This presentation has been corrected. See slides 13, 20, and 21 for corrected slides. The original slides are included at the end of the presentation.

Risk-Benefit Analysis of RSV Vaccination in Older Adults

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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.

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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 ABRYSVO
  - 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)

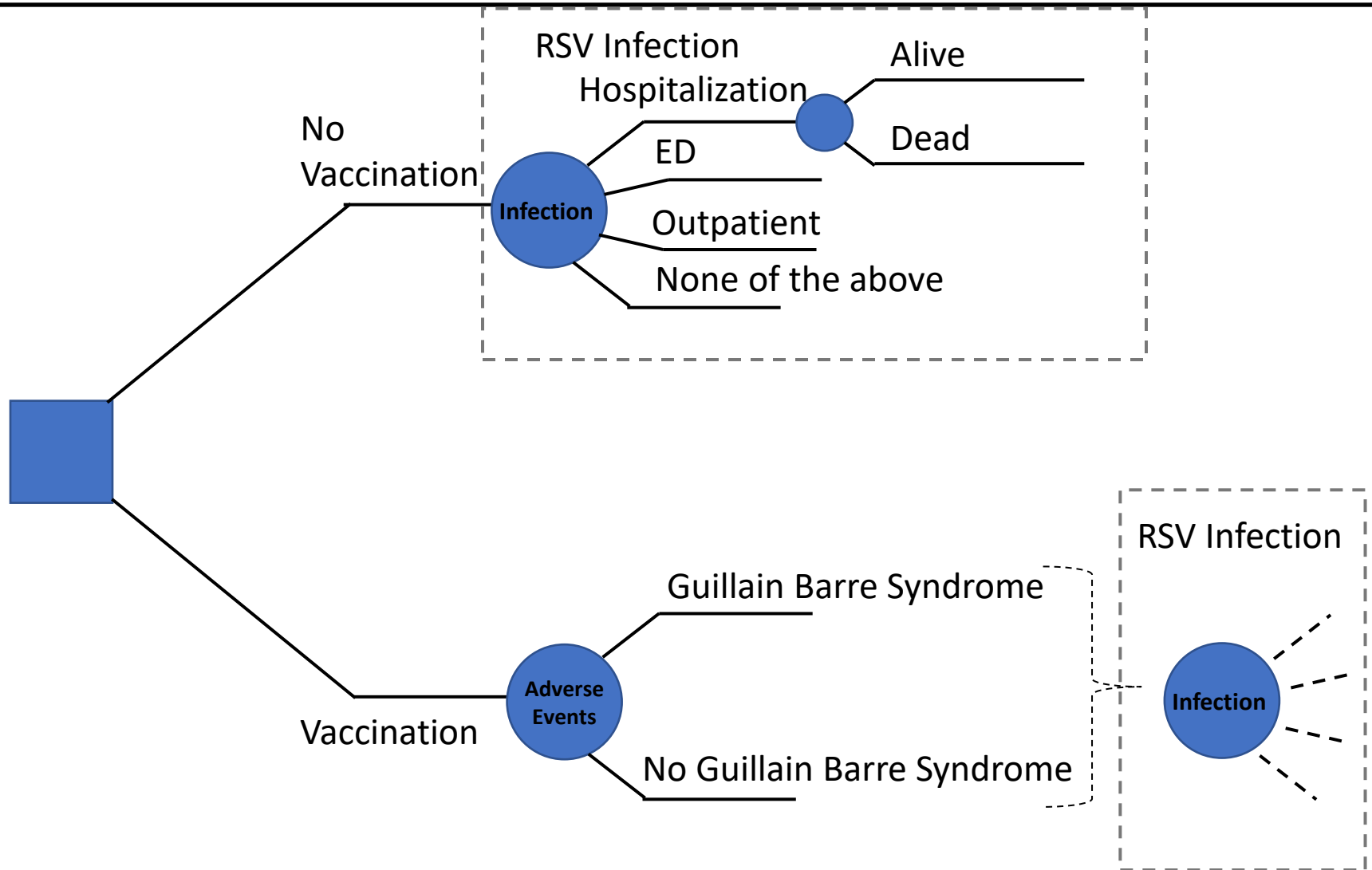
  - Heart failure
  - Immune Compromise
    - Lung Transplant
    - Hematopoietic cell transplant, allogeneic
    - Hematopoietic cell transplant, autologous

Assumed that vaccine effectiveness was reduced by <u>half</u> 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 ABRYSVO**: **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

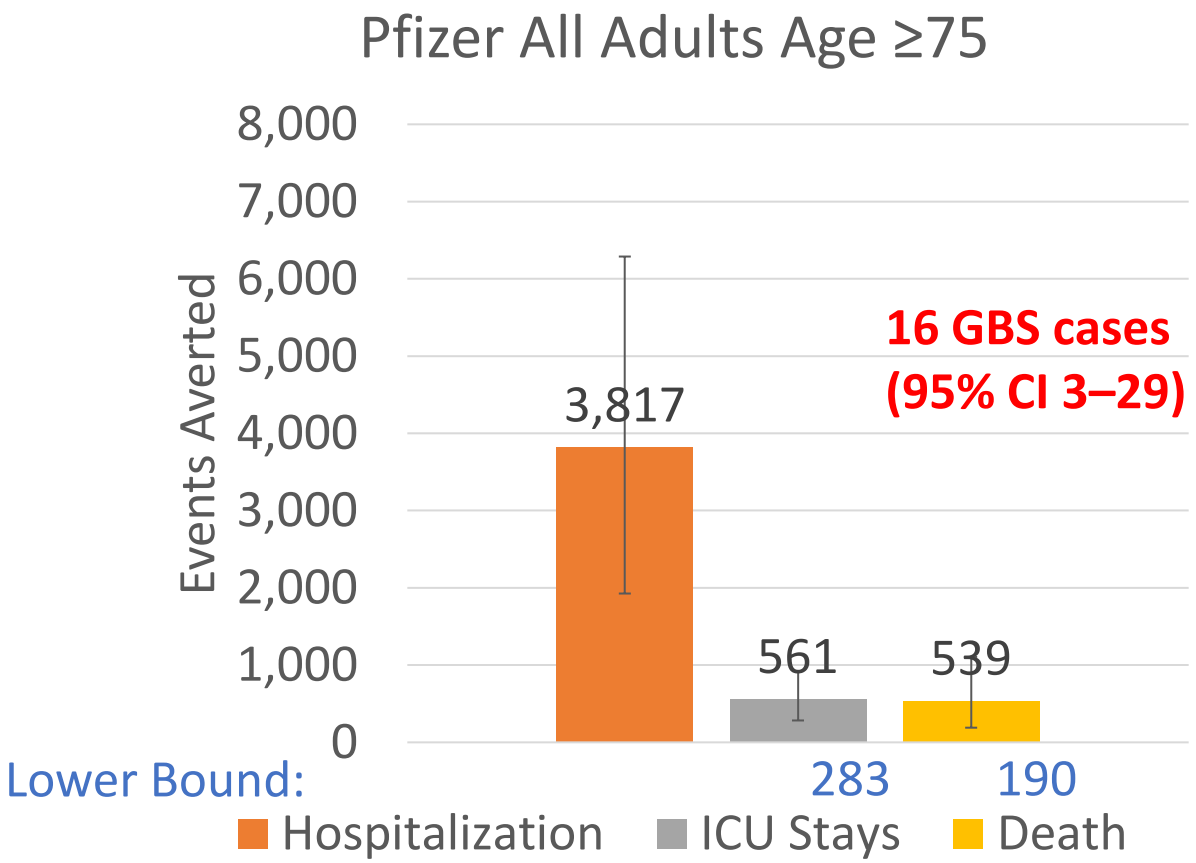
* Attributable risk for GSK's AREXVY was estimated to be 3 GBS cases (95% CI: -3, 10) per 1 million doses. For this analysis, the lower end of the 95% CI was truncated at 0 to evaluate potential **risk** of GBS. Potential protective effects were not evaluated.

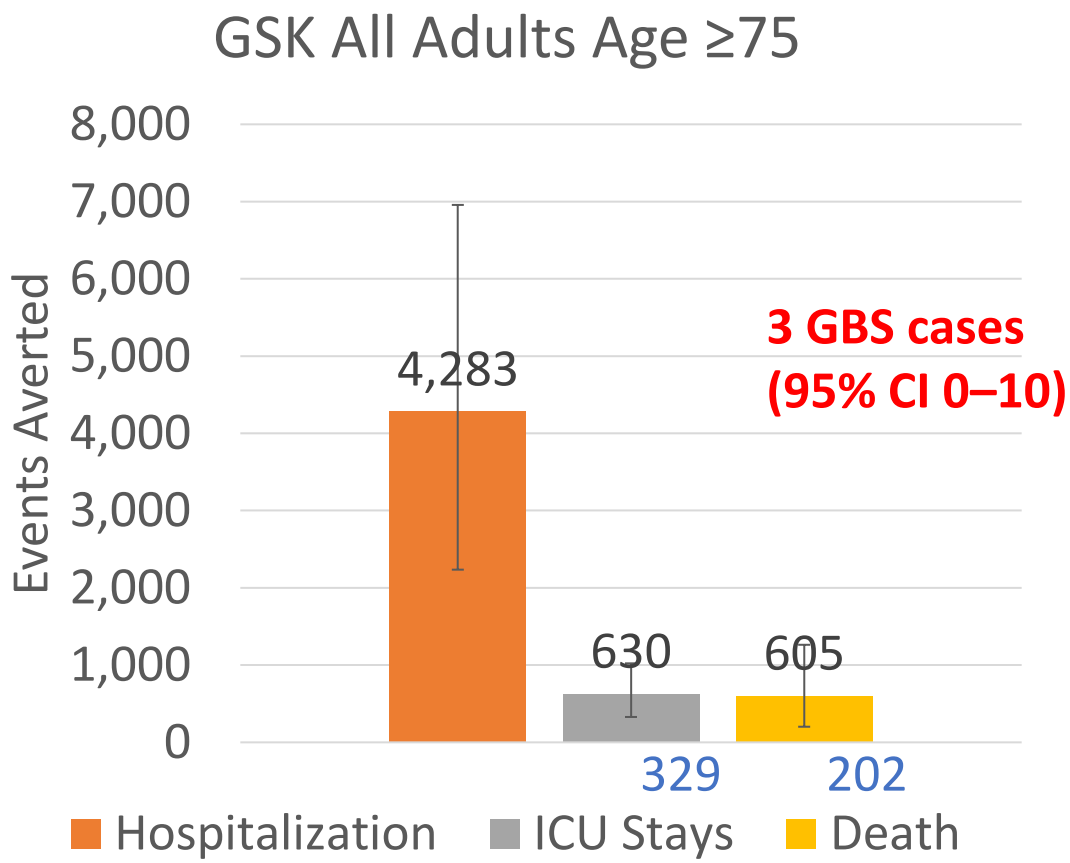
Results: Estimated Benefits and Potential Risk

- 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**.

