Evidence to Recommendations Framework (EtR): RSV Vaccination in Adults Aged 50–59 years

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Policy questions

- **Should adults aged 50–59 years at increased risk of severe RSV disease be recommended to receive a single dose of RSV vaccination?**

We plan to consider adults aged 18–49 years at increased risk of severe RSV disease at the June 2025 meeting.

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 uncertainty about, or variability in, how much people value the main outcomes?
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 the impact of the intervention on health equity?

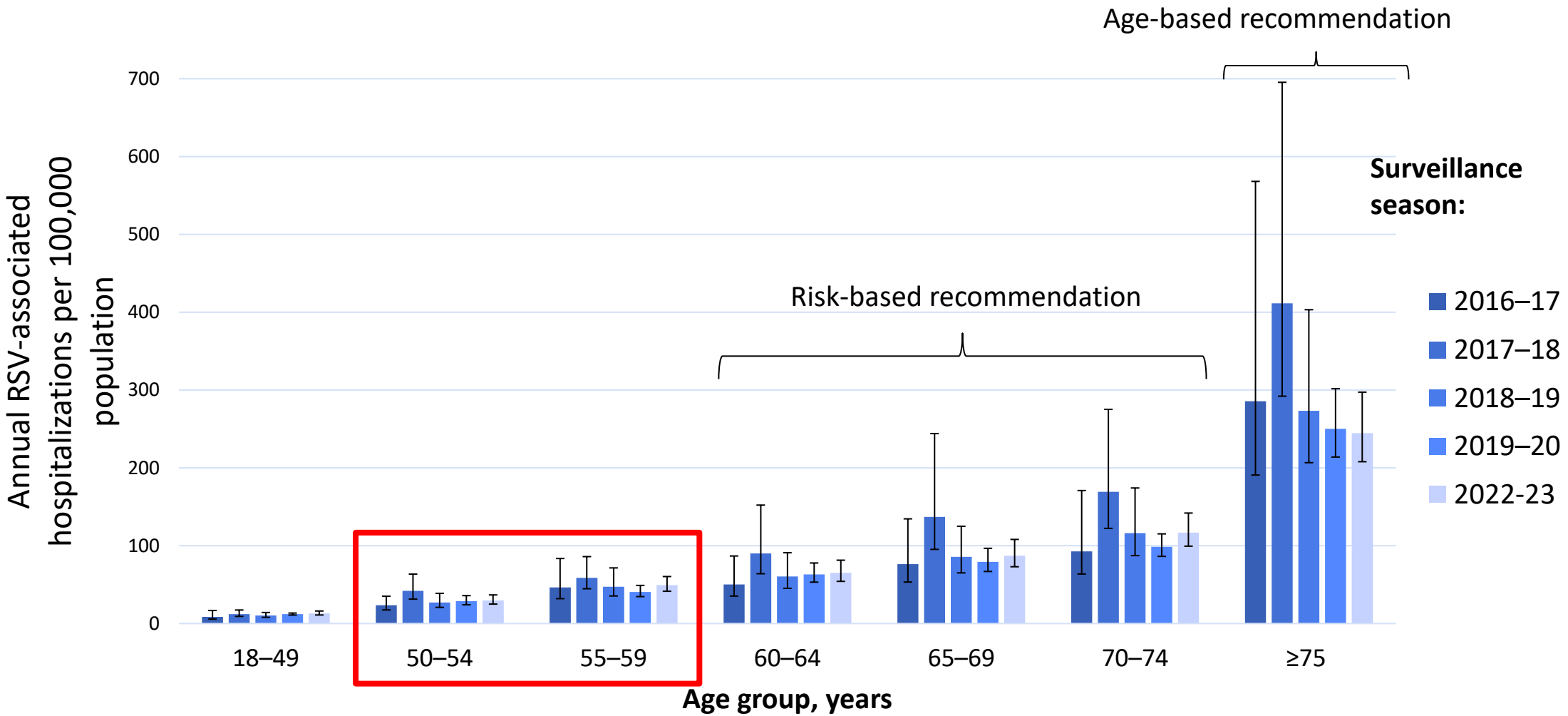
EtR Domain: Public Health Problem

Is the problem of public health importance **among adults aged 50-59 years at increased risk of severe RSV disease?**

What do we know about RSV epidemiology in adults aged 50–59 years?

- Population-based rates of RSV disease among adults aged 50–59 years are lower than those among older adults

Estimated annual RSV-associated **hospitalization** rates per 100,000 adults* aged **≥18 years** by age group and year, RSV-NET, 2016–17 to 2019–20 and 2022–23

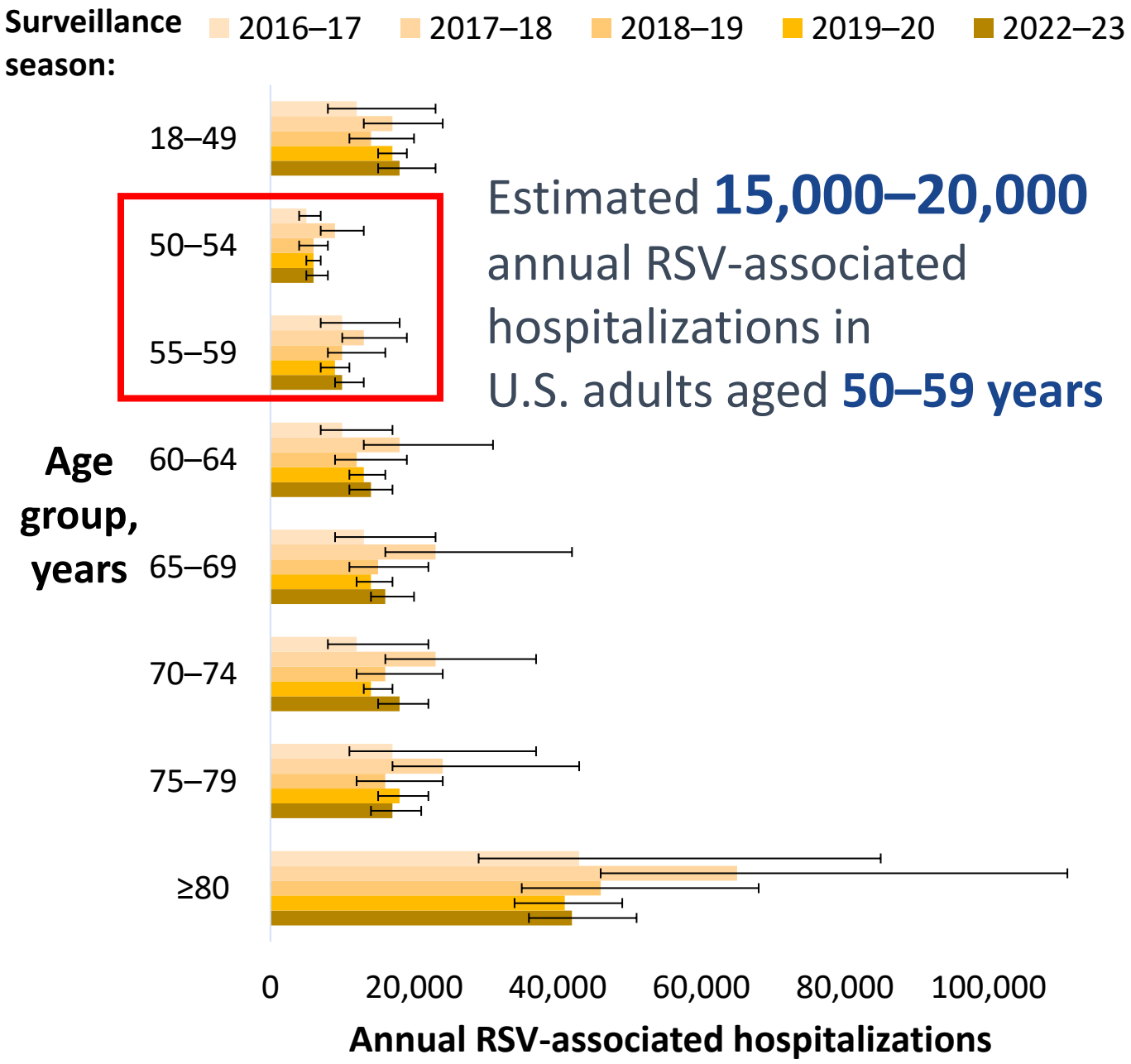


Havers FP, et al. Burden of Respiratory Syncytial Virus–Associated Hospitalizations in US Adults, October 2016 to September 2023. JAMA Netw Open. 2024;7(11):e2444756. https://pmc.ncbi.nlm.nih.gov/articles/PMC11561688/

Hospitalization rates were adjusted for under-detection of RSV infection due to testing practices and diagnostic test sensitivity. Season is defined as October to April for 2016 to 2017 through 2019 to 2020 and as October to September for 2022 to 2023. Error bars represent 95% CIs.

*Estimated rates exclude recorded hospitalizations among pregnant women.

Estimated annual number of RSV-associated hospitalizations* among adults aged ≥18 years by age group and year, RSV-NET, 2016–17 to 2019–20, 2022–23



Estimated **15,000–20,000** annual RSV-associated hospitalizations in U.S. adults aged **50–59 years**

Havers FP, et al. Burden of Respiratory Syncytial Virus-Associated Hospitalizations in US Adults, October 2016 to September 2023. JAMA Netw Open. 2024 Nov 4;7(11):e2444756. https://pubmed.ncbi.nlm.nih.gov/39535791/

*Estimated hospitalizations exclude recorded hospitalizations among pregnant women.

What do we know about RSV epidemiology in adults aged 50–59 years?

- Population-based rates of RSV disease among adults aged 50–59 years are lower than those among older adults
- However, we know that some younger adults are at increased risk of RSV hospitalization, even if the risk in the general population is low

Top 10 most common underlying medical conditions among adults aged ≥50 years hospitalized with RSV are similar by age

Major medical condition categories among persons aged 50–59 years hospitalized with RSV	Weighted %
Cardiovascular disease	46.3
Diabetes mellitus	37.0
Asthma	29.7
COPD or chronic bronchitis	26.5
Immunocompromised condition	25.5
Severe obesity (BMI ≥40 kg/m^2)	21.3
Chronic kidney disease	19.8
Neurologic disorder	19.4
Gastrointestinal, liver, or pancreatic disease	9.8
Blood disorder	4.5

Major medical condition categories among persons aged ≥60 years hospitalized with RSV	Weighted %
Cardiovascular disease	66.7
Diabetes mellitus	36.9
COPD or chronic bronchitis	35.0
Chronic kidney disease	29.1
Neurologic disorder	26.5
Immunocompromised condition	18.5
Asthma	18.1
Severe obesity (BMI ≥40 kg/m^2)	10.7
Gastrointestinal, liver, or pancreatic disease	6.5
Rheumatologic disease	4.2

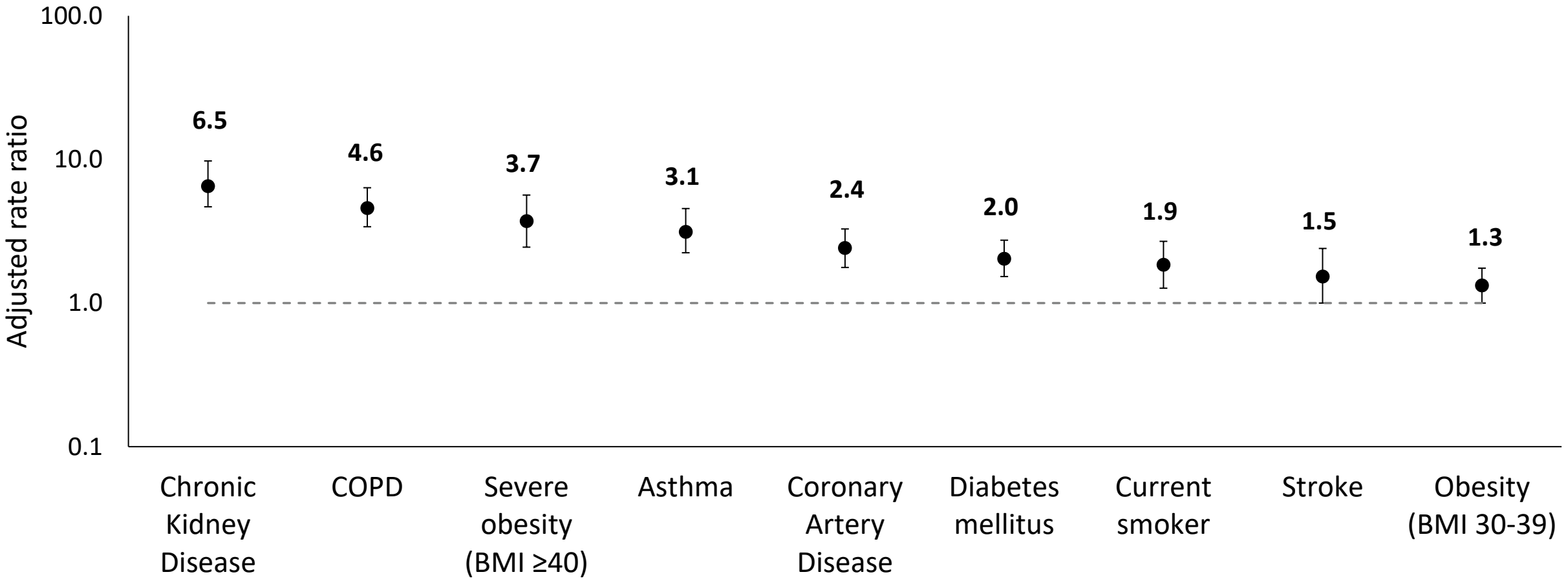
BMI: body mass index; COPD: chronic obstructive pulmonary disease

Unpublished RSV-NET data, 2015–2016 to 2017–2018, 2022–2023, and 2023–2024

Categories are not mutually exclusive; individual patients may have underlying conditions in more than one category

Slide credit: Dr. Monica Patton

Adjusted Rate Ratios for RSV-Associated Hospitalization by Chronic Condition among Community-Dwelling Adults Aged ≥50 Years



Unpublished data. Update on analysis from Woodruff et al. First presented to ACIP in February 2024: https://www.cdc.gov/acip/downloads/slides-2024-02-28-29/03-RSV-Adults-Woodruff-508.pdf

BMI: Body Mass Index (kg/m^2), COPD: Chronic Obstructive Pulmonary Disease. Data are preliminary and unpublished. Current smoking is defined as smoking cigarettes every day or some days at the time of survey response. Adjusted rate ratios and 95% confidence intervals are derived from Poisson regression using Monte Carlo simulation methods and adjust for age, sex and race and ethnicity group. Error bars represent 95% confidence intervals.

