

# 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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ACIP Meeting

February 23, 2023

# Evidence to Recommendations (EtR) Framework

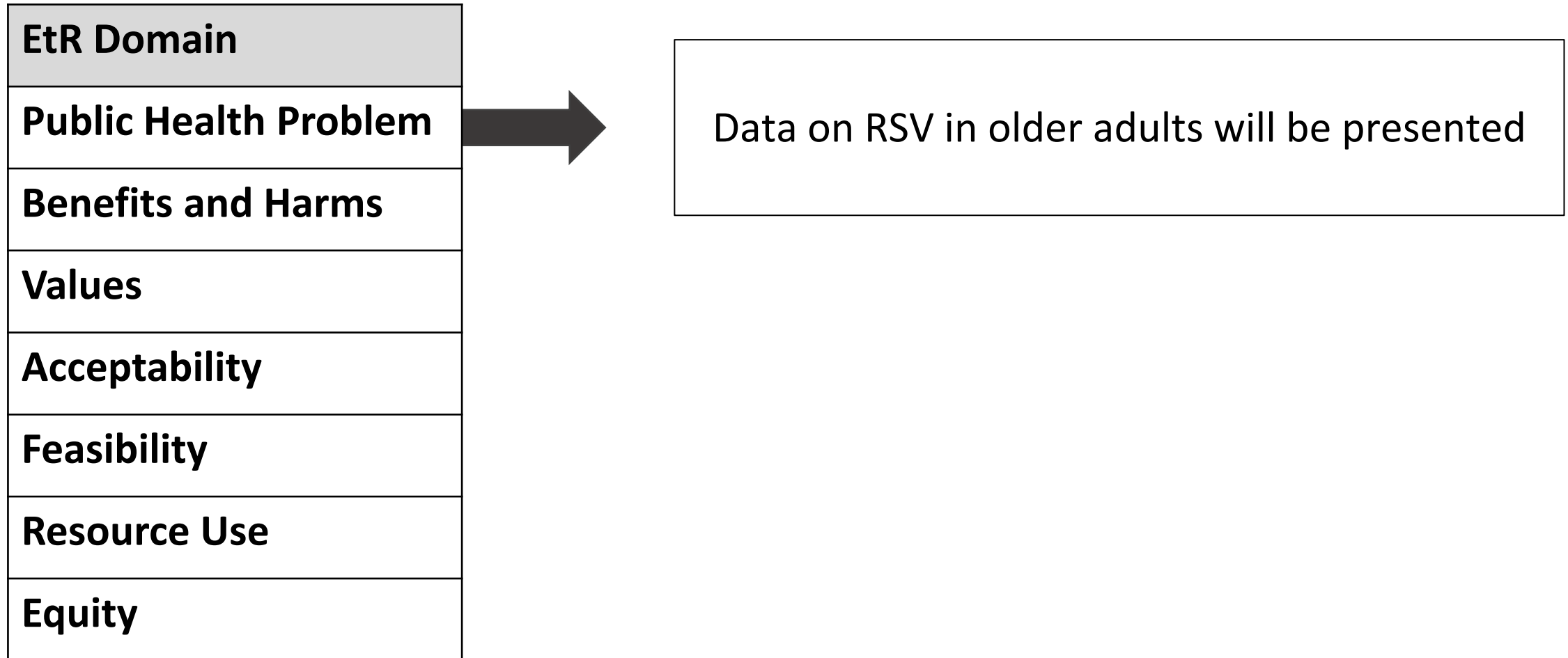
## Policy Questions

- 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?

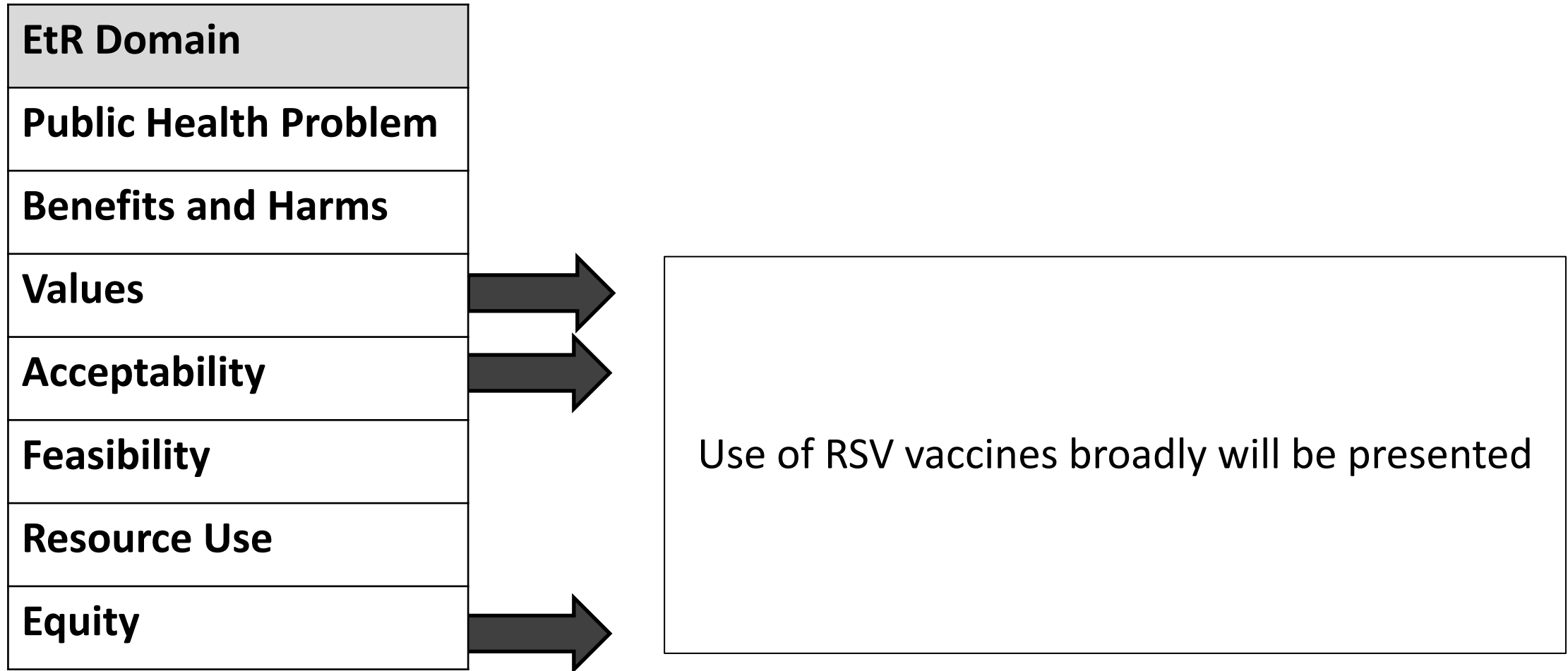
# Evidence to Recommendations (EtR) Framework

EtR Domain	Question(s)
<b>Public Health Problem</b>	<ul style="list-style-type: none"> <li>Is the problem of public health importance?</li> </ul>
<b>Benefits and Harms</b>	<ul style="list-style-type: none"> <li>How substantial are the desirable anticipated effects?</li> <li>How substantial are the undesirable anticipated effects?</li> <li>Do the desirable effects outweigh the undesirable effects?</li> </ul>
<b>Values</b>	<ul style="list-style-type: none"> <li>Does the target population feel the desirable effects are large relative to the undesirable effects?</li> <li>Is there important variability in how patients value the outcome?</li> </ul>
<b>Acceptability</b>	<ul style="list-style-type: none"> <li>Is the intervention acceptable to key stakeholders?</li> </ul>
<b>Feasibility</b>	<ul style="list-style-type: none"> <li>Is the intervention feasible to implement?</li> </ul>
<b>Resource Use</b>	<ul style="list-style-type: none"> <li>Is the intervention a reasonable and efficient allocation of resources?</li> </ul>
<b>Equity</b>	<ul style="list-style-type: none"> <li>What would be the impact of the intervention on health equity?</li> </ul>