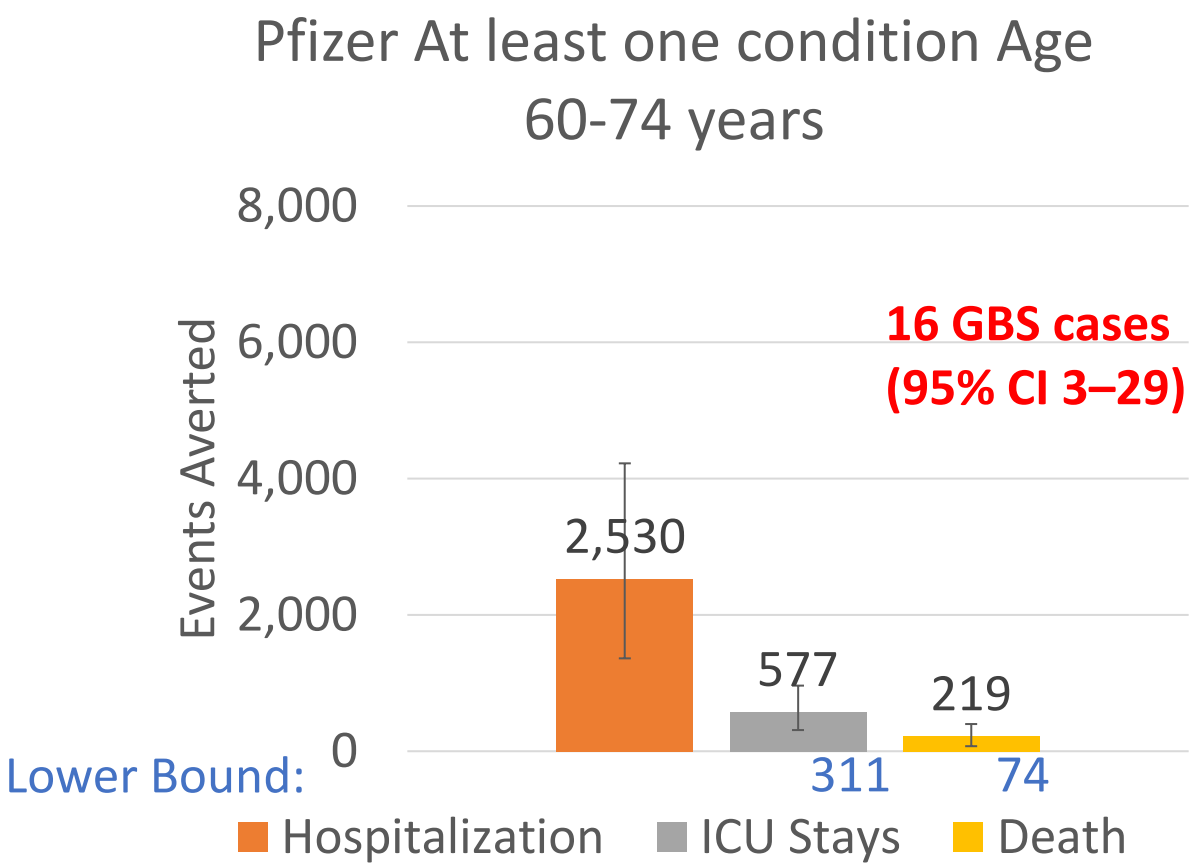
This slide contains corrections. To see the slide as originally presented, without corrections, please see slide 32.

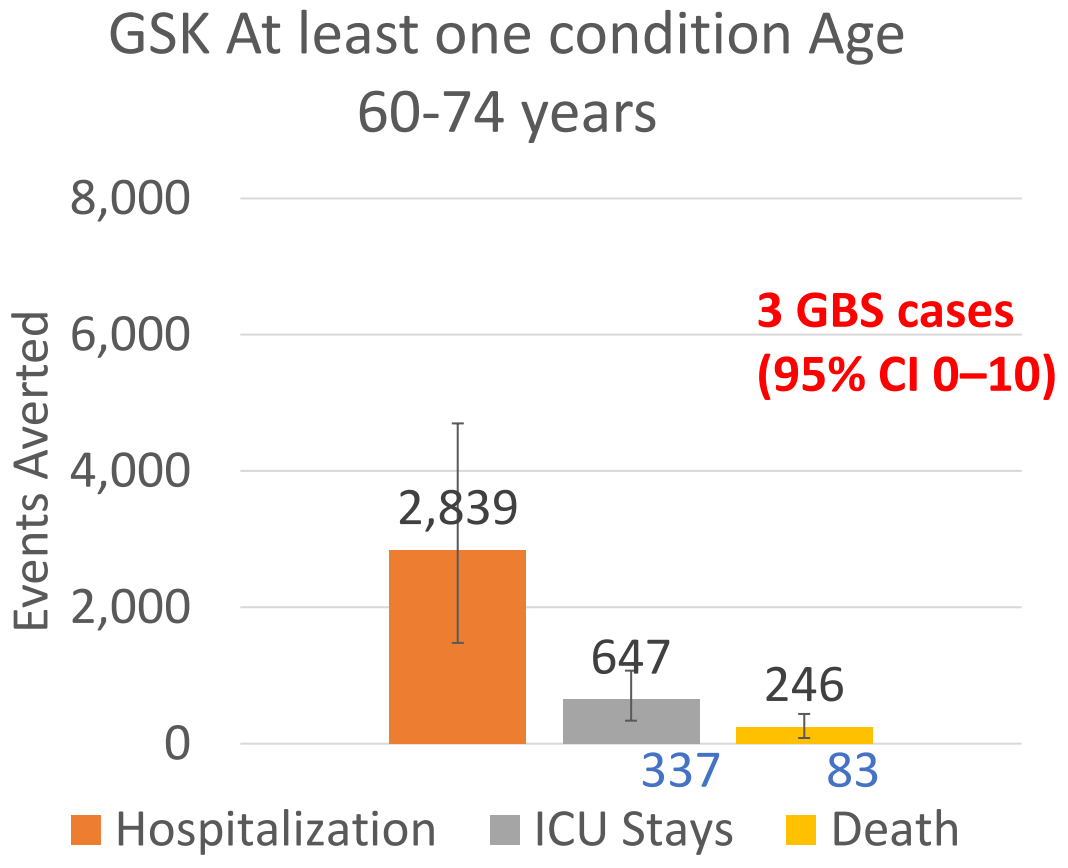
Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in adults ≥75 years (general population)





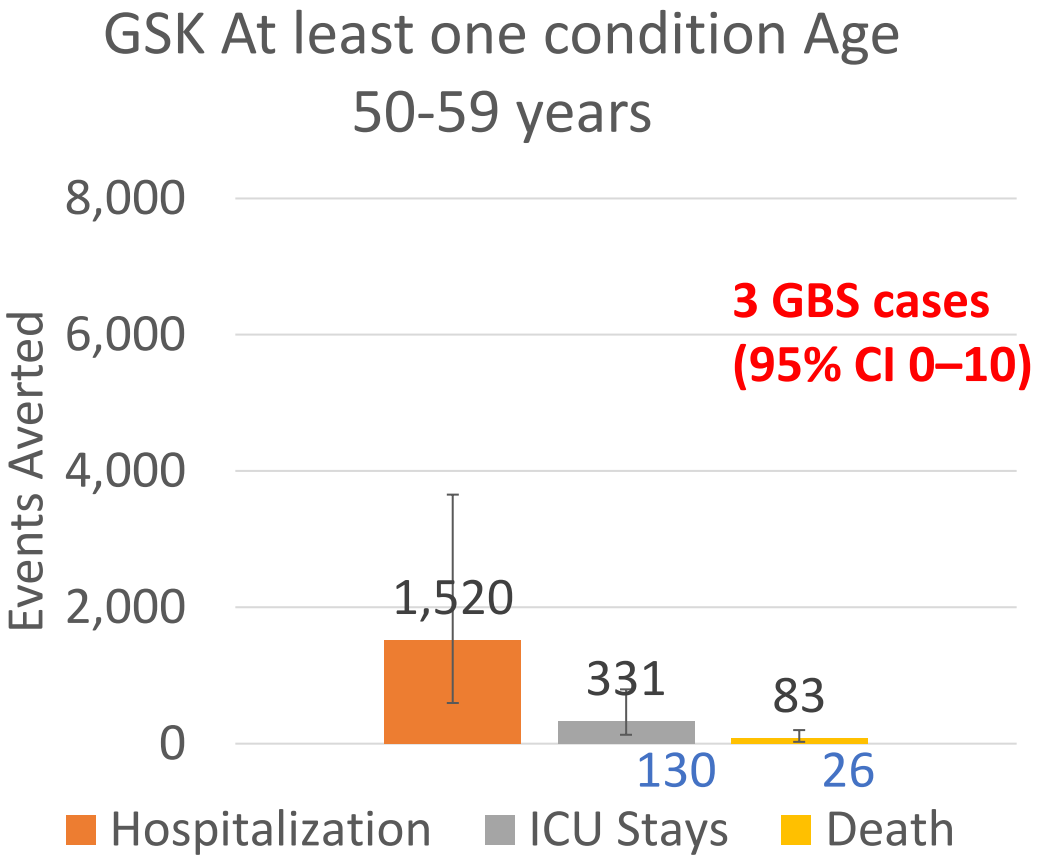
Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in adults 60-74 years with ≥1 chronic condition*





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

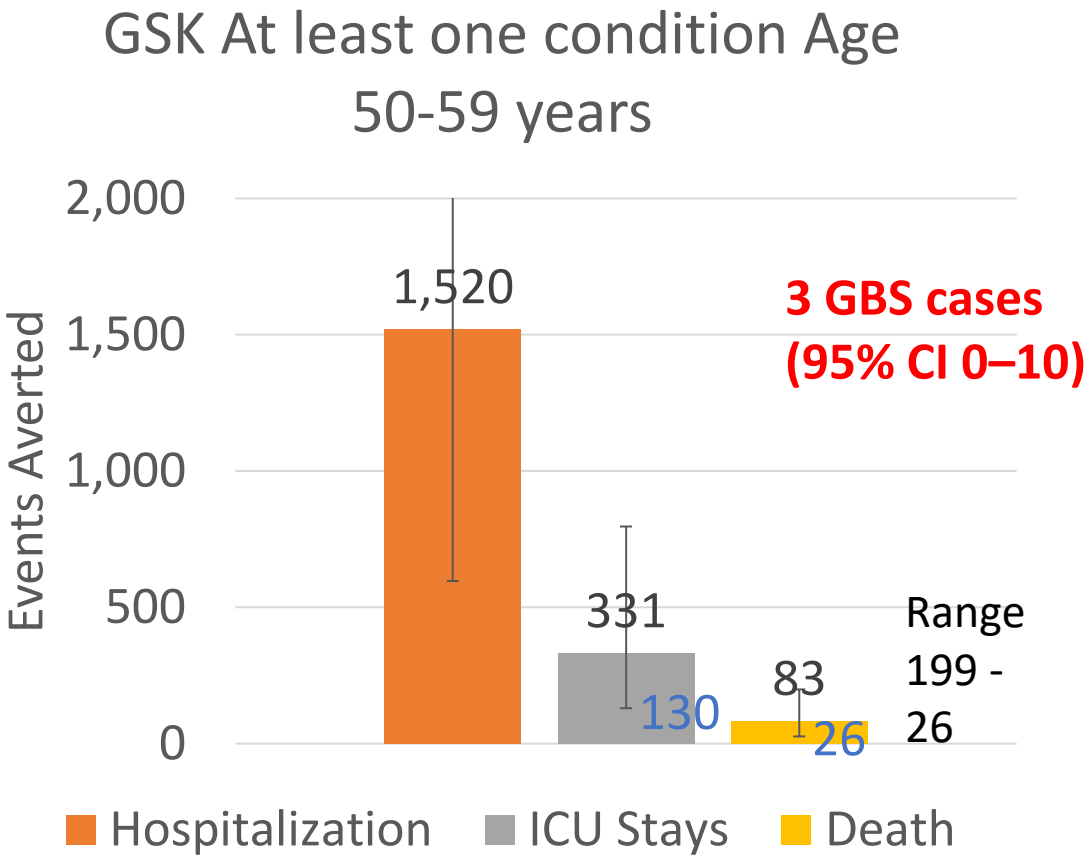
Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in adults 50-59 years with ≥1 chronic condition*



