Evidence to Recommendations Framework

Respiratory Syncytial Virus (RSV) in Adults

GSK adjuvanted RSVpreF3 vaccine in older adults
Pfizer bivalent RSVpreF vaccine in older adults

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Evidence to Recommendations (EtR) Framework
Policy Questions

- Should vaccination with GSK RSVpreF3 vaccine (120µg antigen + AS01E adjuvant, 1 dose IM), rather than no vaccine, be recommended in persons aged ≥65 years?
- Should vaccination with GSK RSVpreF3 vaccine (120µg antigen + AS01E adjuvant, 1 dose IM), rather than no vaccine, be recommended in persons aged ≥60 years?

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

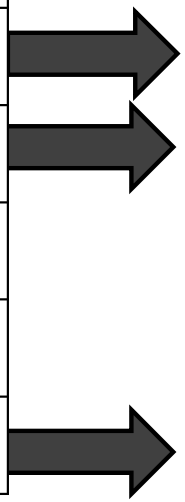
Evidence to Recommendations (EtR) Framework

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

Data on RSV in older adults will be presented

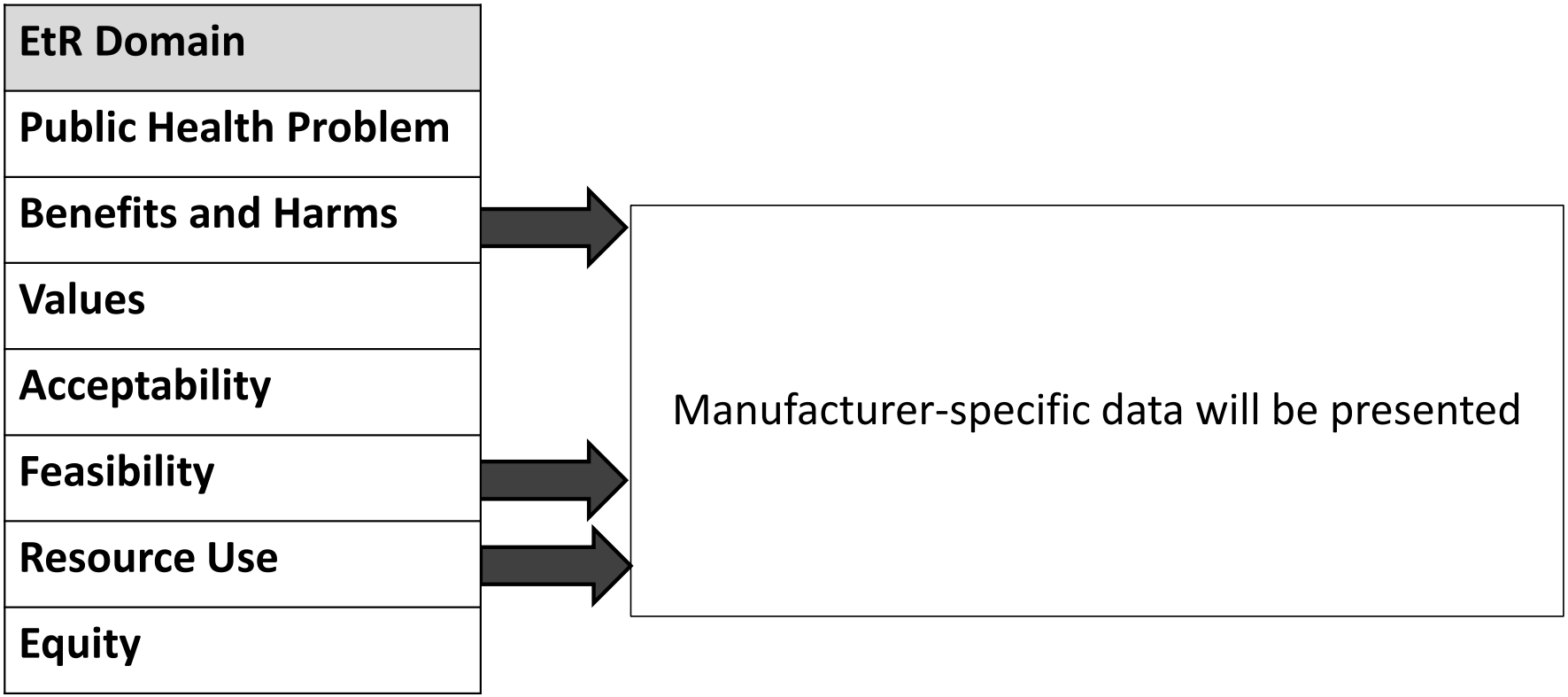
Evidence to Recommendations (EtR) Framework

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



Use of RSV vaccines broadly will be presented

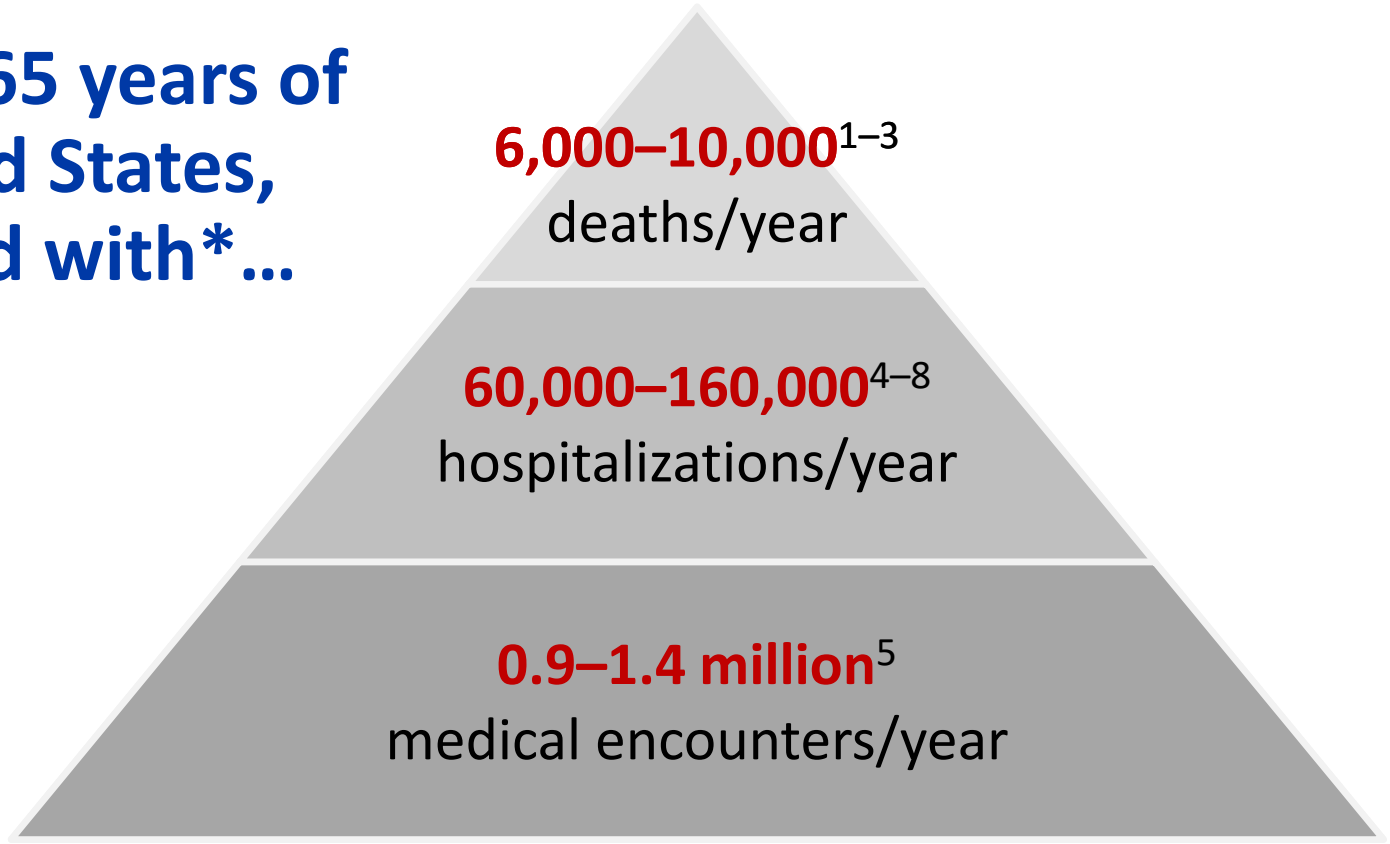
Evidence to Recommendations (EtR) Framework



Public Health Problem

Is RSV among older adults of public health importance?

