Economic Analysis of RSV Vaccination in Adults 50 years and Older

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Conflicts of interest statements

- No known conflict of interests.

Updates from last presentation before ACIP in June 2023*

- Risk-Based Analysis
  - Groups based on chronic medical conditions (CMCs) and age
- Added Moderna Vaccine
- Other New Inputs
  - RSV Epidemiology
    - Hospitalization incidence by chronic medical conditions
    - Outpatient incidence by chronic medical condition
    - RSV-mortality inclusive of deaths in ***and out of hospital***
  - Real-world observational vaccine effectiveness of RSV protein subunit vaccination (Pfizer/GSK)
    - Duration of protection derived from clinical trial efficacy waning over time using all available follow up time
  - Vaccine adverse events after protein subunit RSV vaccination
    - Real world evidence on local and systemic vaccine reactions (V-safe)
    - Risk of Guillain-Barre syndrome (GBS) observed after RSV vaccination in administrative claims data through FDA/CMS partnership

* DW Hutton, "Economic Analysis of RSV Vaccination in Older Adults" June 21, 2023 (cdc.gov)

Methods

Methods: Study question

- Determine the cost-effectiveness of RSV vaccination by:
  - Comparing vaccination to no vaccination using the incremental cost-effectiveness ratio
  - Scenario analyses.
- Perspective: Societal

Methods: Intervention(s)

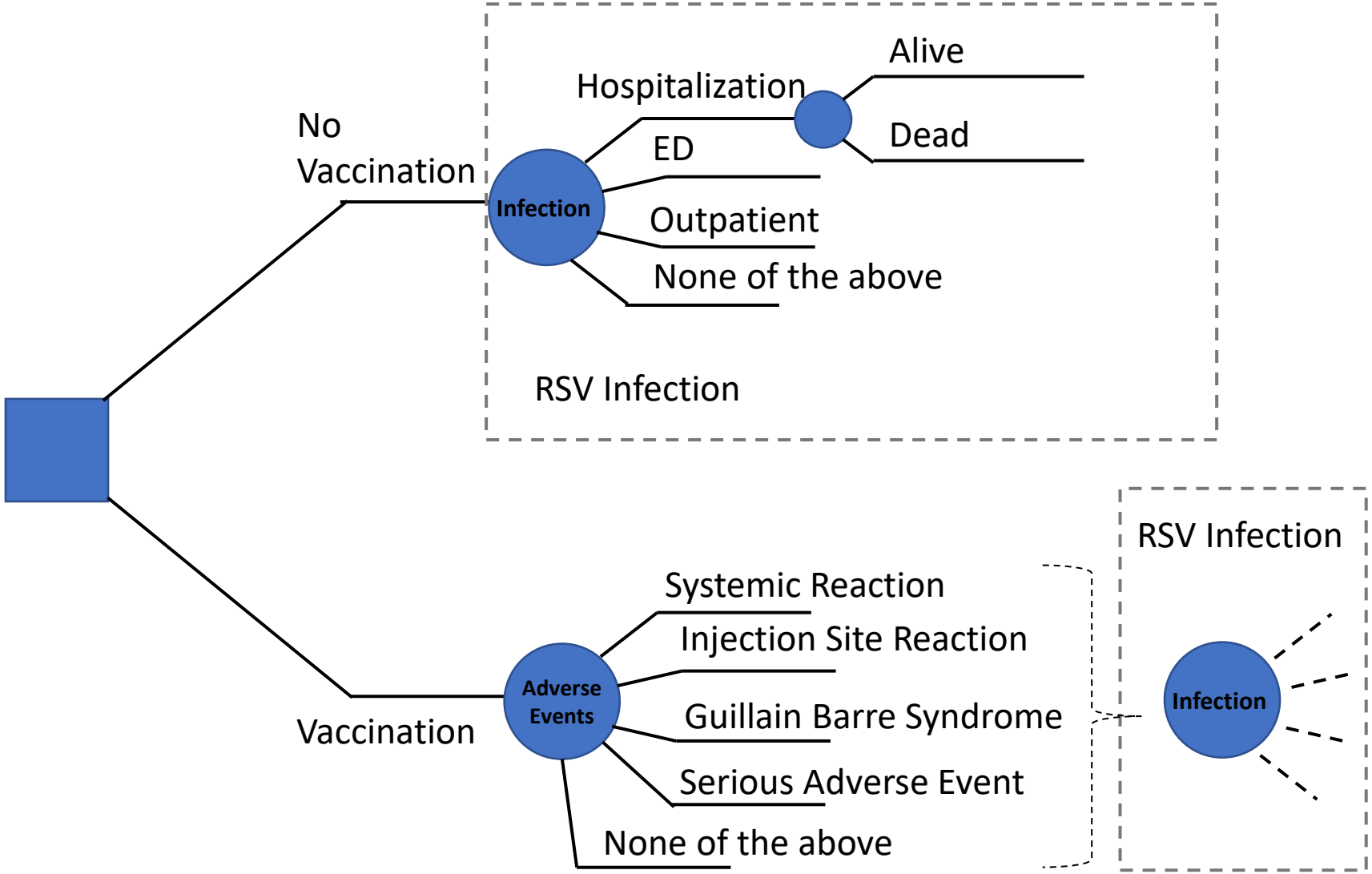
- Target population: US adults aged ≥50 years, stratified by age, chronic medical conditions
  - **Adults aged ≥75 years**
  - **Adults aged 60-74 years with at least one chronic medical condition***
  - **Adults aged 50-59 years with at least one chronic medical condition***
- Interventions: RSV vaccination
  - Protein subunit RSV vaccination (Pfizer's ABRYSVO, GSK's AREXVY)
  - Moderna RSV vaccination (Moderna's mRESVIA)
- Each compared to no vaccination

*At least one of: chronic obstructive pulmonary disease (COPD), asthma, coronary artery disease, chronic kidney disease, diabetes mellitus, severe obesity (BMI ≥40)

Combining Pfizer and GSK in base case

- ACIP has previously seen that product-specific cost effectiveness for the two currently licensed protein subunit RSV vaccines is similar
- Policy question does not distinguish between the two products
- Combining products allows simplification of results and enables us to focus on the policy questions
- Product-specific results will still be shown in scenario analyses
- Benefit/risk analyses evaluating GBS risk will be shown at the end and continue to be product-specific, understanding whether there is meaningful difference between products in terms of benefit/risk balance

Methods: Decision Tree Model



Annual RSV Incidence

- Hospitalizations
  - RSV-NET estimated annual hospitalizations per 100,000 population (adjusted for under-detection, including a 1.5x multiplier to account for RSV test sensitivity)
    - Source, age stratification only: Havers et al. manuscript draft, ***2016-2020***
    - Source, stratification by age AND presence/absence of chronic medical conditions: Update to Woodruff et al. analysis presented to ACIP in February 2024, ***2017-2018***[1]
- Emergency Department visits:
  - From McLaughlin et al. meta-analysis[2] (main results incorporating a 1.5x multiplier to account for RSV laboratory test sensitivity).
  - No differences by presence or absence of chronic medical conditions*
- Outpatient:
  - The base values (all-comers) are from the McLaughlin et al. meta-analysis.[2]
  - Values for adults with chronic cardiopulmonary conditions (e.g., COPD) are drawn from Belongia et al.[3] and multiplied by 1.5x for test sensitivity to align with RSV-NET and McLaughlin et al. methods.
  - Non-cardiopulmonary conditions (e.g., diabetes) utilize the base values (same as for all-comers)

*Values were assumed to be the same for adults with and without chronic medical conditions. This is a conservative assumption made in the absence of reliable risk-stratified data on the incidence of emergency department visits.

1. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2024-02-28-29/03-RSV-Adults-Woodruff-508.pdf
2. Pfizer-sponsored: McLaughlin JM, et al. Rates of Medically Attended RSV Among US Adults: A Systematic Review and Meta-analysis. Open Forum Infect Dis. 2022 Jun 17;9(7):ofac300. doi: 10.1093/ofid/ofac300. PMID: 35873302; PMCID: PMC9301578.
3. Novavax sponsored: Belongia EA, et al. Clinical features, severity, and incidence of RSV illness during 12 consecutive seasons in a community cohort of adults ≥60 years old. In Open forum infectious diseases 2018 Dec (Vol. 5, No. 12, p. ofy316). US: Oxford University Press

Annual RSV incidence

- **At least one** chronic medical condition (source RSV-NET):
  - Chronic obstructive pulmonary disease (COPD), OR
  - Asthma, OR
  - Coronary artery disease (CAD), OR
  - Diabetes mellitus, OR
  - Chronic kidney disease (CKD), OR
  - Severe obesity (body mass index [BMI] ≥40 kg/m^2)
- Additional chronic medical conditions evaluated in scenario analyses:
  - Heart failure[1]
  - Immune compromised
    - Lung transplant[2]
    - Hematopoietic cell transplant, allogeneic[3,4]
    - Hematopoietic cell transplant, autologous[3,4]

These conditions are considered separately because RSV epidemiologic parameters were derived from different published sources and cannot be combined with RSV-NET hospitalization rate estimates under “at least one” condition.

1. Kujawski SA, et al. Rates of respiratory syncytial virus (RSV)-associated hospitalization among adults with congestive heart failure-United States, 2015-2017. PLoS One. 2022 Mar 9;17(3):e0264890. doi: 10.1371/journal.pone.0264890
2. Testaert H, et al. Incidence, management and outcome of respiratory syncytial virus infection in adult lung transplant recipients: a 9-year retrospective multicentre study. Clin Microbiol Infect. 2021 Jun;27(6):897-903. doi: 10.1016/j.cmi.2020.07.050.
3. Martino R, et al. Prospective study of the incidence, clinical features, and outcome of symptomatic upper and lower respiratory tract infections by respiratory viruses in adult recipients of hematopoietic stem cell transplants for hematologic malignancies. Biol Blood Marrow Transplant. 2005 Oct;11(10):781-96. doi: 10.1016/j.bbmt.2005.07.007
4. Waghmare A, et al. Supplemental Oxygen-Free Days in Hematopoietic Cell Transplant Recipients With Respiratory Syncytial Virus. J Infect Dis. 2017 Dec 5;216(10):1235-1244. doi: 10.1093/infdis/jix390

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    - Hematopoietic cell transplant, allogeneic[3,4]
    - Hematopoietic cell transplant, autologous[3,4]

Assumed that vaccine effectiveness was reduced by <u>half</u> in immune compromised populations, compared with all others

1. Kujawski SA, et al. Rates of respiratory syncytial virus (RSV)-associated hospitalization among adults with congestive heart failure-United States, 2015-2017. PLoS One. 2022 Mar 9;17(3):e0264890. doi: 10.1371/journal.pone.0264890
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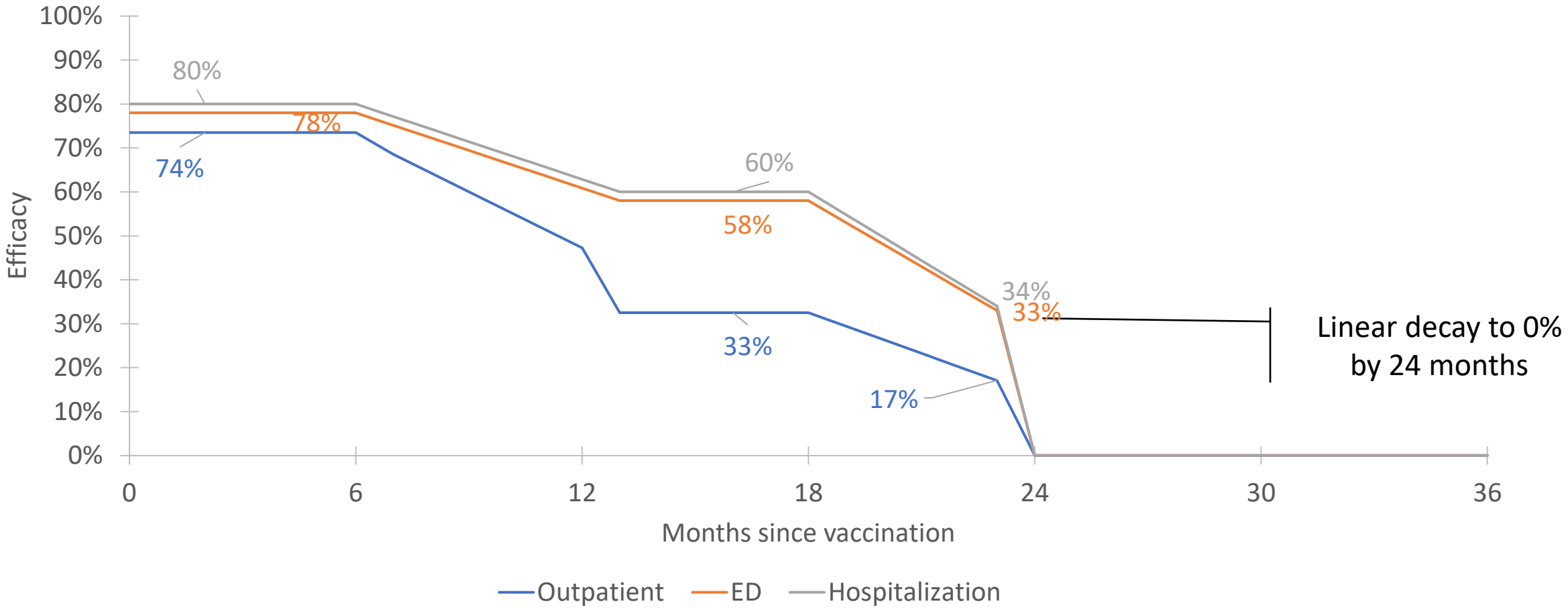
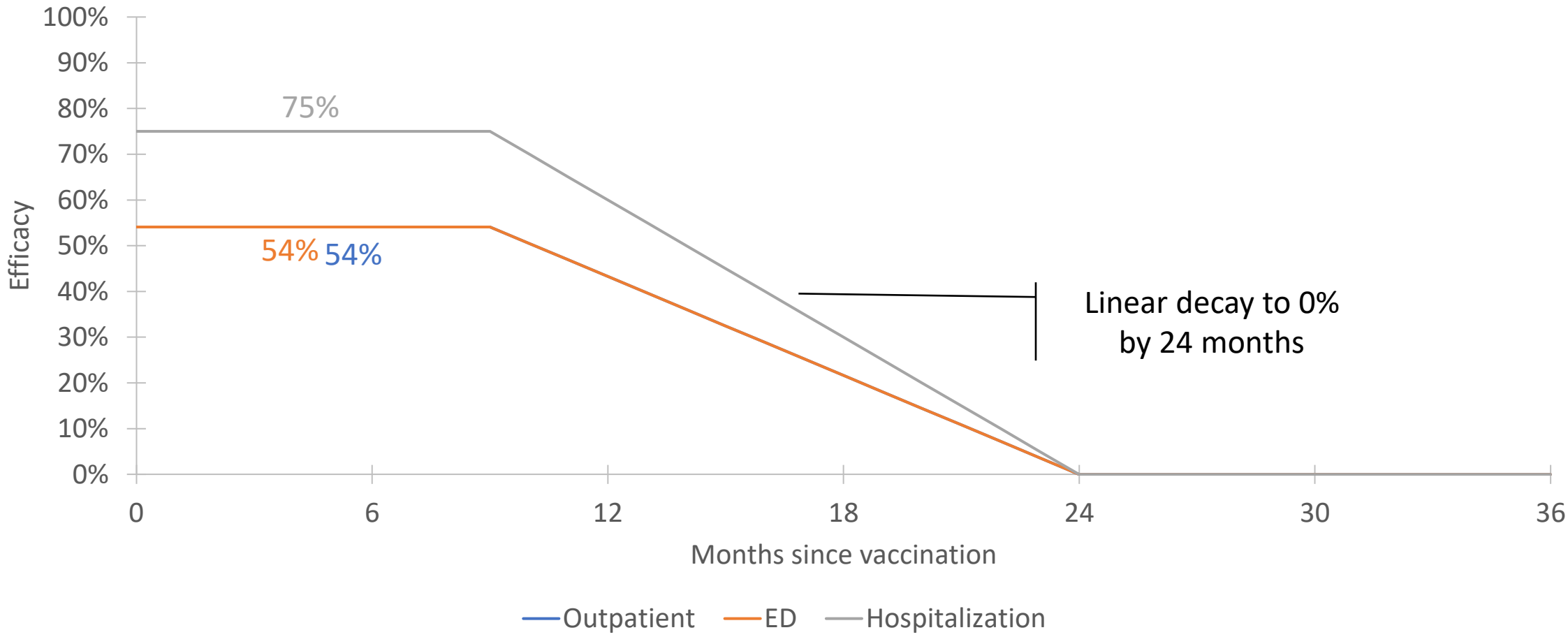
Vaccine effectiveness (VE) of a single dose over time: protein subunit RSV vaccine (combined Pfizer/GSK)



