

Centers for Disease Control and Prevention
National Center for Immunization and Respiratory Diseases



RSV Vaccination in Older Adults: Work Group Interpretations

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Advisory Committee on Immunization Practices

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First, the Work Group would like to acknowledge that there are multiple concurrent policy issues to consider in the older adult RSV vaccine landscape.

- This includes follow-up of the **implementation and experience of the current shared clinical decision-making** recommendation, **understanding uptake** of RSV vaccines across age and demographic groups, consideration of **new vaccine products**, and potential expansion of RSV vaccines to **younger age groups**.
- **However, the Work Group believes that contextualization and understanding of current safety data are paramount in determining future preferred policy options for the adult RSV vaccination program.**
- Therefore, today's Work Group interpretations focus primarily on the safety and benefit/risk data reviewed today.
- We will then briefly review the proposed roadmap for expected future policy decisions.

Objectives

- Summarize Work Group interpretations of current RSV vaccine safety surveillance data and the balance of estimated benefits vs potential risks associated with use of RSV vaccines in adults ages 60 years and older
- Share updated clinical considerations incorporating timing of RSV vaccine administration in shared clinical decision-making
- Update on plans for future policy considerations in the older adult RSV vaccine program



Work Group interpretation of current RSV vaccine safety data and benefit/risk of RSV vaccination in adults ages 60 years and older

The initial RSV vaccine recommendation for adults 60 years and older was made in the setting of a small number of cases of inflammatory neurologic events (particularly GBS) observed in the clinical trials for both GSK and Pfizer's RSV vaccines for older adults.

- Due to the small number of cases, it was **unclear whether the cases observed in the trials represented a genuine association** between RSV vaccination and risk of GBS or whether the cases observed in the trials were due to chance alone.
- The potential for increased risk of GBS was discussed extensively during deliberations for the older adult recommendation. ACIP concluded that the estimated benefits of RSV vaccination outweighed potential risks.
- **However, ACIP recommended RSV vaccines be given using shared clinical decision-making with a healthcare provider. The shared clinical decision-making recommendation was intended to facilitate individualized risk-benefit discussions, acknowledging that the balance of risks and benefits may depend on the characteristics of the individual vaccine recipient.**
- Clinical guidance advised that a patient's risk for severe RSV-associated disease should be the core of shared clinical decision-making, with vaccination targeted to those who are at highest risk for severe RSV disease and therefore most likely to benefit from vaccination.

RSV older adult vaccine safety surveillance timeline

2023

2024



Small number of GBS cases observed in the clinical trials in adults aged ≥ 60 years for GSK and Pfizer RSV vaccines. Safety data shared at FDA VRBPAC and ACIP meetings.

RSV vaccines licensed for use in adults aged ≥ 60 years. Information on trial GBS cases included in product package inserts. Safety monitoring commences immediately post-licensure.

ACIP votes to recommend RSV vaccination for adults aged ≥ 60 years, using shared clinical decision-making.

Number of GBS cases in VAERS raised possibility that cases observed might be above expected background rate. CDC organized CISA calls with clinical experts in neurology to review cases of GBS reported to VAERS.*

VAERS scientists continued monitoring and verifying GBS reports; CISA continued review.

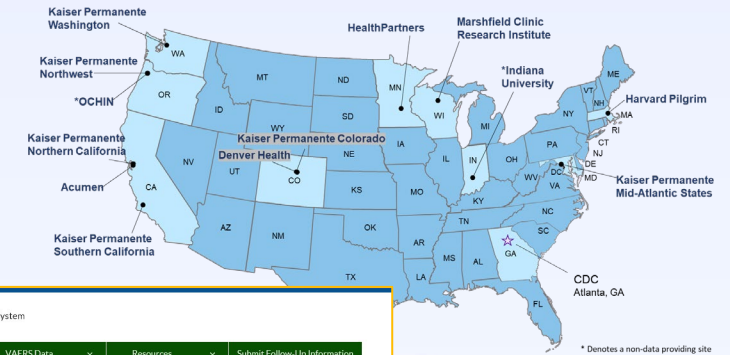
First preliminary safety surveillance data available from CDC V-safe, CDC VSD and FDA CMS.

