Evidence to Recommendations Framework

Respiratory Syncytial Virus (RSV) in Adults

Pfizer bivalent RSVpreF vaccine in older adults
GSK adjuvanted RSVPreF3 vaccine in older adults

Michael Melgar, MD
Amadea Britton, MD

Advisory Committee on Immunization Practices

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Evidence to Recommendations (EtR) Framework
Policy Questions

- Should a single dose of Pfizer bivalent RSVpreF vaccine (120µg antigen, 1 dose IM), rather than no vaccine, be recommended in persons aged ≥65 years?
- Should a single dose of Pfizer bivalent RSVpreF vaccine (120µg antigen, 1 dose IM), rather than no vaccine, be recommended in persons aged 60–64 years?

- Should a single dose of GSK RSVPreF3 vaccine (120µg antigen + $AS01_E$ adjuvant, 1 dose IM), rather than no vaccine, be recommended in persons aged ≥65 years?
- Should a single dose of GSK RSVPreF3 vaccine (120µg antigen + $AS01_E$ adjuvant, 1 dose IM), rather than no vaccine, be recommended in persons aged 60–64 years?

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?

Evidence to Recommendations (EtR) Framework

EtR Domain
Public Health Problem
Benefits and Harms
Values
Acceptability
Feasibility
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Equity

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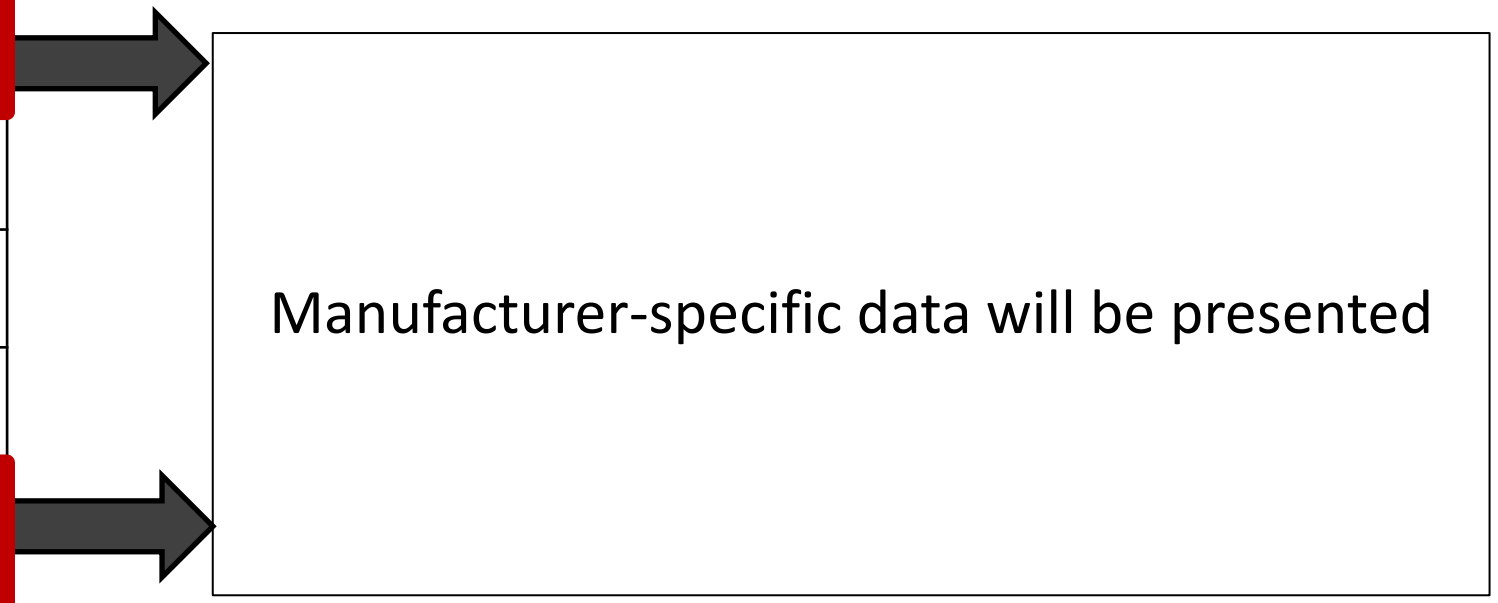

Evidence to Recommendations (EtR) Framework

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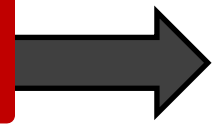

Use of RSV vaccines broadly will be presented

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?

Benefits and Harms

- Pfizer bivalent RSVpreF vaccine
  - Grading of Recommendations, Assessment, Development and Evaluation (**GRADE**) Summary
  - Modeling potential number of RSV-attributable illnesses prevented
- GSK adjuvanted RSVPreF3 vaccine
  - **GRADE** Summary
  - Modeling potential number of RSV-attributable illnesses prevented

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)

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Case definitions of lower respiratory tract illness/disease were not aligned across clinical trials

- ***Pfizer***
- RSV LRTI with ≥2 lower respiratory signs/symptoms (co-primary outcome)
- RSV LRTI with ≥3 lower respiratory signs/symptoms (co-primary outcome)

- Lower respiratory signs/symptoms:
  - Sputum, cough, shortness of breath, wheezing, tachypnea

- ***GSK***
- RSV LRTD (primary outcome)
  - ≥2 lower respiratory **symptoms** or **signs**, including ≥1 **sign**, OR
  - ≥3 lower respiratory **symptoms**

- Lower respiratory **symptoms**:
  - Sputum, cough, dyspnea
- Lower respiratory **signs**:
  - Wheezing, crackles/rhonchi, tachypnea, hypoxemia, O_2 supplementation

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GRADE: Pfizer bivalent RSVpreF

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]

[a] Efficacy estimates were independently calculated using counts of events and total person-time available from the Pfizer pivotal phase 3 trial. Data provided by manufacturer. Efficacy was calculated as 1 – incidence rate ratio. Events of each outcome were included if they occurred on or after day 15 after injection. Manufacturer used the same methodology to calculate efficacy estimates.

[b] Pfizer pivotal phase 3 trial included co-primary outcomes of LRTI with ≥2 lower respiratory signs or symptoms, and LRTI with ≥3 lower respiratory signs or symptoms. In GRADE, the outcome of LRTI with ≥3 lower respiratory signs or symptoms was used.

[c] RCT = randomized controlled trial. Walsh EE, et al. Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults. 2023. NEJM. https://doi.org/10.1056/nejmoa2213836

[d] Mean time from vaccination to end of efficacy follow up, including a gap in RSV surveillance, was 12 months per participant. Among participants who contributed to partial Season 2, this was 13.9 months per participant.

[e] Underrepresentation of adults aged ≥75 years and adults with congestive heart failure. Exclusion of adults with immune compromise.

[f] 95% confidence interval for measure of absolute risk included potential for both benefit and harm. Fragility of estimates.

[g] No RSV-associated deaths were recorded.

Pfizer, Benefits: vaccine efficacy estimates

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[g] No RSV-associated deaths were recorded.

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]

[a] Pfizer pivotal phase 3 trial (Walsh EE, et al. NEJM 2023 https://doi.org/10.1056/nejmoa2213836). Events of each outcome were included if they occurred on or after day 15 after injection. Average time, across participants, from vaccination to end of efficacy follow up was 12 months, including unpublished data provided by manufacturer from partial season 2. Total 36,127 participants (31,986 person-years) under surveillance.

[b] Highlighted text indicates that evidence of statistically significant efficacy is lacking.

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)
≥1 pre-existing comorbidity of interest[b]	4/20	80.0 (40.3, 95.0)
≥1 pre-existing cardiorespiratory comorbidity[c]	3/11	72.7 (-3.2, 95.1)[d]
Adults who are frail	Not assessed[d]	

[a] Pfizer pivotal phase 3 trial (Walsh EE, et al. NEJM 2023 https://doi.org/10.1056/nejmoa2213836). Events of each outcome were included if they occurred on or after day 15 after injection. Average time, across participants, from vaccination to end of efficacy follow up was 12 months, including unpublished data provided by manufacturer from partial season 2. Total 36,127 participants (31,986 person-years) under surveillance.

[b] COPD, asthma, diabetes mellitus, congestive heart failure, liver or renal disease

[c] COPD, asthma, congestive heart failure

[d] Highlighted text indicates that evidence of statistically significant efficacy is lacking.

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 Pfizer pivotal phase 3 trial, 2 events of Guillain-Barré syndrome (GBS) and 1 event of motor-sensory axonal polyneuropathy were reported within 42 days after vaccination with RSVpreF, compared with zero in the placebo arm. One additional case of GBS was reported 8 months after vaccination with RSVpreF and one additional case of GBS was reported 14 months after placebo receipt. No events were recorded in the phase 1/2 formulation selection study.
[e] Measures of relative and absolute risk were not calculated due to zero events within 42 days in placebo recipients.
[f] 95% confidence interval for measure of absolute risk included potential for both benefit and harm.
[g] Fragility of estimate.
[h] Within 7 days after vaccination. RCT = randomized controlled trial.

