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 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 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

- **No Vaccination**
  - RSV Infection
    - Hospitalization
    - Alive
    - Dead
    - ED
    - Outpatient
    - None of the above
  - Adverse Events
    - Guillain Barre Syndrome
    - No Guillain Barre Syndrome

- **Vaccination**
  - RSV Infection
    - Infection

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- **RSV Infection**
  - Alive
  - Dead
  - ED
  - Outpatient
  - None of the above

- **Guillain Barre Syndrome**
  - No Guillain Barre Syndrome

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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\textsuperscript{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**.
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**

- Hospitalization: 3,817
- ICU Stays: 561
- Death: 539

**GSK All Adults Age ≥75**

- Hospitalization: 4,283
- ICU Stays: 630
- Death: 605

Lower Bound:

- 16 GBS cases (95% CI 3–29)
- 3 GBS cases (95% CI 0–10)
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*

*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).
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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*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*

*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.

16 GBS cases (95% CI 3–29)

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

Immune Compromise is not age-stratified
Estimated RSV-associated deaths *avertable* over 2 RSV seasons vs. potential cases of GBS per 1 million Pfizer ABRYSGO doses in adults *60-74 years* with specific chronic conditions.
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**

Lower Bound:

- **Heart Failure**: 278
- **COPD**: 133
- **Asthma**: 42
- **CAD**: 95
- **Diabetes**: 31
- **Obesity BMI >40**: 98
- **CKD**: 75
- **Immune Compromise**: 133
- **Lung Transplant**: 439
- **Autologous HCT**: 230

**3 GBS cases**

(95% CI 0–10)

HCT: hematopoietic cell transplant

Lower bound is labeled if <50

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:
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