

Risk-Benefit Analysis of RSV Vaccination in Older Adults

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Conflicts of interest statements

- No known conflict of interests.

Objective:



- Compare the **estimated benefits of RSV vaccination with the potential risk of Guillain-Barre syndrome (GBS) after RSV vaccination** in adults aged 50-59 years with chronic medical conditions, 60-74 years with chronic medical conditions, and among all adults aged 75 years and older.
- To do this, used the same mathematical models presented in previous presentation. In addition to cost effectiveness, **these models estimate the burden of RSV disease, including RSV-associated hospitalization, ICU admissions, and deaths, that might be averted** through vaccination.
- Will summarize estimated benefit outputs from those models and add information on potential rates of GBS experienced after RSV vaccination.
- **This is an update to the presentation on benefits and risks from the February 2024 ACIP meeting.** Here, we add information on observational (“real-world”) vaccine effectiveness against hospitalization and expand the analysis to evaluate benefits and risks specifically among adults with chronic medical conditions, including adults aged 50-59 years.
- Focus only on the **Protein subunit RSV vaccines** (manufactured by Pfizer and GSK). To date, there are no pre-licensure or observational data indicating risk of GBS after Moderna RSV vaccination (mRESVIA).

Methods: Study question

- Compare the **estimated benefits** of RSV vaccination and the **potential risk of Guillain-Barre syndrome (GBS)** after Protein subunit RSV vaccination (Pfizer/GSK).

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:** Protein subunit RSV vaccines
 - Pfizer's ABRYSSVO
 - GSK's AREXVY
- **Comparator:** 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)

Methods: Scenario analyses

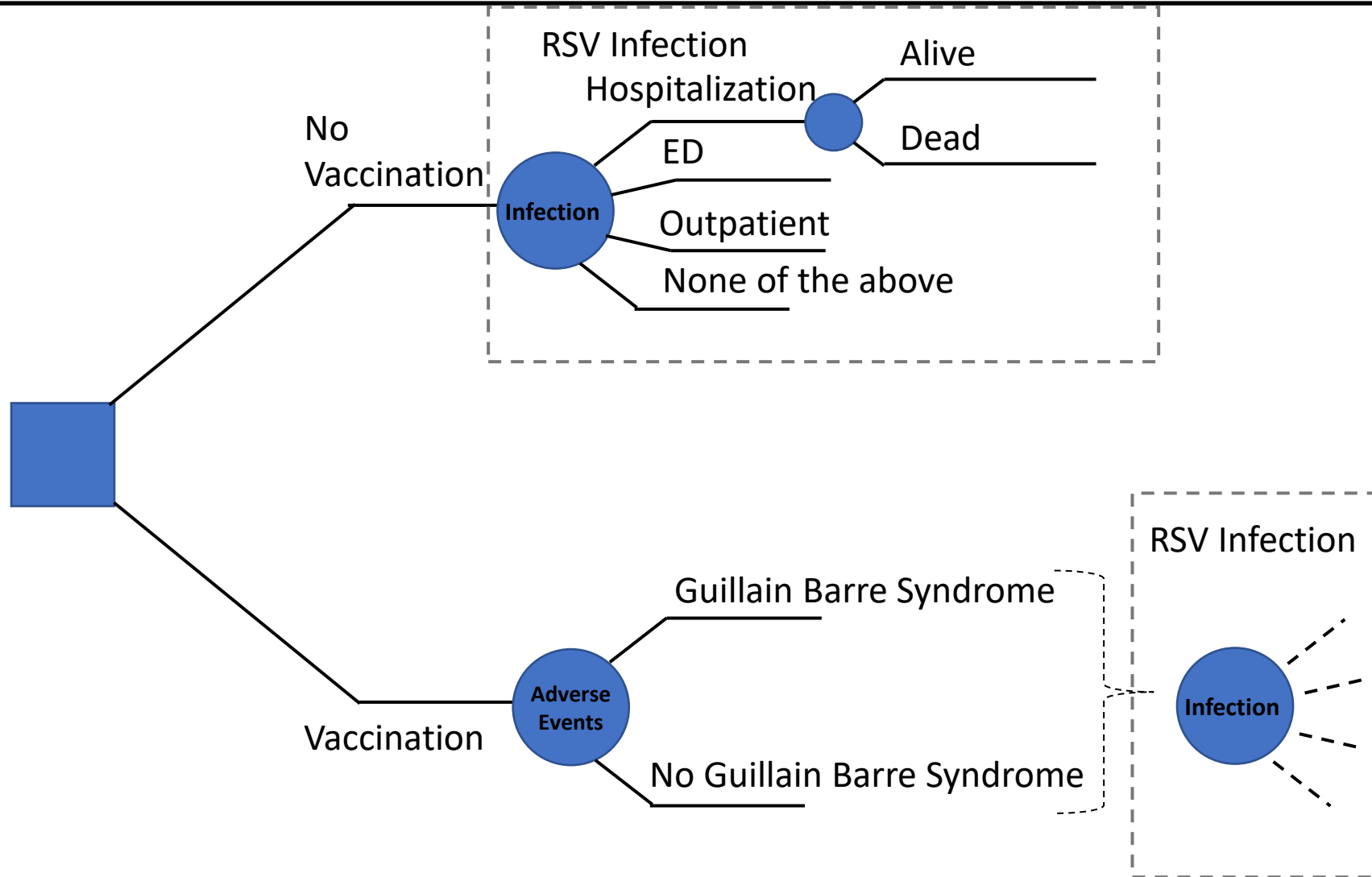
- Adults in each age group (50-59, 60-74, ≥ 75) **without** chronic medical conditions*
- Adults in each age group with **specific** chronic medical conditions:
 - Chronic obstructive pulmonary disease (COPD)
 - Asthma
 - Coronary artery disease
 - Chronic kidney disease
 - Diabetes mellitus
 - Severe obesity (BMI ≥ 40)

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- Heart failure
 - Immune Compromise
 - Lung Transplant
 - Hematopoietic cell transplant, allogeneic
 - Hematopoietic cell transplant, autologous

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

*None of: COPD, asthma, coronary artery disease, chronic kidney disease, diabetes mellitus, severe obesity (BMI ≥ 40)
Heart failure and immune compromise 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.

Methods: Decision Tree Model



Methods: Attributable Risk of Guillain Barre Syndrome (GBS) from RSV vaccination

- GBS risk attributable to RSV vaccination is based on FDA active surveillance using CMS data.
- The FDA analysis was a self-controlled case series based on inpatient claims data.
 - Study population: Medicare beneficiaries **ages ≥ 65 years**¹ who had received either Pfizer or GSK RSV vaccine, from May 2023 (date of FDA approval) to October 8, 2023
 - Used administrative inpatient claims data to identify GBS cases occurring within a **1–42-day risk interval** after RSV vaccination, compared with a 43–90-day control interval
 - Incidence rate ratios and attributable risk were adjusted for outcome-dependent observation time, positive predictive value of inpatient claims in identifying chart-confirmed GBS, and seasonality

Abbreviations: 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.

Reference (Dr. Patricia Lloyd, FDA, June 2024 ACIP meeting)

Methods: Attributable Risk of Guillain Barre Syndrome (GBS) from RSV vaccination

- Attributable risk of GBS:
 - **Pfizer ABRYVO: 16 GBS cases (95% CI: 3, 29) per 1 million doses administered**
 - **GSK AREXVY: 3 GBS cases (95% CI: 0, 10) per 1 million doses administered***
- These risk estimates are **in excess of** background rate of GBS. I.e., they represent excess GBS cases beyond those that would occur in this population without vaccination.
- This analysis remains preliminary. GBS cases identified using diagnostic coding must still undergo chart verification, and the analysis must be updated to include RSV vaccinations occurring after October 8, 2023.
- In the interim, we are using the available estimates, recognizing the associated uncertainty. We are also extrapolating from the study population (age ≥ 65 years) to adults aged 50–64 years.

