Economics of Respiratory Syncytial Virus (RSV) Vaccination in All U.S. Adults≥75 years-old, and Adults aged 60-74 *and* 50-59 years at Increased Risk

SUMMARY COMPARING MODELS FROM:

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

- **Moderna model**: Parinaz Ghaswalla et al., [complete list and affiliations, upon request]
  - Moderna manufacturers the mRNA-1345 (mRESVIA) RSV vaccine
  - Quadrant Health Economics was funded by Moderna

- **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

Three policy questions for economic modeling

1. Should a single dose of RSV vaccination (any licensed product) be recommended for **all** adults 75+?

2. Should a single dose of RSV vaccination (any licensed product) be recommended for adults 60-74 **at increased risk** of severe RSV disease?

3. Should a single dose of RSV vaccination (any licensed product*) be recommended for adults 50-59 **at increased risk** of severe RSV disease?

*Only a single RSV vaccine (GSK AREXVY) is licensed for use in adults aged 50-59 years who are at increased risk of RSV lower respiratory tract disease.

https://www.fda.gov/vaccines-blood-biologics/arexvy
https://www.fda.gov/vaccines-blood-biologics/abrysvo
https://www.fda.gov/vaccines-blood-biologics/vaccines/mresvia

Economic analyses

Cost-effectiveness analyses:

Policy Questions	Comparator	Intervention
1 2 3	**Unvaccinated age and risk groups** -All ≥75yr-olds -Increased risk 60-74yr-olds -Increased risk 50-59yr-olds	**Use of a licensed RSV vaccine among** -All ≥75yr-olds -Increased risk 60-74yr-olds -Increased risk 50-59yr-olds

Base-case scenarios:

- What is the incremental *cost-effectiveness* of vaccinating adults aged ≥75 years against RSV relative to "No vaccination"?
- What is the incremental *cost-effectiveness* of vaccinating adults aged 60-74 years and 50-59 years at increased risk of severe RSV disease relative to "No vaccination"?

GSK, UM-CDC *and* Moderna: incremental analyses of vaccination strategies

Policy question	Incremental analysis	GSK model	UM-CDC model		Moderna model
			Protein Subunit GSK & *Pfizer*	Moderna Vaccine	
1	Vaccinate All ≥75yr-olds ***vs.*** No vaccination	Reviewed in June 2023	Included	Included	Included
2	Vaccinate Increased risk 60-74yr-olds ***vs.*** No vaccination	Not Included	Included (Eight conditions)*		Included
3	Vaccinate Increased risk 50-59yr-olds ***vs.*** No vaccination	Included (Five conditions)**	Included*** (Eight conditions)*	Not Included***	Not Included***

No vaccination was deemed an appropriate comparator under the current shared clinical decision-making recommendation.
* Risk conditions included chronic obstructive pulmonary disease (COPD), asthma, coronary artery disease, chronic kidney disease, diabetes mellitus, severe obesity (BMI ≥40), heart failure, and immune compromise
** Conditions included in GSK model are COPD (base-case), heart failure, coronary artery disease, asthma, diabetes
*** Only a single RSV vaccine (GSK AREXVY) is licensed for use in adults aged 50-59 years who are at increased risk of RSV lower respiratory tract disease. As such, the economic model used GSK-specific inputs for the 50-59-year-old population.