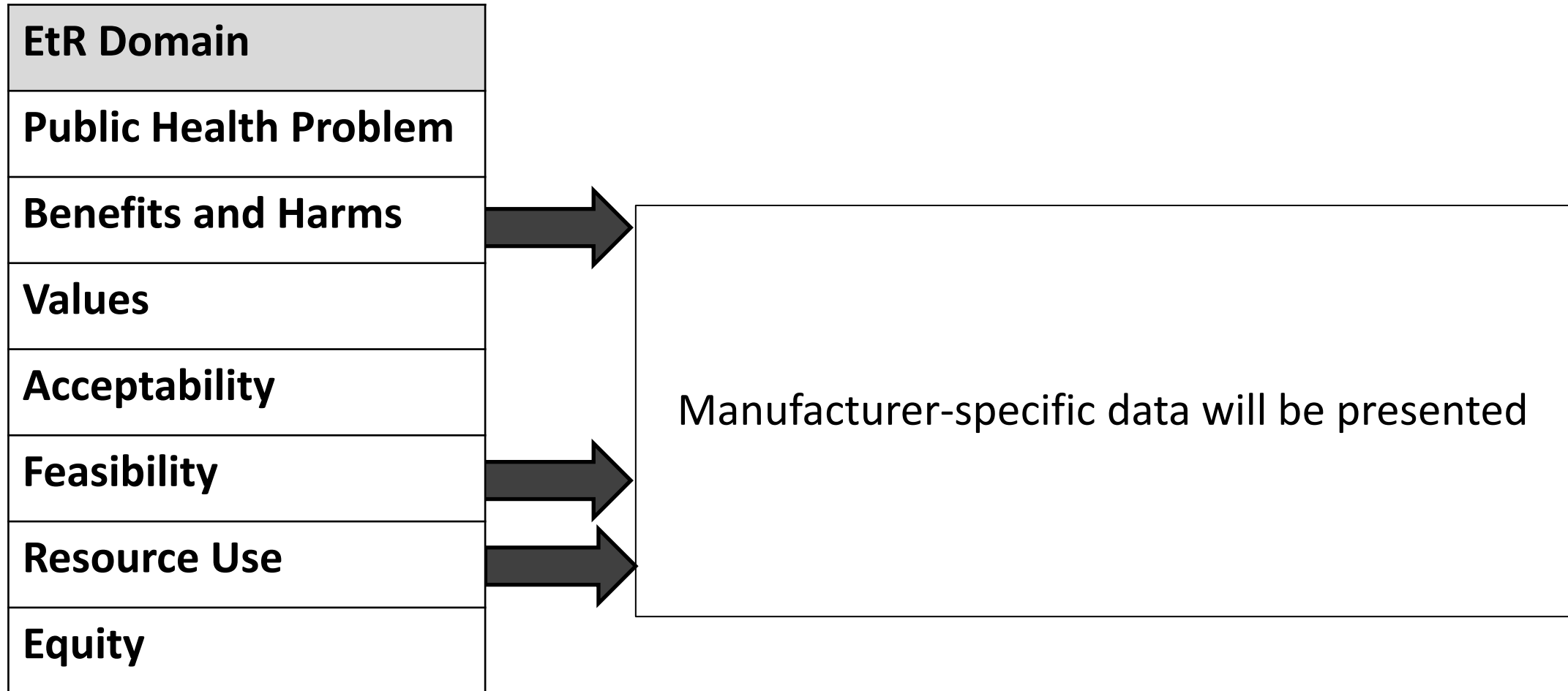
# Evidence to Recommendations (EtR) Framework



# Evidence to Recommendations (EtR) Framework



# Evidence to Recommendations (EtR) Framework

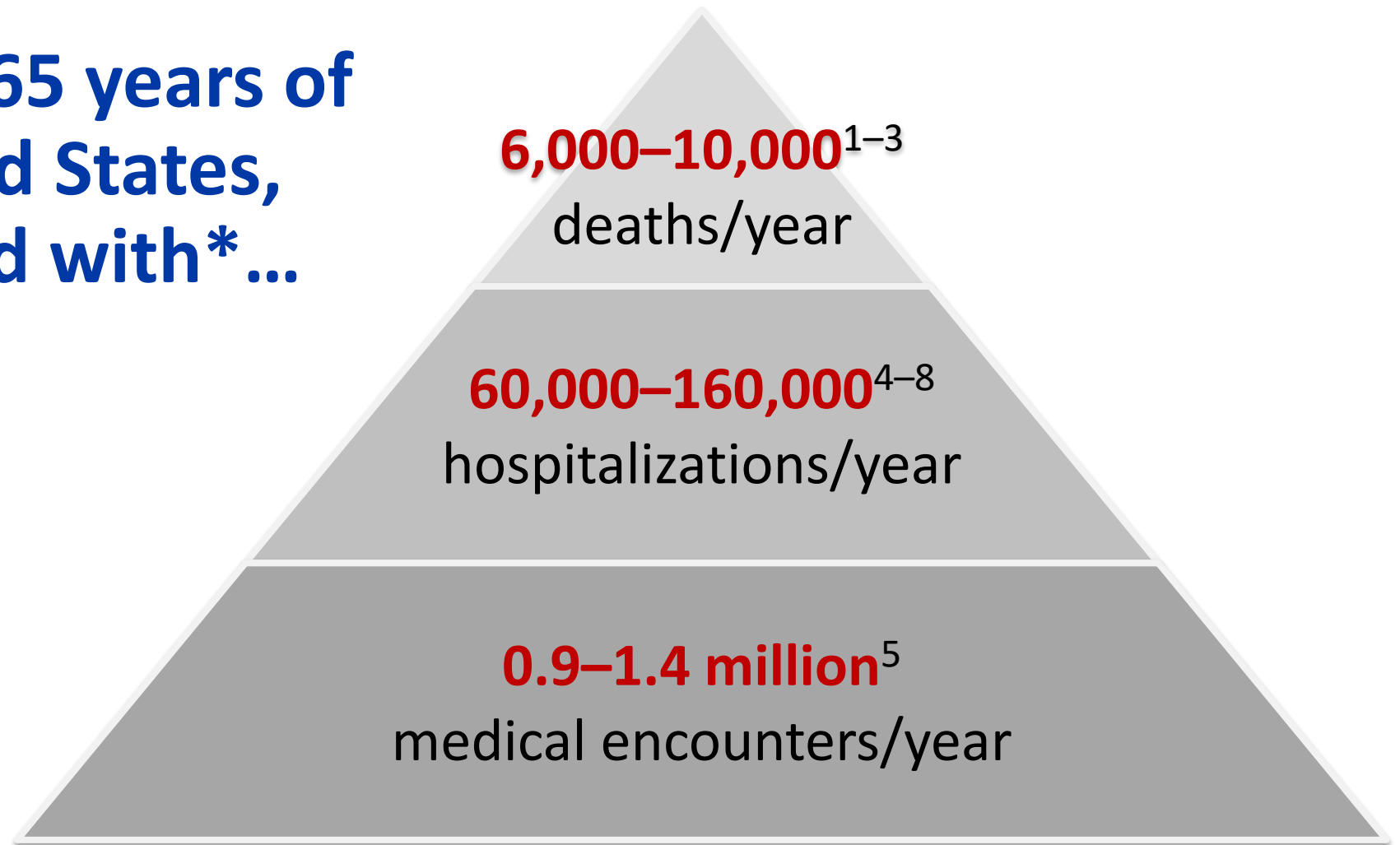


# Public Health Problem

Is RSV among older adults of public health importance?