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

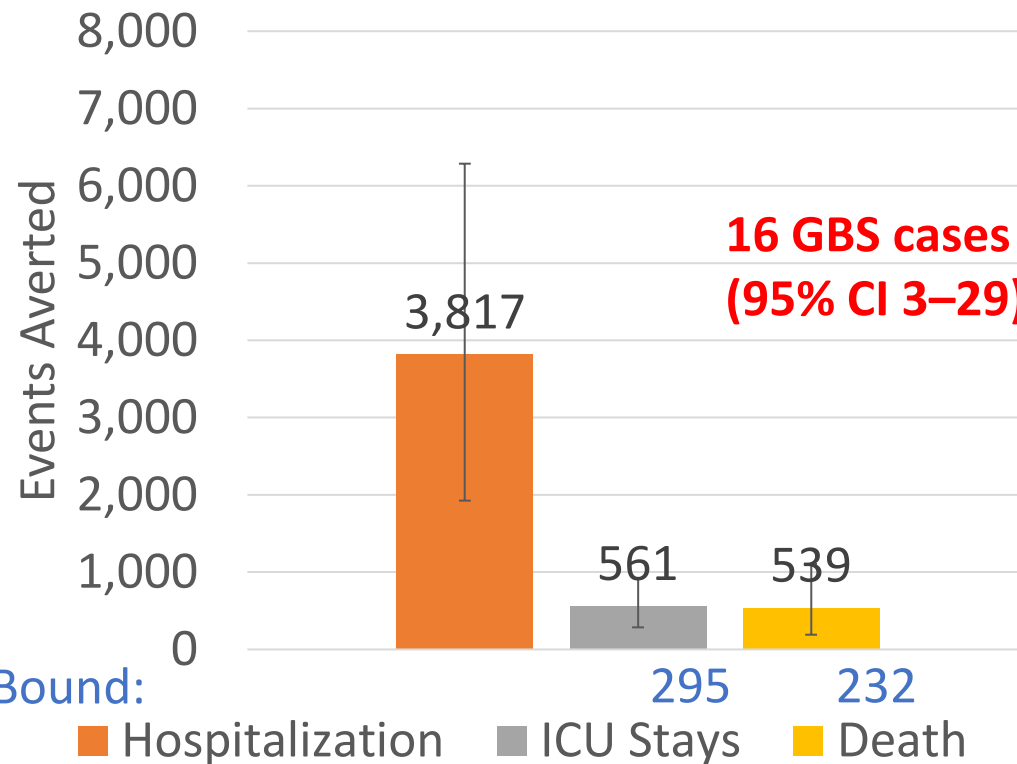
* Attributable risk for GSK's AREXVY was estimated to be 3 GBS cases (95% CI: -3, 10) per 1 million doses. For this analysis, the lower end of the 95% CI was truncated at 0 to evaluate potential **risk** of GBS. Potential protective effects were not evaluated.

Results: Estimated Benefits and Potential Risk

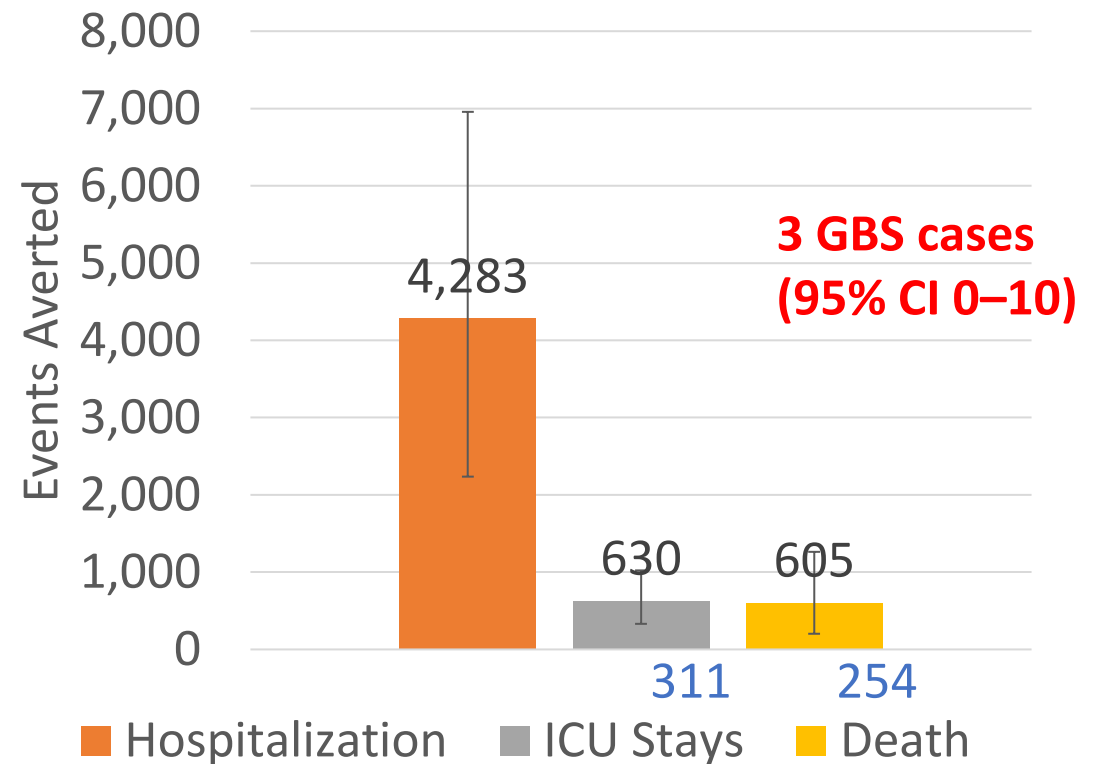
- Results are presented as **RSV outcomes avertable over 2 RSV seasons per 1 million single-dose RSV vaccinations**, and **attributable GBS risk per 1 million single-dose RSV vaccinations**.

Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in adults ≥ 75 years (general population)

