

Thank you for joining

The presentation will begin shortly





Rise to Immunize® Monthly Webinar



Kathryn M. Edwards, MD, Vanderbilt University Medical Center





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- Campaign Expansion/ Extension
- RIZE Action Month
- Resource of the Month

Today's Webinar

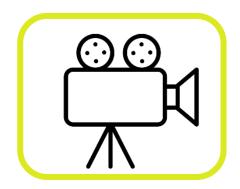
RSV 101

• Kathryn M. Edwards, MD, *Vanderbilt University Medical Center*

Q&A Session

Webinar Reminders





Today's webinar recording will be available the **week** of 08/19

- Will be sent via email
- Will be available on website



Ask questions during the webinar using the **Q&A feature**

Questions will be answered at the end of the presentation

(RiseToImmunize.org → "Resources" → "Webinars")

More Vaccines! More Time!



RSV

Proportion of patients aged 75+ who ever received the RSV vaccination

COVID-19

Proportion of patients
aged 19+ who
received the COVID-19
vaccination in the
Measurement Year

Hepatitis B

Proportion of patients aged 19-59 who completed the hepatitis B series during or prior to the Measurement Year

Together, we can administer 30 million vaccines by 2027 through comprehensive and equitable vaccine initiatives.

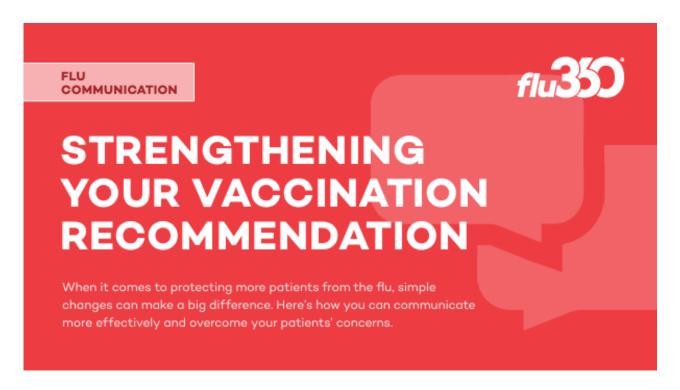


Action Month August 2024

Resource of the Month

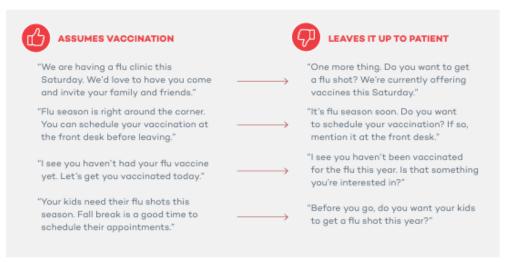


"Best Practices for a Strong Vaccine Recommendation" guide



IT STARTS WITH PRESUMPTIVE LANGUAGE

Presumptive language that assumes the patient is willing to participate can help overcome vaccine hesitancy. Here's a quick look at some strong and weak recommendations.



CSL Segirus

Today's Speaker





Kathryn M. Edwards, MD, Sarah H. Sell and Cornelius Vanderbilt Professor of Pediatrics, *Vanderbilt University Medical Center*

Respiratory Syncytial Virus (RSV) Vaccines for Older Adults

Kathryn M. Edwards MD
Professor of Pediatrics Emerita
Vanderbilt University Medical Center
Nashville, TN

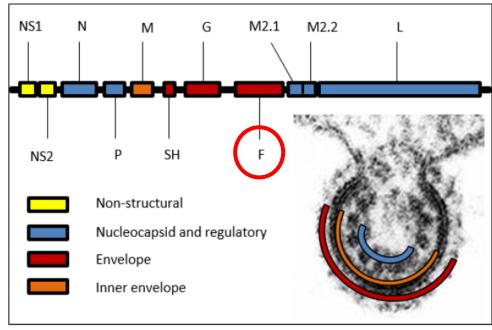
Disclosures

Affiliation / Financial Interest	Organization
Grant Recipient	CDC (Vaccine Safety)
Grant Recipient	NIH (Mentoring young investigators in vaccine sciences)
Consultant	Dynavax (pertussis vaccines), IBM (vaccine safety networks), AstraZeneca (human metapneumovirus vaccine)
Data Safety and Monitoring Board	Sanofi, X-4 Pharma, Seqirus, Moderna, Pfizer, Merck, Roche, Novavax

Objectives of Presentation

- Review the Structural Basis of Immunity to RSV
- Review the Impact of RSV on Older Adults
- Discuss Three Vaccines for RSV prevention
 - GlaxoSmithKline (Arexvy)
 - Pfizer (Abrysvo)
 - Moderna (mResvia)
- Outline efficacy and safety of each vaccine
- Review current recommendations for vaccine use in older adults