# Among adults $\geq 65$ years of age in the United States, RSV is associated with\*...

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

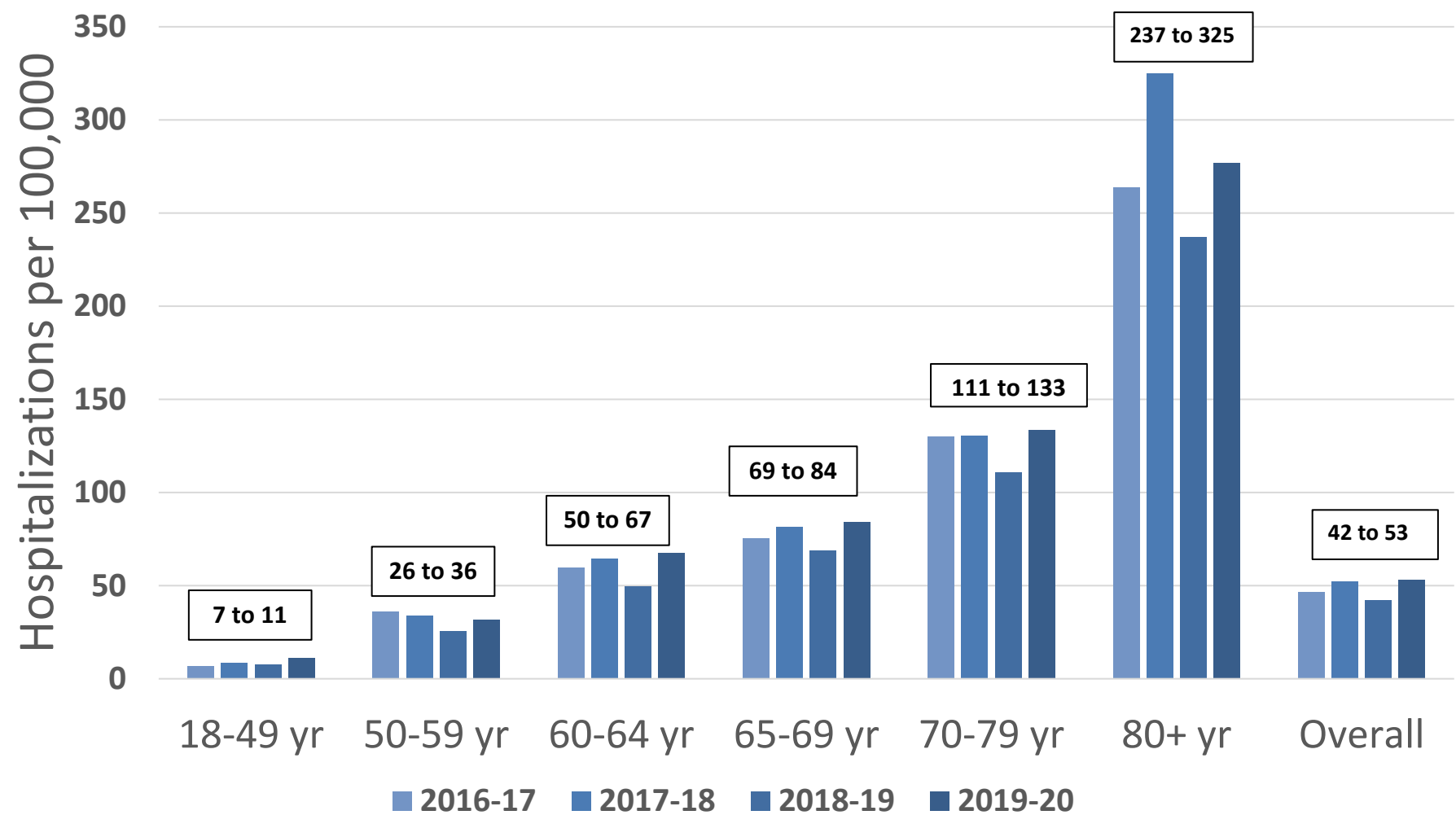


1. Thompson et al, JAMA (2003): <https://doi.org/10.1001/jama.289.2.179>
2. Matias et al, Influenza Other Respi Viruses (2014): <https://doi.org/10.1111/irv.12258>
3. Hansen et al, JAMA Network Open (2022): <https://doi.org/10.1001/jamanetworkopen.2022.0527>
4. Widmer et al, JAMA Network Open (2012): <https://doi.org/10.1093/infdis/jis309>

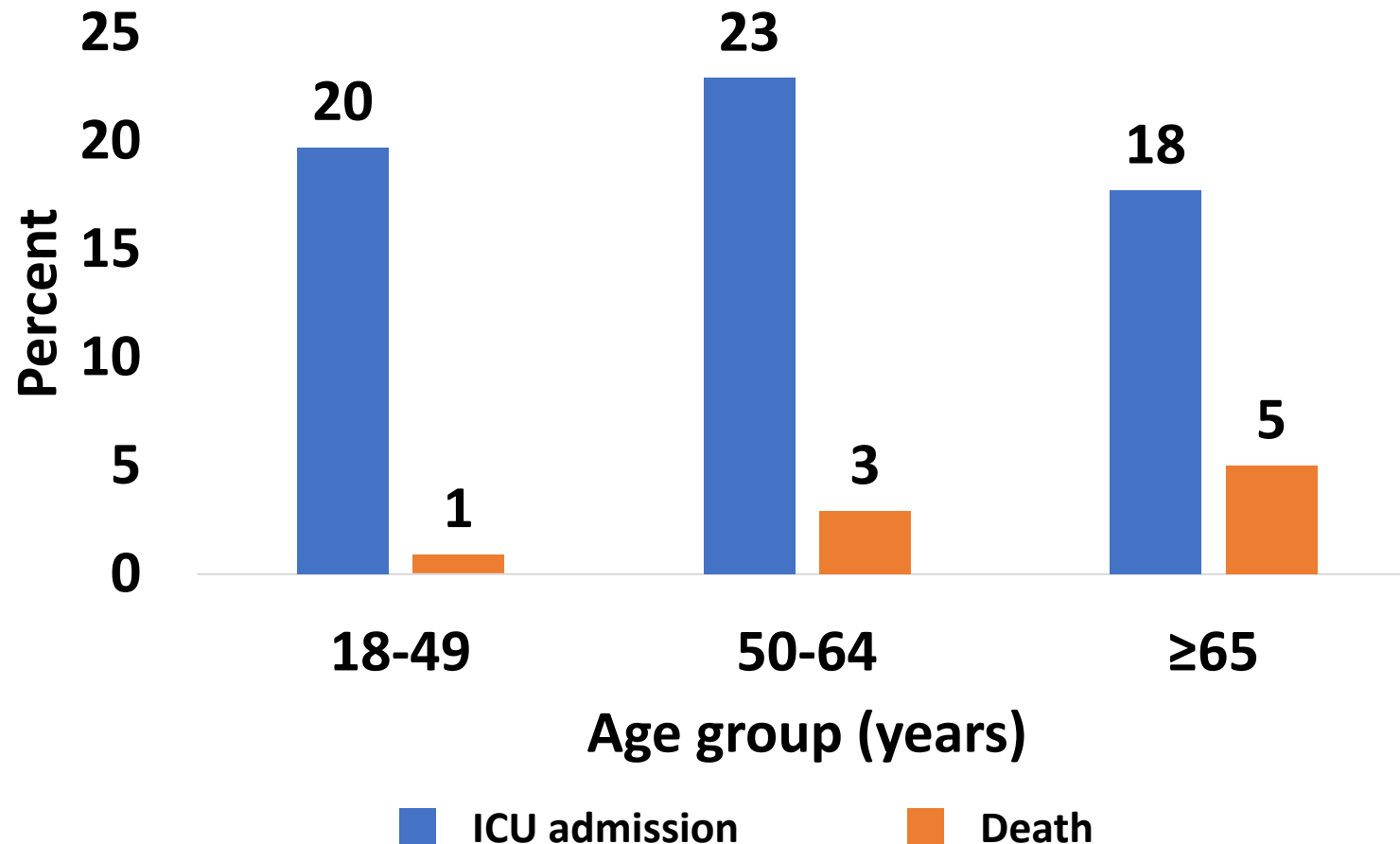
5. McLaughlin et al, Open Forum Infect Dis (2022): <https://doi.org/10.1093/ofid/ofac300>
6. Zheng et al, Pneumonia (2022): <https://doi.org/10.1186/s41479-022-00098-x>
7. Branche et al, Clinical Infect Dis (2022): <https://doi.org/10.1093/cid/ciab595>
8. CDC RSV-NET data 2016–2020 (unpublished)



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



# Outcomes among adults $\geq 18$ 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

# 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  $\geq 65$  years?

No	Probably No	Probably Yes	Yes	Varies	Don't know
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# 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 <b>≥60 years</b>
Intervention	GSK RSVpreF3 vaccine (120 µg antigen + AS01 <sub>E</sub> adjuvant, 1 dose IM) <b>-or-</b> Pfizer bivalent RSVpreF vaccine (120µg antigen, 1 dose IM)
Comparison	No RSV vaccine
Outcomes	<ul style="list-style-type: none"><li>■ RSV lower respiratory tract illness/disease (LRTI/LRTD)</li><li>■ Medically attended RSV LRTI/LRTD</li><li>■ Hospitalization for RSV respiratory illness</li><li>■ Severe RSV respiratory illness requiring supplemental O<sub>2</sub> or other respiratory support</li><li>■ Death due to RSV respiratory illness</li><li>■ Serious Adverse Events (SAEs)</li><li>■ Inflammatory neuropathy (e.g., Guillain-Barré syndrome)</li><li>■ Reactogenicity (grade ≥3)</li></ul>



# GRADE: GSK adjuvanted RSVpreF3

# GSK, Benefits: vaccine efficacy estimates

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

## RCT: Randomized control trial

<sup>a</sup> 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.