Pfizer All Adults Age ≥ 75

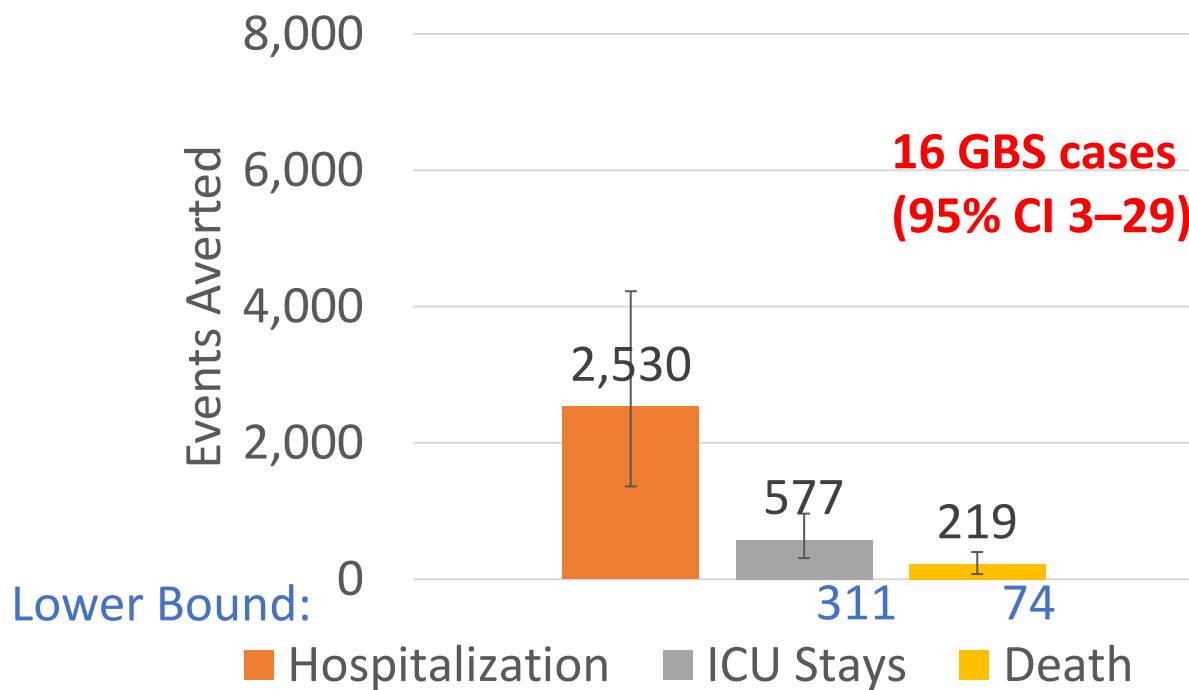


GSK All Adults Age ≥ 75

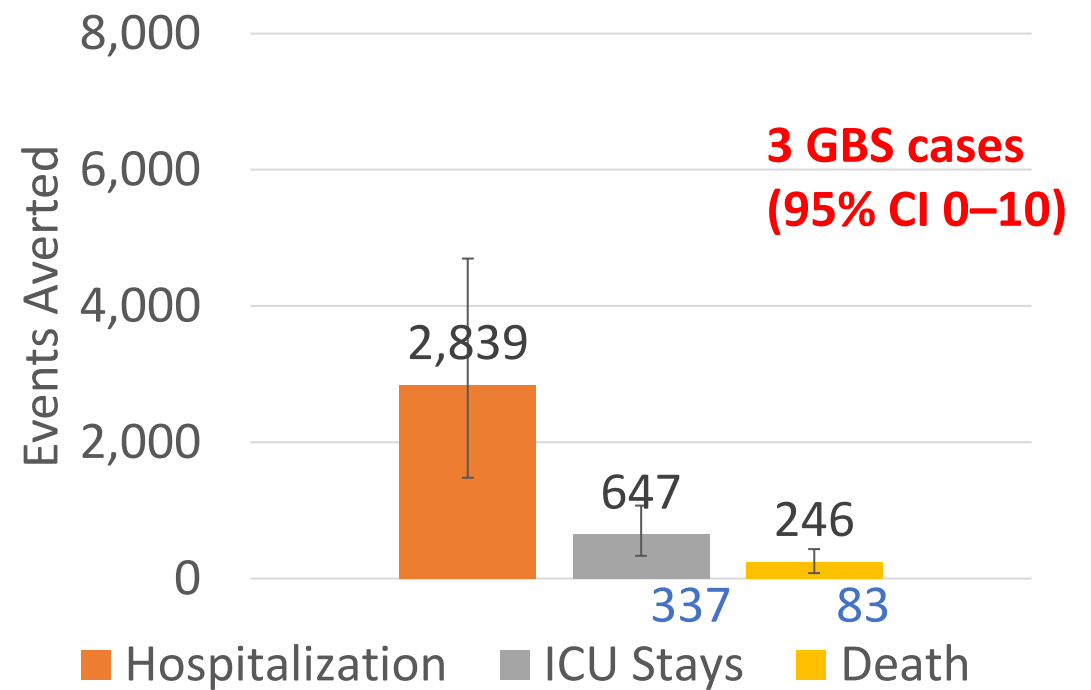


Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in adults 60-74 years with ≥ 1 chronic condition*