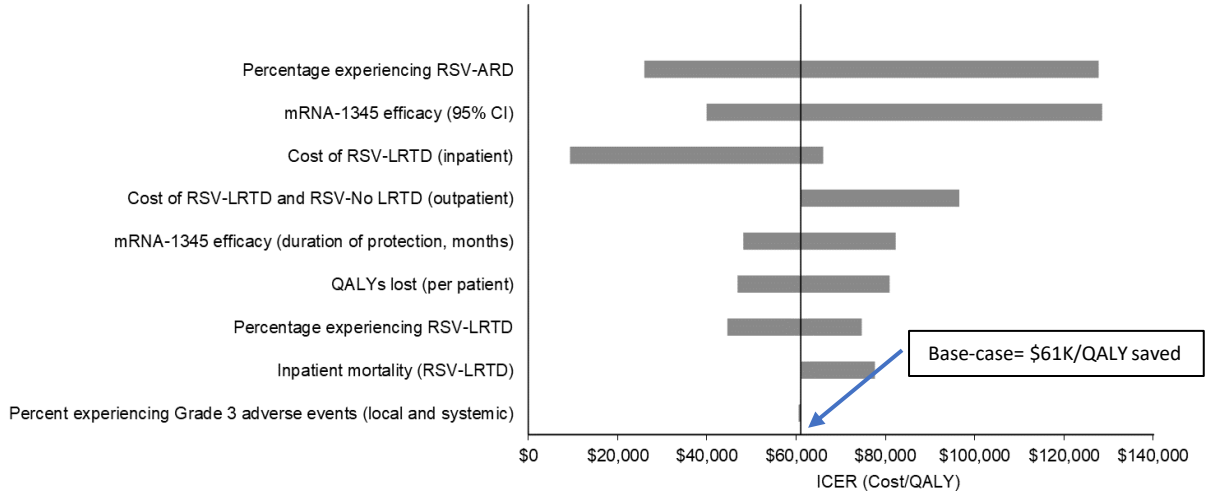
Modeling design and assumptions

	GSK	Moderna	UM-CDC
Static analytical decision-making models	✓	✓	✓
Sensitivity analyses (and probabilistic simulation)	✓(✓)	✓(✓)	✓
Hypothetical populations: ≥75yrs old general population and 60-74yrs old at increased risk (50-59yrs old at increased risk)	(✓)	✓	✓(✓)
Time Frame at least 3 years after a dose of RSV vaccine*	✓	✓	✓
Analytic Horizon: Age- and comorbidity-specific life expectancy**	✓	✓	✓
Discount rate: 3%	✓	✓	✓
Year of economic outcomes measured: 2022/2023	✓	✓	✓
Societal perspective (and healthcare perspective)	✓(✓)	✓(✓)	✓(✓)

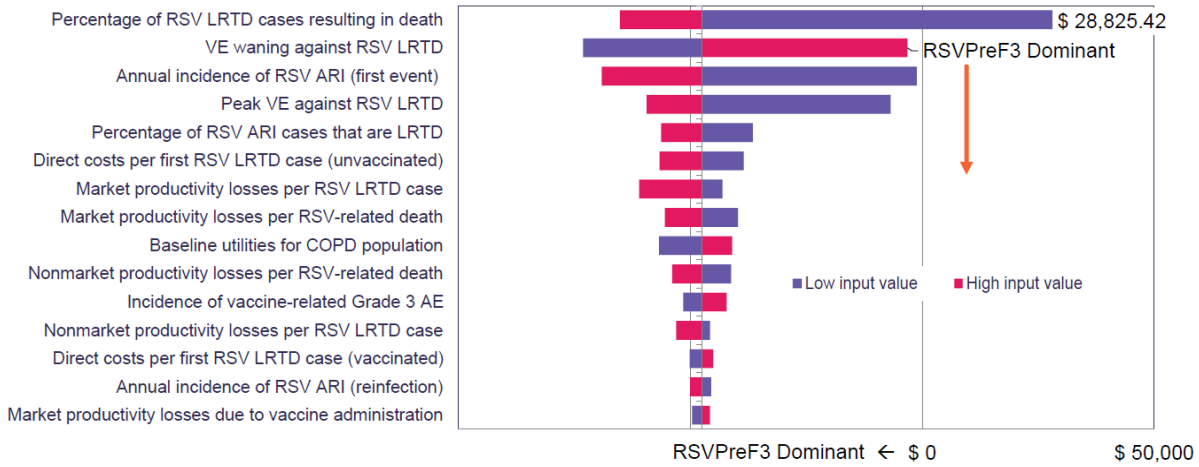
* Base-case in UM-CDC and Moderna models relied on a two-year time frame (three-year timeframe included in scenario analysis) while GSK used a three-year timeframe in the base-case.
In each model, selection of timeframe is based on the duration of protection assumption
** Age and comorbidity specific life expectancy were used for comorbid 50–59-year-old in GSK model.

