Fred Hutch
Cancer Center

Vaccines for respiratory viruses: 2025 updates

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August 26, 2025

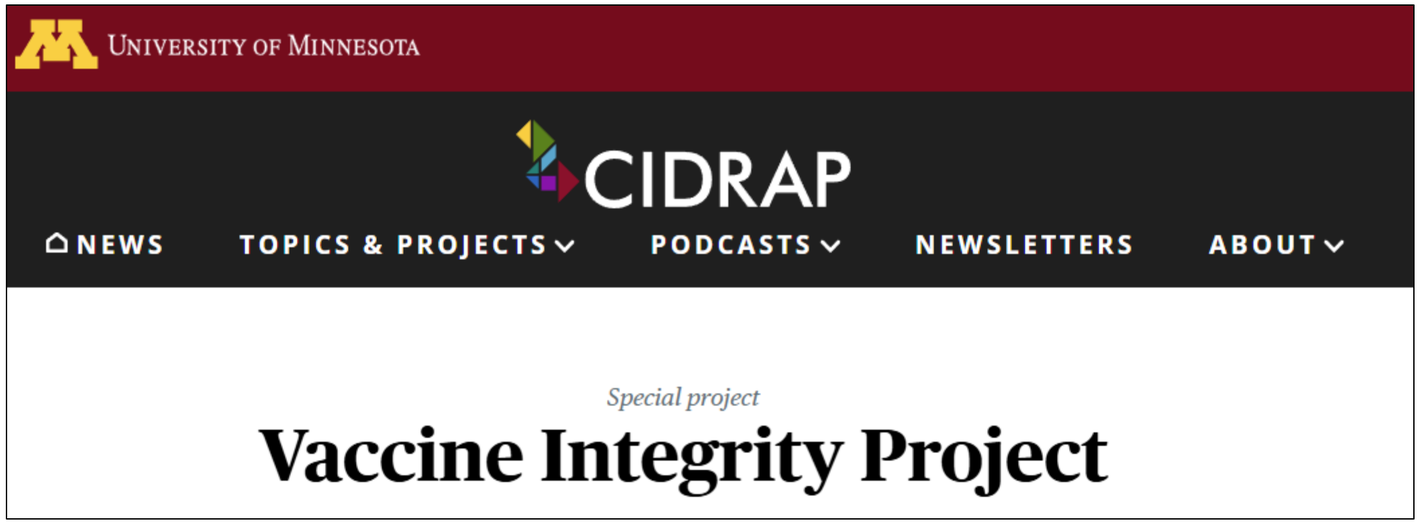
Learning objectives

1. **Influenza**
   a) Examine unique features of the 2024-25 influenza season
   b) Describe updates in influenza vaccination

2. **Respiratory Syncytial Virus (RSV)**
   a) Assess new data on real-world effectiveness of RSV vaccines and mAbs
   b) Identify a novel RSV mAb

3. **COVID-19**
   a) Compare and contrast updated 2025-26 COVID vaccine recommendations

Acknowledgements & References



University of Minnesota - Center for Infectious Disease Research and Policy (CIDRAP) -- https://www.cidrap.umn.edu/vaccine-integrity-project

What’s new in flu?

TIME SUBSCRIBE

HEALTH • DISEASE

This Is One of the Worst Flu Seasons in Decades

5 MINUTE READ

A nurse prepares to administer a flu shot at a COVID-19 and flu vaccination clinic in Chicago on Oct. 10, 2024. Tess Crowley/Chicago Tribune/Tribune News Service—Getty Images

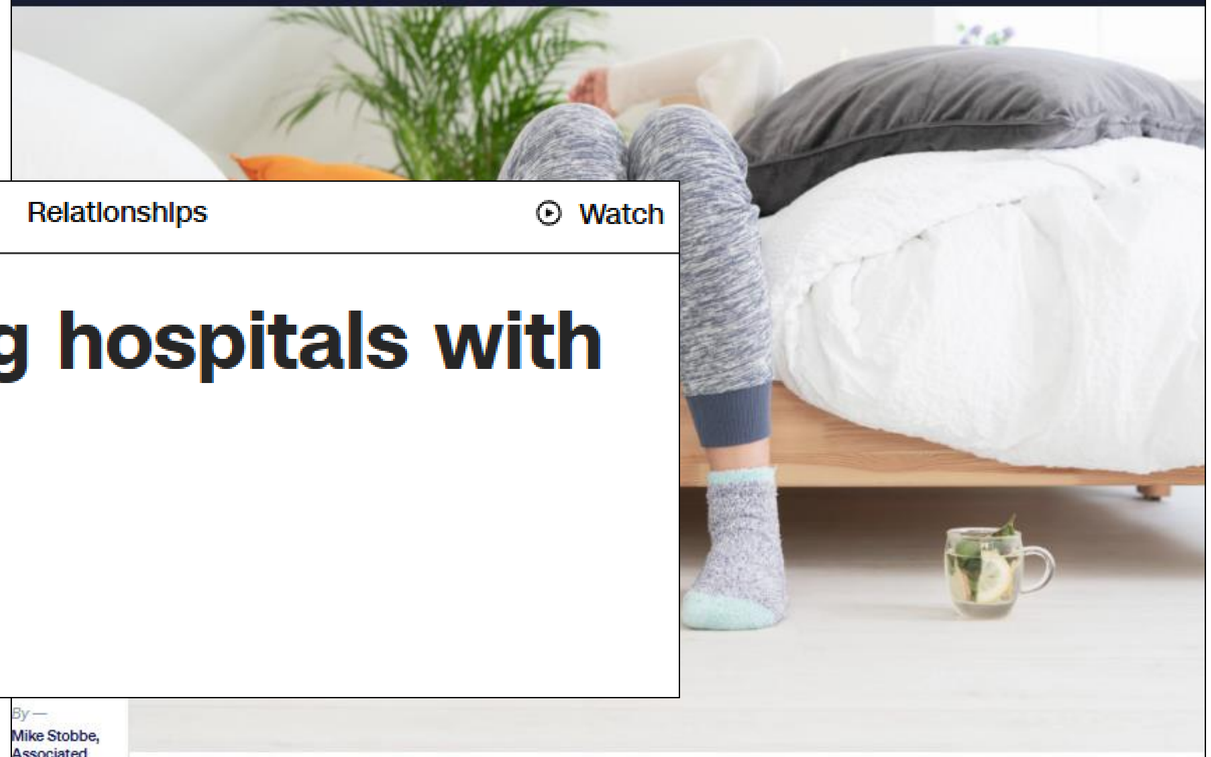
CNN Health Life, But Better Fitness Food Sleep Mindfulness Relationships Watch