Pfizer, Harms: relative risk

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Total of **3** inflammatory neurologic events reported within 42 days of vaccination with RSVpreF among **20,255** older adults across all clinical trials

Pfizer: Total inflammatory neurologic events reported within 42 days of vaccination across all clinical trials

Participant age	Country	Reported as	Onset	Trial	Work group case review
66 years	United States	GBS[a], Brighton Collaboration[b] level 1	14 days post-vaccination	Pivotal phase 3 trial, randomized, blinded, placebo-controlled	Clinical course more consistent with CIDP[c]
66 years	Japan	GBS[a], Miller-Fisher variant, Brighton Collaboration[b] level 4	10 days post-vaccination	Pivotal phase 3 trial, randomized, blinded, placebo-controlled	Possible GBS (Miller Fisher syndrome) though other causes are also possible
68 years	Argentina	Motor-sensory axonal polyneuropathy* *Site investigator reported as not associated with vaccination	21 days post-vaccination* *Participant reported some symptoms preceded vaccination	Pivotal phase 3 trial, randomized, blinded, placebo-controlled	Undifferentiated motor-sensory axonal polyneuropathy

[a] GBS = Guillain Barre syndrome

[b] https://brightoncollaboration.us/guillain-barre-and-miller-fisher-syndromes-case-definition-companion-guide/

[c] CIDP = chronic inflammatory demyelinating polyneuropathy

Background incidence of Guillain-Barré syndrome among older adults

Meta-analysis[a], 13 studies, North America & Europe

Age group, years	Annual rate per 100,000 population (95% CI)
0–9	0.62 (0.52–0.75)
10–19	0.75 (0.60–0.92)
20–29	0.90 (0.67–1.19)
30–39	1.07 (0.74–1.56)
40–49	1.29 (0.80–2.06)
50–59	1.54 (0.87–2.74)
60–69	1.85 (0.94–3.64)
70–79	2.22 (1.01–4.86)
80–89	2.66 (1.09–6.48)

Vaccine Safety Datalink, United States, 2000–2009[b]

Age group, years	Annual rate per 100,000 population (95% CI)	
	Female	Male
0–4	0.51 (0.24–0.78)	0.39 (0.16–0.61)
5–17	0.43 (0.29–0.57)	0.62 (0.46–0.79)
18–24	0.64 (0.39–0.89)	0.75 (0.47–1.03)
25–49	1.00 (0.85–1.15)	1.39 (1.20–1.57)
50–64	2.19 (1.90–2.50)	2.85 (2.49–3.21)
≥65	4.68 (4.14–5.21)	7.06 (6.31–7.81)

[a] Sejvar JJ, et al. Population incidence of Guillain-Barré syndrome: a systematic review and meta-analysis. Neuroepidemiology. 2011;36(2):123-33. https://doi.org/10.1159/000324710

[b] Shui IM, et al. Guillain-Barré syndrome incidence in a large United States cohort (2000-2009). Neuroepidemiology. 2012;39(2):109-15. https://doi.org/10.1159/000339248

Estimated incidence of Guillain-Barre syndrome (GBS) following other recommended vaccinations

- **Seasonal influenza vaccines**[a]: The data on the association between GBS and seasonal flu vaccination are variable and inconsistent across flu seasons. If there is an increased risk of GBS following flu vaccination it is small, on the order of **1–2 additional cases per million doses** of flu vaccine administered.
- **Recombinant zoster vaccine**[b]: **3 excess cases per million doses** administered
  - 6 excess cases per million *first doses* administered, no increased risk following the second dose

a https://www.cdc.gov/flu/prevent/guillainbarre.htm#how1
b https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/fda-requires-warning-about-guillain-barre-syndrome-gbs-be-included-prescribing-information-shingrix

Summary of GRADE for Pfizer RSVpreF vaccine in older adults

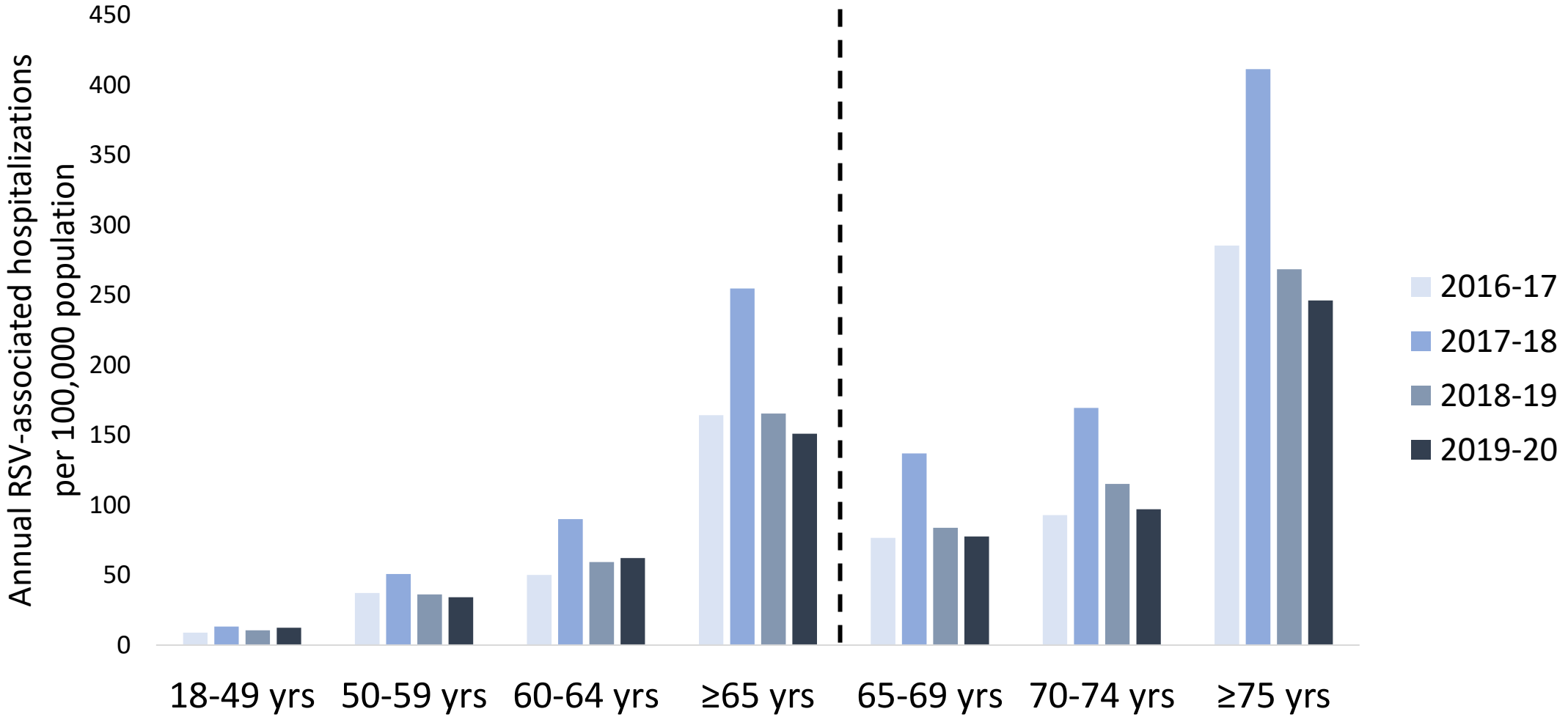
Outcome	Importance	Design (# of studies)	Findings	Evidence type
Benefits				
RSV Lower Respiratory Tract Disease (LTRI)	Critical	RCT (1)	Pfizer RSVpreF likely reduces RSV LRTI.	**Moderate**
Medically attended RSV LRTI	Critical	RCT (1)	Pfizer RSVpreF likely reduces medically attended RSV LRTI.	**Moderate**
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**

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**

Overall evidence rating: Moderate certainty

RSV-NET estimated annual hospitalizations per 100,000 adults: 2016–2017 to 2019–2020



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

Modeling potential RSV-attributable illnesses prevented: Pfizer RSVpreF

- Included in economic analysis performed by U. Michigan, using published incidence estimates and RSV-NET estimated annual hospitalizations per 100,000 adults
- Timeframe: 2 RSV seasons (assumed duration of vaccine protection)

	Number prevented per 1 million vaccinations among: **Adults aged ≥65 years**	Number prevented per 1 million vaccinations among: **Adults aged 60–64 years**
Outpatient visits[a]	25,000	19,000
Hospitalizations[b]	2,500	960
Deaths[c]	130	37

[a] Incidence rates of RSV illness requiring outpatient visit taken from McLaughlin et al, OFID (2022). Vaccine efficacy (VE) against this outcome assumed to be equal to that against medically attended acute respiratory illness (ARI) caused by RSV (Pfizer RENOIR trial, including unpublished data from partial season 2 follow up).
[b] Incidence rates of RSV hospitalization taken from RSV-NET 2016–2020 (unpublished). VE against RSV-associated hospitalization assumed to be equal to that against medically attended lower respiratory tract illness (LRTI) with ≥3 symptoms, caused by RSV (Pfizer RENOIR trial, unpublished).
[c] Probability of in-hospital death among adults hospitalized for RSV taken from RSV-NET 2016–2020 (unpublished). VE against RSV-associated death assumed to be equal to that against medically attended lower respiratory tract illness (LRTI) with ≥3 symptoms, caused by RSV (Pfizer RENOIR trial, unpublished).