*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



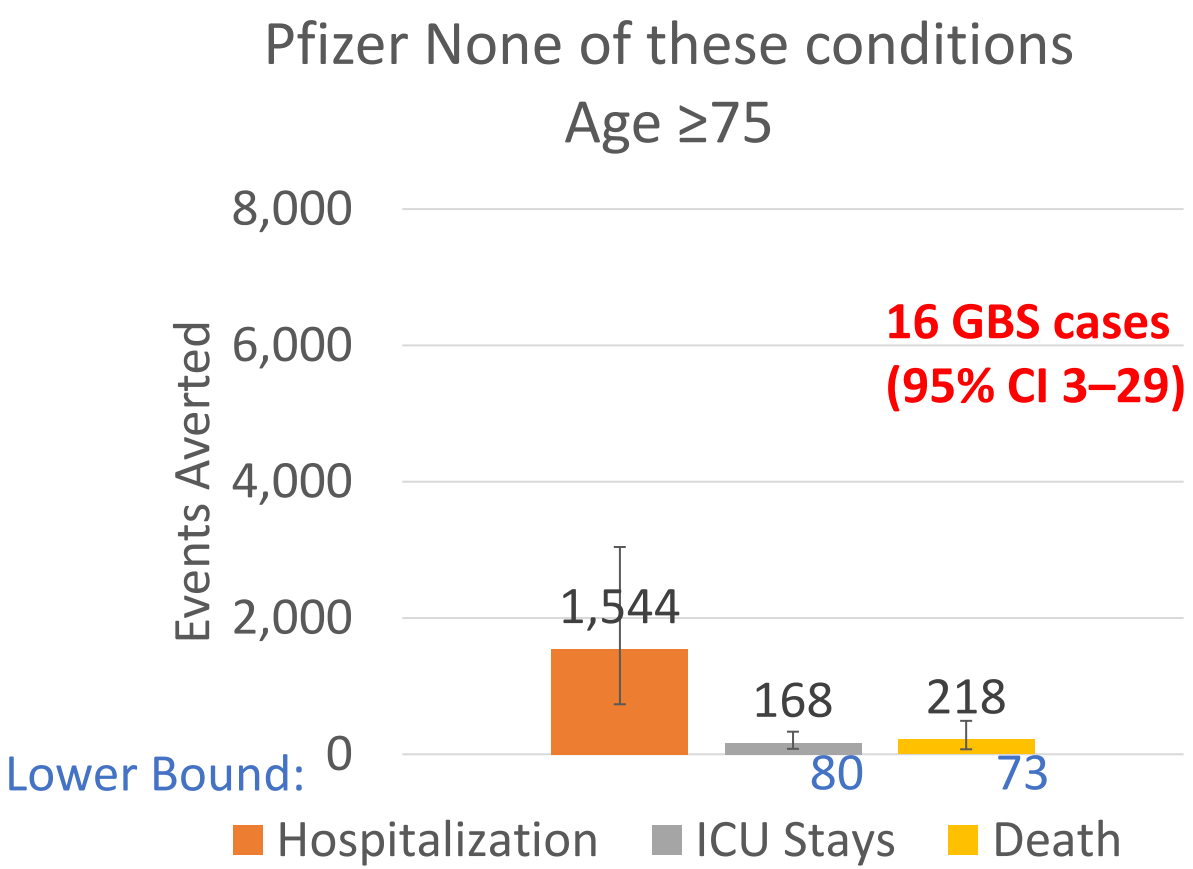
*At least one of: chronic obstructive pulmonary disease, asthma, coronary artery disease, diabetes mellitus, chronic kidney disease, severe obesity (BMI ≥40)

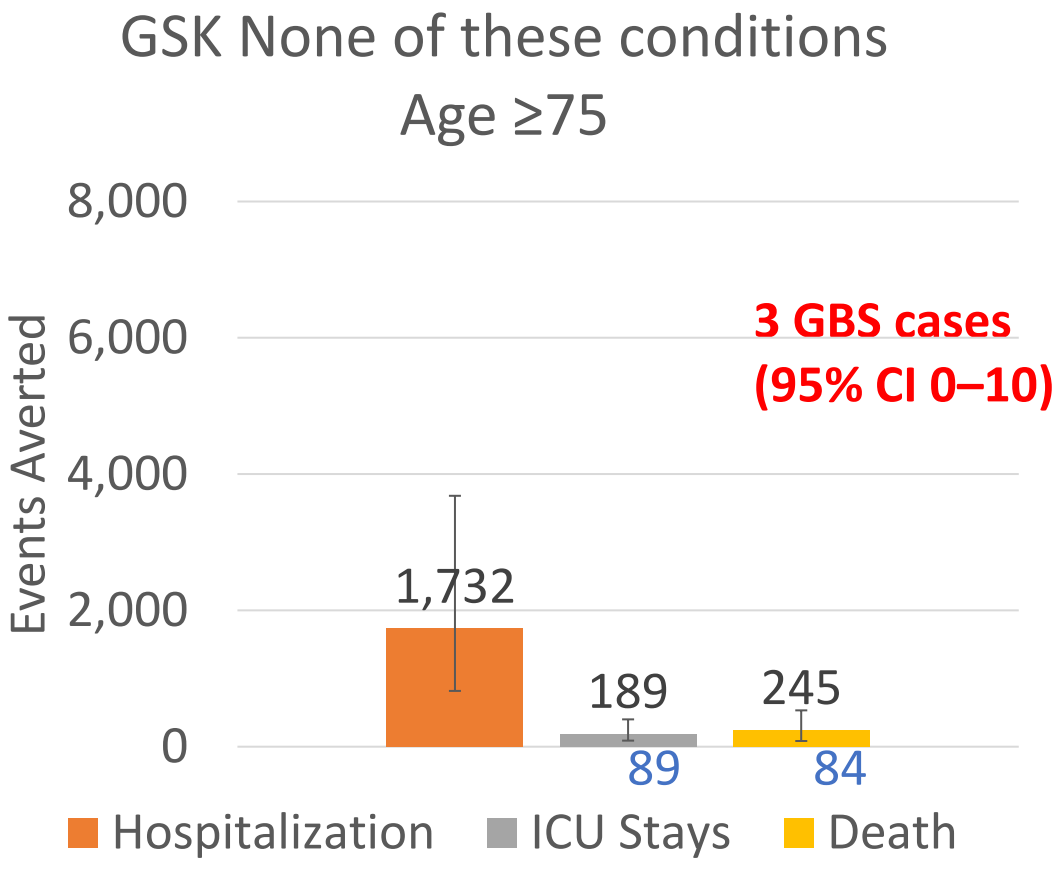
Scenarios

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*



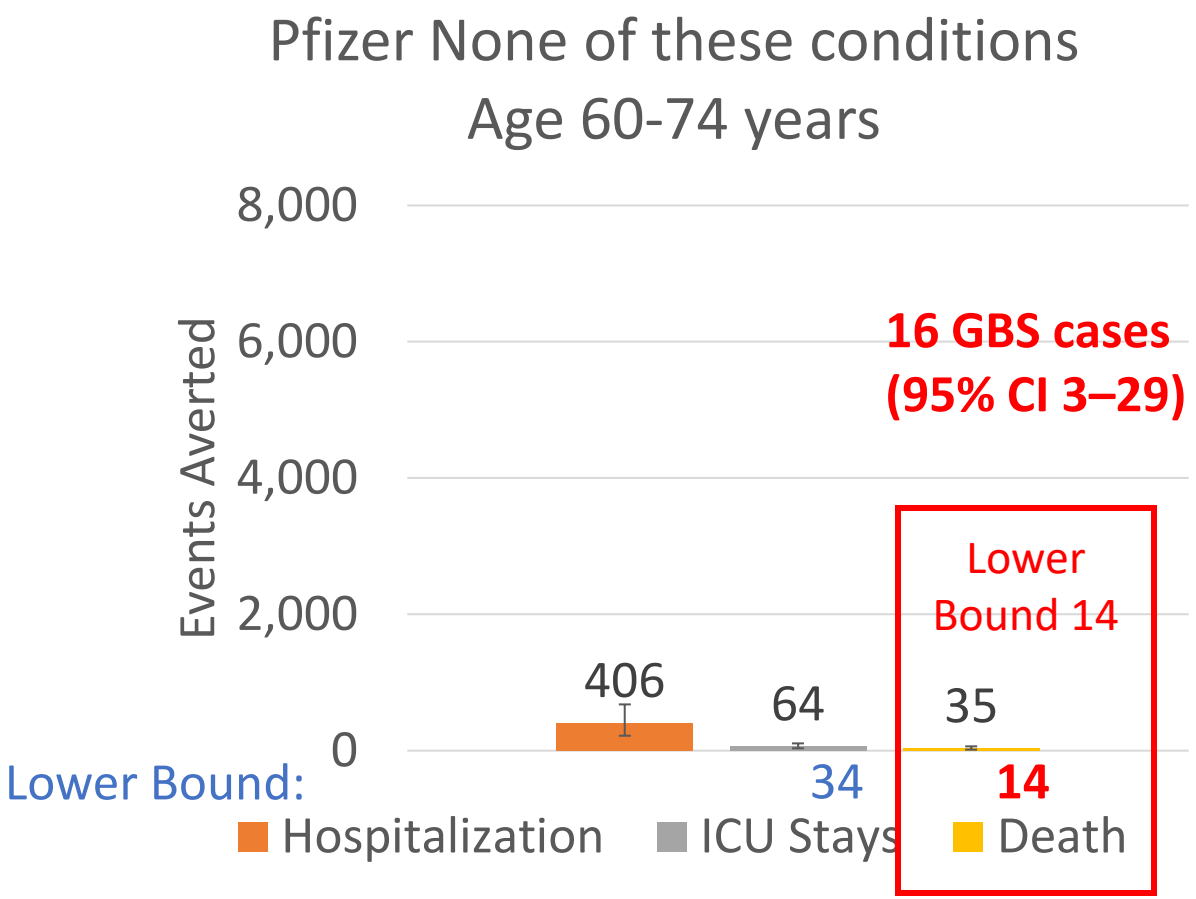


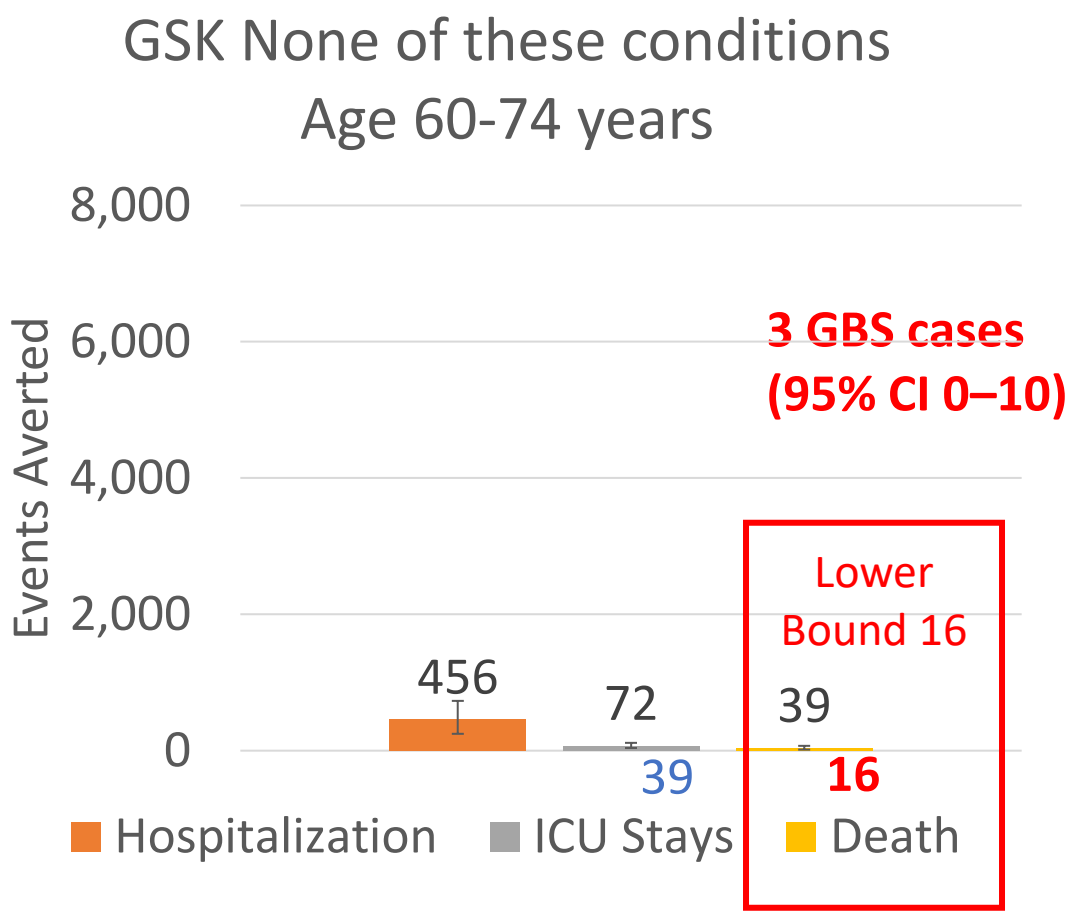
*None of: COPD, asthma, coronary artery disease, chronic kidney disease, diabetes mellitus, severe obesity (BMI ≥40).

