effects of vaccination (i.e., no protection against RSV transmission)

  Except UM-CDC model
  - Manufacturers models do not include RSV-related medical costs incurred after discharge from an RSV-associated hospitalization or emergency department visit:
    - Stay in long-term care or rehabilitation facility
- **Manufacturers models do not include potential vaccine-associated serious adverse events (SAEs)**
    - Quality of life impact, resource utilization and costs associated with hypothetical SAEs
- **Vaccine efficacy beyond clinical trial follow-up time (beyond 14 months, *Pfizer* or 18 months, GSK) is unknown**
  - All 3 models assumed non-zero declining efficacy beyond 14 or18 months

Conclusion

- **Differences in key inputs among GSK, *Pfizer* and UM-CDC models explain differences in results:**
  - Annual incidence of RSV hospitalization and outpatient disease
  - Initial vaccine (season 1) and waning of protection (VE season 2+)
  - Selection of medical costs sources and data extraction approach
- **Resulting ICERs depended heavily on assumptions and selection of input data**
  - Annual incidence of RSV Hospitalization
  - Vaccine costs (e.g., increase in GSK vaccine price)
- **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
- Amadea Britton

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- Andrew Leidner and the Econ Team members at ISD/NCIRD