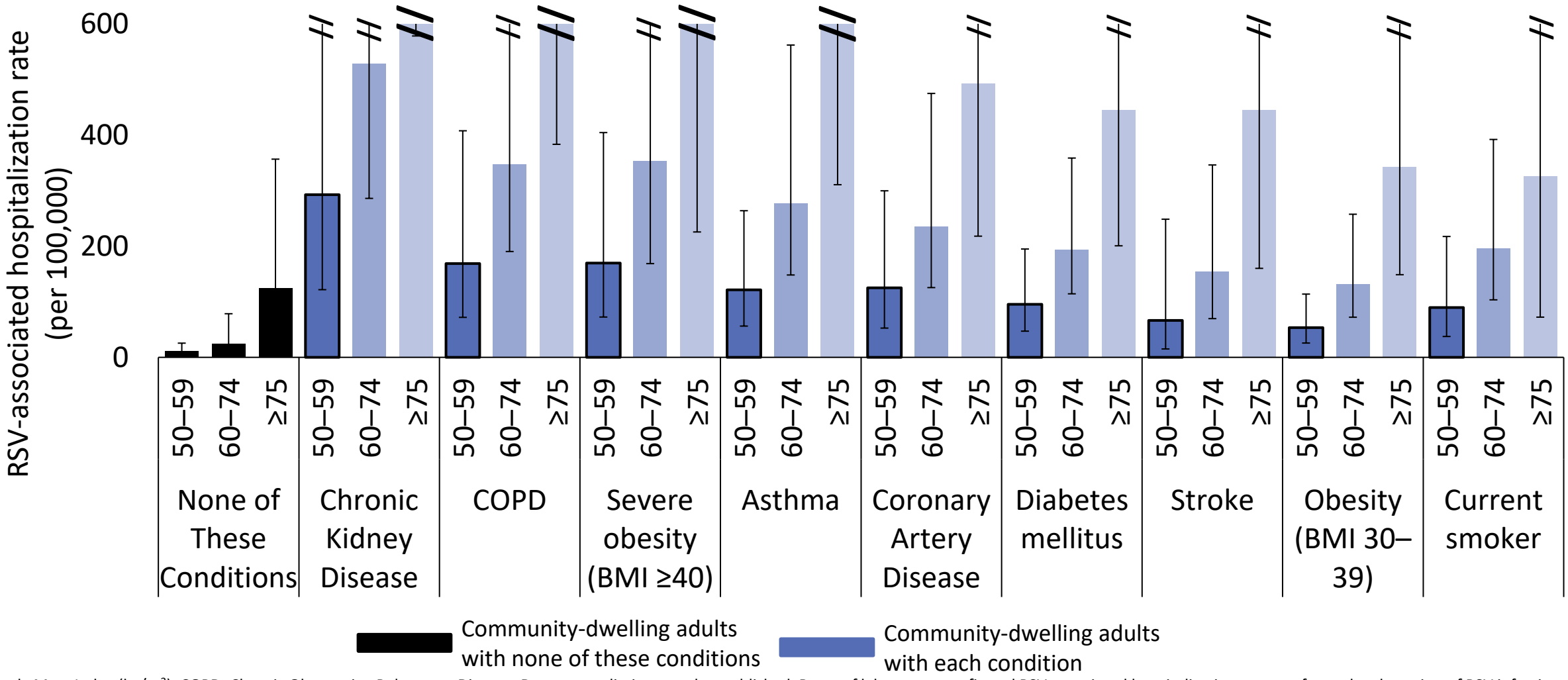
Among community-dwelling adults aged ≥50 years, a history of **≥2 chronic conditions** and **age ≥75 years** were the strongest **independent** risk factors for RSV-associated hospitalization.

	aRR (95% CI)[1]
Number of chronic conditions[2]	
0	ref
1	2.1 (1.4, 3.2)
≥2	**7.3 (5.0, 10.6)**
Age group, years	
50–59	ref
60–74	1.9 (1.3, 2.7)
≥75	**6.0 (4.2, 8.6)**
Race or ethnicity group	
White, non-Hispanic	ref
Black, non-Hispanic	1.1 (0.8, 1.5)
Other race or Hispanic ethnicity	1.7 (1.3, 2.5)
Sex	
Male	Ref
Female	1.3 (1.0, 1.6)

[1] Adjusted rate ratios (aRR) and 95% confidence intervals (CI) were estimated using Poisson regression and Monte Carlo simulation. Adjusted for all covariates in table.
[2] Includes history of asthma, chronic kidney disease, chronic obstructive pulmonary disease, coronary artery disease, current smoker, diabetes, stroke, obesity (body mass index [BMI] 30–39 kg/m^2) or severe obesity (BMI ≥40 kg/m^2)

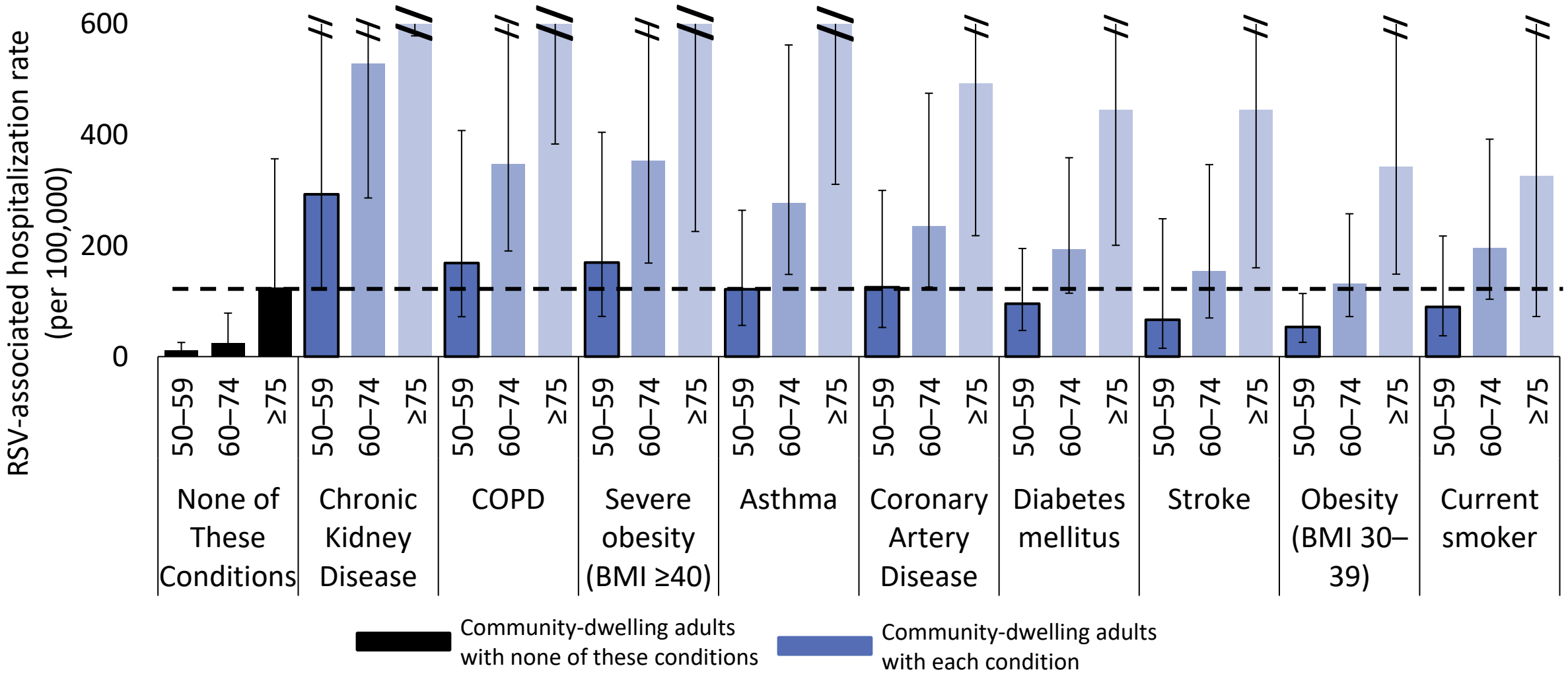
Unpublished data. Update on analysis from Woodruff et al. First presented to ACIP in February 2024: https://www.cdc.gov/acip/downloads/slides-2024-02-28-29/03-RSV-Adults-Woodruff-508.pdf

RSV-associated hospitalization rates among community-dwelling adults aged ≥50 years with chronic medical conditions, 2017–2018 season



BMI: Body Mass Index (kg/m^2), COPD: Chronic Obstructive Pulmonary Disease. Data are preliminary and unpublished. Rates of laboratory-confirmed RSV-associated hospitalization account for under-detection of RSV infection among hospitalized adults and sensitivity of diagnostic tests. Poisson regression using Monte Carlo simulation estimated rates and 95% confidence intervals (represented by error bars). Rates for community-dwelling adults exclude residents of nursing homes and long-term care facilities and are not adjusted for sex or race and ethnicity group.

RSV-associated hospitalization rates among community-dwelling adults aged ≥50 years with chronic medical conditions, 2017–2018 season



BMI: Body Mass Index (kg/m^2), COPD: Chronic Obstructive Pulmonary Disease. Data are preliminary and unpublished. Rates of laboratory-confirmed RSV-associated hospitalization account for under-detection of RSV infection among hospitalized adults and sensitivity of diagnostic tests. Poisson regression using Monte Carlo simulation estimated rates and 95% confidence intervals (represented by error bars). Rates for community-dwelling adults exclude residents of nursing homes and long-term care facilities and are not adjusted for sex or race and ethnicity group.

What do we know about conditions and risk factors not included in the RSV-NET analysis?

- Other medical conditions associated with increased risk of severe RSV disease
  - **Heart failure**
    - As many as **28%** of adults hospitalized with RSV infection have chronic heart failure[1]
    - Among adults <65 years, hospitalization rates are **>14x** higher in those with versus without heart failure[1]
  - **Immune compromise**
    - Severe RSV disease and high RSV-associated mortality (**>20%**), especially among hematopoietic cell transplant and lung transplant recipients[2–4]
    - RSV may account for 20–25% of symptomatic viral respiratory illness after hematopoietic cell transplant[5] and is associated with pulmonary impairment and mortality.[6]
    - RSV infection is associated with increased risk of **allograft dysfunction** after lung transplant[7]

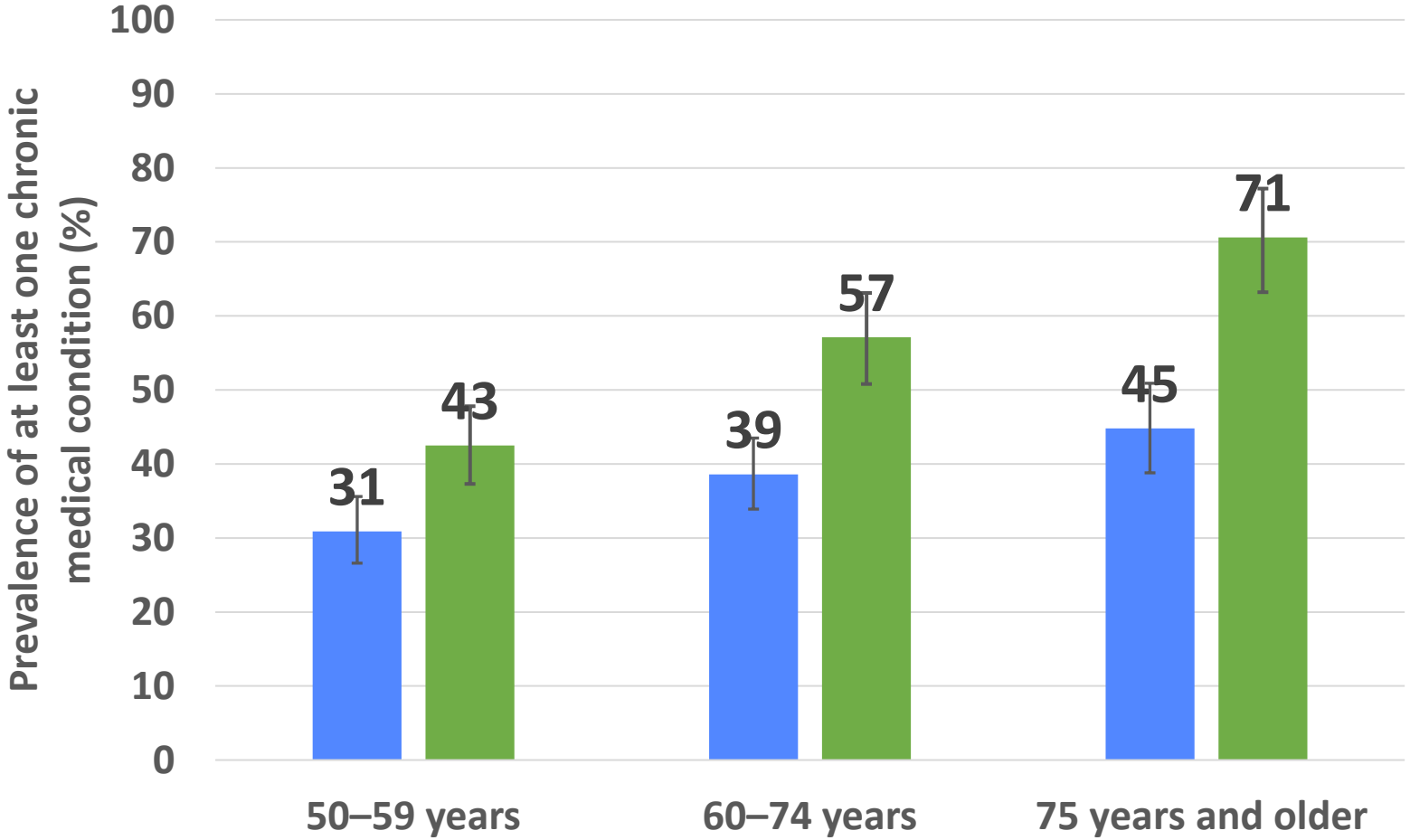
1. Kujawski SA, et al. Rates of respiratory syncytial virus (RSV)-associated hospitalization among adults with congestive heart failure-United States, 2015-2017. PLoS One. 2022 Mar 9;17(3):e0264890. https://pubmed.ncbi.nlm.nih.gov/35263382/
2. Ison MG, Hirsch HH. Community-Acquired Respiratory Viruses in Transplant Patients: Diversity, Impact, Unmet Clinical Needs. Clin Microbiol Rev. 2019 Sep 11;32(4):e00042-19. https://pubmed.ncbi.nlm.nih.gov/31511250/
3. Manuel O, Estabrook M; American Society of Transplantation Infectious Diseases Community of Practice. RNA respiratory viral infections in solid organ transplant recipients: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 2019 Sep;33(9):e13511 https://pubmed.ncbi.nlm.nih.gov/30817023/
4. Waghmare A, et al. Supplemental Oxygen-Free Days in Hematopoietic Cell Transplant Recipients With Respiratory Syncytial Virus. J Infect Dis. 2017 Dec 5;216(10):1235-1244. https://pubmed.ncbi.nlm.nih.gov/28961971/
5. Martino R, et al. Prospective study of the incidence, clinical features, and outcome of symptomatic upper and lower respiratory tract infections by respiratory viruses in adult recipients of hematopoietic stem cell transplants for hematologic malignancies. Biol Blood Marrow Transplant. 2005 Oct;11(10):781-96. https://pubmed.ncbi.nlm.nih.gov/16182179/
6. Sheshadri A, et al. Pulmonary Impairment after Respiratory Viral Infections Is Associated with High Mortality in Allogeneic Hematopoietic Cell Transplant Recipients. Biol Blood Marrow Transplant. 2019 Apr;25(4):800-809. https://pubmed.ncbi.nlm.nih.gov/30521974/
7. Testaert H, et al. Incidence, management and outcome of respiratory syncytial virus infection in adult lung transplant recipients: a 9-year retrospective multicentre study. Clin Microbiol Infect. 2021 Jun;27(6):897-903. https://pubmed.ncbi.nlm.nih.gov/32827713/

Public health problem: Evidence in adults aged 50–59 years

- Population-based rates of RSV disease among adults aged 50–59 years are lower than those among older adults
- However, we know that some younger adults are at increased risk of RSV hospitalization, even if the risk in the general population is low
- Adults aged 50–59 years who are hospitalized with RSV have similar underlying conditions as those in hospitalized adults ≥60 years, but more often have asthma, immune compromise, and severe obesity
- Adults aged 50–59 years with certain chronic conditions experience RSV hospitalization rates similar to those in adults ≥75 years in whom age is the only identified risk factor (who are recommended to receive RSV vaccination)
- Adults with heart failure and immune compromise more often experience severe outcomes from RSV infection

Prevalence of ≥1 chronic medical condition among adults aged 50-59 years is at least 31% using a narrow definition of chronic medical conditions* and may be as high as 43% when using a broad definition**

National Health and Nutrition Examination Survey (NHANES), 2015–2018.