Persons may have other chronic medical conditions (e.g., heart failure, non-severe obesity, immune compromise).

This slide contains corrections. To see the slide as originally presented, without corrections, please see slide 34.

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*



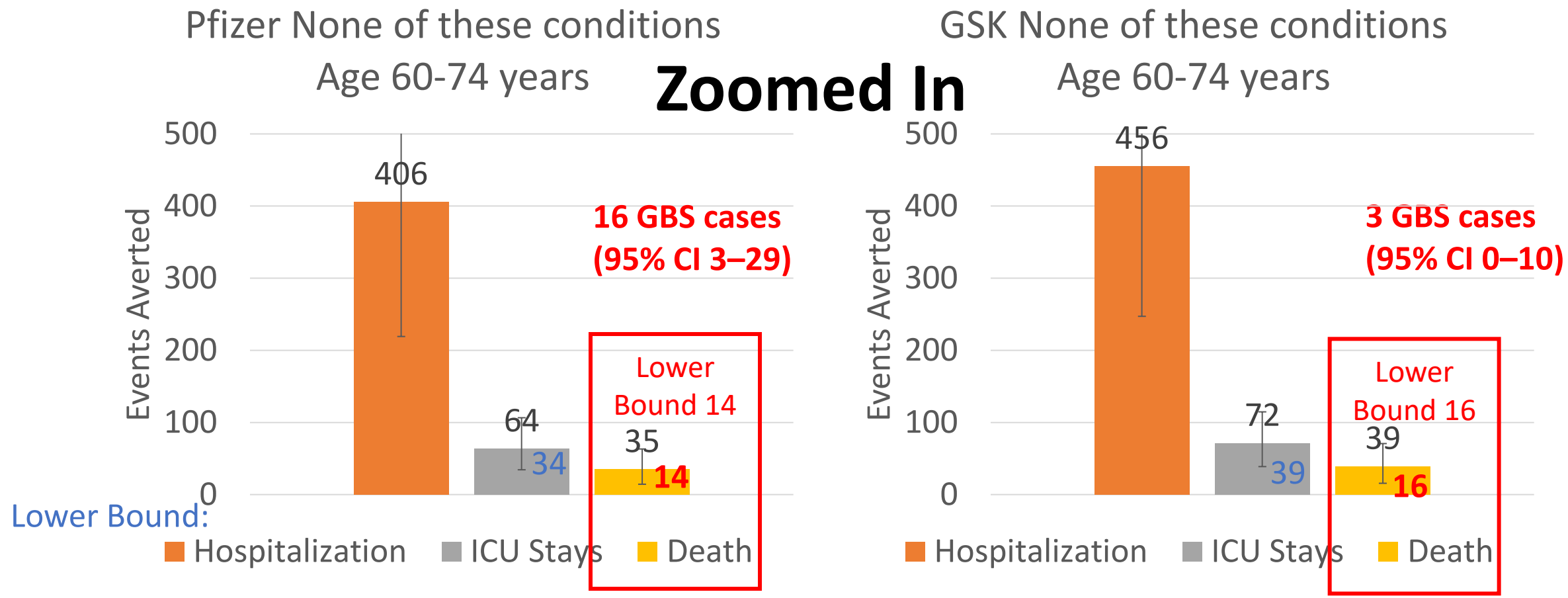


*None of: COPD, asthma, coronary artery disease, chronic kidney disease, diabetes mellitus, severe obesity (BMI ≥40).

Persons may have other chronic medical conditions (e.g., heart failure, non-severe obesity, immune compromise).

This slide contains corrections. To see the slide as originally presented, without corrections, please see slide 36.

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*

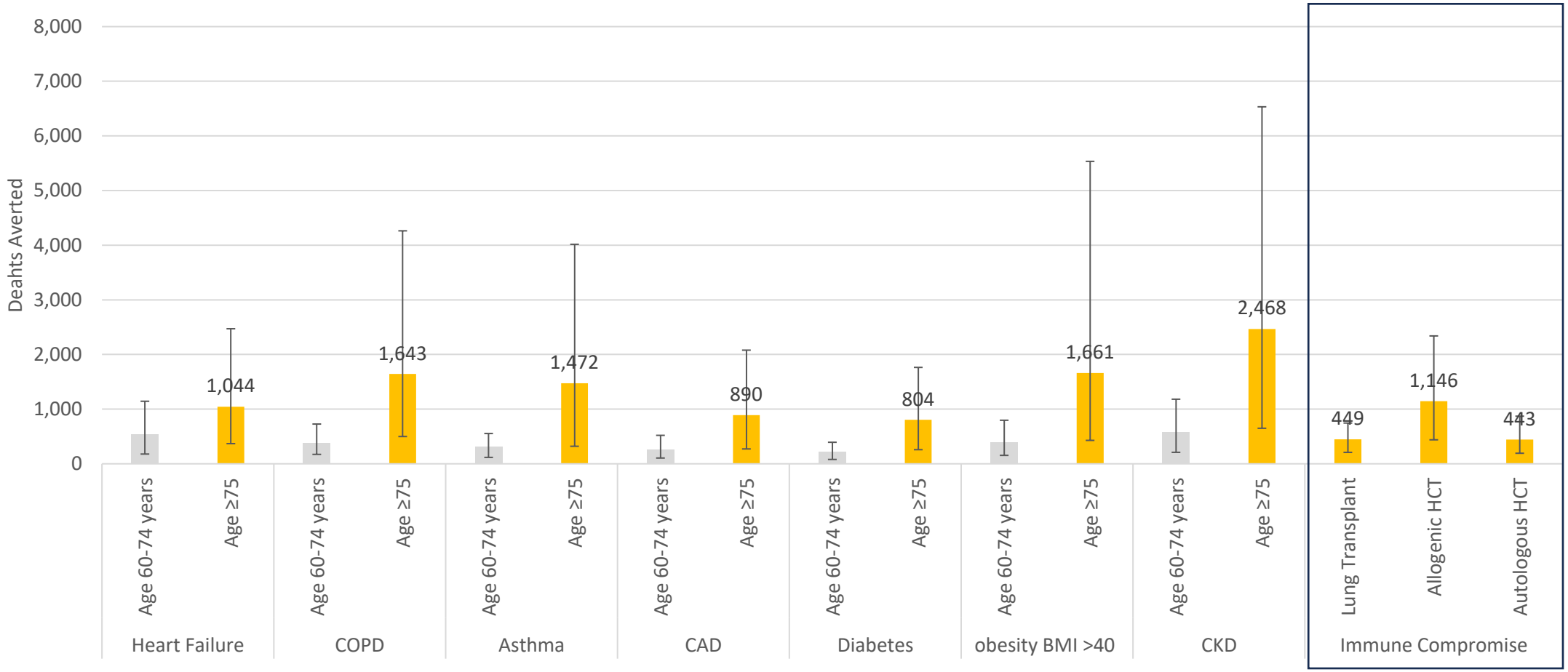


*None of: COPD, asthma, coronary artery disease, chronic kidney disease, diabetes mellitus, severe obesity (BMI ≥40).