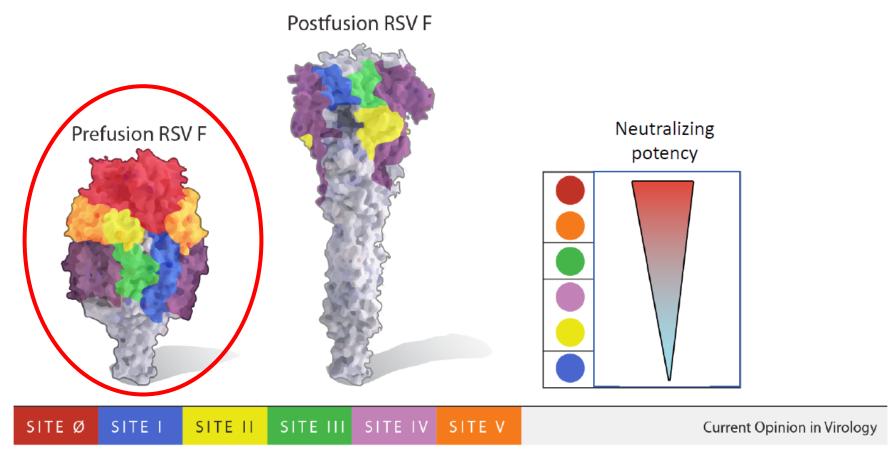
RSV genome



Respiratory Syncytial Virus (RSV) | British Society for Immunology

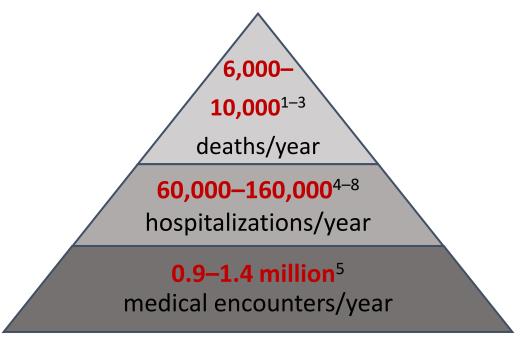
- Filamentous Orthopneumovirus
- 15.2 kbp genome
- Single stranded negative sense
- 11 viral proteins
- Divided into two subgroups / serotypes
 A and B
- RSV A and B co-circulate

The fusion (F) protein exists in two or more structural forms exposes different antigenic regions

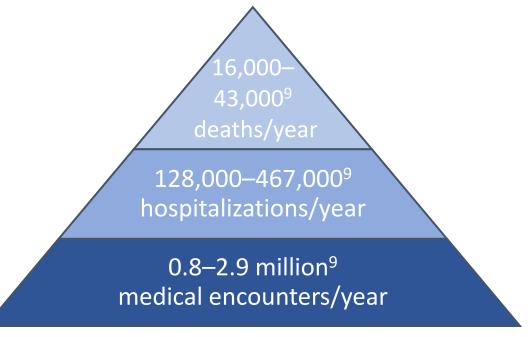


Graham B. Current Opinion in Virology. 23: 107-112. 2017.

RSV and influenza burden, compared



RSV Adults aged ≥65 years

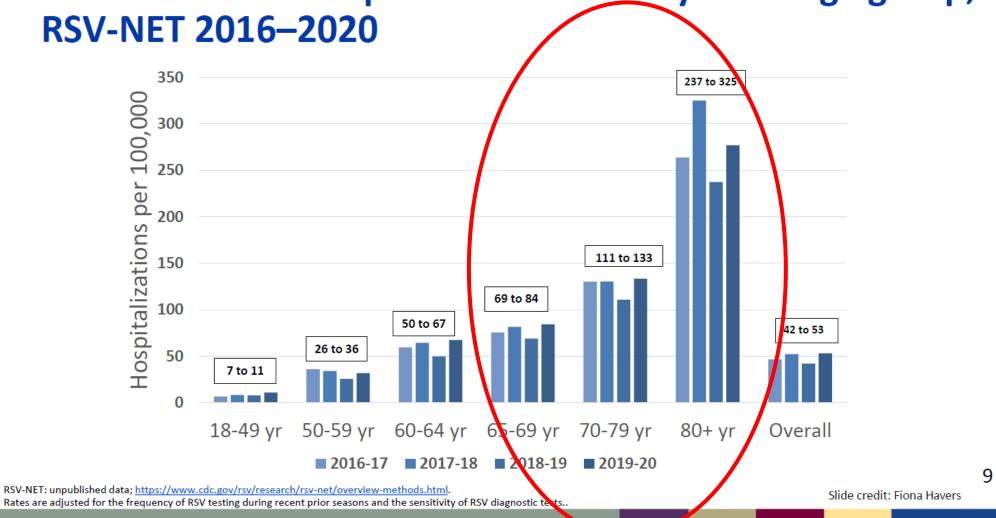


Influenza Adults aged ≥65 years

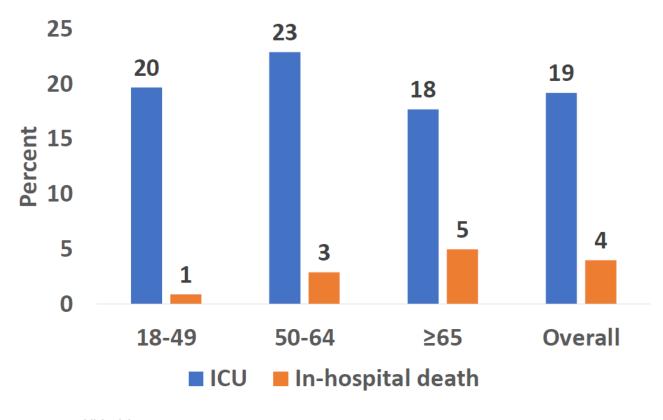
- 1. Thompson et al, JAMA (2003): https://doi.org/10.1001/jama.289.2.179
- Matias et al, Influenza Other Respi Viruses (2014): https://doi.org/10.1111/irv.12258
- 3. Hansen et al, JAMA Network Open (2022):
 - https://doi.org/10.1001/jamanetworkopen.2022.0527
- 4. Widmer et al, JAMA Network Open (2012):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

- . McLaughlin et al, Open Forum Infect Dis (2022): https://doi.org/10.1093/ofid/ofac300
- 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)
- 9. CDC Influenza Burden 2015-2020: https://www.cdc.gov/flu/about/burden/past-seasons.html

RSV-associated hospitalization rates by adult age group,



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



Severe
outcomes
frequent among
adults
hospitalized for
RSV of all ages

15

Source: CDC unpublished data.