An intense flu season is filling hospitals with severely ill patients

By Brenda Goodman and Neha Mukherjee, CNN

9 minute read · Updated 12:40 PM EST, Fri February 14, 2025

PBS NEWS Menu



By — Mike Stobbe, Associated Press

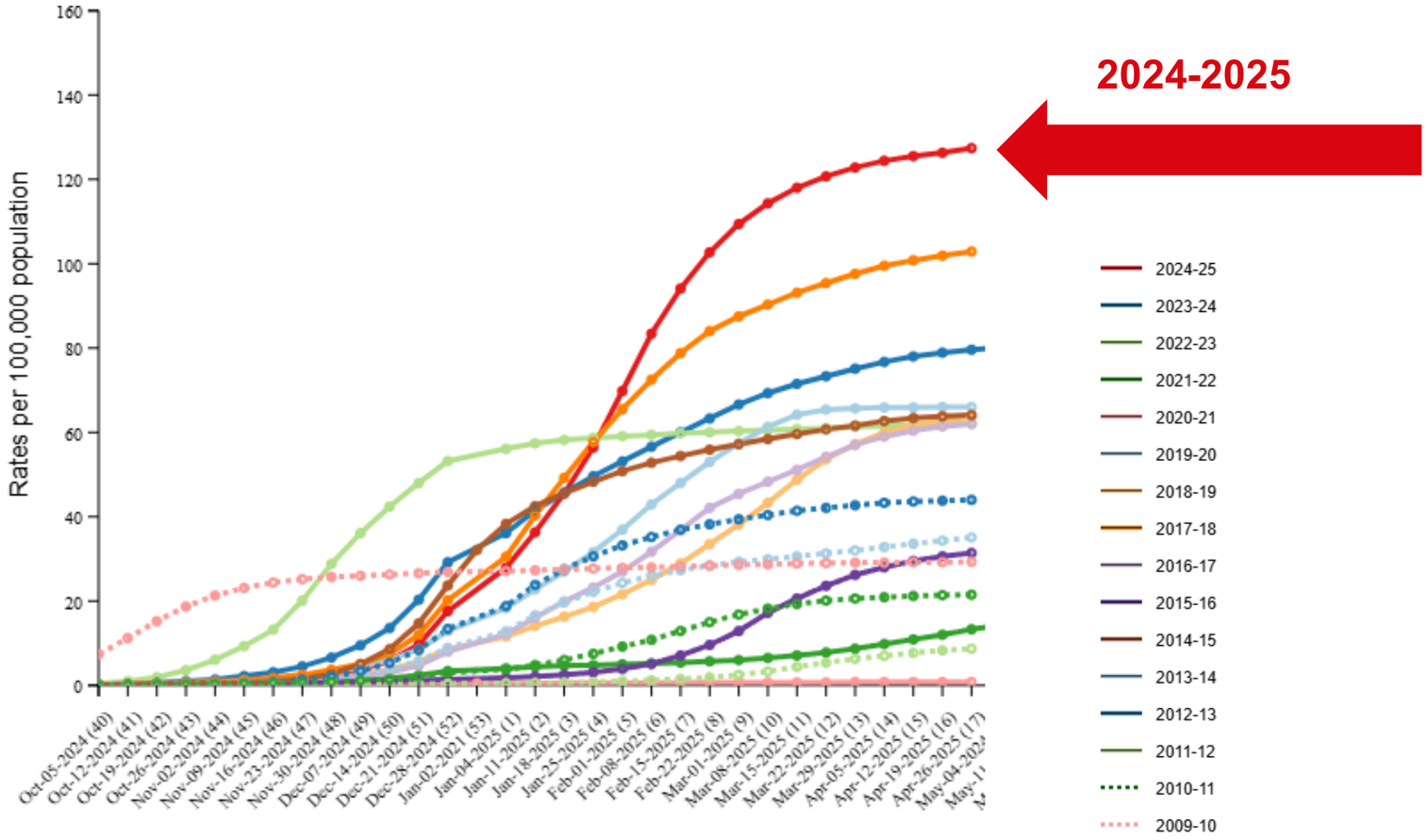
Leave your feedback

Share

U.S. facing most intense flu season in at least 15 years

Health Feb 7, 2025 3:37 PM EDT

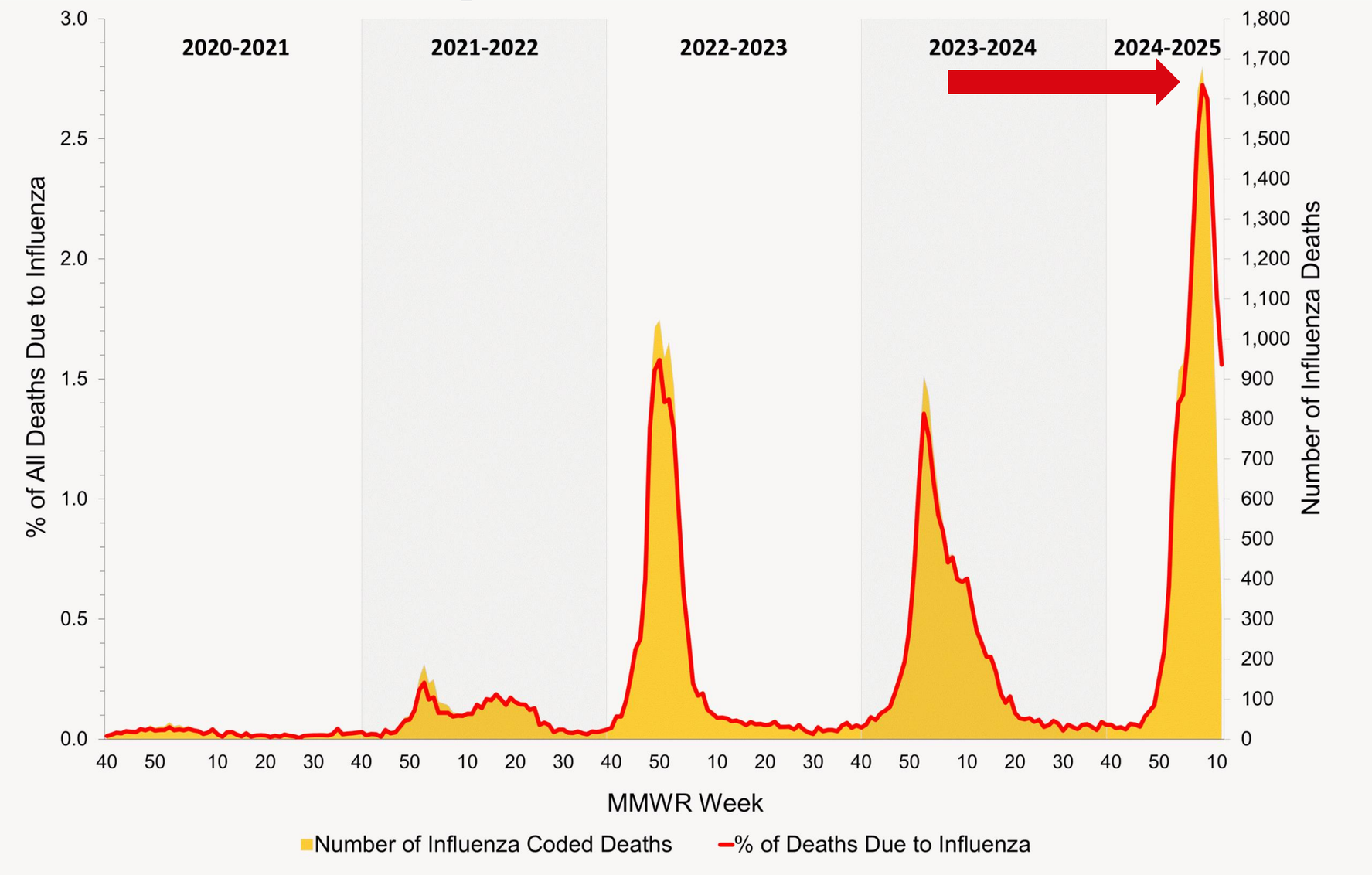
2024-25 flu season: confirmed flu hospitalizations