***Narrow definition**, at least one of:

- Serious heart disease
- Diabetes **with complication**
- Chronic obstructive pulmonary disease
- Asthma
- Severe obesity (BMI ≥40 kg/m^2)
- Liver condition
- Chronic kidney disease, **stage 4 or 5**

****Broad definition**, as above, OR:

- Diabetes **with or without** complication
- Chronic kidney disease, **stage 3, 4, or 5**
- Cancer or malignancy in past 2 years

BMI: body mass index

SOURCE: National Center for Health Statistics (NCHS), National Health and Nutrition Examination Survey (NHANES), 2015–2018. All estimates are crude estimates with no age adjustment and age is age at interview. Error bars represent Korn and Graubard 95% confidence intervals. NHANES is representative of the civilian, non-institutionalized U.S. population. For "narrow" definition: Severe obesity was defined as BMI ≥40 kg/m^2. Diabetes with complication was defined as 1) having diabetes: self-reported diabetes, fasting plasma glucose ≥126 mg/dL, or hemoglobin A1c ≥6.5%, AND 2) having one of the following complications of diabetes assessed within the survey: serious heart disease as defined below, chronic kidney disease (stage 3, 4, or 5) defined as estimated glomerular filtration rate (eGFR) <60 (stages 3–5) further defined below, or having self-reported diabetes and having a doctor previously told them that diabetes affected their eyes or that they have retinopathy. Other complications of diabetes are not included in this definition. Serious heart disease was defined based on self-report as diagnosed congestive heart failure, coronary heart disease, angina, or heart attack, or angina grades 1 or 2 determined by the Rose Angina Questionnaire. Asthma was defined as self-reporting ever being diagnosed with asthma and still having asthma. Chronic kidney disease was defined as estimated glomerular filtration rate (eGFR) <30 (stages 4–5), and using a forward equation for adjustment of creatinine because of methods changes. eGFR calculated using the 2021 CKD-EPI creatinine equation (https://www.nejm.org/doi/10.1056/NEJMoa2102953). Urine albumin is not included in this definition. Chronic obstructive pulmonary disease (COPD) was defined as self-reported diagnosed COPD, emphysema, or current chronic bronchitis. Liver condition was defined as self-reporting ever being diagnosed with any kind of liver condition and still having any kind of liver condition. Having at least one of the above conditions for the narrow definition was defined based on the seven (7) conditions listed. For "broad" definition: conditions were defined identically except diabetes was defined as self-reported diabetes, fasting plasma glucose ≥126 mg/dL, or hemoglobin A1c ≥6.5% without complication; chronic kidney disease was defined as estimated glomerular filtration rate (eGFR) <60 (stages 3,4, or 5); and cancer or malignancy in past 2 years was added. This was defined as self-reporting having "ever been told by a doctor or other health professional that you had cancer or a malignancy of any kind" and reporting age at diagnosis in years as being within 2 years of current age in years. As participant age and age at diagnosis for cancer or malignancy are top-coded for ages 80 years and above, those who are aged 80 years and above and report having diagnosis at age 78 years or above are coded as having cancer or malignancy in the past 2 years; this results in an inflated estimate. Of those with any history of cancer or malignancy ages 50–79 years, 18.6% had a diagnosis within the past 2 years. Of those with any history of cancer or malignancy ages 80 years and above, 36.0% had a diagnosis at ≥ age 78 years. Having at least one of the above conditions for the broad definition was defined based on the eight (8) conditions listed. Among the fasting sample, ~94% had complete data for all reported medical conditions, ~6% were missing data for one (1) medical condition, <1% were missing data for two (2) medical conditions, and none were missing data for three (3) or more medical conditions. Estimates of having ≥1 condition are weighted using fasting sample weight.

Public Health Problem: Work Group interpretation

- **Is RSV of public health importance among adults aged 50–59 years at increased risk of severe RSV disease?**

No	Probably No	Probably Yes	Yes	Varies	Don't know

EtR Domain: Benefits and Harms

Among adults aged 50-59 years at increased risk of severe RSV disease:

- How substantial are the desirable anticipated effects of RSV vaccination?
- How substantial are the undesirable anticipated effects of RSV vaccination?
- Do the desirable effects outweigh the undesirable effects?

GRADE Framework: PICO Question

Population	**Adults aged 50–59 years at increased risk of severe RSV disease**
Intervention	RSV Vaccine: GSK Arexvy (1 dose IM) or Pfizer Abrysvo (1 dose IM) or Moderna mResvia (1 dose IM)
Comparison	No RSV vaccine
Outcomes	▪ Medically attended RSV lower respiratory tract disease (LRTD) ▪ Hospitalization for RSV respiratory illness ▪ Death due to RSV respiratory illness ▪ Serious Adverse Events (SAEs) ▪ Inflammatory neurologic events (e.g., Guillain-Barré syndrome)

IM: intramuscular

For GRADE, we are treating RSV vaccination with any of the three licensed products as a single intervention

- **Protein subunit vaccines**: GSK's Arexvy, Pfizer's Abrysvo
- **mRNA vaccine**: Moderna's mResvia (not currently licensed for use in adults aged <60 years)
- Policy question is not product-specific, so additional RSV vaccines eventually licensed in adults aged 50-59 years at increased risk of severe RSV disease would be included in an existing recommendation
- All three vaccines are based on the same RSV antigen: F protein, stabilized in prefusion conformation (preF)
- Where relevant, we will show product-specific considerations outside of GRADE

GRADE: Grading of Recommendations, Assessment, Development and Evaluation. https://www.cdc.gov/acip/grade/index.html

GSK's Arexvy vaccine in adults aged 50–59 years at increased risk of severe RSV disease, Benefits: Geometric Mean Ratio (GMR) of neutralizing antibody titers[1]

	N	n with sero-response[a], 30 days post-vaccination	N	n with sero-response[a], 30 days post-vaccination	GMR (95% CI)[b], 30 days post-vaccination	Met Noninferiority Objective[c]
	Cohort 1a: Adults aged 50–59 years at increased risk of severe RSV disease		Cohort 2: Adults aged ≥60 years		Cohort 1a vs. Cohort 2	
RSV-A[d]	343	298 (86.9%)	342	275 (80.4%)	1.20 (1.05, 1.37)	Yes
RSV-B[d]	343	280 (81.6%)	341	254 (74.5%)	1.25 (1.10, 1.41)	Yes

Abbreviations: CI = confidence interval; GMR = geometric mean ratio

a) Sero-response was defined as ≥4-fold increase in the neutralization titer compared with pre-vaccination.

b) GMR at 30 days post-vaccination. The manufacturer calculated GMR as Cohort 2 / Cohort 1a. However, here, the reciprocal is shown: Cohort 1a / Cohort 2. GMR values >1 indicate higher geometric mean titers in Cohort 1a (adults 50–59 at increased risk), compared with Cohort 2 (adults ≥60).

c) Noninferiority objective was lower bound of the GMR confidence interval ≥0.67, when evaluating the GMR Cohort 1a / Cohort 2, and the lower limit of the CI around the sero-response rate difference ≥-10%, when evaluating Cohort 1a minus Cohort 2.

d) Serological assays for the determination of antibodies against RSV-A and RSV-B are performed by neutralization assay. The corresponding antibody titers were expressed in ED60 (serum estimated dilution inducing 60% inhibition in plaque-forming units). Assessed at Day 31 , where Day 1 was day of vaccination.

1. Ferguson M, et al. Noninferior Immunogenicity and Consistent Safety of Respiratory Syncytial Virus Prefusion F Protein Vaccine in Adults 50-59 Years Compared to ≥60 Years of Age. Clin Infect Dis. 2024 Oct 15;79(4):1074-1084. https://pubmed.ncbi.nlm.nih.gov/39099093/

Pfizer's Abrysvo vaccine in adults aged 50–59 years at increased risk of severe RSV disease, Benefits: Geometric Mean Ratio (GMR) of neutralizing antibody titers[1]

	N	n with sero-response[a], 1 month post-vaccination	N	n with sero-response[a], 1 month post-vaccination	GMR (95% CI)[b], one month post-vaccination	Met Noninferiority Objective[c]
	Group 1: Adults aged 50–59 years at increased risk of severe RSV disease		Group 2: Adults aged ≥60 years		Group 1 vs. Group 2	
RSV-A	206	193 (93.7%)	534	450 (84.3%)	1.54 (1.33, 1.78)	N/A[c]
RSV-B	207	195 (94.2%)	534	457 (85.6%)	1.52 (1.30, 1.79)	N/A[c]

Abbreviations: CI = confidence interval; GMR = geometric mean ratio

a) Sero-response was defined as achieving a ≥4-fold rise from baseline (before vaccination), if the baseline measurement was above the lower limit of quantification (LLOQ). If the baseline measurement was below the LLOQ, a postvaccination assay result ≥4 x LLOQ was considered a sero-response.

b) GMRs (ratio of geometric mean titers in Group 1, compared to Group 2) and 2-sided CIs were calculated by exponentiating the difference in least square means and the corresponding CIs based on analysis of log-transformed titers using a regression model with population groups, baseline log-transformed titers and sex as covariates.

c) Noninferiority objective was not defined for the subset of participants aged 50-59 years. For the full study population aged 18-59 years, noninferiority criteria were met: lower bound of the GMR confidence interval ≥0.67, and the lower limit of the CI around the sero-response rate difference ≥-10%.

1. https://clinicaltrials.gov/study/NCT05842967, https://pubmed.ncbi.nlm.nih.gov/37018468/, https://www.cdc.gov/acip/downloads/slides-2024-06-26-28/02-RSV-Adult-Munjal-508.pdf, unpublished data obtained from manufacturer

Moderna's mResvia vaccine in adults aged 50–59 years at increased risk of severe RSV disease, Benefits: Geometric Mean Ratio (GMR) of neutralizing antibody titers[1]

	N	n with sero-response[a], 28 days post-vaccination	N	n with sero-response[a], 28 days post-vaccination	GMR (95% CI)[b], 28 days post-vaccination	Met Noninferiority Objective[c]
	Group 1: Adults aged 50–59 years at increased risk of severe RSV disease		Group 2: Adults aged ≥60 years		Group 1 vs. Group 2	
RSV-A	303	259 (85.5%)	1513	1119 (74.0%)	1.13 (1.01, 1.28)	N/A[c]
RSV-B	302	201 (66.6%)	1511	853 (56.5%)	1.10 (0.99, 1.23)	N/A[c]

Abbreviations: CI = confidence interval; GMR = geometric mean ratio

a) Seroresponse at a participant level was defined as a change from below the lower limit of quantification (LLOQ) to equal or above 4 x LLOQ, or at least a 4-fold increase if baseline (pre-vaccine) was equal to or above the LLOQ.

b) GMRs (ratio of geometric mean titers in Group 1, compared to Group 2) and 2-sided CIs were estimated using an Analysis of Covariance model, with log-transformed antibody levels at Day 29 post-baseline as the dependent variable, treatment group as the explanatory variable, and log-transformed baseline antibody level as a covariate. The resulting least square means, difference of least square means, and 95% CIs (based on t-distribution) were back transformed to the original scale for the estimated geometric mean titer and GMR.

c) Noninferiority objective was not defined for the subset of participants aged 50-59 years. For the full study population aged 18-59 years, noninferiority criteria were met: lower bound of the GMR confidence interval ≥0.67, and the lower limit of the CI around the sero-response rate difference ≥-10%.

1. https://clinicaltrials.gov/study/NCT06067230, https://pubmed.ncbi.nlm.nih.gov/38091530/, unpublished data obtained from manufacturer

RSV vaccination in adults aged 50–59 years at increased risk of severe RSV disease
Benefits: *randomized studies*, immunobridging

Outcome	Importance	Data Sources	Effect Estimate, Geometric mean titer ratio[a]	Pooled effect estimate, efficacy[b] (95% CI) in adults aged ≥60 years	Adjustments to certainty assessment
Medically attended RSV LRTD	Important	Three phase 3 RCTs in adults aged <60 years[1–3] Three phase 3 RCTs in adults aged ≥60 years[4–6]	Adults 50–59 at increased risk vs. adults ≥60: RSV-A: 1.20 (95% CI: 1.05, 1.37)[1] RSV-B: 1.25 (95% CI: 1.10, 1.41)[1] RSV-A: 1.54 (95% CI: 1.33, 1.78)[2] RSV-B: 1.52 (95% CI: 1.30, 1.79)[2] RSV-A: 1.13 (95% CI: 1.01, 1.28)[3] RSV-B: 1.10 (95% CI: 0.99, 1.23)[3]	69.3% (51.7, 80.6) Assessed using 16–23 months mean follow up per participant[4–6]	Indirectness (serious)[c]
Hospitalization for RSV respiratory illness	Critical			76.7% (8.3, 94.1) Assessed using 9–16 months mean follow up per participant[4–6]	Indirectness (serious)[c] Imprecision (very serious)[d] Strong association[e]
Death due to RSV respiratory illness	Critical			Zero events observed	Unable to evaluate

CI: confidence interval, LRTD: lower respiratory tract disease, RCT: randomized controlled trial

a) Titers assessed through neutralization assay one month after vaccination. Data from participants aged <50 years were excluded.

b) Pooled estimate using data from all interventional studies for each outcome generated using Mantel-Haenszel random effects model. Efficacy was calculated as 1 – incidence rate ratio. Events were included if they occurred >14 days post-vaccination.

c) Serious concern for indirectness as the outcome was evaluated using immunobridging data as a surrogate for vaccine efficacy and there is no established correlate of protection.

d) Very serious concern for imprecision due to the confidence interval in adults 60 and older containing estimates for which different policy decisions might be considered, and for fragility of the estimate. Fragility refers to a situation in which estimates of the magnitude of effect and CIs may appear robust, but due to small numbers of events, reallocation of <5 events from control to intervention group may render different results.

e) The relative rate for this outcome was <0.5 with consistent evidence from all 3 studies, with no significant concern for confounding. Therefore, this was considered to be a large effect size.