Underlying medical conditions among adults ≥18 years hospitalized for RSV: RSV-NET 2014-2018

Major underlying condition categories		
(n=4,970)	N=4,970	%
Cardiovascular disease	2833	57.0
Chronic lung disease	2486	50.0
Diabetes mellitus	1692	34.0
Renal disease	1378	27.7
Immunocompromised condition	1126	22.7
Neurologic disorder	1041	21.0
Chronic metabolic disease (except diabetes)	934	18.8
Liver disease	332	6.7
Blood disorders/ hemoglobinopathy	132	2.7
Other disease or condition	429	8.7

94% of hospitalized adults have underlying medical conditions:

• 46%: 1-2 conditions

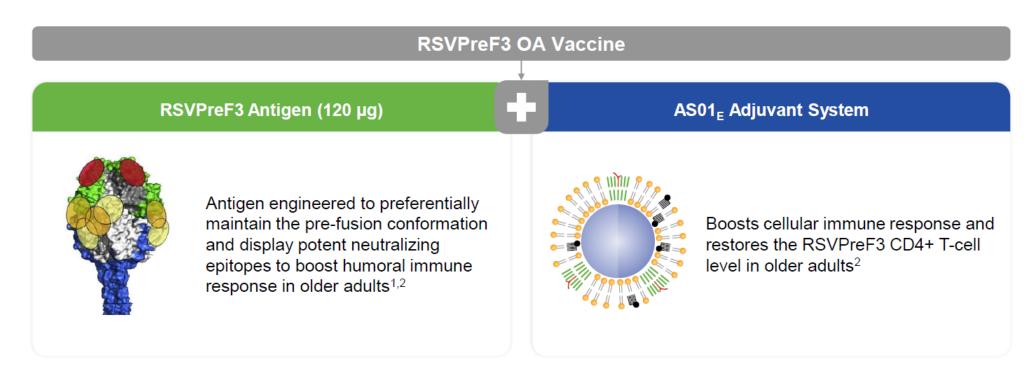
• 48%: ≥3 conditions

12

Source: CDC unpublished data.

► GSK's RSV older adult vaccine

The combination of RSVPreF3 (120 μg) and AS01_E s designed to induce a robust humoral and cellular immune response, to help protect older adults and those with underlying comorbidities

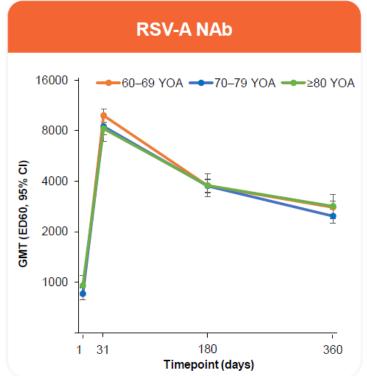


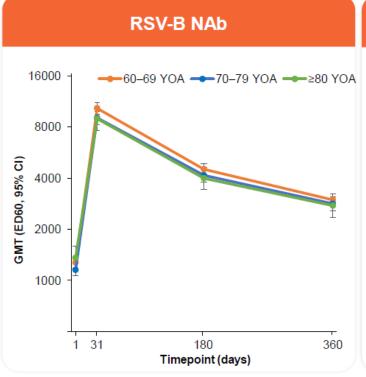


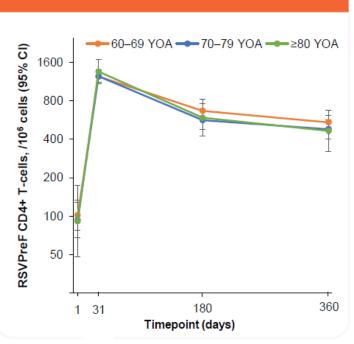
AS01_E, Adjuvant System 01_E (25 µg Quillaja saponaria Molina, fraction 21, 25 µg 3-Odesacyl-4'- monophosphoryl lipid A); OA, older adults. Image of F protein reproduced from Graham BS, et al. Curr Opin Immunol 2015;35:30–38, Copyright 2015, with permission from Elsevier.

1. Graham BS, et al. Curr Opin Immunol. 2015;35:30–38; 2. Leroux-Roels I, et al. J Infect Dis. 2022;jiac327.

Durable RSV-A, RSV-B neutralizing antibody and CD4+ T-cell responses across all age groups, 12 months post vaccination







RSVPreF3-specific CD4+ T-cells*



*CD4+ T-cells expressing ≥2 activation markers including ≥1 cytokine among CD40L, 4-1BB, IL-2, TNF-α, IFN-γ, IL-13, IL-17 (events/10⁶ cells; by intracellular staining). Data at each timepoint for all 3 groups combined: Day 1 N=985 for RSV A, N=986 for RSV B, and N=471 for RSVPreF-specific CD4+ T-cells; Month 6=924 for RSV A and B and N=436 for RSVPreF-specific CD4+ T-cells; Month 12 N=870 for RSV A and B, and N=438 for RSVPreF-specific CD4+ T-cells; Month 12 N=870 for RSV A and B, and N=438 for RSVPreF-specific CD4+ T-cells; NCT0473287. CD, cluster of differentiation; CI, confidence interval; ED, Estimated Dilution; ED60, serum dilution inducing 60% inhibition in plaque-forming units; GMT, geometric mean titer; IL, interleukin; NAb, neutralizing antibody; TNF, tumor necrosis factor; YOA, years of age.

