RSV Vaccines: Moving on to Recommendations

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Disclosures of Interest

- **Member ACIP RSV Work Group**

Goal

- **“On June 21, 2023, ACIP recommended that adults aged ≥60 years may receive a single dose of RSV vaccine, using shared clinical decision-making”***

- **What was the basis for such a recommendation, given the FDA approval of the vaccine for persons 60 years of age and older?**

*https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm

ACIP Review of Vaccines

- **Specialized work group – made up of ACIP voting members, CDC leads, federal agency ex officio members, liaisons from national specialty organizations, outside consultants**
- **PICO question(s)**
  - **Population(s) – ≥65 years, 60-64 years**
  - **Intervention(s):**
    - **Single IM dose Pfizer bivalent RSVpreF vaccine (120 ug antigen)**
    - **Single IM dose GSK RSVPreF3 vaccins (120 ug antigen plus AS01E adjuvant)**
  - **Comparison – no vaccine**
  - **Outcome – efficacy endpoints, safety endpoints**

Adult RSV Work Group Membership

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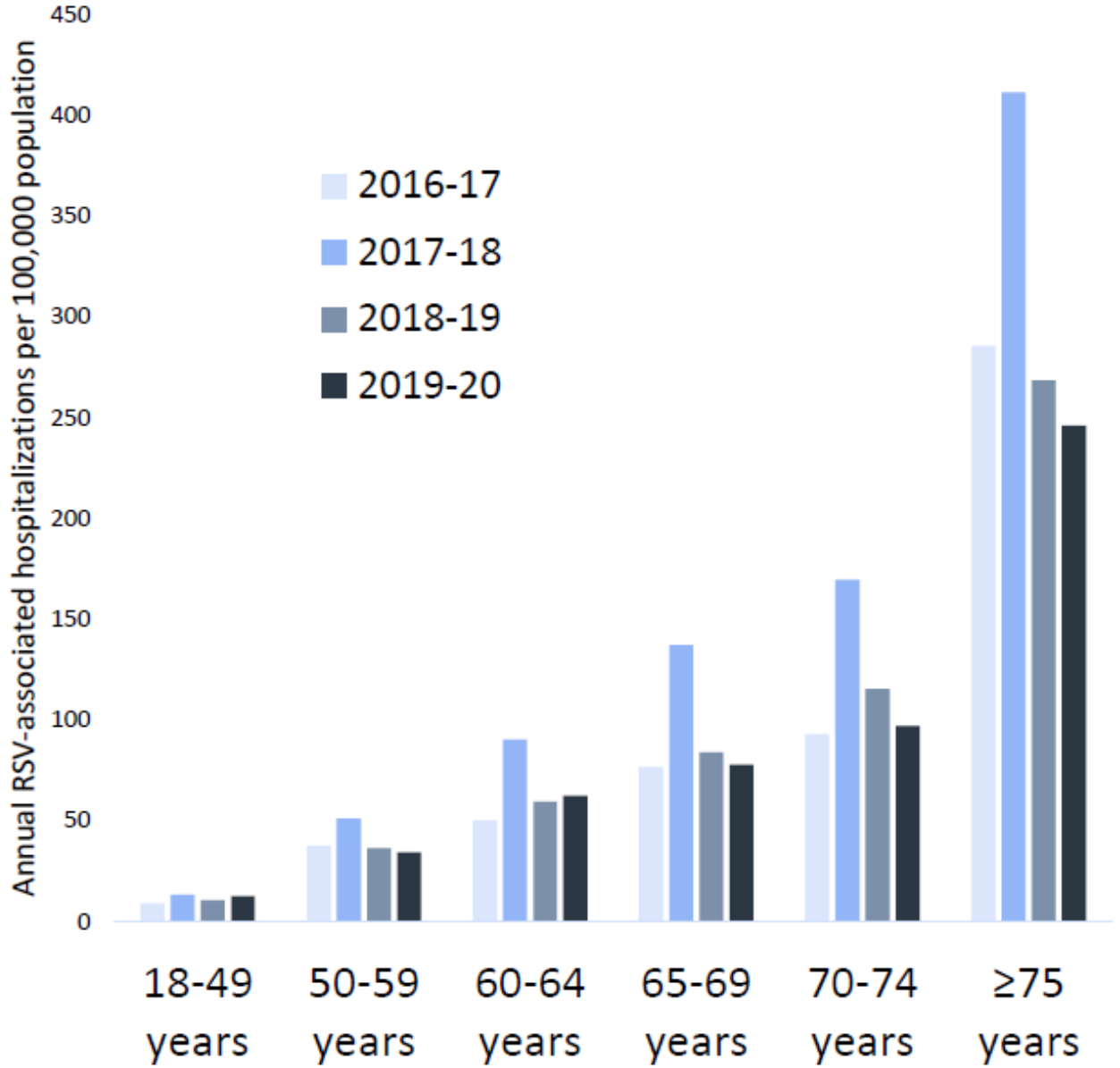
Evidence to Recommendations (EtR) Framework