Pfizer, post-marketing safety requirements and commitments

Study	Aim	Design	Final protocol submission to FDA	Study completion date
C3671031[a]	Evaluate risk of GBS	Retrospective cohort, claims-based	November 30, 2023	May 31, 2029
C3671037	Evaluate risk of atrial fibrillation[b]	Active surveillance study	November 30, 2023	February 28, 2027
C3671013 (main phase 3 trial)	Evaluate safety and immunogenicity of revaccination	Clinical trial	Submitted	March 31, 2025

a Post-marketing requirement under Section 505(o) of the Federal Food, Drug, and Cosmetic Act
b A numerical imbalance in events of atrial fibrillation was noted in the main phase 3 trial, with 10 events in the RSVpreF group and 4 events in the placebo group, within 1 month following vaccination.
Vaccines and Related Biological Products Advisory Committee February 28 - March 1, 2023 Meeting Briefing Document- FDA: Applicant Pfizer

May 31, 2023 Approval Letter - ABRYSVO (fda.gov)

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

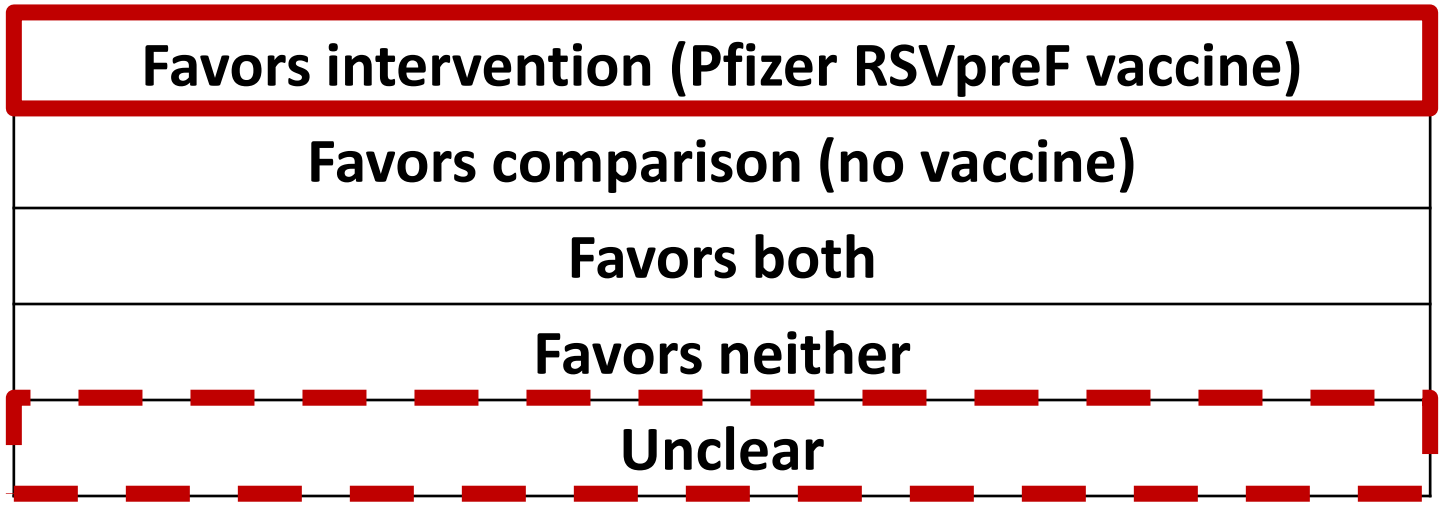
Benefits and Harms Pfizer bivalent RSVpreF vaccine

- 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

Benefits and Harms Pfizer bivalent RSVpreF vaccine

- How substantial are the desirable anticipated effects among adults aged **60–64 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

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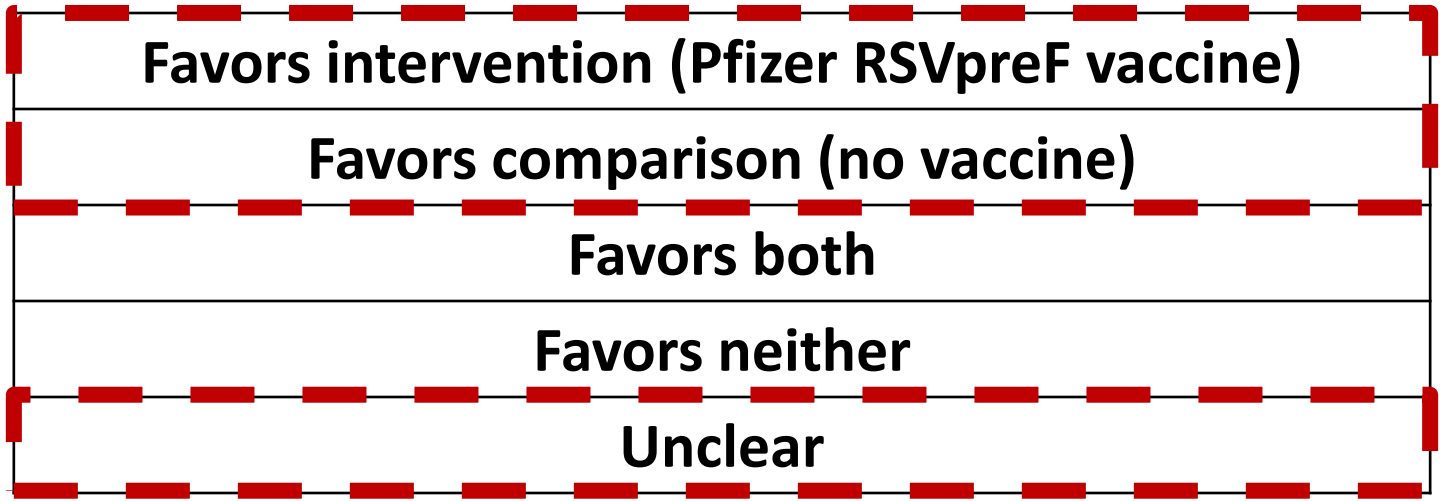
Benefits and Harms Pfizer bivalent RSVpreF vaccine

- Do the desirable effects outweigh the undesirable effects among adults aged **60–64 years**?
  - What is the balance between the desirable effects relative to the undesirable effects?



Minority opinion

GRADE: GSK adjuvanted RSVPreF3

GSK, Benefits: vaccine efficacy estimates

Outcome	Importance	Data sources	Vaccine efficacy of a single dose (%)[a] (95% confidence interval)	Concerns in certainty assessment
Benefits				
RSV Lower Respiratory Tract Disease (LTRD)	Critical	One phase 3 RCT[b], - 15.3 months mean follow up time, including season 2[c] - 31,932 – 32,023 person-years under surveillance, varied by outcome	74.6 (62.1, 83.5) Vaccine: n=30, Placebo: n=139	Indirectness (serious)[d]
Medically attended RSV LRTD	Critical		77.5 (57.9, 89.0) Vaccine: n=12, Placebo: n=63	Indirectness (serious)[d]
Hospitalization for RSV respiratory illness	Important		76.4 (-111, 99.5) Vaccine: n=1, Placebo: n=5	Indirectness (serious)[d] Imprecision (very serious)[e]
Severe RSV respiratory illness requiring O2/respiratory support	Important		76.4 (-111, 99.5) Vaccine: n=1, Placebo: n=5	Indirectness (serious)[d] Imprecision (very serious)[e]
Death due to RSV respiratory illness	Important		Vaccine: n=0/14,677 person-years Placebo: n=0/17,346 person-years	Unable to evaluate[f]

[a] Efficacy estimates were independently calculated using counts of events and total person-time available from the GSK pivotal phase 3 trial. Data provided by manufacturer. Efficacy was calculated as 1 – incidence rate ratio. Events of each outcome were included if they occurred on or after day 15 after injection. Due to exclusion of follow up time after RSVPreF3 dose 2 among participants randomized to annual re-vaccination, person-time in the placebo arm exceeded that in the intervention arm. CDC method of efficacy estimation differed from manufacturer method (Poisson model adjusted by season, participant age, & region). Adjustment by season resulted in substantially different estimates.

[b] RCT = randomized controlled trial. Papi A, et al. Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults. 2023. NEJM. https://doi.org/10.1056/nejmoa2209604

[c] Mean efficacy follow up time inclusive of person-time after dose 2 of RSVPreF3 was 16.6 months. Median time of efficacy follow up was 17.8 months.

[d] Underrepresentation of adults aged ≥75 years, adults with congestive heart failure, and frail adults. Exclusion of adults with immune compromise.

[e] 95% confidence interval for measure of absolute risk included potential for both benefit and harm. Fragility of estimates.

[f] No RSV-associated deaths were recorded.

GSK, Benefits: vaccine efficacy estimates

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[f] No RSV-associated deaths were recorded.

GSK: RSV lower respiratory tract disease (LRTD)

Age group in years	Case split (vaccine/placebo)[a]	Manufacturer-calculated vaccine efficacy[b], % (CI)	
		No adjustment by season	Adjusted by season
≥60 (all)	30/139	74.5 (60.0, 84.5)	67.2 (48.2, 80.0)
≥65	25/100	70.3 (53.5, 81.6)	61.2 (39.0, 76.1)
≥70	13/65	76.4 (56.7, 88.1)	69.3 (43.4, 84.6)
≥75	8/24	Not shared[c]	49.3 (-18.2, 80.6)[c]
≥80	4/10	52.6 (-64.2, 89.2)[c]	38.4 (-118, 86.1)[c]

[a] GSK pivotal phase 3 trial (Papi A, et al. NEJM 2023 https://doi.org/10.1056/nejmoa2209604). Events of each outcome were included if they occurred on or after day 15 after injection. Median time, across participants, of efficacy follow up was 17.8 months, including unpublished data provided by manufacturer from season 2. Total 24,967 participants (31,932 person-years) under surveillance.

[b] Calculated using Poisson model, adjusted by season and participant age and region. Adjustment by season resulted in efficacy estimates substantially different from those estimated by CDC. Due to exclusion of follow up time after dose 2 of RSVPreF3 among participants randomized to annual re-vaccination, person-time follow up in the placebo arm exceeded that in the intervention arm.

[c] Highlighted text indicates that evidence of statistically significant efficacy is lacking.

