ACIP Adult RSV Work Group Considerations

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ACIP Adult RSV WG Lead

Policy questions being considered by the work group

- Should vaccination with GSK RSVpreF3 vaccine (120 µg antigen + AS01E adjuvant, 1 dose IM) be recommended for all older adults*?

- Should vaccination with Pfizer RSVpreF vaccine (120 µg antigen, 1 dose IM) be recommended for all older adults*?

*Age ≥60 years? Age ≥65 years? Other?
RSV-associated hospitalization rates by adult age group, RSV-NET 2016–2020

RSV-NET: unpublished data. Rates are adjusted for the frequency of RSV testing during recent prior seasons and the sensitivity of RSV diagnostic tests.
Evidence reviewed by the work group includes (but is not limited to):

- Epidemiology and burden of RSV in U.S. adults
  - RSV seasonality
  - Population-based rates of RSV-associated outpatient visits, hospitalizations, and deaths
- RSV virology, immunology
- Safety and efficacy of GSK RSVpreF3
  - Pivotal phase 3 study in adults aged ≥60 years, earlier phase studies
- Safety and efficacy of Pfizer RSVpreF
  - Pivotal phase 3 study in adults aged ≥60 years, earlier phase studies
Work group interpretation of data presented
Both clinical trials showed significant efficacy against lower respiratory tract disease/illness caused by RSV

- Efficacy point estimates against the primary outcomes in both trials exceeded 60%

<table>
<thead>
<tr>
<th>Outcome</th>
<th>GSK Efficacy (%) 96.95% CI</th>
<th>Pfizer Efficacy (%) 95% CI</th>
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<tbody>
<tr>
<td>RSV LRTD&lt;sup&gt;a&lt;/sup&gt;</td>
<td>82.6 (57.9–94.1)</td>
<td>66.7 (32.5–84.8)</td>
</tr>
<tr>
<td>RSV LRTI ≥2 symptoms&lt;sup&gt;b&lt;/sup&gt;</td>
<td>85.7 (37.9–98.4)</td>
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<sup>a</sup> Lower respiratory tract disease: ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign OR ≥3 lower respiratory symptoms for ≥24 hours

<sup>b</sup> Lower respiratory tract illness: ≥2 or ≥3 lower respiratory signs/symptoms lasting more than 1 day
Both clinical trials showed significant efficacy against lower respiratory tract disease/illness caused by RSV

- Efficacy point estimates against the primary outcomes in both trials exceeded 60%
- Based on a small number of total events (<50 in each trial)

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<td>RSV LRTD(^a)</td>
<td>7/12,466</td>
<td>11/16,306</td>
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<tr>
<td></td>
<td>40/12,494</td>
<td>33/16,308</td>
</tr>
<tr>
<td>RSV LRTI ≥2 symptoms(^b)</td>
<td>2/16,306</td>
<td>14/16,308</td>
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\(^a\) Lower respiratory tract disease: ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign OR ≥3 lower respiratory symptoms for ≥24 hours

\(^b\) Lower respiratory tract illness: ≥2 or ≥3 lower respiratory signs/symptoms lasting more than 1 day
Incidence of symptomatic RSV infection was low in both trials

Why?

- Clinical trials may enroll a healthier population, compared with the general U.S. population
- Both trials were conducted during periods of atypical RSV seasonality in the United States, attributable to the COVID-19 pandemic
Monthly RSV-associated hospitalizations among adults aged ≥65 years reported to RSV-NET, 2017–2022

RSV-NET: unpublished data. Data are preliminary and subject to change.
Monthly RSV-associated hospitalizations among adults aged ≥65 years reported to RSV-NET, 2017–2022

RSV-NET: unpublished data. Data are preliminary and subject to change.
Trials were underpowered to estimate efficacy against more severe RSV outcomes (e.g., hospitalization, death)

- There were <5 RSV hospitalizations in each trial, and no RSV-associated deaths
- However, the burden of RSV-associated hospitalizations is high among older adults in the United States
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- However, the burden of RSV-associated hospitalizations is high among older adults in the United States

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<th>95% confidence interval</th>
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<td>2016-17</td>
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CDC unpublished data from RSV-NET (https://www.cdc.gov/rsv/research/rsv-net.html). Note that rates are adjusted for test sensitivity (using 95% for rRT-PCR testing) and undertesting for RSV among patients with acute respiratory illnesses. Data are preliminary and subject to change.

Trials were underpowered to estimate efficacy against more severe RSV outcomes (e.g., hospitalization, death)

- There were <5 RSV hospitalizations in each trial, and no RSV-associated deaths
- However, the burden of RSV-associated hospitalizations is high among older adults in the United States
- Industry-sponsored 2022 meta-analysis* estimated ≥106,165 annual RSV hospitalizations among adults aged ≥65 years

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Estimates for 2018-19 and 2019-20:
Havers et al. Hospitalization rates and outcomes for RSV-associated hospitalizations in adults ≥18 years in the United States during two respiratory seasons, October 2018 - April 2020. Presentation at: 12th International RSV Symposium; 2022 Sep 29 – Oct 2; Belfast, United Kingdom.

