

Risk-Benefit Analysis of RSV Vaccination in Older Adults

David W. Hutton, PhD, MS

Associate Professor, Health Management and Policy, School of Public Health

Associate Professor of Global Public Health, School of Public Health

Associate Professor, Industrial and Operations Engineering, College of Engineering



University of Michigan



Disclaimer

- An error in the market productivity calculation for adults aged 50–64 years has been identified in this presentation.
- Correction of this error and additional updates have been incorporated into a more recent analysis.
- Please refer to the ACIP agenda on **April 16, 2025** and the presentation titled, “Economic Analysis of Adult RSV Vaccination, including benefits and risk discussion” by Dr. Ismael Ortega-Sanchez for the most updated version of this analysis.

Research Team

University of Michigan

- David Hutton, PhD
- Lisa Prosser, PhD
- Angela Rose, MPH
- Christina Nyamuswa, MS

CDC

- Michael Melgar, MD
- Amadea Britton, MD
- Lauren Roper, MPH
- Mila Prill, MSPH
- Jamison Pike, PhD
- Ismael Ortega-Sanchez, PhD
- Andrew Leidner, PhD
- Fiona Havers, MD
- Michael Whitaker, MPH
- Rebecca Woodruff, PhD
- Huong Pham, MPH

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)

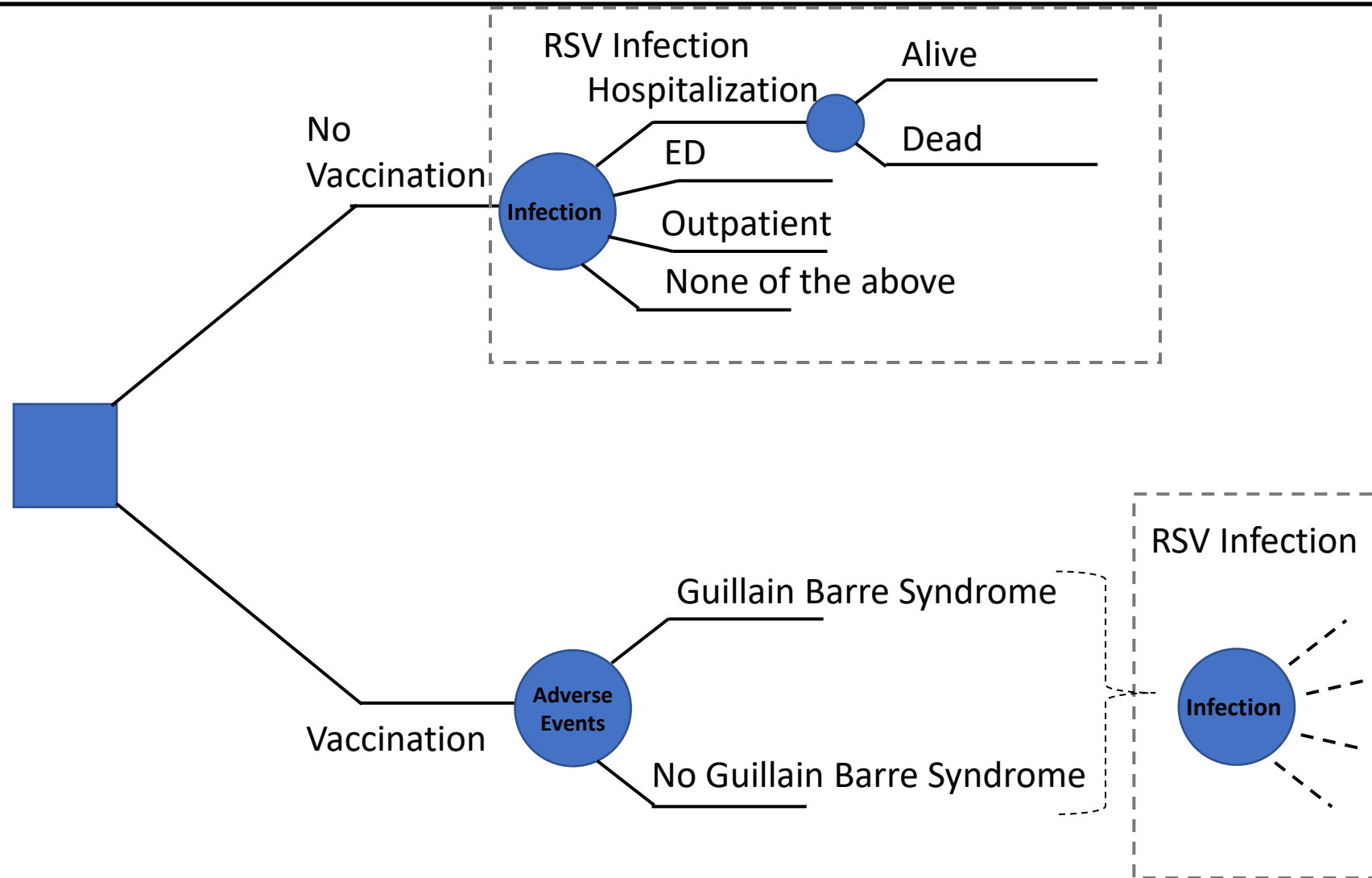
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- Heart failure
 - Immune Compromise
 - Lung Transplant
 - Hematopoietic cell transplant, allogeneic
 - Hematopoietic cell transplant, autologous

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

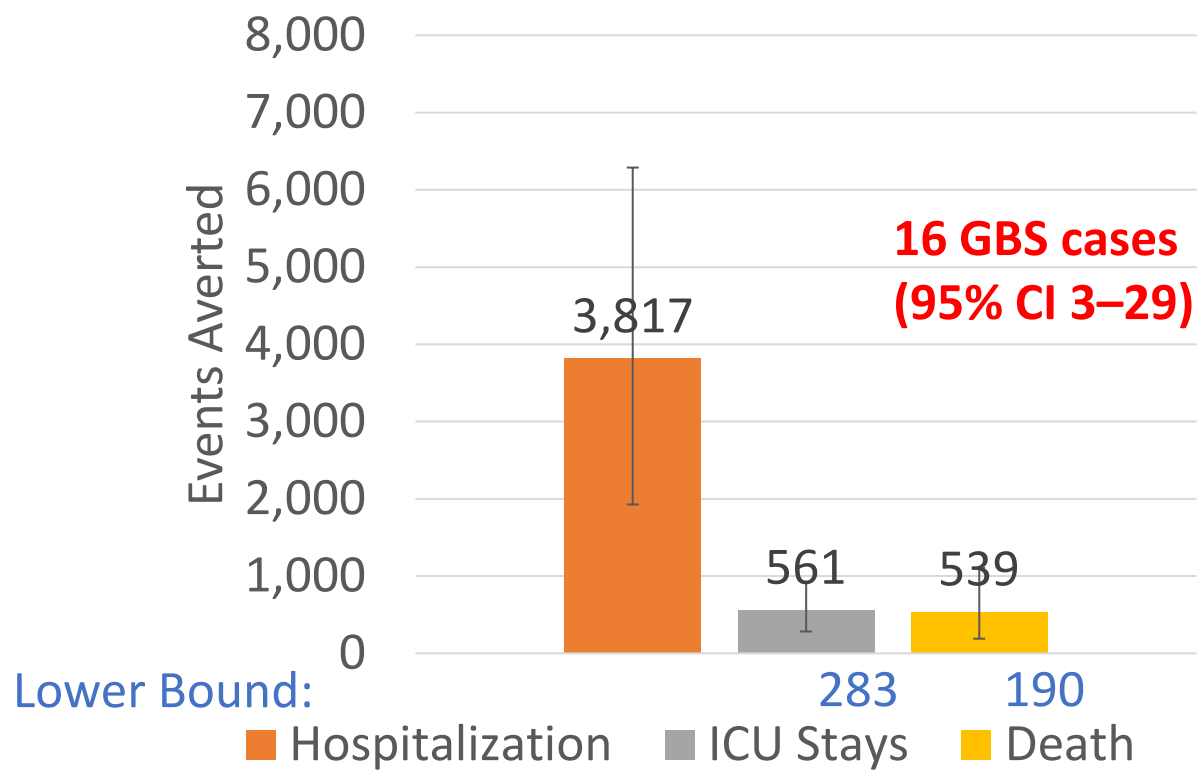
* Attributable risk for GSK's AREXVY was estimated to be 3 GBS cases (95% CI: -3, 10) per 1 million doses. For this analysis, the lower end of the 95% CI was truncated at 0 to evaluate potential risk of GBS. Potential protective effects were not evaluated.

Results: Estimated Benefits and Potential Risk

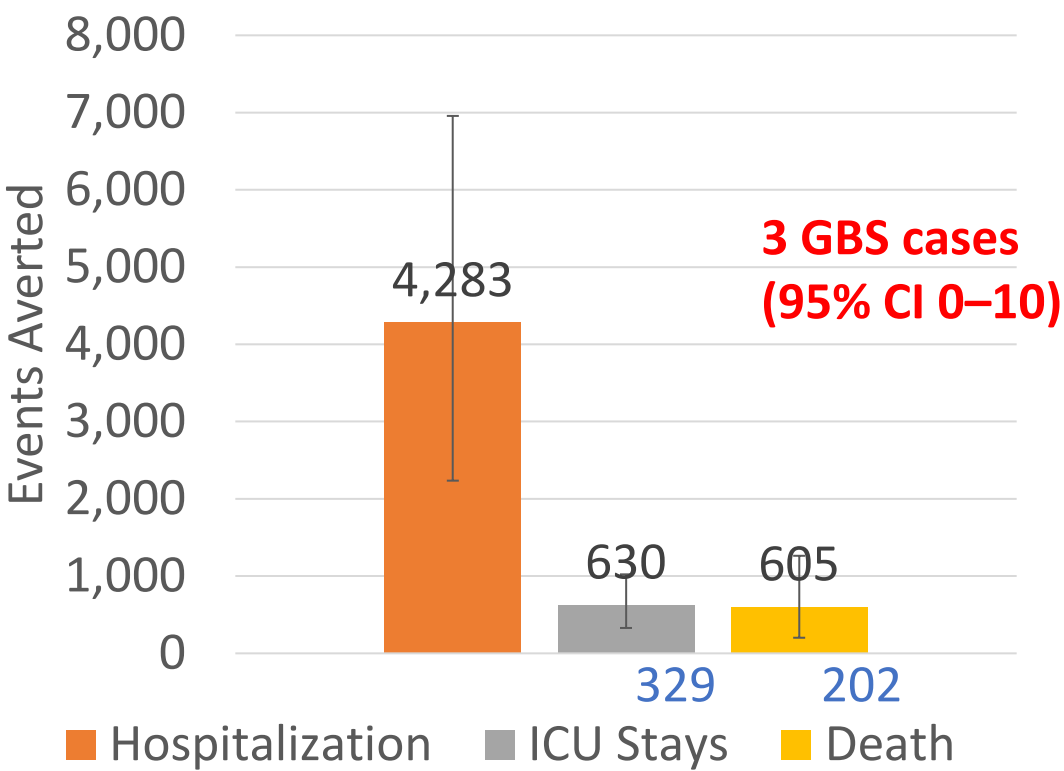
- Results are presented as **RSV outcomes avertable over 2 RSV seasons per 1 million single-dose RSV vaccinations**, and **attributable GBS risk per 1 million single-dose RSV vaccinations**.