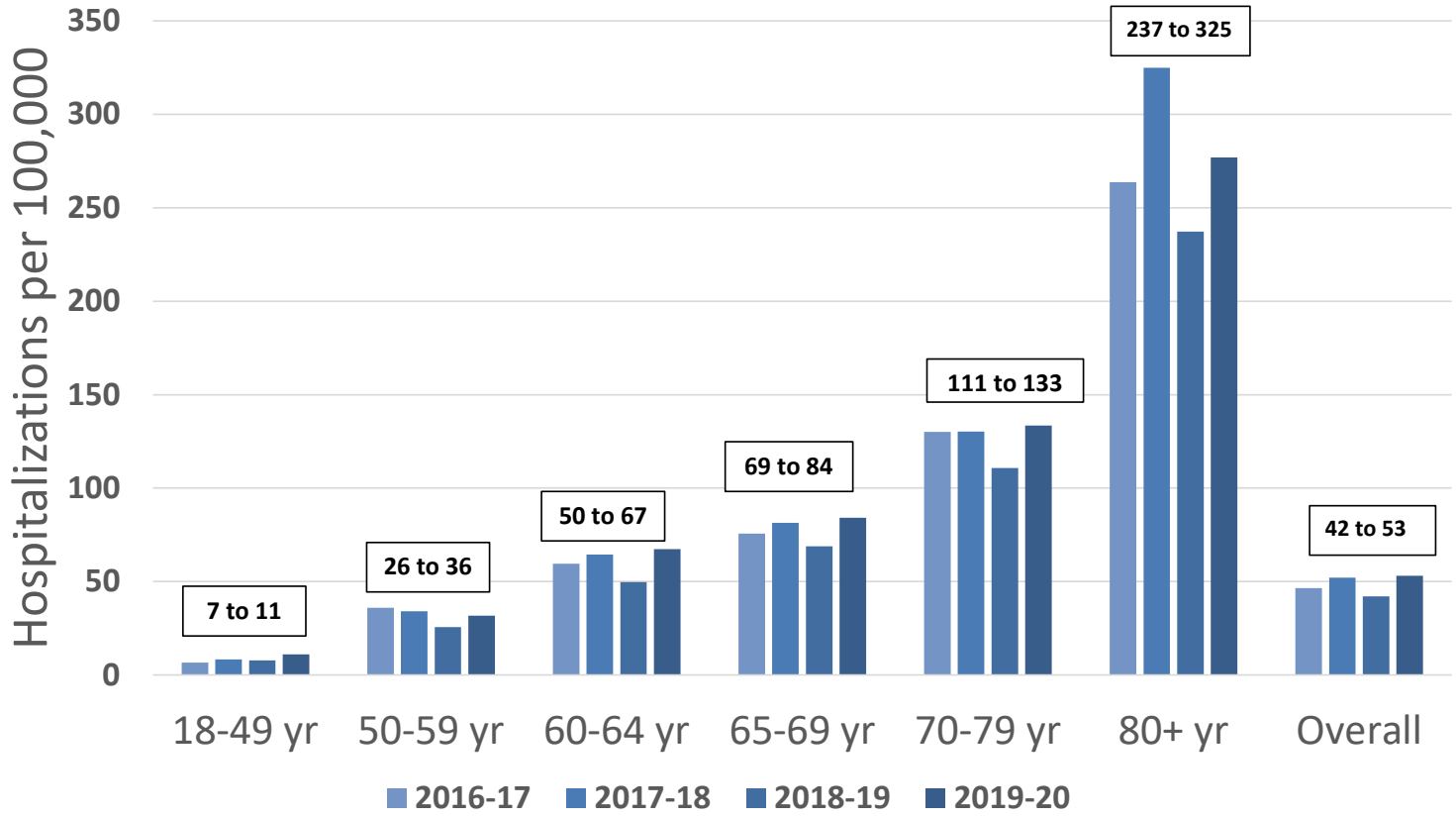
Among adults ≥65 years of age in the United States, RSV is associated with*…



*There is substantial uncertainty in burden of disease, reflected in wide ranges here.

1. Thompson et al, JAMA (2003): https://doi.org/10.1001/jama.289.2.179
2. Matias et al, Influenza Other Respi Viruses (2014): https://doi.org/10.1111/irv.12258
3. Hansen et al, JAMA Network Open (2022): https://doi.org/10.1001/jamanetworkopen.2022.0527
4. Widmer et al, JAMA Network Open (2012): https://doi.org/10.1093/infdis/jis309
5. McLaughlin et al, Open Forum Infect Dis (2022): https://doi.org/10.1093/ofid/ofac300
6. Zheng et al, Pneumonia (2022): https://doi.org/10.1186/s41479-022-00098-x
7. Branche et al, Clinical Infect Dis (2022): https://doi.org/10.1093/cid/ciab595
8. CDC RSV-NET data 2016–2020 (unpublished)

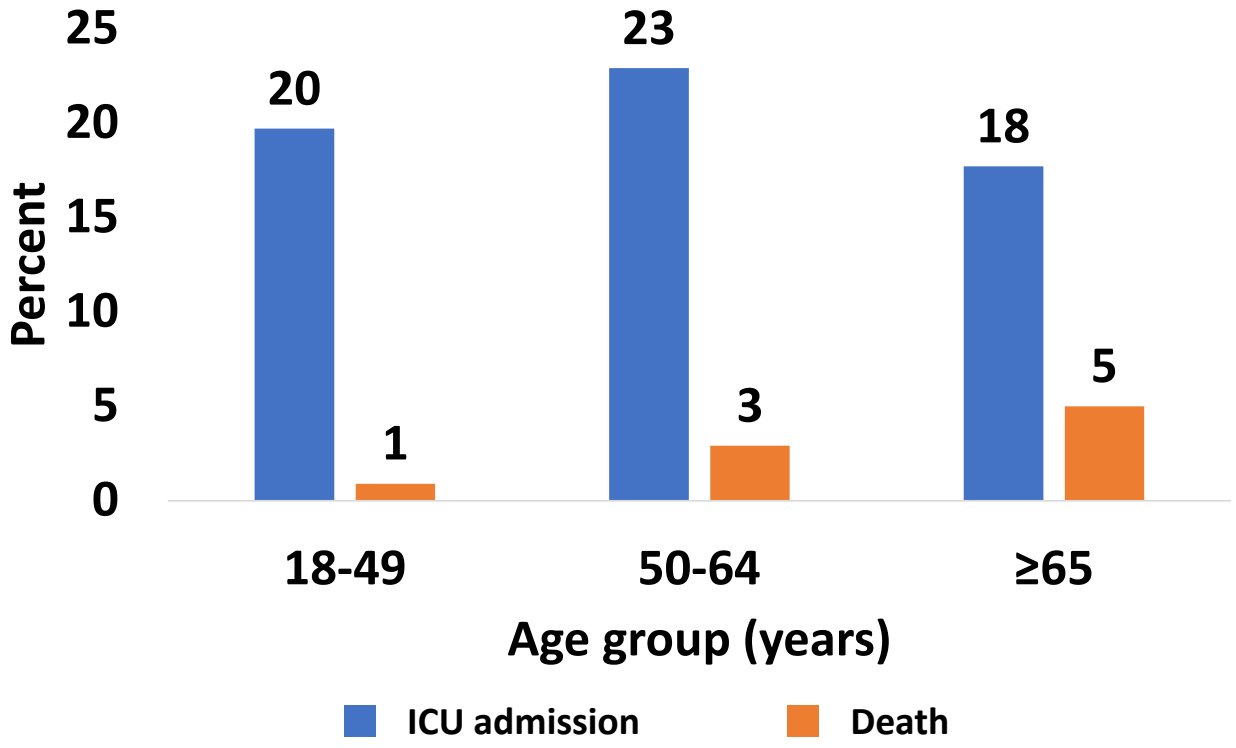
RSV-associated hospitalization rates by adult age group, RSV-NET 2016–2020



RSV-NET: unpublished data; https://www.cdc.gov/rsv/research/rsv-net/overview-methods.html.
Rates are adjusted for the frequency of RSV testing during recent prior seasons and the sensitivity of RSV diagnostic tests..

Slide credit: Fiona Havers

Outcomes among adults ≥18 years hospitalized for RSV: RSV-NET 2017–18 to 2019–20 seasons (n=8,214)



Severe outcomes frequent among adults of all ages hospitalized for RSV

Slide credit: Fiona Havers

Adults with certain underlying medical conditions are at higher risk of RSV hospitalization

- Immune compromise, especially hematopoietic stem cell transplant and solid organ transplant
- Cardiovascular disease (e.g., congestive heart failure)
- Diabetes mellitus
- Chronic obstructive pulmonary disease (COPD)
- Asthma

1. Anderson et al, Diagn Microbiol Infect Dis (2016): https://doi.org/10.1016/j.diagmicrobio.2016.02.025
2. Prasad et al, Clin Infect Dis (2020): https://doi.org/10.1093/cid/ciaa730
3. Kujawski et al, Plos One (2022): https://doi.org/10.1371/journal.pone.0264890
4. Branche et al, Clin Infect Dis (2022): https://doi.org/10.1093/cid/ciab595

Summary

- RSV is a frequent, often unrecognized, cause of severe respiratory illness, with incidence increasing with age among older adults
- High proportion of those hospitalized with RSV have severe outcomes, including ICU admission and death
- Death is more common with increasing age

Public Health Problem- Work Group Interpretation

- **Is RSV disease of public health importance among adults aged ≥65 years?**

No	Probably No	Probably Yes	**Yes**	Varies	Don't know

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

- GSK adjuvanted RSVpreF3 vaccine
  - Grading of Recommendations, Assessment, Development and Evaluation (**GRADE**) Summary
  - Number-needed-to-vaccinate (NNV) analysis
- Pfizer bivalent RSVpreF vaccine
  - **GRADE** Summary
  - NNV analysis

GRADE Framework: PICO Question

Population	Persons aged ≥60 years
Intervention	GSK RSVpreF3 vaccine (120 µg antigen + $AS01_E$ adjuvant, 1 dose IM) **-or-** Pfizer bivalent RSVpreF vaccine (120µg antigen, 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 neuropathy (e.g., Guillain-Barré syndrome) ▪ Reactogenicity (grade ≥3)

GRADE: GSK adjuvanted RSVpreF3

GSK, Benefits: vaccine efficacy estimates

Outcome	Importance	Data sources	Vaccine efficacy estimate[a] (95% confidence interval)	Concerns in certainty assessment
Benefits				
RSV Lower Respiratory Tract Disease (LTRD)	Critical	One phase 3 RCT[b]	82.5% (60.9%, 92.1%)	Indirectness (serious)[c]
Medically attended RSV LRTD	Critical	One phase 3 RCT[b]	87.5% (58.4%, 96.2%)	Indirectness (serious)[c]
Hospitalization for RSV respiratory illness	Important	One phase 3 RCT[b]	Unable to evaluate[d]	
Severe RSV respiratory illness requiring O2/respiratory support	Important	One phase 3 RCT[b]	Unable to evaluate[e]	
Death due to RSV respiratory illness	Important	One phase 3 RCT[b]	Unable to evaluate[f]	

RCT: Randomized control trial

[a] Efficacy estimates were independently calculated using counts of events and participants in the GSK pivotal phase 3 trial interim analysis. Data provided by manufacturer. Efficacy was calculated as 1 – relative risk. Events of each outcome were included if they occurred on or after day 15 after injection.