Pfizer At least one condition Age 60-74 years

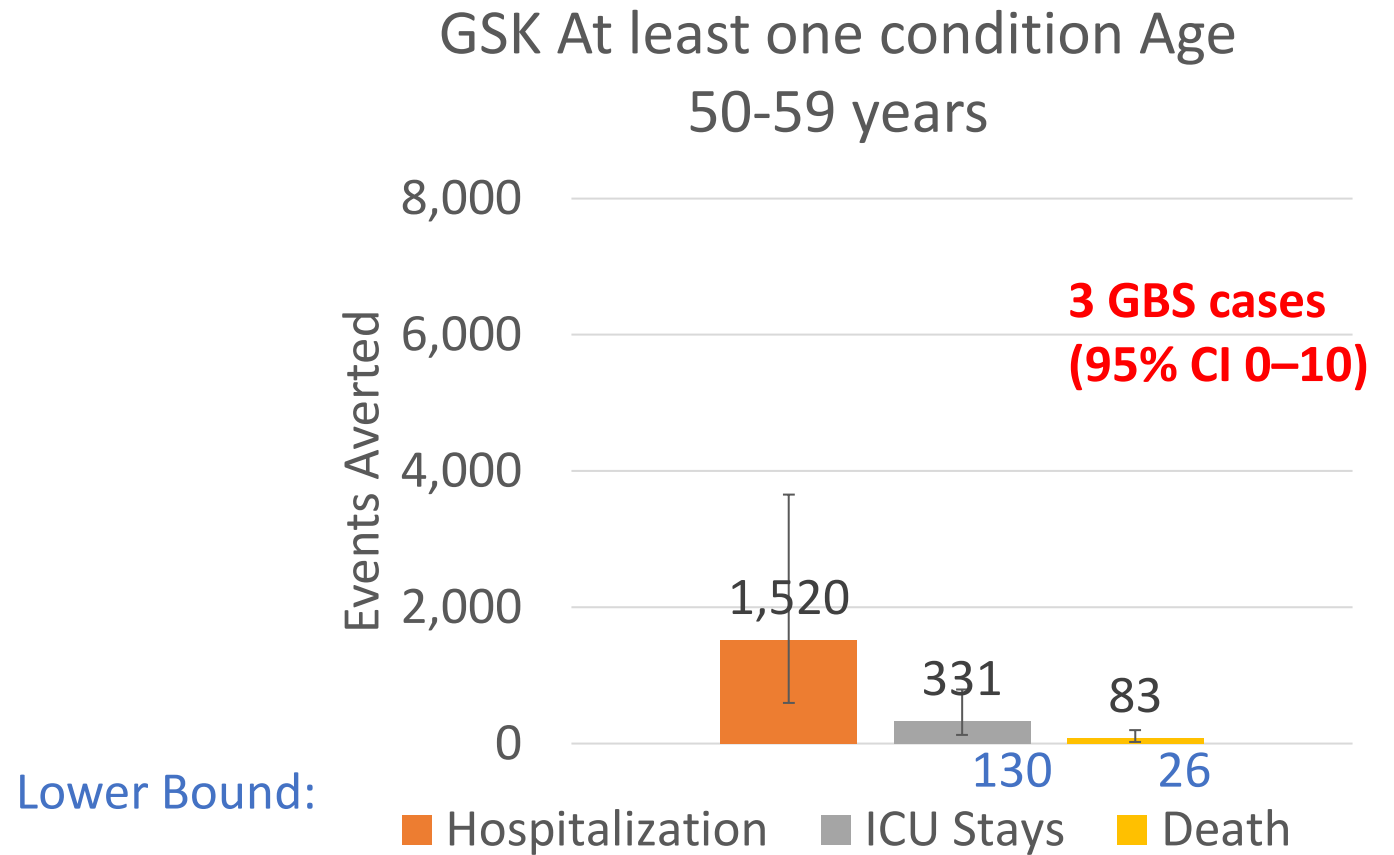


GSK At least one condition Age 60-74 years



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

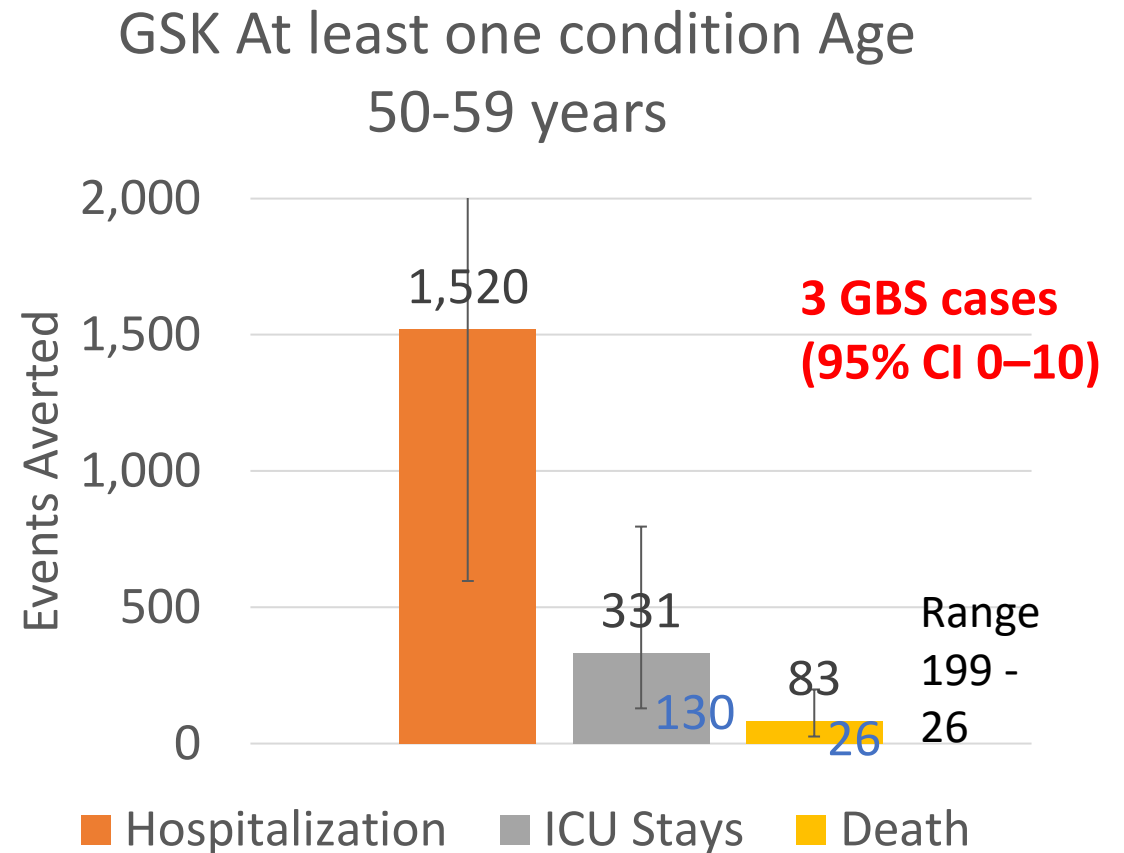
Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in adults 50-59 years with ≥ 1 chronic condition*



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

Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in **adults 50-59 years with ≥ 1 chronic condition***

Zoomed In



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

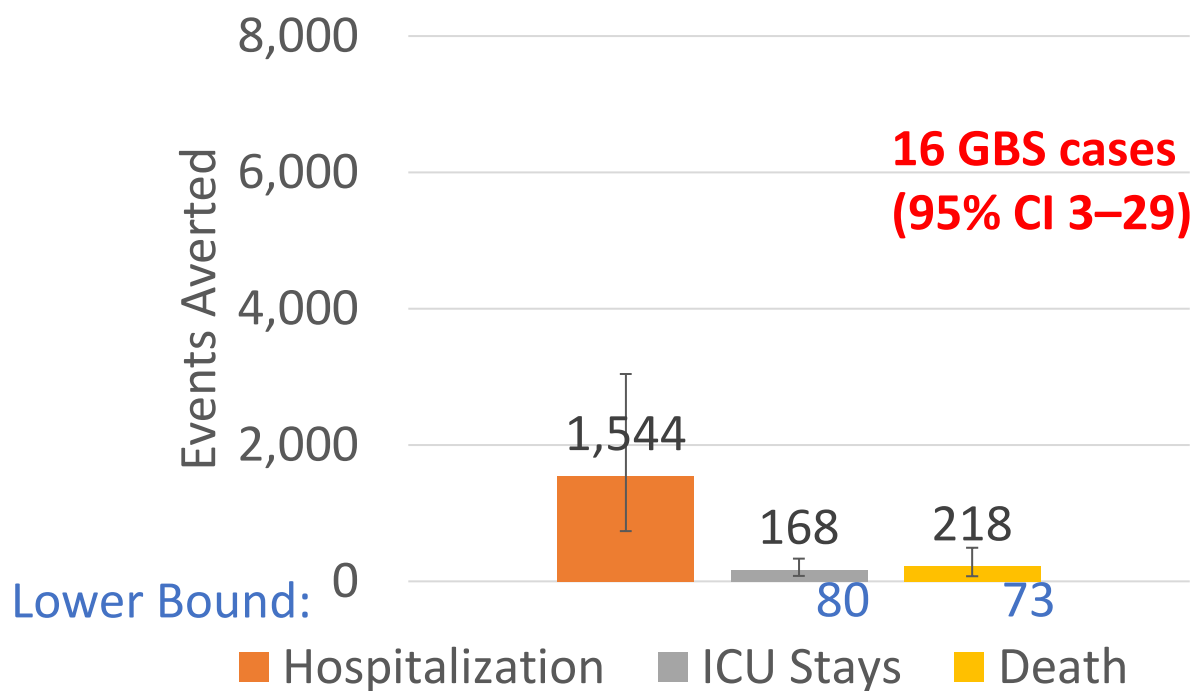
Scenarios

Scenario 1: Estimated RSV-associated outcomes avertable among adults without chronic medical conditions*

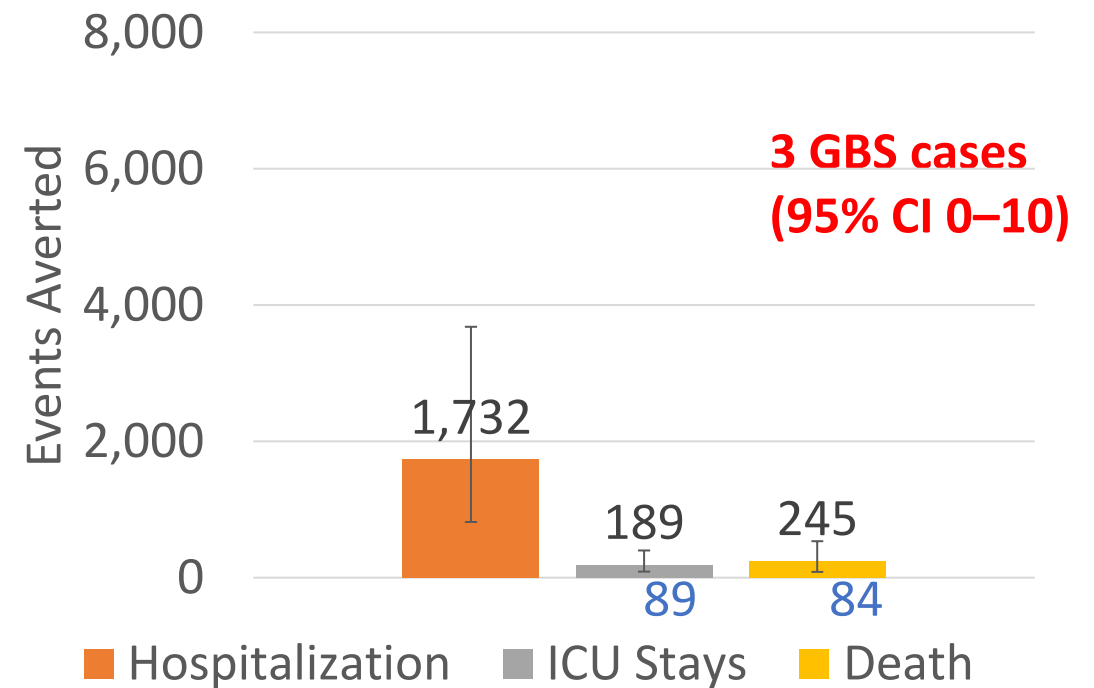
*None of: COPD, asthma, coronary artery disease, chronic kidney disease, diabetes mellitus, severe obesity (BMI ≥ 40)

Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in **adults ≥ 75 years with none of these conditions***