Abbreviations: ACIP = Advisory Committee on Immunization Practices, CISA = Clinical Immunization Safety Assessment Project, CMS = Centers for Medicare & Medicaid Services, FDA = Federal Drug Administration, GBS = Guillain-Barre syndrome, RSV = respiratory syncytial virus, VAERS = Vaccine Adverse Event Reporting System, VRBPAC = Vaccines and Related Biological Products Advisory Committee Meeting; VSD = Vaccine Safety Datalink

*CISA is covered by a CDC Assurance of Confidentiality

Surveillance with a focus on early detection of increased risk of GBS after RSV vaccination began immediately post-licensure.

- Today, CDC's Immunization Safety Office and FDA shared preliminary data from multiple surveillance systems: VAERS, VSD, and the FDA-CMS partnership.
- The data from these systems have been shared as near real-time findings and allow us to be immediately responsive to early signals.
- Together, the data support a potential increased risk for GBS after RSV vaccination among adults aged ≥ 60 years.
- However, due to uncertainty and limitations in these early data, there is currently insufficient evidence to confirm whether RSV vaccination is associated with increased risk for GBS in older adults, or to estimate the magnitude of any increase in GBS risk after RSV vaccination.
- Assessing the risk for GBS following receipt of the RSV vaccine among older adults in more robust analyses in active vaccine safety surveillance systems will be crucial and is underway.



How do these new data impact the Work Group's thinking about RSV vaccine for older adults?

- Any increase in potential risk of GBS should be placed in the context of the benefits of RSV vaccination.
- Earlier in this session, we summarized what we know about the estimated benefits of RSV vaccine and compared that to what we know currently about potential risk of GBS. This benefit-risk analysis showed that:
 - From a population perspective, the estimated benefits of RSV vaccination **outweigh** the estimated risks for adults 60 years and older.
 - Benefits of RSV vaccination **vary by age group and RSV incidence.**
 - Benefits likely also **vary by individual-level risk** of severe RSV disease and by **timing of vaccination** relative to the RSV season.
- We also saw data demonstrating that adults with certain chronic conditions are at increased risk of severe RSV disease, even at younger ages.

The Work Group also reviewed examples from other licensed and recommended vaccines of benefit-risk considerations in practice.

- **Seasonal influenza vaccine:** routine annual influenza vaccination is recommended for all persons aged ≥ 6 months who do not have contraindications. Adults aged ≥ 65 years should preferentially receive high-dose, recombinant, or adjuvanted influenza vaccines.¹
 - *The data on the association between GBS and seasonal influenza vaccination are variable and inconsistent across influenza seasons. If there is an increased risk of GBS following influenza vaccination it is small, on the order of **1–2 additional cases per million doses** of influenza vaccine administered. Studies also suggest that it is more likely that a person will get GBS after getting the influenza disease than after influenza vaccination.*²

1. Grohskopf LA, et al. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023–24 Influenza Season. *MMWR Recomm Rep* 2023;72(No. RR-2):1–25. <http://dx.doi.org/10.15585/mmwr.rr7202a1>
2. Vellozzi C, Iqbal S, and Broder K. Guillain-Barré Syndrome, Influenza, and Influenza Vaccination: The Epidemiologic Evidence, *Clinical Infectious Diseases*, Volume 58, Issue 8, 15 April 2014, Pages 1149–1155, <https://doi.org/10.1093/cid/ciu005>.

Summary of RSV and Influenza disease-associated hospitalizations, estimated vaccine-avertable disease hospitalizations, and **potential vaccine-associated GBS risk**

	Disease-associated hospitalizations per 1 million population per year in the U.S.	Estimated disease-associated hospitalizations avertable per 1 million persons vaccinated	Potential vaccine-associated GBS cases per 1 million persons vaccinated
RSV	1,700 – 2,800 ¹ among adults ages 65 and older	Over two RSV seasons, among adults ages 60 and older GSK: 2,400 (1,800 – 3,700) ² Pfizer: 2,700 (2,100 – 4,200) ²	GSK: 10 (2–18) cases ³ Pfizer: 25 (7–43) cases ³ Not adjusted for background rate of GBS Expected from background rate: 5 cases of GBS (95% CI: 4.8, 5.4) per 1 million doses given⁴
Influenza	3,200 – 9,200 ⁵ among adults ages 65 and older	Over one influenza season, among adults ages 65 and older 2,000 (300 – 5,500) ⁶	Variable and inconsistent across influenza seasons. If there is an increased risk, it is small: ~1–2 additional cases per million doses given^{7,8}