EtR Domain	Question(s)
Public Health Problem	▪ Is the problem of public health importance?
Benefits and Harms	▪ How substantial are the desirable anticipated effects? ▪ How substantial are the undesirable anticipated effects? ▪ Do the desirable effects outweigh the undesirable effects?
Values	▪ Does the target population feel the desirable effects are large relative to the undesirable effects? ▪ Is there important variability in how patients value the outcome?
Acceptability	▪ Is the intervention acceptable to key stakeholders?
Feasibility	▪ Is the intervention feasible to implement?
Resource Use	▪ Is the intervention a reasonable and efficient allocation of resources?
Equity	▪ What would be in the impact of the intervention on health equity?

GRADE Framework: PICO Question

Population	Persons aged ≥60 years
Intervention	Pfizer bivalent RSVpreF vaccine (120µg antigen, 1 dose IM) **-or-** GSK RSVPreF3 vaccine (120 µg antigen + $AS01_E$ adjuvant, 1 dose IM)
Comparison	No RSV vaccine
Outcomes	▪ RSV lower respiratory tract illness/disease (LRTI/LRTD) ▪ Medically attended RSV LRTI/LRTD ▪ Hospitalization for RSV respiratory illness ▪ Severe RSV respiratory illness requiring supplemental O_2 or other respiratory support ▪ Death due to RSV respiratory illness ▪ Serious Adverse Events (SAEs) ▪ Inflammatory neurologic events (e.g., Guillain-Barré syndrome) ▪ Reactogenicity (grade ≥3)

RSV-NET estimated annual hospitalizations per 100,000 adults, 2016–17 to 2019–20



CDC RSV-NET unpublished data. Estimates are adjusted for under-testing and incomplete test sensitivity. https://www.cdc.gov/rsv/research/rsv-net/index.html

Pfizer, Benefits: vaccine efficacy estimates

Outcome	Importance	Data sources	Vaccine efficacy (%)[a] (95% confidence interval)	Concerns in certainty assessment
Benefits				
RSV Lower Respiratory Tract Illness (LRTI)[b]	Critical	One phase 3 RCT[c], - 10.6 months mean follow up time under surveillance, including partial season 2[d] - 31,986 person-years under surveillance	84.4 (59.6, 95.2) Vaccine: n=5, Placebo: n=32	Indirectness (serious)[e]
Medically attended RSV LRTI[b]	Critical		81.0 (43.5, 95.2) Vaccine: n=4, Placebo: n=21	Indirectness (serious)[e]
Hospitalization for RSV respiratory illness	Important		66.7 (-315, 99.4) Vaccine: n=1, Placebo: n=3	Indirectness (serious)[e] Imprecision (very serious)[f]
Severe RSV respiratory illness requiring O2/respiratory support	Important		0 (-7750, 98.7) Vaccine: n=1, Placebo: n=1	Indirectness (serious)[e] Imprecision (very serious)[f]
Death due to RSV respiratory illness	Important		Vaccine: n=0/16,010 person-years Placebo: n=0/15,976 person-years	Unable to evaluate[g]