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

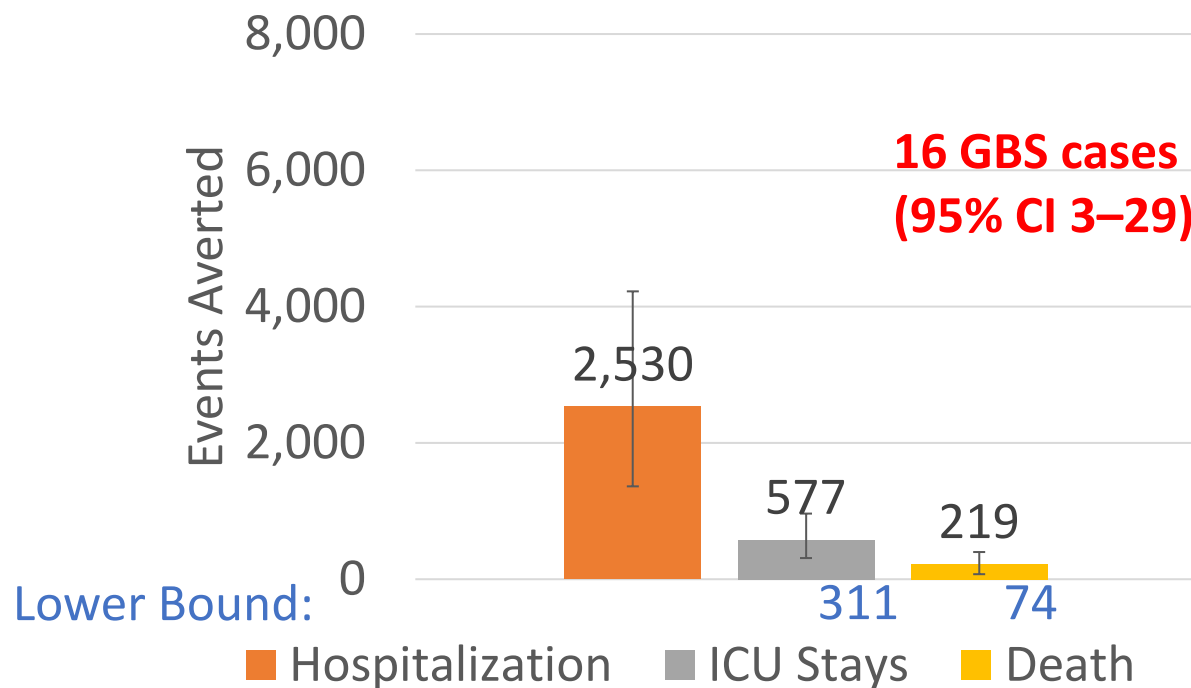


GSK All Adults Age ≥75

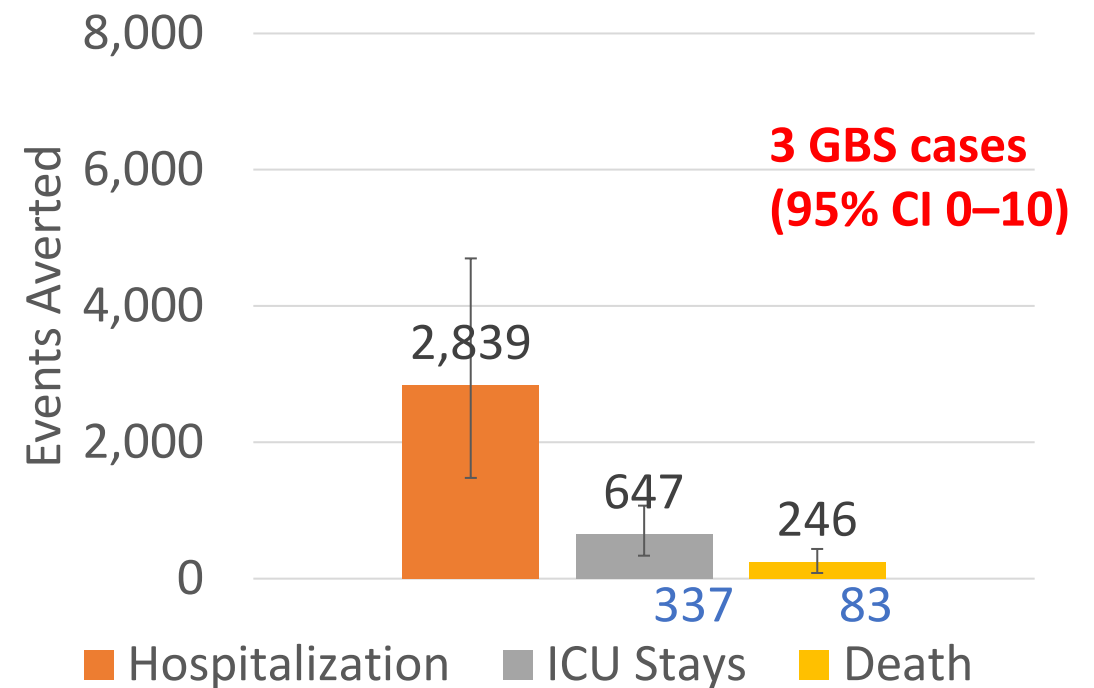


Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in adults 60-74 years with ≥ 1 chronic condition*

Pfizer At least one condition Age 60-74 years

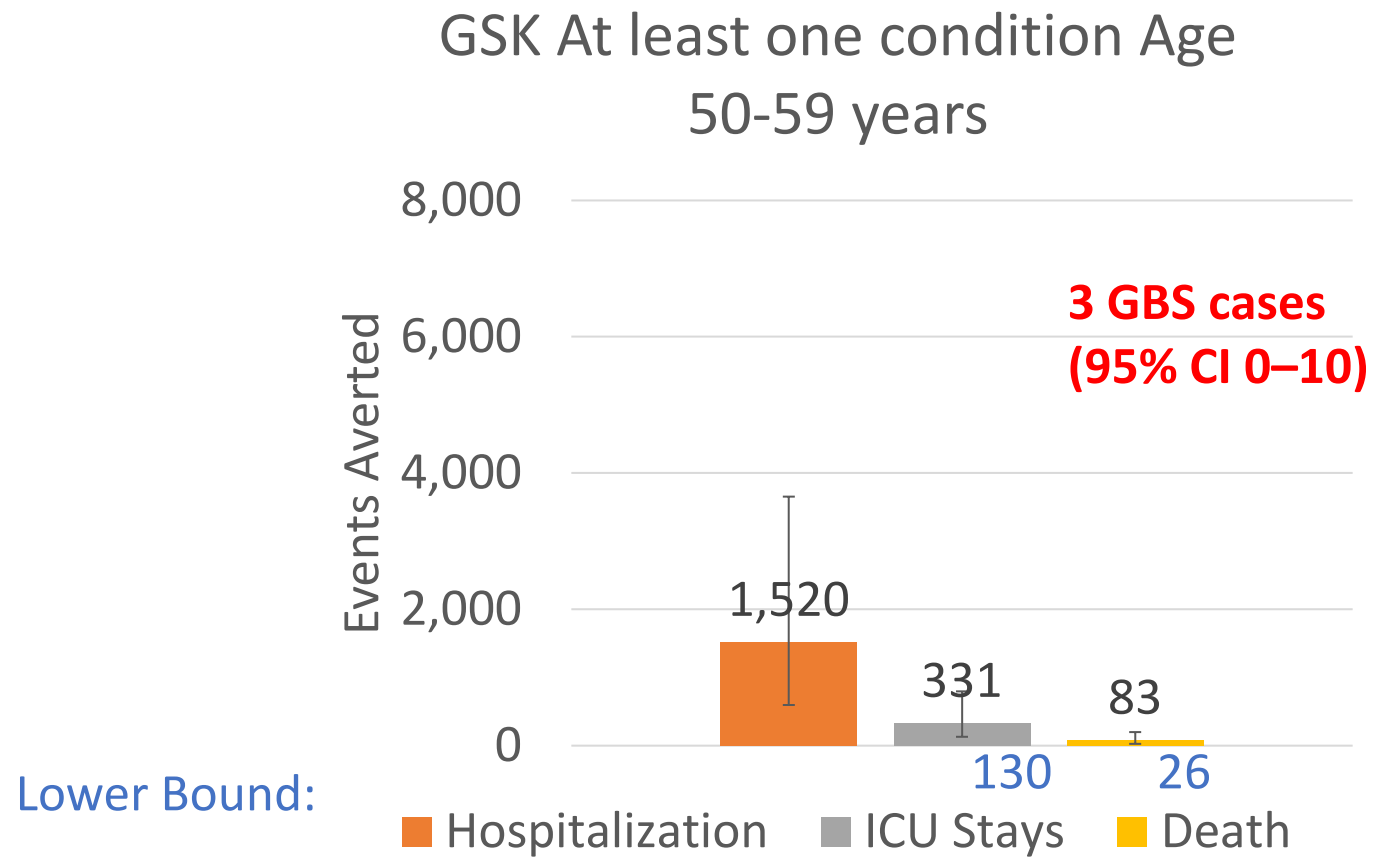


GSK At least one condition Age 60-74 years



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

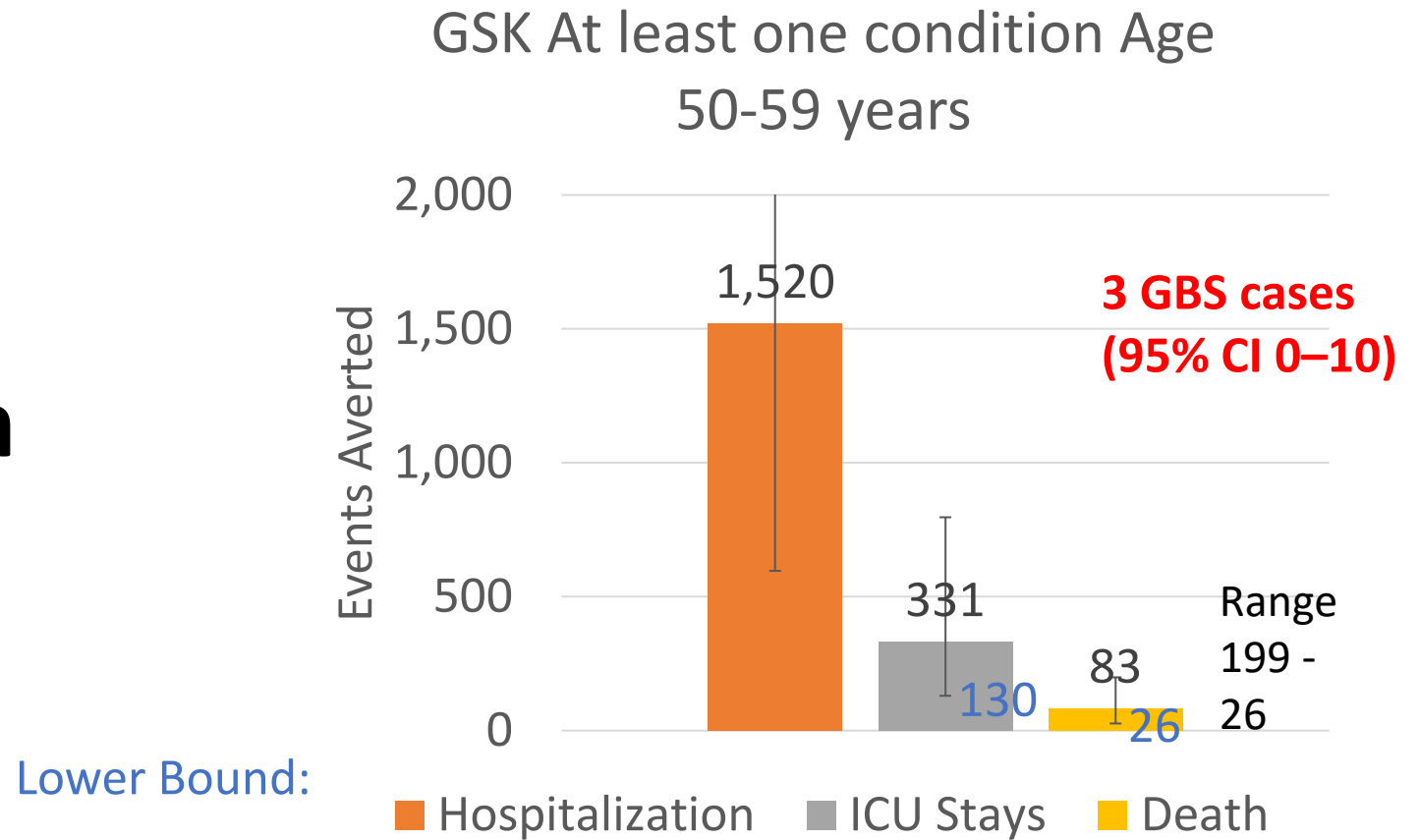
Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in adults 50-59 years with ≥ 1 chronic condition*