VE against hospitalization and emergency department visits during months 0-6 post-vaccination was assumed to be equal to results of a meta-analysis of observational VE estimates from CDC and Veterans Health Administration analyses from the first RSV season of vaccine availability. Proportional waning was applied from clinical trial vaccine efficacy over time against RSV lower respiratory tract illness with ≥3 signs/symptoms (Pfizer ABRYSVO) and RSV lower respiratory tract disease (GSK AREXVY) (data provided by manufacturers). VE against outpatient illness was assumed to be the mean across the two products of trial efficacy against RSV acute respiratory illness.

Vaccine effectiveness (VE) of a single dose over time: Moderna RSV vaccine (mRESVIA)



VE against hospitalization during months 0-9 post-vaccination was assumed to be equal to clinical trial vaccine efficacy against medically attended RSV lower respiratory tract disease with ≥3 signs/symptoms. VE against emergency department visits and outpatient illness during months 0-9 was assumed to be equal to clinical vaccine efficacy against medically attended RSV acute respiratory illness. VE was assumed to decline to zero by month 24 post-vaccination.

Methods: Adverse Events

- Pfizer and GSK systemic and injection site adverse event rates updated based on real-world V-safe data:
  - Pfizer: 6% experienced severe injection site reaction or systemic reaction
  - GSK: 10% experienced severe injection site reaction or systemic reaction
- Pfizer and GSK Guillain Barre syndrome (GBS) risk updated based on FDA active surveillance through partnership with CMS, Medicare beneficiaries ages ≥65 years[1], vaccinations during May–October 8, 2023:
  - Pfizer: 16 GBS cases (95% CI 3–29) per 1 million doses administered[2]
  - GSK: 3 GBS cases (95% CI 0–10) per 1 million doses administered[2,3]
- Moderna data based on trial
  - Moderna: 7% experienced severe injection site reaction or systemic reaction
  - Assumed no vaccine-attributable GBS risk
- All Vaccines: rare, unnamed serious adverse event of 1 per million doses administered

Abbreviations: CI = confidence interval, CMS = Centers for Medicare & Medicaid Services, FDA = U.S. Food and Drug Administration, GBS = Guillain-Barre syndrome

1. Must have been enrolled in Medicare Parts A, B and D. Must not have had a diagnostic code for GBS in the 365 days preceding vaccination.
2. These estimates reflect vaccine-attributable risk of GBS in excess of background rate of GBS among adults ages ≥65 years vaccinated with the same product. This analysis extrapolated from the study population and assumed the same risk applied to adults ages 50–64 years.
3. Attributable risk for GSK's AREXVY was estimated to be 3 GBS cases (95% CI: -3, 10) per 1 million doses. For mathematical modeling, lower end of the 95% CI was truncated at 0 to evaluate potential **risk** of GBS. Potential protective effects were not evaluated.

Methods: Base RSV Medical Costs

Variable	Value	Range	Source
Disease-specific hospitalization costs (per hospitalization)			
age 50 to <60 years	$20,330	9,511 – 39,544	Ackerson 2020*
age 60 to <65 years	$21,417	9,288 – 45,454	
age 65 to <75 years	$21,417	10,491 – 43,619	
age ≥75 years	$22,425	10,491 – 43,619	
Disease-specific ED costs (per ED visit)			
age 60 to <65 years	$1,210	-	2016 Marketscan*
age 65 to <75 years	$1,210	-	
age ≥75 years	$1,210	-	
Disease-specific outpatient costs (per outpatient visit)			
age 60 to <65 years	$117.58	65.88-145.38	MarketScan and Medicare FFS, 2020-2021
age 65 to <75 years	$100.86	50.48-120.08	
age ≥75 years	$100.86	50.48-120.08	

*Updated to 2023 using GDP Deflator

Methods: Hospitalization cost multiplier based on chronic medical conditions

Condition	Condition-specific multiplier, based on median length of stay (RSV-NET)
At least one condition*	1.06
With COPD	1.22
With Asthma	1.0
With CAD	1.13
With Diabetes	1.11
With severe obesity, BMI ≥40	1.0
With CKD	1.26
None of these conditions**	0.84
With Heart Failure	1.28
Immune Compromise	1.06

*Have at least one of: chronic obstructive pulmonary disease, asthma, coronary artery disease, diabetes mellitus, severe obesity (BMI ≥40), chronic kidney disease; may also have other conditions such as heart failure or immune compromise

** None of the conditions in the at least one definition, but may have other conditions such as heart failure or immune compromise

Methods: Vaccination-Related Costs

Variable	Value	Range	Source
Vaccine, per dose			
Pfizer	$295		List price
GSK	$280		List price
Moderna	$290		Manufacturer Assumption
Vaccine administration	$16.96	-	HCPCS 90460 (Physician Fee Schedule 2022)

Methods: Additional Inputs

- Also included
  - RSV illness QALYs lost
  - RSV illness productivity costs
  - Vaccination healthcare and productivity costs
  - Vaccination adverse events
    - Medical costs
    - Productivity costs
- *These assumptions remain unchanged from October 2023*

* DW Hutton, “Economic Analysis of RSV Vaccination in Older Adults” June 21, 2023 (cdc.gov)

Methods: Scenarios

- Manufacturer-specific (Pfizer and GSK-specific models; Moderna is considered separately in the base case, so no scenario needed)
- Assuming longer duration of protection (efficacy declines to 0 at 36 rather than at 24 months)
- Among persons *without* chronic medical conditions
- Condition-specific (e.g., among persons with heart failure)

Base case results

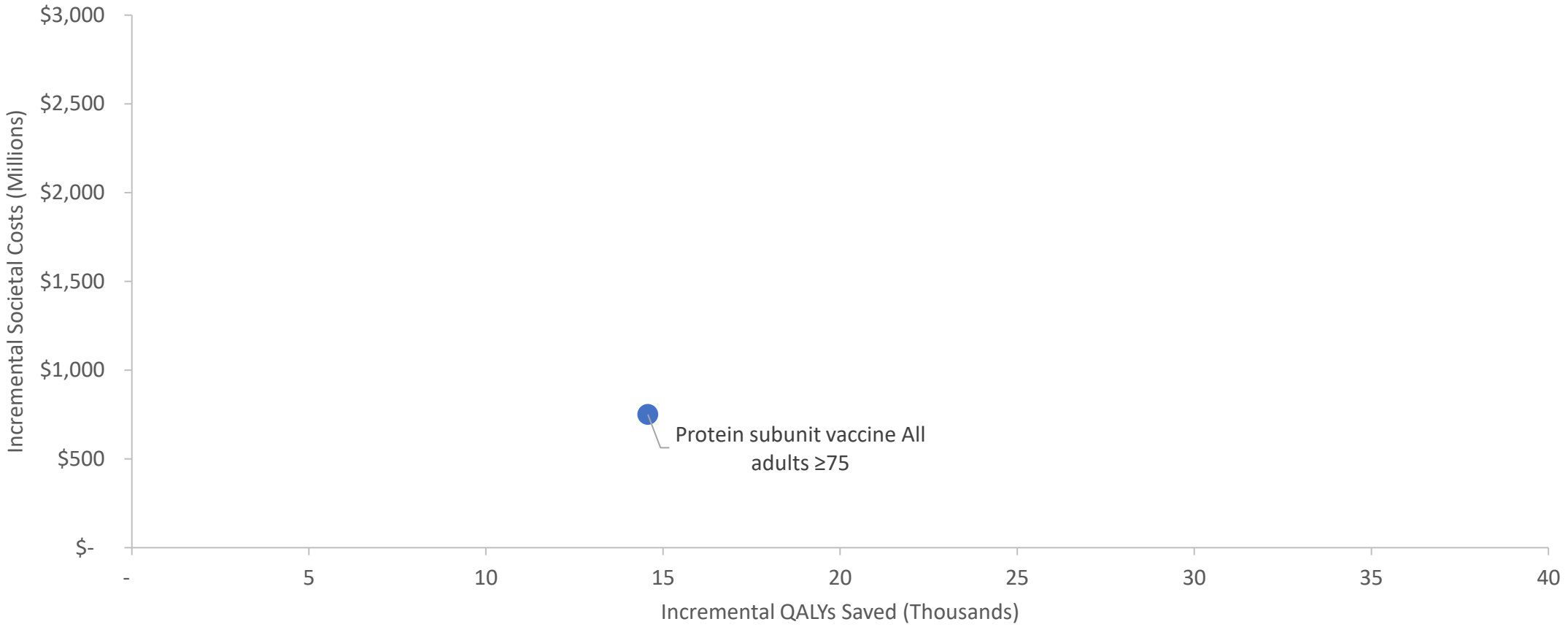
Base case Incremental Cost-Effectiveness Ratios ($/QALY)