Pfizer None of these conditions
Age ≥ 75



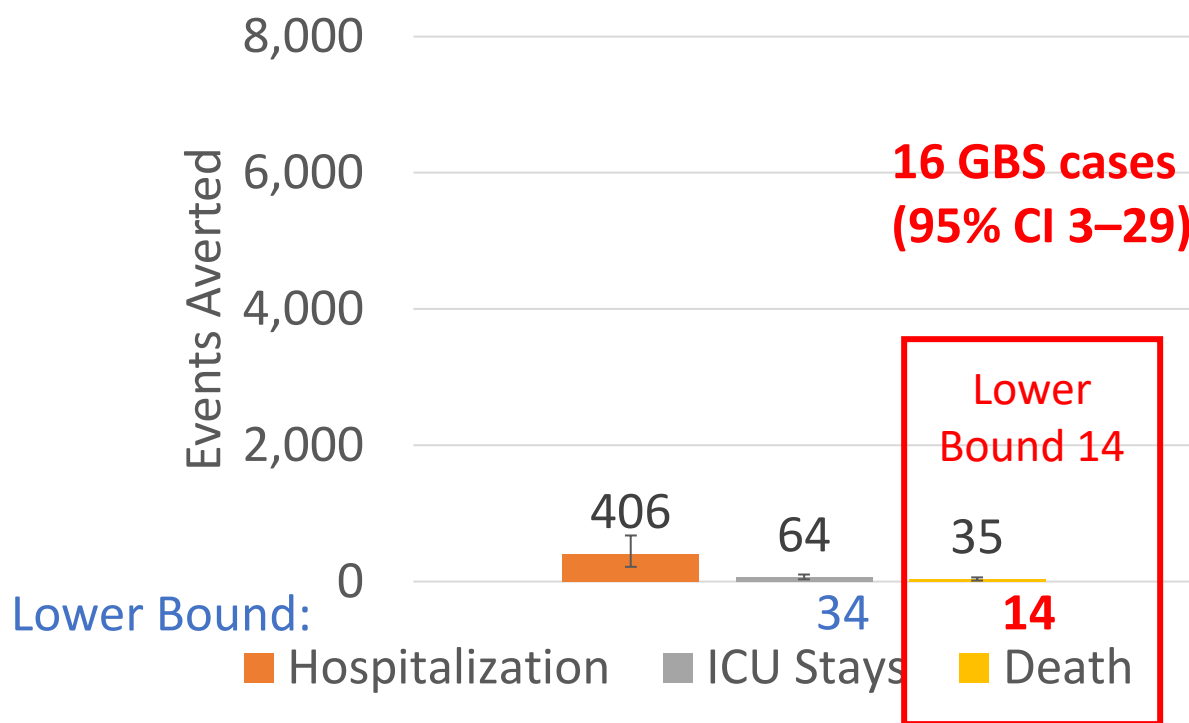
GSK None of these conditions
Age ≥ 75



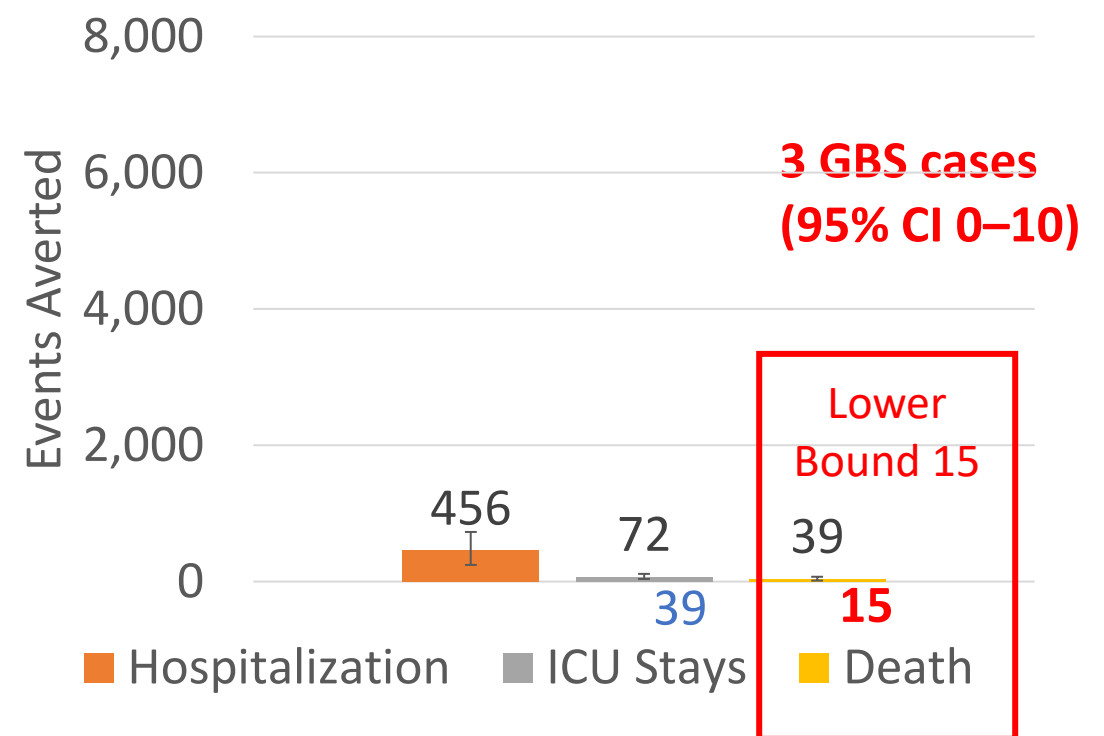
*None of: COPD, asthma, coronary artery disease, chronic kidney disease, diabetes mellitus, severe obesity (BMI ≥ 40). Persons may have other chronic medical conditions (e.g., heart failure, non-severe obesity, immune compromise). ¹⁸

Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in **adults 60-74 years with none of these conditions***

Pfizer None of these conditions
Age 60-74 years



GSK None of these conditions
Age 60-74 years



*None of: COPD, asthma, coronary artery disease, chronic kidney disease, diabetes mellitus, severe obesity (BMI ≥40). Persons may have other chronic medical conditions (e.g., heart failure, non-severe obesity, immune compromise).¹⁹

Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in **adults 60-74 years with none of these conditions***