1. https://clinicaltrials.gog/ct2/show/NCT04732871 (accessed October 2022).

TABLE 1. Efficacy of 1 dose of GSK respiratory syncytial virus RSV preF3 vaccine against respiratory syncytial virus—associated disease among adults aged ≥60 years — multiple countries, 2021–2023

	Vaccine efficacy against outcome*			
Efficacy evaluation period	RSV-associated LRTD [†]	RSV-associated medically attended LRTD [§]		
Season 1 [¶]	82.6 (57.9-94.1)**	87.5 (58.9-97.6) ^{††}		
Season 2 ^{§§}	56.1 (28.2-74.4) ^{††}	11		
Combined seasons 1 and 2 (Interim)***	74.5 (60.0–84.5)†††	77.5 (57.9–89.0) ^{††}		

Abbreviations: LRTD = lower respiratory tract disease; RSV = respiratory syncytial virus.

Melgar M, Britton A, Roper LE, et al. Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023. 20 MMWR Morb Mortal Wkly Rep 2023;72:793–801. DOI: http://dx.doi.org/10.15585/mmwr.mm7229a4

TABLE 2. Safety* of 1 dose of GSK respiratory syncytial virus RSVPreF3 vaccine in adults aged ≥60 years — multiple countries, 2021–2023

	Risk for event			
Safety event	RSVPreF3 recipients no./No. (%) [†]	Placebo recipients no./No. (%) [§]	Relative risk (95% CI)¶	
Serious AE**	549/12,570 (4.4)	540/12,604 (4.3)	1.02 (0.91–1.15)	
Severe reactogenicity events ^{††}	37/979 (3.8)	9/976 (0.9)	4.10 (1.99–8.45)	
Inflammatory neurologic events ^{§§}	3 events in trials without placebo recipients¶	¶'		

Abbreviations: AE = adverse event; GBS = Guillain-Barré syndrome.

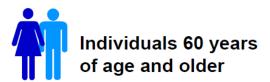
Melgar M, Britton A, Roper LE, et al. Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023. MMWR Morb Mortal Wkly Rep 2023;72:793–801. DOI: http://dx.doi.org/10.15585/mmwr.mm7229a4

PFIZER RSV Vaccine

Bivalent RSV Prefusion F Vaccine

Proposed Indication:

Prevention of acute respiratory disease and lower respiratory tract disease caused by respiratory syncytial virus (RSV)





DOSE LEVEL

- 120 µg without an adjuvant
- Dose contains 60 µg dose of each prefusion protein antigen, in a 0.5 mL injection



PRESENTATION

- Single dose 2 mL vial
- 1 mL Pre-filled syringe
- Vial adaptor



STORAGE

- Refrigeration at 2°C to 8°C (36°F to 46°F)
- After reconstitution: 15°C to 30°C (used within 4 hours of reconstitution)

RSV Neutralizing Titer GMFRs at 1, 6, and 12 months After Vaccination Compared with Pre-vaccination for RSV Subgroups A and B in Participants 65–85 Years of Age

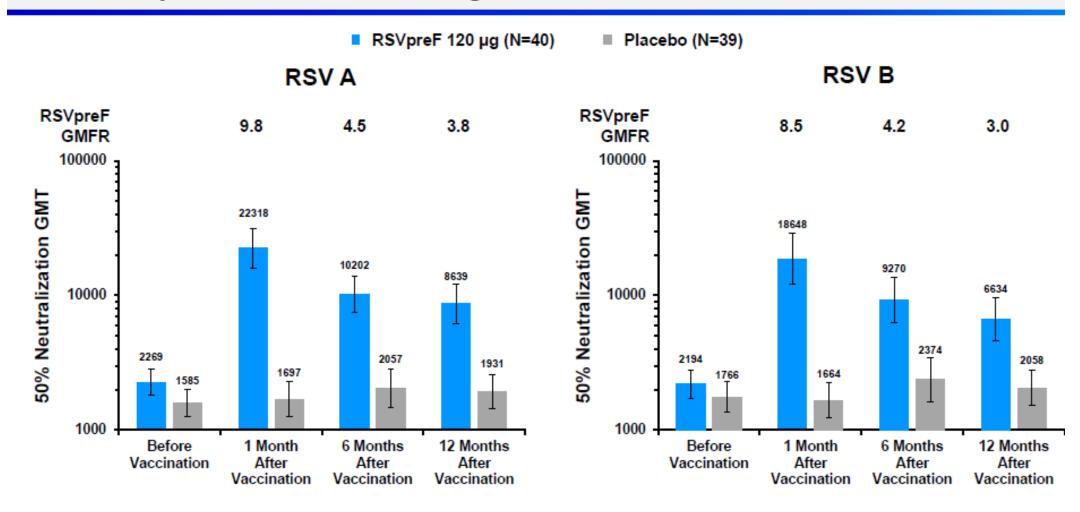


TABLE 3. Efficacy of 1 dose of Pfizer respiratory syncytial virus RSVpreF vaccine against respiratory syncytial virus—associated disease among adults aged ≥60 years — multiple countries, 2021–2023

Vaccine efficacy against outcome, % (95% CI)*

Efficacy evaluation period	RSV-associated LRTD [†]	RSV-associated medically attended LRTD [§]
Season 1 [¶]	88.9 (53.6-98.7)	84.6 (32.0-98.3)
Season 2 (interim)**	78.6 (23.2-96.1)	††
Combined seasons 1 and 2 (Interim)§§	84.4 (59.6–95.2)	81.0 (43.5–95.2)

Abbreviations: LRTD = lower respiratory tract disease; LRTI = lower respiratory tract illness; RSV = respiratory syncytial virus.