GSK, Moderna and UM-CDC models comparison: From one-way sensitivity analyses

Moderna: Adults ≥60yrs at high risk



GSK: Adults 50-59 yrs. at high risk



We will compare:

- Incidence of RSV hospitalization and outpatient care
- Medical and indirect costs
- Initial vaccine effectiveness
- Vaccine waning
- Age and risk groups

Moderna and UM-CDC models: Key differences in model inputs, adults ≥60 years

	UM-CDC	Moderna
Incidence of RSV outpatient illness (per 100,000 persons per year)	2,940 for adults ≥60 with cardiopulmonary disease (including COPD)[a] 1,722 for adults ≥60 with other chronic conditions (e.g., diabetes mellitus)[b]	1,833 for adults 60-64 and 2,478 for adults ≥65 years, general population
Incidence of RSV hospitalization (per 100,000 persons per year)	Age-dependent: 198–527 for adults ≥60 with at least one chronic condition[d] 32–121 for adults ≥60 without chronic conditions[d]	66.5 for adults 60-64 and 266.7 for adults ≥65 years, general population
Direct medical costs per RSV hospitalization	Age-dependent: $21,417 – $22,425,[e] adjusted using median length of stay by chronic conditions from RSV-NET	$11,876 ($8,407 - $47,512)[f,g]

a Adapted from Belongia et al. Open Forum Infect Dis (2018): https://doi.org/10.1093/ofid/ofy316.
b McLaughlin et al. Open Forum Infect Dis (2022): https://doi.org/10.1093/ofid/ofac300
c Adapted from McLaughlin et al. Open Forum Infect Dis (2022): https://doi.org/10.1093/ofid/ofac300; (Outpatient targets include both emergency department and outpatient visits)
d RSV-NET, CDC unpublished data. Crude surveillance rates were adjusted using multipliers for the frequency of RSV testing during each season and the sensitivity of RSV diagnostic tests.
e 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
f Wyffels V et al (2020) A Real-World Analysis of Patient Characteristics and Predictors of Hospitalization Among US Medicare Beneficiaries with Respiratory Syncytial Virus Infection: https://pubmed.ncbi.nlm.nih.gov/32026380/ (range values $8,407 is from Choi and $47,512 is from Pastula)
g Merative MarketScan Commercial Claims and Encounters (CCAE) and Medicare Supplemental Coordination of Benefits (MDCR) Databases (2016-2019)

GSK and UM-CDC models: Key differences in model inputs, adults 50-59 years

	UM-CDC	GSK
Incidence of RSV outpatient illness (per 100,000 persons per year)	2,940 for adults 50-59 with cardiopulmonary disease (e.g., COPD)[a] 1,722 for adults 50-59 with other chronic conditions (e.g., diabetes mellitus)[b]	2,925 for adults 50-59 with COPD[a]
Incidence of RSV hospitalization (per 100,000 persons per year)	**106** for adults 50-59 with at least one chronic condition[c] **169** for adults 50-59 with COPD, specifically[c]	**312** for adults 50-59 with COPD[d]
Direct medical costs per RSV hospitalization	**$20,330** for adults 50-59,[e] adjusted using median length of stay, by chronic condition, from RSV-NET	**$35,308** for adults 50-59[f]

a Adapted from Belongia et al. Open Forum Infect Dis (2018): https://doi.org/10.1093/ofid/ofy316. Adjusted by a factor of 1.5 for PCR sensitivity (McLaughlin et al. [2022])
b McLaughlin et al. Open Forum Infect Dis (2022): https://doi.org/10.1093/ofid/ofac300
c RSV-NET, CDC unpublished data. Crude surveillance rates were adjusted using multipliers for the frequency of RSV testing during each season and the sensitivity of RSV diagnostic tests.
d Adapted from Branche et al. (2022) across Rochester and New York City sites adjusted by a factor of 1.5 for PCR sensitivity (McLaughlin et al. [2022])
e 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
f CMS Medicare Inpatient Hospitals - by Geography and Service (CMS, 2023a); (DRG Average Payments from 2019 dataset); Falsey et al. (2005); KFF (2020)