	Protein subunit RSV vaccines (combined Pfizer + GSK)	Moderna RSV vaccine
All adults 75+	$ 51,447	$ 66,287
Adults 60-74 with at least 1 condition[1]	$ 60,933	$ 80,953
Adults 50-59 with at least 1 condition[1,2]	$ 154,501	

1. At least one of: chronic obstructive pulmonary disease, asthma, coronary artery disease, diabetes mellitus, chronic kidney disease, severe obesity (BMI ≥40)
2. Only a single vaccine (GSK AREXVY) is licensed in adults 50-59. So, this uses GSK-specific input parameters for this age group.

BMI: body mass index, QALY: Quality-Adjusted Life-Year

Incremental Cost-Effectiveness



QALY: Quality-Adjusted Life-Year

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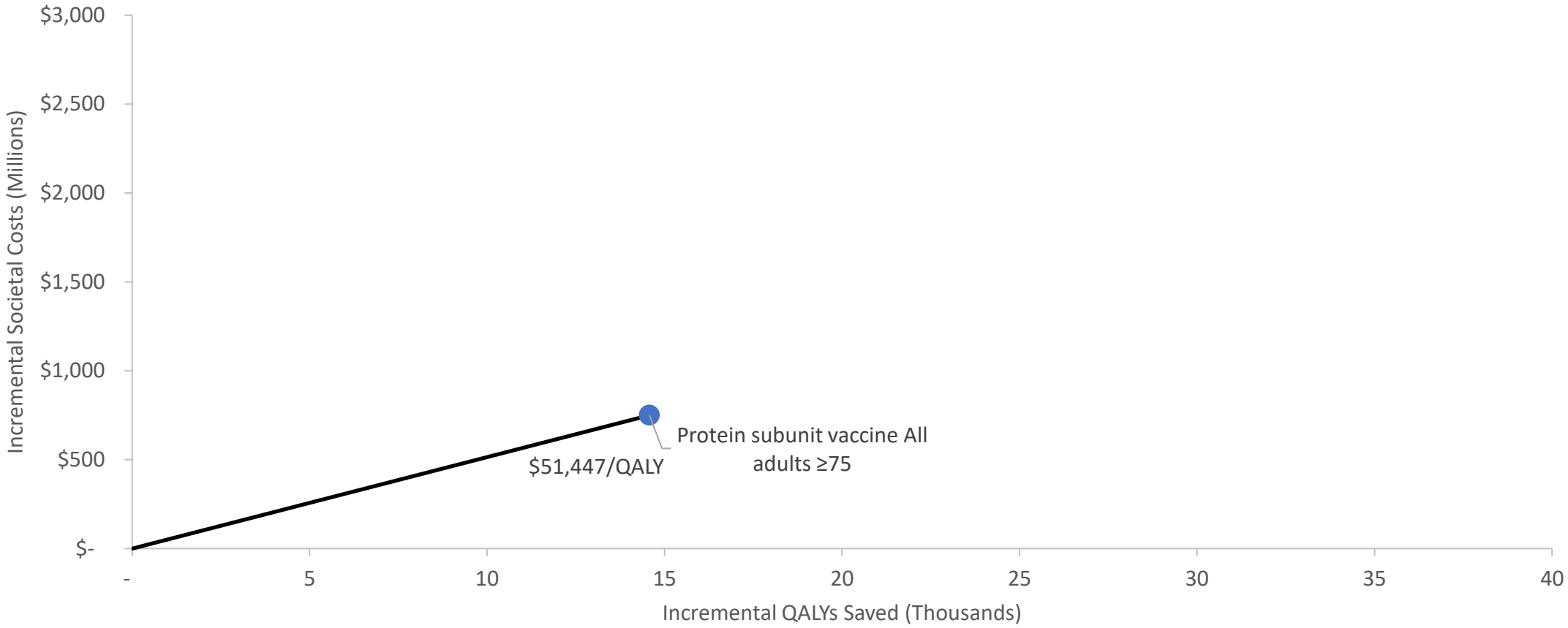

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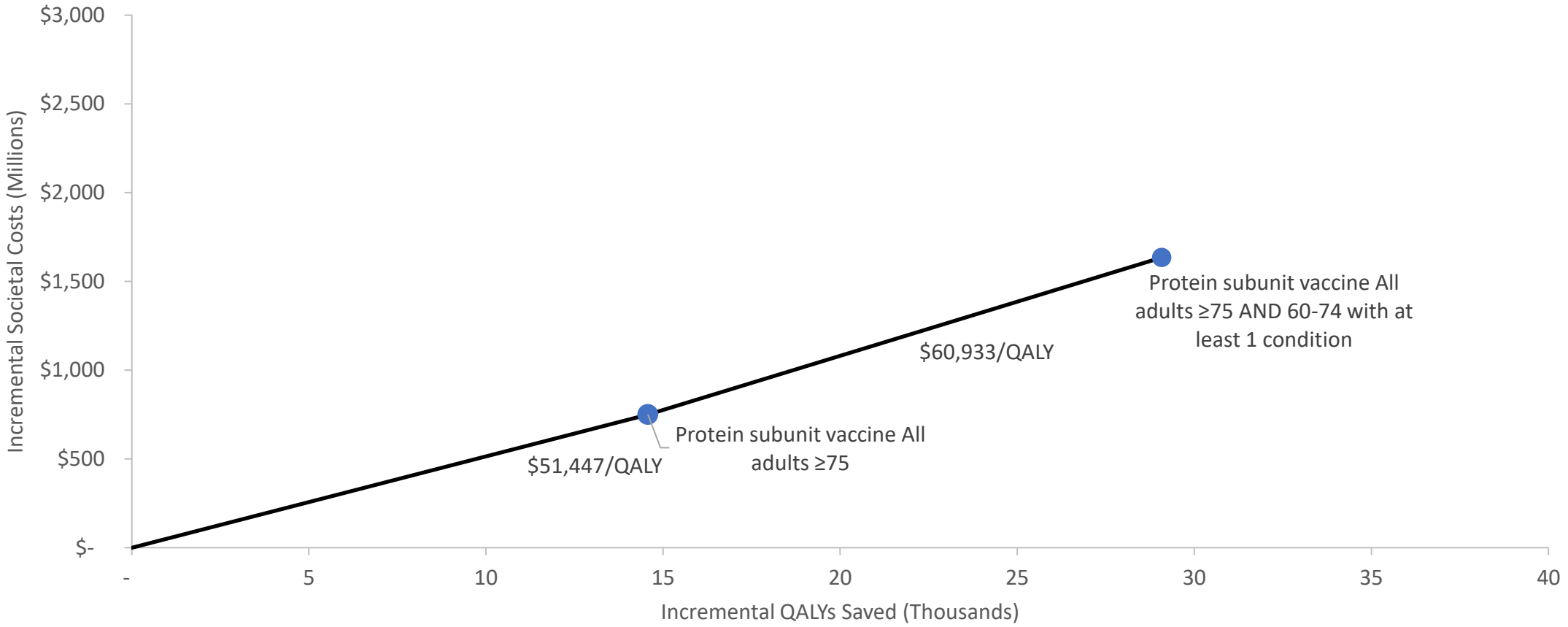