1. CDC RSV-NET data 2016–2020, 2022–2023 (unpublished)
2. Unpublished benefit/risk analysis presented at this ACIP meeting (February 2024).
3. FDA analysis of CMS data. Includes GBS cases in a 42-day risk interval post-RSV-vaccination, adjusted for claims delay, among beneficiaries 65 and older with Parts A and B coverage who did not have a GBS claim in the 365 days before vaccination. These are rates of GBS identified by inpatient claims data and are decreased by 29% to account for the positive predictive value of diagnostic codes in identifying chart-confirmed GBS cases. A GBS background rate is not subtracted from these rates.
4. FDA analysis of CMS data. Background rate based on GBS cases observed per 100,000 person-years among Medicare beneficiaries 65 and older with Parts A and B coverage in 2022. Beneficiaries must not have had an International Classification of Diseases, 10th revision, clinical modification (ICD-10-CM) diagnostic code for GBS in the 365 days preceding January 1, 2022. Rate per 100,000 person-years applied used to estimate cases expected over 42-day follow-up for 1 million persons.
5. CDC Influenza Burden 2016–2020, 2022–2023: <https://www.cdc.gov/flu/about/burden/past-seasons.html>
6. Ellen KD, Gebremariam A, Rose A, et al. Cost-effectiveness of routine annual influenza vaccination by age and risk status. *Vaccine*. 41 (29): 4239-4248. 2023. <https://doi.org/10.1016/j.vaccine.2023.04.069>
7. Vellozzi C, Iqbal S, and Broder K. Guillain-Barré Syndrome, Influenza, and Influenza Vaccination: The Epidemiologic Evidence. *Clinical Infectious Diseases*, Volume 58, Issue 8, 15 April 2014, Pages 1149–1155, <https://doi.org/10.1093/cid/ciu005>.
8. Committee to Review Adverse Effects of Vaccines; Institute of Medicine; Stratton K, Ford A, Rusch E, et al., editors. *Adverse Effects of Vaccines: Evidence and Causality*. Washington (DC): National Academies Press (US); 2011 Aug 25. 6, Influenza Vaccine. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK190013/>
Influenza Vaccine - Adverse Effects of Vaccines - NCBI Bookshelf (nih.gov).

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- **Recombinant zoster vaccine:** CDC recommends two doses of recombinant zoster vaccine (RZV, Shingrix) 2–6 months apart for adults aged ≥ 50 years and for adults aged ≥ 19 years who are or will be immunocompromised, for prevention of herpes zoster (shingles) and related complications.^{3,4}
 - **3-6 additional cases of GBS projected per million RZV vaccinated.**⁵
 - *Risk-benefit analysis incorporated available data on risk of GBS following zoster disease and vaccination with RZV*

1. Grohskopf LA, et al. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023–24 Influenza Season. MMWR Recomm Rep 2023;72(No. RR-2):1–25. <http://dx.doi.org/10.15585/mmwr.rr7202a1>

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3. Dooling KL, et al. Recommendations of the Advisory Committee on Immunization Practices for Use of Herpes Zoster Vaccines. MMWR Morb Mortal Wkly Rep 2018;67:103–108. <http://dx.doi.org/10.15585/mmwr.mm6703a5>

4. Anderson TC, et al. Use of Recombinant Zoster Vaccine in Immunocompromised Adults Aged ≥ 19 Years: Recommendations of the Advisory Committee on Immunization Practices — United States, 2022. MMWR Morb Mortal Wkly Rep 2022;71:80–84. <http://dx.doi.org/10.15585/mmwr.mm7103a2>

5. Janusz CB, et al. Projected risks and health benefits of vaccination against herpes zoster and related complications in US adults. *Hum Vaccin Immunother.* 2022 Nov 30;18(5):2060668. <https://doi.org/10.1080/21645515.2022.2060668>

Experience with recombinant zoster vaccine (Shingrix)