*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)

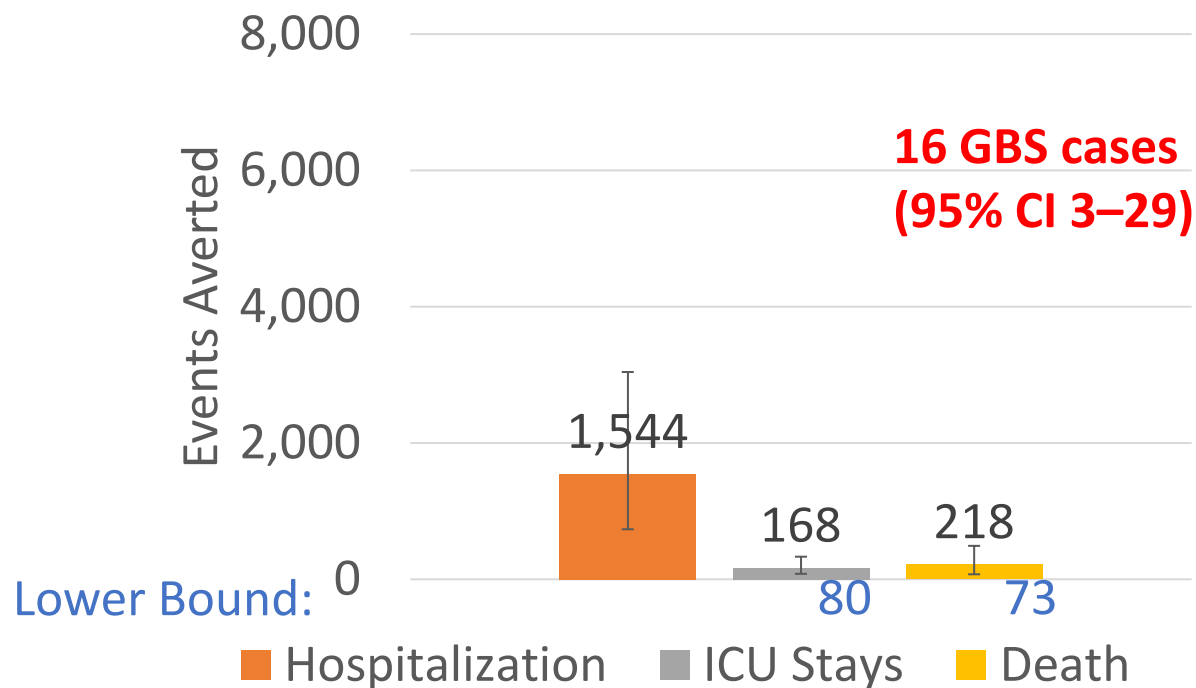
Scenarios

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

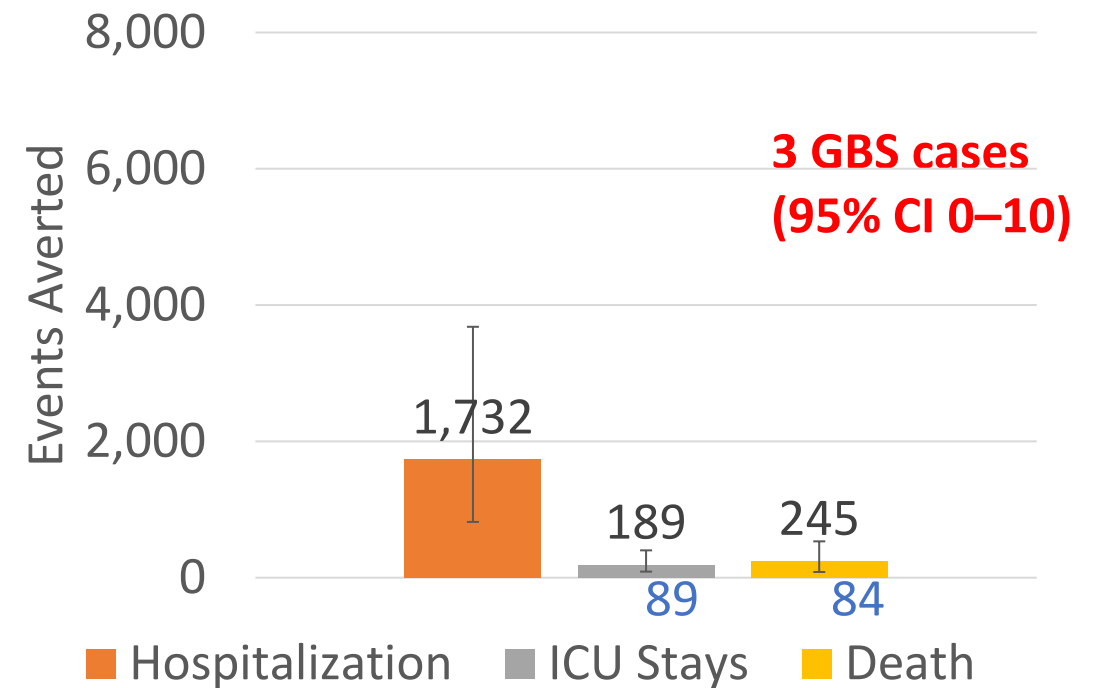
*None of: COPD, asthma, coronary artery disease, chronic kidney disease, diabetes mellitus, severe obesity (BMI ≥ 40)

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



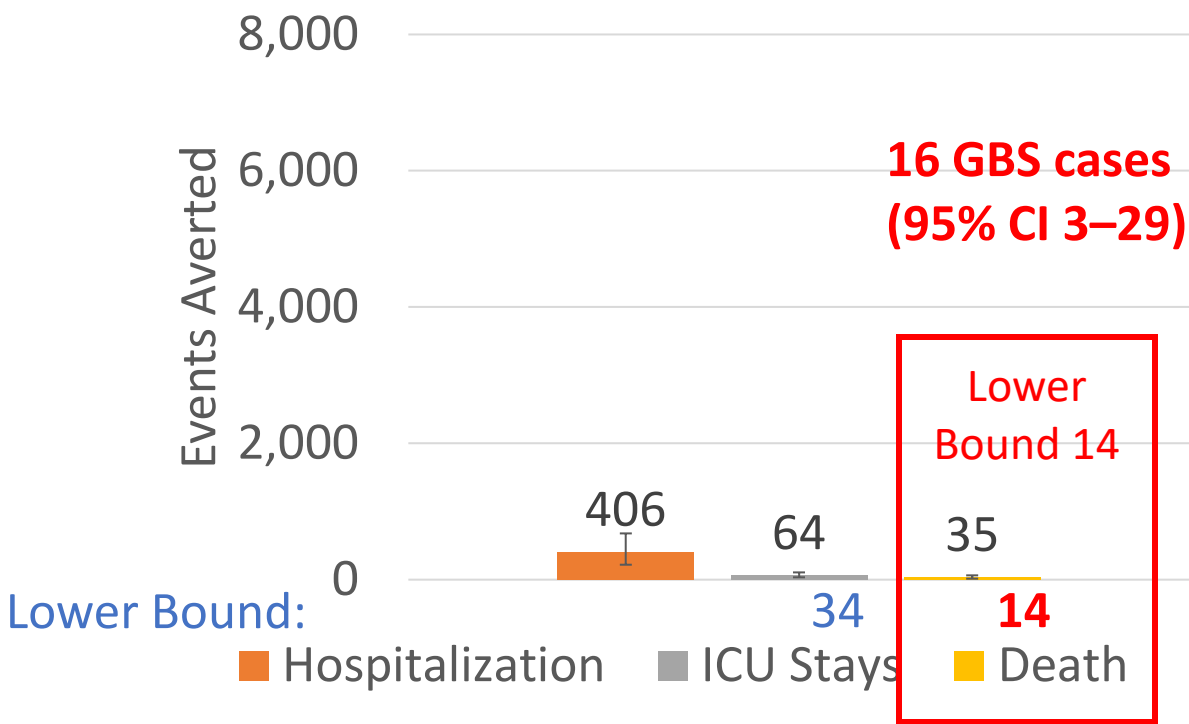
GSK None of these conditions
Age ≥ 75



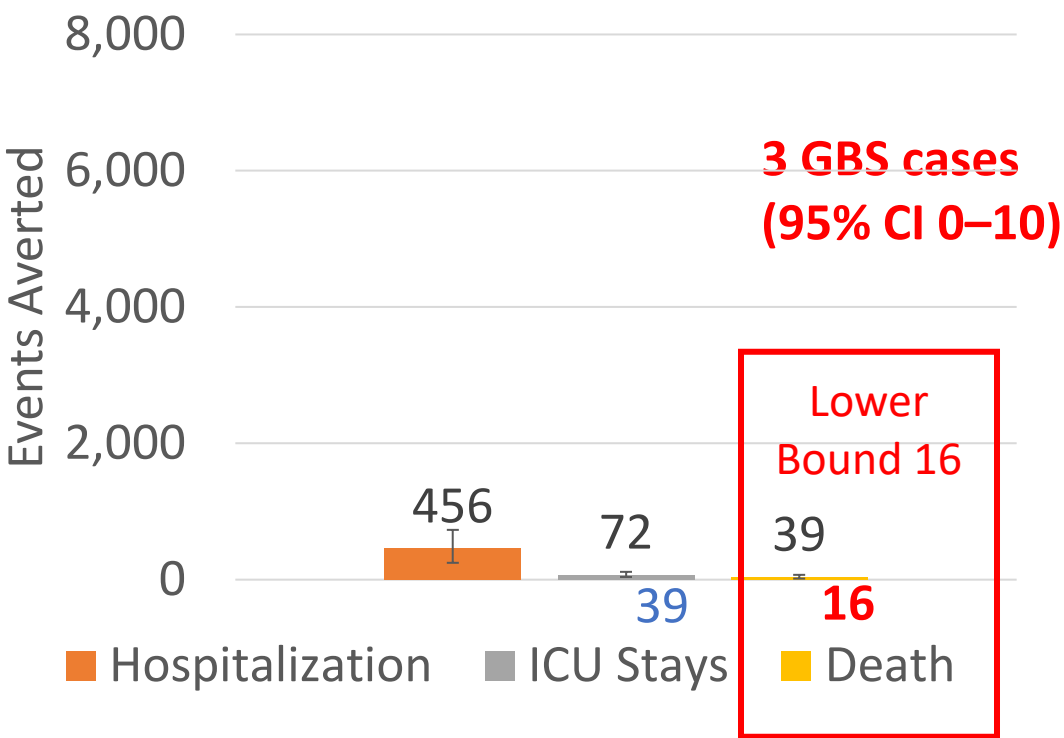
*None of: COPD, asthma, coronary artery disease, chronic kidney disease, diabetes mellitus, severe obesity (BMI ≥ 40). Persons may have other chronic medical conditions (e.g., heart failure, non-severe obesity, immune compromise).