Indirectness → underrepresentation of adults ≥75 years of age
Less data evaluating severe outcomes

Pfizer: RSV lower respiratory tract illness (LRTI), defined by ≥3 lower respiratory signs or symptoms

Population	Case split (vaccine/placebo)[a]	Manufacturer-calculated vaccine efficacy, % (95% CI)
All (age ≥60 years)	5/32	84.4 (59.6, 95.2)
Age ≥65 years	3/23	87.0 (56.8, 97.5)
Age ≥70 years	1/11	90.9 (37.5, 99.8)
Age ≥75 years	1/7	85.7 (-11.2, 99.7)[b]
Age ≥80 years	0/4	100.0 (-51.5, 100.0)[b]

Pfizer, Harms: relative risk

Outcome	Importance	Data sources	Relative risk estimate[a] (95% confidence interval)	Concerns in certainty assessment
Harms				
Serious adverse events (SAEs)	Critical	One phase 3 RCT, one phase 1/2 RCT[b]	1.04 (0.94, 1.15) N=36,953 total participants	None serious
Inflammatory neurologic events	Important	One phase 3 RCT[c] one phase 1/2 RCT[c]	Vaccine: n=3/18,622 participants[d] Placebo: n=0/18,335 participants[e]	Imprecision (very serious)[f,g]
Reactogenicity (grade ≥3)	Important	One phase 3 RCT[h] one phase 1/2 RCT[h]	1.43 (0.85, 2.39) N=7,164 total participants	Imprecision (serious)[f]

[a] Pooled relative risk estimates were independently calculated using counts of events and participants in the Pfizer pivotal phase 3 trial (Walsh EE et al. NEJM 2023 https://doi.org/10.1056/nejmoa2213836), as well as from a placebo-controlled phase 1/2 dosing selection study (Falsey AR, et al. J Infect Dis. 2022 https://doi.org/10.1093/infdis/jiab611). Data provided by manufacturer.

[b] After dose 1, but before dose 2 (day 61). RCT = randomized controlled trial.

[c] Within 42 days after injection. RCT = randomized controlled trial.

[d] In the Pfize reported within 42 da after vaccination v phase 1/2 formulation

[e] Measures c

[f] 95% confid

[g] Fragility of

[h] Within 7 days after vaccination. RCT = randomized controlled trial.

Total of **3** inflammatory neurologic events reported within 42 days of vaccination with RSVpreF among approximately **20,000** older adults across all clinical trials

Summary of GRADE for Pfizer RSVpreF vaccine in older adults

Outcome	Importance	Design (# of studies)	Findings	Evidence type
Benefits				
RSV Lower Respiratory Tract Disease (LTRI)	Critical	RCT (1)	Pfizer RSVpreF likely reduces RSV LRTI.	**Moderate**
Medically attended RSV LRTI	Critical	RCT (1)	Pfizer RSVpreF likely reduces medically attended RSV LRTI.	**Moderate**
Hospitalization for RSV respiratory illness	Important	RCT (1)	Pfizer RSVpreF may reduce hospitalization for RSV respiratory illness, but the effect is very uncertain.	**Very low**
Severe RSV respiratory illness requiring O2/respiratory support	Important	RCT (1)	Pfizer RSVpreF may not impact severe RSV respiratory illness requiring supplemental oxygen or other respiratory support, but the effect is very uncertain.	**Very low**
Death due to RSV respiratory illness	Important	RCT (1)	No events observed	Unable to evaluate
Harms				
Serious adverse events	Critical	RCT (2)	Pfizer RSVpreF results in little to no differences in SAEs.	**High**
Inflammatory neurologic events	Important	RCT (2)	Pfizer RSVpreF may increase inflammatory neurologic events.	**Low**
Reactogenicity (grade ≥3)	Important	RCT (2)	Pfizer RSVpreF likely increases severe reactogenicity events.	**Moderate**