- In 2019, a statistical safety signal for GBS following recombinant zoster vaccine was identified in VSD; evidence was insufficient to confirm the initial signal.
- FDA, CDC, and collaborators conducted additional extensive safety assessments.^{1,2}
- Using data from this safety surveillance, a formal analysis evaluating health risks and benefits was undertaken. Epidemiologic data suggesting a potentially elevated risk of GBS following an episode of herpes zoster (HZ) in the U.S. adult population was also included.³
- In this analysis, benefits were assumed to accrue over a period of 20 years after vaccination.
- Vaccination averted 43,000–63,000 cases of HZ, including GBS complications, per million vaccinated per 10-year age cohort compared to 3–6 additional cases of GBS projected per million vaccinated with recombinant zoster vaccine in the same population.⁴
- Importantly, RSV disease is not directly comparable to herpes zoster disease.

Projected cases* of postherpetic neuralgia, ocular complications, and death averted through recombinant zoster vaccine per million vaccinated, compared to incremental GBS increase per million⁴

Age group (years)	Postherpetic neuralgia	Ocular complications	Deaths	Incremental GBS increase	Notes
50-59	5,500	4,300	47	3 – 6	<ul style="list-style-type: none"> • 20-year time horizon • Incremental GBS increase subtracts background rate of GBS and HZ-associated GBS averted • Outcomes averted per million 1-dose or 2-dose series
60-69	9,400	5,500	62		
70-79	12,000	5,700	171		
80-89	12,000	5,200	155		
90-99	11,000	3,900	116		

* Projected number of averted cases of postherpetic neuralgia and ocular complications have been rounded to two significant figures. For exact numbers see Janusz et al. below.

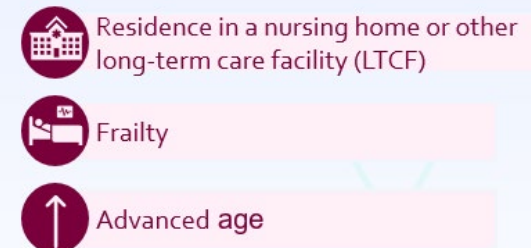
1. Goud R, et al. Risk of Guillain-Barré Syndrome Following Recombinant Zoster Vaccine in Medicare Beneficiaries. JAMA Intern Med. 2021 Dec 1;181(12):1623-1630. doi: 10.1001/jamainternmed.2021.6227.
2. Nelson JC, et al. Active Postlicensure Safety Surveillance for Recombinant Zoster Vaccine Using Electronic Health Record Data. Am J Epidemiol. 2023 Feb 1;192(2):205-216. doi: 10.1093/aje/kwac170.
3. Anderson TC, et al. Risk of Guillain-Barré syndrome following herpes zoster, United States, 2010-2018. Hum Vaccin Immunother. 2021 Dec 2;17(12):5304-5310. doi: 10.1080/21645515.2021.1985890.
4. Janusz CB, et al. Projected risks and health benefits of vaccination against herpes zoster and related complications in US adults. Hum Vaccin Immunother. 2022 Nov 30;18(5):2060668. <https://doi.org/10.1080/21645515.2022.2060668>

Based on this review of currently available data, the Work Group continues to believe that the estimated benefits of RSV vaccination outweigh potential risks when vaccination is implemented using the current recommendation: **Adults aged ≥ 60 years may receive RSV vaccination, using shared clinical decision-making.**