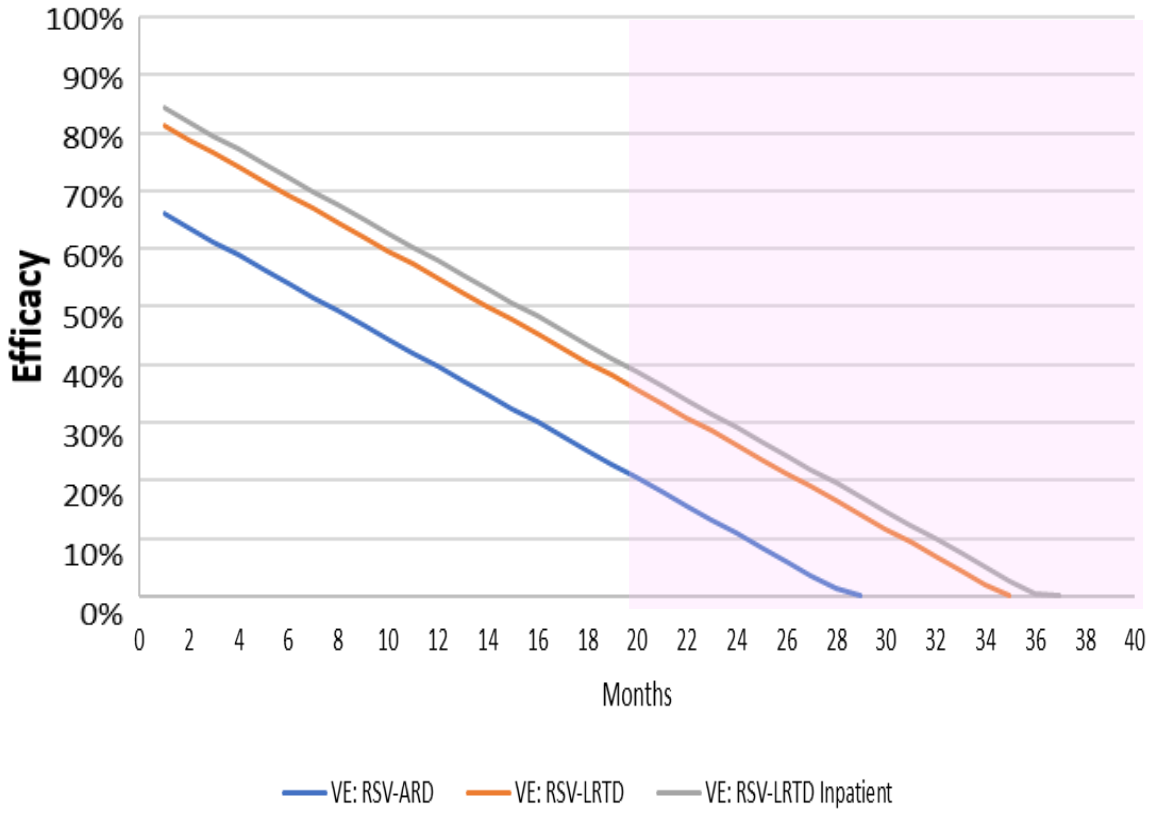
Moderna and UM-CDC:
Initial or Early Peak of Vaccine Efficacy & Decline

		UM-CDC Model	Moderna Model
		Moderna vaccine	**Moderna vaccine**
Vaccine efficacy against RSV *outpatient* illness[a]	**Year 1**	54 (0–83)[b]	Peak: 68.4 (50.9–79.7)[c]
	Year 2	Linear decline reaching zero at month 24	40.1 Weighted least square regression
Vaccine efficacy against RSV *hospitalization* and emergency department visit[a]	**Year 1**	75 (0–95)[d]	Peak: 86.7 (41.9–97.0)[e]
	Year 2	Linear decline reaching zero at month 24	57.9 Weighted least square regression