<sup>b</sup> 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>

<sup>c</sup> Underrepresentation of adults aged ≥80 years, exclusion of persons with immune compromise.

<sup>d</sup> 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.

<sup>e</sup> 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.

<sup>f</sup> No RSV-associated deaths were recorded in the interim analysis.

# GSK, Harms: relative risk

Outcome	Importance	Data sources	Relative risk estimate <sup>a</sup> (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 <sup>b</sup>	
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**

<sup>a</sup> 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.

<sup>b</sup> 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 <sup>a</sup> (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 <sup>b</sup>	
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

<sup>a</sup> 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.

<sup>b</sup> 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
<b>Benefits</b>				
RSV Lower Respiratory Tract Disease (LRTD)	Critical	RCT (1)	GSK RSVpreF3 likely reduces RSV LRTD.	<b>Moderate</b>
Medically attended RSV LRTD	Critical	RCT (1)	GSK RSVpreF3 likely reduces medically attended RSV LRTD.	<b>Moderate</b>
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
<b>Harms</b>				
Serious adverse events	Critical	RCT (2)	GSK RSVpreF3 results in little to no differences in SAEs.	<b>High</b>
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 $\geq 3$ )	Important	RCT (2)	GSK RSVpreF3 increases severe reactogenicity events.	<b>High</b>

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 <sup>a</sup>	84 vaccinations	90 vaccinations
1 RSV hospitalization <sup>b</sup>	1,097 vaccinations	1,348 vaccinations
1 RSV death <sup>c</sup>	21,442 vaccinations	27,284 vaccinations

<sup>a</sup> 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).

<sup>b</sup> 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).

<sup>c</sup> 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  $\geq 65$  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 O<sub>2</sub>/respiratory support
    - Death due to RSV respiratory illness

Minimal	Small	Moderate	Large	Varies	Don't know
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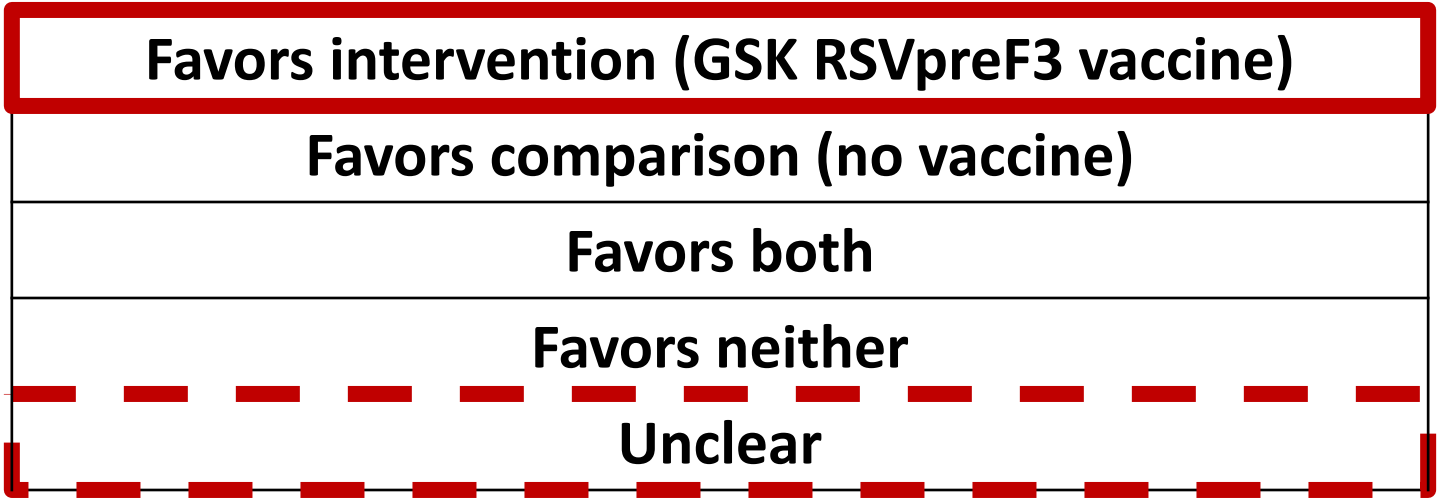
# Benefits and Harms GSK adjuvanted RSVpreF3 vaccine

- How substantial are the undesirable anticipated effects among adults aged  $\geq 65$  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  $\geq 3$ )

Minimal	Small	Moderate	Large	Varies	Don't know
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# Benefits and Harms GSK adjuvanted RSVpreF3 vaccine

- Do the desirable effects outweigh the undesirable effects among adults aged  $\geq 65$  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 <sup>a</sup> (95% confidence interval)	Concerns in certainty assessment
<b>Benefits</b>				
RSV Lower Respiratory Tract Illness (LRTI) <sup>b</sup>	Critical	One phase 3 RCT	85.7% (37.9%, 98.4%)	Indirectness (serious) <sup>c</sup>
Medically attended RSV LRTI <sup>b</sup>	Critical	One phase 3 RCT	80.0% (6.3%, 97.9%)	Indirectness (serious) <sup>c</sup>
Hospitalization for RSV respiratory illness	Important	Counts not provided	Unable to evaluate <sup>d</sup>	
Severe RSV respiratory illness requiring O2/respiratory support	Important	Counts not provided	Unable to evaluate <sup>d</sup>	
Death due to RSV respiratory illness	Important	One phase 3 RCT	Unable to evaluate <sup>e</sup>	

## RCT: Randomized control trial

<sup>a</sup> 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.

<sup>b</sup> 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.

<sup>c</sup> Underrepresentation of adults aged ≥80 years, exclusion of persons with immune compromise.

<sup>d</sup> Counts of event were not provided by manufacturer.

<sup>e</sup> No RSV-associated deaths were recorded in the interim analysis.

# Pfizer, Harms: relative risk

Outcome	Importance	Data sources	Relative risk estimate <sup>a</sup> (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 <sup>b</sup>	
Reactogenicity (grade ≥3)	Important	One phase 3 RCT one phase 1/2 RCT	1.47 (0.88 to 2.46)	Imprecision (serious) <sup>c</sup>

## RCT: Randomized control trial

<sup>a</sup> 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.

<sup>b</sup> 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.

<sup>c</sup> 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 <sup>a</sup> (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 <sup>b</sup>	
Reactogenicity (grade ≥3)	Important	One phase 3 RCT one phase 1/2 RCT	1.47 (0.88 to 2.46)	Imprecision (serious) <sup>c</sup>

**RCT: Randomized control trial**

<sup>a</sup> 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.

<sup>b</sup> 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.