[b] Papi A, Ison MG, Langley JM, et al. Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults. 2023. NEJM. https://doi.org/10.1056/nejmoa2209604

[c] Underrepresentation of adults aged ≥80 years, exclusion of persons with immune compromise.

[d] Three RSV-associated hospitalizations occurred in the modified exposed set up to the data lock point for the interim analysis. Information was not provided by study arm (intervention vs. placebo) to avoid unblinding of cases.

[e] 31 cases of LRTD requiring oxygen supplementation were identified; 4 of the 31 cases were associated with RSV. All 4 cases occurred in the placebo arm. Measures of relative and absolute risk were not calculated due to small number of events.

[f] No RSV-associated deaths were recorded in the interim analysis.

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, one phase 1/2 RCT	1.03 (0.92, 1.17)	None serious
Inflammatory neuropathy	Important	One phase 3 RCT one phase 1/2 RCT	Unable to evaluate[b]	
Reactogenicity (grade ≥3)	Important	One phase 3 RCT one phase 1/2 RCT	4.10 (1.99, 8.45)	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 interim analysis (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] No events recorded in studies included in GRADE. One event of Guillain-Barré syndrome recorded 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.

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, one phase 1/2 RCT	1.03 (0.92, 1.17)	None serious
Inflammatory neuropathy	Important	One phase 3 RCT one phase 1/2 RCT	Unable to evaluate[b]	
Reactogenicity (grade ≥3)	Important	One phase 3 RCT one phase 1/2 RCT	4.10 (1.99, 8.45)	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 interim analysis (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] No events recorded in studies included in GRADE. One event of Guillain-Barré syndrome recorded 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.

Total of 1 case of inflammatory neuropathy among approximately 15,000 investigational vaccine recipients across all clinical trials

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)	Only three events, unknown whether in vaccine or placebo arm	Unable to evaluate
Severe RSV respiratory illness requiring O2/respiratory support	Important	RCT (1)	Measures of relative and absolute risk not calculated due to small number of events.	Unable to evaluate
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 neuropathy	Important	RCT (2)	No events observed in placebo-controlled trials. Single case observed in an open-label uncontrolled study.	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)	Only three events, unknown whether in vaccine or placebo arm	Unable to evaluate
Severe RSV respiratory illness requiring O2/respiratory support	Important	RCT (1)	Measures of relative and absolute risk not calculated due to small number of events.	Unable to evaluate
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 neuropathy	Important	RCT (2)	No events observed in placebo-controlled trials. Single case observed in an open-label uncontrolled study.	Unable to evaluate
Reactogenicity (grade ≥3)	Important	RCT (2)	GSK RSVpreF3 increases severe reactogenicity events.	**High**

Overall evidence rating: Moderate certainty

Number needed to vaccinate (NNV): GSK RSVpreF3

- Derived from cost effectiveness analysis performed by U. Michigan
- Time horizon: one year

Number of vaccinations required to prevent…	Adults aged ≥65 years	Adults aged ≥60 years
1 RSV outpatient visit[a]	84 vaccinations	90 vaccinations
1 RSV hospitalization[b]	1,097 vaccinations	1,348 vaccinations
1 RSV death[c]	21,442 vaccinations	27,284 vaccinations

[a] Incidence rates of RSV illness requiring outpatient visit taken from McLaughlin et al, OFID (2022) (unadjusted for RSV under-detection by NP swab RT-PCR). 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, unpublished).
[b] Incidence rates of RSV hospitalization taken from RSV-NET 2015–2019 (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 2015–2019 (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).

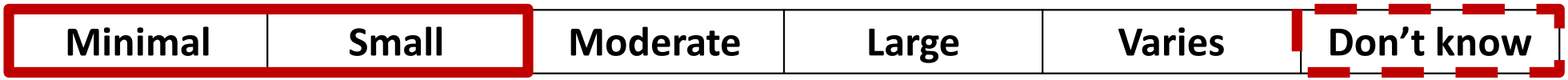
Benefits and Harms GSK adjuvanted RSVpreF3 vaccine

- 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

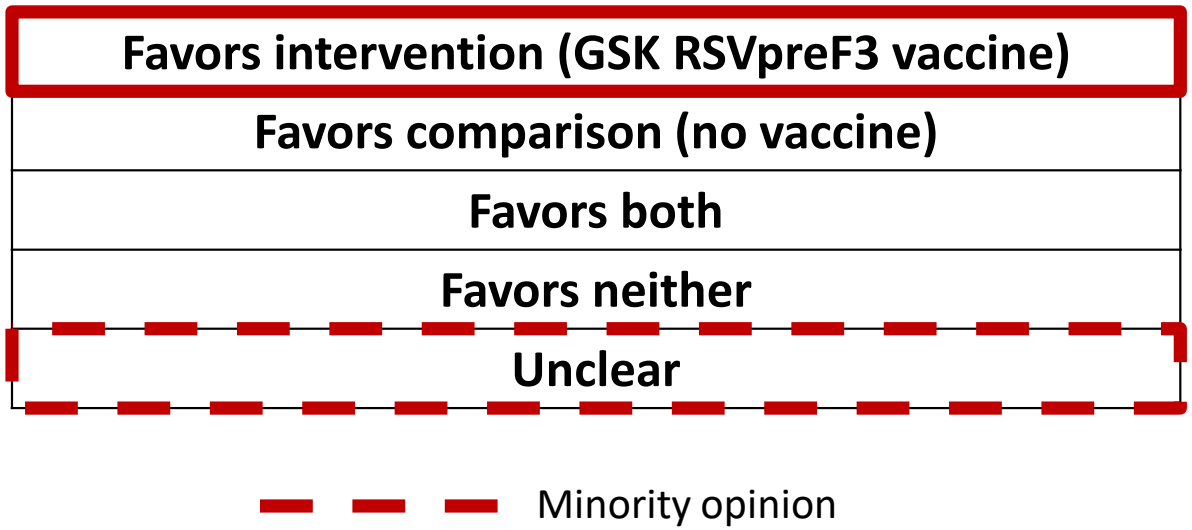
- How substantial are the undesirable anticipated effects among adults aged ≥65 years (relative to no RSV vaccine)?
  - How substantial is the anticipated effect on:
    - Serious Adverse Events (SAEs)
    - Inflammatory neuropathy (e.g., Guillain-Barré Syndrome)
    - Reactogenicity (grade ≥3)



Minority opinion

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?



GRADE: Pfizer bivalent RSVpreF

Pfizer, Benefits: vaccine efficacy estimates

Outcome	Importance	Data sources	Vaccine efficacy estimate[a] (95% confidence interval)	Concerns in certainty assessment
Benefits				
RSV Lower Respiratory Tract Illness (LRTI)[b]	Critical	One phase 3 RCT	85.7% (37.9%, 98.4%)	Indirectness (serious)[c]
Medically attended RSV LRTI[b]	Critical	One phase 3 RCT	80.0% (6.3%, 97.9%)	Indirectness (serious)[c]
Hospitalization for RSV respiratory illness	Important	Counts not provided	Unable to evaluate[d]	
Severe RSV respiratory illness requiring O2/respiratory support	Important	Counts not provided	Unable to evaluate[d]	
Death due to RSV respiratory illness	Important	One phase 3 RCT	Unable to evaluate[e]	

RCT: Randomized control trial

[a] Efficacy estimates were independently calculated using counts of events and person-time observation in the Pfizer pivotal phase 3 trial interim analysis. 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.
[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] Underrepresentation of adults aged ≥80 years, exclusion of persons with immune compromise.
[d] Counts of event were not provided by manufacturer.
[e] No RSV-associated deaths were recorded in the interim analysis.

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	1.01 (0.88 to 1.16)	None serious
Inflammatory neuropathy	Important	One phase 3 RCT one phase 1/2 RCT	Unable to evaluate[b]	
Reactogenicity (grade ≥3)	Important	One phase 3 RCT one phase 1/2 RCT	1.47 (0.88 to 2.46)	Imprecision (serious)[c]

RCT: Randomized control trial

[a] Pooled relative risk estimates were independently calculated using counts of events and participants in the Pfizer pivotal phase 3 trial interim analysis, as well as from a placebo-controlled phase 1/2 formulation selection study (Falsey A, et al. J Infect Dis. 2022 https://doi.org/10.1093/infdis/jiab611p). Data provided by manufacturer.

[b] In the Pfizer pivotal phase 3 trial interim analysis, 2 events of Guillain-Barré syndrome were recorded in the intervention arm, compared with zero in the placebo arm. No events were recorded in the phase 1/2 formulation selection study. Measures of relative and absolute risk were not calculated due to small number of events.