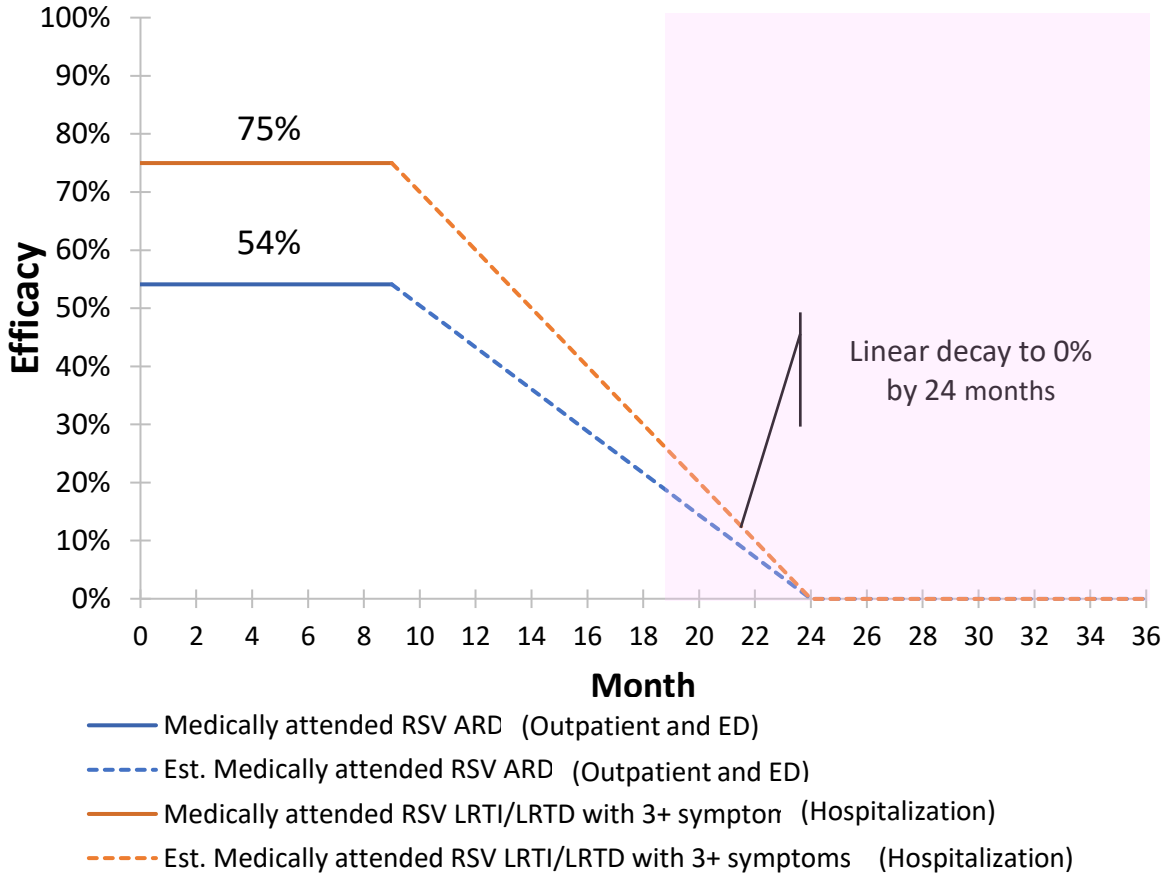
a Efficacy over median 19 months (Moderna) as reported in the phase 3 clinical trials
b Moderna phase 3 trial data; VE against medically attended acute respiratory illness
c Moderna mRNA-1345 Efficacy from the Phase 2/3 Clinical Trial for RSV-ARD (primary analysis: 1-4 months)
d Moderna phase 3 trial data; VE against medically attended lower respiratory tract disease with ≥3 lower respiratory symptoms
e Moderna mRNA-1345 Efficacy from the Phase 2/3 Clinical Trial for RSV-LRTD with ≥2 symptoms associated with shortness of breath (primary analysis: 1-4 months)

Moderna and UM-CDC: Assumption on waning of vaccine effectiveness (VE) per outcome

MODERNA (two-year model timeframe)



UM-CDC (two-year model timeframe)



ARD = Acute respiratory disease
LRTD =Lower respiratory tract disease
Est. = estimated
ED = Emergency department

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

GSK and UM-CDC:
Initial or Early Peak of Vaccine Efficacy & Decline

		UM-CDC Model	GSK Model
		GSK vaccine	**GSK vaccine**
Vaccine efficacy against RSV *outpatient* illness[a]	**Year 1**	79 (54–92)[b]	Peak: 73.3 (57.9–87.4)[c]
	Year 2+	28 (0–60)[b]	Weighted linear regression over time (-2.1% monthly waning)[c]
Vaccine efficacy against RSV *hospitalization* and emergency department visit[a]	**Year 1**	84 (74–90)[d]	Peak: 86.5 (67.7–98.7)[f]
	Year 2+	60 (43–72)[e]	Weighted linear regression over time (-1.8% monthly waning)[f]