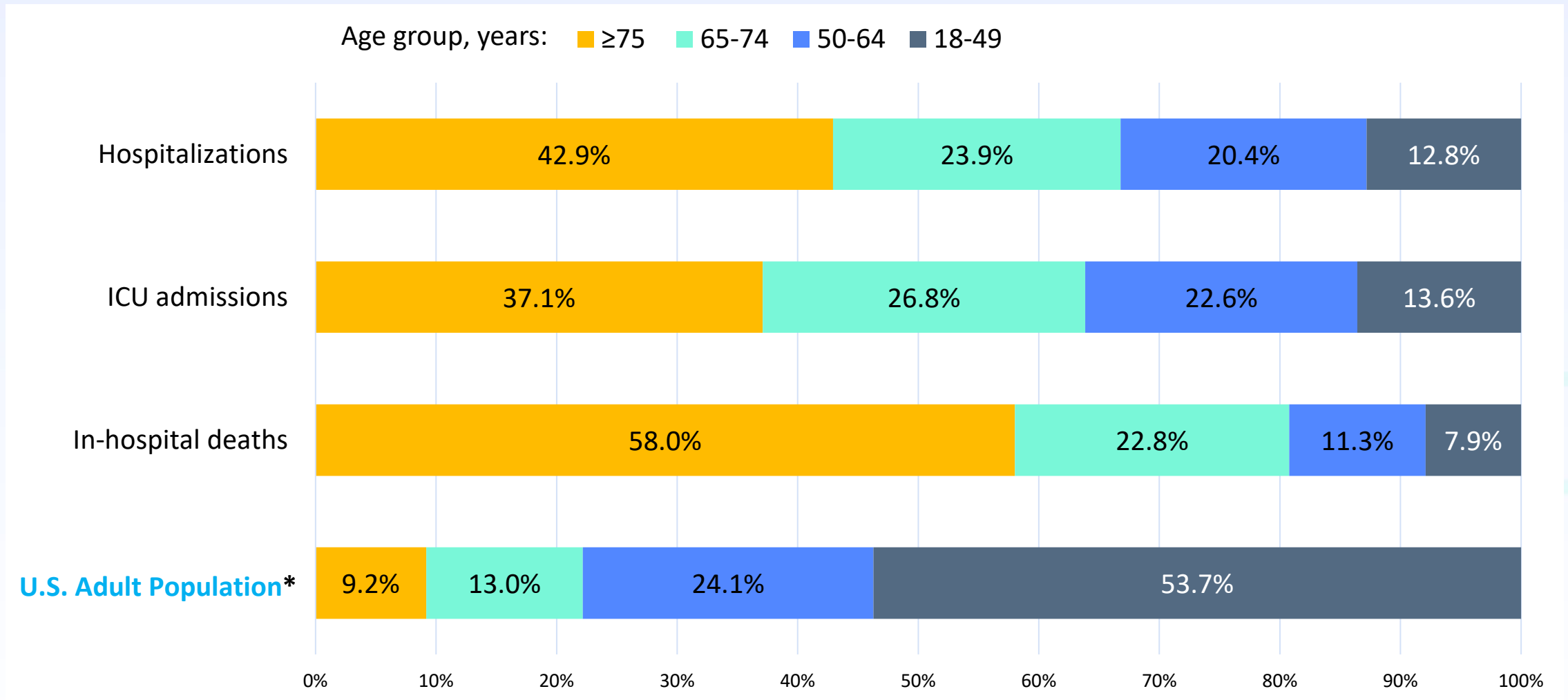


A majority of Work Group members expressed that the balance of estimated benefits outweighed potential risks for all adults 60 and older.

- However, the Work Group expressed that estimated benefits **most clearly outweigh potential risks among adults 60 and older who are at increased risk of severe RSV disease.**
- This includes adults who are 60 and older with chronic medical conditions such as **chronic lung diseases, heart failure, immune compromise, those of more advanced age, and those living in long-term care facilities (e.g., nursing homes).**



Estimated age distribution of national RSV-associated hospitalizations, ICU admissions, and in-hospital deaths among adults ≥ 18 years, RSV-NET, 2022–2023, compared with U.S. population



Unpublished data. Underlying rates are adjusted using multipliers for the frequency of RSV testing during each season and for the sensitivity of RSV diagnostic tests. Estimates from 2022-2023 are preliminary. These estimates use the same multipliers as for 2019-2020.

*As of 2022. <https://www.census.gov/popclock/>

Underlying medical conditions* among non-pregnant adults ≥ 18 years with RSV-associated hospitalizations — RSV-NET, 2014–2015 to 2017–2018 and 2022–2023

Major underlying condition categories	Unweighted N=7,479	Weighted %
Cardiovascular disease (overall)	5,141	57.4
Obesity	2,798	39.0
Diabetes	2,484	34.1
COPD	2,248	31.4
Heart failure	1,984	28.0
Chronic kidney disease	2,003	27.0
Asthma	1,789	24.0
Coronary artery disease (includes CABG, MI)	1,718	24.0
Neurologic condition	1,628	22.6
Immune compromised	1,567	20.8
Chronic metabolic disease, not including diabetes	1,417	19.3
Other chronic lung disease	995	17.1
Chronic liver disease	538	7.2
Autoimmune/inflammatory disease	310	4.5
Blood disorders	287	4.1