ACIP Jun 21, 2023 mtg

Benefits and Harms Pfizer bivalent RSVpreF vaccine

- How substantial are the desirable anticipated effects among adults aged **≥65 years** (relative to no RSV vaccine)?
  - How substantial is the anticipated protective effect against:
    - RSV lower respiratory tract disease (LRTD)
    - Medically attended RSV LRTD
    - Hospitalization for RSV respiratory illness
    - Severe RSV respiratory illness requiring supplemental O2/respiratory support
    - Death due to RSV respiratory illness

Minimal	Small	**Moderate**	Large	Varies	Don't know

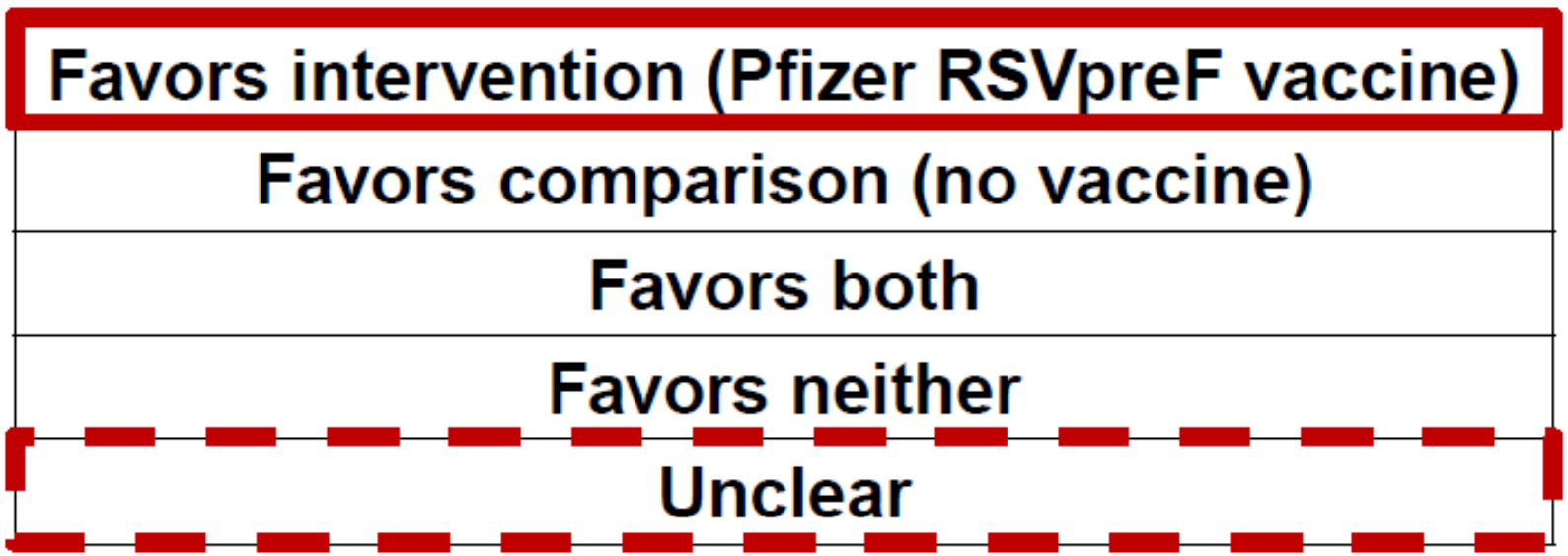
Benefits and Harms Pfizer bivalent RSVpreF vaccine

- How substantial are the undesirable anticipated effects among adults aged **≥65 years** (relative to no RSV vaccine)?
  - How substantial is the anticipated effect on:
    - Serious Adverse Events (SAEs)
    - Inflammatory neuropathy (e.g., Guillain-Barré Syndrome)
    - Reactogenicity (grade ≥3)

Minimal	**Small**	Moderate	Large	Varies	Don't know

Benefits and Harms Pfizer bivalent RSVpreF vaccine

- Do the desirable effects outweigh the undesirable effects among adults aged **≥65 years**?
  - What is the balance between the desirable effects relative to the undesirable effects?