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

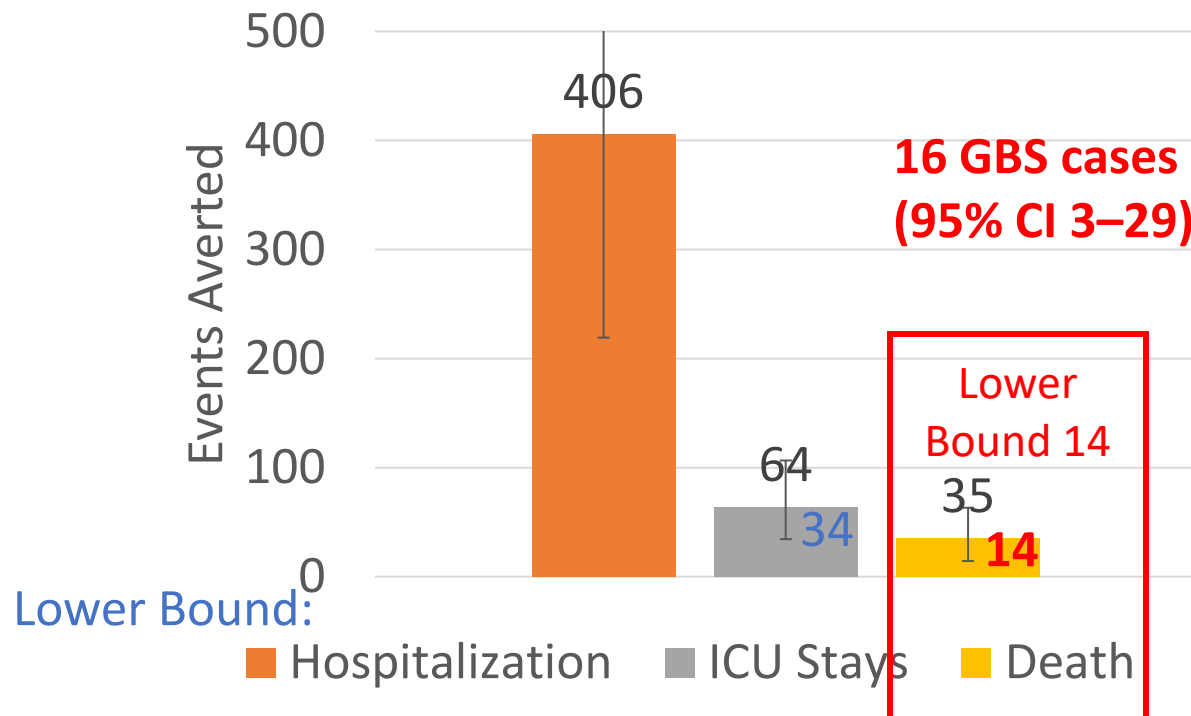


*None of: COPD, asthma, coronary artery disease, chronic kidney disease, diabetes mellitus, severe obesity (BMI ≥40).
Persons may have other chronic medical conditions (e.g., heart failure, non-severe obesity, immune compromise).

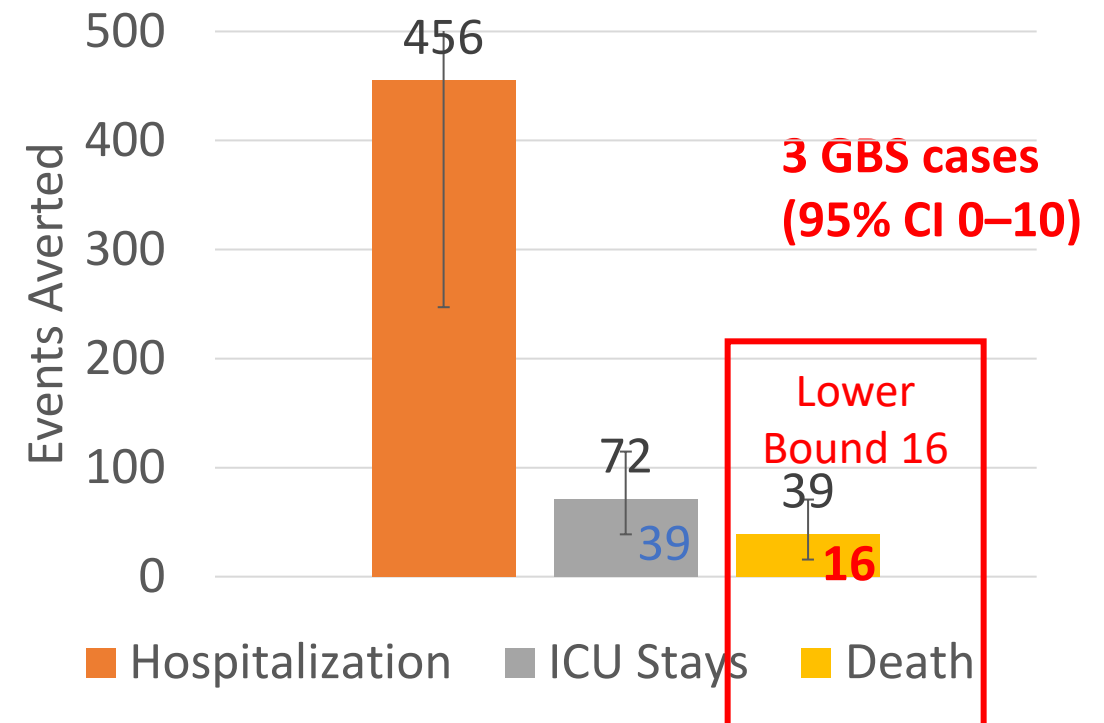
Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in **adults 60-74 years** **with none of these conditions***

Pfizer None of these conditions
Age 60-74 years

Zoomed In



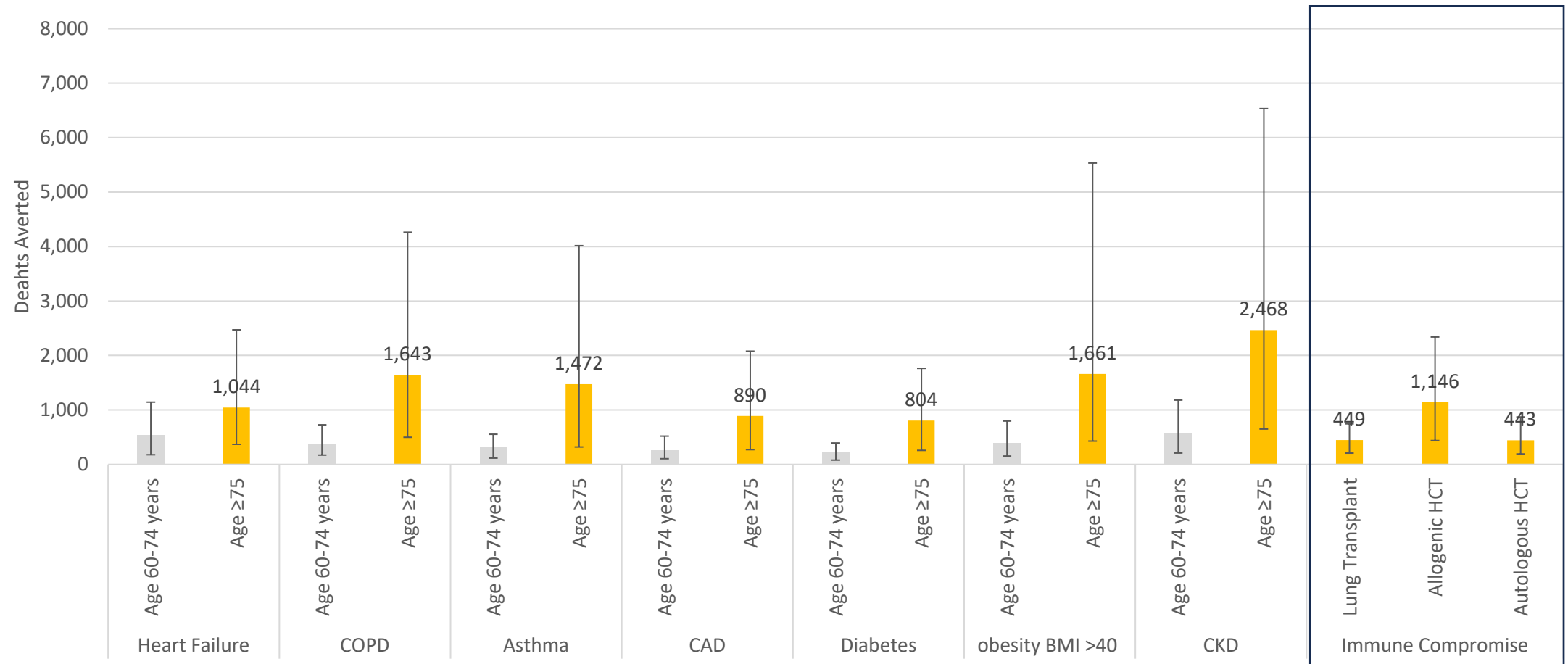
GSK None of these conditions
Age 60-74 years



*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 ABRYSV0 doses in adults 75**
years and older with specific chronic conditions