GSK: RSV lower respiratory tract disease (LRTD)

Population	Case split (vaccine/ placebo)[a]	Manufacturer-calculated vaccine efficacy[b], % (CI)	
		No adjustment by season	Adjusted by season
≥1 pre-existing comorbidity of interest[c]	16/72	74.5 (55.7, 86.1)	66.7 (41.8, 82.0)
≥1 pre-existing cardiorespiratory comorbidity[d]	10/56	80.1 (60.6, 91.0)	73.8 (47.9, 88.2)
Gait speed ≥1.0 m/s (*fit*)	20/89	73.4 (56.5, 84.5)	66.2 (44.3, 80.4)
Gait speed 0.4–0.99 m/s (*pre-frail*)	8/47	80.0 (57.3, 91.8)	73.3 (42.4, 89.2)
Gait speed <0.4 m/s or unable to complete assessment (*frail*)	2/1	-116 (-12,800, 88.9)[e]	-148 (-15,800, 88.2)[e]

[a] GSK pivotal phase 3 trial (Papi A, et al. NEJM 2023 https://doi.org/10.1056/nejmoa2209604). Events of each outcome were included if they occurred on or after day 15 after injection. Median time, across participants, of efficacy follow up was 17.8 months, including unpublished data provided by manufacturer from season 2. Total 24,967 participants (31,932 person-years) under surveillance.

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[c] COPD, asthma, any chronic respiratory/pulmonary disease, diabetes mellitus, chronic heart failure, advanced liver or renal disease

[d] COPD, asthma, any chronic respiratory/pulmonary disease, chronic heart failure

[e] Highlighted text indicates that evidence of statistically significant efficacy is lacking.

GSK, 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[b], one phase 1/2 RCT[c]	1.02 (0.91, 1.15) N=25,174 total participants	None serious
Inflammatory neurologic events	Important	One phase 3 RCT[d] one phase 1/2 RCT[d]	Vaccine: n=0/12,570 participants Placebo: n=0/12,604 participants	Unable to evaluate
Reactogenicity (grade ≥3)	Important	One phase 3 RCT[f] one phase 1/2 RCT[g]	4.06 (1.97, 8.36) N=1,955 total participants	None serious

RCT: Randomized control trial

[a] Pooled relative risk estimates were independently calculated using counts of events and participants in the GSK pivotal phase 3 trial (Papi A, et al. NEJM 2023 https://doi.org/10.1056/nejmoa2209604), as well as from a placebo-controlled phase 1/2 dosing selection study (Leroux-Roels I, et al. J Infect Dis. 2022 https://doi.org/10.1093/infdis/jiac327). Data provided by manufacturer.

[b] Up to 6 months after injection

[c] After dose 1, but before dose 2 (day 61)

[d] Within 42 days after injection

[e] No events recorded in studies included in GRADE. One event of Guillain-Barré syndrome (GBS) reported within 42 days after vaccination in a recipient of the investigational vaccine in an open label trial without a placebo arm. This study was not included in GRADE assessment due to lack of an unvaccinated comparator. Two events of acute disseminated encephalomyelitis (ADEM) reported in a co-administration study of the investigational vaccine with standard dose seasonal influenza vaccine. Both cases were reported in the co-administration arm within 42 days after the intervention; none in the sequential administration control arm. This study was not included in GRADE assessment due to lack of an unvaccinated comparator.

[f] Within 7 days after vaccination

[g] Within 4 days after vaccination

GSK, Harms: relative risk

Outcome	Importance	Data sources	Relative risk estimate[a] (95% confidence interval)	Concerns in certainty assessment
Harms				
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Total of **3** inflammatory neurologic events reported within 42 days of vaccination with RSVpreF3 among **17,922** older adults across all clinical trials

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GSK: Total inflammatory neurologic events reported within 42 days of vaccination across all clinical trials

Participant age	Country	Reported as	Onset	Trial	Work group case review
78 years	Japan	GBS[a], Brighton Collaboration[b] level 3	9 days post-vaccination	• Open-label phase 3 trial without a placebo control, evaluating the immunogenicity of different revaccination intervals	Likely GBS[a]
71 years	South Africa	ADEM[c], fatal* *Site investigator updated diagnoses: hypoglycemia & dementia	7 days post-vaccination	• Randomized, blinded co-administration study with standard dose seasonal influenza vaccine • Case occurred in the simultaneous administration arm of the study	ADEM[c] cannot be ruled out, however, other diagnoses appear more likely
71 years	South Africa	ADEM[c]	22 days post-vaccination	• Randomized, blinded co-administration study with standard dose seasonal influenza vaccine • Case occurred in the simultaneous administration arm of the study	ADEM[c] cannot be ruled out, however, other diagnoses appear more likely

[a] GBS = Guillain Barre syndrome

[b] https://brightoncollaboration.us/guillain-barre-and-miller-fisher-syndromes-case-definition-companion-guide/

[c] ADEM = acute disseminated encephalomyelitis

Summary of GRADE for GSK RSVPreF3 vaccine in older adults

Outcome	Importance	Design (# of studies)	Findings	Evidence type
Benefits				
RSV Lower Respiratory Tract Disease (LTRD)	Critical	RCT (1)	GSK RSVPreF3 likely reduces RSV LRTD.	**Moderate**
Medically attended RSV LRTD	Critical	RCT (1)	GSK RSVPreF3 likely reduces medically attended RSV LRTD.	**Moderate**
Hospitalization for RSV respiratory illness	Important	RCT (1)	GSK RSVPreF3 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)	GSK RSVPreF3 may reduce severe RSV respiratory illness requiring oxygen supplementation 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)	GSK RSVPreF3 results in little to no differences in SAEs.	**High**
Inflammatory neurologic events	Important	RCT (2)	No events observed in placebo-controlled trials. Three cases observed in clinical trials without placebo controls.	Unable to evaluate
Reactogenicity (grade ≥3)	Important	RCT (2)	GSK RSVPreF3 increases severe reactogenicity events.	**High**

Summary of GRADE for GSK RSV vaccine in older adults

Outcome	Importance	Design (# of studies)	Findings	Evidence type
Benefits				
RSV Lower Respiratory Tract Disease (LTRD)	Critical	RCT (1)	GSK RSVpreF3 likely reduces RSV LRTD.	**Moderate**
Medically attended RSV LRTD	Critical	RCT (1)	GSK RSVpreF3 likely reduces medically attended RSV LRTD.	**Moderate**
Hospitalization for RSV respiratory illness	Important	RCT (1)	GSK RSVpreF3 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)	GSK RSVpreF3 may reduce severe RSV respiratory illness requiring oxygen supplementation 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)	GSK RSVpreF3 results in little to no differences in SAEs.	**High**
Inflammatory neurologic events	Important	RCT (2)	No events observed in placebo-controlled trials. Three cases observed in clinical trials without placebo controls.	Unable to evaluate
Reactogenicity (grade ≥3)	Important	RCT (2)	GSK RSVpreF3 increases severe reactogenicity events.	**High**

Overall evidence rating: Moderate certainty

Modeling potential RSV-attributable illnesses prevented: GSK RSVPreF3

- Included in economic analysis performed by U. Michigan, using published incidence estimates and RSV-NET estimated annual hospitalizations per 100,000 adults
- Timeframe: 2 RSV seasons (assumed duration of vaccine protection)

	Number prevented per 1 million vaccinations among: **Adults aged ≥65 years**	Number prevented per 1 million vaccinations among: **Adults aged 60–64 years**
Outpatient visits[a]	23,000	18,000
Hospitalizations[b]	2,300	890
Deaths[c]	120	35

[a] Incidence rates of RSV illness requiring outpatient visit taken from McLaughlin et al, OFID (2022). Vaccine efficacy (VE) against this outcome assumed to be equal to that against medically attended acute respiratory illness (ARI) caused by RSV (GSK AReSVi-006 trial, including unpublished data from season 2 follow up).
[b] Incidence rates of RSV hospitalization taken from RSV-NET 2016–2020 (unpublished). VE against RSV-associated hospitalization assumed to be equal to that against medically attended lower respiratory tract disease (LRTD) caused by RSV (GSK AReSVi-006 trial, unpublished).
[c] Probability of in-hospital death among adults hospitalized for RSV taken from RSV-NET 2016–2020 (unpublished). VE against RSV-associated death assumed to be equal to that against medically attended lower respiratory tract disease (LRTD) caused by RSV (GSK AReSVi-006 trial, unpublished).

GSK, post-marketing safety requirements and commitments

Aim	Design	Final protocol submission to FDA	Study completion date
Evaluate risk of GBS, ADEM[a]	Self-controlled risk interval design	June 30, 2024	June 30, 2030
Evaluate risk of atrial fibrillation[b]	Self-controlled risk interval design	June 30, 2024	June 30, 2030

a Post-marketing requirement under Section 505(o) of the Federal Food, Drug, and Cosmetic Act

b A numerical imbalance in events of atrial fibrillation was noted in the main phase 3 trial, with 7 events in the RSVPreF3 group and 1 event in the placebo group, within 1 month following vaccination (dose 1).