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

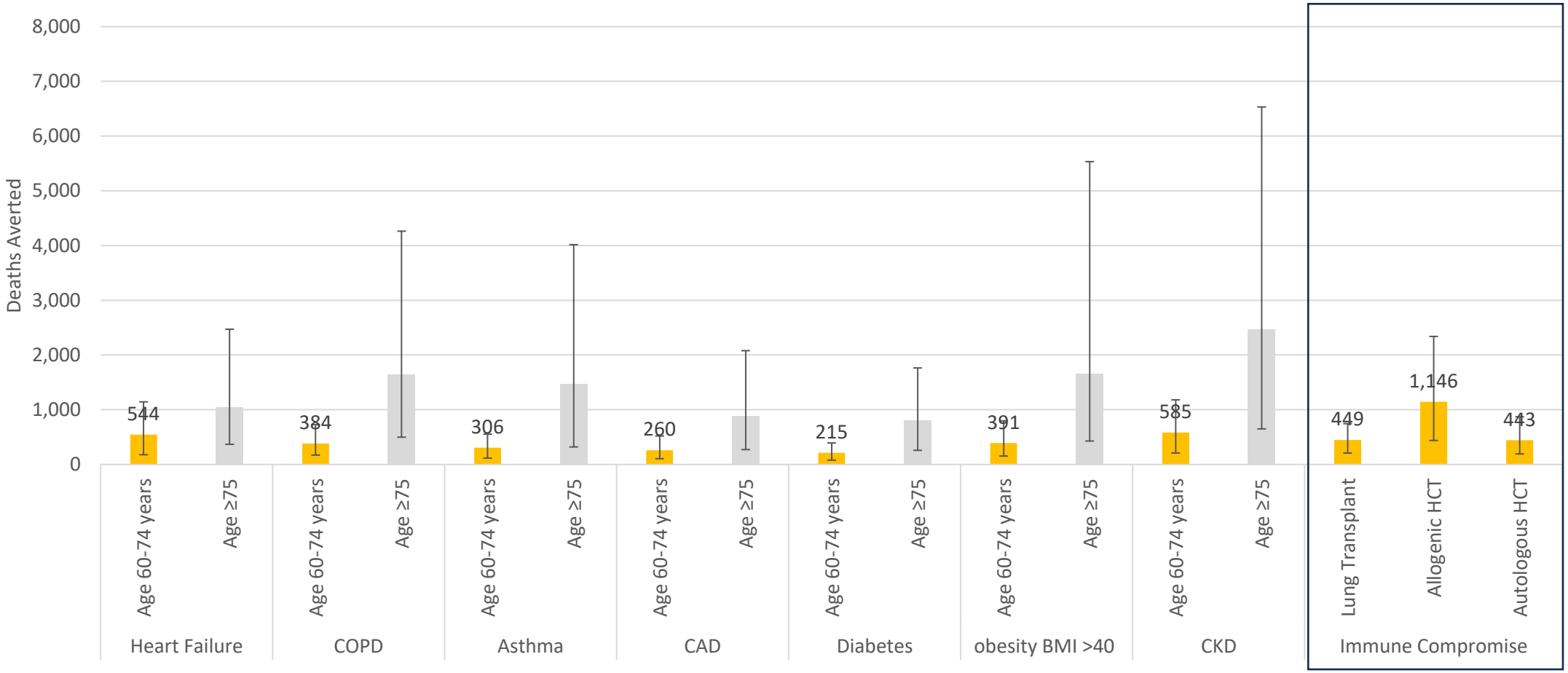


HCT: hematopoietic cell transplant
Lower bound is labeled if <50

16 GBS cases (95% CI 3–29)

Immune Compromise is not age-stratified

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

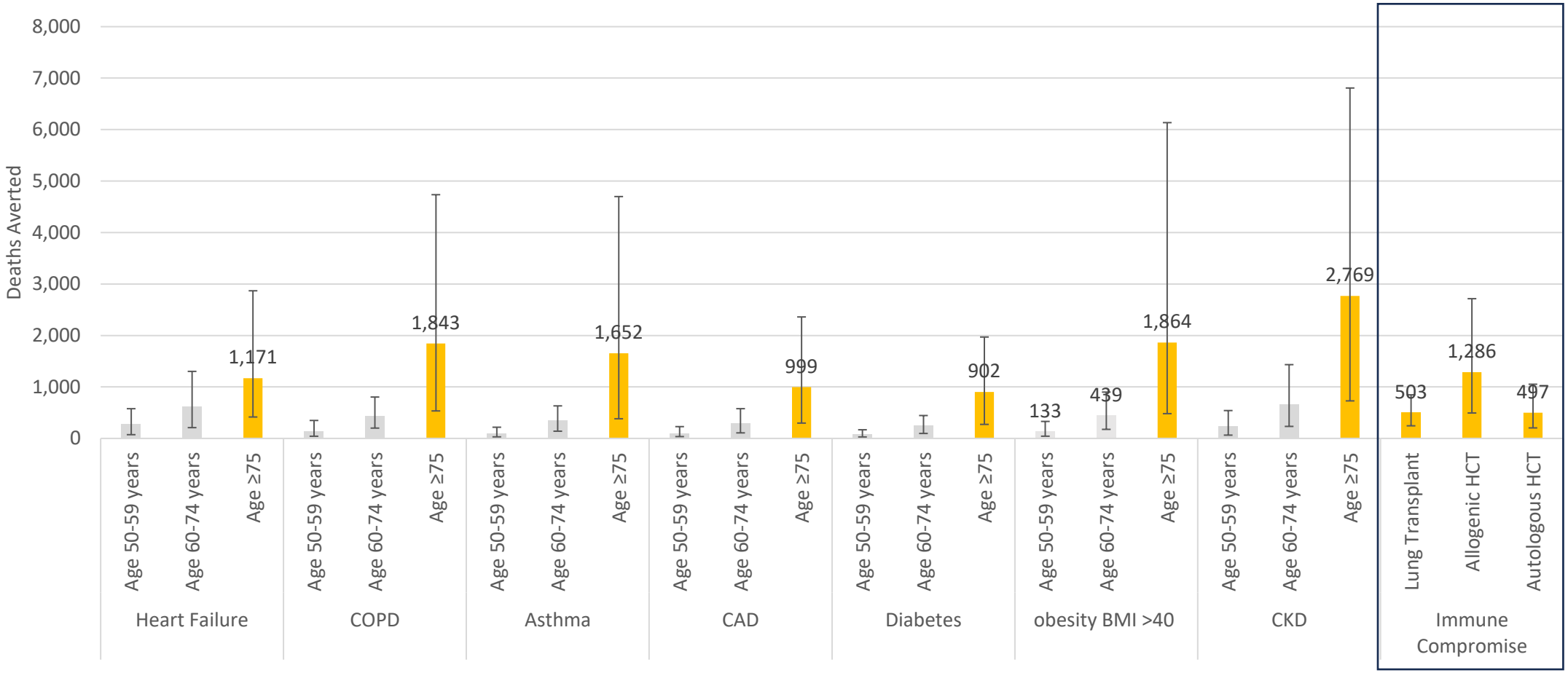


HCT: hematopoietic cell transplant
Lower bound is labeled if <50

16 GBS cases (95% CI 3–29)

Immune Compromise is not age-stratified

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

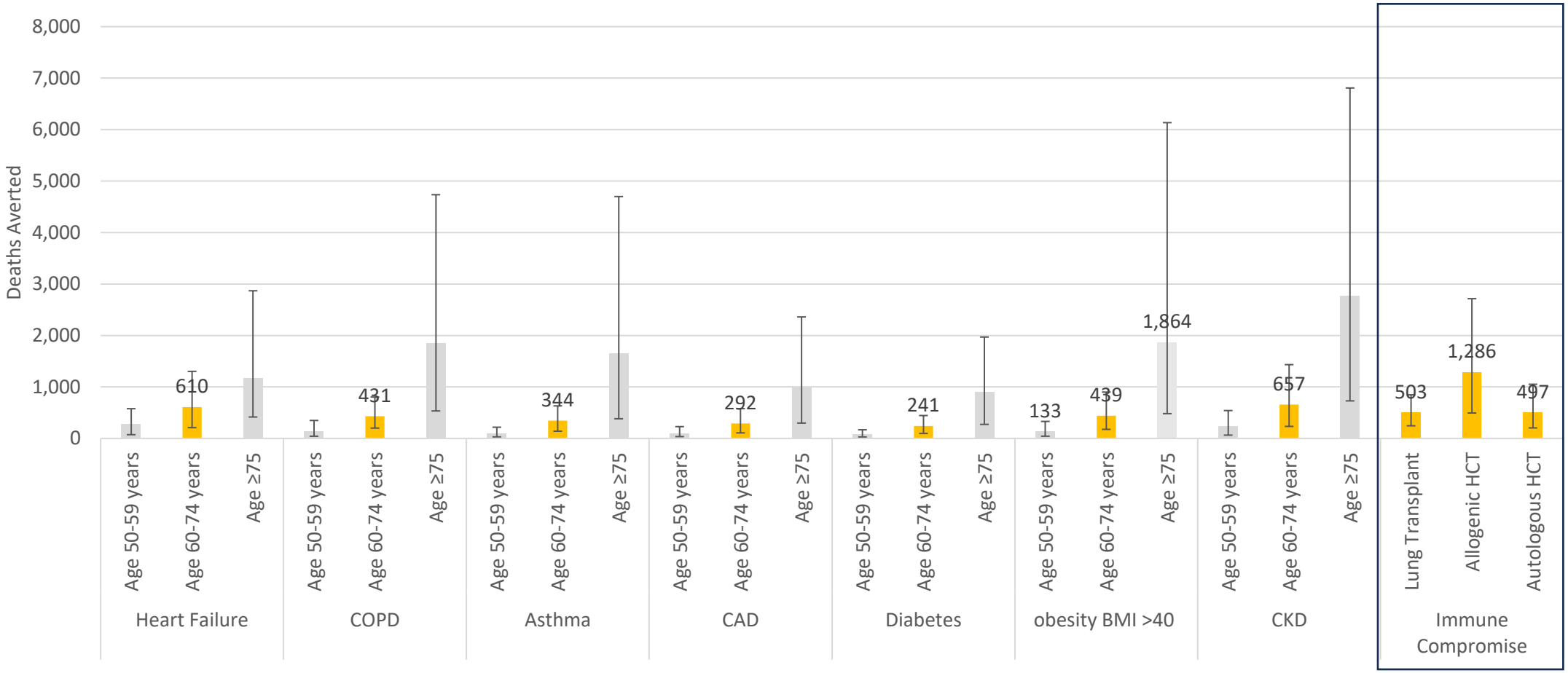


HCT: hematopoietic cell transplant
Lower bound is labeled if <50

3 GBS cases (95% CI 0–10)

Immune Compromise is not age-stratified

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

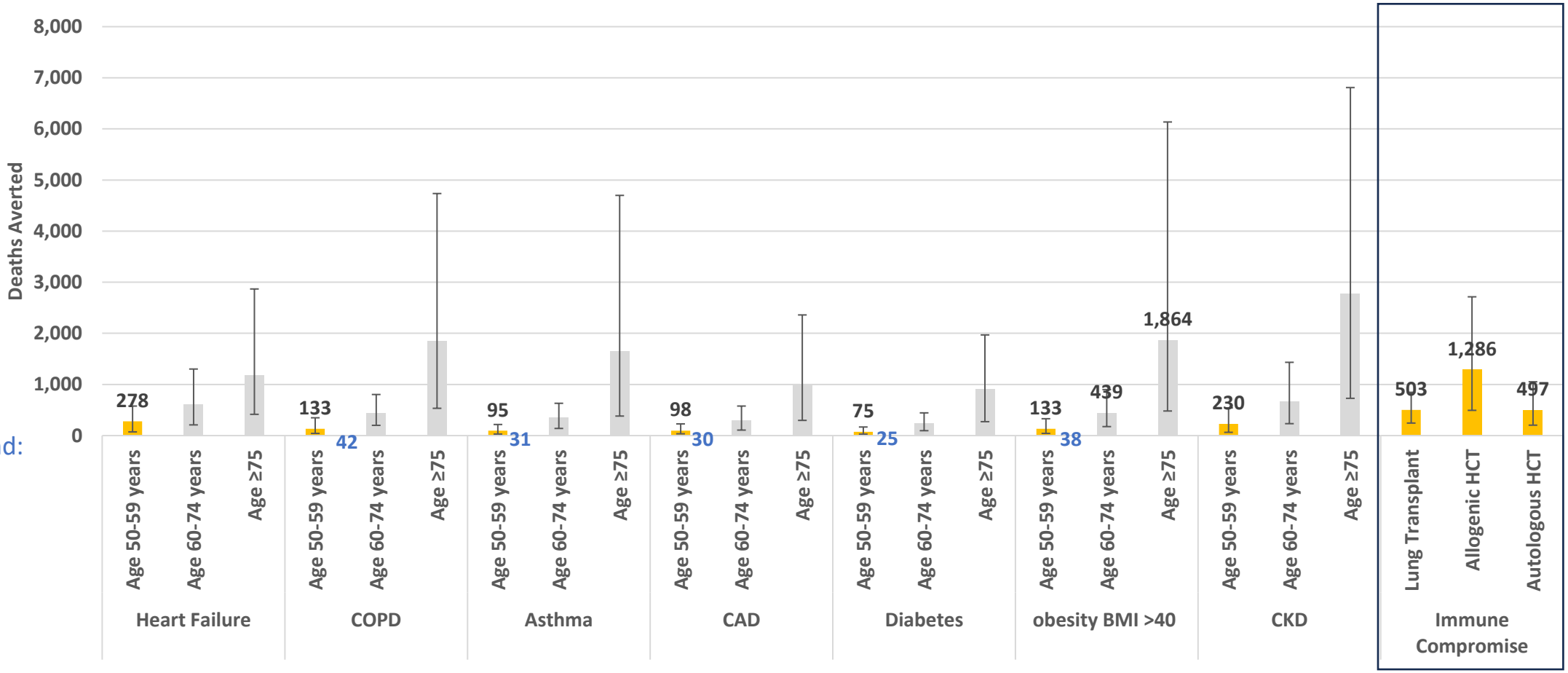


HCT: hematopoietic cell transplant
Lower bound is labeled if <50

3 GBS cases (95% CI 0–10)

Immune Compromise is not age-stratified

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



HCT: hematopoietic cell transplant

Lower bound is labeled if <50

3 GBS cases (95% CI 0–10)

Immune Compromise is not age-stratified

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 ABRYSVO.
- 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 ABRYSVO 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.