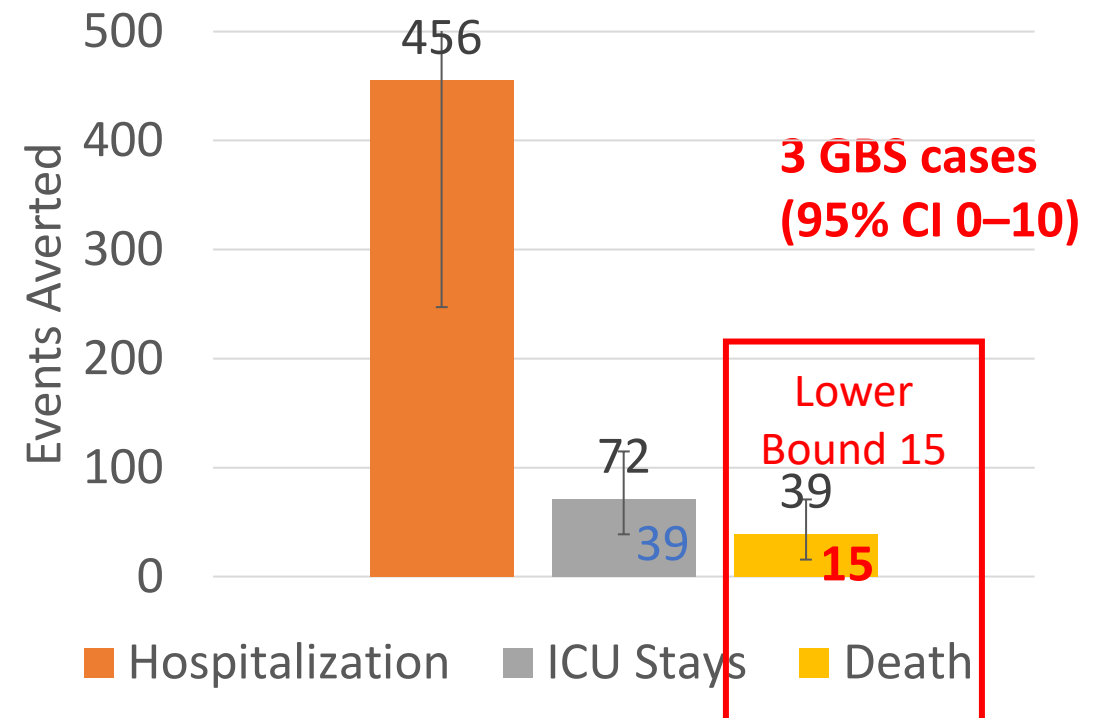
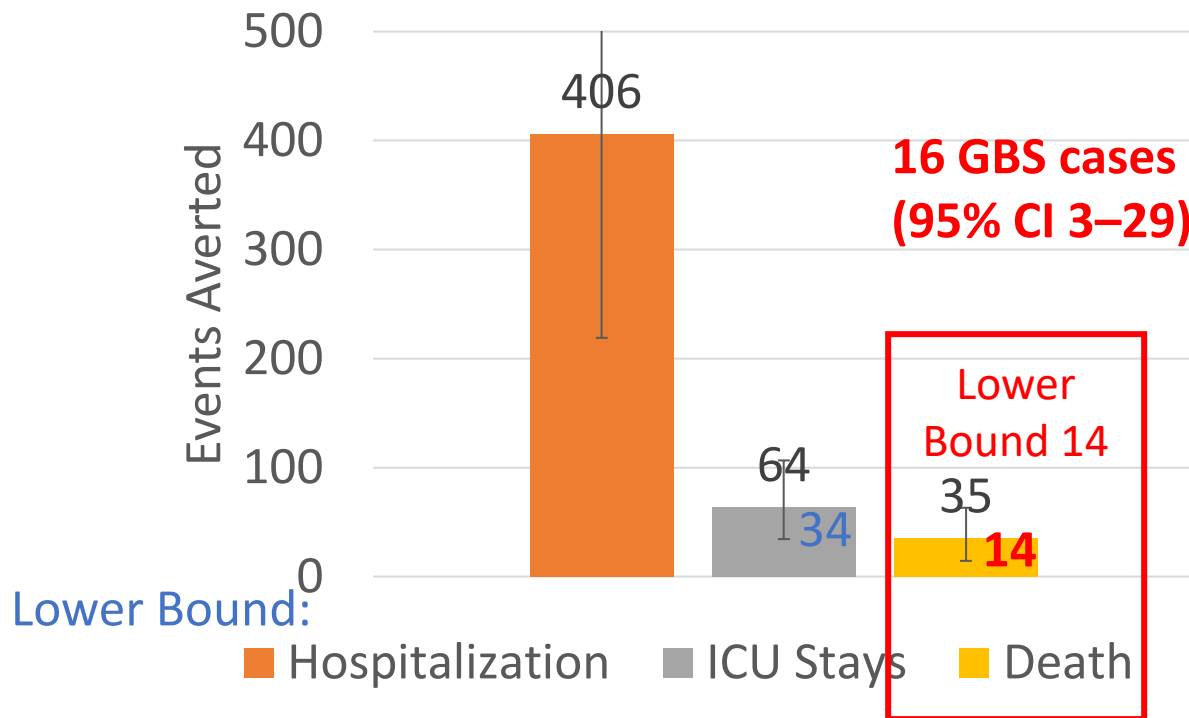
Pfizer None of these conditions

Age 60-74 years

Zoomed In

GSK None of these conditions

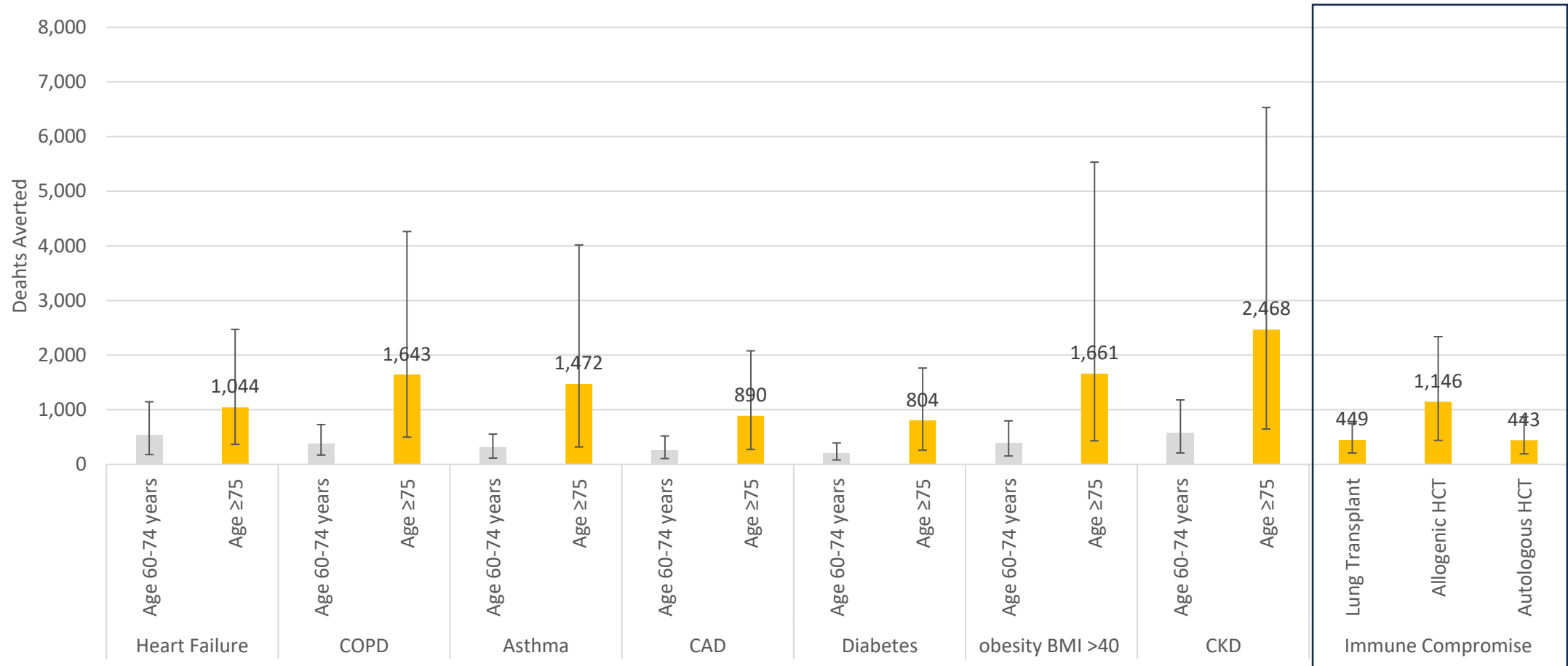
Age 60-74 years



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

Scenario 2: RSV-attributable deaths avertable among adults by age and presence of specific chronic conditions

Estimated RSV-associated **deaths avertable** over 2 RSV seasons vs. potential cases of GBS per 1 million Pfizer ABRYSCO doses in adults **75 years and older with specific chronic conditions**