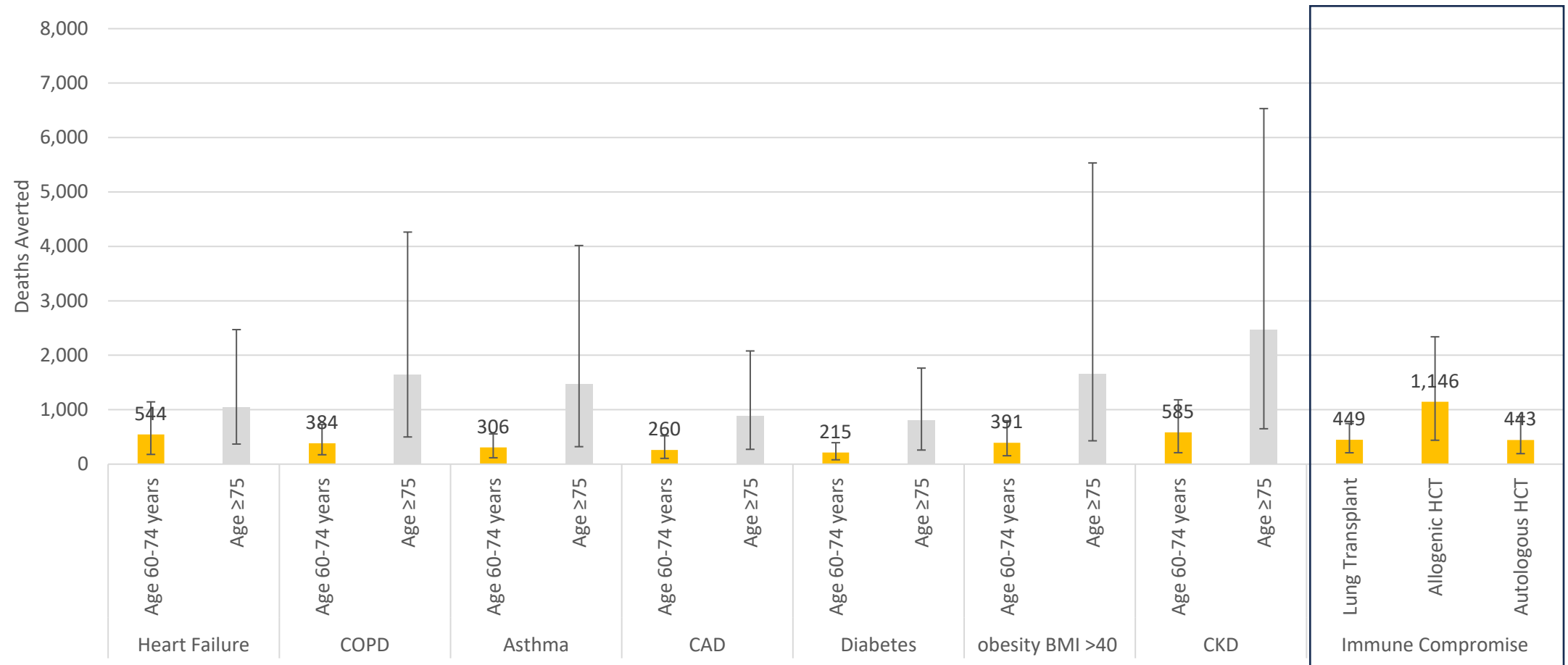


16 GBS cases
(95% CI 3–29)

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

Immune Compromise is not age-stratified 23

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**

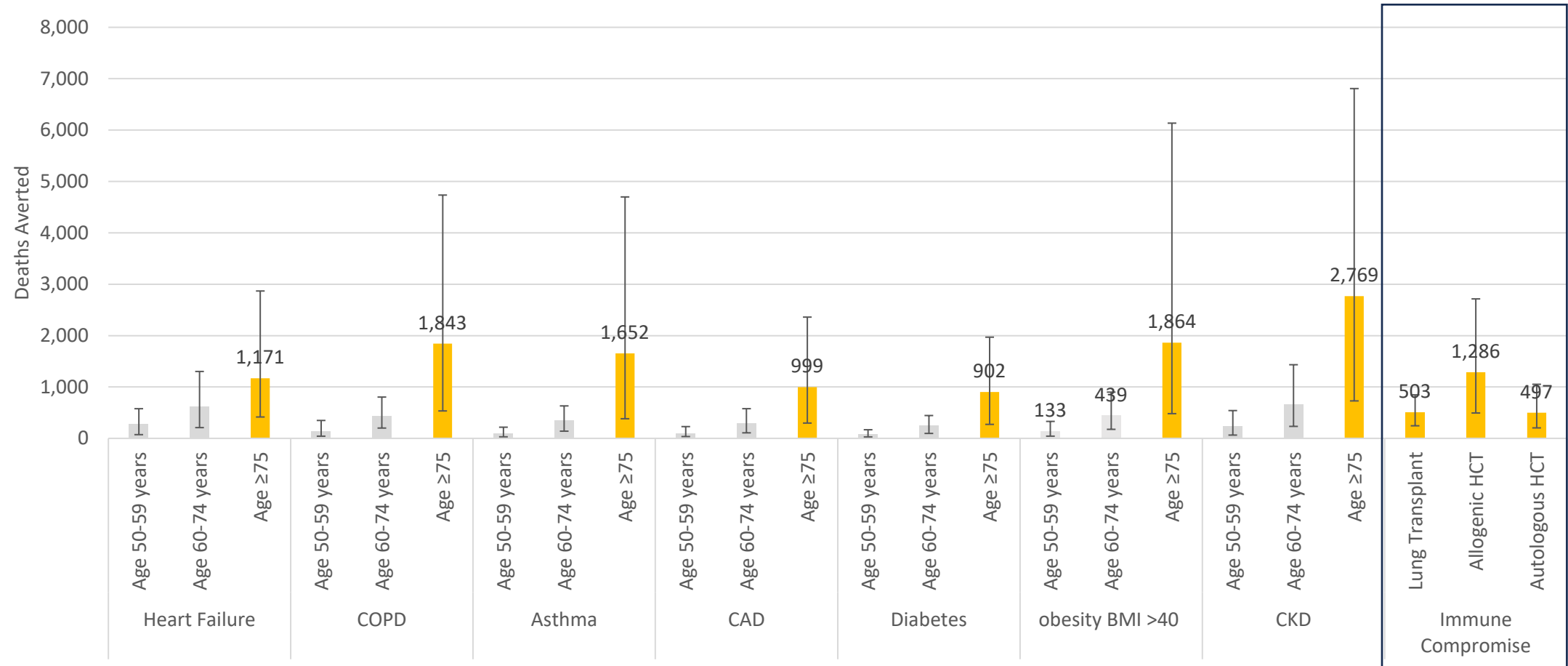


HCT: hematopoietic cell transplant
Lower bound is labeled if <50

**16 GBS cases
(95% CI 3–29)**

Immune Compromise is not age-stratified 24

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**

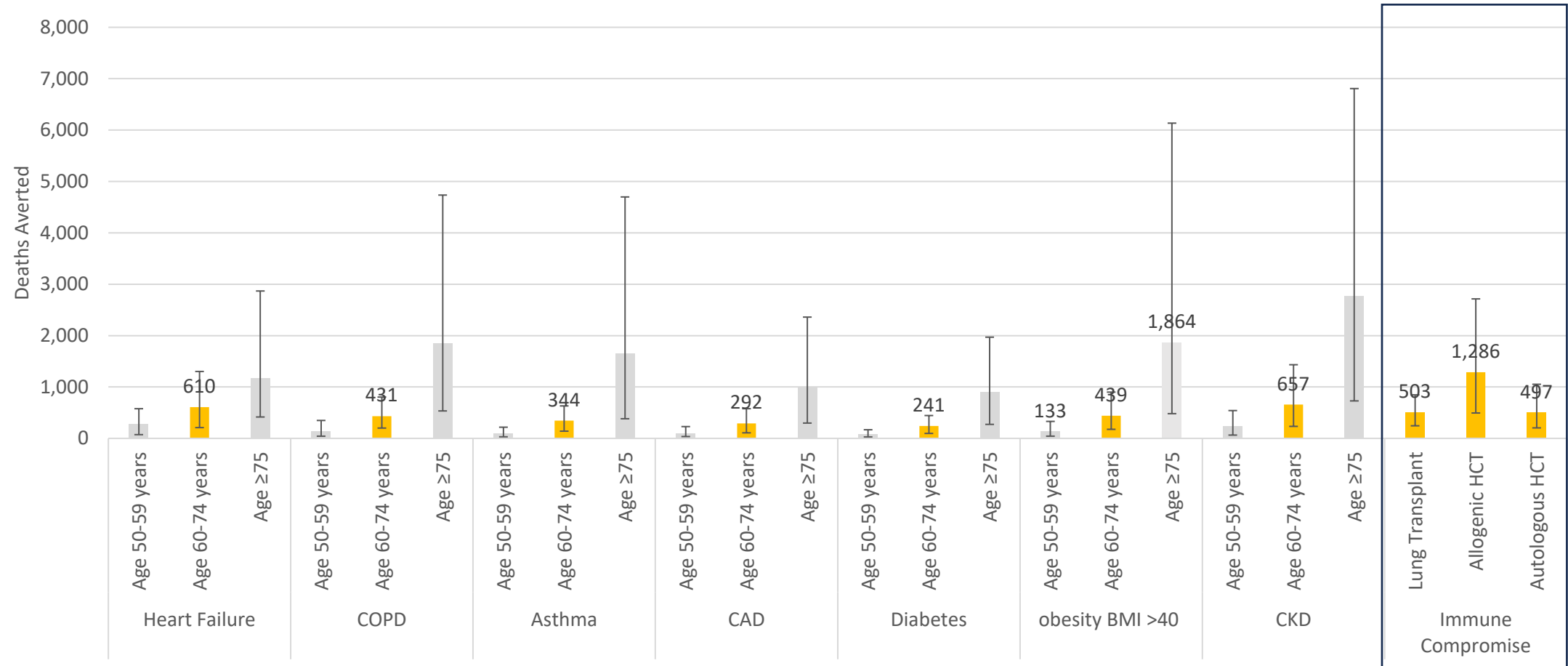


**3 GBS cases
(95% CI 0–10)**

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

Immune Compromise is not age-stratified 25

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**

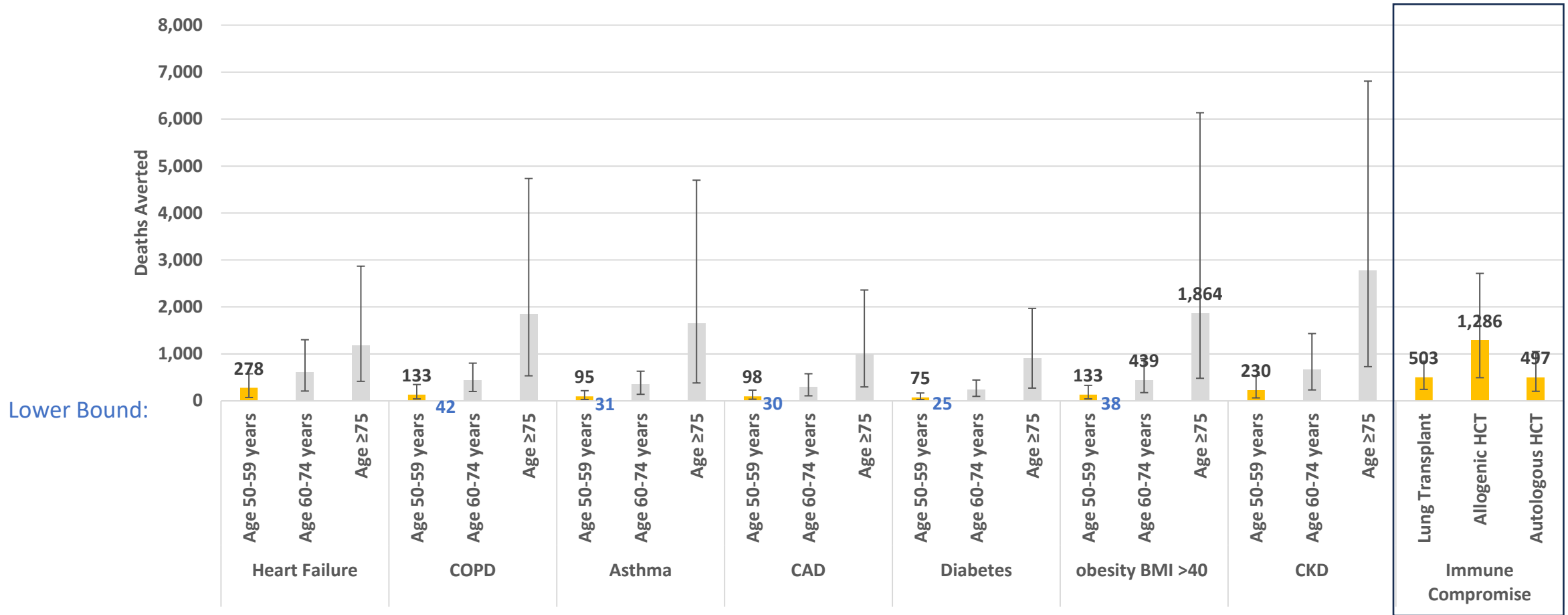


**3 GBS cases
(95% CI 0–10)**

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

Immune Compromise is not age-stratified 26