1. Ferguson M, et al. Noninferior Immunogenicity and Consistent Safety of Respiratory Syncytial Virus Prefusion F Protein Vaccine in Adults 50-59 Years Compared to ≥60 Years of Age. Clin Infect Dis. 2024 Oct 15;79(4):1074-1084. https://pubmed.ncbi.nlm.nih.gov/39099093/
2. https://clinicaltrials.gov/study/NCT05842967, https://www.cdc.gov/acip/downloads/slides-2024-06-26-28/02-RSV-Adult-Munjal-508.pdf, unpublished data obtained from manufacturer
3. https://clinicaltrials.gov/study/NCT06067230, unpublished data obtained from manufacturer
4. Papi A, et al. Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults. NEJM 2023; 388:595–608. https://pubmed.ncbi.nlm.nih.gov/36791160/, unpublished data obtained from manufacturer
5. Walsh EE, et al. Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults. N Engl J Med. 2023 Apr 20;388(16):1465-1477. https://pubmed.ncbi.nlm.nih.gov/37018468, unpublished data obtained from manufacturer
6. Wilson E, et al. Efficacy and Safety of an mRNA-Based RSV PreF Vaccine in Older Adults. N Engl J Med. 2023 Dec 14;389(24):2233-2244. https://pubmed.ncbi.nlm.nih.gov/38091530/, unpublished data obtained from manufacturer

RSV vaccination in adults aged 50–59 years at increased risk of severe RSV disease

Benefits: *observational studies*

Outcome	Importance	Data Sources	Pooled effect estimate, Vaccine Effectiveness (95% CI)[a]	Adjustments to certainty assessment
Medically attended RSV LRTD[b]	Important	Three case-control studies (test-negative design) in adults ≥60 years[1–3] One retrospective cohort study (target trial emulation) in adults ≥60 years[4]	78% (74, 82)[c]	Indirectness (serious)[d] Strong association[e]
Hospitalization for RSV respiratory illness	Critical		80% (73, 85)[c]	Indirectness (serious)[d] Strong association[e]
Death due to RSV respiratory illness	Critical		No data available	Unable to evaluate

CI: confidence interval, LRTD: lower respiratory tract disease

a) Pooled estimate using data from observational studies for each outcome generated using Mantel-Haenszel random effects model with weights assigned using standard error back calculation.

b) Surrogate outcome was used to evaluate this outcome: RSV-associated ED visit, or either RSV-associated ED visit or hospitalization, depending availability by study.

c) Pooled effectiveness estimate reflects a mean or median of 2–4 months after vaccination in each study.

d) Serious concern for indirectness because study participants were from the general population 60 and older, not 50-59 with conditions that increase risk.

e) The relative rate for this outcome was <0.5 with consistent evidence from all 4 studies, with no significant concern for confounding. Therefore, this was considered to be a large effect size.

1. Surie D, et al. RSV Vaccine Effectiveness Against Hospitalization Among US Adults 60 Years and Older. JAMA. 2024 Oct 1;332(13):1105-1107. https://pubmed.ncbi.nlm.nih.gov/39230920/
2. Payne AB, et al. Respiratory syncytial virus (RSV) vaccine effectiveness against RSV-associated hospitalisations and emergency department encounters among adults aged 60 years and older in the USA, October, 2023, to March, 2024: a test-negative design analysis. Lancet. 2024 Oct 19;404(10462):1547-1559. https://pubmed.ncbi.nlm.nih.gov/39426837/
3. Pfizer-sponsored study: Tartof SY, et al. Estimated Vaccine Effectiveness for Respiratory Syncytial Virus-Related Lower Respiratory Tract Disease. JAMA Netw Open. 2024 Dec 2;7(12):e2450832. https://pubmed.ncbi.nlm.nih.gov/39671195/
4. Bajema KL, et al. Respiratory syncytial virus vaccine effectiveness among US veterans, September, 2023 to March 2024: a target trial emulation study. Lancet Infect Dis. 2025 Jan 20:S1473-3099(24)00796-5. https://pubmed.ncbi.nlm.nih.gov/39848264/

RSV vaccination in adults aged 50–59 years at increased risk of severe RSV disease
Harms

Outcome	Importance	Data Sources	Pooled effect estimate, relative risk (95% CI)	Concerns in certainty assessment
Serious adverse events (SAEs)[a]	Critical	Two phase 3 RCTs in adults aged <60 years at increased risk of severe RSV disease[1,2]	1.13 (0.50, 2.59)[b]	Imprecision (serious)[c] Inconsistency (serious)[d]
Inflammatory neurologic events[e]	Critical		Zero events observed	Unable to evaluate

a) Within 6 months after study intervention.
b) Pooled estimate using data from all studies for this outcome generated using a Mantel-Haenszel fixed effect model. Data were limited to participants aged 50–59 years.
c) Serious concern for imprecision due to the confidence interval containing estimates for which different policy decisions might be considered.
d) Serious concern for inconsistency because the point estimates between the studies differed substantially, although the confidence intervals overlapped.
e) Within 42 days after vaccination.

1. Ferguson M, et al. Noninferior Immunogenicity and Consistent Safety of Respiratory Syncytial Virus Prefusion F Protein Vaccine in Adults 50-59 Years Compared to ≥60 Years of Age. Clin Infect Dis. 2024 Oct 15;79(4):1074-1084. https://pubmed.ncbi.nlm.nih.gov/39099093/ , unpublished data obtained from manufacturer
2. https://clinicaltrials.gov/study/NCT05842967, https://www.cdc.gov/acip/downloads/slides-2024-06-26-28/02-RSV-Adult-Munjal-508.pdf, unpublished data obtained from manufacturer

Summary of GRADE for RSV vaccination in adults aged 50–59 years at increased risk of severe RSV disease

Outcome	Importance	Design (# of studies)	Findings In adults aged 50-59 years at increased risk of severe RSV disease:	Evidence type
Benefits				
Medically attended RSV lower respiratory tract disease (LRTD)	Important	RCT (3)	RSV vaccination likely reduces medically attended RSV LRTD	**Moderate**
		Observational (3)	RSV vaccination may reduce medically attended RSV LRTD	**Low**
Hospitalization for RSV respiratory illness	Critical	RCT (3)	RSV vaccination may reduce hospitalization for RSV respiratory illness	**Low**
		Observational (4)	RSV vaccination may reduce hospitalization for RSV respiratory illness	**Low**
Death due to RSV respiratory illness	Critical	RCT (3)	Zero events observed	Unable to evaluate
Harms				
Serious adverse events	Critical	RCT (2)	RSV vaccination may result in little to no difference in serious adverse events	**Low**
Inflammatory neurologic events	Critical	RCT (2)	Zero events observed	Unable to evaluate

RCT: randomized controlled trial

Additional information on benefits/harms for adults aged 50–59 years at increased risk of severe RSV disease

- Population benefits of RSV vaccination compared with risk of Guillain-Barre syndrome (GBS), for protein subunit vaccines
- Duration of vaccine protection and potential to restore protection through revaccination
- Immunogenicity in immunocompromised persons

Available FDA data support existence of increased risk of GBS after protein subunit RSV vaccination[1] in adults ≥65yrs

- On January 7th, the U.S. Food and Drug Administration (FDA) required revision of the Prescribing Information for GSK's Arexvy[2] and Pfizer's Abrysvo[3] Warnings and Precautions section to include the following:
  - *The results of a postmarketing observational study suggest an increased risk of Guillain-Barré syndrome (GBS) during the 42 days following vaccination with [Abrysvo/Arexvy].*
- Available data suggest that risk is similar to, and potentially greater than, that of other currently licensed and recommended adult vaccines.
  - *The analyses of all GBS cases based on claims data suggest an increased risk of GBS during the 42 days following vaccination, […] with an estimated 9 excess cases of GBS per million doses of Abrysvo, and an estimated 7 excess cases of GBS per million doses of Arexvy administered to individuals 65 years of age and older.*

1. GSK's Arexvy and Pfizer's Abrysvo are protein subunit RSV vaccines. Moderna's mResvia is an mRNA RSV vaccine, not a protein subunit vaccine. To date, Moderna's mResvia vaccine has NOT been associated with increased risk of Guillain-Barré syndrome. Post-licensure safety surveillance for mResvia began recently in June 2024.
2. https://www.fda.gov/media/167805/download
3. https://www.fda.gov/media/168889/download

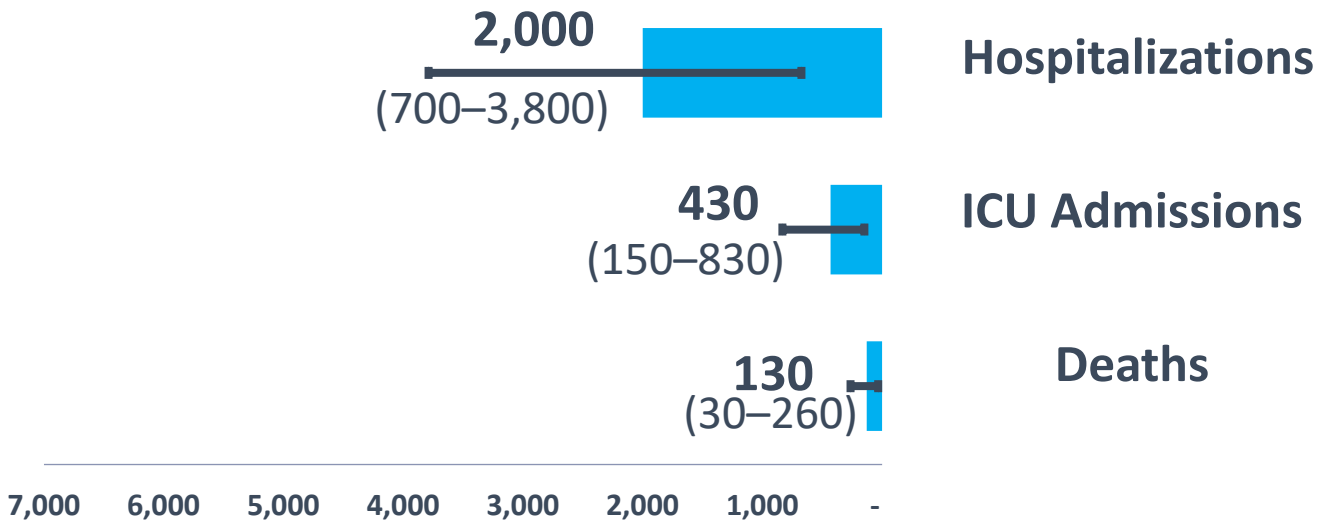
Available FDA data support existence of increased risk of GBS after protein subunit RSV vaccination[1] in adults ≥65yrs

- The Work Group emphasized that risk of Guillain-Barre syndrome (GBS) associated with protein subunit RSV vaccines[1] should be considered in the context of the public health benefits of RSV vaccination.
- In June and October 2024, ACIP reviewed results of mathematical modeling analyses comparing the numbers of RSV-associated hospitalizations, intensive care unit (ICU) admissions, and deaths preventable per 1 million persons vaccinated vs. the numbers of potential vaccine-attributable GBS cases.[2]
- This analysis has been updated to account for the most up to date information on protein subunit RSV vaccine effectiveness, duration of protection, and GBS risk[1], and has been applied to adults aged 50–59 years at increased risk of severe RSV disease.
- *The background risk of GBS in a study population influences the excess GBS case estimates and may differ between studies, precluding direct comparisons to excess GBS case estimates from other vaccine studies or populations.*

1. GSK's Arexvy and Pfizer's Abrysvo are protein subunit RSV vaccines. Moderna's mResvia is an mRNA RSV vaccine, NOT a protein subunit vaccine. To date, Moderna's mResvia vaccine has NOT been associated with increased risk of Guillain-Barré syndrome. Post-licensure safety surveillance for mResvia began recently in June 2024.
2. https://www.cdc.gov/acip/downloads/slides-2024-10-23-24/06-RSV-Adult-Melgar-508.pdf

Estimated RSV-associated outcomes[1] preventable over 3 RSV Seasons vs. attributable risk of Guillain-Barre syndrome (GBS) estimated from self-controlled case series analysis through FDA-CMS partnership data among adults aged ≥65 years, 42-day risk interval[2]

Per 1 Million Doses of Protein Subunit RSV Vaccines Administered to Adults Aged 50–59 Years[3] at Increased Risk of Severe RSV Disease:



Base case

Absolute risk from adults ≥65 years applied directly to adults aged 50-59 years:

0–18[4] attributable cases of GBS per 1 million people vaccinated

1. Range of outcomes avertable was calculated using adjusted 95% confidence interval of RSV-associated incidence of the outcome observed in RSV-NET.
2. FDA self-controlled case series analysis, among CMS Medicare beneficiaries ≥65 years with Parts A, B, and D coverage who did not have a GBS claim in the 365 days before vaccination. Analysis based on diagnoses of GBS in inpatient claims data in risk interval (1–42 days after RSV vaccination) compared to control interval (43–90 days after RSV vaccination). GBS cases identified using ICD-10 diagnosis of GBS in primary position of inpatient claims coding with chart verification requiring Brighton Collaboration Level 1–3 certainty. Estimates adjusted for outcome-dependent observation time, seasonality, and (when chart review could not be performed) the positive predictive value of diagnostic codes in identifying chart-confirmed GBS cases. Analysis includes patients with RSV vaccinations only through January 28, 2024 to allow for 90-day post-vaccination observation and 90% or greater claims data completeness. Claims data through July 13, 2024.
3. Although CMS data were limited to Medicare beneficiaries aged ≥65 years, results are extrapolated here to apply to adults aged 50-59 years.
4. Credible range spans the lowest lower bound and highest upper bound of attributable risk estimates for the GSK and Pfizer RSV vaccines.

Credit: Dr. David Hutton, U. Michigan

What do we know so far about duration of protection and the need for revaccination with adult RSV vaccines?

- **In the clinical trials, protection provided by a single dose of RSV vaccine appears to wane over time.[1,2,3]**
  - Clinical trial data are available through 2–3 RSV seasons, depending on manufacturer.
  - Do not yet have real-world effectiveness data beyond the first RSV season.
- **Clinical trial efficacy data evaluating revaccination are available only from GSK's pivotal phase 3 trial (12-month revaccination interval).[1]**
  - Clinical efficacy in GSK's pivotal phase 3 trial did not improve after revaccination at a 12-month interval.

1. Ison MG, et al. Efficacy and Safety of Respiratory Syncytial Virus (RSV) Prefusion F Protein Vaccine (RSVPreF3 OA) in Older Adults Over 2 RSV Seasons. Clin Infect Dis. 2024 Jun 14;78(6):1732-1744. https://pubmed.ncbi.nlm.nih.gov/38253338/
2. Walsh EE, Eiras D, Woodside J, et al. Efficacy, Immunogenicity, and Safety of the Bivalent RSV Prefusion F (RSVpreF) Vaccine in Older Adults Over 2 RSV Seasons, Clinical Infectious Diseases, 2025; ciaf061. Feb 2025. https://doi.org/10.1093/cid/ciaf061
3. Das R. Update on Moderna's RSV vaccine, mRESVIA (mRNA-1345), in adults ≥60 years of age [Presentation slides]. Presented at the Advisory Committee on Immunization Practices meeting, Atlanta, GA; June 26, 2024. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2024-06-26-28/04-RSV-Adult-Das-508.pdf

Clinical efficacy of 1 and 2 doses of GSK RSV vaccine (Arexvy) from GSK's phase 3 clinical trial

GSK RSV vaccine doses	Vaccine efficacy (%) against RSV-associated lower respiratory tract disease
Single dose, season 1 only (median follow-up 6.7 months during season 1)[1]	82.6 (96.95% CI: 57.9, 94.1)
Single dose, season 2 only (median follow-up 6.3 months during season 2)[2]	56.1 (95% CI: 28.2, 74.4)
Two doses, season 2 only (median follow-up 6.3 months during season 2)[3]	55.9 (95% CI: 27.9, 74.3)

Revaccination at 12 months did not improve protection against clinical disease

CI=confidence interval

Ison MG, et al. Efficacy and Safety of Respiratory Syncytial Virus (RSV) Prefusion F Protein Vaccine (RSVPreF3 OA) in Older Adults Over 2 RSV Seasons. Clin Infect Dis. 2024 Jun 14;78(6):1732-1744. https://pubmed.ncbi.nlm.nih.gov/38253338/

1. Efficacy of 1 dose RSVPreF3 OA given pre-season 1 in preventing RSV-LRTD over season 1.
2. Efficacy of 1 dose RSV PreF3 OA given pre-season 1 in preventing RSV-LRTD over season 2.
3. Efficacy of 1 dose RSV PreF3 OA given pre-season 1 and a 2nd dose given pre-season 2 in preventing RSV-LRTD over season 2. Analysis includes data collected from participants who received RSVPreF3 OA as dose 1 and dose 2 for the analysis of the revaccination regimen, and from participants who received placebo as dose 1 and 2 (comparator group).