https://gis.cdc.gov/GRASP/Fluview/FluHospRates.html

2024-25 flu mortality

- Timing
- Strains
- Decreased vaccine uptake



https://www.cdc.gov/fluview/surveillance/2025-week-11.html

2024-2025 Flu Season

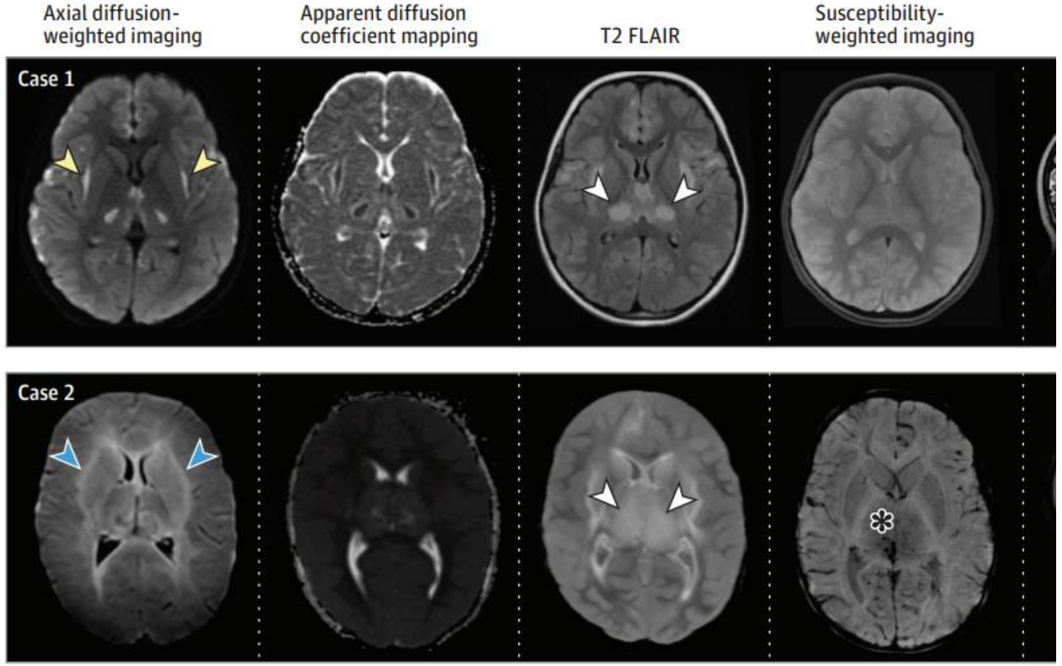
Pediatric complications and deaths

Morbidity and Mortality Weekly Report

Reports of Encephalopathy Among Children with Influenza-Associated Mortality — United States, 2010–11 Through 2024–25 Influenza Seasons

Amara Fazal, MD[1]; Katie Reinhart, PhD[1]; Stacy Huang, MPH[1]; Krista Kniss, MPH[1]; Samantha M. Olson, MPH[1]; Vivien G. Dugan, PhD[1]; Sascha Ellington, PhD[1]; Alicia P. Budd, MPH[1]; Carrie Reed, DSc[1]; Timothy M. Uyeki, MD[1]; Shikha Garg, MD[1]

Figure 1. Neuroimaging Findings of Children With Influenza-Associated Necrotizing Encephalopathy



Research

JAMA | Original Investigation

Influenza-Associated Acute Necrotizing Encephalopathy in US Children

Influenza-Associated Acute Necrotizing Encephalopathy (IA-ANE) Working Group

- 41 cases of influenza-associated ANE
- Median age: 5 years
- 76% no significant medical history
- 84% had not received the flu vaccine
- 27% mortality
  - 91% had not received age-appropriate seasonal flu vaccine

Silverman, JAMA, 2025. Fazal, MMWR, 2025. https://www.cdc.gov/mmwr/volumes/74/wr/pdfs/mm7406a3-H.pdf