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**



**3 GBS cases
(95% CI 0–10)**

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

Immune Compromise is not age-stratified 27

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

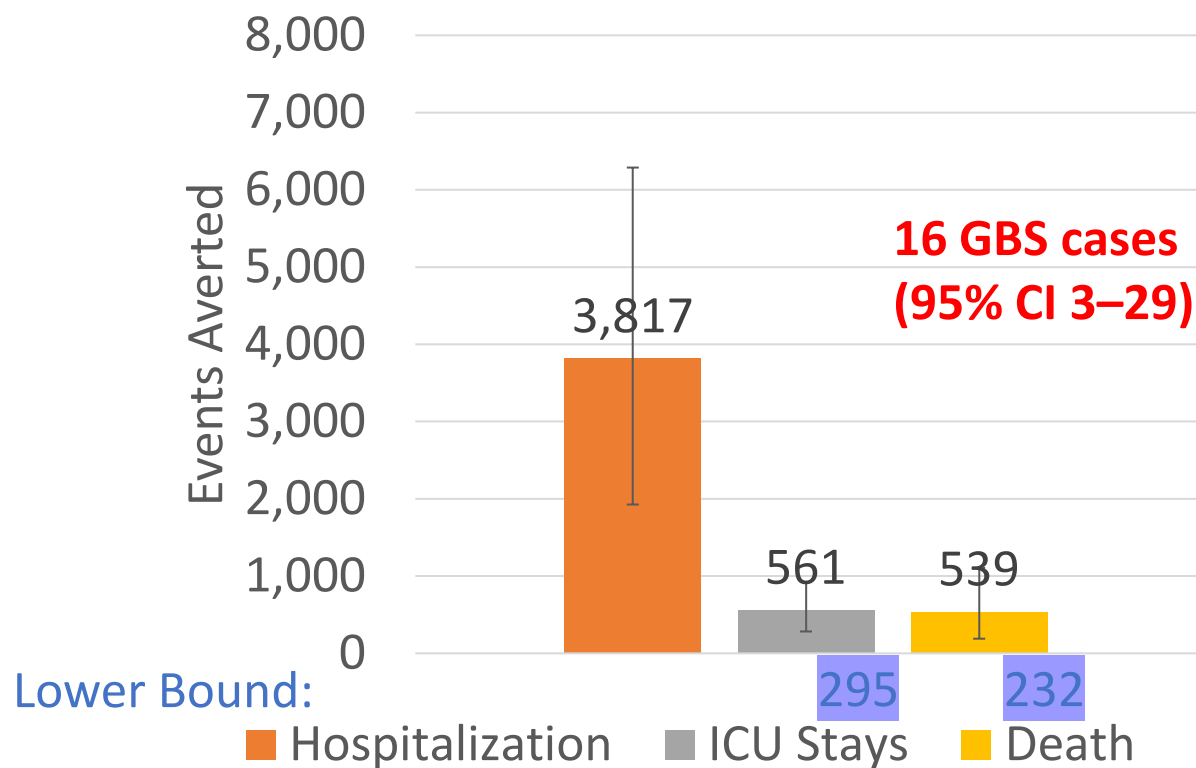
- Please send comments to:
- dwhutton@umich.edu

Original slides

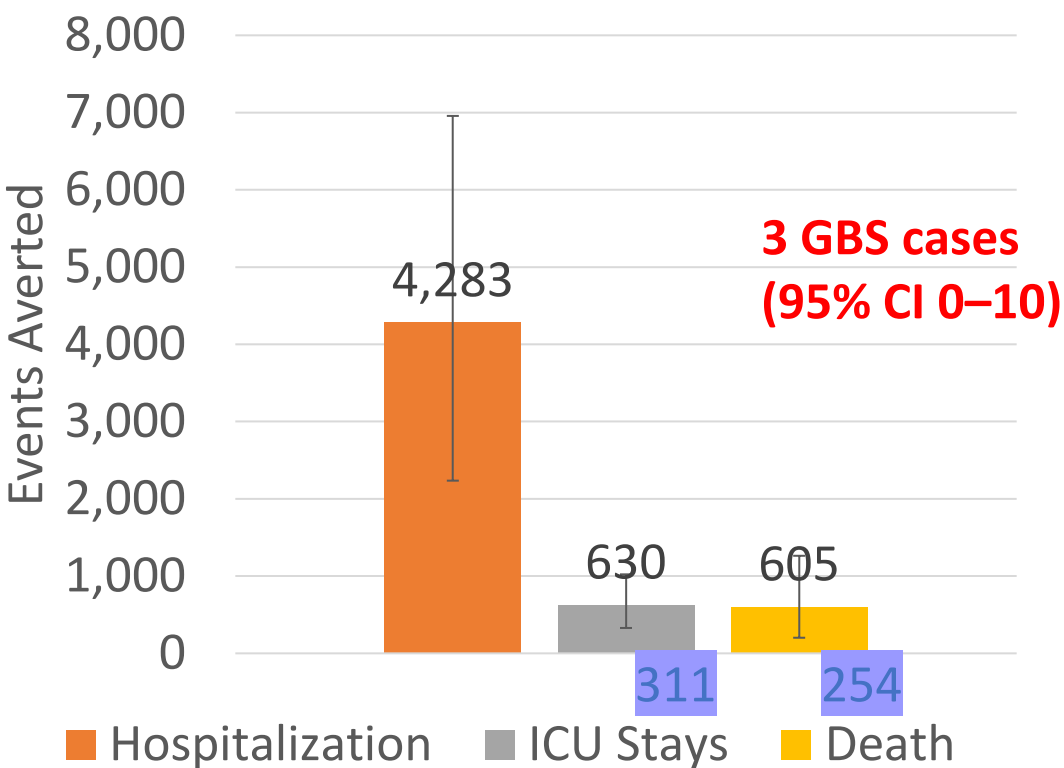
- The following slides contain errata. They are being shared here for a record of what was presented at the June 26, 2024, ACIP meeting.
- Corrected slides are available in the main presentation.
- Corrected slides with changes highlighted are included in the following slides.

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

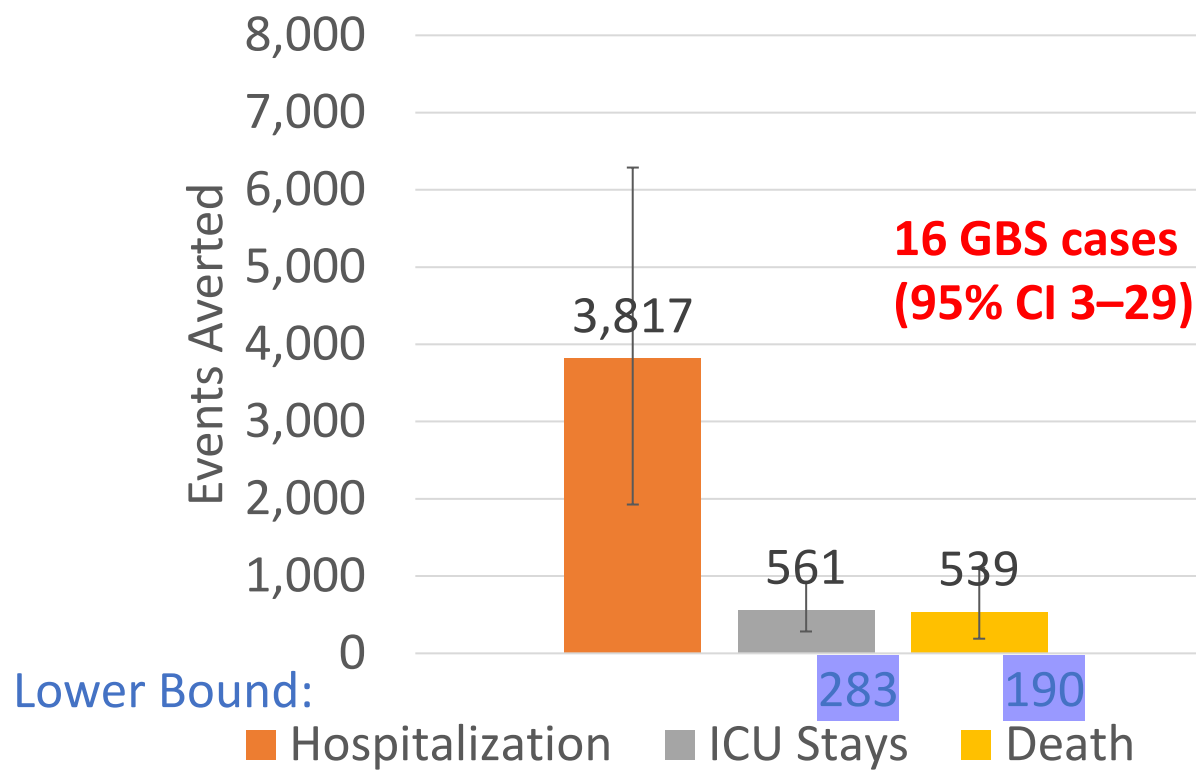


GSK All Adults Age ≥75

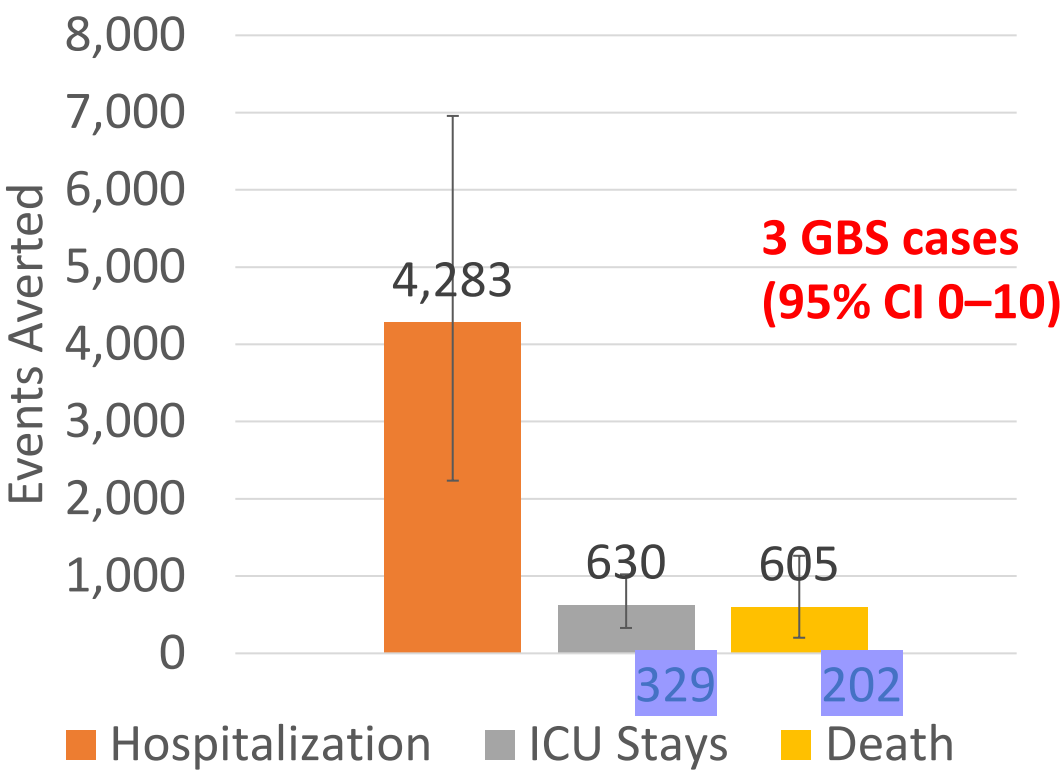


Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in adults ≥75 years (general population)