Expect efficacy against more severe outcomes to be at least as high as efficacy against lower respiratory tract disease/illness

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<td>RSV acute respiratory illness(^a)</td>
<td>71.7%</td>
<td>RSV acute respiratory illness(^b)</td>
<td>62.1%</td>
</tr>
<tr>
<td>RSV lower respiratory tract disease(^c)</td>
<td>82.6%</td>
<td>RSV lower respiratory tract illness ≥2 symptoms(^d)</td>
<td>66.7%</td>
</tr>
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<td>RSV lower respiratory tract disease with ≥2 lower respiratory signs or assessed as ‘severe’ by investigator</td>
<td>94.1%</td>
<td>RSV lower respiratory tract illness ≥3 symptoms(^d)</td>
<td>85.7%</td>
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\(^a\) Acute respiratory illness: ≥2 respiratory symptoms/signs for ≥24 hours OR ≥1 respiratory symptom/sign +1 systemic sign for ≥24 hours

\(^b\) Acute respiratory illness: ≥1 respiratory symptom lasting more than 1 day

\(^c\) Lower respiratory tract disease: ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign OR ≥3 lower respiratory symptoms for ≥24 hours

\(^d\) Lower respiratory tract illness: ARI with ≥2 or ≥3 lower respiratory signs/symptoms
Efficacy beyond one RSV season is unknown

- Both trials are ongoing, with multiple years of follow up planned
- However, data from only the first year will be available for consideration of the first policy recommendations
- There is no established immunologic correlate of protection for RSV
- Need for revaccination, and the time interval, are yet to be determined
Cases of Guillain Barré syndrome (GBS) were reported after vaccination with both investigational vaccines.

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<td>No cases of GBS observed in main phase 3 trial (N=24,966 participants, 12,467 received investigational vaccine)</td>
<td>2 cases of GBS (1 case Miller-Fisher syndrome) observed in main phase 3 trial (N=34,283 participants, 17,214 received investigational vaccine)</td>
</tr>
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<td>1 case of GBS was reported in a randomized open-label study evaluating safety &amp; long-term immunogenicity of different revaccination schedules (N=1,650 participants)</td>
<td>• Onset 8 and 11 days after receipt of investigational vaccine No cases of GBS observed in any other trials of this investigational vaccine</td>
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<td>• Onset 9 days after receipt of investigational vaccine</td>
<td></td>
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Total: 1 case of GBS / ~15,000 persons who received the investigational vaccine

Total: 2 cases of GBS / ~26,000 persons who received the investigational vaccine
Cases of Guillain Barré syndrome (GBS) were reported after vaccination with both investigational vaccines

- All cases had onset during the 42-day risk window post-vaccination used in CDC surveillance
- The significance of 1–2 cases in safety databases of 15,000–26,000 persons is unclear
- Population-based rates of GBS increase with age\(^a\)
- RSV infection has also been associated with GBS in case reports and case series\(^b,c\), but causal link has not been established
- The work group continues to review and interpret safety evidence


Uptake of a novel RSV vaccine among older adults will depend on patient and clinician education

- Adult immunization schedule is becoming more complex
  - Primary series only: pneumococcal vaccine, recombinant zoster vaccine
  - Revaccination: influenza vaccine, COVID-19 vaccine, Td/Tdap, RSV?
- RSV is likely less well known as a pathogen in adults, compared with influenza and SARS-CoV-2
- Safety and efficacy of coadministration of influenza, COVID-19, and RSV vaccines must be established
Next steps for the work group

- Review GRADE of evidence for GSK RSVpreF3
- Review GRADE of evidence for Pfizer RSVpreF
- Review cost effectiveness analysis (CEA)
- Review Evidence to Recommendations
  - Public health problem, benefits and harms, values and preferences, equity, resource use (cost effectiveness), acceptability, feasibility
- All of these will inform age threshold for an RSV vaccine recommendation
  - Both trials enrolled adults aged ≥60 years
  - There may be other considerations that inform an age threshold for a recommendation
Acknowledgements

Coronavirus and Other Respiratory Viruses Division (proposed)
- Katherine Fleming-Dutra
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- Lauren Roper
- Diya Surie

Immunization Safety Office
- Anne Hause
- Christine Olson
- David Shay
- Tom Shimabukuro
Questions for ACIP

1. Are there additional data needed prior to ACIP voting on recommendations for the use of either of these investigational vaccines in older adults?
2. What additional data would ACIP like to see to determine an age threshold for an adult RSV vaccine recommendation?
3. Other questions from ACIP?
Thank you