Melgar M, Britton A, Roper LE, et al. Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023. MMWR Morb Mortal Wkly Rep 2023;72:793–801. DOI: http://dx.doi.org/10.15585/mmwr.mm7229a4

TABLE 4. Safety* of 1 dose of Pfizer respiratory syncytial virus RSVpreF vaccine in adults aged ≥60 years — multiple countries, 2021–2023

	Risk for event			
Safety event	RSVpreF recipients no./No. (%) [†]	Placebo recipients no./No. (%) [§]	Relative risk (95% CI)¶	
Serious AE**	792/18619 (4.3%)	749/18334 (4.1%)	1.04 (0.94–1.15)	
Severe reactogenicity events ^{††}	36/3673 (1.0%)	24/3491 (0.7%)	1.43 (0.85–2.39)	
Inflammatory neurologic events [§]	3/18622 (—)¶¶	0/18335 (—)	11	

Abbreviations: AE = adverse events; GBS = Guillain-Barré syndrome.

Melgar M, Britton A, Roper LE, et al. Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023. MMWR Morb Mortal Wkly Rep 2023;72:793–801. DOI: http://dx.doi.org/10.15585/mmwr.mm7229a4

Cases of Guillain Barré syndrome (GBS) were reported after vaccination with both investigational vaccines

- All cases had onset during the 42-day risk window post-vaccination used in CDC surveillance
- The significance of 1–2 cases in safety databases of 15,000–26,000 persons is unclear
- Population-based rates of GBS increase with age^a
- RSV infection has also been associated with GBS in case reports and case series^{b,c}, but causal link has not been established
- The work group continues to review and interpret safety evidence

^a Sejvar JJ, Baughman AL, Matthew Wise, Morgan OW. Population incidence of Guillain-Barré syndrome: a systematic review and meta-analysis. Neuroepidemiology. 2011;36(2):123-33.

^b Helgeson SA, Heckman AJ, Harris DM. First Reported Case of Respiratory Syncytial Virus Infection Causing Guillain-Barré Syndrome. Indian J Crit Care Med. 2018 Apr;22(4):309-310.

^c Munayco CV, Gavilan RG, Ramirez G, et al. Large Outbreak of Guillain-Barré Syndrome, Peru, 2019. Emerg Infect Dis. 2020 Nov;26(11):2778-2780.

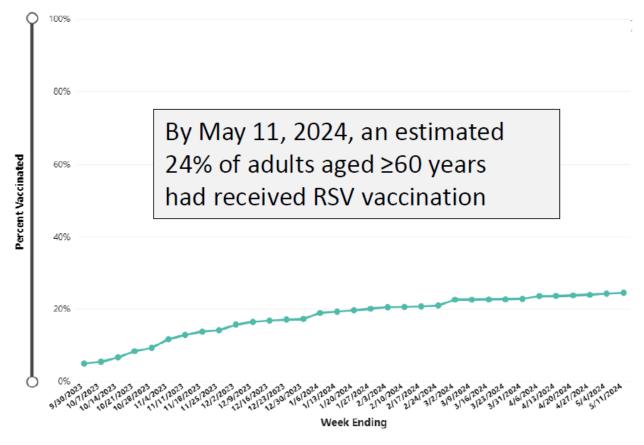
Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023

Michael Melgar, MD¹; Amadea Britton, MD¹; Lauren E. Roper, MPH¹; H. Keipp Talbot, MD²; Sarah S. Long, MD³; Camille N. Kotton, MD⁴; Fiona P. Havers, MD¹

Recommendations for Use of RSV Vaccines in Older Adults

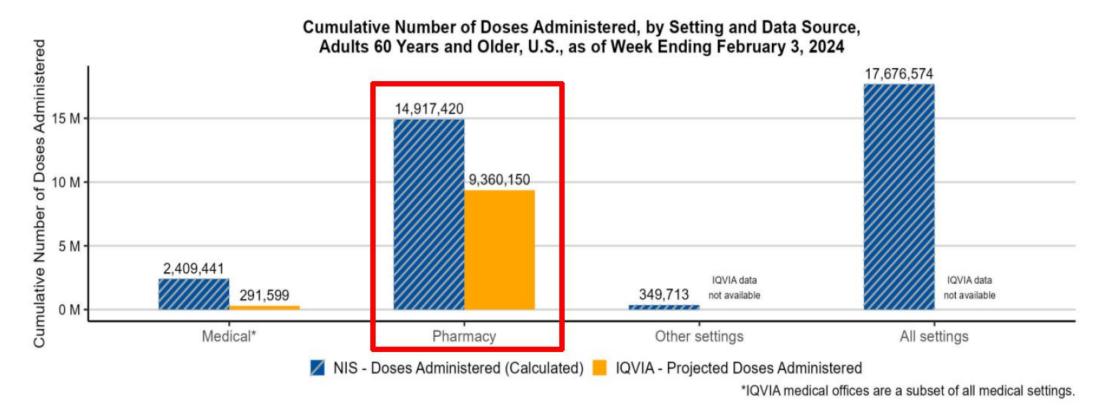
On June 21, 2023, ACIP recommended that adults aged ≥60 years may receive a single dose of RSV vaccine, using shared clinical decision-making. §§§§§

Cumulative RSV vaccine coverage among adults aged ≥60 years, September 30, 2023 – May 11, 2024



Data source: National Immunization Survey – Adult COVID Module. Available at: Respiratory Syncytial Virus (RSV) Vaccination Coverage and Intent for Vaccination, Adults 60 Years and Older, United States | CDC. Accessed on June 13, 2024.