Minority opinion

Work group considerations

- RSV vaccination for older adults **could** be a cost-effective intervention
- There is substantial uncertainty in the net societal costs of an RSV vaccination program for older adults, driven by:
  - **Uncertainty in vaccine acquisition cost**
    - Current assumptions: $200 Pfizer RSVpreF, $270 GSK RSVPreF3
  - Uncertainty in incidence of RSV illness (e.g., hospitalization)
  - Uncertainty in duration of protection from RSV vaccination
    - Current assumption: 2 RSV seasons
- Vaccination of older age groups would be more cost effective than vaccination of younger age groups

Other Considerations

- Resource Use – reasonable and efficient use of resources
  - ≥65 years – probably yes
  - 60-64 – probably no

- Equity – greater prevalence of chronic medical conditions in Black, non-Hispanic and median age of RSV-associated hospitalization lower in this group (60 years of age vs 65 in Hispanic and 73 in white, NH)
  - Lower equity if recommendation restricted to ≥65 yo

Shared clinical decision-making

- One policy option that the Work Group discussed to address the varied risk of severe RSV disease (e.g., hospitalization) among 60–64 year-olds is shared clinical decision-making (SCDM) for adults aged 60–64 years.
- Ideally, this would allow adults aged 60–64 years at high risk of RSV hospitalization to be vaccinated and decrease age-based racial and ethnic health disparities.
- Prior experience with SCDM can inform the expected impact on equity.

In studies assessing knowledge, attitude, and practices around SCDM for other vaccines, providers have reported mixed views and understanding of recommendations

- Some in favor of SCDM recommendations because they give more flexibility in decisions about use of a vaccine[1]

- Some think that SCDM requires more time than routine recommendations, that SCDM creates confusion, and many do not know vaccines recommended for SCDM would be covered by most health insurance[1,2]
- Providers unsure of what points to emphasize in discussions with patients[2]

Evidence to Recommendations Framework

Summary: Work Group Interpretations (Pfizer RSVpreF, GSK RSVPreF3)

Type of recommendation, adults aged ≥65 years

We do not recommend the intervention

We recommend the intervention for individuals based on shared clinical decision-making

We recommend the intervention

Type of recommendation, adults aged 60–64 years

We do not recommend the intervention

We recommend the intervention for individuals based on shared clinical decision-making

We recommend the intervention

Minority opinion

ACIP Discussion

- **Concerns about outright recommendation and different age thresholds**
  - **Lack of data in highest risk groups – older adults, frail adults, adults with multiple co-morbidities**
  - **Unknown significance of neuroinflammatory diseases (GBS-like) in recipients of both vaccines**
  - **Concerns of equity if restricted by age to decrease potential benefits to some demographics**
  - **Lack of thorough consideration of other approaches, e.g., risk-based assessment**