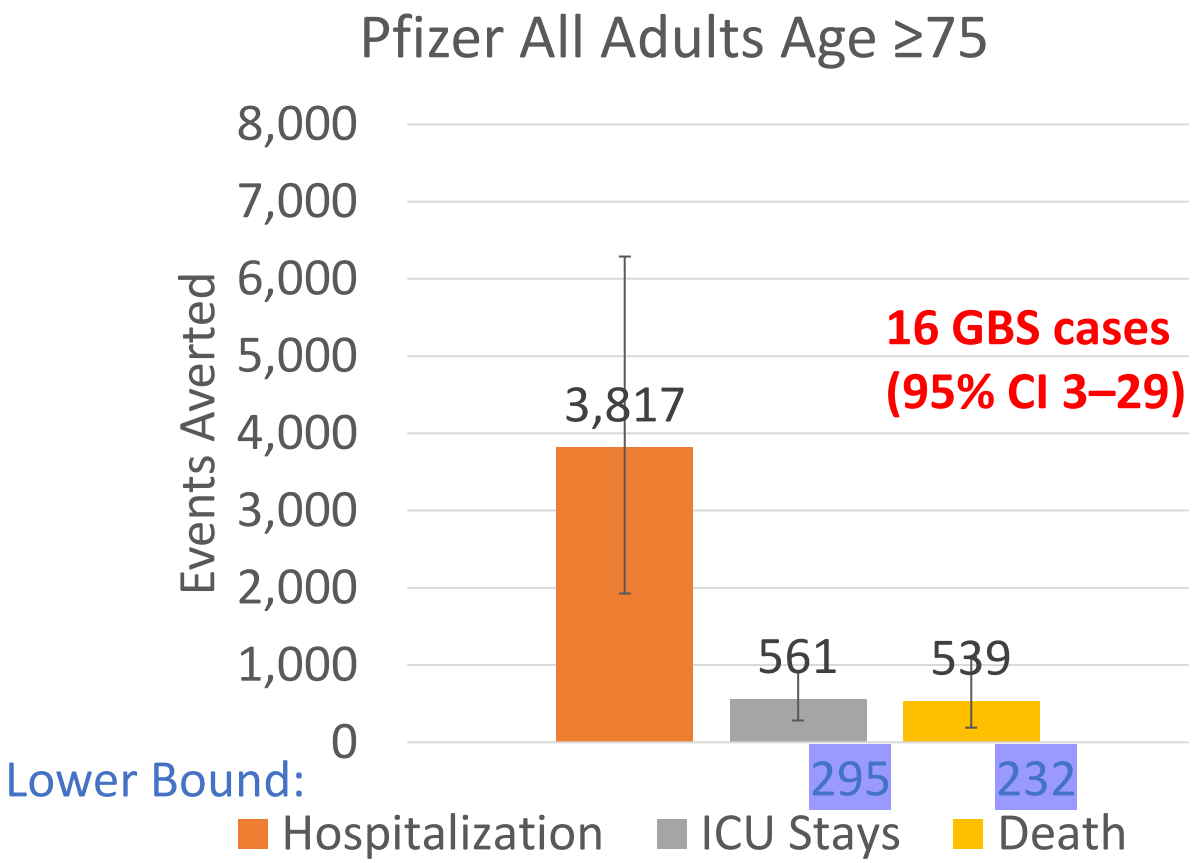
Thank You

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

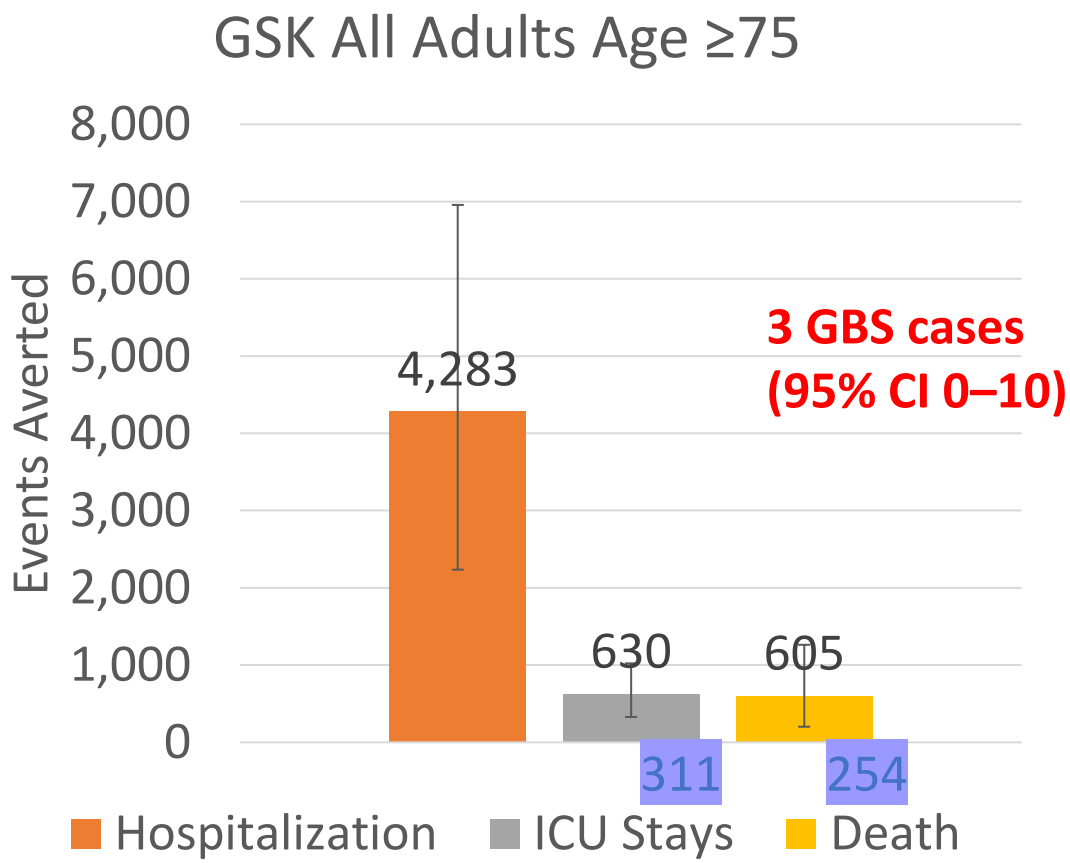
Original slides

- 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)

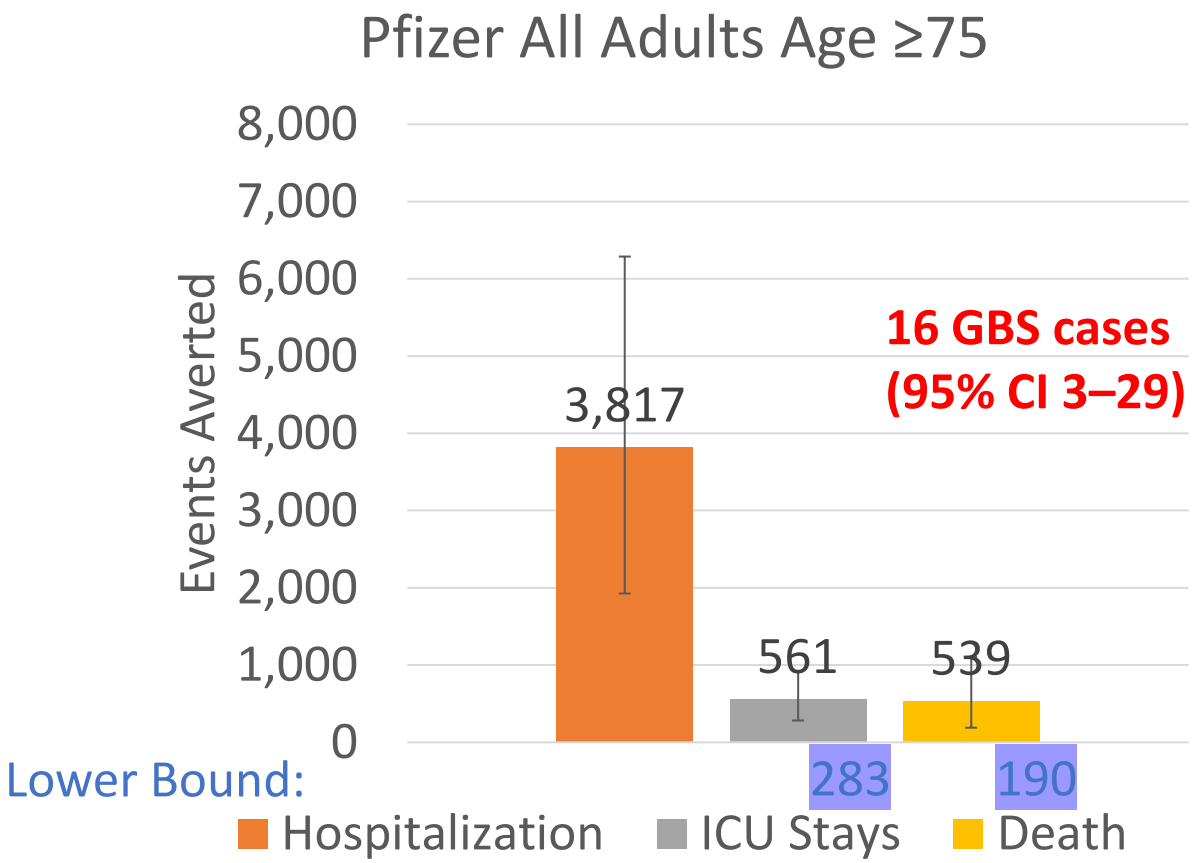


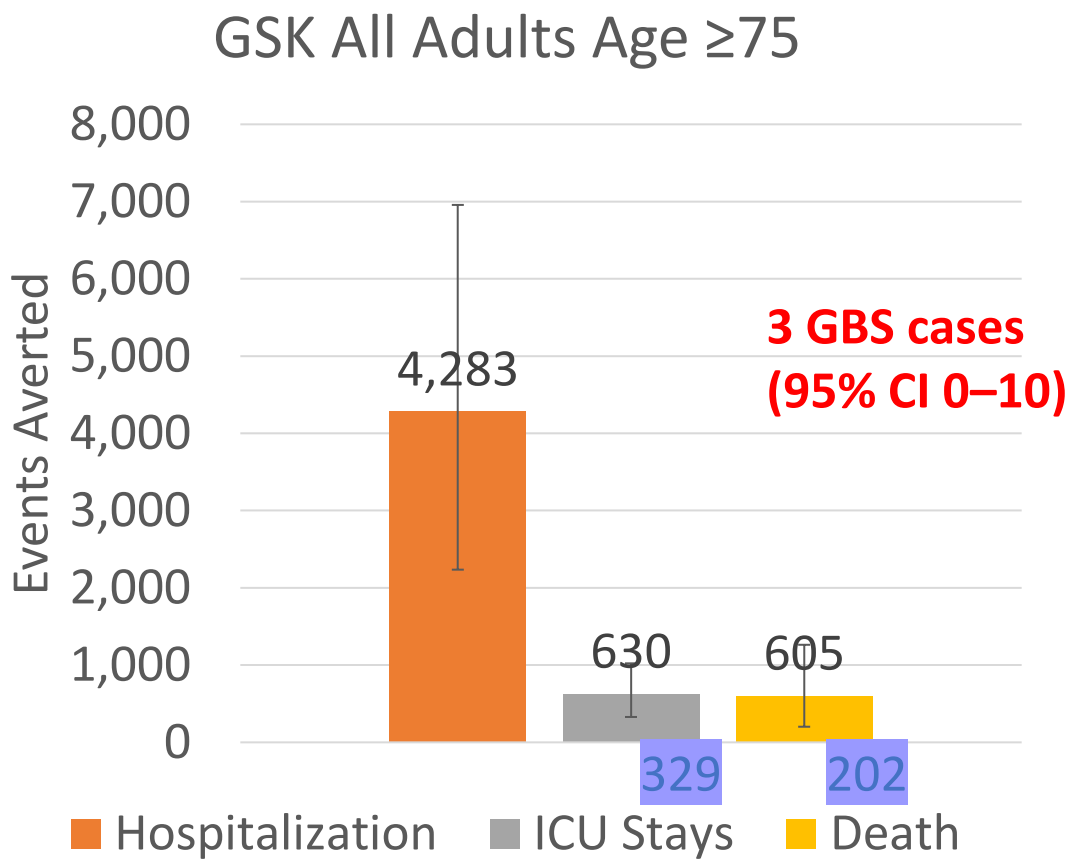
Lower Bound:



This slide has been corrected (highlighted). To see the slide as originally presented at the June 26, 2024 meeting, please see slide 32; to see a corrected, unhighlighted version, see slide 13.