What do we know so far about duration of protection and the need for revaccination with adult RSV vaccines?

- **In the clinical trials, protection provided by a single dose of RSV vaccine appears to wane over time.[1,2,3]**
  - Clinical trial data are available through 2–3 RSV seasons, depending on manufacturer.
  - Do not yet have real-world effectiveness data beyond the first RSV season.
- **Clinical trial efficacy data evaluating revaccination are available only from GSK's pivotal phase 3 trial (12-month revaccination interval).[1]**
  - Clinical efficacy in GSK's pivotal phase 3 trial did not improve after revaccination at a 12-month interval.
- **Immunogenicity data at various revaccination intervals are being studied**
  - GSK immunogenicity data at 12-, 24-, and 36-month revaccination intervals have shown a weaker humoral immune response compared with the response after dose 1.[4]
  - Pfizer immunogenicity data at a 12-month revaccination interval has also shown a weaker humoral immune response compared with the response after dose 1.[5]
  - Moderna immunogenicity data at 12- and 24-month revaccination intervals have met prespecified **non-inferiority** objectives compared with dose 1,[3,6] but revaccination with a 24-month interval showed lower peak GMT compared with dose 1.

1. Ison MG, et al. Efficacy and Safety of Respiratory Syncytial Virus (RSV) Prefusion F Protein Vaccine (RSVPreF3 OA) in Older Adults Over 2 RSV Seasons. Clin Infect Dis. 2024 Jun 14;78(6):1732-1744. https://pubmed.ncbi.nlm.nih.gov/38253338/
2. Walsh EE, Eiras D, Woodside J, et al. Efficacy, Immunogenicity, and Safety of the Bivalent RSV Prefusion F (RSVpreF) Vaccine in Older Adults Over 2 RSV Seasons, Clinical Infectious Diseases, 2025; ciaf061. Feb 2025. https://doi.org/10.1093/cid/ciaf061
3. Das R. Update on Moderna's RSV vaccine, mRESVIA (mRNA-1345), in adults ≥60 years of age [Presentation slides]. Presented at the Advisory Committee on Immunization Practices meeting, Atlanta, GA; June 26, 2024. https://www.cdc.gov/acip/downloads/slides-2024-06-26-28/04-RSV-Adult-Das-508.pdf
4. Gerber, S. Arexvy (Adjuvanted RSVPreF3) 2-Year Update. Presented at the Advisory Committee on Immunization Practices meeting, Atlanta, GA; June 26, 2024. https://www.cdc.gov/acip/downloads/slides-2024-06-26-28/03-RSV-Adult-Gerber-508.pdf.
5. Walsh EE, et al. Respiratory Syncytial Virus Prefusion F Vaccination: Antibody Persistence and Revaccination. J Infect Dis. 2024 Oct 16;230(4):e905-e916. https://pubmed.ncbi.nlm.nih.gov/38606958/
6. Shaw CA et al. Safety and Immunogenicity of an mRNA-Based RSV Vaccine Including a 12-Month Booster in a Phase 1 Clinical Trial in Healthy Older Adults, *The Journal of Infectious Diseases*, Volume 230, Issue 3, 15 September 2024, Pages e647–e656, https://pubmed.ncbi.nlm.nih.gov/38385566/

Revaccination summary

Knowns

- Efficacy data with revaccination at 12 months did not show any improvement in clinical protection
- Revaccination DOES elicit a “boost” in neutralizing antibody immune response
- For GSK, neutralizing antibody response does not appear to reach post-dose 1 antibody levels, even after waiting 3 years to revaccinate after the initial dose
- For Moderna, neutralizing antibody response to revaccination at 12 and 24-months met *non-inferiority criteria** when compared with titers post-dose 1, but were lower with the 24-month interval
- Cellular immune response data available from GSK shows that revaccination boosts T-cell response to post-dose 1 level or higher

Unknowns

- No clear trend yet visible in available data indicating longer revaccination intervals yield more robust antibody responses
  - Would longer revaccination intervals result in a stronger neutralizing antibody response? How long would that be (5 years)?
- Are the “boosted” revaccination antibody responses sufficient to provide clinical protection (even if lower than the post-dose 1 response)?
- What is the relative importance of humoral versus cellular immune responses in providing protection against clinical disease?
- Do immunocompromised adults experience different immune responses to revaccination?

* Prespecified non-inferiority criteria were met when the lower bounds of the 95% confidence interval (CI) of the Geometric Mean Titer Ratio (GMR) of RSV-A and RSV-B neutralizing antibodies one month after dose #2 / one month after dose #1 were >0.667. 24-month revaccination GMR of RSV-A was 0.719 (95% CI: 0.68, 0.76); 24-month GMR of RSV-B was 0.705 (95% CI: 0.67, 0.74). Despite the statistically significant difference, prespecified non-inferiority criteria were met because the lower bound of the 95% CI was >0.667.

Summary of GSK Arexvy immunogenicity studies among adults with immune compromise

- Trial included adults aged ≥18 years with renal or lung transplant
- One month after a single dose of Arexvy, these participants had lower RSV neutralizing antibody titers, compared with immunocompetent adults aged ≥50 years
- After a second dose of Arexvy one month after the first, RSV neutralizing antibody titers increased and were similar to those in immunocompetent adults aged ≥50 years at 2 months post-vaccination
- Measures of cellular immunity after Arexvy vaccination were similar between immunocompromised participants and immunocompetent participants
- **No specific safety concerns identified. One participant experienced renal transplant rejection after RSV vaccination*.**

*Not interpreted as vaccine-related by the investigator

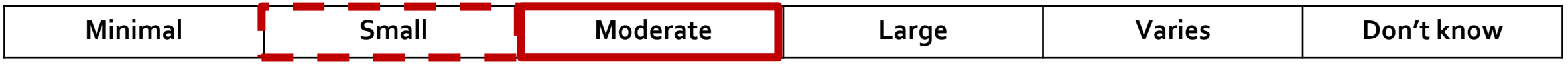
Summary of Pfizer Abrysvo immunogenicity studies among adults with immune compromise

- Trial included adults aged ≥18 years with autoimmune disorders on immunomodulator therapy, solid organ transplant, end-stage renal disease on dialysis, or non-small cell lung cancer on therapy
- One month after a single dose of Abrysvo, these participants had similar RSV neutralizing antibody titers, compared with immunocompetent adults aged ≥60 years from Pfizer's main phase 3 trial
- The neutralizing antibody response in participants with autoimmune disorders on immunomodulator therapy and solid organ transplant appeared lower than in adults with end-stage renal disease
- A second dose of Abrysvo one month after the first did not appreciably increase neutralizing antibody titers
- **No specific safety concerns identified. One participant experienced renal transplant rejection* and one participant experienced lung transplant rejection* after RSV vaccination.**

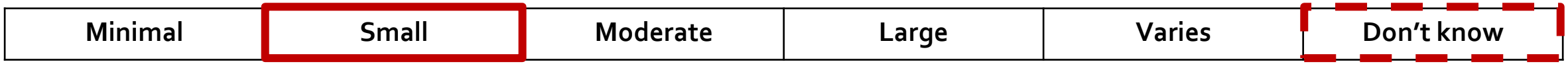
*Not interpreted as vaccine-related by the investigator

Benefits and Harms of RSV vaccine in adults aged 50–59 years at increased risk of severe RSV disease

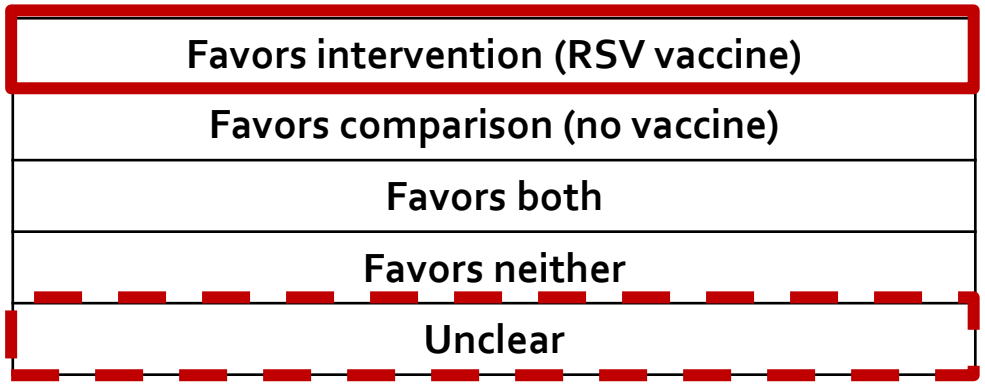
- How substantial are the **desirable anticipated effects** among adults aged 50–59 years at increased risk of severe RSV disease



- How substantial are the **undesirable anticipated effects** among adults aged 50–59 years at increased risk of severe RSV disease?



- Do the **desirable effects outweigh the undesirable effects** among adults aged 50–59 years at increased risk of severe RSV disease?

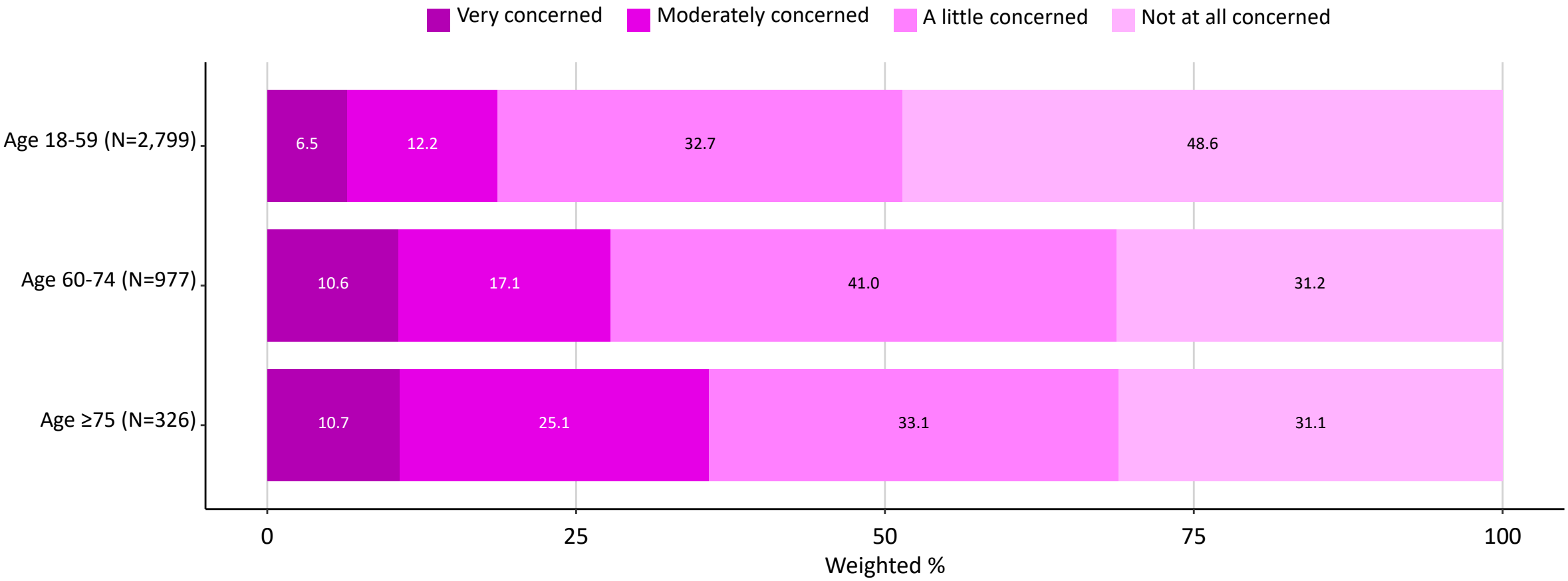


Values and preferences

- Do **adults aged 50–59 years at increased risk of severe RSV disease** feel the desirable effects of RSV vaccination are large relative to the undesirable effects?

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

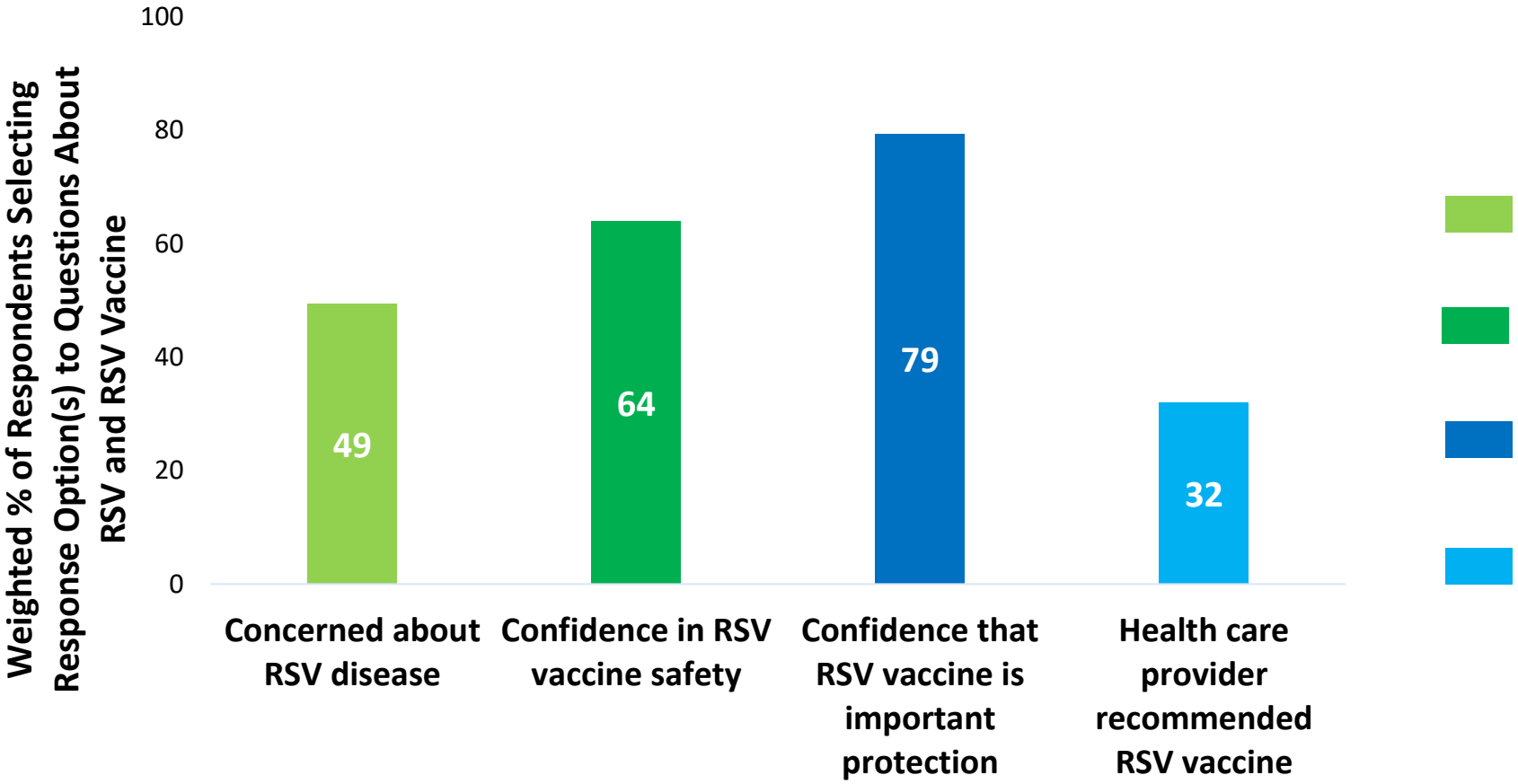
Concern About Getting RSV Disease Among Adults Aged ≥18 Years, by Age Group, Omnibus Surveys, April 4–26, 2024 (N=4,102)



Omnibus Surveys: data for this analysis were collected through the Ipsos KnowledgePanel and NORC AmeriSpeak Omnibus Surveys, which use probability-based panels to survey a nationally representative sample of U.S. adults aged 18 years and older. CDC fields questions about vaccination status, intent, knowledge, attitudes, beliefs, and behaviors on each survey for 2 waves each month, for a combined sample size of ~4,000 respondents. These slides present results from April 2024. Data were weighted to represent the non-institutionalized U.S. population and mitigate possible non-response bias. All responses are self-reported.