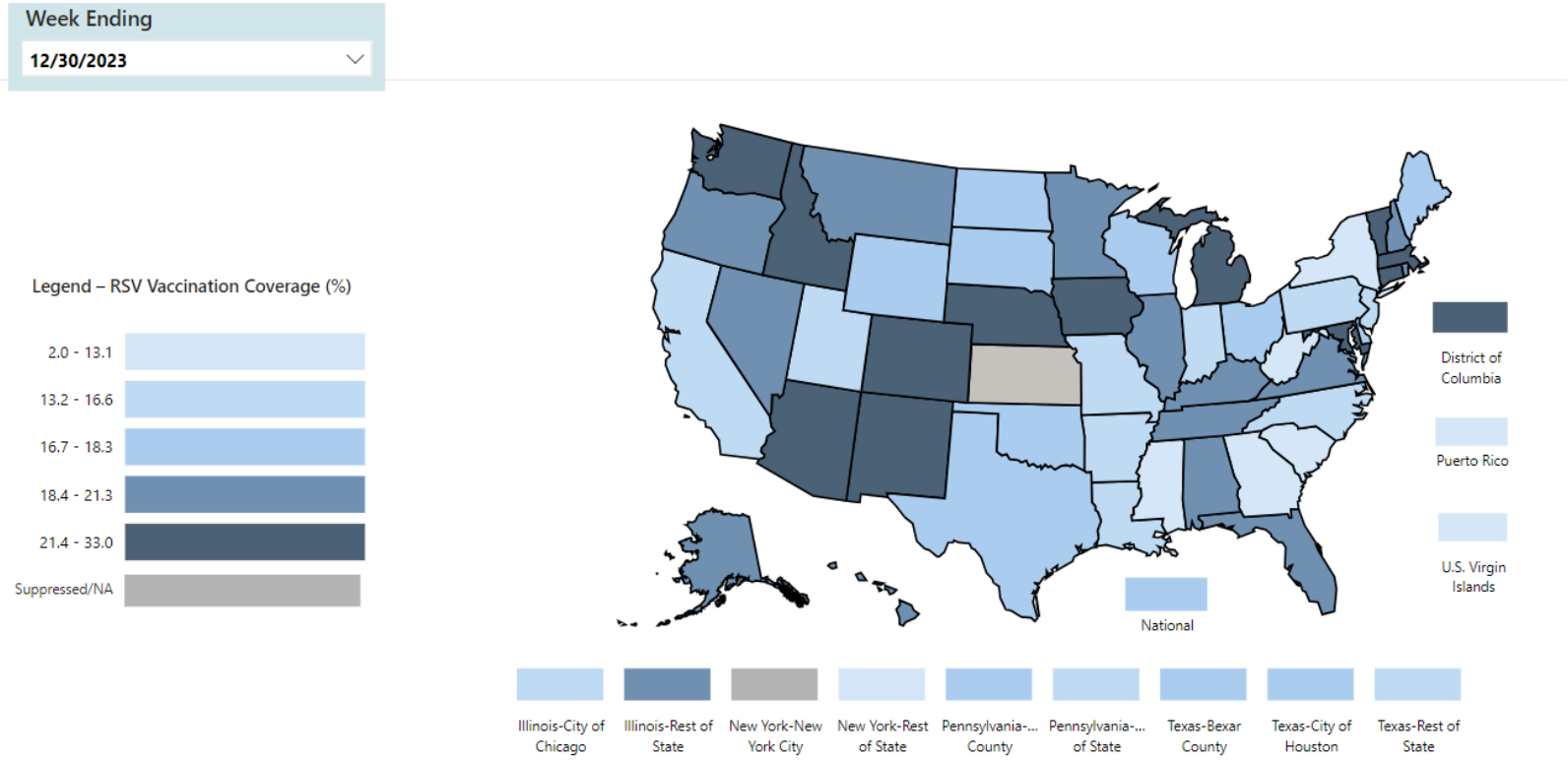
Decisions

- **Make vaccine available using shared clinical decision making**
  - **Allows use in persons potentially at greatest risk**
  - **Can monitor vaccine effectiveness**
  - **Can assess vaccine safety**

- **Reassess recommendations as new data become available and new vaccines are considered**

Where are we now?

- As of Dec 30, ~17.7% of persons 60+ yo vaccinated (7.61 million doses by Dec 16, 2023)
  - 60-69 yo → 13.1%
  - 70-79 yo → 23.0%
  - ≥ 80 yo → 21.3%
- By race/ethnicity:
  - White, NH → 20.1%
  - Black, NH → 11.8%
  - Asian, NH → 15.3%
  - Hispanic → 8.8%



https://www.cdc.gov/vaccines/imz-managers/coverage/rsvvaxview/index.html

Expectations as to what’s next?