Vaccines and Related Biological Products Advisory Committee February 28 - March 1, 2023 Meeting Briefing Document- FDA: Applicant- GSK

May 23, 2023 Approval Letter - AREXVY (fda.gov)

Benefits and Harms GSK adjuvanted RSVPreF3 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

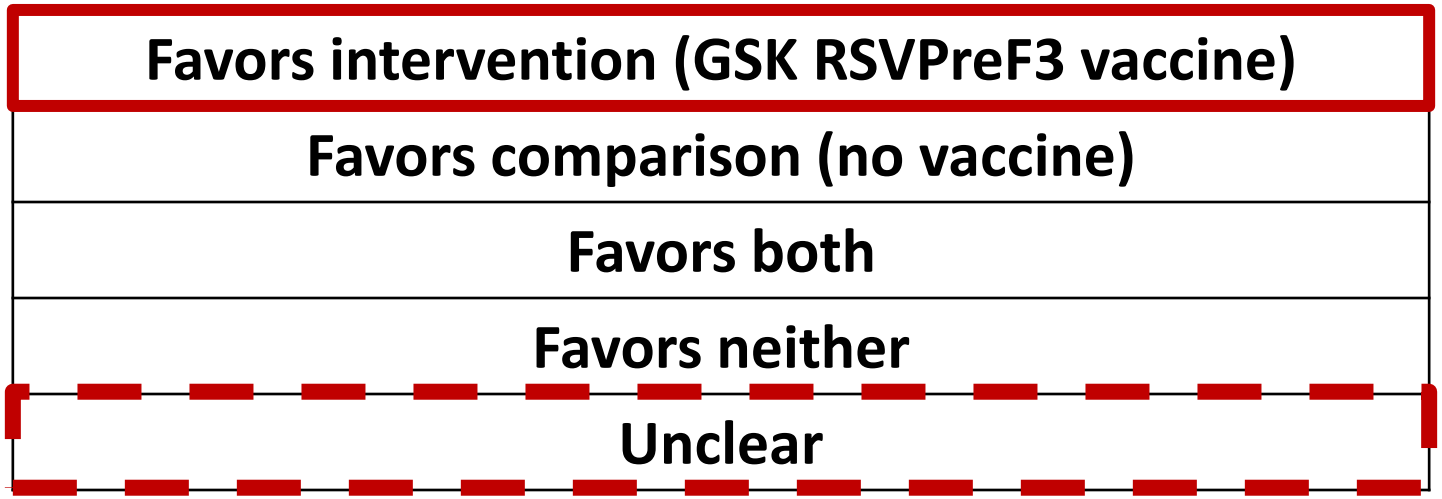
Benefits and Harms GSK adjuvanted RSVPreF3 vaccine

- 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 GSK adjuvanted RSVPreF3 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

Benefits and Harms GSK adjuvanted RSVPreF3 vaccine

- How substantial are the desirable anticipated effects among adults aged **60–64 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

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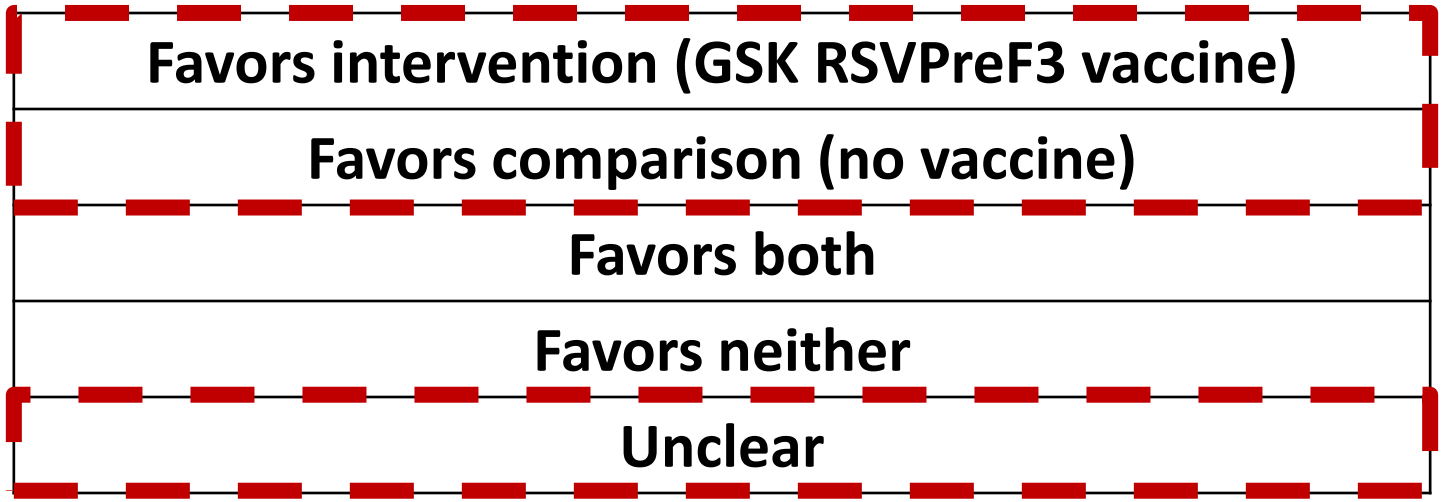


Minority opinion

Resource Use

Is an RSV vaccine program for older adults a reasonable and efficient allocation of resources?

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

Resource Use

- Is use of **Pfizer bivalent RSVpreF** vaccine among adults aged **≥65 years** a reasonable and efficient allocation of resources, compared with no RSV vaccine?
- Is use of **GSK adjuvanted RSVPreF3** vaccine among adults aged **≥65 years** a reasonable and efficient allocation of resources, compared with no RSV vaccine?

No	Probably No	Probably Yes	Yes	Varies	Don't know

Resource Use

- Is use of **Pfizer bivalent RSVpreF** vaccine among adults aged **60–64 years** a reasonable and efficient allocation of resources, compared with no RSV vaccine?
- Is use of **GSK adjuvanted RSVPreF3** vaccine among adults aged **60–64 years** a reasonable and efficient allocation of resources, compared with no RSV vaccine?

No	Probably No	Probably Yes	Yes	Varies	Don’t know

Equity

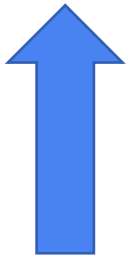
What would be the impact on health equity of recommending RSV vaccines in older adults?

The Work Group discussed multiple equity concerns.

- Not all persons experience the same **risk of RSV** disease.
- An RSV vaccine **might increase equity** by protecting those disproportionately impacted by RSV.
- However, if access or uptake of the vaccine is not equal, an RSV vaccine **might decrease equity.**
- The **age groups** in which the vaccine might be recommended were felt to have **important equity implications.**

First the Work Group considered the impact on equity of a recommendation for RSV vaccination in adults aged 65 years and older.

Anticipated impact on equity of an age-based recommendation for RSV vaccination in adults ≥65



RSV vaccination in adults aged ≥65 years **might increase equity** by decreasing RSV burden among persons from racial and ethnic minority groups and in persons with lower income levels.

Next the Work Group considered the impact on equity of a recommendation for RSV vaccination in adults aged 60–64 years.

Age of adults hospitalized with RSV, by race and ethnicity, RSV-NET

	N	Median age, years (interquartile range)
All	9,163	70 (58–81)
Race and ethnicity		
White, non-Hispanic	5,596	73 (62–83)
Black, non-Hispanic	1,731	60 (50–70)
Hispanic	713	65 (50–77)
Asian or Pacific Islander, non-Hispanic	518	77 (64–85)
American Indian or Alaska Native, non-Hispanic	56	57 (47–71)

CDC RSV-NET data 2015–2020 (unpublished). https://www.cdc.gov/rsv/research/rsv-net/index.html

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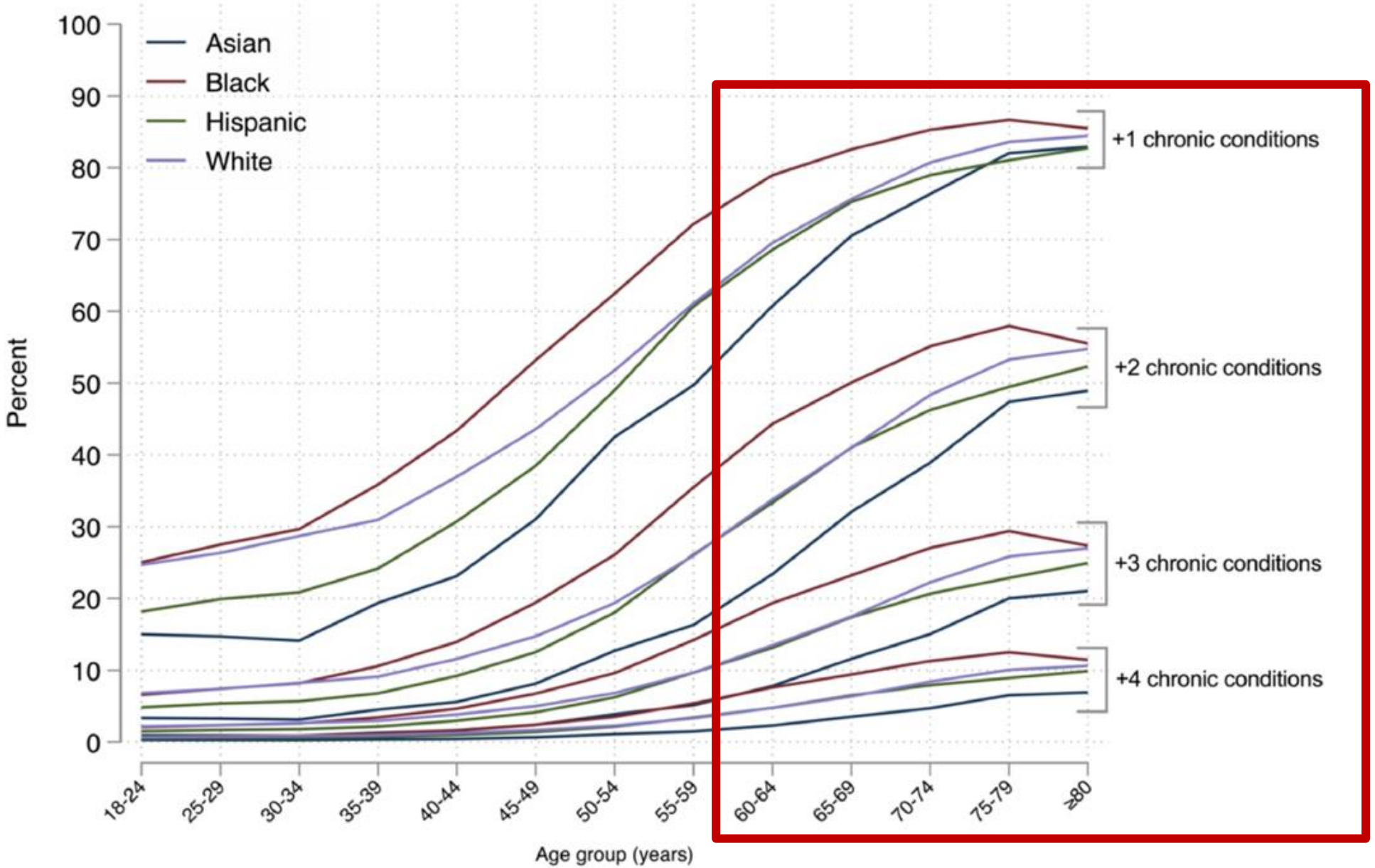
Number of chronic conditions by age among Asian, Black, Latino/Hispanic, and White adults in the National Health Interview Survey (NHIS), 1999 to 2018