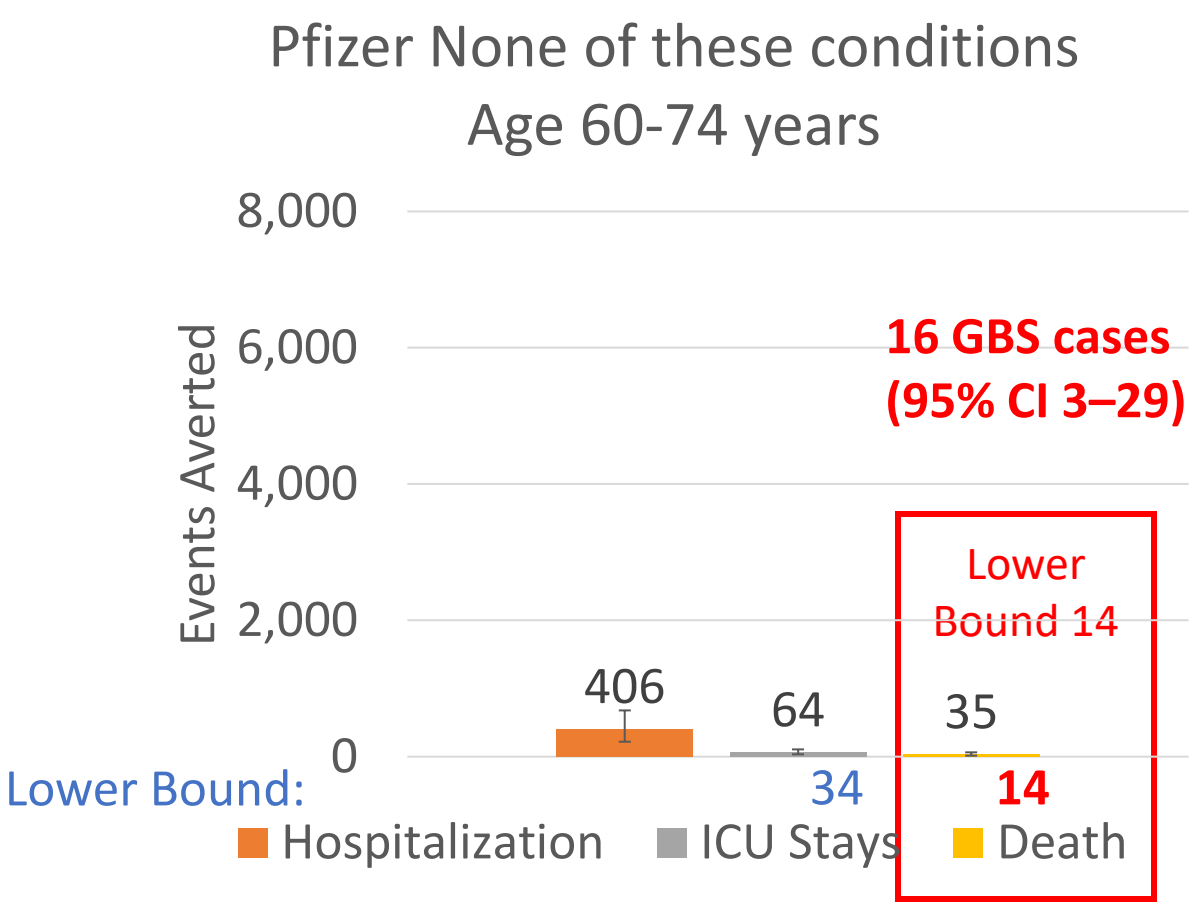
Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in adults ≥75 years (general population)

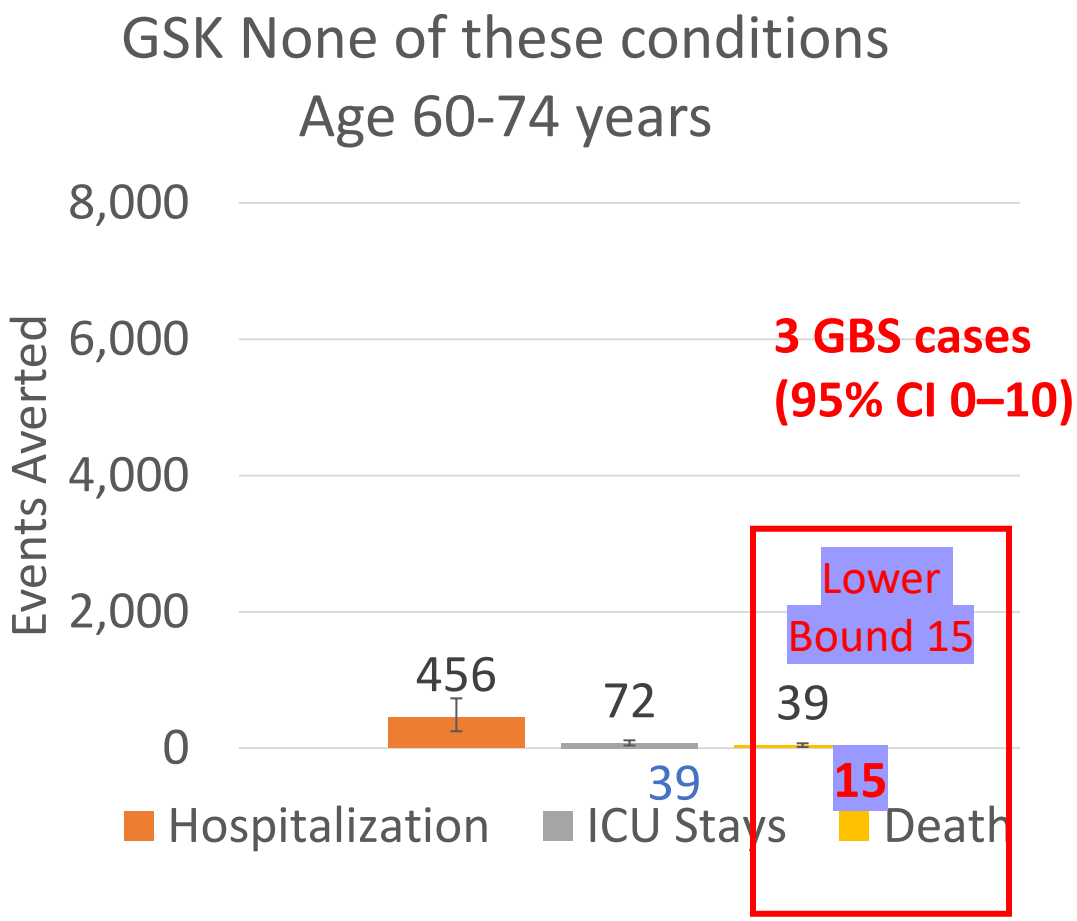




Lower Bound:

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*





*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).

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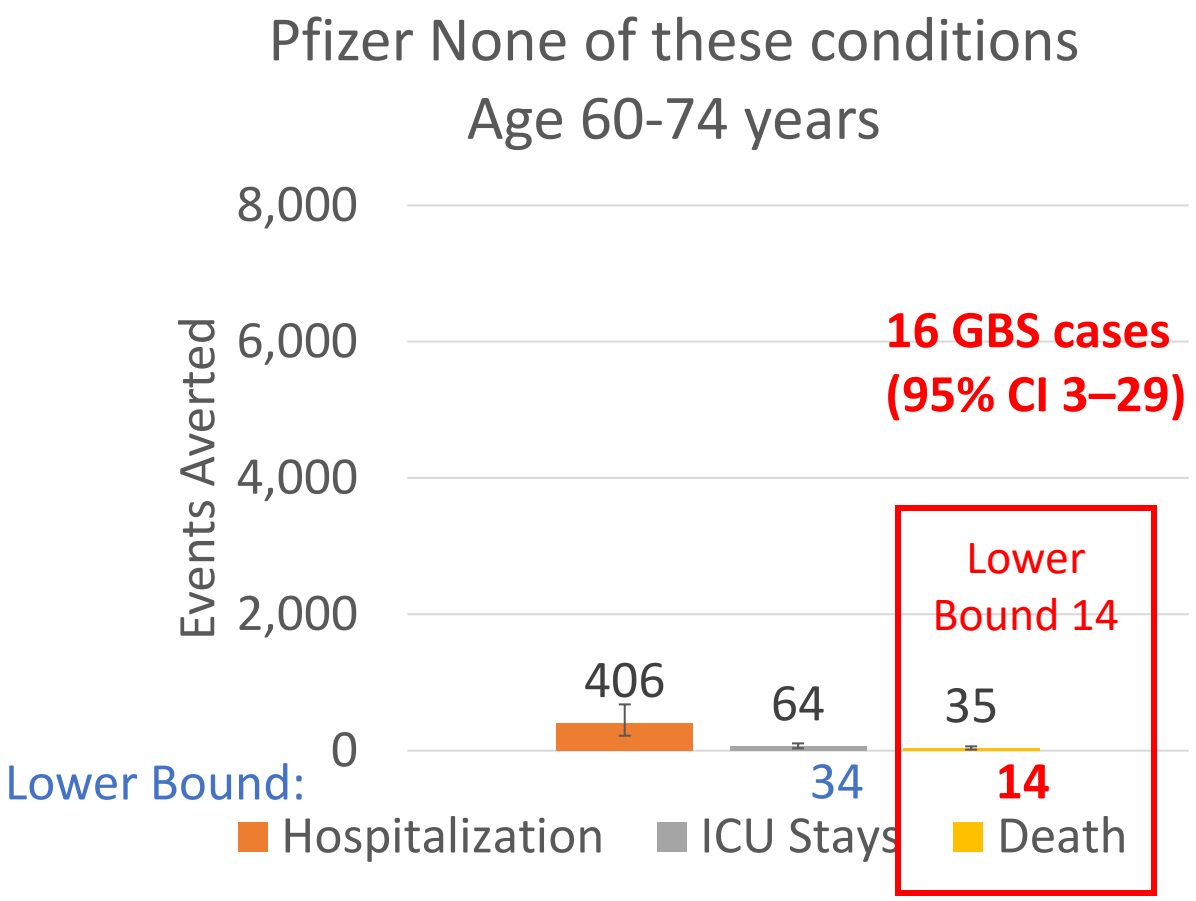
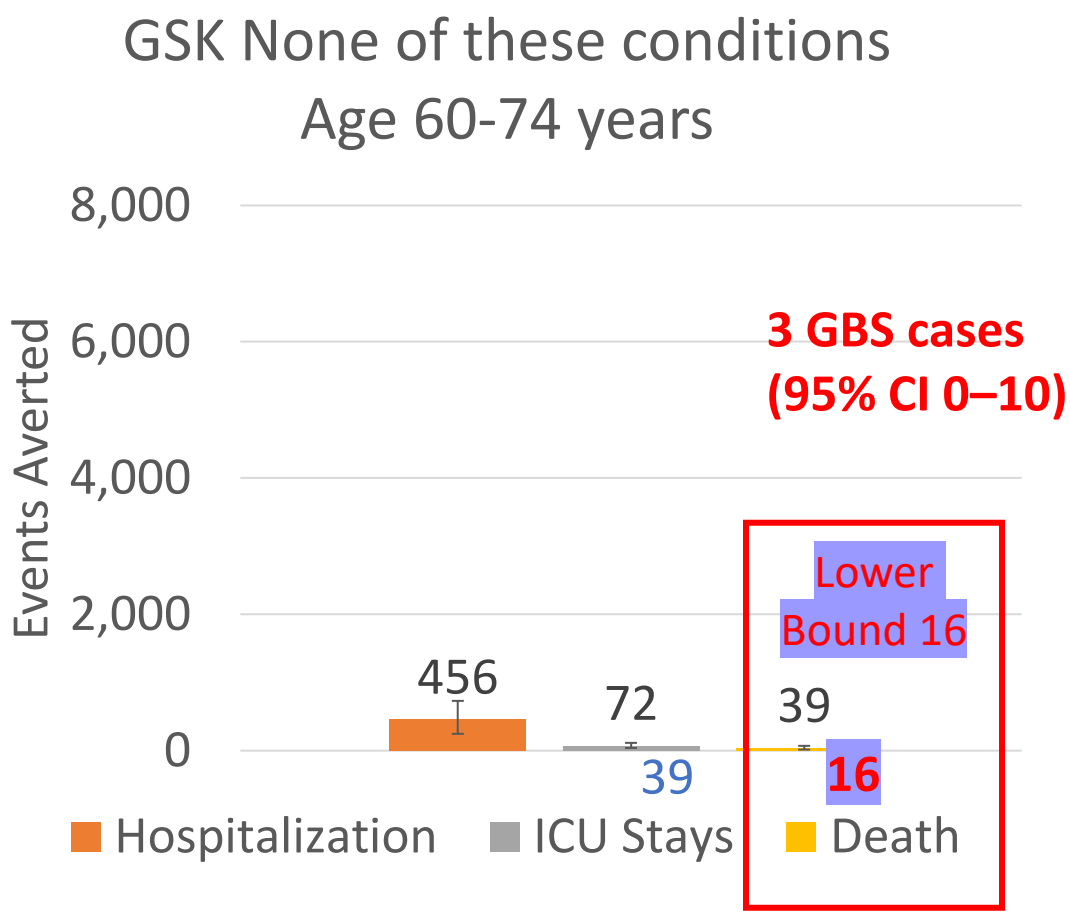
Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in **adults 60-74 years with** none of these conditions*