<sup>c</sup> 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
<b>Benefits</b>				
RSV Lower Respiratory Tract Illness (LRTI)	Critical	RCT (1)	Pfizer RSVpreF likely reduces RSV LRTI.	<b>Moderate</b>
Medically attended RSV LRTI	Critical	RCT (1)	Pfizer RSVpreF likely reduces medically attended RSV LRTI.	<b>Moderate</b>
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
<b>Harms</b>				
Serious adverse events (SAEs)	Critical	RCT (2)	Pfizer RSVpreF results in little to no difference in SAEs.	<b>High</b>
Inflammatory neuropathy	Important	RCT (2)	Measures of relative and absolute risk not calculated due to small number of events.	Unable to evaluate
Reactogenicity (grade $\geq 3$ )	Important	RCT (2)	Pfizer RSVpreF likely increases severe reactogenicity events.	<b>Moderate</b>

# Summary of GRADE for Pfizer RSV vaccine in older adults

Outcome	Importance	Design (# of studies)	Findings	Evidence type
<b>Benefits</b>				
RSV Lower Respiratory Tract Illness (LRTI)	Critical	RCT (1)	Pfizer RSVpreF likely reduces RSV LRTI.	<b>Moderate</b>
Medically attended RSV LRTI	Critical	RCT (1)	Pfizer RSVpreF likely reduces medically attended RSV LRTI.	<b>Moderate</b>
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
<b>Harms</b>				
Serious adverse events (SAEs)	Critical	RCT (2)	Pfizer RSVpreF results in little to no difference in SAEs.	<b>High</b>
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.	<b>Moderate</b>

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 <sup>a</sup>	95 vaccinations	103 vaccinations
1 RSV hospitalization <sup>b</sup>	1,275 vaccinations	1,567 vaccinations
1 RSV death <sup>c</sup>	24,927 vaccinations	31,717 vaccinations

<sup>a</sup> 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).

<sup>b</sup> 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).

<sup>c</sup> 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  $\geq 65$  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 O<sub>2</sub>/respiratory support
    - Death due to RSV respiratory illness

Minimal	Small	Moderate	Large	Varies	Don't know
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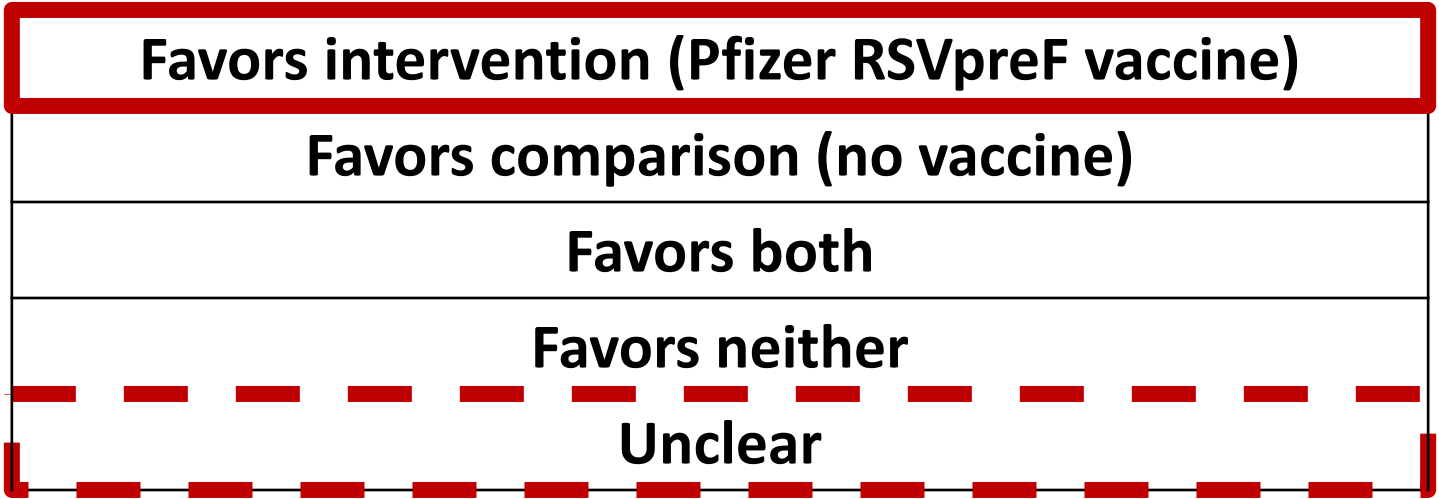
# Benefits and Harms Pfizer bivalent RSVpreF vaccine

- How substantial are the undesirable anticipated effects among adults aged  $\geq 65$  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  $\geq 3$ )

Minimal	Small	Moderate	Large	Varies	Don't know
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# Benefits and Harms Pfizer bivalent RSVpreF vaccine

- Do the desirable effects outweigh the undesirable effects among adults aged  $\geq 65$  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 $\geq 60$ 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**



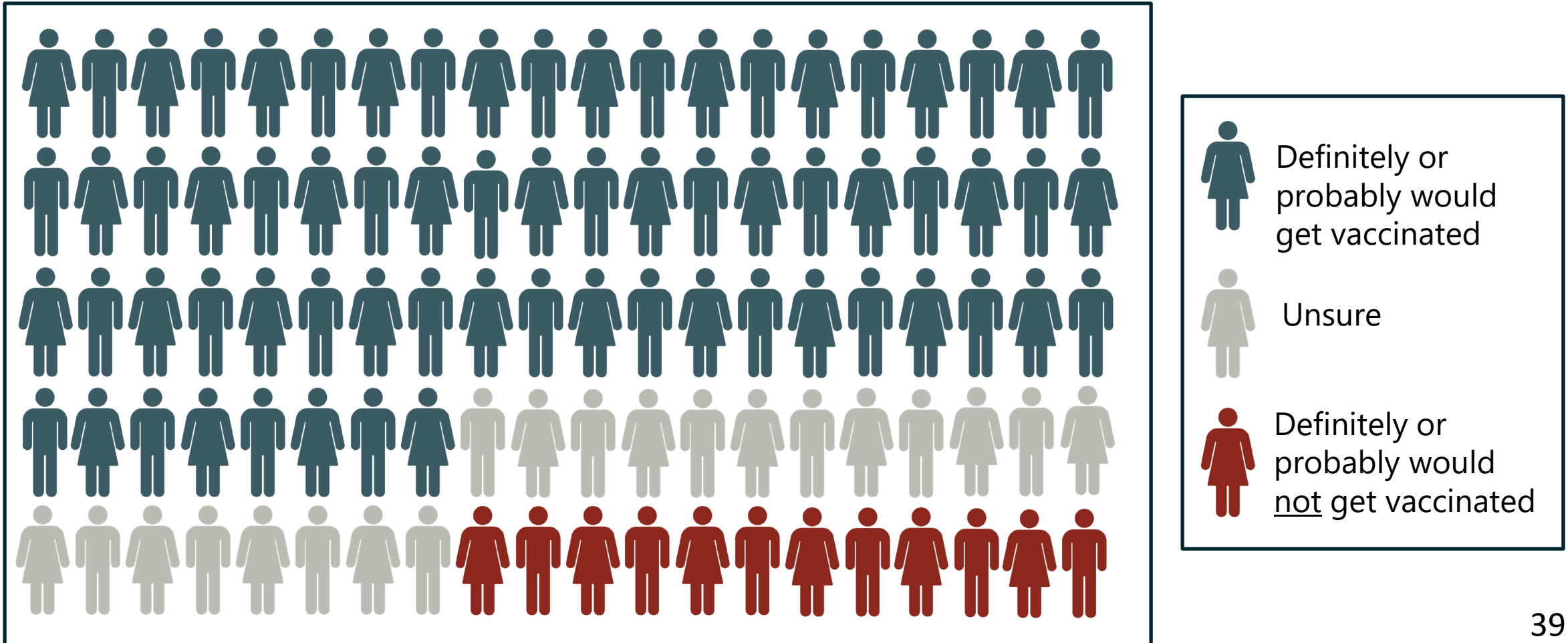
**RACE/ETHNICITY**



**AGE**

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% $\geq 70$ years
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68% of respondents said they 'definitely' or 'probably' would get vaccinated if a safe and effective FDA-approved RSV vaccine was available