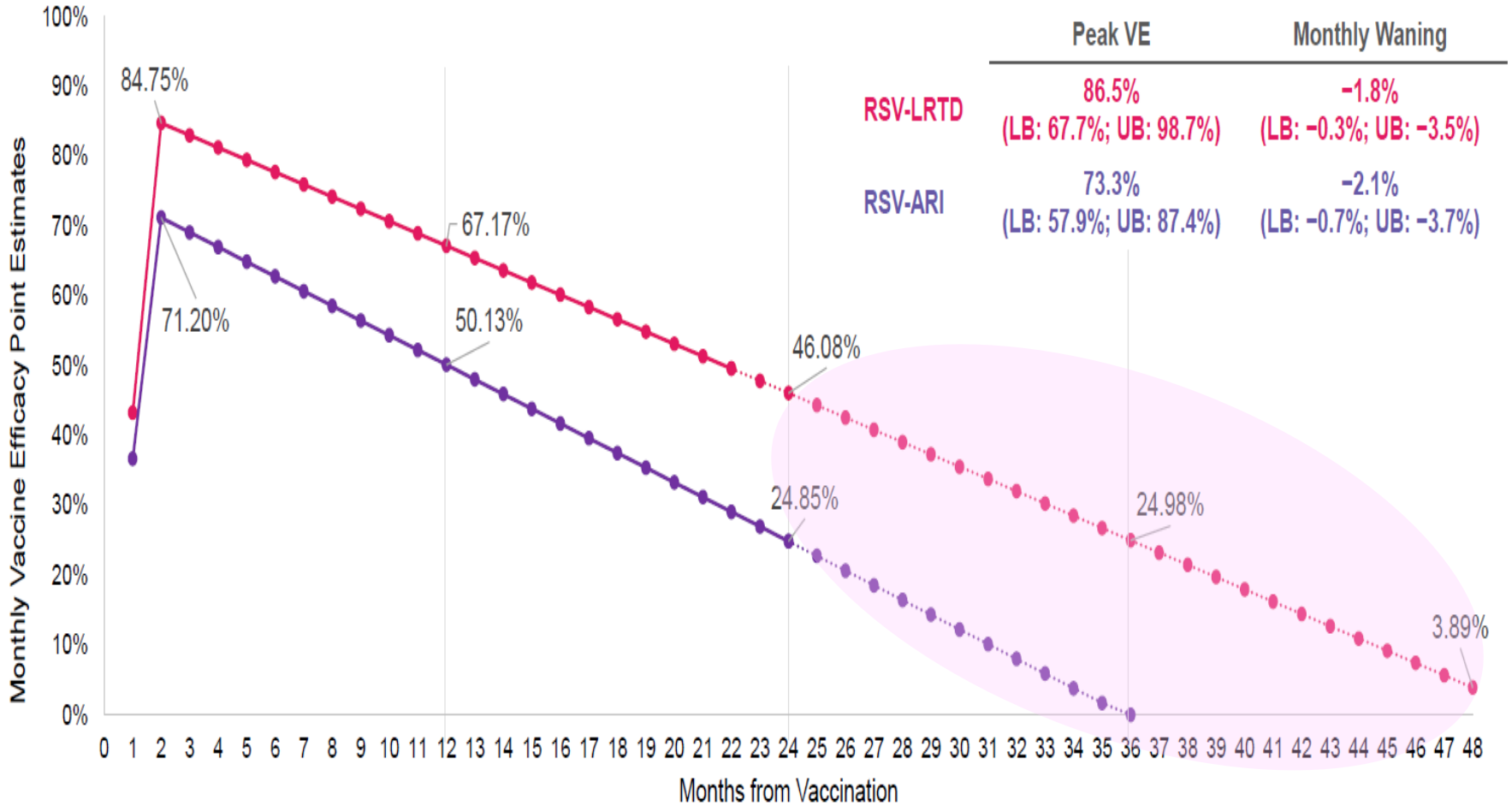
a Efficacy over median 23 months follow up (GSK) as reported in the phase 3 clinical trials
b GSK phase 3 trial data; VE against medically attended acute respiratory illness
c GSK phase 3 trial data; VE against acute respiratory illness, regardless of whether medically attended. During month 1, 50% of peak VE is assumed, with linear waning in months 2+ based on weighted linear regression.
d Observational vaccine effectiveness, GSK-specific.
e Proportional waning applied to Season 1 efficacy, from GSK phase 3 trial efficacy against lower respiratory tract disease (Season 2 vs. Season 1)
f GSK phase 3 trial data; VE against lower respiratory tract disease, regardless of whether medically attended. During month 1, 50% of peak VE is assumed, with linear waning in months 2+ based on weighted linear regression.