Source: Caraballo C, Herrin J, Mahajan S, et al. Temporal Trends in Racial and Ethnic Disparities in Multimorbidity Prevalence in the United States, 1999-2018. *Am J Med*. 2022;135(9):1083-1092.e14. doi:10.1016/j.amjmed.2022.04.010

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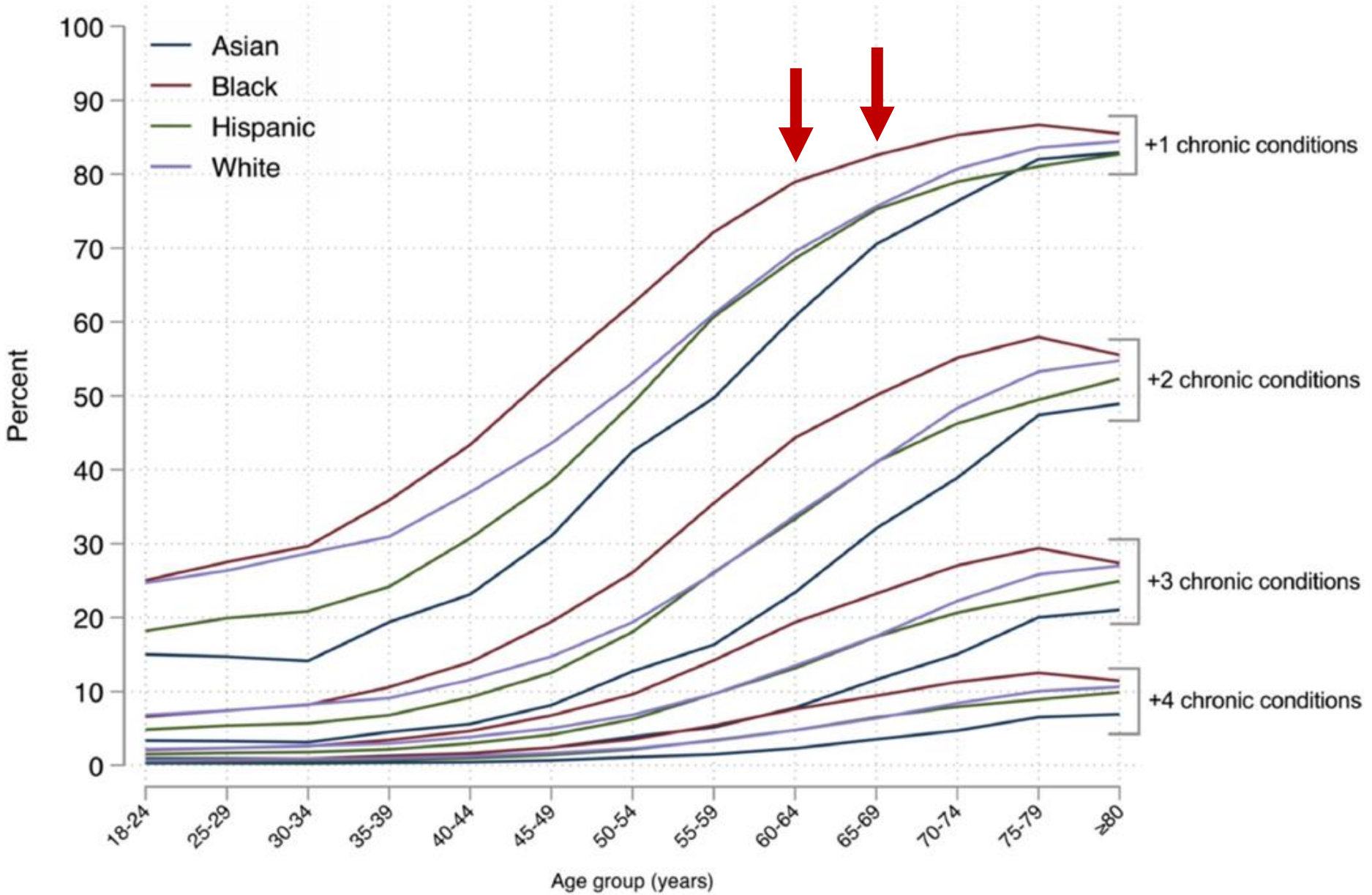

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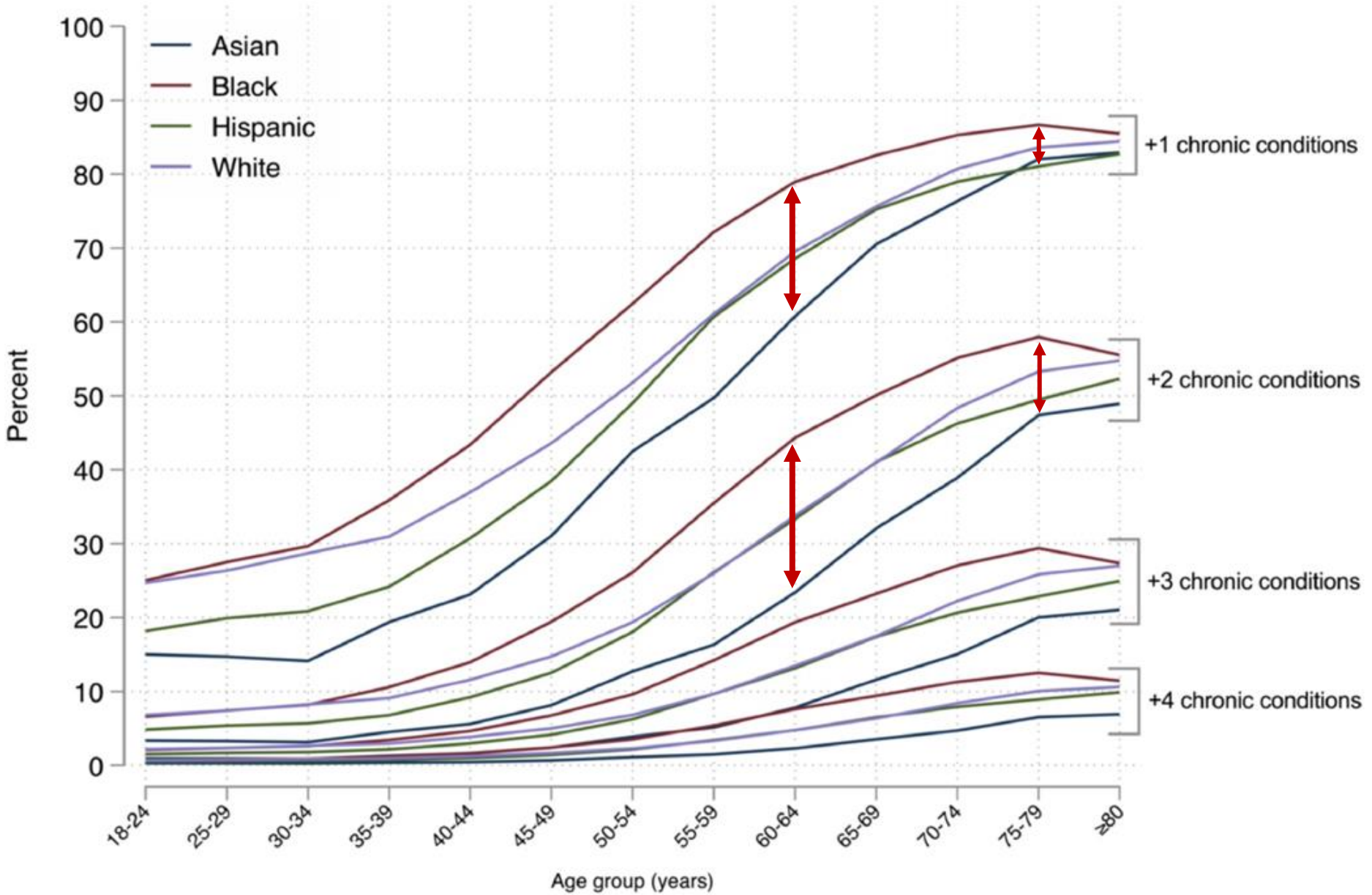