Most RSV vaccinations were administered in pharmacy settings



Data source: Dr. Carla Black. Implementation update: older adult RSV vaccination. ACIP Meeting, February 29, 2024. Available at: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2024-02-28-29/04-RSV-Adults-Black-508.pdf



50 μg mRNA encoding prefusion F protein

NEWS RELEASE

Moderna Receives U.S. FDA Approval for RSV Vaccine mRESVIA(R)

5/31/2024

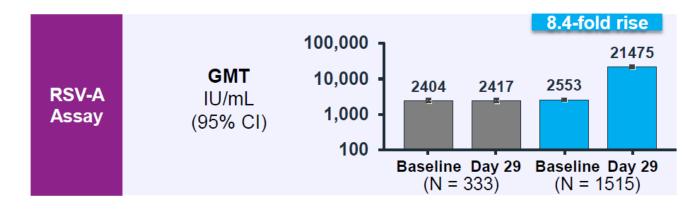
mRESVIA is Moderna's second approved product and the only RSV vaccine available in single-dose pre-filled syringes

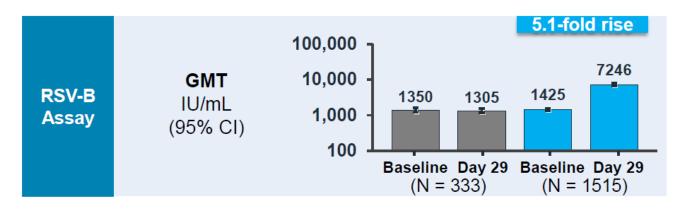
CAMBRIDGE, MA / ACCESSWIRE / May 31, 2024 Moderna, Inc. (NASDAQ:MRNA) today announced that the U.S. Food and Drug Administration (FDA) has approved mRESVIA (mRNA-1345), an mRNA respiratory syncytial virus (RSV) vaccine, to protect adults aged 60 years and older from lower respiratory tract disease caused by RSV infection. The approval was granted under a breakthrough therapy designation and marks the second approved mRNA product from Moderna.

Neutralizing Antibody Response by RSV Subtype – Baseline and Day 29

Study 301 - Microneutralization Antibody (IU/mL)

Per Protocol Immunogenicity Set







- Participants had baseline titers consistent with prior exposure to RSV
- One dose of 50 µg of mRNA-1345 increased titers by:
 - >8-fold for RSV-A
 - >5-fold for RSV-B



Figure 2. Solicited Local and Systemic Adverse Reactions.

Adverse Events of Special Interest (AESI)

Study 301

Safety Set

Neurological Disorders

- No cases of acute disseminated encephalomyelitis (ADEM)
- No safety concern with Guillain-Barre syndrome (3 unrelated cases reported >500 days postinjection [1 vaccine, 2 placebo])
- No imbalance observed for other neurological disorders including Bell's palsy/facial paralysis

Cardiac Events

- No imbalance observed in cardiac arrhythmias such as atrial fibrillation
- No confirmed cases of:
 - Acute myocarditis in vaccine recipients
 - Acute pericarditis in vaccine recipients with onset < 42 days

Efficacy of mRNA-1345 Against RSV LRTD among Adults ≥ 60 Years

Study 301 – Primary and Additional Analyses

Per Protocol Analysis

	Primary Analysis (Case Driven) ¹ 3.7 Months Median (range 0.5 - 12.6) Follow-up		Additional Analysis¹ 8.6 Months Median (range 0.4 – 17.7) Follow-up			
Cases, n (%)	RSV Vaccine (mRNA-1345) (N = 17,561)	Placebo (N = 17,503)	Vaccine Efficacy (%Cl*)	RSV Vaccine (mRNA-1345) (N = 18,074)	Placebo (N = 18,010)	Vaccine Efficacy (% CI*)
RSV LRTD ≥ 2 symptoms	15 (0.09%)	70 (0.40%)	78.7% (62.8%, 87.9%)	48 (0.27%)	127 (0.71%)	62.5% (47.7%, 73.1%)
RSV LRTD ≥ 3 symptoms	5 (0.03%)	26 (0.15%)	80.9% (50.1%, 92.7%)	20 (0.11%)	51 (0.28%)	61.1% (34.7%, 76.8%)

- Vaccine protection continued through a high incidence RSV season (2022/2023)
- Lower bound of confidence interval continued to exceed 20%