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

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	1.01 (0.88 to 1.16)	None serious
Inflammatory neuropathy	Important	One phase 3 RCT one phase 1/2 RCT	Unable to evaluate[b]	
Reactogenicity (grade ≥3)	Important	One phase 3 RCT one phase 1/2 RCT	1.47 (0.88 to 2.46)	Imprecision (serious)[c]

RCT: Randomized control trial

[a] Pooled relative risk estimates were independently calculated using counts of events and participants in the Pfizer pivotal phase 3 trial interim analysis, as well as from a placebo-controlled phase 1/2 formulation selection study (Falsey A, et al. J Infect Dis. 2022 https://doi.org/10.1093/infdis/jiab611p). Data provided by manufacturer.

[b] In the Pfizer pivotal phase 3 trial interim analysis, 2 events of Guillain-Barré syndrome were recorded in the intervention arm, compared with zero in the placebo arm. No events were recorded in the phase 1/2 formulation selection study. Measures of relative and absolute risk were not calculated due to small number of events.

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

Total of 2 cases of inflammatory neuropathy among approximately 26,000 investigational vaccine recipients across all clinical trials

Summary of GRADE for Pfizer RSV vaccine in older adults

Outcome	Importance	Design (# of studies)	Findings	Evidence type
Benefits				
RSV Lower Respiratory Tract Illness (LRTI)	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		No data	Unable to evaluate
Severe RSV respiratory illness requiring O2/respiratory support	Important		No data	Unable to evaluate
Death due to RSV respiratory illness	Important	RCT (1)	No events observed	Unable to evaluate
Harms				
Serious adverse events (SAEs)	Critical	RCT (2)	Pfizer RSVpreF results in little to no difference in SAEs.	**High**
Inflammatory neuropathy	Important	RCT (2)	Measures of relative and absolute risk not calculated due to small number of events.	Unable to evaluate
Reactogenicity (grade ≥3)	Important	RCT (2)	Pfizer RSVpreF likely increases severe reactogenicity events.	**Moderate**

Summary of GRADE for Pfizer RSV vaccine in older adults

Outcome	Importance	Design (# of studies)	Findings	Evidence type
Benefits				
RSV Lower Respiratory Tract Illness (LRTI)	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		No data	Unable to evaluate
Severe RSV respiratory illness requiring O2/respiratory support	Important		No data	Unable to evaluate
Death due to RSV respiratory illness	Important	RCT (1)	No events observed	Unable to evaluate
Harms				
Serious adverse events (SAEs)	Critical	RCT (2)	Pfizer RSVpreF results in little to no difference in SAEs.	**High**
Inflammatory neuropathy	Important	RCT (2)	Measures of relative and absolute risk not calculated due to small number of events.	Unable to evaluate
Reactogenicity (grade ≥3)	Important	RCT (2)	Pfizer RSVpreF likely increases severe reactogenicity events.	**Moderate**

Overall evidence rating: Moderate certainty

Number needed to vaccinate (NNV): Pfizer RSVpreF

- Derived from cost effectiveness analysis performed by U. Michigan
- Time horizon: one year

Number of vaccinations required to prevent…	Adults aged ≥65 years	Adults aged ≥60 years
1 RSV outpatient visit[a]	95 vaccinations	103 vaccinations
1 RSV hospitalization[b]	1,275 vaccinations	1,567 vaccinations
1 RSV death[c]	24,927 vaccinations	31,717 vaccinations

[a] Incidence rates of RSV illness requiring outpatient visit taken from McLaughlin et al, OFID (2022) (unadjusted for RSV under-detection by NP swab RT-PCR). 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, unpublished).
[b] Incidence rates of RSV hospitalization taken from RSV-NET 2015–2019 (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 2015–2019 (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).

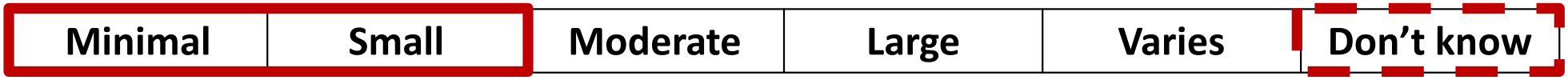
Benefits and Harms Pfizer bivalent RSVpreF vaccine

- 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

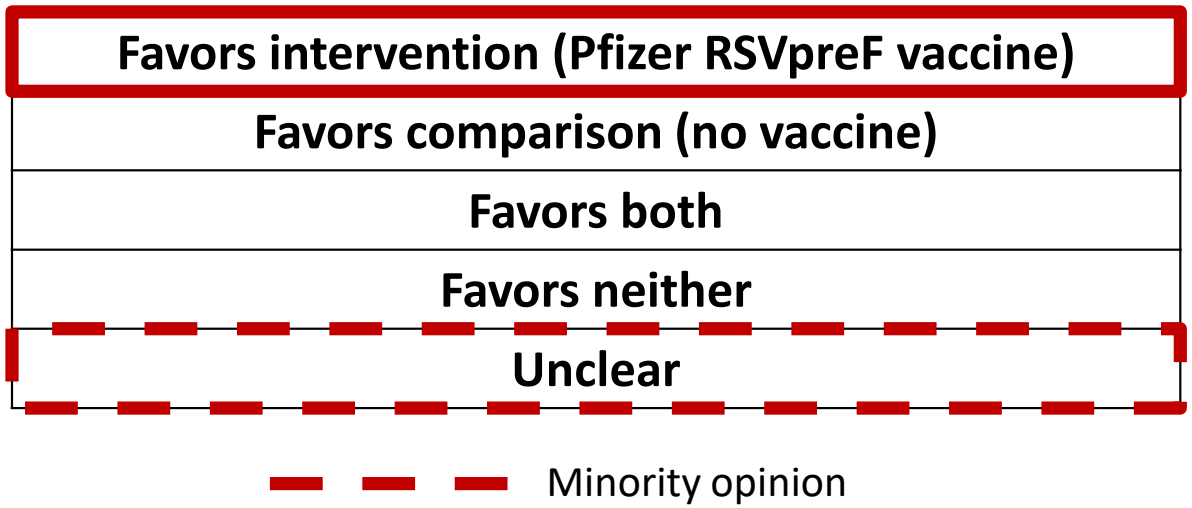
- How substantial are the undesirable anticipated effects among adults aged ≥65 years (relative to no RSV vaccine)?
  - How substantial is the anticipated effect on:
    - Serious Adverse Events (SAEs)
    - Inflammatory neuropathy (e.g., Guillain-Barré Syndrome)
    - Reactogenicity (grade ≥3)



Minority opinion

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?



Values

Do older adults feel the desirable effects of RSV vaccination are large relative to the undesirable effects?

Is there important variability in how older adults value the main outcomes?

Survey of vaccination intent for an RSV vaccine among U.S. adults aged ≥60 years

- Designed to assess vaccination intentions for a hypothetical RSV vaccine
- Data collection period: December 23–31, 2022
- Final sample: 586 respondents (98.7% completion rate)

GENDER

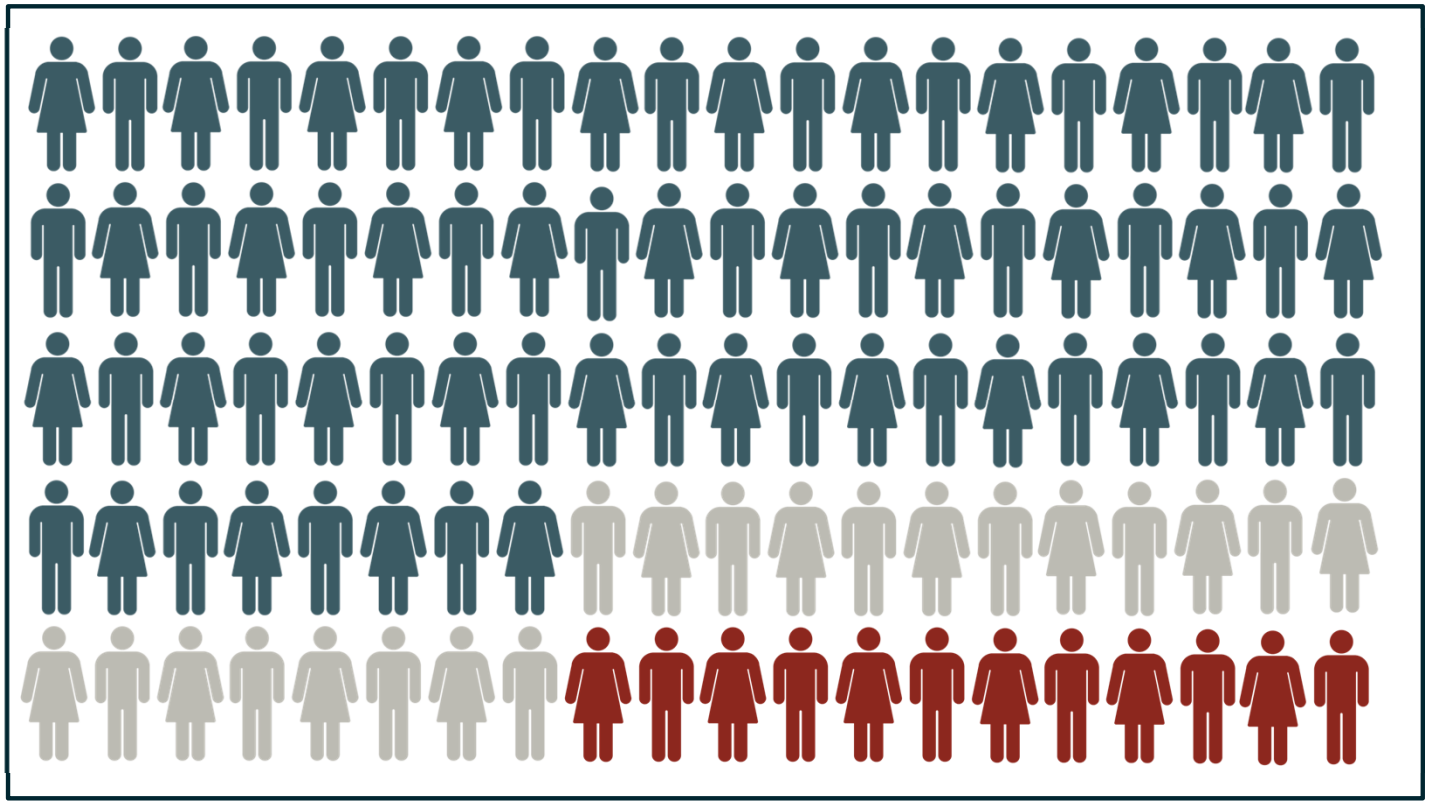
RACE/ETHNICITY

AGE

GENDER	RACE/ETHNICITY	AGE
56.3% Female 43.7% Male or other gender identity	74.9% Non-Hispanic White 12.4% Non-Hispanic Black 9.1% Hispanic	70.6% 60–70 years 29.4% ≥70 years