GSK: Residual Vaccine Effectiveness (VE) analyses (3-year timeframe)

RSV LRTD: 50% of peak VE (86.5%) assumed in month 1, peak VE declines by 1.8% monthly rate beginning in month 2 though 23-month follow up of trial. Assumed to follow linear decline trend afterwards. Reaches 0% near month 48

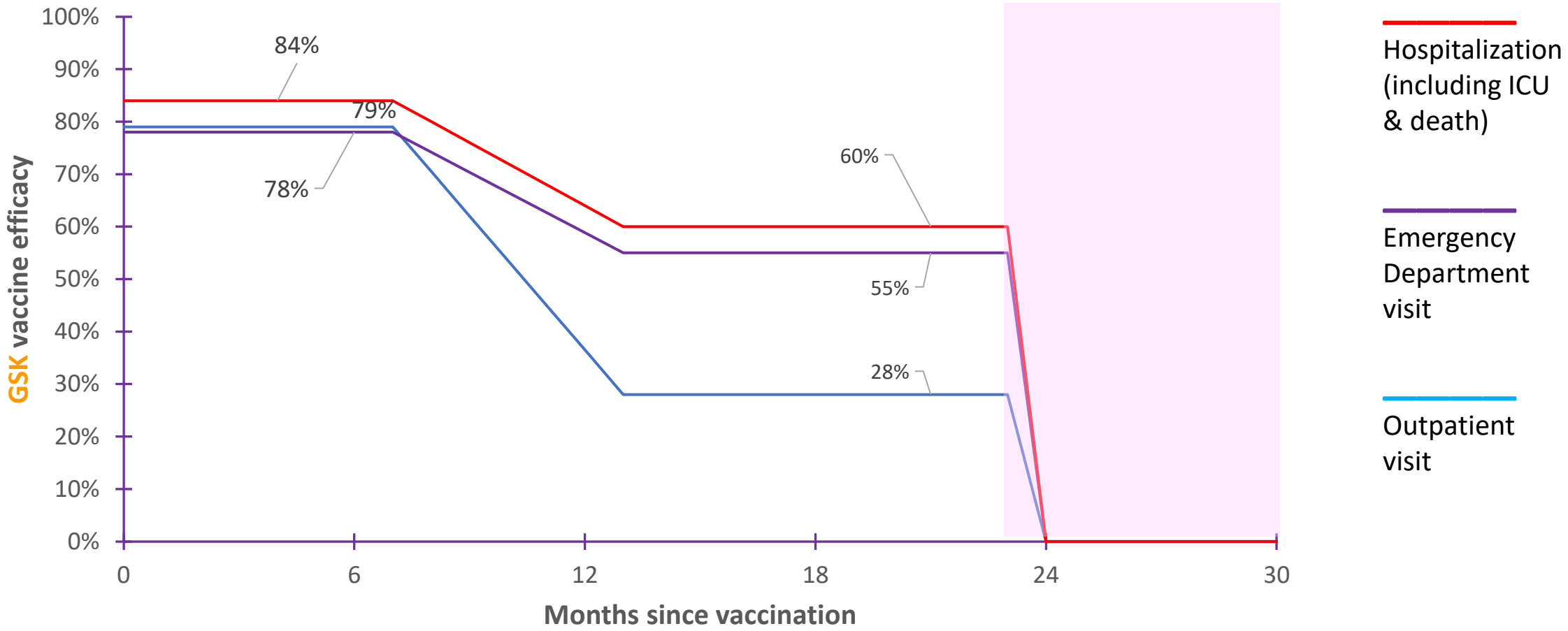
RSV ARI: 50% of peak VE (73.3%) assumed in month 1, peak VE declines by 2.1% monthly rate beginning in month 2 though 23-month follow up of trial. Assumed to follow linear decline trend afterwards. Reaches 0% in month 36

Source: GSK Technical report and Slides June 2024
LRTD= Lower respiratory tract disease
ARI= Acute respiratory illness
LB= Lower bound



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

UM-CDC: Assumption of waning of vaccine efficacy (GSK vaccine) (2-year timeframe)



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

Policy questions 1 & 2: Moderna and UM-CDC

Policy question 1. What is the incremental cost-effectiveness of vaccinating ***all adults aged ≥75 years old*** against RSV illness ***relative*** to "No vaccination"?