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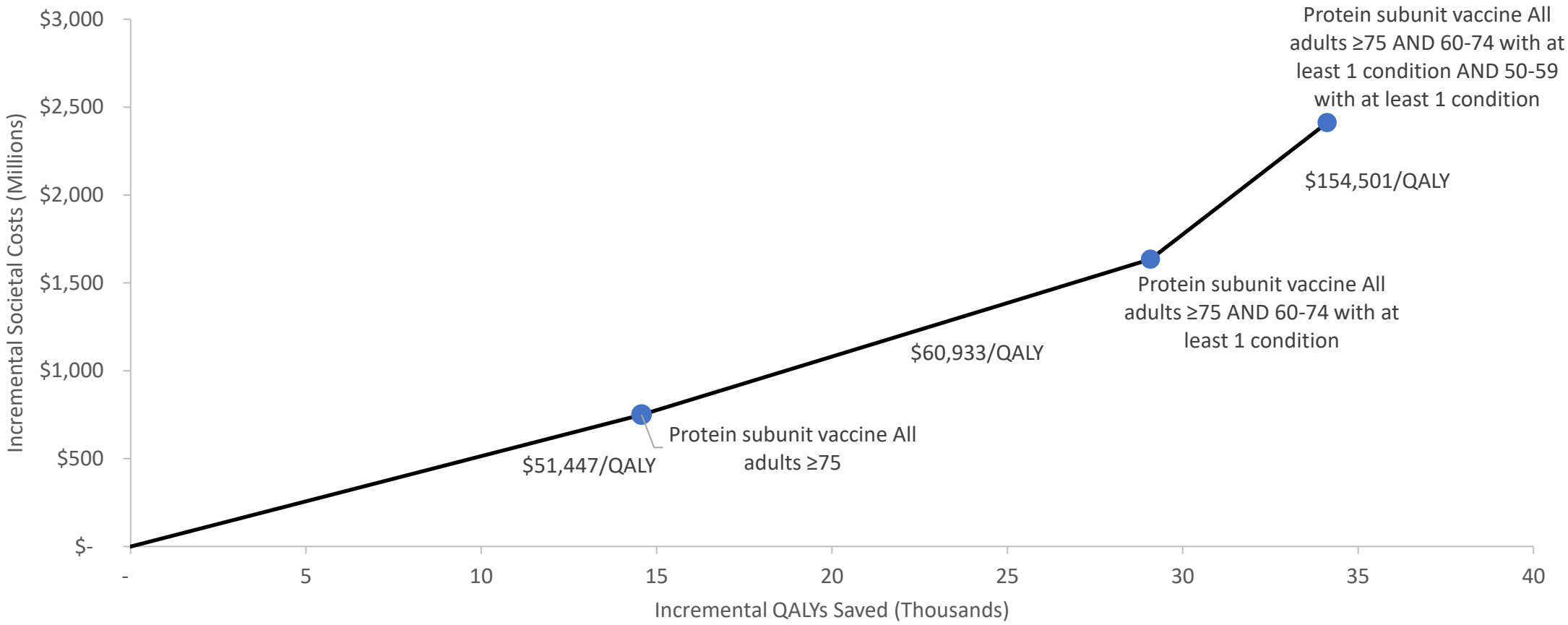

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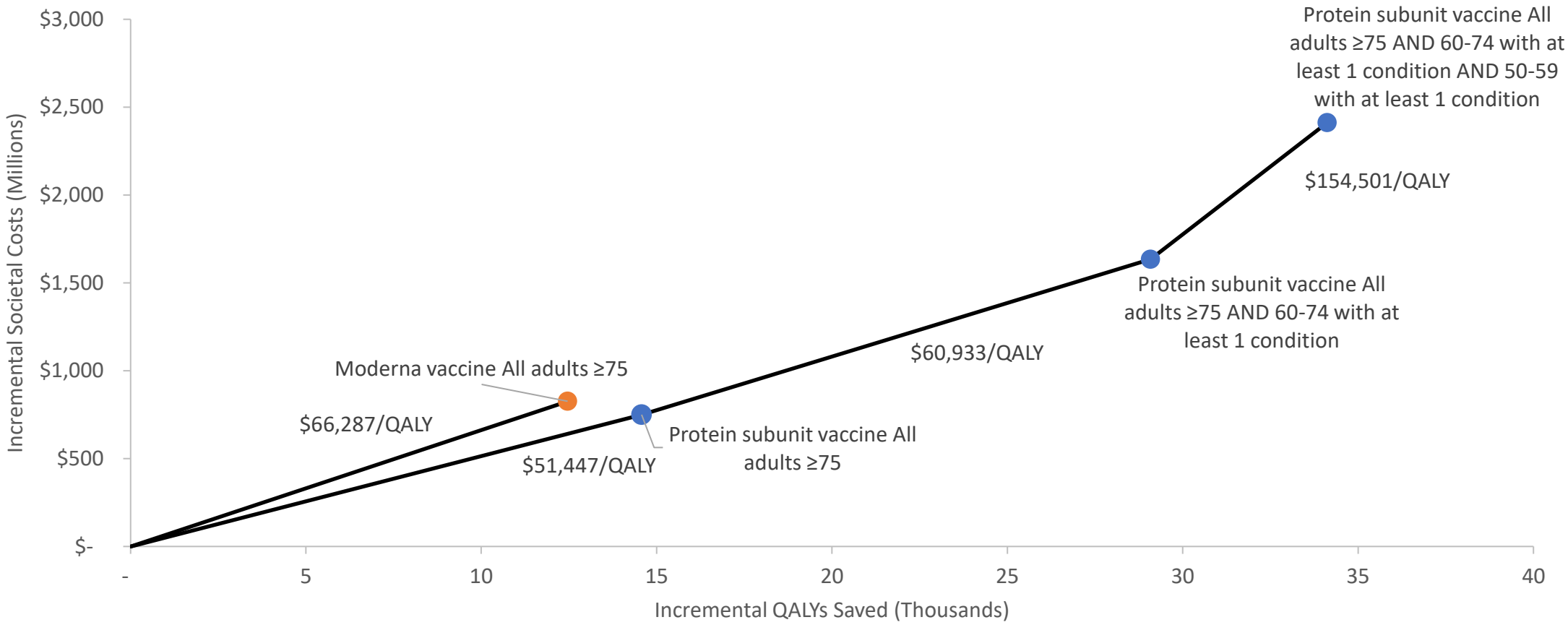