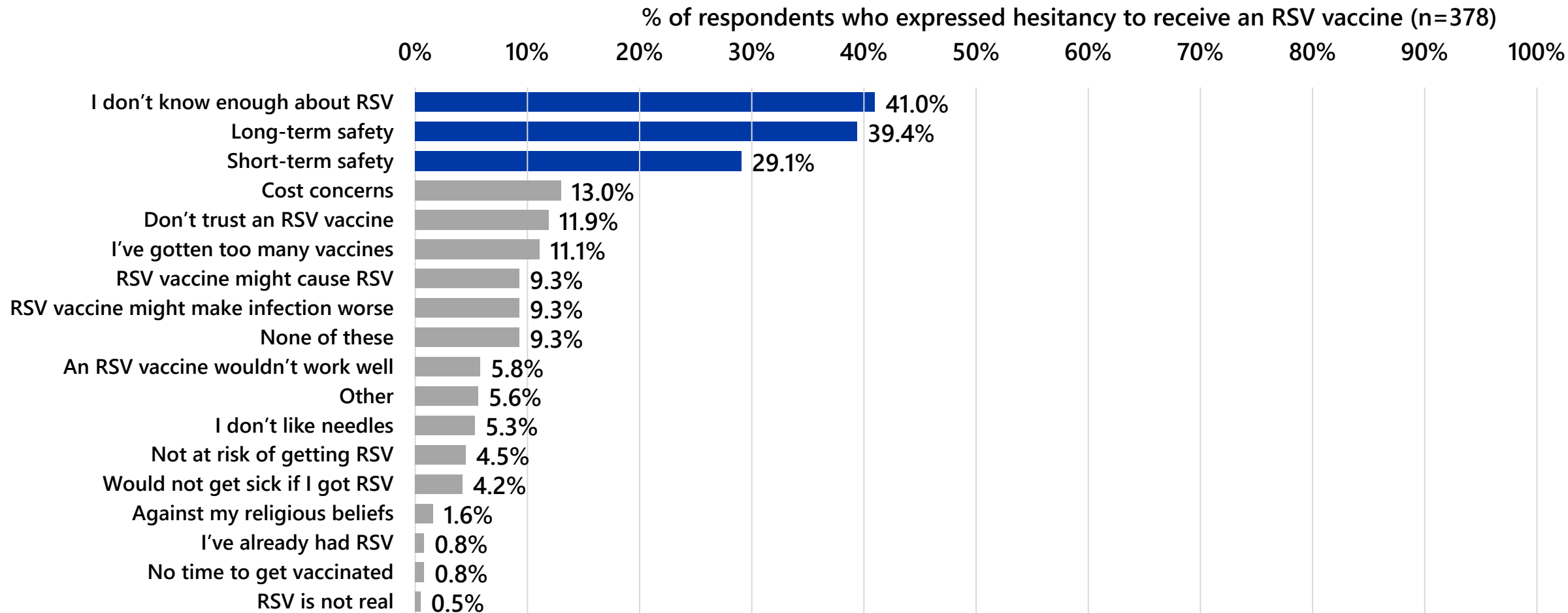


# 77% said they 'definitely' or 'probably' would get an RSV vaccine if it were recommended by a **healthcare provider**





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



# 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
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# 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?

<b>Important uncertainty or variability</b>
<b>Probably important uncertainty or variability</b>
<b>Probably not important uncertainty or variability</b>
<b>No important uncertainty or variability</b>
<b>No known undesirable outcomes</b>

# Acceptability

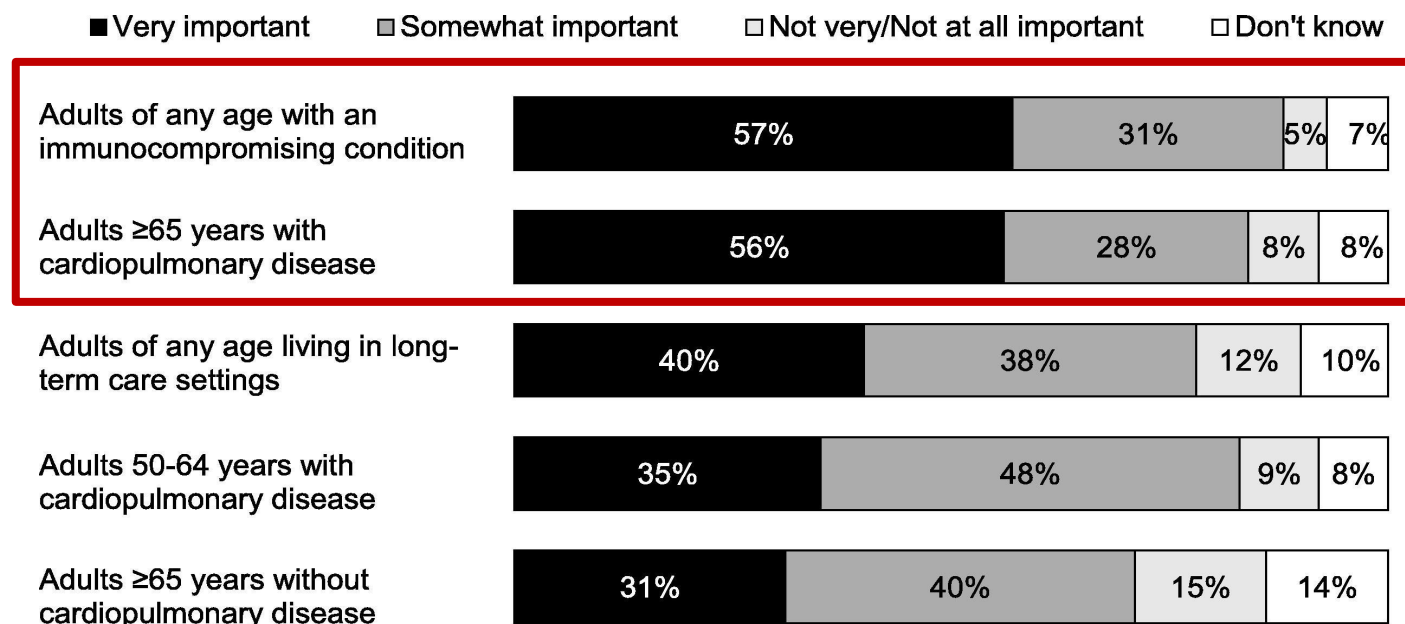
**Would recommending RSV vaccines for older adults be acceptable to key stakeholders?**

# Vaccine Policy Collaborative Initiative

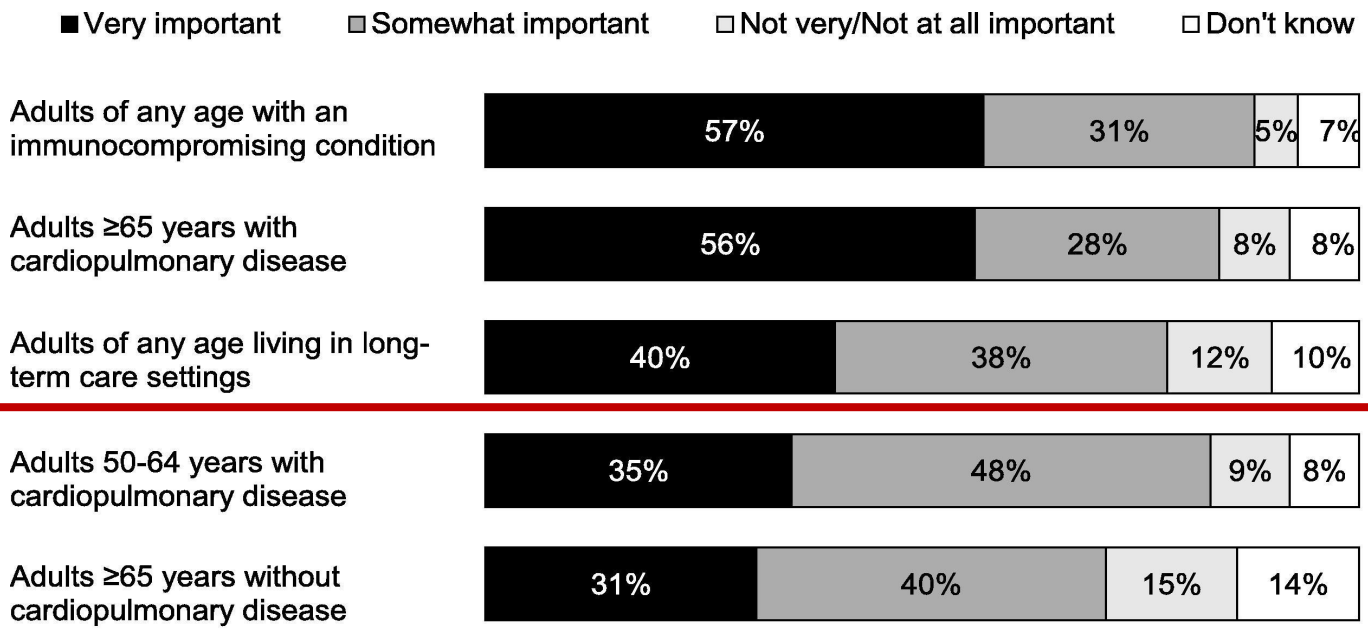
- Survey of physicians, February–March 2017
- National network of 930 primary care physicians who agreed to participate in surveys about vaccine policy issues
  - 620 physicians (67%) completed the survey
  - Responses analyzed from 317 respondents (51%) who reported caring for  $\geq 1$  adult patient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