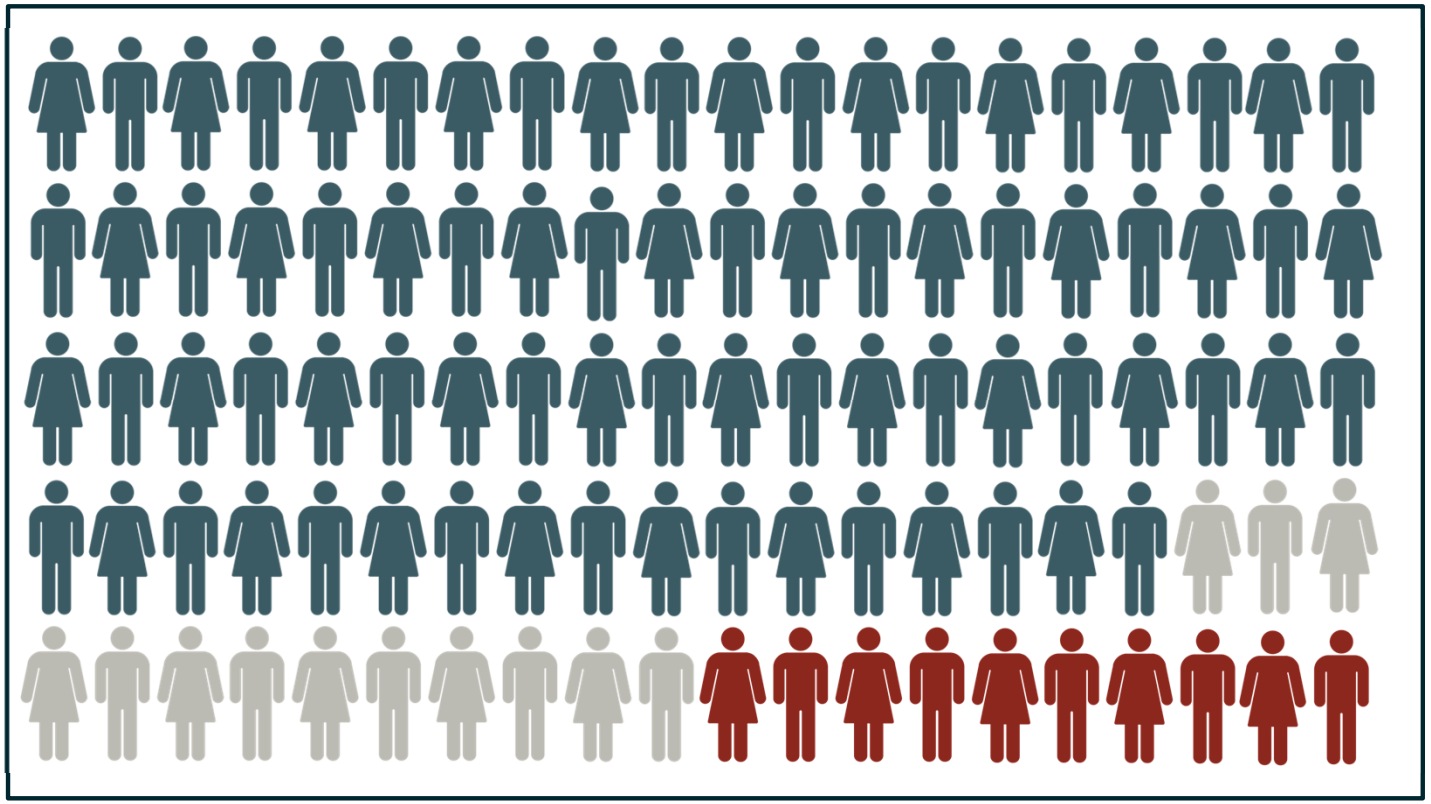
CDC and University of Iowa/RAND survey, unpublished

68% of respondents said they ‘definitely’ or ‘probably’ would get vaccinated if a safe and effective FDA-approved RSV vaccine was available



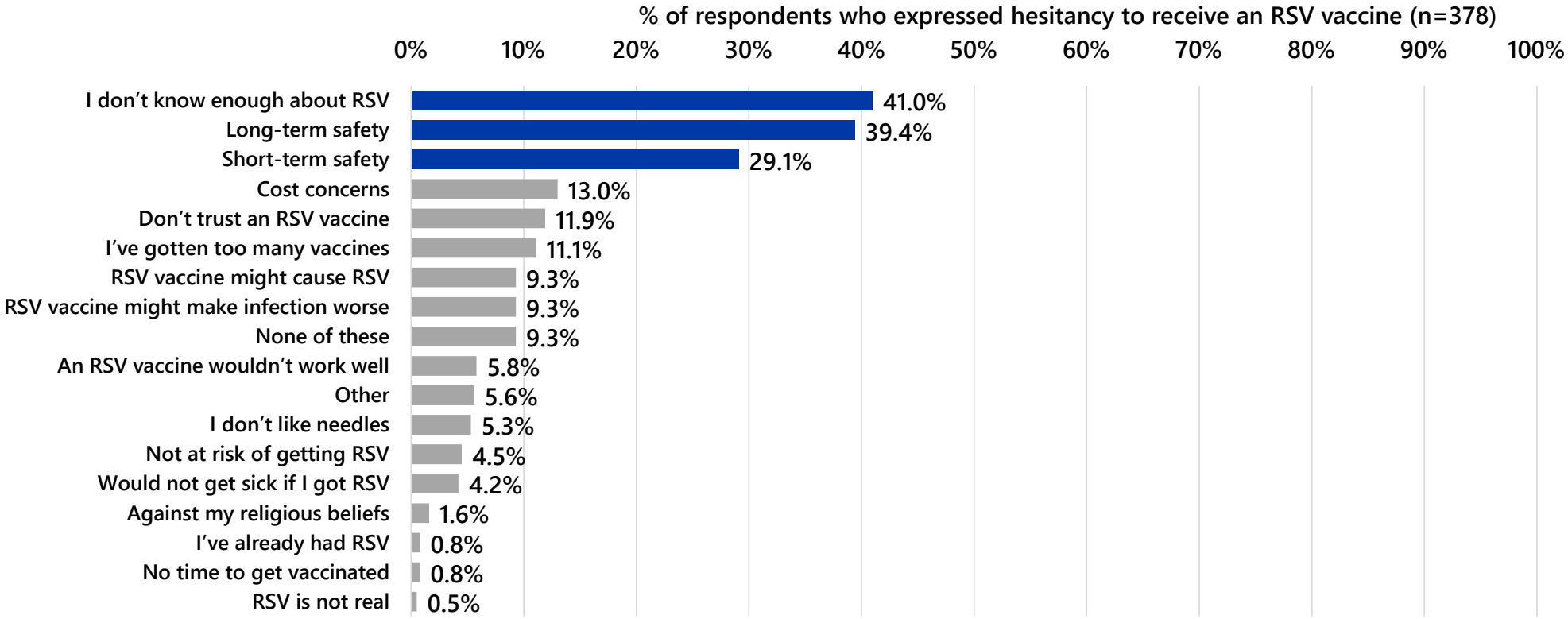
CDC and University of Iowa/RAND survey, unpublished

77% said they ‘definitely’ or ‘probably’ would get an RSV vaccine if it were recommended by **a healthcare provider**



CDC and University of Iowa/RAND survey, unpublished

Lack of RSV knowledge and **safety concerns** were among the top reasons for not wanting an RSV vaccine



CDC and University of Iowa/RAND survey, unpublished

Values

- Do older adults feel that the desirable effects of RSV vaccination are large relative to the undesirable effects?
  - How do older adults view the balance of desirable versus undesirable effects?
  - Would older adults feel that the benefits outweigh the harms?

No	Probably no	Probably Yes	Yes	Varies	Don't know

Values

- Is there important uncertainty about, or variability in, how much older adults value the main outcomes?
  - Is there evidence that the variability is large enough to lead to different decisions?

Important uncertainty or variability
Probably important uncertainty or variability
Probably not important uncertainty or variability
No important uncertainty or variability
No known undesirable outcomes

Acceptability

Would recommending RSV vaccines for older adults be acceptable to key stakeholders?