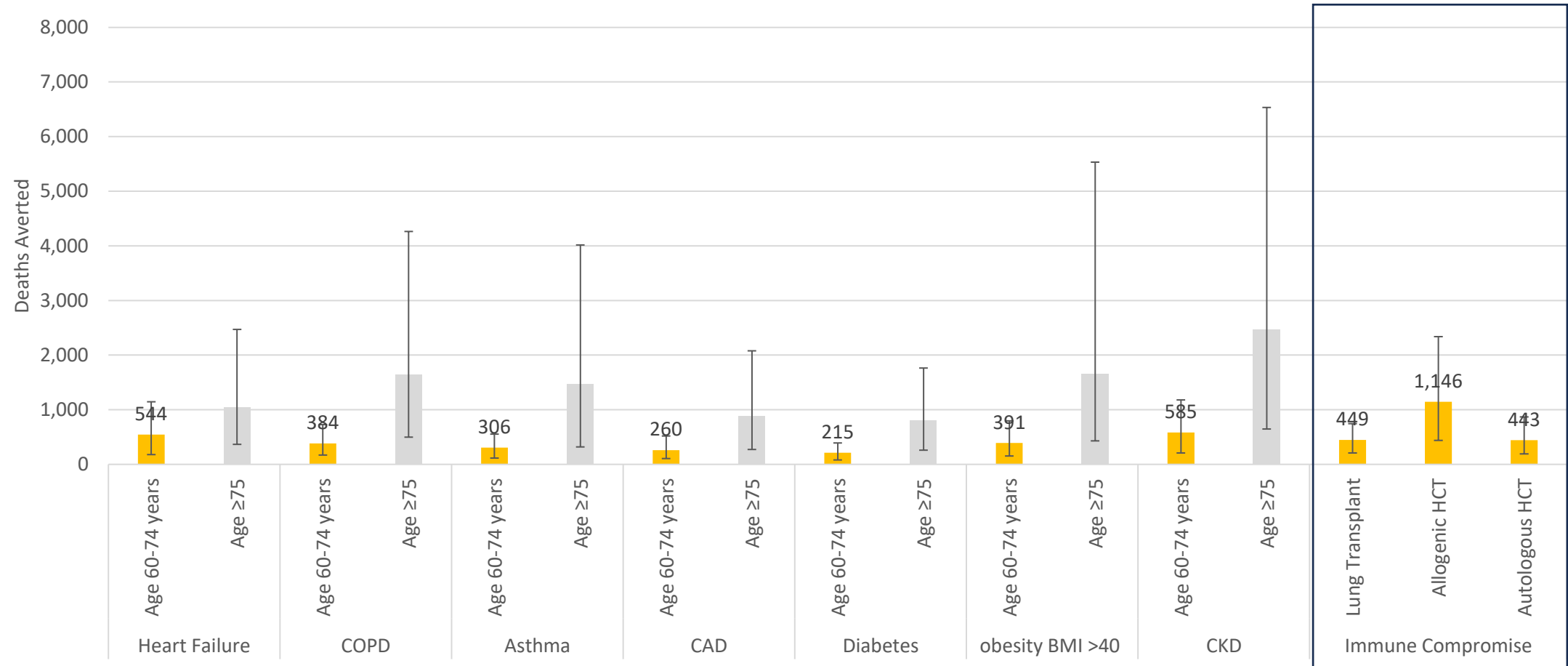


HCT: hematopoietic cell transplant
Lower bound is labeled if <50

**16 GBS cases
(95% CI 3–29)**

Immune Compromise is not age-stratified 22

Estimated RSV-associated **deaths avertable** over 2 RSV seasons vs. potential cases of GBS per 1 million Pfizer ABRYSVO doses in adults **60-74 years with specific chronic conditions**

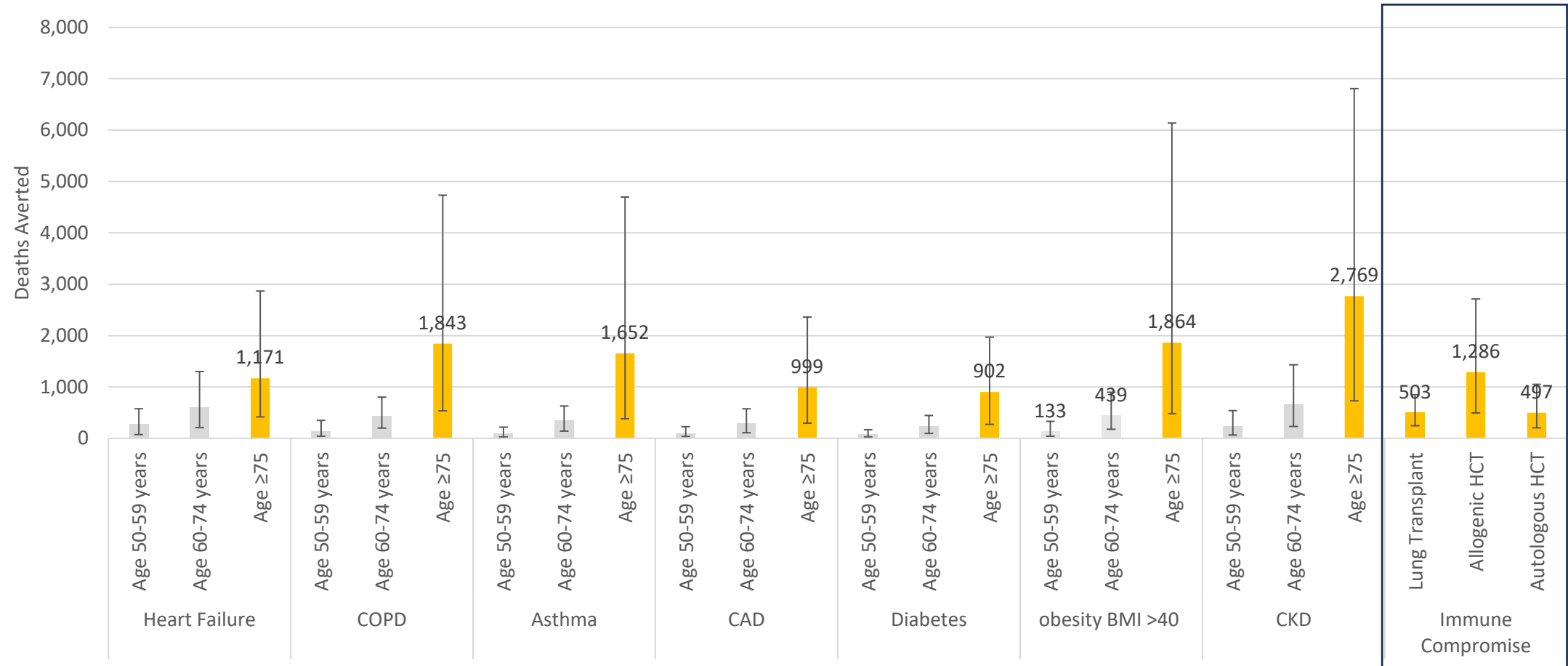


HCT: hematopoietic cell transplant
Lower bound is labeled if <50

**16 GBS cases
(95% CI 3–29)**

Immune Compromise is not age-stratified 23

Estimated RSV-associated **deaths avertable** over 2 RSV seasons vs. potential cases of GBS per 1 million **GSK AREXVY** doses in **adults 75 years and older with specific chronic conditions**