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)



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



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%).

# Acceptability

- Would recommending RSV vaccines for adults aged  $\geq 65$  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
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# 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
<b>Reconstitution required:</b> single dose vial of lyophilized powder (antigen component) + single dose vial of liquid (adjuvant component)	<b>Reconstitution required:</b> 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 <b>4 hours</b> , otherwise discarded	After reconstitution, the product should be administered within <b>4 hours</b> , 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
<u>Influenza inactivated</u> (IIV4) or <u>Influenza recombinant</u> (RIV4)	1 dose annually	
<u>Tetanus, diphtheria, pertussis</u> (Tdap or Td)	1 dose Tdap, then Td or Tdap booster every 10 years	
<u>Zoster recombinant</u> (RZV)	2 doses	
<u>Pneumococcal</u> (PCV15, PCV20, PPSV23)	1 dose PCV15 followed by PPSV23 OR 1 dose PCV20 ( <u>see notes</u> )	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  $\geq 65$  years?
- Is the Pfizer bivalent RSVpreF vaccine feasible to implement among adults aged  $\geq 65$  years?

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

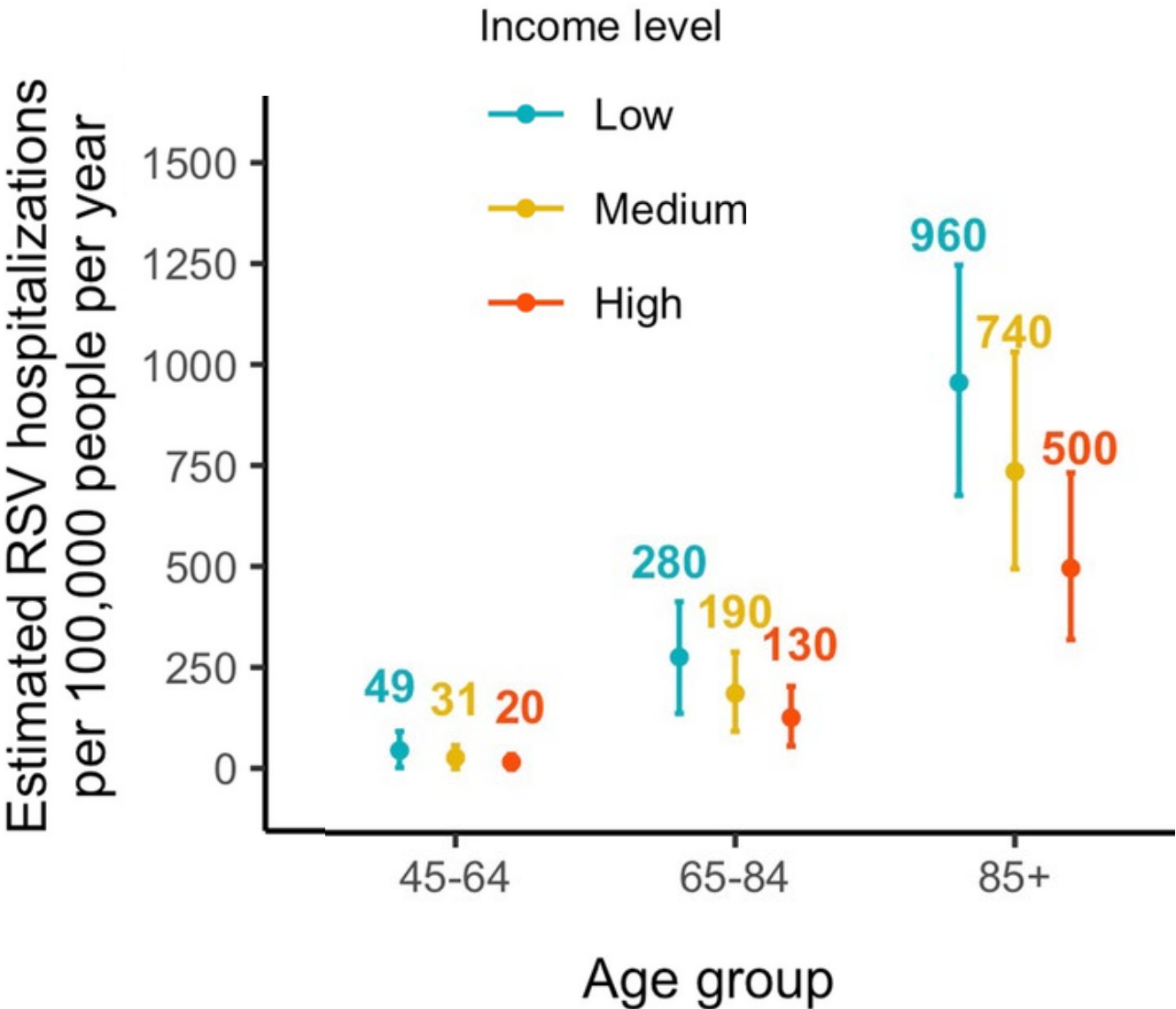
- Is use of GSK adjuvanted RSVpreF3 vaccine among adults aged  $\geq 65$  years a reasonable and efficient allocation of resources, compared with no RSV vaccine?
- Is use of Pfizer bivalent RSVpreF vaccine among adults aged  $\geq 65$  years a reasonable and efficient allocation of resources, compared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

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



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

	N	Median age, years (interquartile range)
<b>All</b>	9,163	70 (58–81)
<b>Race and ethnicity</b>		
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)

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# 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 <sup>a</sup>	Asthma
Black, non-Hispanic <sup>b</sup>	↑ <sup>c</sup>	↑ ↑ <sup>c</sup>	↑ <sup>c,d</sup>		↑ <sup>e,f</sup>
AI/AN <sup>g</sup> , non-Hispanic <sup>b</sup>		↑ ↑ <sup>h</sup>	↑ ↑ <sup>h</sup>		↑ <sup>e</sup>
Hispanic <sup>a</sup>			↑ <sup>c,d,h</sup>		↓ <sup>e,f</sup>
Asian, non-Hispanic <sup>b</sup>	↓ <sup>c</sup>	↓ <sup>c</sup>	↑ <sup>c,d</sup>	↓ <sup>h</sup>	↓ <sup>e</sup>
Lower income or SES <sup>i</sup>	↑ <sup>j</sup>	↑ <sup>h,j,k</sup>	↑ <sup>h,l</sup>	↑ <sup>h</sup>	↑ <sup>e,f,h</sup>

<sup>a</sup> COPD = chronic obstructive pulmonary disease

<sup>b</sup> Compared with non-Hispanic White adults

<sup>c</sup> Tsao et al, Circulation (2022): <https://doi.org/10.1161/cir.0000000000001052>

<sup>d</sup> Cheng et al, JAMA (2019): <https://doi.org/10.1001/jama.2019.19365>

<sup>e</sup> [https://www.cdc.gov/asthma/most\\_recent\\_national\\_asthma\\_data.htm](https://www.cdc.gov/asthma/most_recent_national_asthma_data.htm)

