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

Decision Tree Model:

- **No Vaccination**
  - **Infection**
    - RSV Infection
    - Hospitalization
      - ED
      - Outpatient
      - None of the above
    - Alive
    - Dead

- **Vaccination**
  - **Adverse Events**
    - Guillain Barre Syndrome
    - No Guillain Barre Syndrome
  - RSV Infection

Adverse Events:

- **RSV Infection**
  - Infection
  - Guillain Barre Syndrome
  - No Guillain Barre Syndrome
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.
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

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** *

**Pfizer None of these conditions**
Age 60-74 years

- Hospitalization: 406
- ICU Stays: 64
- Death: 35

- Lower Bound: 14

<table>
<thead>
<tr>
<th>Events Averted</th>
<th>8,000</th>
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<tbody>
<tr>
<td>6,000</td>
<td>16 GBS cases (95% CI 3–29)</td>
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<tr>
<td>4,000</td>
<td>3 GBS cases (95% CI 0–10)</td>
</tr>
<tr>
<td>2,000</td>
<td>3 GBS cases (95% CI 0–10)</td>
</tr>
</tbody>
</table>

**GSK None of these conditions**
Age 60-74 years

- Hospitalization: 456
- ICU Stays: 72
- Death: 39

- Lower Bound: 15

*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
- Hospitalization: 406
- ICU Stays: 64
- Death: 35
- Lower Bound: 14

**GSK**
- None of these conditions
- Age 60-74 years
- Hospitalization: 456
- ICU Stays: 72
- Death: 39
- Lower Bound: 15

Lower Bound:
- 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**

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 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)
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:

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

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