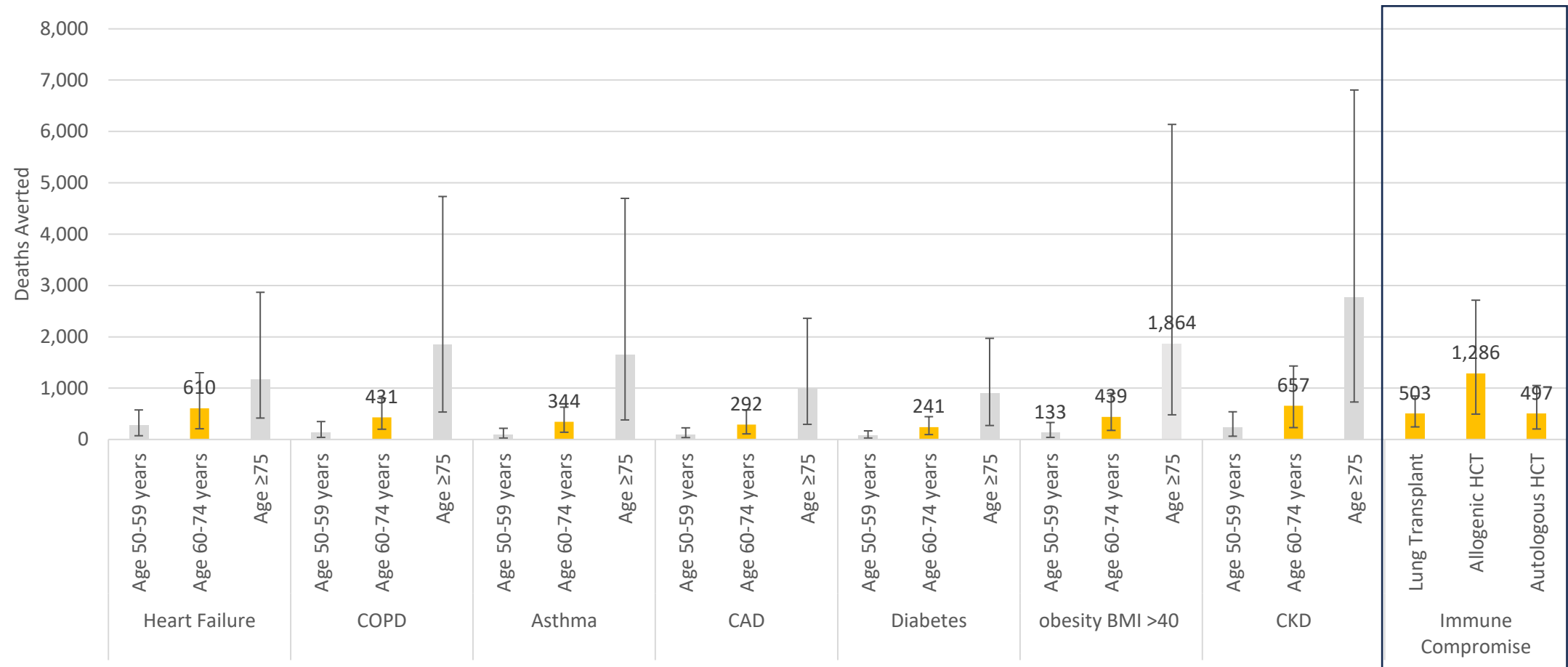


**3 GBS cases
(95% CI 0–10)**

HCT: hematopoietic cell transplant
Lower bound is labeled if <50

Immune Compromise is not age-stratified 24

Estimated RSV-associated **deaths avertable** over 2 RSV seasons vs. potential cases of GBS per 1 million **GSK AREXVY** doses in **adults 60-74 years with specific chronic conditions**

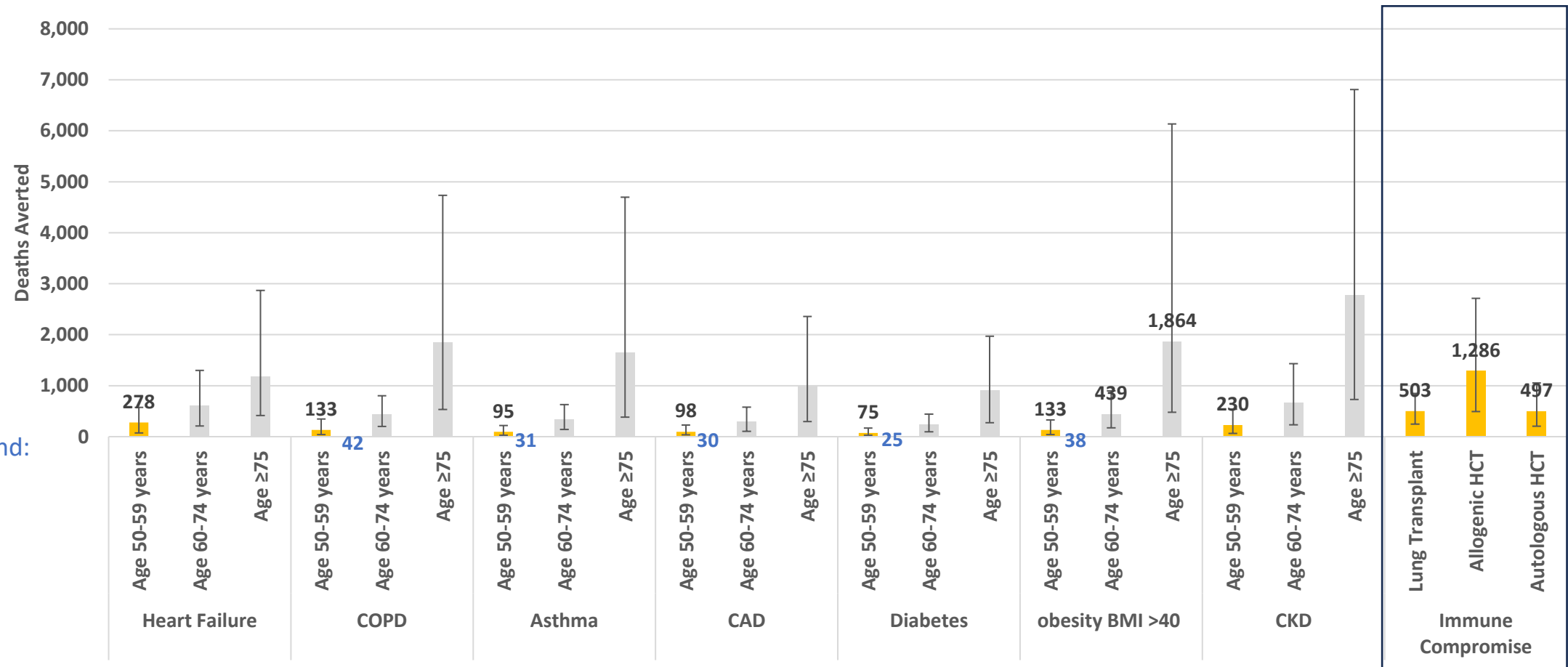


HCT: hematopoietic cell transplant
Lower bound is labeled if <50

**3 GBS cases
(95% CI 0–10)**

Immune Compromise is not age-stratified 25

Estimated RSV-associated **deaths avertable** over 2 RSV seasons vs. potential cases of GBS per 1 million **GSK AREXVY** doses in adults **50-59 years with specific chronic conditions**



Lower Bound:

HCT: hematopoietic cell transplant
Lower bound is labeled if <50

**3 GBS cases
(95% CI 0–10)**

Immune Compromise is not age-stratified 26

Summary

- Estimated numbers of avertable deaths are much larger than potential GBS cases for:
 - Adults 75 and older
 - Adults 60-74 with at least one chronic condition
- Estimated numbers of avertable hospitalizations and ICU admissions are much larger than potential GBS cases for all age groups, for both GSK's AREXVY and Pfizer's ABRYSSVO.
- Estimated numbers of avertable deaths are larger, but more similar in magnitude, than potential GBS cases for:
 - Adults 50-59 with at least one chronic condition
 - Adults 60-74 without chronic conditions, particularly for the Pfizer ABRYSSVO vaccine

Limitations

- Uncertain Inputs
 - RSV hospitalization incidence by age and condition
 - RSV-NET represents ~9% of the United States and hospitalization rates observed in RSV-NET may not be generalizable to the U.S.
 - Could not include all conditions that may increase risk of severe RSV disease in this analysis
 - Vaccine effectiveness (VE)
 - Observational VE data only available for first few months after vaccination—protection over time was extrapolated from waning in efficacy against symptomatic illness observed in clinical trials
 - Risk of Guillain-Barre Syndrome
 - GBS risk estimates were calculated using a small number of events observed after RSV vaccination, resulting in high uncertainty.
 - GBS was identified by diagnostic codes in administrative data and may be subject to coding errors. Not all cases of GBS occurring after RSV vaccination may have received a diagnostic code.
 - Attributable risk of GBS may be different among adults 50-59 than among adults 60 and older.

Thank You

- Please send comments to:
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