Behavioral & Social Drivers of RSV Vaccination Among Adults Aged 60–74 Years at Increased Risk** for Severe RSV Disease, November 2024

National Immunization Survey-Adult COVID Module (NIS-ACM)



Responses to questions:

"Very or moderately concerned about getting RSV"

"Thinks the RSV vaccine is completely or very safe"

"Thinks the RSV vaccine is very or somewhat important to protect yourself against RSV"

"Doctor, nurse, or other health professional recommended that you get an RSV vaccine since Fall 2023"

**A respondent was considered to be at increased risk for severe RSV disease if they had any of the following: chronic lung diseases, diabetes with insulin use, heart conditions, immunocompromised state, solid organ or blood stem cell transplant (including bone marrow transplant), cancer, liver disease, sickle cell disease or thalassemia, or currently lives in a nursing home.

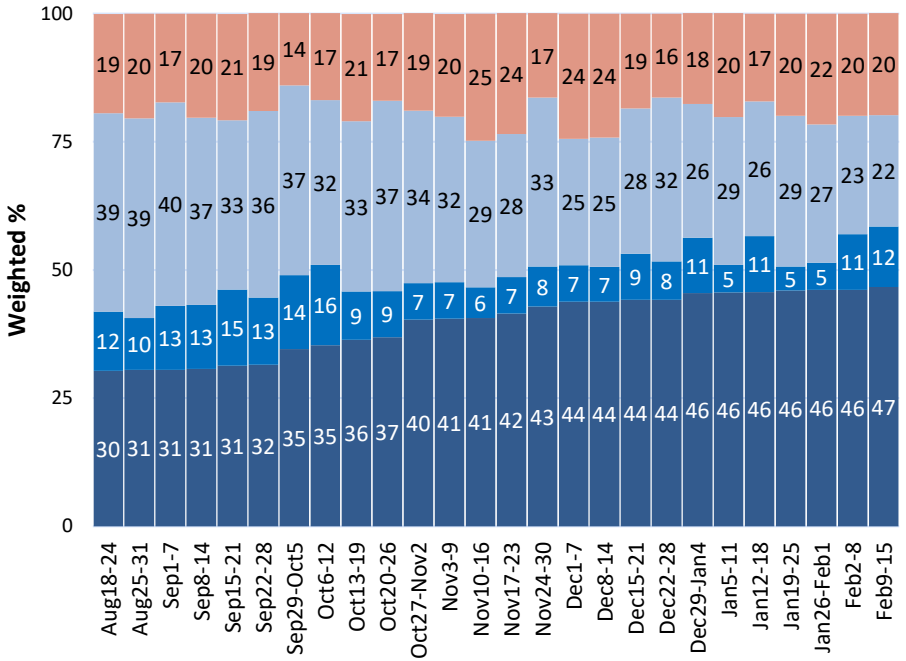
NIS-ACM methods: Data from adults age ≥18 years are collected by telephone interview using a random-digit-dialed sample of cell telephone numbers stratified by state, the District of Columbia, five local jurisdictions (Bexar County TX, Chicago IL, Houston TX, New York City NY, and Philadelphia County PA), and Puerto Rico and the U.S. Virgin Islands. Data are weighted to represent the non-institutionalized U.S. population and mitigate possible bias that can result from an incomplete sample frame (exclusion of households with no phone service or only landline telephones) or non-response. All responses are self-reported. For more information about the survey, see https://www.cdc.gov/nis/about/index.html and https://www.cdc.gov/nis/media/pdfs/2025/02/NISACMQuestionnaireQ12025_508-2_2025.pdf.

RSV Vaccination Status and Intent Among Adults Aged ≥75 Years and 60–74 Years at Increased Risk** for Severe RSV, through February 15, 2025

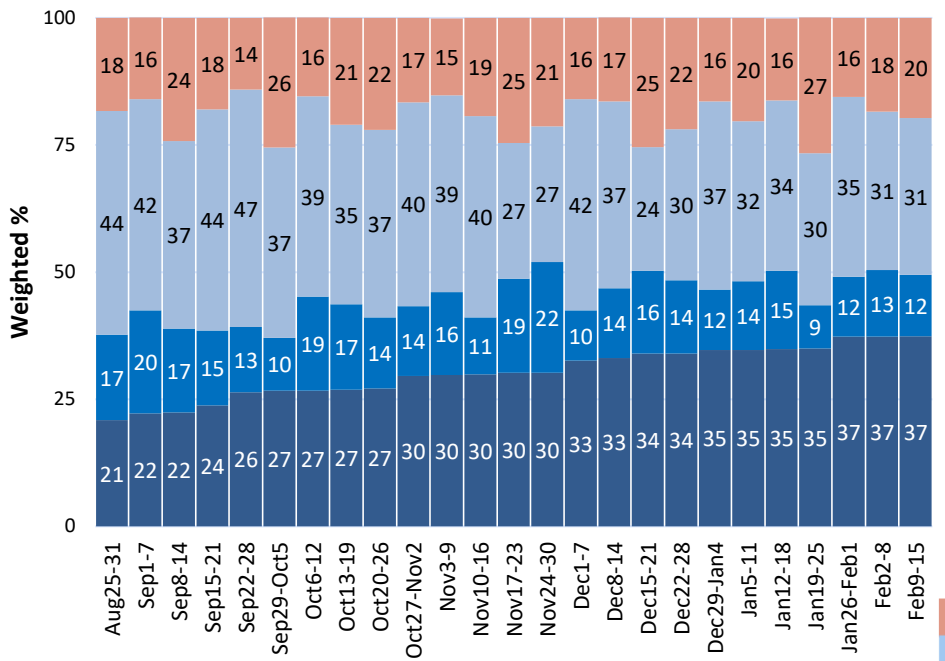
National Immunization Survey-Adult COVID Module (NIS-ACM)

Weekly RSV Vaccination Status and Intent, NIS-ACM

Adults Aged ≥75 Years (n=95,706)



Adults Aged 60–74 Years at Increased Risk (n=18,880)



Aged ≥75 years

- **47%** (95% CI: 45.0-48.3) received an RSV vaccine
- **12%** (95% CI: 6.1-17.5) definitely will get vaccinated

Aged 60–74 years at increased risk

- **37%** (95% CI: 34.1-40.6) received an RSV vaccine
- **12%** (95% CI: 5.8-18.5) definitely will get vaccinated

Probably or definitely will not get RSV vaccine
Probably will get RSV vaccine or unsure
Definitely will get RSV vaccine
Received RSV vaccine

**A respondent was considered to be at increased risk for severe RSV disease if they had any of the following: chronic lung diseases, diabetes with insulin use, heart conditions, immunocompromised state, solid organ or blood stem cell transplant (including bone marrow transplant), cancer, liver disease, sickle cell disease or thalassemia, or currently lives in a nursing home.

NIS-ACM methods: Data from adults age ≥18 years are collected by telephone interview using a random-digit-dialed sample of cell telephone numbers stratified by state, the District of Columbia, five local jurisdictions (Bexar County TX, Chicago IL, Houston TX, New York City NY, and Philadelphia County PA), and Puerto Rico and the U.S. Virgin Islands. Data are weighted to represent the non-institutionalized U.S. population and mitigate possible bias that can result from an incomplete sample frame (exclusion of households with no phone service or only landline telephones) or non-response. All responses are self-reported. For more information about the survey, see https://www.cdc.gov/nis/about/index.html.

Risk of Guillain-Barre Syndrome (GBS)

There are no data assessing how adults value protection against RSV relative to potential risk of GBS.

A few considerations:

- Adults are willing to accept some rate of vaccine-associated adverse events for the benefit of preventing disease[1]
- Individual baseline and vaccine-associated risk of GBS may differ by age group and presence of chronic conditions
- Willingness to accept risk of GBS after vaccination may differ by age and health status and perceived risk of RSV-associated disease[2]

1. Scherer LD, Shaffer VA, Patel N, Zikmund-Fisher BJ. Can the vaccine adverse event reporting system be used to increase vaccine acceptance and trust? Vaccine. 2016 May 5;34(21):2424-2429. https://pubmed.ncbi.nlm.nih.gov/27049120/
2. Prosser LA, Payne K, Rusinak D, et al. Valuing health across the lifespan: health state preferences for seasonal influenza illnesses in patients of different ages. Value Health. 2011;14(1):135-143. https://pubmed.ncbi.nlm.nih.gov/21211495/

Values: summary of the available evidence

Adults aged 50–59 years at increased risk of severe RSV disease

- About 20% of adults aged 18–59 years say they are very or moderately concerned about RSV, compared with approximately 30–35% of adults aged ≥60 years.
- Uptake of RSV vaccine through February 2025 was 37–47% among adults aged ≥60 years.
- We do not have data on how adults value protection against RSV versus potential risk of GBS, but this may vary by age or other factors.

Values

- **Do adults aged 50–59 years at increased risk of severe RSV disease feel that the desirable effects of RSV vaccination are large relative to the undesirable effects?**

No	Probably no	Probably Yes	Yes	Varies	Don't know

- **Is there important uncertainty about, or variability in, how much adults aged 50–59 years at increased risk of severe RSV disease value the main outcomes?**

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

Minority opinion

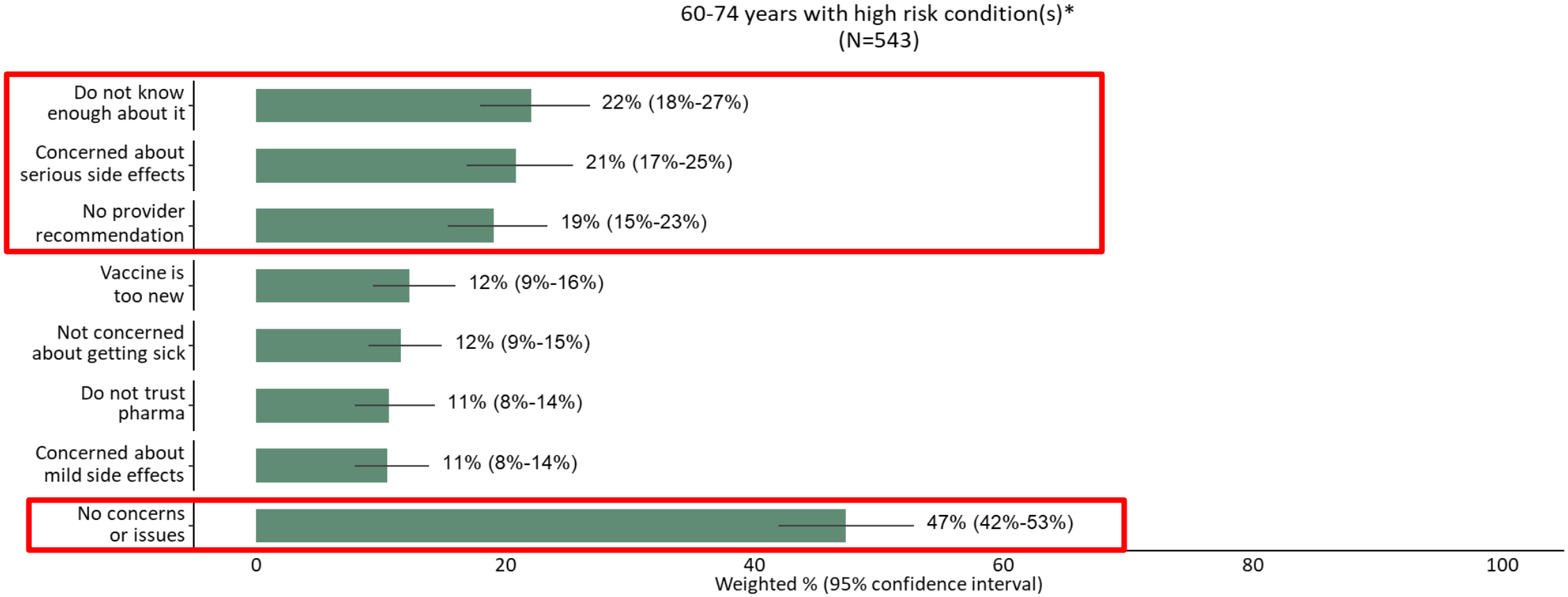
Acceptability

Would recommending RSV vaccination for **adults aged 50–59 years at increased risk of severe RSV disease** be acceptable to key stakeholders?

Feasibility

Is it feasible to implement RSV vaccination for **adults aged 50–59 years at increased risk of severe RSV disease**?