Pfizer All Adults Age ≥75

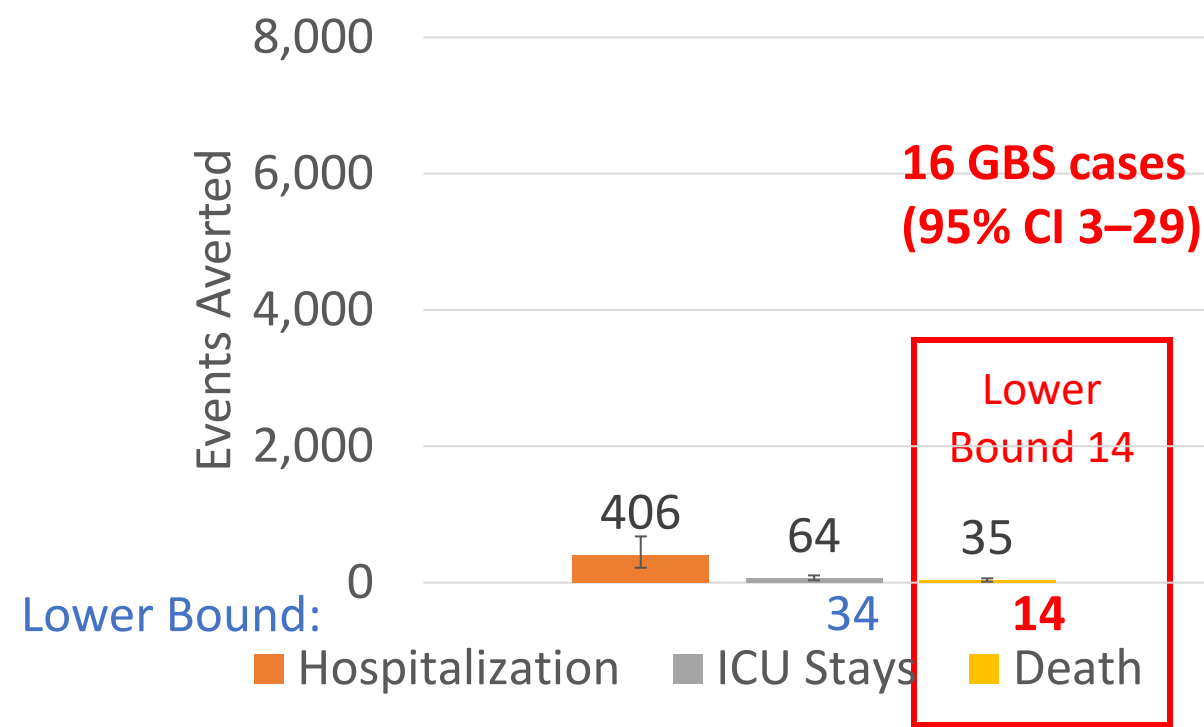


GSK All Adults Age ≥75

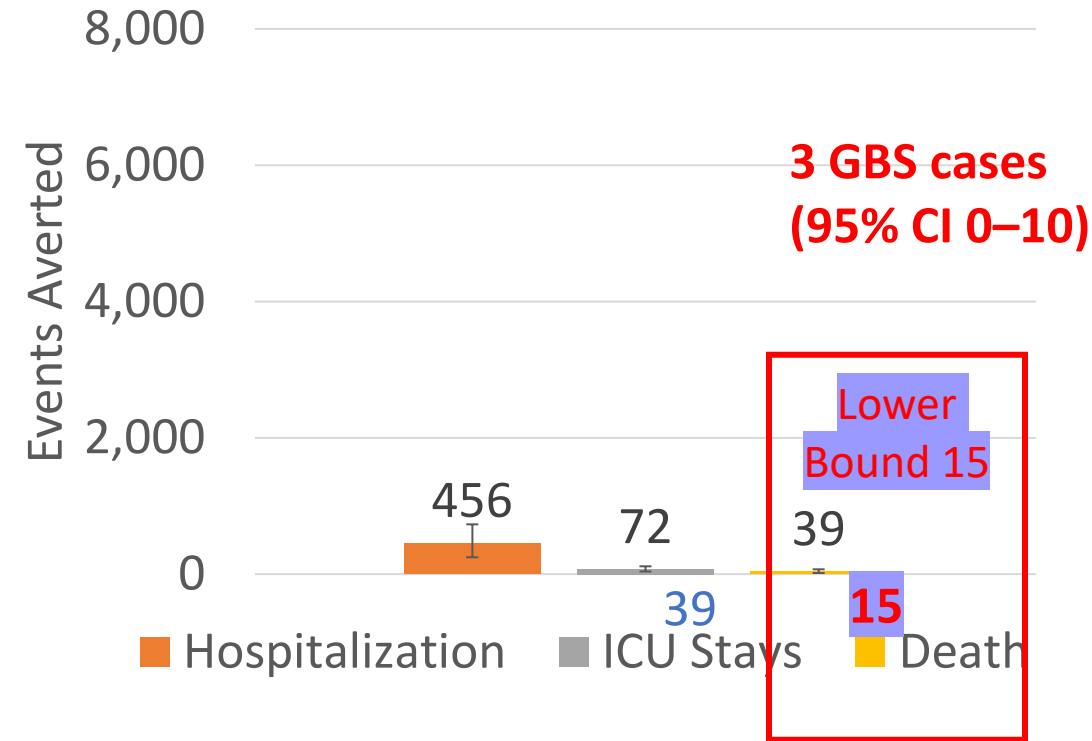


Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in **adults 60-74 years with none of these conditions***

Pfizer None of these conditions
Age 60-74 years



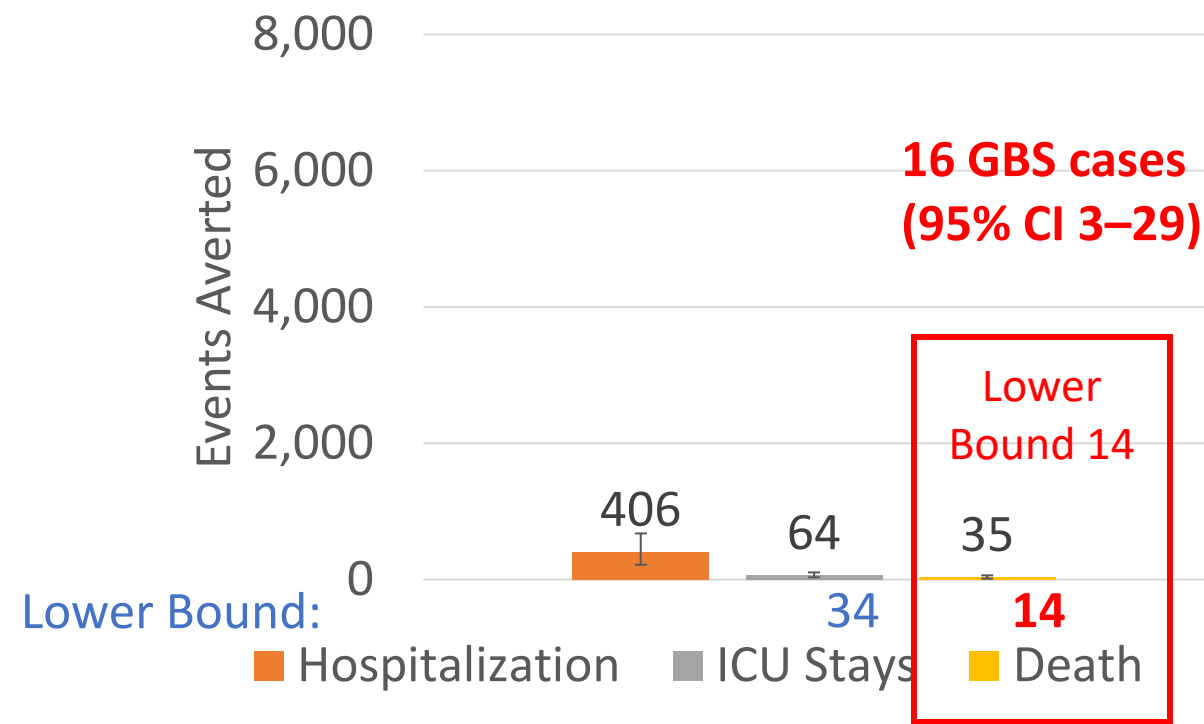
GSK None of these conditions
Age 60-74 years



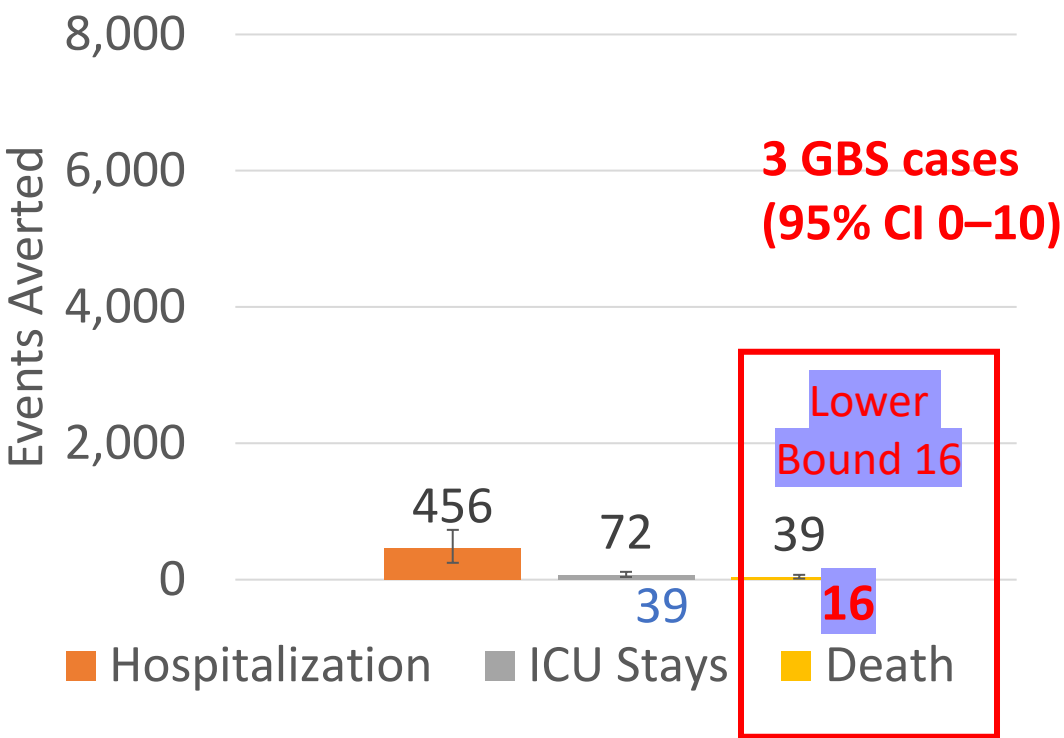
*None of: COPD, asthma, coronary artery disease, chronic kidney disease, diabetes mellitus, severe obesity (BMI ≥40). Persons may have other chronic medical conditions (e.g., heart failure, non-severe obesity, immune compromise).