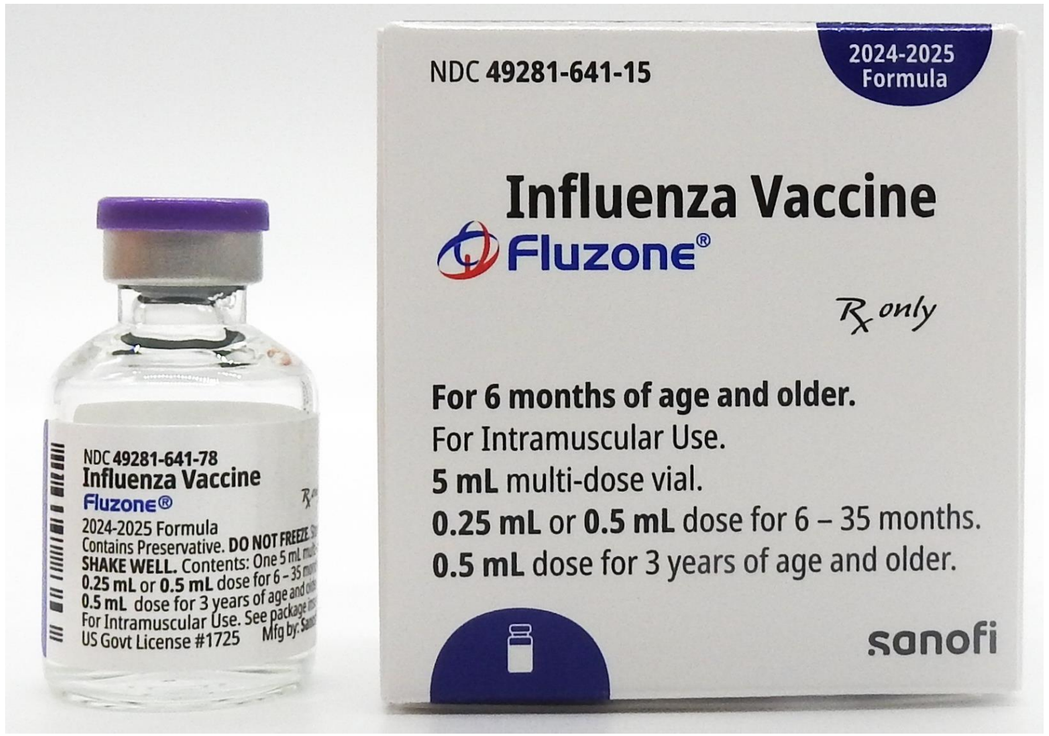
Updated 2025 ACIP recommendations

- Routine **annual influenza vaccination for everyone** aged ≥ 6 months
  – *Unless contraindications*

- ACIP recommends **only single-dose formulations** of annual flu vaccines
  – *Free of thimerosal as a preservative*

https://www.cdc.gov/acip/vaccine-recommendations/index.html

Thimerosal



- Preservative in multi-dose vials
- Prevents microbial growth
- Vax containing 0.01% thimerosal contains 50 mcg per 0.5 mL dose
  - Roughly the same amount of elemental mercury as a 3-oz can of tuna

- Single-dose formulation
- Prefilled syringe
- Does not require preservatives

https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/thimerosal-and-vaccines#rati

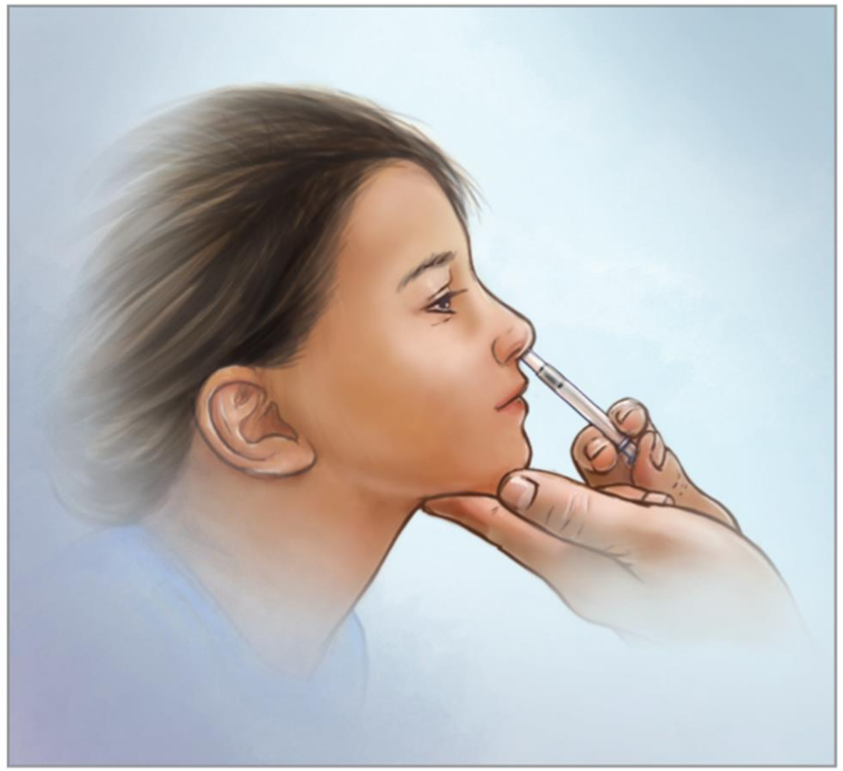
Influenza vaccine options

Intramuscular, single-dose formulation
Inactivated

Intra-nasal
Live attenuated

Images: L: Jeffrey Hamilton/Getty Images; R: The Lancet Respiratory Medicine

Self-Administered Home Flu Vaccination



- FDA approved for home use
- Prescription required
- Screening & eligibility assessment
- Nasal spray mailed home
- Ages 2 – 49
- Caregiver administration < 18 years

JAMA doi:10.1001/jama.2024.21299

Self-Administered Home Flu Vaccination

FluMist Home is as easy as 1, 2, 3...4

1

Order online for yourself and your household

2

Order reviewed by a healthcare professional*

*Eligible orders receive approval based on medical questionnaire.