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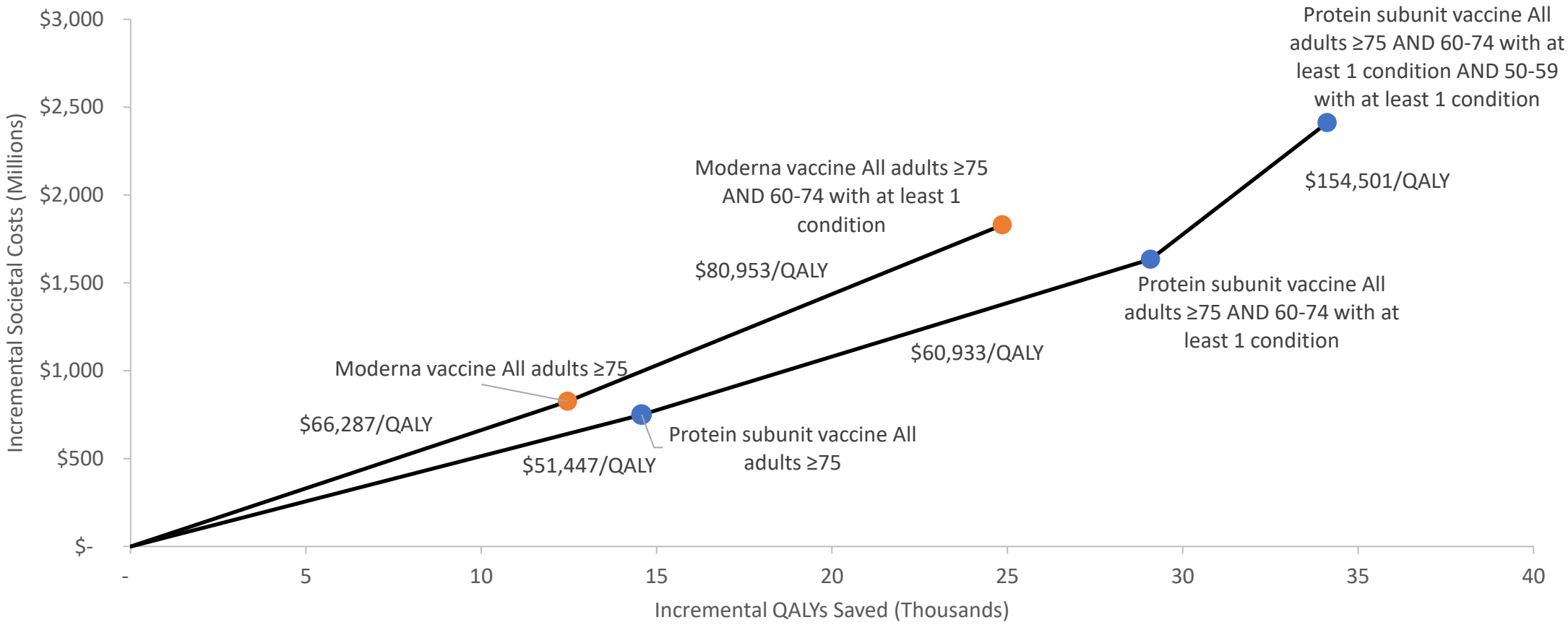


QALY: Quality-Adjusted Life-Year

At least one of: chronic obstructive pulmonary disease, asthma, coronary artery disease, diabetes mellitus, chronic kidney disease, severe obesity (BMI ≥40)

Scenario analyses

Protein subunit RSV vaccination: product-specific

	GSK AREXVY	Pfizer ABRYSVO
All adults 75+	$ 47,050	$ 58,739
Adults 60-74 with at least 1 condition	$ 55,006	$ 70,624

At least one of: chronic obstructive pulmonary disease, asthma, coronary artery disease, diabetes mellitus, chronic kidney disease, severe obesity (BMI ≥40)

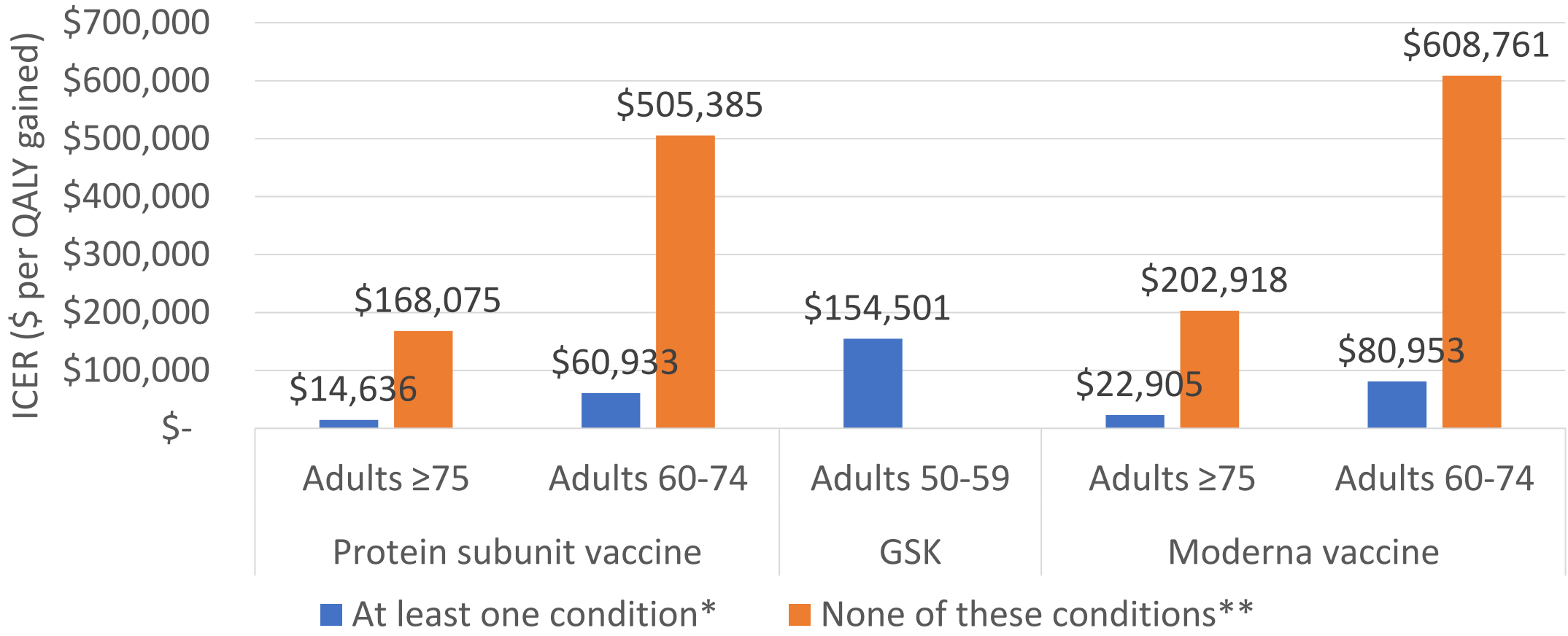
Time Horizon Comparison

	Base case (**24 months of efficacy**)		Scenario (**36 months of efficacy**)	
	Protein subunit RSV vaccines (combined Pfizer + GSK)	**Moderna RSV vaccine**	**Protein subunit RSV vaccines (combined Pfizer+GSK)**	**Moderna RSV vaccine**
All adults 75+	$ 51,447	$ 66,287	$ 39,833	$ 42,495
Adults 60-74 with at least 1 condition	$ 60,933	$ 80,953	$ 45,445	$ 49,198
Adults 50-59 with at least 1 condition*	$ 154,501		$ 112,949	

*Only a single manufacturer (GSK) has applied for FDA licensure in adults 50-59. So, this scenario uses GSK-specific inputs.

At least one of: chronic obstructive pulmonary disease, asthma, coronary artery disease, diabetes mellitus, chronic kidney disease, severe obesity (BMI ≥40)