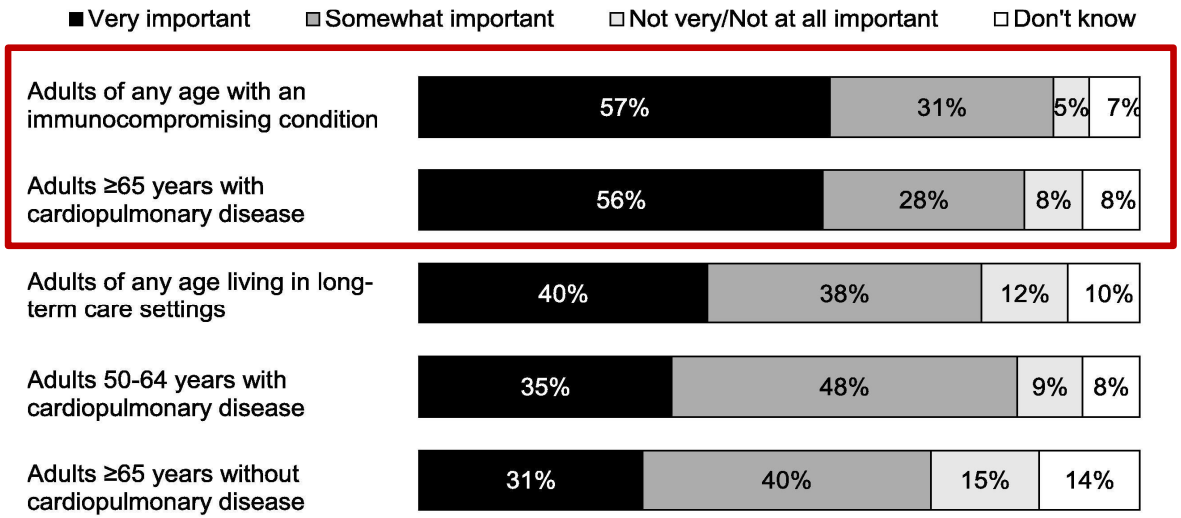
Vaccine Policy Collaborative Initiative

- Survey of physicians, February–March 2017
- National network of 930 primary care physicians who agreed to participate in surveys about vaccine policy issues
  - 620 physicians (67%) completed the survey
  - Responses analyzed from 317 respondents (51%) who reported caring for ≥1 adult patient with possible RSV in the preceding 12 months

Hurley LP, Allison MA, Kim L, et al. Primary care physicians' perspectives on respiratory syncytial virus (RSV) disease in adults and a potential RSV vaccine for adults. 2019 Vaccine 37(4): 565-570. ISSN 0264-410X. https://doi.org/10.1016/j.vaccine.2018.12.031.

A majority of physicians believed that RSV was a very important pathogen in adults of any age with an **immunocompromising condition** (57%) and adults aged **≥65 years *with* cardiopulmonary disease** (56%).

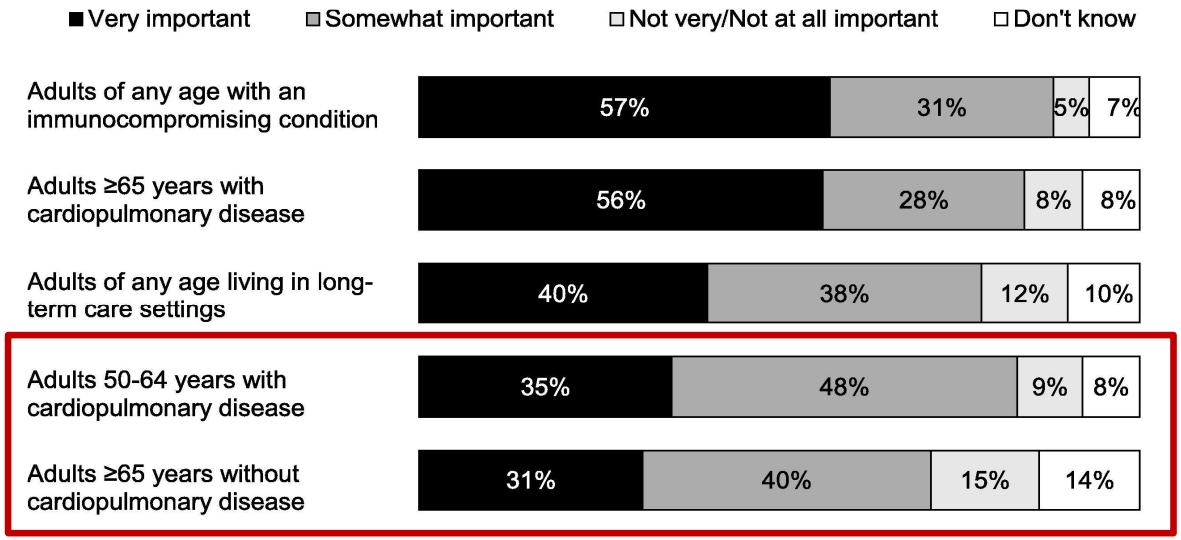
Physician Perception of Importance of RSV as a pathogen in the following groups of patients, United States, 2017 (n = 317)



Hurley LP, Allison MA, Kim L, et al. Primary care physicians' perspectives on respiratory syncytial virus (RSV) disease in adults and a potential RSV vaccine for adults. 2019 Vaccine 37(4): 565-570. ISSN 0264-410X. https://doi.org/10.1016/j.vaccine.2018.12.031.

One third of physicians believed that RSV was a very important pathogen in adults **50–64 years *with* cardiopulmonary disease** (35%) and **adults ≥65 years *without* cardiopulmonary disease** (31%).

Physician Perception of Importance of RSV as a pathogen in the following groups of patients, United States, 2017 (n = 317)



Hurley LP, Allison MA, Kim L, et al. Primary care physicians' perspectives on respiratory syncytial virus (RSV) disease in adults and a potential RSV vaccine for adults. 2019 Vaccine 37(4): 565-570. ISSN 0264-410X. https://doi.org/10.1016/j.vaccine.2018.12.031.

Acceptability

- Would recommending RSV vaccines for adults aged ≥65 years be acceptable to key stakeholders?
  - Are there key stakeholders that would not accept the distribution of benefits and harms?
  - Are there key stakeholders that would not accept the undesirable effects in the short term for the desirable effects (benefits) in the future?

No	Probably No	Probably Yes	Yes	Varies	Don't know

Feasibility

Is RSV vaccination for older adults feasible to implement?

Barriers to implementation of a novel RSV vaccine may include:

- Vaccine storage and handling requirements
- Complexity of the adult vaccination schedule (including coadministration)
- Financial barriers

Storage & handling requirements

GSK RSVpreF3	Pfizer RSVpreF
Supplied as single dose	Supplied as single dose, or as a 5-pack or 10-pack of single-dose kits
Reconstitution required: single dose vial of lyophilized powder (antigen component) + single dose vial of liquid (adjuvant component)	**Reconstitution required**: single dose vial of lyophilized powder, reconstitution supplies included in kit
Both components should be refrigerated (2–8°C) in original container, protected from light	Product should be refrigerated (2–8°C) in original container, protected from light
After reconstitution, the product should be administered within **4 hours**, otherwise discarded	After reconstitution, the product should be administered within **4 hours**, otherwise discarded

Older adult routine immunization schedule is becoming more complex

https://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html

	50-64 years	≥65 years
Influenza inactivated (IIV4) or Influenza recombinant (RIV4)	1 dose annually	
Tetanus, diphtheria, pertussis (Tdap or Td)	1 dose Tdap, then Td or Tdap booster every 10 years	
Zoster recombinant (RZV)	2 doses	
Pneumococcal (PCV15, PCV20, PPSV23)	1 dose PCV15 followed by PPSV23 OR 1 dose PCV20 (see notes)	1 dose PCV15 followed by PPSV23 OR 1 dose PCV20

- Potential fall or other regularly scheduled COVID-19 vaccine
- Clinicians may face competing vaccine priorities

Time/financial barriers

- Older adults without health insurance coverage may experience financial hardship obtaining an RSV vaccine.
- Financial hardship may also arise if vaccine recipients need to take time off from work to receive an RSV vaccine, or due to post-vaccination reactogenicity.

Feasibility

- Is the GSK adjuvanted RSVpreF3 vaccine feasible to implement among adults aged ≥65 years?
- Is the Pfizer bivalent RSVpreF vaccine feasible to implement among adults aged ≥65 years?

No	Probably No	Probably Yes	Yes	Varies	Don't know

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 incidence of severe RSV illness
  - Uncertainty in vaccine acquisition cost
  - Uncertainty in duration of protection from RSV vaccination
- None of the three models incorporated medical costs of longer-term sequelae of RSV infection (e.g., admission to skilled nursing facilities)
- Vaccination of older age groups would be more cost effective than vaccination of younger age groups