Top RSV vaccination concerns and issues among adults aged 60–74 years with high-risk conditions*, Omnibus Surveys, December 12–30, 2024

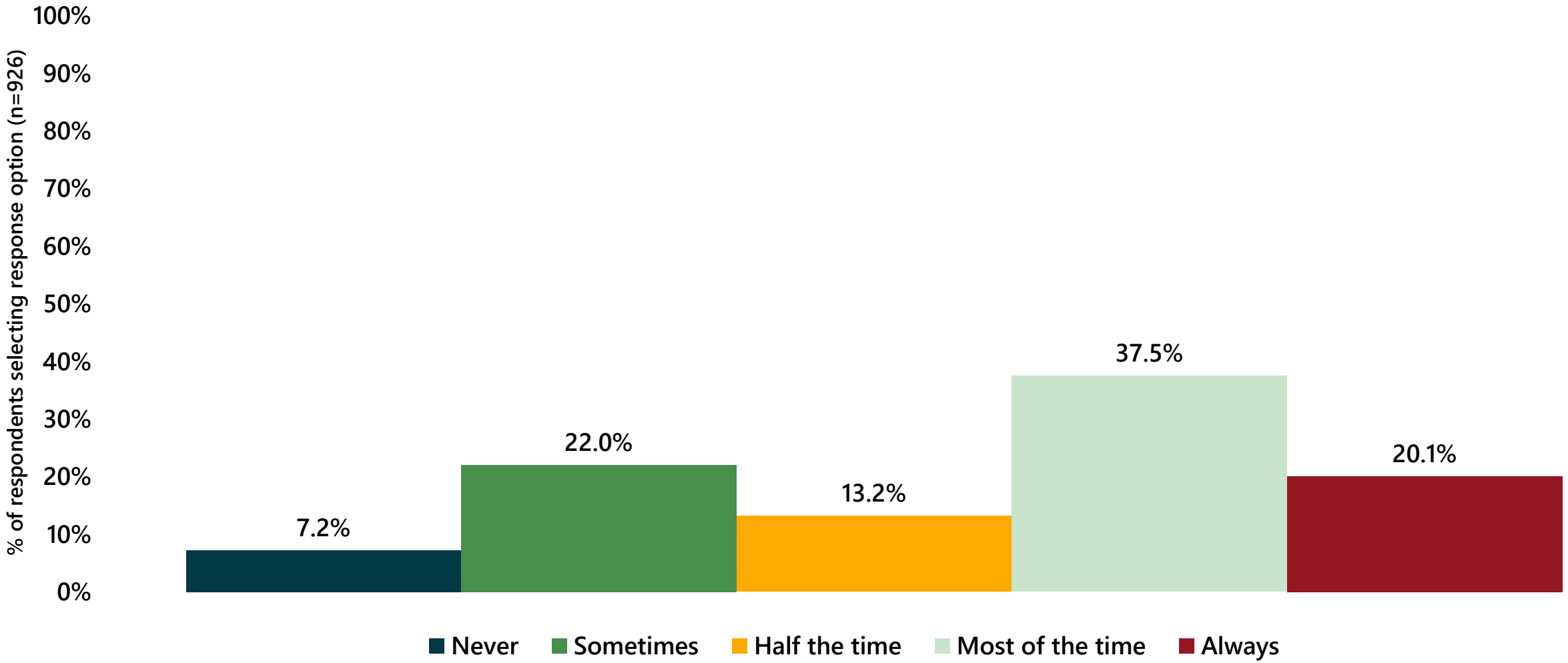


*Includes self-reported chronic lung disease, heart conditions, solid organ or blood stem cell transplant, cancer (excluding basal cell carcinoma and squamous cell carcinoma), diabetes, liver disease, sickle cell disease or thalassemia, BMI (body mass index) ≥40, and immunocompromised state.

Other response options included: "Have not had time," "Vaccine fatigue," "Not eligible/ unsure if eligible," "Too close to another vaccine," "Have enough immunity," "Concerned about effectiveness," "Other," "Cost," "Got sick from past vaccine," "Could not find vaccine," "Allergic/other medical reason."

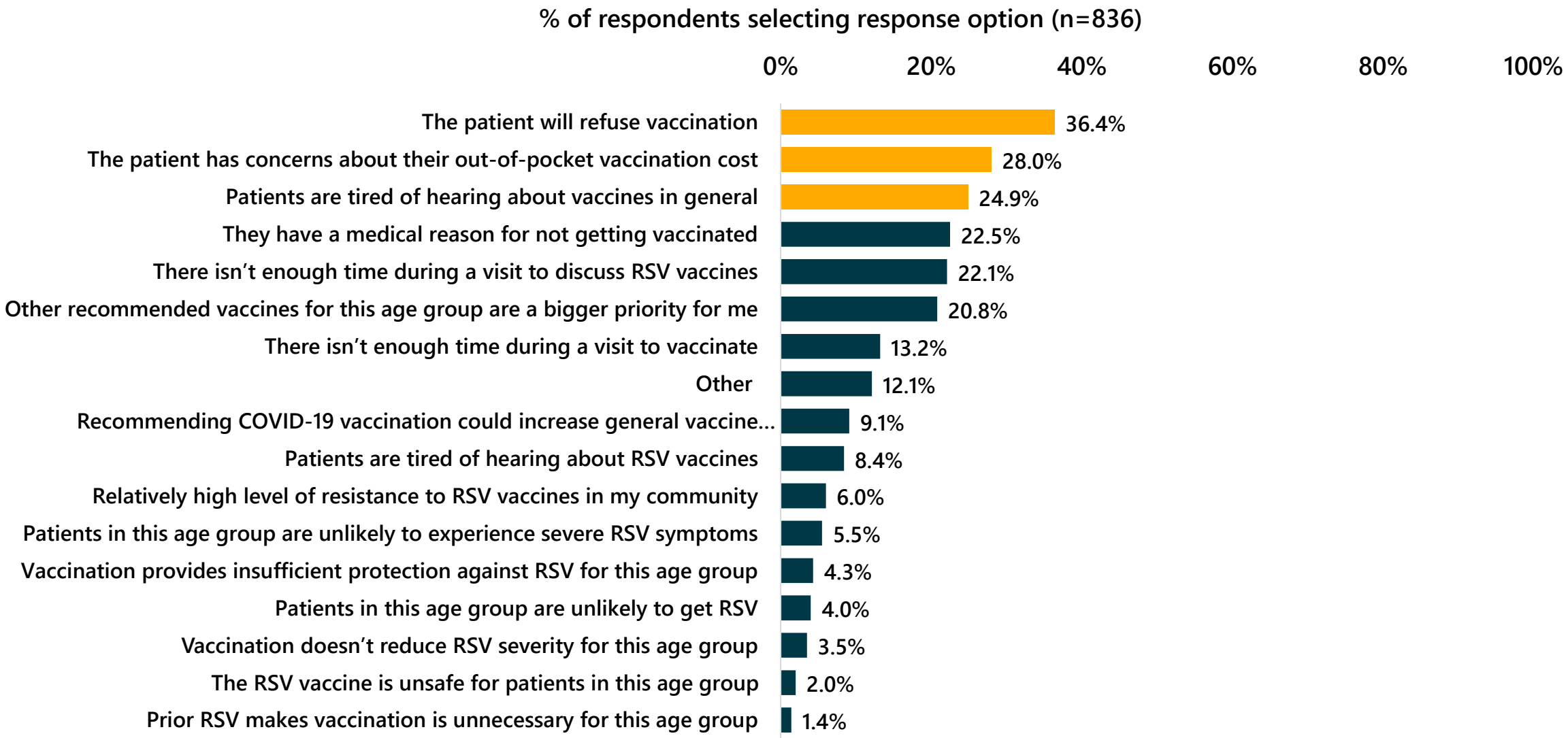
Omnibus Surveys: Data for this analysis were collected through the Ipsos KnowledgePanel and NORC AmeriSpeak Omnibus Surveys, which use probability-based panels to survey a nationally representative sample of U.S. adults aged 18 years and older. CDC fields questions about vaccination status, intent, knowledge, attitudes, beliefs, and behaviors on each survey for 2 waves each month, for a combined sample size of ~4,000 respondents. This slide presents results from December 2024. Data were weighted to represent the non-institutionalized U.S. population and mitigate possible non-response bias. All responses are self-reported.

58% of respondents report checking RSV vaccination eligibility for their adult (aged ≥60 years) patients prior to an appointment most or all the time



Unpublished data—CDC/University of Iowa/RAND survey conducted 6/3-6/24/24. Question respondents (N=926) included Family Medicine providers (N=300), General Internists (N=306), Pharmacists (N=295), and Pediatricians (N=25).

Anticipated vaccine refusal, patient financial concerns, and perceived patient vaccine fatigue were the top reasons for not recommending RSV vaccination



Unpublished data—CDC/University of Iowa/RAND survey conducted 6/3-6/24/24. Respondents for this question included Family Medicine providers, General Internists, Pharmacists, and Pediatricians. Respondents could select multiple answer choices. N=836.

Potential barriers to implementation of a risk-based recommendation for RSV vaccine among adults aged 50–59 years

- **Vaccine acquisition cost is relatively high**
  - Costly upfront investment to carry RSV vaccines
- **Most RSV vaccines are administered in pharmacies**
  - Risk assessment and billing for risk-based recommendations may be challenging
- **Increased vaccine schedule complexity for adults**
  - Limited time to discuss vaccines at appointments
  - Increasing number of adult vaccines
  - Multiple adult RSV vaccine products with different temperature requirements for storage and handling

Acceptability and Feasibility: Summary of the available evidence

Adults aged 50–59 years at increased risk of severe RSV disease

- **Approximately 50% of adults aged 60–74 years with risk conditions have no concerns about RSV vaccine**
  - Among those with concerns, top responses indicated lack of knowledge about RSV vaccine, concern about serious side effects and lack of provider recommendation
- **Providers check RSV vaccine eligibility about 60% of the time**
  - Top barriers for making a recommendation are related to concern about patient vaccine fatigue and vaccine refusal
- **Other implementation barriers include cost, challenges of a risk-based recommendation in pharmacy settings, and schedule complexity**

Acceptability

- **Would recommending RSV vaccines for adults aged 50-59 years at increased risk of severe RSV disease be acceptable to key stakeholders?**

No	Probably No	Probably Yes	Yes	Varies	Don’t know

Feasibility

- **Is it feasible to implement RSV vaccination among adults aged 50-59 years at increased risk of severe RSV disease?**

Minority opinion

Resource Use

Is an RSV vaccine program for **adults aged 50–59 years at increased risk of severe RSV disease** a reasonable and efficient allocation of resources

Work Group considerations regarding societal resource use toward RSV vaccination in older adults at current list prices

- **RSV vaccination for adults aged 50–59 years with risk factors for severe RSV disease has an incremental cost-effectiveness ratio (ICER) of $43,070 (3-year time horizon for protein subunit vaccines) to $152,293 (2-year time horizon for mRNA vaccine)**
- **Vaccination is likely cost-saving for certain risk conditions**
- **Substantial uncertainty in key parameters that impact cost effectiveness:**
  - Uncertainty in incidence of medically attended RSV illness, particularly hospitalizations
  - Uncertainty in RSV-attributable mortality
  - Uncertainty in duration of protection from a single dose of RSV vaccination
  - Real-world vaccine effectiveness of Moderna mResvia; analyses currently rely on clinical trial efficacy estimates
- **If RSV vaccine list prices were substantially reduced, then RSV vaccination may be a cost-effective intervention for a broader adult population**

Resource use

- **Is RSV vaccination a reasonable and efficient allocation of resources in adults aged 50-59 years at increased risk of severe RSV disease?**

No	Probably No	Probably Yes	Yes	Varies	Don't know

Equity

What would be the impact on health equity of recommending RSV vaccination for:

Adults aged 50–59 years at increased risk of severe RSV disease?

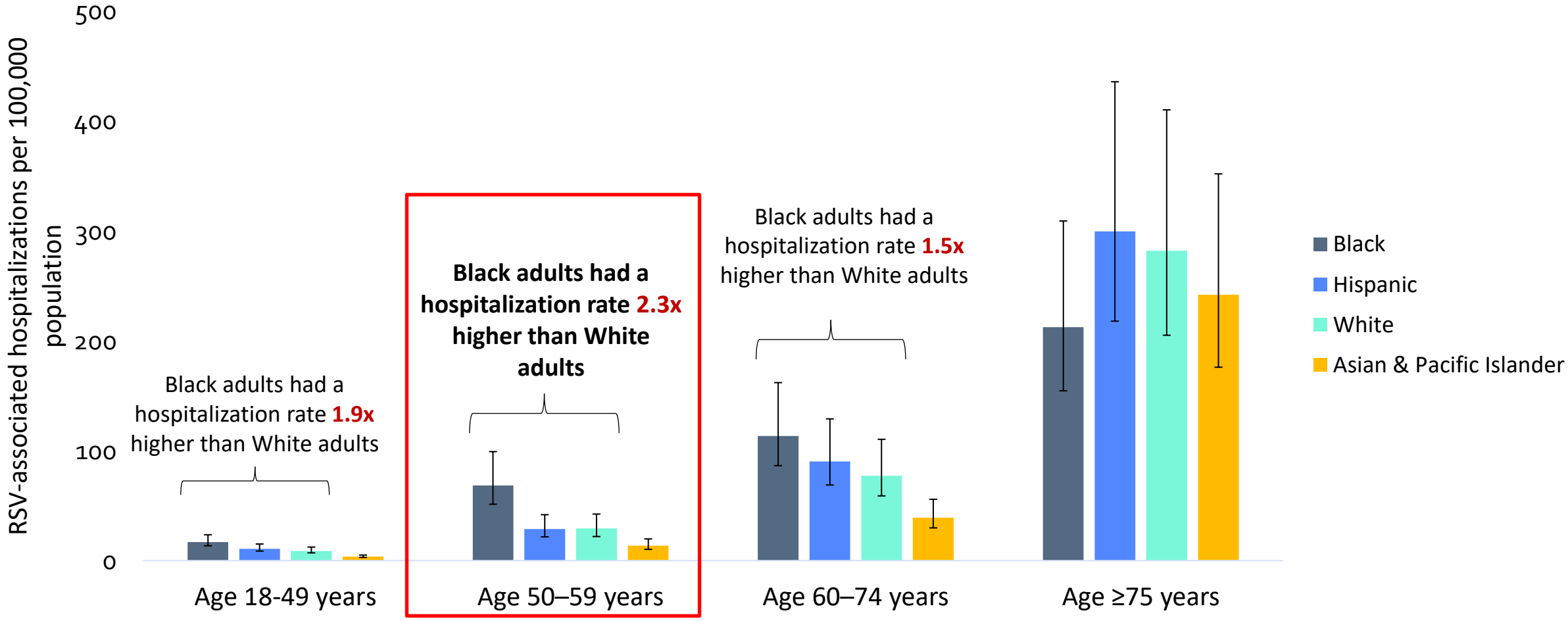
Median age of non-pregnant adults* aged ≥18 years with RSV-associated hospitalizations by race and ethnicity** — RSV-NET, 2014–2015 to 2022–2023

	Unweighted	Weighted %	Median Age	Interquartile range (IQR)
Overall	17,847	-	69	(58–81)
White	10,755	62.2	73	(63–82)
Black	3,529	20.4	**62**	**(50–71)**
Hispanic	1,434	8.3	**62**	**(48–76)**
Asian or Pacific Islander	1,020	5.9	73	(59–83)
American Indian or Alaska Native	90	0.5	**64**	**(54–73)**
Multiple races	89	0.5	75	(58–84)
Unknown	367	2.1	68	(57–78)

Median **age of hospitalization is lower among Black, Hispanic, and American Indian/Alaska Native** persons than White and Asian/Pacific Islander persons.

*Includes men and non-pregnant women.
**Black, White, American Indian/Alaska Native and Asian/Pacific Islander people were categorized as non-Hispanic; Hispanic people could be of any race.

RSV-associated hospitalization rates by age group and by race and ethnicity, RSV-NET, 2018–2019



Unpublished data from RSV-NET. Rates are adjusted using multipliers for the frequency of RSV testing during each season and the sensitivity of RSV diagnostic tests. Error bars represent 95% confidence intervals. Estimated rates exclude recorded hospitalizations among pregnant women. Black, White, and Asian/Pacific Islander people were categorized as non-Hispanic; Hispanic people could be of any race. Hospitalization rates among American Indian and Alaska Native persons are not shown due to small numbers. There may be unmeasured confounding, especially in the oldest age group. Although incidence appears lower in Black adults aged ≥75 years than in White adults, if Black adults are less likely to survive to age 80 or 90 years, then differences in underlying age distribution may be driving this finding.