Cost-Effectiveness by age and conditions



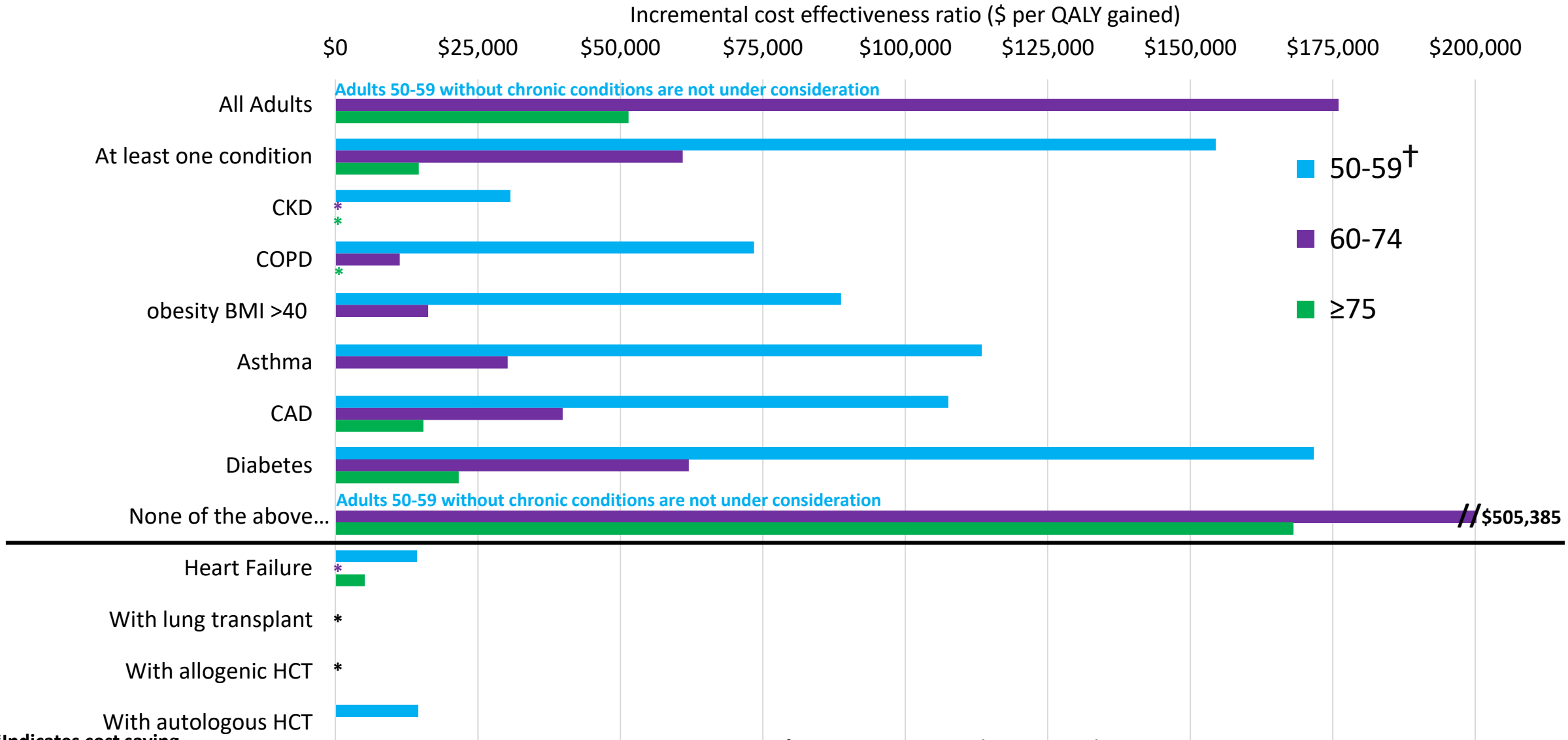
* At least one of: chronic obstructive pulmonary disease, asthma, coronary artery disease, diabetes mellitus, chronic kidney disease, severe obesity (BMI ≥40)
** None of the above conditions. Persons may have other chronic medical conditions (e.g., heart failure, non-severe obesity, immune compromise).

Scenarios: Cost-effectiveness of vaccinating adults with specific chronic conditions

	Protein subunit RSV vaccines (combined Pfizer+GSK)	Moderna RSV vaccine
Adults 60-74 with specific conditions: heart failure, immune compromise, COPD, asthma, CAD, diabetes, severe obesity, chronic kidney disease	10 Scenarios	10 Scenarios
Adults 50-59 with specific conditions: as above	10 Scenarios (GSK-specific)*	

*Only a single vaccine (GSK AREXVY) is licensed in adults 50-59. So, this uses GSK-specific inputs for this age group.

Scenarios: Adults with specific chronic medical conditions, **protein subunit RSV vaccines (Pfizer/GSK)**



***Indicates cost saving**

At least one condition refers to: COPD, asthma, coronary artery disease, diabetes mellitus, chronic kidney disease, severe obesity (BMI ≥40)

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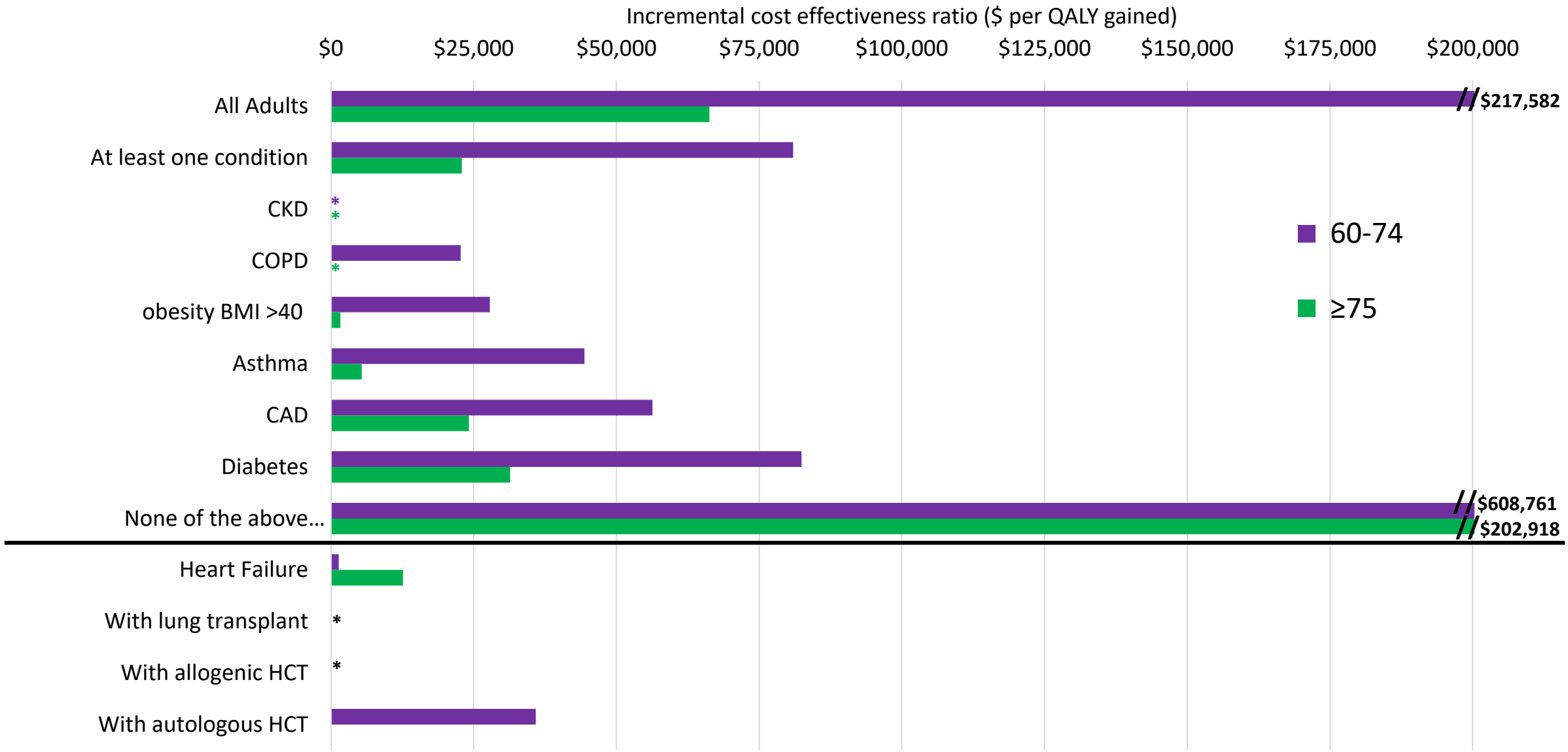
HCT: Hematopoietic Cell Transplant

Scenarios: Adults with specific chronic medical conditions, **Moderna RSV vaccine**