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

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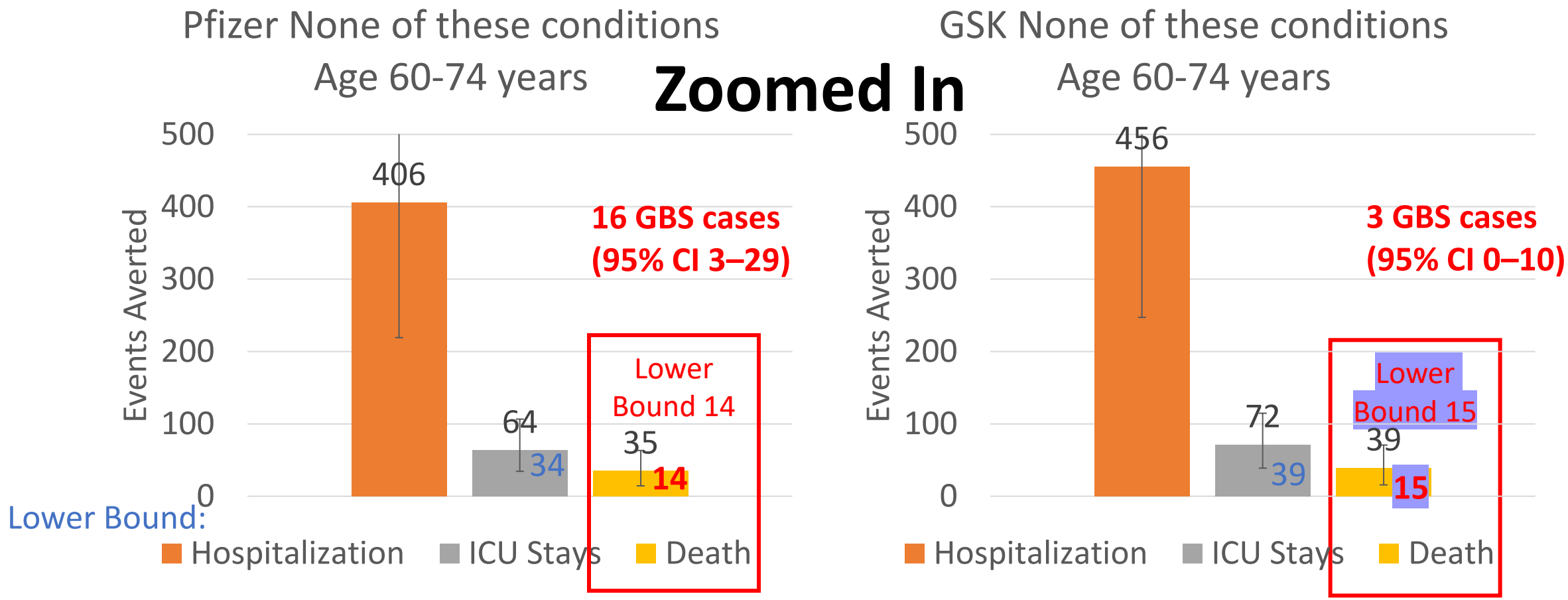
Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in **adults 60-74 years** with none of these conditions*



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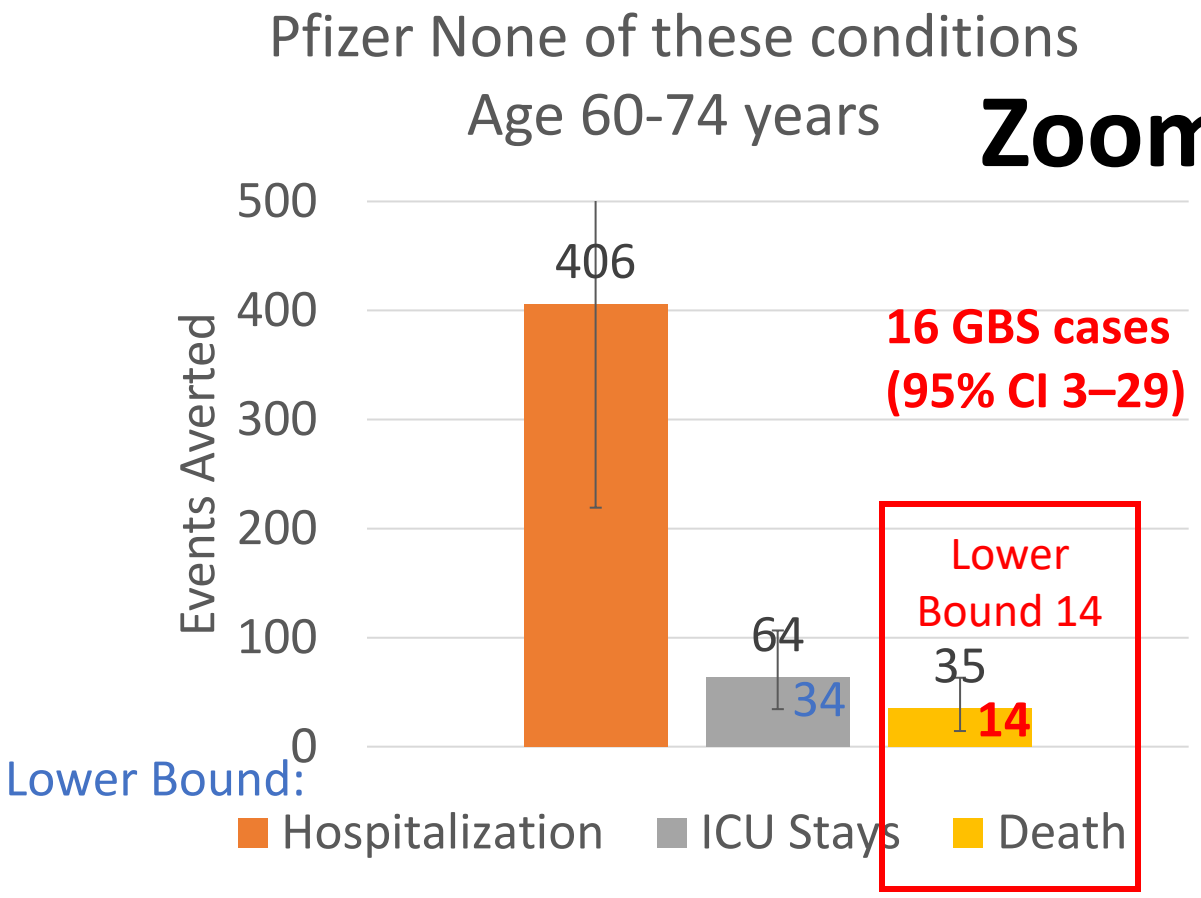
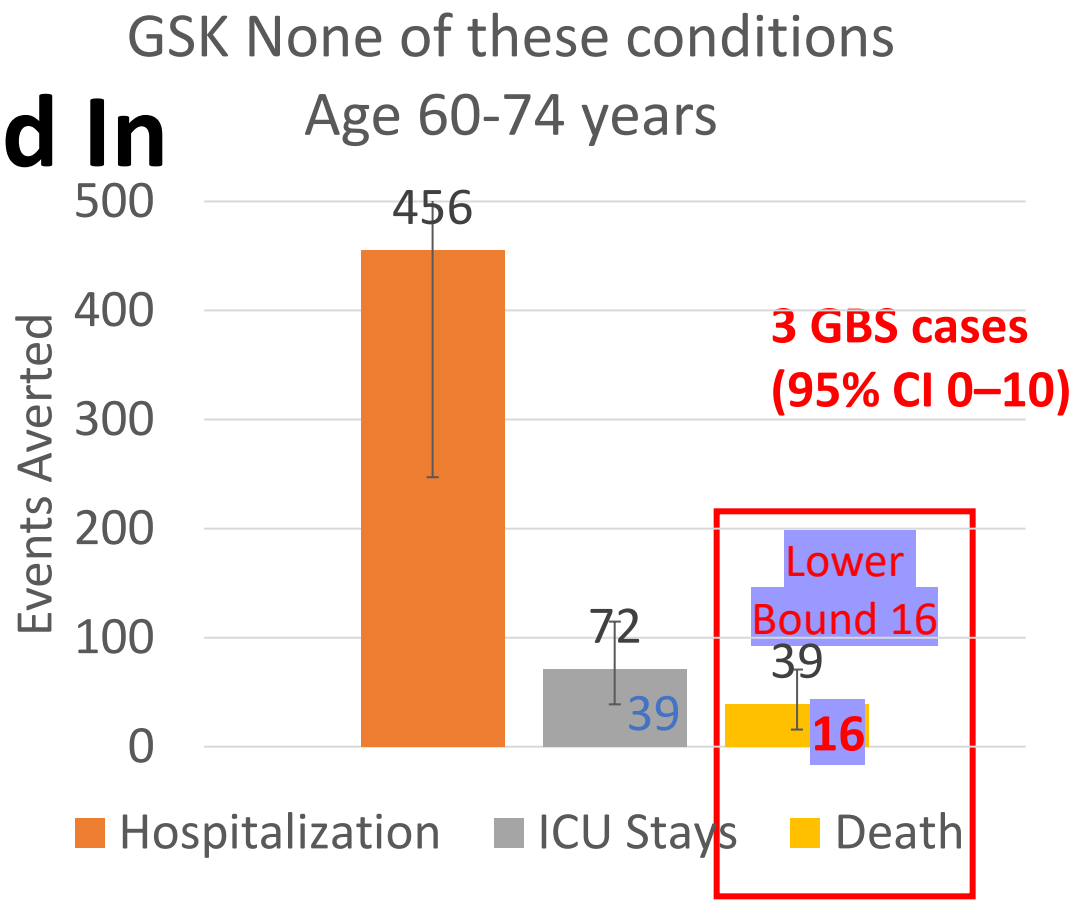
Estimated RSV-associated outcomes avertable over 2 RSV seasons vs. potential cases of GBS per 1 million vaccine doses in **adults 60-74 years** with none of these conditions*

Zoomed In





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