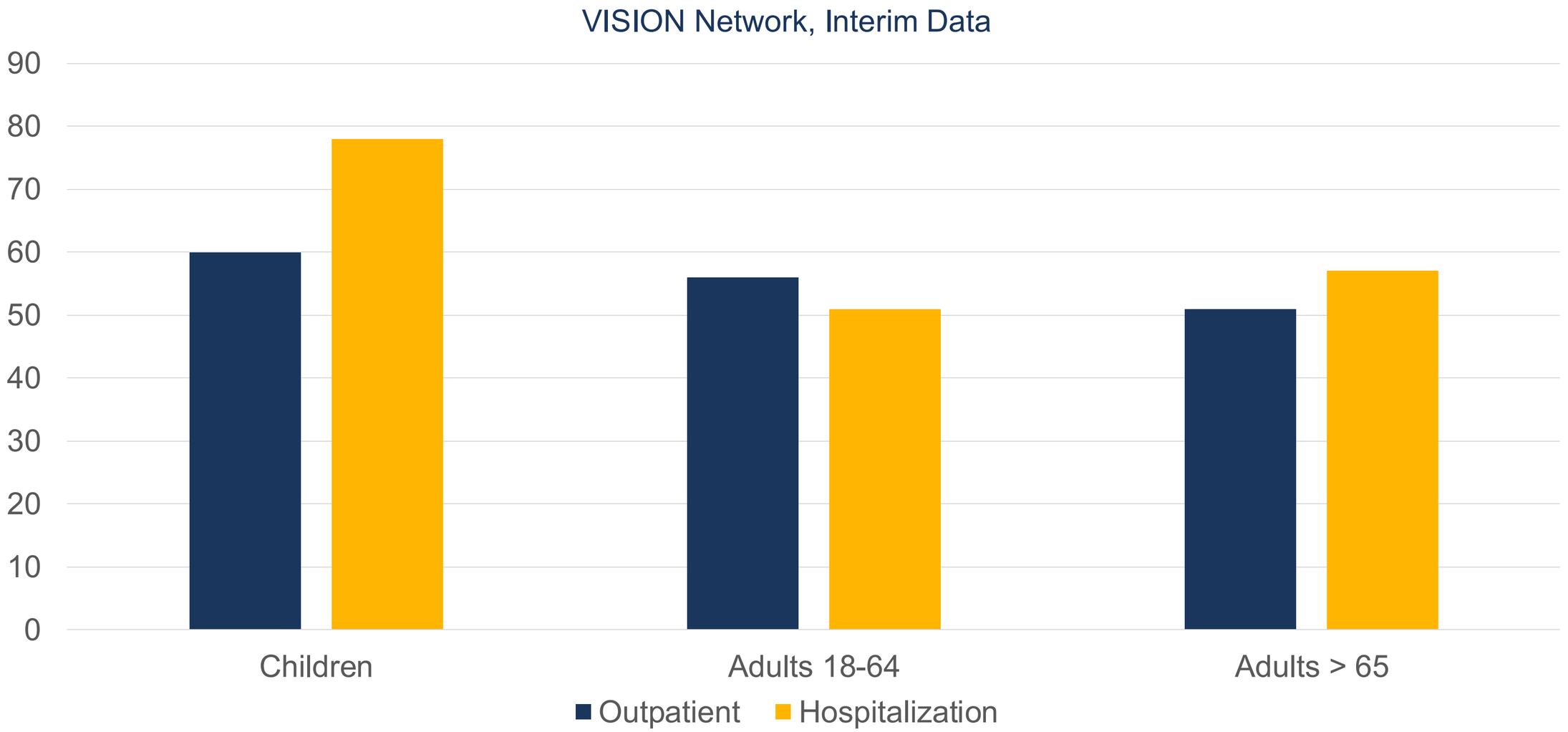
3

Get FluMist delivered to your door

4

Use FluMist at home!

2024-25 Influenza vaccine effectiveness (VE)



https://www.cdc.gov/flu-vaccines-work/php/effectiveness-studies/2024-2025.html

Reeves, 2025

What’s new in RSV

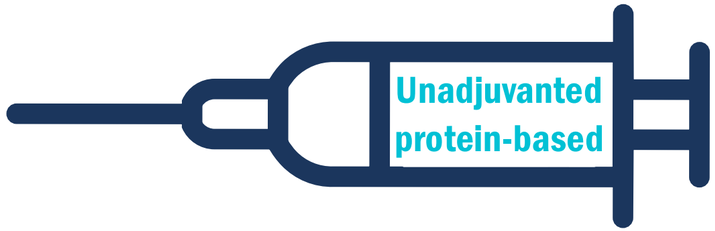
3 FDA-approved RSV vaccines

GSK - Arexvy

Approved for:

- Adults ≥ 60 years
- Adults 50 - 59 years at increased risk

Pfizer - ABRYSVO



Approved for:

- Adults ≥ 60 years
- Adults 18 - 59 years at increased risk
- Pregnant women at 32 through 36 weeks gestational age

Moderna

Approved for:

- Adults ≥ 60 years
- Adults 18 - 59 years at increased risk

https://www.cdc.gov/vaccine-safety/vaccines/rsv.html

Real world vaccine effectiveness (VE)

Post-licensure data for the Pfizer and GSK protein subunit RSV vaccines

RSV-associated hospitalization

Adults >60

General population: 75-82% effective

Immunocompetent adults

Effective across age groups 50-74 and > 75

Similar for Pfizer & GSK products

Britton A. MMWR, August 6, 2024

ACIP recommendations

- Adults ≥ 75 years of age: receive a single dose of RSV vaccine
- Adults 50–74 years of age at increased risk of severe RSV disease: receive a single dose of RSV vaccine
- Single lifetime dose