	Moderna model **Moderna vaccine**	UM-CDC model **Moderna vaccine**
$/QALY saved (2-year timeframe)	**$55,995***	**$66,287**
$/QALY saved (3-year timeframe)	Not reported	$42,495

Policy question 2: What is the incremental cost-effectiveness of vaccinating ***adults aged 60-74 years old at increased risk*** of severe RSV illness ***relative*** to "No vaccination"?

$/QALY saved (2-year timeframe)	**$89,064****	**$80,953**
$/QALY saved (3-year timeframe)	Not reported	$49,198

* Target population: All adults ≥75yrs (Table 27, Moderna Technical report June13,2024)

** Target population: High-risk 60-74yrs (Table 27, Moderna Technical report June13,2024)

Policy question 3: GSK and UM-CDC

Policy question 3: What is the incremental cost-effectiveness of vaccinating ***adults aged 50-59 years at increased risk*** of severe RSV illness ***relative*** to "No vaccination"?

	GSK*	UM-CDC**
$/QALY saved (2-year timeframe)	Not reported	$154,501
$/QALY saved (3-year timeframe)	Cost-saving to $2,445	$112,949

* GSK estimated cost-saving values for four high risk conditions: COPD, heart failure, CAD and Diabetes. For Asthma, GSK estimated societal cost of $2,445/ QALY saved
** In the base case (2-year vaccine effectiveness timeframe), Michigan estimated a *societal cost of $154,501 /QALY saved* for adults with at least one chronic condition (COPD, asthma, CAD, CKD, Severe Obesity, or Diabetes). For individual conditions, societal costs ranged from $30,720 (CKD) to $171,661 (Diabetes) per QALY saved. When evaluating other specific conditions not included in "at least one", $/QALY ranged from cost-saving (lung transplant, allogeneic hematopoietic cell transplant) to $14,335 (heart failure) and $14,521 (autologous hematopoietic cell transplant).

Limitations

- **Factors not considered that may result in underestimating the cost-effectiveness of RSV vaccination**
  - No impact of RSV on long-term prognosis of COPD or of other higher risk conditions
  - No indirect effects of vaccination (i.e., no protection against RSV transmission)
  - No productivity or quality of life impact on caregivers during RSV illness
- **All models *partially* 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
- **Manufacturer models *partially* include** *potential* vaccine-associated serious adverse events (SAEs) or from Guillain Barre syndrome (GBS): Quality of life impact, resource utilization, and costs associated with SAEs, including GBS specifically for protein subunit RSV vaccines.
- **Vaccine efficacy beyond median clinical trial follow-up time (beyond 19 months, Moderna; or 23 months, GSK) is unknown**
  - All 3 models assumed non-zero declining efficacy beyond trial time data
- **All 3 models assumed seasonal vaccination** (with optimal timing in the late summer and early fall) without off-RSV-season vaccination impact.

Conclusion

- **Differences in key inputs and assumptions among GSK, Moderna and UM-CDC models explain differences in results:**
  - Annual incidence of RSV hospitalization and outpatient disease
  - Initial vaccine effectiveness and waning of protection
  - Medical cost per RSV hospitalization

Resulting ICERs for policy questions vary by age and high-risk group:

- **1:** Vaccinating *all adults aged ≥75 years old* against RSV illness
  - **Moderna** and **UM-CDC** models reported societal costs between $51K to $66K per QALY saved
- **2:** Vaccinating *adults aged 60-74 years old at higher risk* of severe RSV disease
  - **Moderna** and **UM-CDC** models reported societal costs between $61K to $89K per QALY saved
- **3:** Vaccinating *adults aged 50-59 years old at higher risk* showed more discrepant $/QALY ratios
  - Outcomes ranged from societal *cost-saving* (**GSK**) to $154K per QALY saved (**UM-CDC**)

Overall, vaccination would significantly reduce RSV disease burden in adults 50-59 and 60-74 years old at higher risk of RSV disease and in the general population of adults aged ≥75 years old.

- Efficacy clinical trial data and assumptions support impact on disease reduction

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- Katherine Fleming-Dutra

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- Adult RSV working group members
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End of Summary

For more information, contact CDC
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TTY: 1-888-232-6348 www.cdc.gov