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

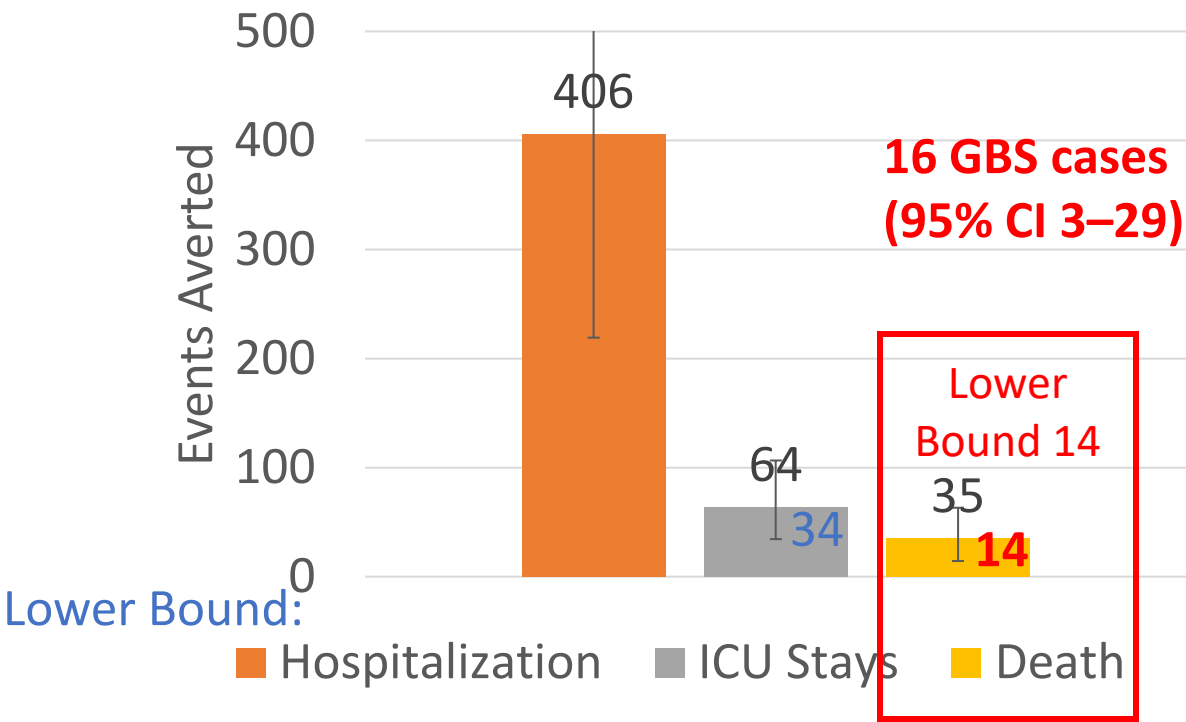


*None of: COPD, asthma, coronary artery disease, chronic kidney disease, diabetes mellitus, severe obesity (BMI ≥40). Persons may have other chronic medical conditions (e.g., heart failure, non-severe obesity, immune compromise).

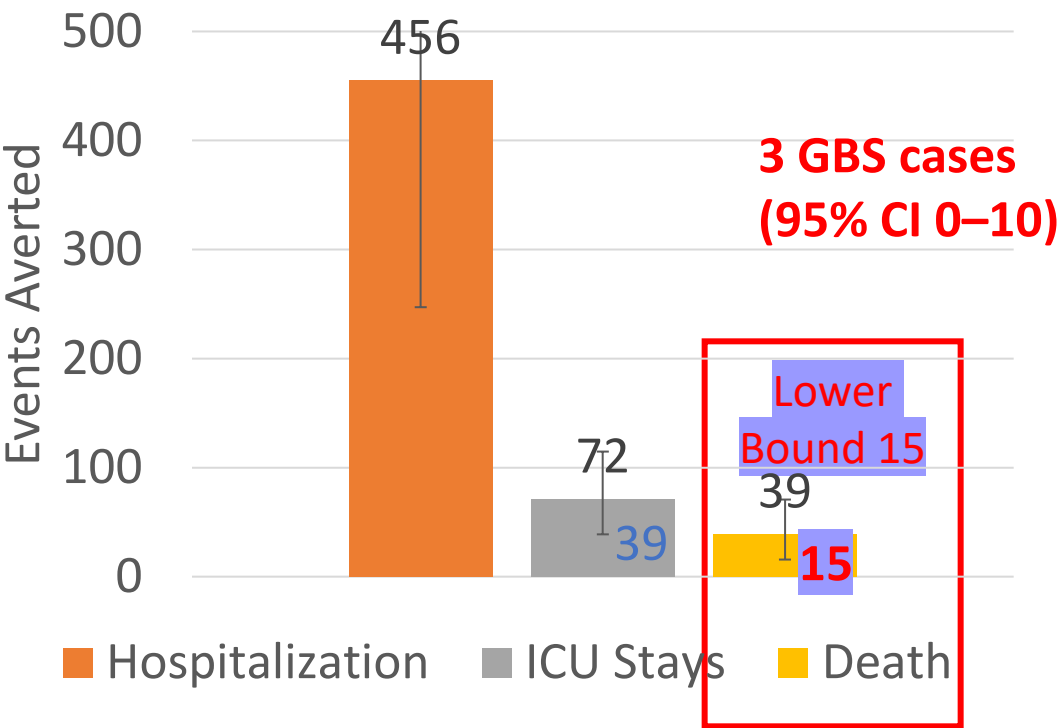
Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in **adults 60-74 years** **with none of these conditions***

Pfizer None of these conditions
Age 60-74 years

Zoomed In



GSK None of these conditions
Age 60-74 years

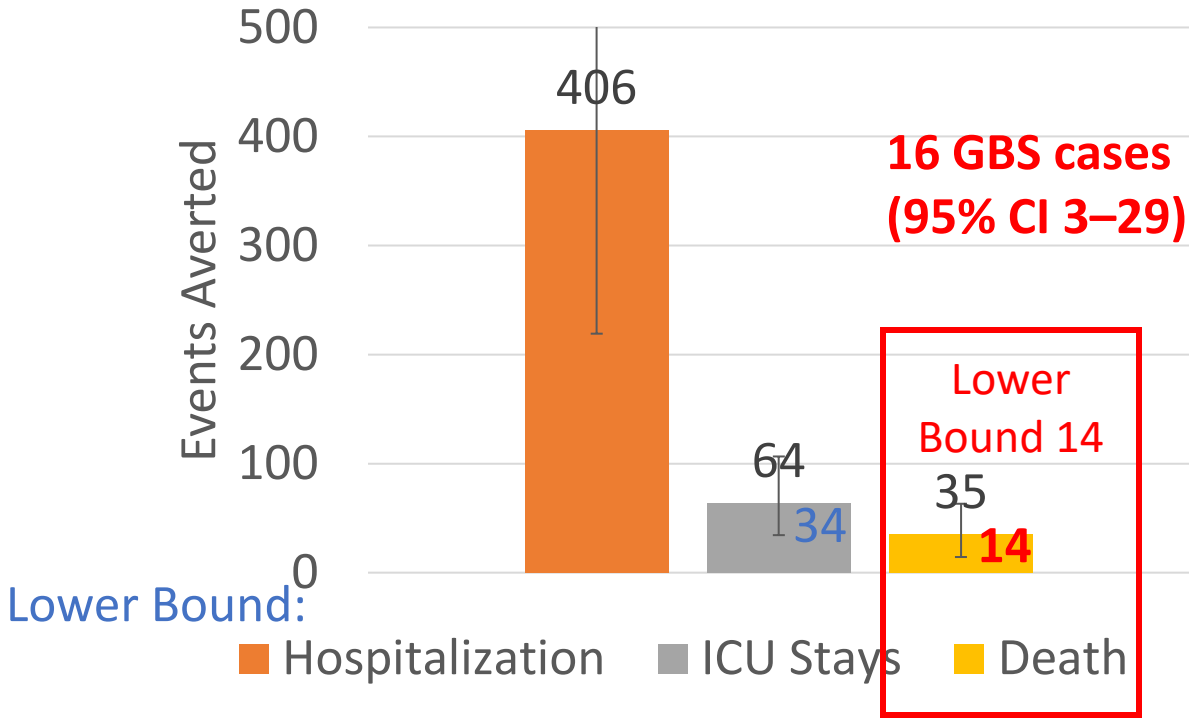


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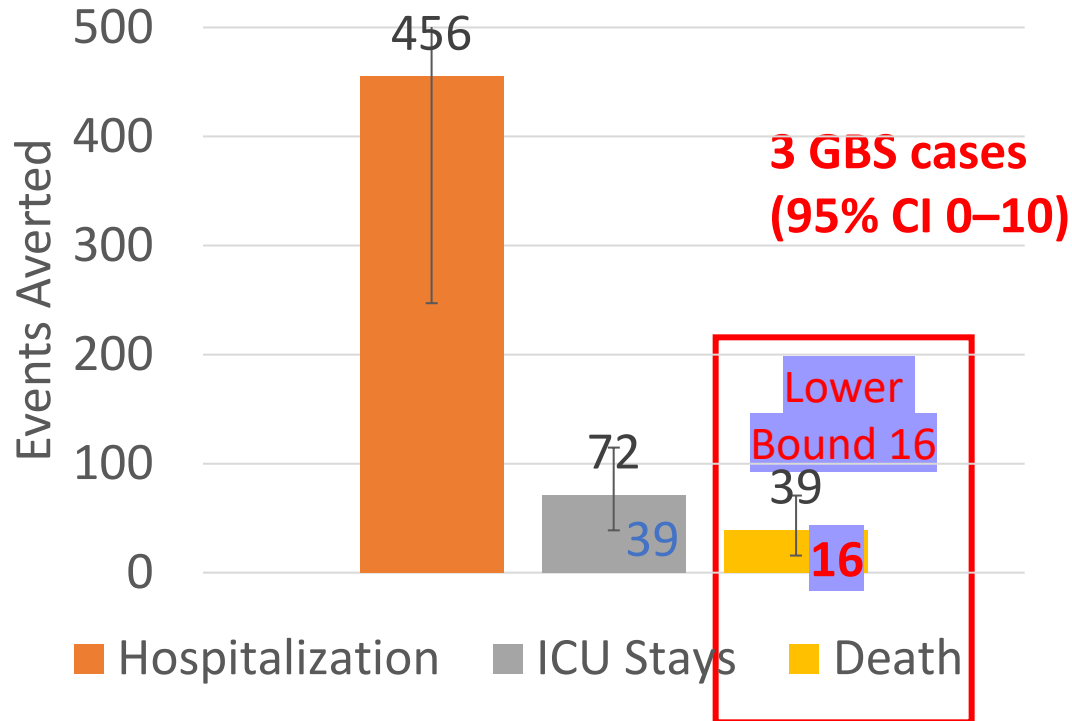
Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in **adults 60-74 years** **with none of these conditions***

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).