MMWR, August 6 2024; https://www.cdc.gov/vaccine-safety/vaccines/rsv.html

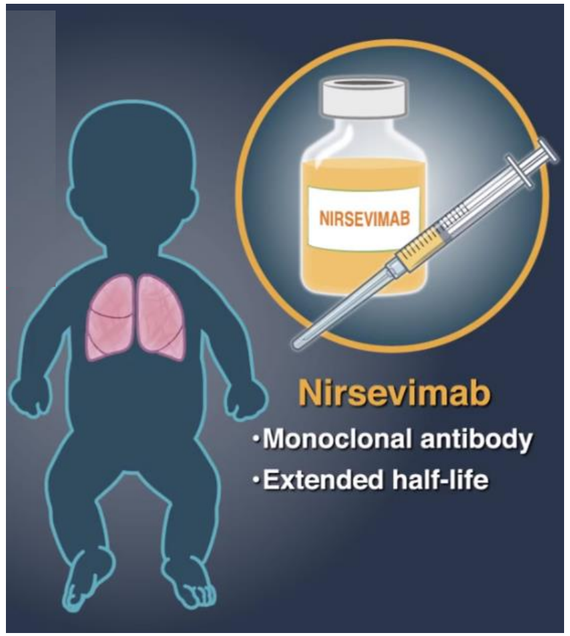
Pediatric RSV prevention

Infant RSV prevention options

Vaccination during pregnancy: 32-36 weeks

- Transplacental antibody transfer
- Protects infants in first few months of life
- Abrysvo (Pfizer) bivalent vaccine

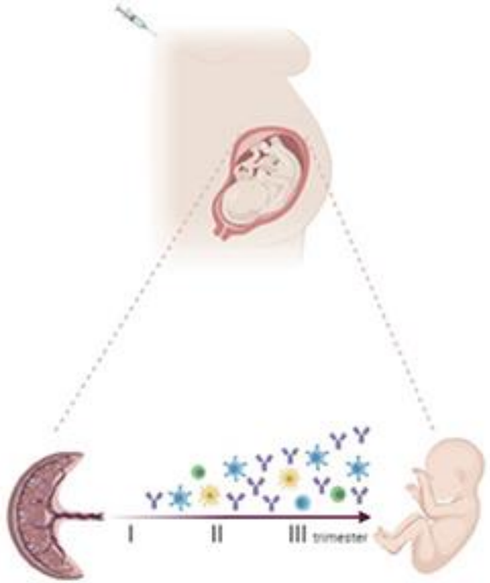
Infant mAb: Single dose, long-acting IM



- **Infants <8 months** entering 1st RSV season
- Infants & children **8–19 months at ↑ risk**
- Nirsevimab or clesrovimab

Images: L: Jeffrey Hamilton/Getty Images; R: The Lancet Respiratory Medicine

Immunization during pregnancy



Efficacy:

– RCT: 70% efficacy in clinical trial

– 3 studies of preventing RSV hospitalization under 6 months:

- **72% pooled effectiveness** (62-79%)

Safety:

- **RCT:** possible signal (NS) of increased **pre-eclampsia** (1.8% vs. 1.4%) and **preterm birth** (5.7% vs 4.7%)
- Subgroup analysis: **No increased risk** in high income countries. Increased risk in low-income countries
- Real-world data study of Abrysvo at 32-36 weeks: no increased risk.

Kampmann, NEJM 2023 and FDA press release

Image: Cinicola, Front. Pediatr., 28 April 2021

Nirsevimab (Beyfortus)

Highly effective in preventing adverse outcomes due to RSV:

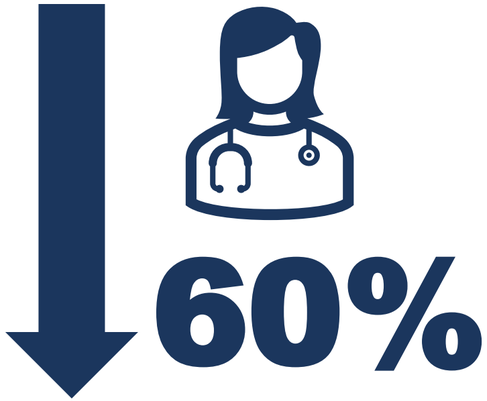
Medically-attended RSV
5 studies:
17-89% effective

Hospitalization
13 studies:
64% - 93% effectiveness

ICU admission
6 studies:
51-91% effectiveness

A second mAb for RSV prevention: Clesrovimab

Single-dose, long-acting monoclonal antibody



Reduction in medically-attended RSV LRTI through 5 months

Favorable safety profile

SAE balanced in drug & placebo arms

ACIP meeting slides : https://www.cdc.gov/acip/downloads/slides-2025-04-15-16/02-Moulia-maternal-peds-RSV-508.pdf

Monoclonals for RSV prevention in infants

- No head-to-head data; trial outcomes defined differently
- ACIP: no preferential recommendation between the two

- Implementation:
  - **Clesrovimab** = single dose regardless of infant weight
  - **Nirsevimab** = additional approval for high-risk kids entering 2nd RSV season

- **Benefits of 2 mAbs:**
  - Different binding sites – resistance
  - Product availability
  - Competition & pricing

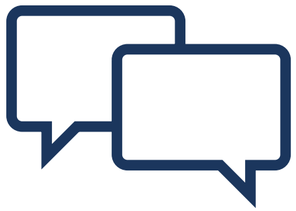
ACIP meeting slides : https://www.cdc.gov/acip/downloads/slides-2025-04-15-16/02-Moulia-maternal-peds-RSV-508.pdf

Covid updates

Conflicting pediatric recommendations

CDC:

"Parents of children ages 6 months to 17 years should discuss the benefits of vaccination with a healthcare provider."