1. US product insert mRESVIA

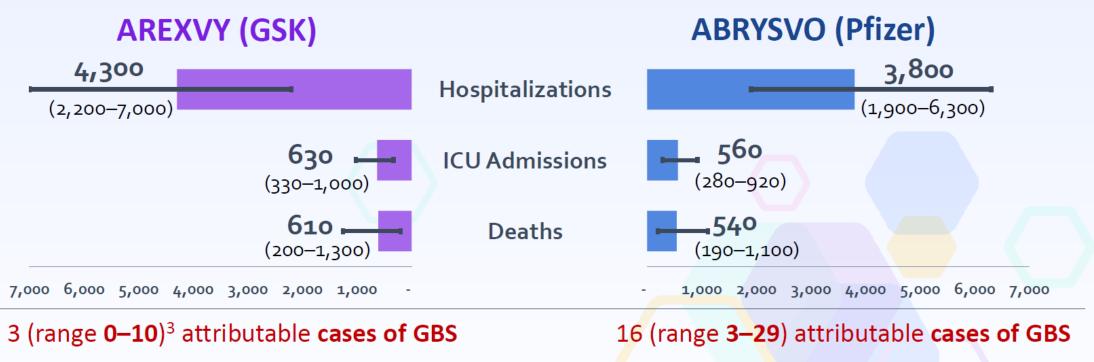
^{*} For primary analysis, the alpha-adjusted 95.04% CI and 95.10% CI for RSV LRTD ≥ 2 symptoms and ≥ 3 symptoms are presented, respectively. For additional analysis, 95% CIs are presented. Efficacy based on hazard ratios

Use of Respiratory Syncytial Virus Vaccines in Adults Aged ≥60 Years: Updated Recommendations of the Advisory Committee on Immunization Practices — United States, 2024

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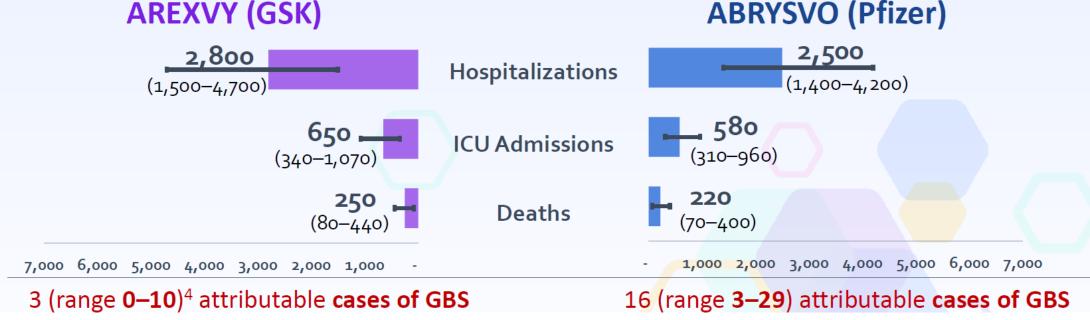
Estimated RSV-Associated Outcomes¹ Preventable <u>over 2 RSV Seasons</u> vs. potential cases of GBS (positive predictive value-adjusted attributable risk of GBS in FDA-CMS partnership data among adults aged ≥65 years, 42-day risk interval²)

Per 1 Million Vaccine Doses Administered to Adults Aged ≥75 Years:



Estimated RSV-Associated Outcomes¹ Preventable <u>over 2 RSV Seasons</u> vs. potential cases of GBS (positive predictive value-adjusted attributable risk of GBS in FDA-CMS partnership data among adults aged ≥65 years, 42-day risk interval²,³)

Per 1 Million Vaccine Doses Administered to Adults Aged 60–74 Years at Increased Risk of Severe RSV Disease:



Chronic medical conditions associated with increased risk of severe RSV disease



Lung disease



Cardiovascular disease



Moderate or severe immune compromise



Diabetes Mellitus with end-organ damage



Severe obesity (body mass index ≥40 kg/m²)



Neurologic or neuromuscular conditions



Chronic kidney disease, advanced



Liver disorders



Hematologic disorders



Other chronic medical conditions that a healthcare provider determines increases risk of severe disease due to respiratory infection

Other factors associated with increased risk of severe RSV disease



Residence in a nursing home or other long-term care facility (LTCF)*



Frailty



Other factors determined to increase risk of severe disease due to respiratory infection

*Long-term care facilities do NOT include retirement communities or senior independent living communities in which residents are able to perform activities of daily living without assistance.

RSV vaccination will have the most benefit if given in late summer or early fall.

- This means from August to October in most of the United States.
- Note this is not a formal seasonal recommendation for RSV vaccination. Older adults may continue to receive RSV vaccination year-round.

Adults who have already received a dose of RSV vaccine DO NOT need to receive another dose this year.

- RSV vaccination should be given ONLY to adults who have not yet received a dose of RSV vaccine.
- At this time, it is anticipated that adults may need additional doses of RSV vaccine in the future, but ideal revaccination timing is not yet known.

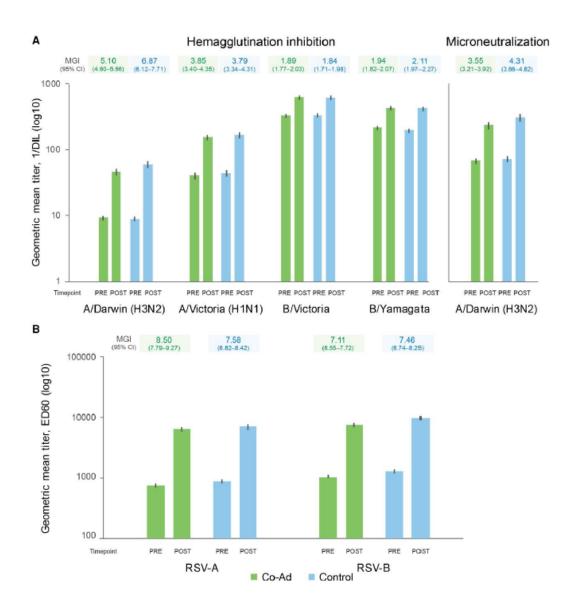
Co-administration of RSV vaccines and other vaccines

In accordance with General Best Practice Guidelines for Immunization, coadministration of RSV vaccines with other adult vaccines is acceptable.*

This includes giving RSV vaccines simultaneously with seasonal influenza vaccines, COVID-19 vaccines, pneumococcal vaccines, Td/Tdap, and recombinant zoster vaccine (Shingrix).