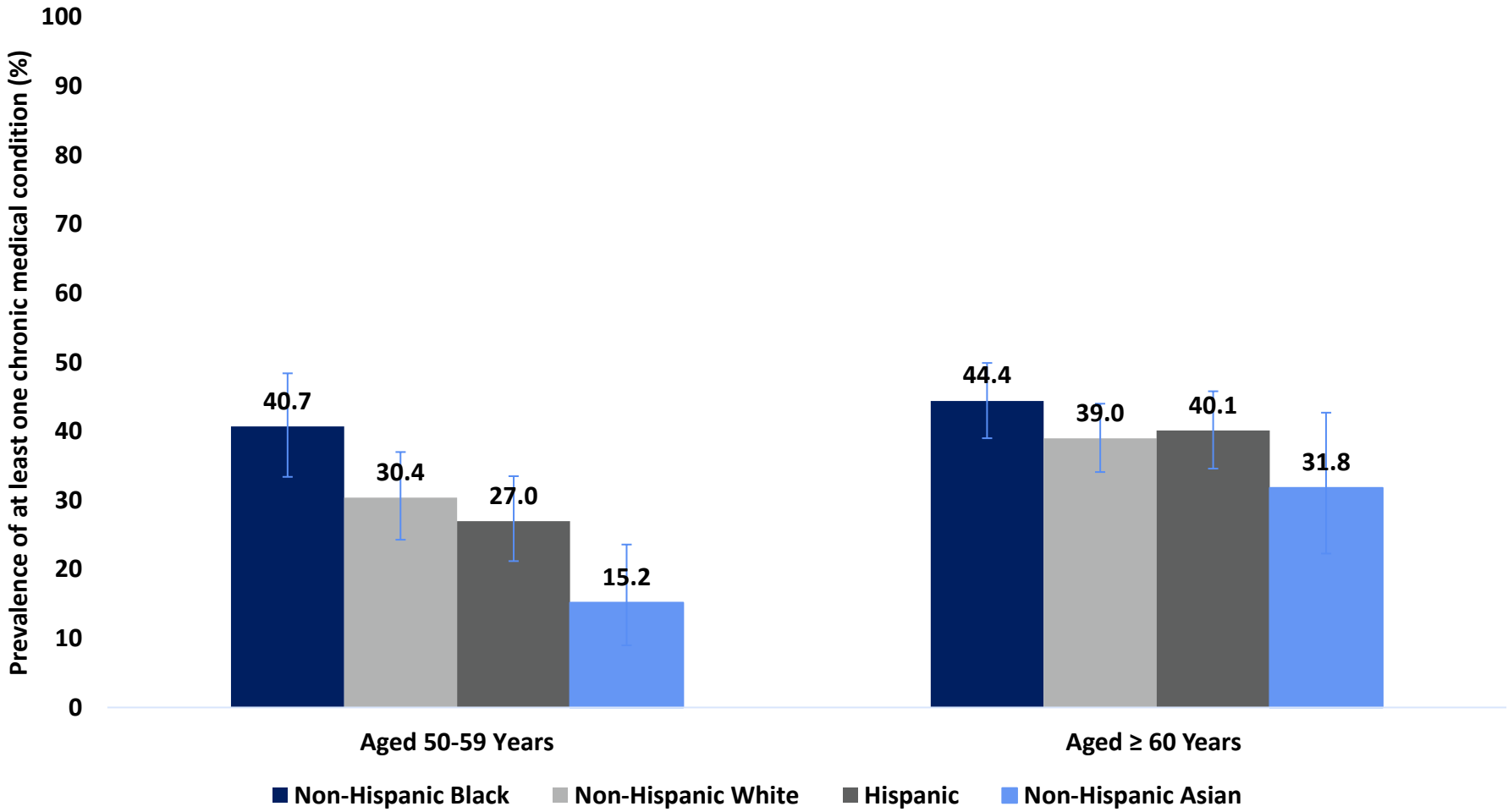
Prevalence of U.S. adults with ≥1 chronic medical condition using narrow definition of chronic medical conditions*, by age and race

National Health and Nutrition Examination Survey (NHANES), 2015—2018

***Narrow definition**, at least one of:

- Serious heart disease
- Diabetes **with complication**
- Chronic obstructive pulmonary disease
- Asthma
- Severe obesity (BMI ≥40 kg/m^2)
- Liver condition
- Chronic kidney disease, **stage 4 or 5**

BMI: body mass index

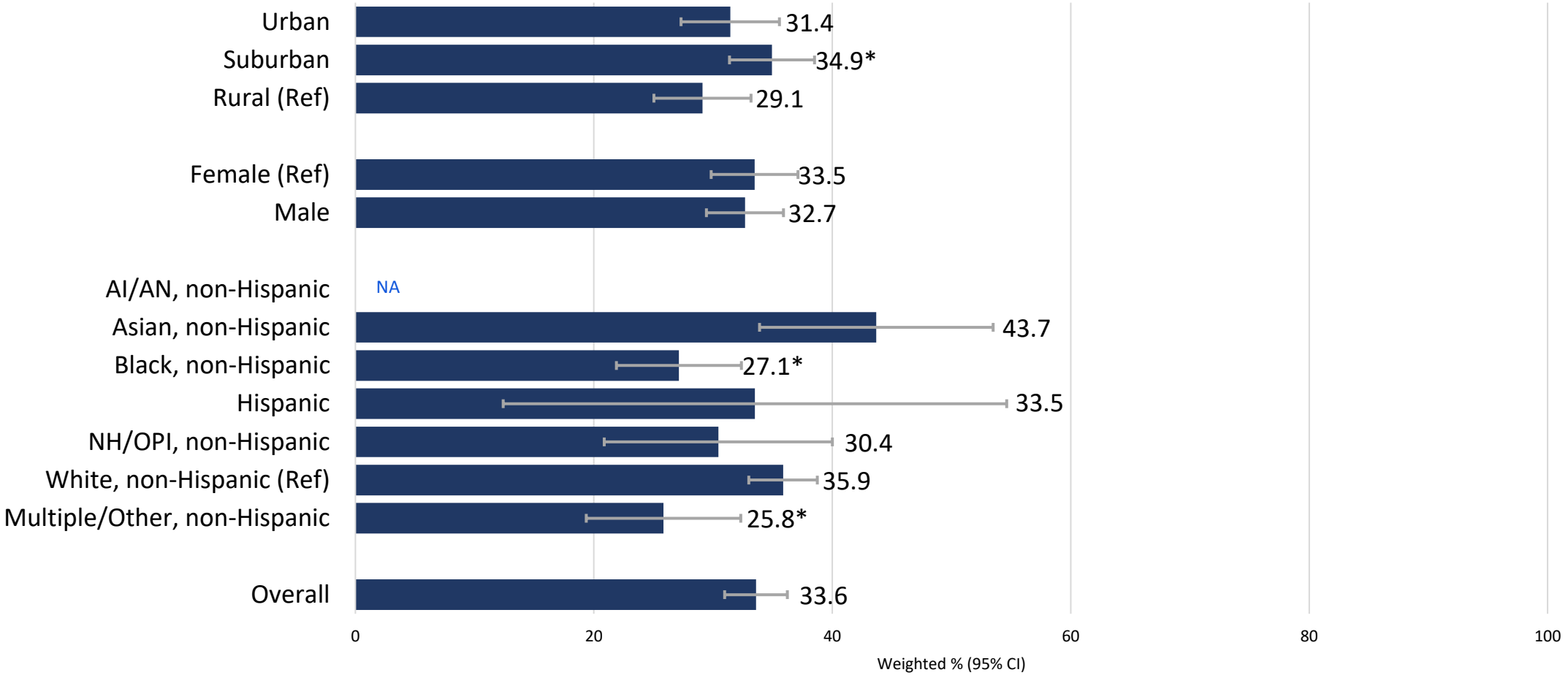


SOURCE: National Center for Health Statistics (NCHS), National Health and Nutrition Examination Survey (NHANES), 2015–2018. All estimates are crude estimates with no age adjustment and age is age at interview. Error bars represent Korn and Graubard 95% confidence intervals. NHANES is representative of the civilian, non-institutionalized U.S. population. For "narrow" definition: Severe obesity was defined as BMI ≥40 kg/m^2. Diabetes with complication was defined as 1) having diabetes: self-reported diabetes, fasting plasma glucose ≥126 mg/dL, or hemoglobin A1c ≥6.5%, AND 2) having one of the following complications of diabetes assessed within the survey: serious heart disease as defined below, chronic kidney disease (stage 3, 4, or 5) defined as estimated glomerular filtration rate (eGFR) <60 (stages 3–5) further defined below, or having self-reported diabetes and having a doctor previously told them that diabetes affected their eyes or that they have retinopathy. Other complications of diabetes are not included in this definition. Serious heart disease was defined based on self-report as diagnosed congestive heart failure, coronary heart disease, angina, or heart attack, or angina grades 1 or 2 determined by the Rose Angina Questionnaire. Asthma was defined as self-reporting ever being diagnosed with asthma and still having asthma. Chronic kidney disease was defined as estimated glomerular filtration rate (eGFR) <30 (stages 4–5), and using a forward equation for adjustment of creatinine because of methods changes. eGFR calculated using the 2021 CKD-EPI creatinine equation (https://www.nejm.org/doi/10.1056/NEJMoa2102953). Urine albumin is not included in this definition. Chronic obstructive pulmonary disease (COPD) was defined as self-reported diagnosed COPD, emphysema, or current chronic bronchitis. Liver condition was defined as self-reporting ever being diagnosed with any kind of liver condition and still having any kind of liver condition. Having at least one of the above conditions for the narrow definition was defined based on the seven (7) conditions listed. Among the fasting sample, ~94% had complete data for all reported medical conditions, ~6% were missing data for one (1) medical condition, <1% were missing data for two (2) medical conditions, and none were missing data for three (3) or more medical conditions. Estimates of having ≥1 condition are weighted using fasting sample weights.

RSV Vaccination Coverage Among Adults Aged 60–74 Years at Increased Risk** for Severe RSV, by December 28, 2024

National Immunization Survey-Adult COVID Module (NIS-ACM)

Age 60–74 Years, at Increased Risk (n=13,919)



NA: estimate not reported because denominator is <30; AI/AN: American Indian or Alaska Native; NH/OPI: Native Hawaiian or Other Pacific Islander; CI: 95% confidence interval; Ref: Referent category.

*Statistically significant at p<0.05 compared to the referent category.

**A respondent was considered to be at increased risk for severe RSV disease if they had any of the following: self-reported chronic lung diseases, diabetes with insulin use, heart conditions, immunocompromised state, solid organ or blood stem cell transplant (including bone marrow transplant), cancer, liver disease, sickle cell disease or thalassemia, or currently lives in a nursing home.

NIS-ACM methods: Data from adults age ≥18 years are collected by telephone interview using a random-digit-dialed sample of cell telephone numbers stratified by state, the District of Columbia, five local jurisdictions (Bexar County TX, Chicago IL, Houston TX, New York City NY, and Philadelphia County PA), and Puerto Rico and the U.S. Virgin Islands. Data are weighted to represent the non-institutionalized U.S. population and mitigate possible bias that can result from an incomplete sample frame (exclusion of households with no phone service or only landline telephones) or non-response. All responses are self-reported. For more information about the survey, see https://www.cdc.gov/nis/about/index.html.

Equity: Summary of the available evidence

Adults 50–59 years at increased risk of severe RSV disease

- Overall rates of RSV among all race and ethnicity groups remain lower in adults aged <60 years than adults 60–74 and 75 years and older; however, Black adults aged 50–59 years had higher RSV hospitalization rates than White adults
- Chronic conditions that increase risk of severe RSV disease occur more frequently among certain racial and ethnic groups aged 50–59
- RSV vaccine uptake varies by race and ethnicity

Equity

- What would be the impact on health equity of recommending RSV vaccination in **adults aged 50-59 years at increased risk of severe RSV disease?**

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

Summary

Domain	Among adults aged 50–59 years at increased risk of severe RSV disease	Work Group Majority Opinion
Public Health Problem	Is RSV of public health importance?	Yes/Probably yes
Benefits and Harms	How substantial are the desirable anticipated effects?	Moderate
	How substantial are the undesirable anticipated effects?	Small
	Do the desirable effects outweigh the undesirable effects?	Favors intervention
Values	Does the target population feel the desirable effects are large relative to the undesirable effects?	Probably yes
	Is there important variability in how patients value the outcomes?	Probably important uncertainty or variability
Acceptability	Is the intervention acceptable to key stakeholders?	Yes/Probably yes
Feasibility	Is the intervention feasible to implement?	Yes/Probably yes
Resource Use	Is the intervention a reasonable and efficient allocation of resources?	Yes/Probably yes
Equity	What would be the impact on health equity?	Probably increased

Proposed ACIP vote language

1. ACIP recommends that adults 50–59 years of age who are at increased risk of severe RSV disease[a] receive a single dose of RSV vaccine.[b,c]

a. CDC will publish Clinical Considerations that describe chronic medical conditions and other risk factors for severe RSV disease for use in this risk-based recommendation.

b. RSV vaccination is recommended as a single dose only. Persons who have already received RSV vaccination are NOT recommended to receive another dose.

c. RSV vaccine can be administered with any product licensed in this age group.

Evidence to Recommendations Framework

Summary: Work Group Interpretations

Among adults aged 50-59 years at increased risk of severe RSV disease:

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

Minority opinion

Evidence to Recommendations Framework

Summary: Work Group Interpretations

Is there sufficient information to move forward with a recommendation?

Among adults aged 50-59 years at increased risk of severe RSV disease:

Minority opinion

Evidence to Recommendations Framework

Summary: Work Group Interpretations

Type of recommendation, adults aged 50-59 years at increased risk of severe RSV disease:

We do not recommend the intervention
We recommend the intervention for individuals based on shared clinical decision-making
We recommend the intervention

Work Group considerations

- **The Work Group also discussed which risk conditions should be included in a risk-based recommendation for adults aged 50-59 years.**
  - Should risk conditions be the same as those for adults aged 60-74 years? Or should they be different?
- **Discussion points favoring the same risk conditions as those outlined for adults aged 60-74 years:**
  - Significant concerns about complexity for providers and patients in having a different list of risk conditions for adults aged 50-59 years than adults aged 60-74 years.
  - Adults aged 50-59 years have similar conditions that increase risk of severe RSV disease as adults aged 60-74 years.
- **Discussion points favoring a narrower list of risk conditions than those outlined for adults aged 60-74 years:**
  - Due to increasing vaccine fatigue and complexity of the adult immunization schedule, perhaps focus for providers and patients should be on a adults with a narrower list of risk conditions, who are at highest risk of severe RSV disease
  - While the vaccine looks to be cost-saving for certain risk conditions, recommending RSV vaccine for the same list of risk conditions among adults aged 50-59 as 60-74 years is less cost-effective in adults aged 50-59 than in those 60-74.
  - There remains important uncertainty in whether revaccination can restore protection to levels seen after the first dose. This may be a more important consideration when developing a recommendation for younger adults with longer remaining life expectancy.

Work Group considerations

- **Overall, the Work Group majority feels that risk conditions for a recommendation in adults aged 50-59 years should include the same conditions already outlined in the risk-based recommendation for adults aged 60-74 years**
- **With this recommendation, the Work Group stresses that additional data will be critical to understand the optimal revaccination interval and that studies supporting the preferred policy around revaccination are needed**
- **The Work Group also stresses the importance of ongoing safety surveillance monitoring**

Acknowledgements

- Adult RSV Vaccine Work Group
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- CDC Immunization Services Division
- CDC Immunization Safety Office
- FDA Center for Biologics Evaluation and Research
- David Hutton, University of Michigan

For more information, contact CDC
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