<sup>f</sup> Bhan et al, Am J Public Health (2015): <https://doi.org/10.2105/ajph.2014.302172>

<sup>g</sup> AI/AN = American Indian or Alaska Native

<sup>h</sup> NHIS 2018: <https://www.cdc.gov/nchs/nhis/shs/tables.htm>

<sup>i</sup> SES = socio-economic status

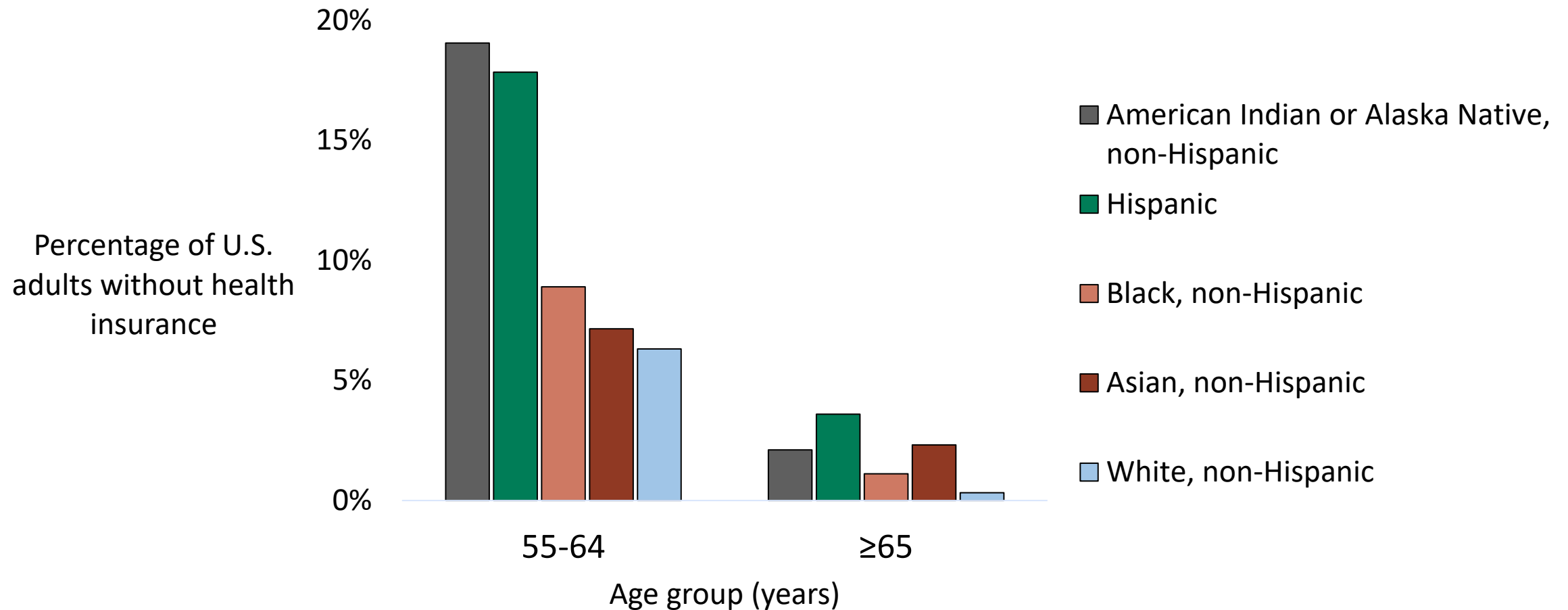
<sup>j</sup> Abdalla et al, JAMA Netw Open (2020):

<https://doi.org/10.1001%2Fjamanetworkopen.2020.18150>

<sup>k</sup> Hamad et al, JAMA Cardiol (2020): <https://doi.org/10.1001/jamacardio.2020.1458>

<sup>l</sup> 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



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

Age group (years)	Percentage of population without health insurance			
	<i>Below poverty</i>	<i>1.0–1.9x poverty</i>	<i>2.0–2.9x poverty</i>	<i>≥3.0x poverty</i>
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



# Equity

- What would be the impact on health equity of recommending RSV vaccines in adults aged  $\geq 65$  years?

<b>Reduced</b>
<b>Probably reduced</b>
<b>Probably no impact</b>
<b>Probably increased</b>
<b>Increased</b>
<b>Varies</b>
<b>Don't know</b>

# Summary

Domain	Question	Work Group Judgements	
		GSK	Pfizer
	<b>Adults aged ≥65 years</b>		
<b>Public Health Problem</b>	Is RSV of public health importance?	Yes	
<b>Benefits and Harms</b>	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
<b>Values</b>	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	
<b>Acceptability</b>	Is the intervention acceptable to key stakeholders?	Yes/Probably yes	
<b>Feasibility</b>	Is the intervention feasible to implement?	Yes/Probably yes	Yes/Probably yes
<b>Resource Use</b>	Is the intervention a reasonable and efficient allocation of resources?	Yes/Probably yes	Yes/Probably yes
<b>Equity</b>	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	<ul style="list-style-type: none"> <li>• 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)</li> <li>• Aligns with licensure for adjuvanted and high-dose influenza vaccines and age-based pneumococcal vaccination</li> </ul>	<ul style="list-style-type: none"> <li>• 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</li> </ul>
Age ≥60 years	<ul style="list-style-type: none"> <li>• Potential to prevent a greater total burden of disease (e.g., number of hospitalizations)</li> <li>• 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)</li> </ul>	<ul style="list-style-type: none"> <li>• Uninsured adults would have difficulty obtaining vaccination (disproportionately aged 60–64 in racial, ethnic and socioeconomic groups at greater risk)</li> <li>• May experience more difficulty achieving clinician adoption of the recommendation among patients 60–64</li> <li>• Less efficient allocation of societal resources</li> </ul>

\*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)

Among adults aged  $\geq 65$  years:

--- Minority opinion

<b>Balance of consequences</b>	Undesirable consequences <i>clearly outweigh</i> desirable consequences in most settings	Undesirable consequences <i>probably outweigh</i> desirable consequences in most settings	The balance between desirable and undesirable consequences is <i>closely balanced</i> or <i>uncertain</i>	Desirable consequences <i>probably outweigh</i> undesirable consequences in most settings	Desirable consequences <i>clearly outweigh</i> undesirable consequences in most settings	There is insufficient evidence to determine the balance of consequences
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Among adults aged  $\geq 60$  years:

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



# Evidence to Recommendations Framework

Summary: Work Group Interpretations (Pfizer RSVpreF)

# Evidence to Recommendations Framework

## Summary: Work Group Interpretations (Pfizer RSVpreF)

Among adults aged  $\geq 65$  years:

--- Minority opinion

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

Among adults aged  $\geq 60$  years:

<b>Balance of consequences</b>	Undesirable consequences <i>clearly outweigh</i> desirable consequences in most settings	Undesirable consequences <i>probably outweigh</i> desirable consequences in most settings	The balance between desirable and undesirable consequences is <i>closely balanced</i> or <i>uncertain</i>	Desirable consequences <i>probably outweigh</i> undesirable consequences in most settings	Desirable consequences <i>clearly outweigh</i> undesirable consequences in most settings	There is insufficient evidence to determine the balance of consequences
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# Evidence to Recommendations Framework

## Summary: Work Group Interpretations (Pfizer RSVpreF)

### Type of recommendation, adults aged $\geq 65$ 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 $\geq 60$ 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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# 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  $\geq 65$  years?
- Should vaccination with **GSK RSVpreF3 vaccine** (120µg antigen + AS01E adjuvant, 1 dose IM), rather than no vaccine, be recommended in persons aged  $\geq 60$  years?
- Should vaccination with **Pfizer bivalent RSVpreF vaccine** (120µg antigen, 1 dose IM), rather than no vaccine, be recommended in persons aged  $\geq 65$  years?
- Should vaccination with **Pfizer bivalent RSVpreF vaccine** (120µg antigen, 1 dose IM), rather than no vaccine, be recommended in persons aged  $\geq 60$  years?

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

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