^{*}ACIP Timing and Spacing Guidelines for Immunization | CDC

Safety and Immunogenicity of Respiratory Syncytial Virus Prefusion F Protein Vaccine when Co-administered with Adjuvanted Seasonal Quadrivalent Influenza Vaccine in Older Adults: A Phase 3 Randomized Trial

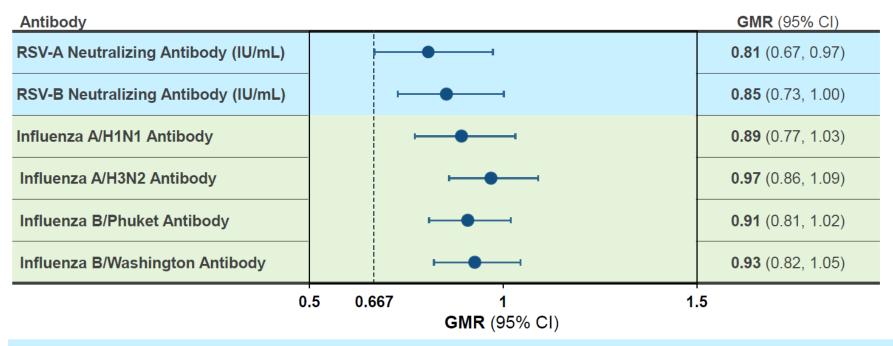


Received 12 March 2024; editorial decision 03 June 2024; published online 5 August 2024 Correspondence: S. Kotb, GSK, Ave Fleming 20, 1300 Wavre, Belgium (shady.x.kotb@gsk com). N. Meyer, GSK, Ave Fleming 20, 1300 Wavre, Belgium (nadia.x.meyer@gsk.com).

Clinical Infectious Diseases®

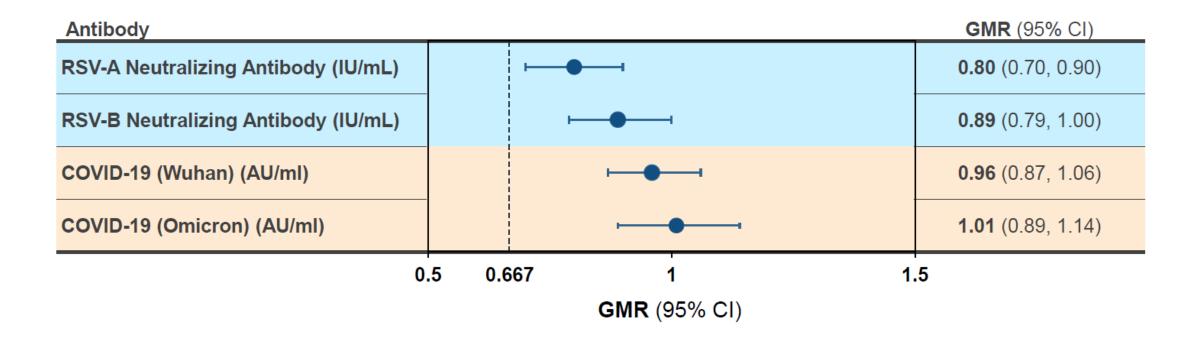
© The Author(s) 2024. Published by Oxford University Press on behalf of Infectious Diseases Society of America.

Comparison of Day 29 Geometric Mean Titer Ratio (GMR) – Concomitant vs Nonconcomitant Administration of mRNA-1345 and Quadrivalent Influenza Vaccine Study 302, Part A



All GMR non-inferiority criteria met (LB of the 2-sided 95% CI of GMR > 0.667)

Comparison of Day 29 Geometric Mean Titer Ratio (GMR) – Concomitant vs Nonconcomitant Administration of mRNA-1345 and COVID-19 Bivalent Vaccine Study 302, Part B



Presented at ACIP meeting February 29, 2024





Morbidity and Mortality Weekly Report (MMWR)

Use of Respiratory Syncytial Virus Vaccines in Adults Aged ≥60 Years: Updated Recommendations of the Advisory Committee on Immunization Practices — United States, 2024

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Summary

What is already known about this topic?

On June 21, 2023, the Advisory Committee on Immunization Practices (ACIP) recommended that adults aged ≥60 years may receive a single dose of respiratory syncytial virus (RSV) vaccine, using shared clinical decision-making.

What is added by this report?

On June 26, 2024, ACIP voted to update these recommendations as follows: all adults aged ≥75 years and adults aged 60–74 years who are at increased risk for severe RSV disease should receive a single dose of RSV vaccine.

What are the implications for public health practice?

These updated recommendations are intended to maximize RSV vaccination coverage among persons most likely to benefit. Continued postlicensure monitoring will guide future recommendations.

Upcoming Webinar





Topic: Learning from the RIZE Pneumococcal Vaccination Collaborative



Date/ Time: Thursday, September 19 at 2pm ET



Presenters: Participants from the RIZE Pneumococcal Vaccination Best Practices Learning Collaborative, moderated by Carolyn Bridges, MD, FACP (*Immunize.org*)

Questions?





Submit your questions using the **Q&A feature** at the bottom of the screen