Resource Use

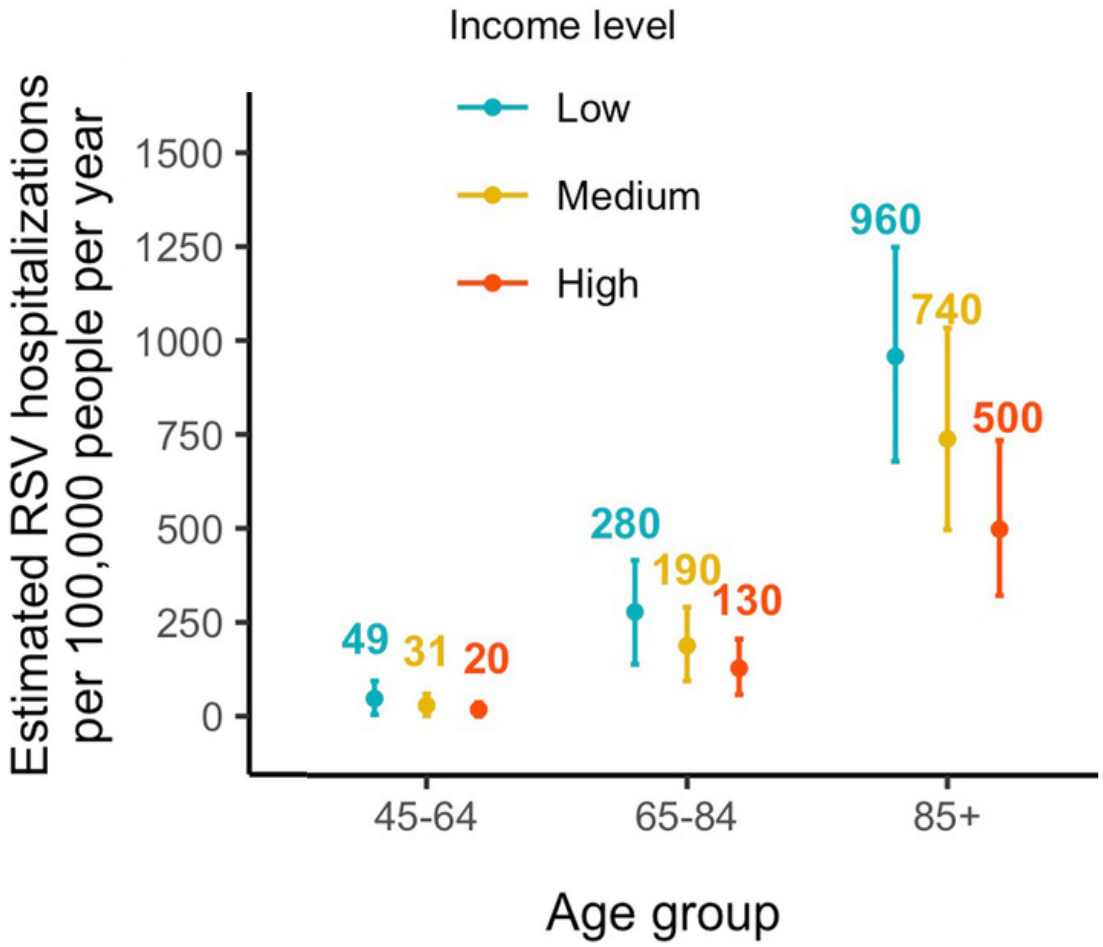
- Is use of GSK adjuvanted RSVpreF3 vaccine among adults aged ≥65 years a reasonable and efficient allocation of resources, compared with no RSV vaccine?
- Is use of Pfizer bivalent RSVpreF vaccine among adults aged ≥65 years a reasonable and efficient allocation of resources, compared with no RSV vaccine?

No	Probably No	Probably Yes	Yes	Varies	Don't know

Equity

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

Incidence of RSV hospitalization is higher among persons in low-income ZIP codes



Zheng Z, et al. Estimated incidence of respiratory hospitalizations attributable to RSV infections across age and socioeconomic groups. Pneumonia (Nathan). 2022 Oct 25;14(1):6. doi: 10.1186/s41479-022-00098-x.

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)

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

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

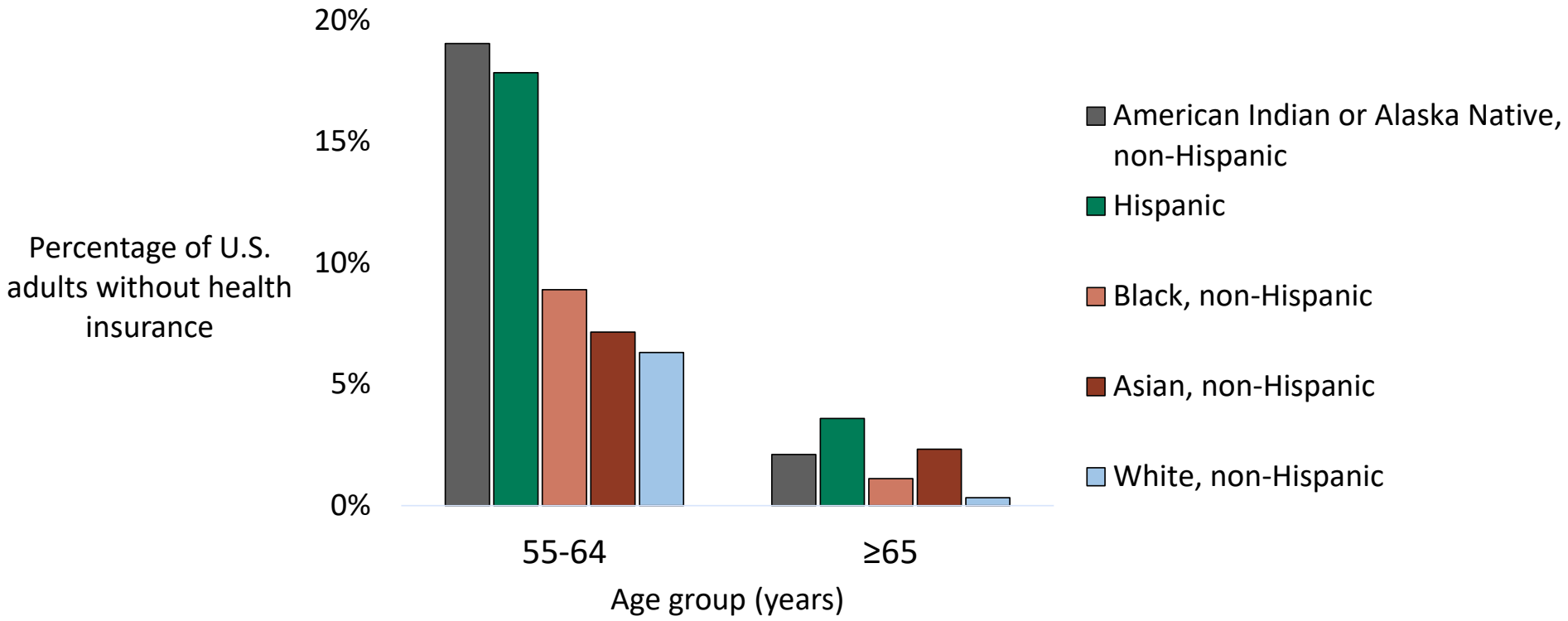
CDC RSV-NET data 2015–2020 (unpublished)

Chronic medical conditions associated with increased risk of RSV disease are more prevalent in U.S. adults in certain demographic groups

	Heart failure	Coronary heart disease	Diabetes mellitus	COPD[a]	Asthma
Black, non-Hispanic[b]	↑[c]	↑↑[c]	↑[c,d]		↑[e,f]
AI/AN[g], non-Hispanic[b]		↑↑[h]	↑↑[h]		↑[e]
Hispanic[a]			↑[c,d,h]		↓[e,f]
Asian, non-Hispanic[b]	↓[c]	↓[c]	↑[c,d]	↓[h]	↓[e]
Lower income or SES[i]	↑[j]	↑[h,j,k]	↑[h,l]	↑[h]	↑[e,f,h]

[a] COPD = chronic obstructive pulmonary disease
[b] Compared with non-Hispanic White adults
[c] Tsao et al, Circulation (2022): https://doi.org/10.1161/cir.0000000000001052
[d] Cheng et al, JAMA (2019): https://doi.org/10.1001/jama.2019.19365
[e] https://www.cdc.gov/asthma/most_recent_national_asthma_data.htm
[f] Bhan et al, Am J Public Health (2015): https://doi.org/10.2105/ajph.2014.302172
[g] AI/AN = American Indian or Alaska Native
[h] NHIS 2018: https://www.cdc.gov/nchs/nhis/shs/tables.htm
[i] SES = socio-economic status
[j] Abdalla et al, JAMA Netw Open (2020): https://doi.org/10.1001%2Fjamanetworkopen.2020.18150
[k] Hamad et al, JAMA Cardiol (2020): https://doi.org/10.1001/jamacardio.2020.1458
[l] Beckles and Chou, MMWR (2016): http://dx.doi.org/10.15585/mmwr.mm6545a4

Access to an RSV vaccine may be determined by health insurance coverage



U.S. Census Bureau, 2021 American Community Survey 1-year estimates: https://data.census.gov/table

Access to an RSV vaccine may be determined by health insurance coverage

Age group (years)	Percentage of population without health insurance			
	Below poverty	*1.0–1.9x poverty*	*2.0–2.9x poverty*	*≥3.0x poverty*
19–64	23.0%	22.2%	16.8%	6.5%
≥65	2.3%	1.0%	0.9%	0.5%

Example income for 2-person household without children, age <65 years

$18,145 $36,290 $54,435

U.S. Census Bureau, 2021 American Community Survey 1-year estimates: https://data.census.gov/table

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

Summary

Domain	Question Adults aged ≥65 years	Work Group Judgements GSK	 Pfizer
Public Health Problem	Is RSV of public health importance?	Yes	
Benefits and Harms	How substantial are the desirable anticipated effects?	Moderate – Large	Moderate – Large
	How substantial are the undesirable anticipated effects?	Minimal – Small	Minimal – 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?	Yes/Probably yes	Yes/Probably yes
Equity	What would be the impact on health equity?	Increased/Probably increased	

Work Group interpretation

- GSK's adjuvanted RSVpreF3 and Pfizer's bivalent RSVpreF vaccines both have demonstrated significant efficacy against lower respiratory tract illness caused by RSV among older adults
  - Trials underpowered to show efficacy against RSV hospitalization
  - Groups at highest risk of severe RSV disease were under-represented in clinical trials
- At least one case of inflammatory neuropathy has been observed among recipients of each investigational vaccine
- If licensed, 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	• Greater risk of RSV disease and therefore more favorable population-wide balance of risks and benefits of vaccination (in light of 1–2 cases of inflammatory neuropathy observed) • Aligns with licensure for adjuvanted and high-dose influenza vaccines and age-based 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
Age ≥60 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)	• Uninsured adults would have difficulty obtaining vaccination (disproportionately aged 60–64 in racial, ethnic and socioeconomic groups at greater risk) • May experience more difficulty achieving clinician adoption of the recommendation among patients 60–64 • Less efficient allocation of societal resources

*FDA has not yet completed review of safety and efficacy data for the GSK RSVpreF3 vaccine and the Pfizer RSVpreF vaccine. ACIP recommendations would be made only if the vaccines are approved and licensed by the FDA.