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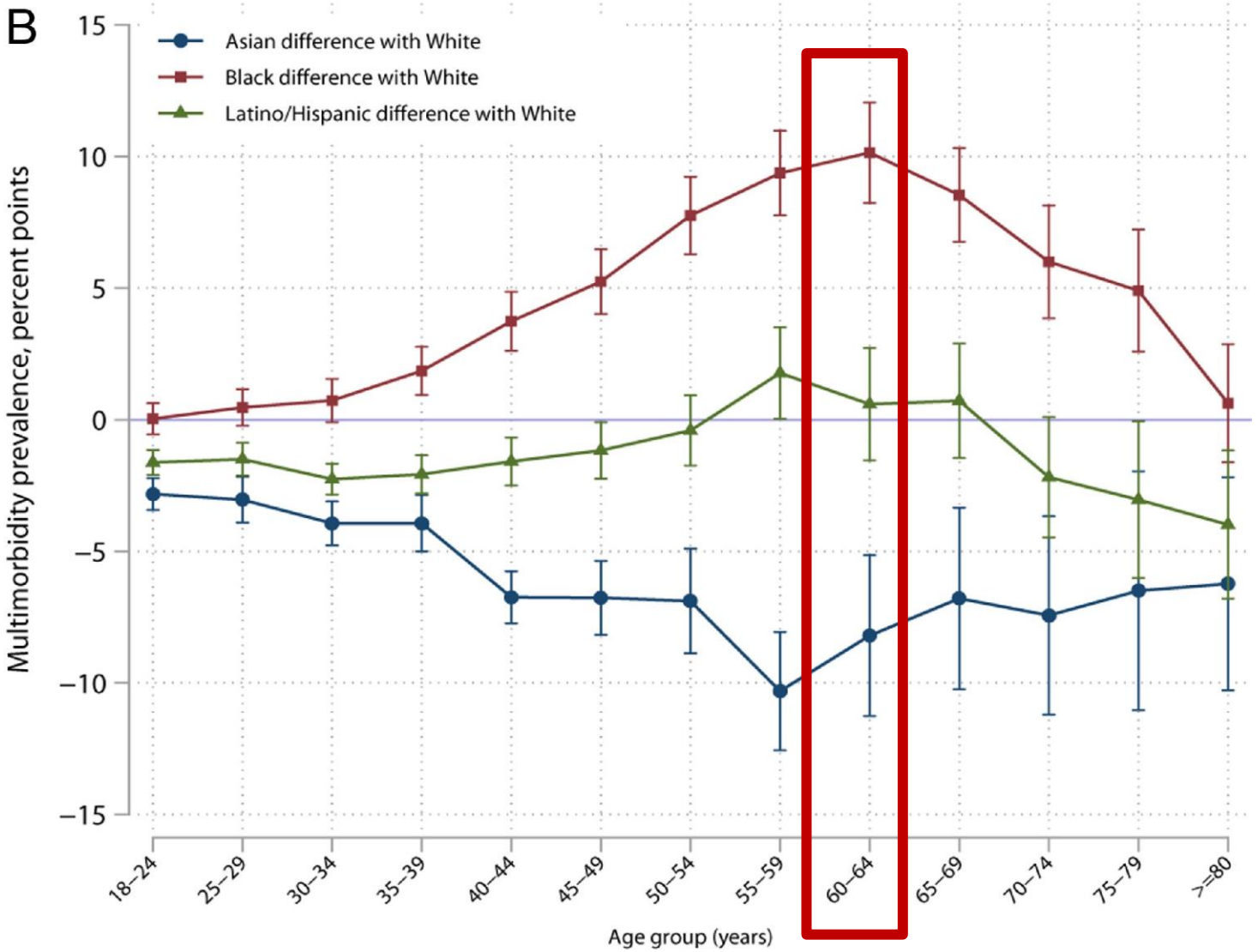
Difference in prevalence of multiple chronic conditions by age and race/ethnicity, National Health Interview Survey, 1999 to 2018



- Prevalence of multimorbidity (≥2 concurrent conditions) diverged between Black individuals and White individuals
- Reached maximum difference of 10% among those aged 60-64 years

Source: Caraballo C, Herrin J, Mahajan S, et al. Temporal Trends in Racial and Ethnic Disparities in Multimorbidity Prevalence in the United States, 1999-2018. *Am J Med*. 2022;135(9):1083-1092.e14. doi:10.1016/j.amjmed.2022.04.010

Anticipated impact on equity of an age-based recommendation for RSV vaccination in adults ≥65

RSV vaccination in adults aged ≥65 years **might increase equity** by decreasing RSV burden among persons from racial and ethnic minority groups and persons with lower income levels.

An RSV vaccination recommendation that excludes adults aged 60-64 years **might decrease equity** by excluding persons from racial and ethnic minority groups that would benefit from the vaccine at earlier ages due to risk conditions.

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 might inform the expected impact on equity.

ACIP recommendations for vaccination based on shared clinical decision-making (SCDM) that appear (or appeared) on the tables and/or notes of the immunization schedules

- *Historical:* Pneumococcal conjugate vaccination (PCV13) for adults aged 65 years and older who do not have an immunocompromising condition, cerebrospinal fluid leak, or cochlear implant (recommendation revised in 2021 with introduction of PCV15 and PCV20)
- *Historical:* Hepatitis B (HepB) vaccination for adults aged 60 years and older with diabetes mellitus (recommendation revised in 2022)
- Meningococcal B (MenB) vaccination for adolescents and young adults aged 16–23 years
- Human papillomavirus (HPV) vaccination for adults aged 27–45 years

History of Hepatitis B and SCDM

- In 2011, ACIP recommended Hepatitis B vaccination for all unvaccinated adults with diabetes mellitus aged <60 years but for unvaccinated adults with diabetes mellitus aged ≥60 years, ACIP recommended Hepatitis B vaccination at the discretion of their healthcare provider.
- *(This recommendation was revised in 2022. Now HepB vaccination is universally recommended for adults aged 19–59 years and adults aged ≥60 years with risk factors for hepatitis B; adults aged ≥60 years without known risk factors for hepatitis B may also receive HepB vaccines).*

Source: Weng MK, Doshani M, Khan MA, et al. Universal Hepatitis B Vaccination in Adults Aged 19–59 Years: Updated Recommendations of the Advisory Committee on Immunization Practices — United States, 2022. MMWR Morb Mortal Wkly Rep 2022;71:477–483.
DOI: http://dx.doi.org/10.15585/mmwr.mm7113a1external icon.

Hep B vaccine coverage remained suboptimal when recommended to be given *at provider discretion*

- Lu et al. analyzed 2014–2018 NHIS data to determine hepatitis B vaccination coverage (≥3 doses) among adults ≥60 years by diabetes mellitus status
- Hepatitis B vaccination coverage **remained low among older adults** with diabetes mellitus even 7 years after the recommendation was made

Race and ethnicity	Vaccination coverage with ≥3 Hep B doses among adults ≥60 *with diabetes mellitus*	Vaccination coverage with ≥3 Hep B doses among adults ≥60 *without diabetes mellitus*
All	15.3 (13.3 – 17.4)	15.9 (14.8-17.0)
White, non-Hispanic	15.5 (13.1-18.1)	15.9 (14.7-17.2)
Black, non-Hispanic	17.3 (12.2-23.9)	13.4 (10.5-17.2)
Hispanic	9.2 (4.9-16.7)	16.0 (12.0-21.0)
Asian, non-Hispanic	15.7 (8.1-28.2)	18.4 (13.4-24.8)

Source: Lu PJ, Hung MC, Srivastav A, Williams WW, Harris AM. Hepatitis B Vaccination Among Adults With Diabetes Mellitus, U.S., 2018. Am J Prev Med. 2021 Nov;61(5):652-664. doi: 10.1016/j.amepre.2021.04.029. Epub 2021 Jul 20. PMID: 34294463; PMCID: PMC9077536.

Hep B vaccine coverage remained suboptimal when recommended to be given *at provider discretion*

- Lu et al. analyzed 2014–2018 NHIS data to determine hepatitis B vaccination coverage (≥3 doses) among adults ≥60 years by diabetes mellitus status
- Hepatitis B vaccination coverage **remained low among older adults** with diabetes mellitus even 7 years after the recommendation was made
- However, coverage may have been higher among Black, non-Hispanic older adults with diabetes mellitus

Race and ethnicity	Vaccination coverage with ≥3 Hep B doses among adults ≥60 *with diabetes mellitus*	Vaccination coverage with ≥3 Hep B doses among adults ≥60 *without diabetes mellitus*
All	15.3 (13.3 – 17.4)	15.9 (14.8-17.0)
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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]

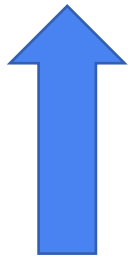
- Some think that SCDM requires more time than routine recommendations, that SCDM creates confusion, and many do not know vaccines recommended for SCDM would be covered by most health insurance[1,2]
- Providers unsure of what points to emphasize in discussions with patients[2]

1. Kempe A, Lindley MC, O'Leary ST, et al. Shared Clinical Decision-Making Recommendations for Adult Immunization: What Do Physicians Think?. *J Gen Intern Med*. 2021;36(8):2283-2291. doi:10.1007/s11606-020-06456-z
2. Hurley LP, O'Leary ST, Kobayashi M, et al. Physician survey regarding updated PCV13 vaccine recommendations for adults ≥65 years. *J Am Geriatr Soc*. 2021;69(9):2612-2618. doi:10.1111/jgs.17274

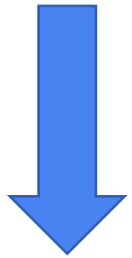
Brief summary of SCDM equity considerations

- Ideally SCDM would increase access for adults aged 60–64 years with medical risk factors for severe RSV disease (disproportionately in racial and ethnic groups impacted by RSV at earlier ages)
- Limited evidence regarding the impact of conditional recommendations, like SCDM, in older adults suggests they may not substantially increase uptake in the target population
- However, without a recommendation for adults aged 60–64 years, adults with medical risk factors for severe RSV disease would likely face additional barriers to RSV vaccination, increasing health disparities

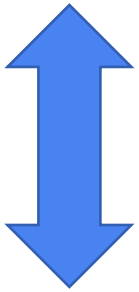
Anticipated impact on equity



RSV vaccination in adults aged ≥65 years might increase equity by decreasing RSV burden among persons from racial and ethnic minority groups and persons with lower income levels.