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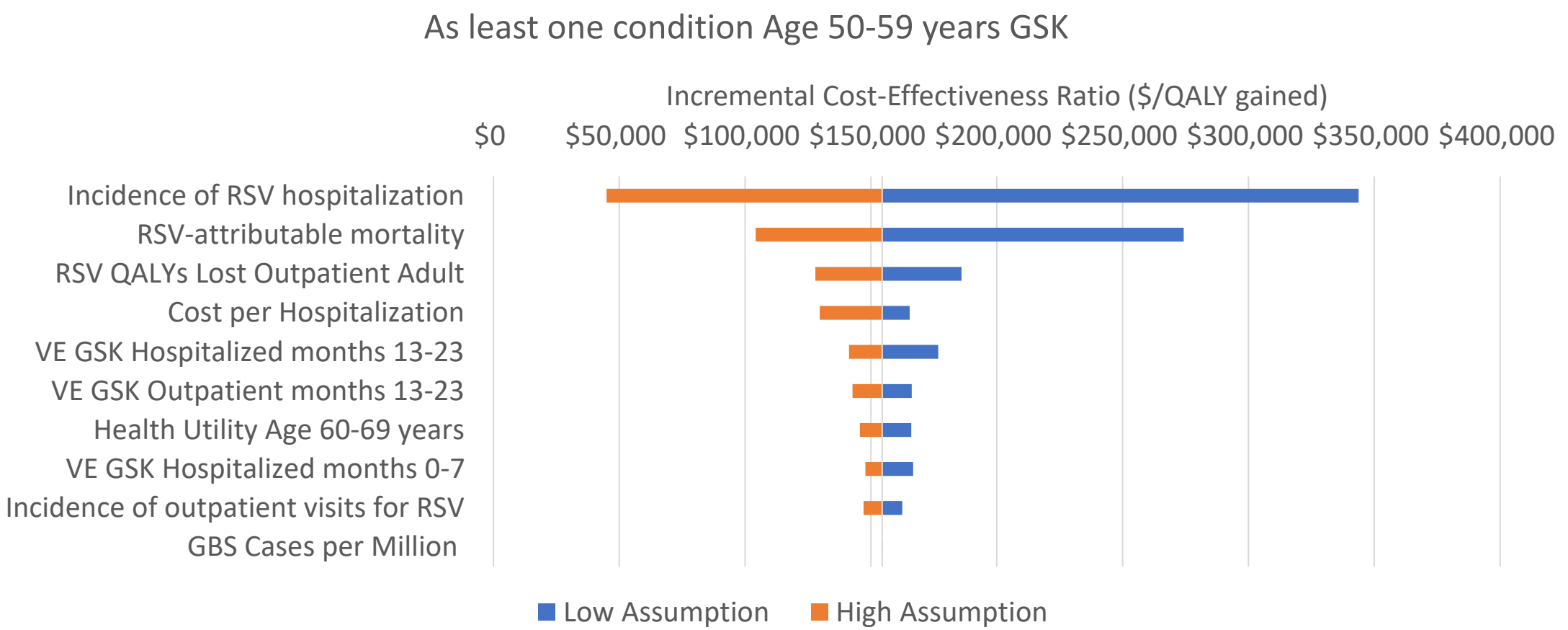
At least one condition refers to: COPD, asthma, coronary artery disease, diabetes mellitus, chronic kidney disease, severe obesity (BMI ≥40)

HCT: Hematopoietic Cell Transplant

Sensitivity Analysis:
Changing Parameter Assumptions

GSK RSV vaccine at least 1 condition age 50-59



Limitations

- Model Structure
  - No dynamic transmission. No impact of the vaccine on transmission and indirect effects
- We did not include or analyze all potential RSV risk factors.
  - Some medical conditions (e.g., interstitial lung disease) are likely associated with high risk of severe RSV disease, but literature on population-based hospitalization rates and other outcomes are lacking.
  - RSV vaccination may be cost effective for adults with additional conditions that were not evaluated.
- Uncertain inputs
  - Moderna real-world vaccine effectiveness
  - Moderna vaccine cost
  - RSV burden of disease, especially hospitalization and mortality
  - Duration and waning pattern of vaccine protection

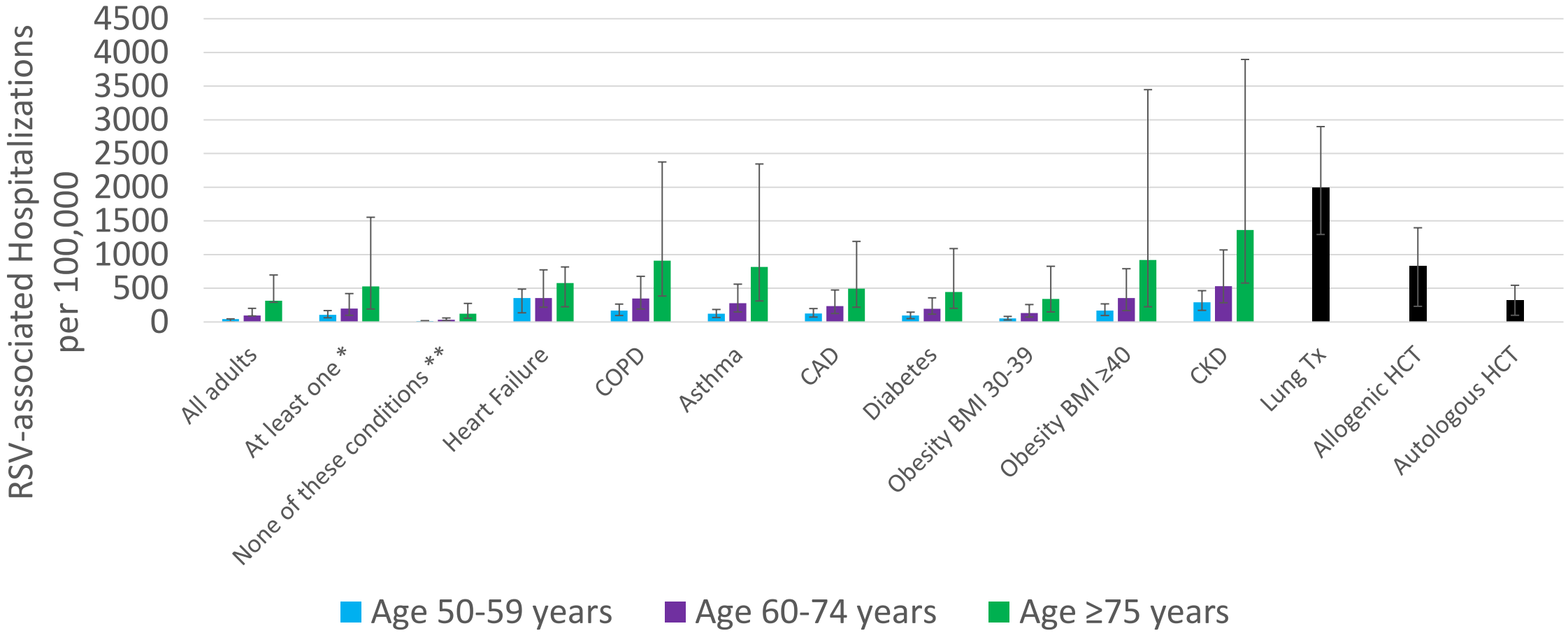
Conclusions

- If there were a recommendation for RSV vaccination **for all adults 75 and older** the ICER would be **$51,447 societal cost/QALY saved (Pfizer/GSK)** and **$66,287/QALY (Moderna)**.
  - If instead we limited the recommendation only to adults 75 and older with at least one chronic medical condition the **ICER would be $14,636/QALY (Pfizer/GSK) and $22,905 (Moderna)**
- If we add in adults **60-74 with at least one chronic medical condition**, the ICER would be **$60,933 societal cost/QALY (Pfizer/GSK)** and **$80,953/QALY (Moderna)**.
  - Vaccination of adults 60-74 *without* chronic conditions has an ICER of **$505,385/QALY (Pfizer/GSK) and $608,761/QALY (Moderna)**
- If we add in adults **50-59 with at least one chronic medical condition** the ICER would be **$154,501 societal cost/QALY saved (GSK only).**
  - By specific condition, $/QALY saved was lowest among adults 50-59 with heart failure **($14,335/QALY**) and immune compromise (**cost-saving or $14,521/QALY**) and highest among those with diabetes **($171,661/QALY**).
- Longer duration of protection (36 months rather than 24 months) or higher baseline RSV disease burden made all policy options more cost effective.

Thank You

- Please send comments to:
- dwhutton@umich.edu

Methods: Epidemiology
RSV Hospitalization Incidence by Age and Chronic Medical Condition *"back-up slide not shown at meeting"*



Source: CDC RSV-NET data from RSV seasons: 2016-17, 2017-18, 2018-19, 2019-2020

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** None of the above conditions. Persons may have other chronic medical conditions (e.g., heart failure, non-severe obesity, immune compromise).