Evidence to Recommendations Framework
Summary: Work Group Interpretations (GSK RSVpreF3)

Evidence to Recommendations Framework

Summary: Work Group Interpretations (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 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 (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 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: shared clinical decision-making for individual adults aged 60–64 years**

Minority opinion

Evidence to Recommendations Framework
Summary: Work Group Interpretations (Pfizer RSVpreF)

Evidence to Recommendations Framework

Summary: Work Group Interpretations (Pfizer RSVpreF)

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 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)

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 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: shared clinical decision-making for individual adults aged 60–64 years**

Minority opinion

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- Michael Whitaker
- Patricia Wodi

Policy questions for ACIP

- Should vaccination with **GSK RSVpreF3 vaccine** (120µg antigen + AS01E adjuvant, 1 dose IM), rather than no vaccine, be recommended in persons aged ≥65 years?
- Should vaccination with **GSK RSVpreF3 vaccine** (120µg antigen + AS01E adjuvant, 1 dose IM), rather than no vaccine, be recommended in persons aged ≥60 years?

- Should vaccination with **Pfizer bivalent RSVpreF vaccine** (120µg antigen, 1 dose IM), rather than no vaccine, be recommended in persons aged ≥65 years?
- Should vaccination with **Pfizer bivalent RSVpreF vaccine** (120µg antigen, 1 dose IM), rather than no vaccine, be recommended in persons aged ≥60 years?

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Back up slides

Background incidence of GBS increases with increasing age

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

GSK pivotal phase 3 trial

- GSK phase III randomized controlled trial (RCT) (unpublished, data obtained from manufacturer)
- Persons aged ≥60 years in Australia, Belgium, Canada, Estonia, Finland, Germany, Italy, Japan, Republic of Korea, Mexico, New Zealand, Poland, Russian Federation, South Africa, Spain, United Kingdom, United States
  - 32% from United States; 92% from Northern Hemisphere
- Data evaluated: data cut-off April 11, 2022; median follow-up 6.7 months
  - Enrollment and efficacy follow up: May 2021–April 2022
- Exposed set: 12,467 participants in vaccine arm; 12,499 in placebo arm
  - Per-protocol set: 1 excluded from vaccine arm; 5 from placebo arm
  - 8.2% aged ≥80 years, 1.5% with gait speed <0.4 m/s, 1.2% long term care facility residents

https://clinicaltrials.gov/ct2/show/NCT04886596

GSK, Outcome 1: RSV lower respiratory tract disease (LRTD) (n=1 study)

- PCR-confirmed RSV infection with presence of ≥2 lower respiratory **signs** or **symptoms** for ≥24 hours including ≥1 lower respiratory **sign** OR ≥3 lower respiratory **symptoms** for ≥24 hours
- Lower respiratory **signs**
  - New or increased wheezing
  - New or increased crackles/rhonchi on chest auscultation
  - Respiratory rate ≥20 breaths per minute
  - SaO_2 <95% (or ≤90% if baseline is <95%)
  - Need for oxygen supplementation
- Lower respiratory **symptoms**
  - New or increased sputum
  - New or increased cough
  - New or increased dyspnea

GSK, Outcome 1: RSV lower respiratory tract disease (LRTD) (n=1 study)

Population	Events/Vaccine[a,b] (n/N)	Events/Placebo[a,b] (n/N)	Vaccine efficacy (1 – RR) (95% CI)
Age ≥60 years	7/12,466	40/12,494	82.5% (60.9%, 92.1%)
Age ≥65 years	5/9,253	29/9,325	82.6% (55.2%, 93.3%)
Age ≥70 years	3/5,503	19/5,515	84.2% (46.6%, 95.3%)
Age ≥80 years	2/1,016	3/1,028	32.5% (–303%, 88.7%)

[a]12,467 persons received on dose of RSVpreF3 vaccine and 12,499 received one dose of placebo (6 patients excluded due to RSV acute respiratory illness prior to day 15 post injection)
[b]Events diagnosed on or after day 15 post injection

GSK: Inflammatory neuropathy

- A single case of Guillain-Barré syndrome (GBS) was observed in an open-label phase 3 randomized clinical trial without a placebo arm (not included in GRADE)
  - Randomized, open-label study evaluating safety and long-term persistence of immunogenicity indicators following different revaccination schedules
  - Enrolled 1,650 adults aged ≥60 years in 5 countries
  - Data currently available up to 6 months of follow up post-dose 1
  - 3.9% of participants have reported at least 1 SAE
    - 1 case of GBS occurred **9 days** after vaccination, reported as related to the investigational vaccine by the investigator
    - 78 year-old female in Japan; Brighton Collaboration level 3
    - Led to hospitalization, lasted 179 days, patient recovered
- No additional cases of inflammatory neuropathy observed across clinical trials
  - **Total of 1 case among ~15,000 RSVpreF3 recipients**

Pfizer pivotal phase 3 trial

- Pfizer phase 3 randomized controlled trial (RCT), RENOIR, (unpublished, data obtained from manufacturer)
- Persons aged ≥60 years in Argentina, Canada, Finland, Japan, Netherlands, South Africa, and United States
  - 60% from United States; 76% from Northern Hemisphere
- Data evaluated: data cut-off July 8, 2022; mean follow-up 6.8 months per participant
  - Enrollment and efficacy follow up: August 2021–July 2022
- Exposed set: 17,214 participants in vaccine arm; 17,069 in placebo arm
  - Per protocol set: 908 participants excluded from vaccine arm; 761 from placebo
    - <15 days of follow up, ineligibility for study, incorrect intervention, major protocol deviations

Pfizer, Outcome 1: RSV lower respiratory tract illness (LRTI) (n=1 study)

- Acute Respiratory Illness (ARI) with **≥2 or ≥3** of 5 lower respiratory signs/symptoms with PCR confirmed RSV infection within 7 days of ARI symptom onset
- Lower respiratory signs/symptoms:
  - Cough
  - Wheezing
  - Sputum production
  - Shortness of breath
  - Tachypnea
- In this GRADE assessment, we used efficacy against 3-symptom LRTI

Pfizer, Outcome 1: RSV lower respiratory tract illness (LRTI) *≥2 symptoms* (n=1 study)

Population	Events/PYO Vaccine[a,b] (n/N)	Events/PYO Placebo[a,b] (n/N)	Vaccine efficacy (1 – IRR) (95% CI)[c]
Age ≥60 years	11/9,226	33/9,211	66.7% (32.5%, 84.8%)
Age ≥65 years	4/6,251	24/6,230	83.4% (51.7%, 95.8%)
Age ≥70 years	3/3,526	14/3,507	78.7% (23.6%, 96.1%)
Age ≥80 years	1/532	5/527	80.2% (-76.9%, 99.6%)

[a]16,306 persons in the vaccine arm and 16,308 in the placebo arm, contributing 9,226 and 9,211 person-years observation (PYO), respectively

[b]Events diagnosed on or after day 15 post injection

[c]Confidence intervals for vaccine efficacy adjusted by person-time follow-up were calculated using the conditional exact test based on the binomial distribution of the proportion of cases occurring in the vaccine arm

Pfizer, Outcome 1: RSV lower respiratory tract illness (LRTI) *≥3 symptoms* (n=1 study)

Population	Events/PYO Vaccine[a,b] (n/N)	Events/PYO Placebo[a,b] (n/N)	Vaccine efficacy (1 – IRR) (95% CI)[c]
Age ≥60 years	2/9,226	14/9,211	85.7% (37.9%, 98.4%)
Age ≥65 years	1/6,251	10/6,230	90.0% (29.9%, 99.8%)
Age ≥70 years	0/3,526	0/3,507	Not estimated
Age ≥80 years	0/532	0/527	Not estimated

[a]16,306 persons in the vaccine arm and 16,308 in the placebo arm, contributing 9,226 and 9,211 person-years observation (PYO), respectively

[b]Events diagnosed on or after day 15 post injection

[c]Confidence intervals for vaccine efficacy adjusted by person-time follow-up were calculated using the conditional exact test based on the binomial distribution of the proportion of cases occurring in the vaccine arm

Pfizer, Outcome 7: Inflammatory neuropathy (e.g., Guillain Barré syndrome) (n=2 studies)

Study	Events/Vaccine (n/N)	% GBS Vaccine	Events/Placebo (n/N)	% GBS Placebo
Pfizer Phase 3[a]	2/17,214	<0.1	0/17,069	0.0
Pfizer Phase 1/2[b]	0/45	0.0	0/46	0.0

[a] Up to 6 months of follow up post-vaccination
[b] 12 months of follow up post-vaccination

No additional cases of inflammatory neuropathy observed across clinical trials

- **Total of 2 cases among ~26,000 RSVpreF recipients**

Details of Pfizer GBS cases (pivotal phase 3 trial)

- 66 year-old male in the United States
  - Suffered non-ST elevation myocardial infarction 7 days after vaccination with RSVpreF
  - The day after, had onset of weakness
  - Nerve conduction study – acute demyelinating polyneuritis of lower extremities
  - Certainty: Brighton Collaboration Level 1
- 66 year-old female in Japan
  - Miller-Fisher syndrome variant
  - Onset 11 days after vaccination with RSVpreF
  - Certainty: Brighton Collaboration Level 4