American Academy of Pediatrics:

- 6-23 months: recommend complete initial vaccine series
- 2-18 years: recommend a single dose of age-appropriate 2025-2026 COVID-19 vaccine for at-risk groups
- 2-18 years, not in a risk group: offer vaccination

Data updates:

- No new safety concerns with booster dose
- Highest incidence after 2-dose primary series, esp among adolescent males
- Lower incidence with subsequent doses

https://www.cdc.gov/covid/vaccines/stay-up-to-date.html
Committee on Infectious Diseases; Recommendations for COVID-19 Vaccines in Infants, Children, and Adolescents: Policy Statement. *Pediatrics* 2025; 10.1542/peds.2025-073924

Conflicting obstetric recommendations

CDC:

Vaccine	Pregnancy
COVID-19	No Guidance/Not Applicable

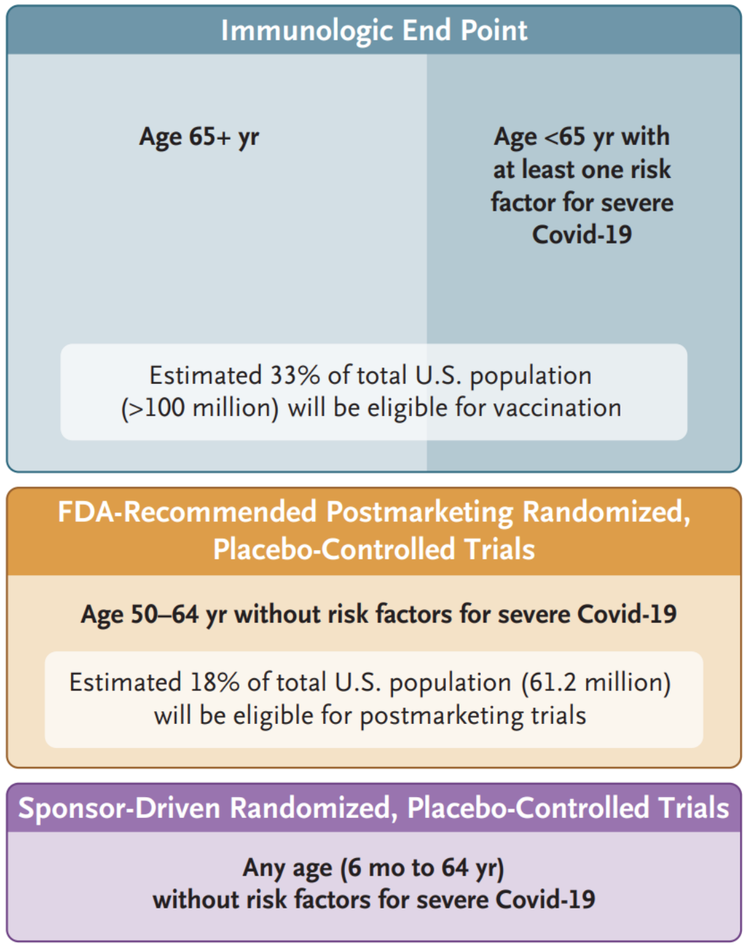
American College of Obstetricians & Gynecologists (ACOG)

- Recommend that all pregnant and lactating individuals receive an updated COVID-19 vaccine or “booster.”

Data updates:

- No association between COVID-19 vaccination during pregnancy and SGA
- Some studies demonstrate a protective effect of COVID-19 vaccination an preterm birth

COVID-19 vaccines for older adults



FDA approval expected for >65 and those with risk factors

"On the basis of immunogenicity — proof that a vaccine can generate antibody titers in people — the FDA anticipates that it will be able to make favorable benefit–risk findings for adults over the age of 65 years and for all persons above the age of 6 months with one or more risk factors"

Data updates:

2024–2025 COVID-19 vaccine VE:

45% vs. hospitalizations among immunocompetent adults ≥65

NEJM: https://www.nejm.org/doi/pdf/10.1056/NEJMsb2506929

Take home points

Conclusions

Influenza

- Annual vaccination continues to be recommended; effectiveness is modest

RSV

- 3 safe & effective RSV vaccines are approved for older and high-risk adults
- Infants can be protected either through maternal vaccination or long-acting mAb

COVID-19

- Updated vaccines – expect approval soon for >65, high-risk

Vaccines and antimicrobial stewardship

RSV, Influenza & Covid vaccines + monoclonals

↓ Acute respiratory illnesses

↓ Antibiotic use[1-8]

1. Smith, CID, 2020
2. Buckley, Clin Micro Infect, 2019.
3. Rodgers, PloS One, 2021.
4. Jorgensen, CID, 2024.
5. MacFadden, CID, 2023
6. Simoes, Lancet CAH, 2023
7. Molnar, Infect Dis Ther, 2024
8. Lewnard, PNAS, 2022

Thank you

Teaching Peer Evaluation
for Dr. Denise McCulloch