RSV vaccination that excludes adults aged 60-64 years might decrease equity by excluding persons from racial and ethnic minority groups that would benefit from the vaccine at earlier ages due to risk conditions.



RSV vaccination that includes both adults aged 65 and older and adults aged 60-64 years under shared clinical decision-making (SCDM) would increase access for adults 60–64 with medical risk factors for severe RSV disease (disproportionately in racial and ethnic groups impacted by RSV at earlier ages). However, SCDM may not substantially increase uptake in the target population.

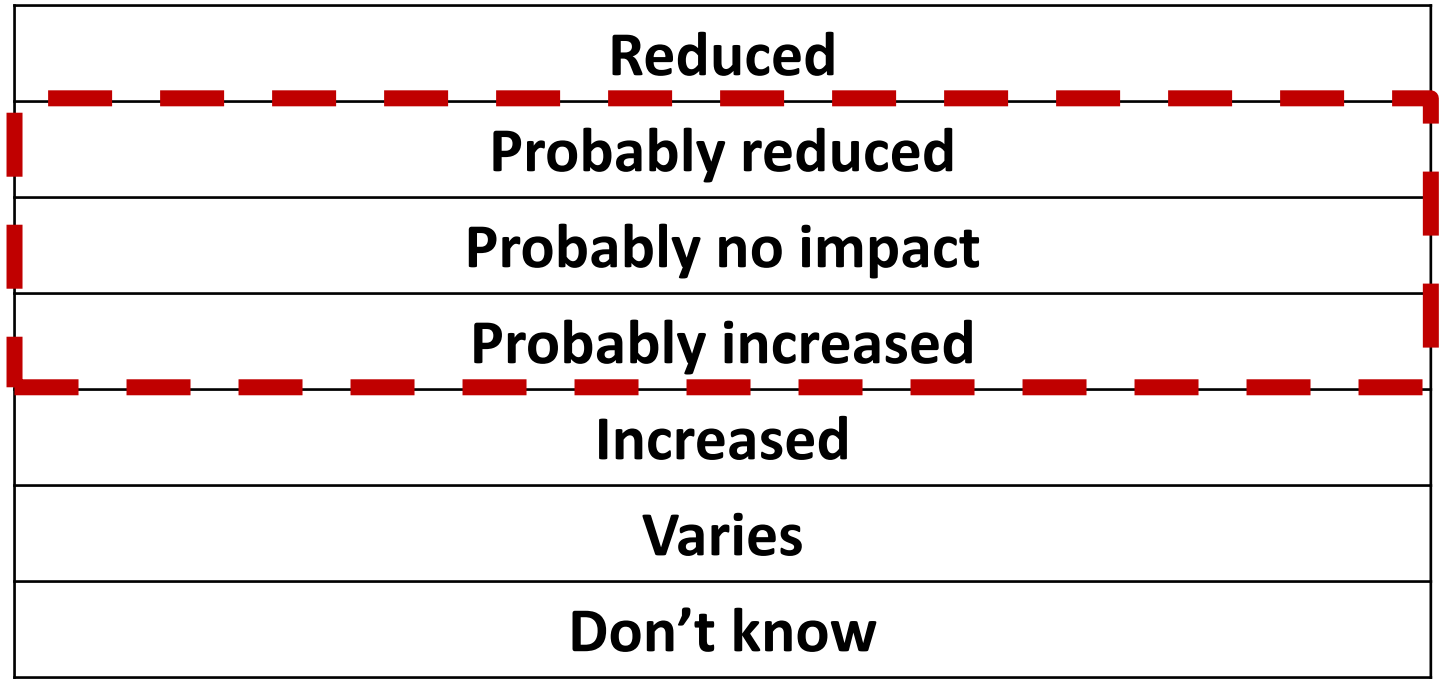
Equity

- What would be the impact on health equity of recommending RSV vaccines in adults aged **≥65 years**?

Reduced
Probably reduced
Probably no impact
Probably increased
Increased
Varies
Don’t know

Equity

- What would be the impact on health equity of recommending RSV vaccines in adults aged **60–64 years**?



Minority opinion

Summary

Domain	Question Adults aged ≥65 years	Work Group Judgements Pfizer	 GSK
Public Health Problem	Is RSV of public health importance?	Yes	
Benefits and Harms	How substantial are the desirable anticipated effects?	Moderate	Moderate
	How substantial are the undesirable anticipated effects?	Small	Small
	Do the desirable effects outweigh the undesirable effects?	Favors intervention	Favors intervention
	What is the overall certainty of the evidence profile?	Moderate	Moderate
Values	Does the target population feel the desirable effects are large relative to the undesirable effects?	Yes/Probably yes	
	Is there important variability in how patients value the outcomes?	Important variability/Probably important variability	
Acceptability	Is the intervention acceptable to key stakeholders?	Yes/Probably yes	
Feasibility	Is the intervention feasible to implement?	Yes/Probably yes	Yes/Probably yes
Resource Use	Is the intervention a reasonable and efficient allocation of resources?	Probably yes	Probably yes
Equity	What would be the impact on health equity?	Probably increased/Probably no impact	

Domain	Question Adults aged 60–64 years	Work Group Judgements Pfizer	 GSK
Public Health Problem	Is RSV of public health importance?	Yes	
Benefits and Harms	How substantial are the desirable anticipated effects?	Small – Moderate	Small – Moderate
	How substantial are the undesirable anticipated effects?	Small	Small
	Do the desirable effects outweigh the undesirable effects?	Unclear	Unclear
	What is the overall certainty of the evidence profile?	Moderate	Moderate
Values	Does the target population feel the desirable effects are large relative to the undesirable effects?	Yes/Probably yes	
	Is there important variability in how patients value the outcomes?	Important variability/Probably important variability	
Acceptability	Is the intervention acceptable to key stakeholders?	Yes/Probably yes	
Feasibility	Is the intervention feasible to implement?	Yes/Probably yes	Yes/Probably yes
Resource Use	Is the intervention a reasonable and efficient allocation of resources?	Probably no	Probably no
Equity	What would be the impact on health equity?	Unclear	

Work Group interpretation (part 1)

- Pfizer's bivalent RSVpreF and GSK's adjuvanted RSVPreF3 vaccines both have demonstrated significant efficacy against lower respiratory tract illness caused by RSV among older adults over at least two seasons
  - Trials were underpowered to show efficacy in the oldest adults and in adults who are frail
  - Trials were underpowered to show efficacy against RSV hospitalization
    - Efficacy against symptomatic illness may indicate efficacy against more severe disease
- RSV vaccination has the potential to prevent considerable morbidity from RSV disease among older adults, particularly in those with chronic medical conditions and those who are frail (e.g., long-term care facility residents)

Work Group interpretation (part 2)

- Cases of inflammatory neurologic events have been reported within 42 days after vaccination with each RSV vaccine
- Clinical trials were not sufficiently powered to determine whether the small number of cases occurred due to random chance
- Whether there is an increased risk of GBS or other inflammatory neurologic events from RSV vaccination is not known at this time
- Post-licensure surveillance for both safety and vaccine effectiveness will be critical

Choice of age threshold at which to recommend RSV vaccines

	Pros	Cons
Age ≥65 years only	• Greater risk of RSV disease and therefore more favorable population-wide balance of risks and benefits of vaccination (in light of cases of inflammatory neurologic events observed) • Aligns with recommendations for high-dose and adjuvanted influenza vaccines, and universal pneumococcal vaccination	• Lost opportunity to prevent additional disease in the 60–64 age group, who are disproportionately from racial and ethnic groups impacted by RSV at earlier ages
Also in ages 60–64 years	• Potential to prevent a greater total burden of disease (e.g., number of hospitalizations) • Increases access to adults 60–64 with medical risk factors for severe RSV disease (disproportionately in racial and ethnic groups impacted by RSV at earlier ages)	• Risk/benefit balance depends on the patient population that seeks and receives vaccination among those 60–64 • Uninsured adults would face financial barriers obtaining vaccination (disproportionately aged 60–64 in racial, ethnic and socioeconomic groups at greater risk of severe RSV) • May experience more difficulty achieving clinician adoption of the recommendation among patients 60–64 • Less efficient allocation of societal resources

Evidence to Recommendations Framework
Summary: Work Group Interpretations

- Work Group interpretations were similar for:
  - Pfizer bivalent RSVpreF
  - GSK adjuvanted RSVPreF3

Evidence to Recommendations Framework

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

Minority opinion

Among adults aged ≥65 years:

Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings	Undesirable consequences *probably outweigh* desirable consequences in most settings	The balance between desirable and undesirable consequences is *closely balanced* or *uncertain*	Desirable consequences *probably outweigh* undesirable consequences in most settings	Desirable consequences *clearly outweigh* undesirable consequences in most settings	There is insufficient evidence to determine the balance of consequences

Among adults aged 60–64 years:

Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings	Undesirable consequences *probably outweigh* desirable consequences in most settings	The balance between desirable and undesirable consequences is *closely balanced* or *uncertain*	Desirable consequences *probably outweigh* undesirable consequences in most settings	Desirable consequences *clearly outweigh* undesirable consequences in most settings	There is insufficient evidence to determine the balance of consequences

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

Minority opinion

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

Proposed ACIP Voting Language

- Adults 65 years of age and older are recommended to receive a single dose of RSV vaccine.

- Individual adults aged 60–64 years may receive a single dose of RSV vaccine, using shared clinical decision-making based on risk assessment.

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