94.3% of adults ≥ 18 years with RSV-associated hospitalization had at least one underlying medical condition:

- **31.4%: 1–2 conditions**
- **62.9%: ≥ 3 conditions**

*Clinical data, including underlying medical conditions, were collected for all patients with laboratory-confirmed RSV hospitalizations during the 2014–2015 to 2017–2018 seasons, and for an age- and site-stratified random sample of patients with laboratory-confirmed RSV hospitalizations during the 2022–2023 season. Data are presented as unweighted case counts and weighted percentages that were weighted for the probability of selection.

The Work Group noted that for older adults who do not have any chronic medical conditions and who do not live in long-term care facilities, the risk of severe RSV disease is lower.

- For these adults, the benefit from RSV vaccination may be lower.
- However, the Work Group felt **that these adults might still benefit from vaccination depending on their individual situation** and the decision to get vaccinated should be based on discussion with a healthcare provider.
- The shared clinical decision-making recommendation continues to support this flexibility.



The Work Group also stresses that discussion of benefits vs potential risks should remain the core of shared clinical decision-making.

- Providers will need support in appropriately framing shared clinical decision-making discussions with their older adult patients.
- Providers may need additional communications materials clarifying which of their patients aged ≥ 60 years are at increased risk of severe RSV disease and would benefit most from vaccination.
- Providers may need more materials to support discussing current safety data.



The Work Group acknowledges the challenge of multiple sources of uncertainty.

■ **Uncertainty in estimates of risk**

- Estimated risk is uncertain and confidence intervals are wide
- Among adults electing to receive RSV vaccine, background rates of GBS are uncertain
 - Adults receiving RSV vaccine may differ from those who do not choose vaccines in underlying health status or other ways that could impact background risk of GBS
 - It is unclear if recipients of different RSV vaccine products may also differ in ways that could affect their underlying risk of GBS independent of RSV vaccination

■ **Uncertainty in estimates of benefit**

- Although estimated benefits are based on the best available data, we do not yet have estimates of real-world vaccine effectiveness against RSV-associated hospitalization and death
- The extent to which effectiveness will extend to older adults at highest risk of severe RSV disease (those aged ≥ 75 years, those who are frail, those with immune compromise) is also unknown

■ **There may be other important sources of uncertainty**

- What do we need to understand about coadministration of RSV vaccine with other recommended vaccines?
- Is RSV disease itself associated with a risk of GBS?

Safety surveillance is ongoing and new data will be shared as soon as they become available. The preliminary data shared today are the first in what will be a series of rigorous analyses across multiple different platforms.

- V-safe data monitoring ongoing
- VAERS data monitoring ongoing with CISA experts reviewing selected reports
- Vaccine Safety Datalink
 - Rapid cycle analysis (RCA) will be performed as soon as sufficient data (plan for first RCA March 2024)
 - Power may be limited, especially for Pfizer RSV vaccine
- FDA-CMS partnership ongoing
 - Plan for self-controlled case series as soon as sufficient follow-up time accrued
- Both manufacturers (Pfizer and GSK) conducting post-marketing studies
 - GSK: Sentinel system self-controlled risk interval active surveillance, final report 2031
 - Pfizer: CMS claims data active surveillance, final report 2030
- Will conduct more robust risk-benefit analysis once active surveillance analyses are able to characterize risk and estimates of real-world vaccine effectiveness are available

CDC and the Adult RSV Work Group will be engaged in ongoing assessment. Future older adult RSV policy will be responsive to what is learned over the coming months.

- In the interim, the Work Group wishes to affirm the importance of the RSV vaccination program. RSV is a disease that causes significant morbidity and mortality among persons across the age spectrum.
- The Work Group is cognizant that premature changes in the RSV vaccination program have the potential to limit access to RSV vaccine.
- **CDC and the Work Group are committed to incorporating what we are learning from post-licensure data in a transparent way that ensures safety for the public and clarity for providers.**

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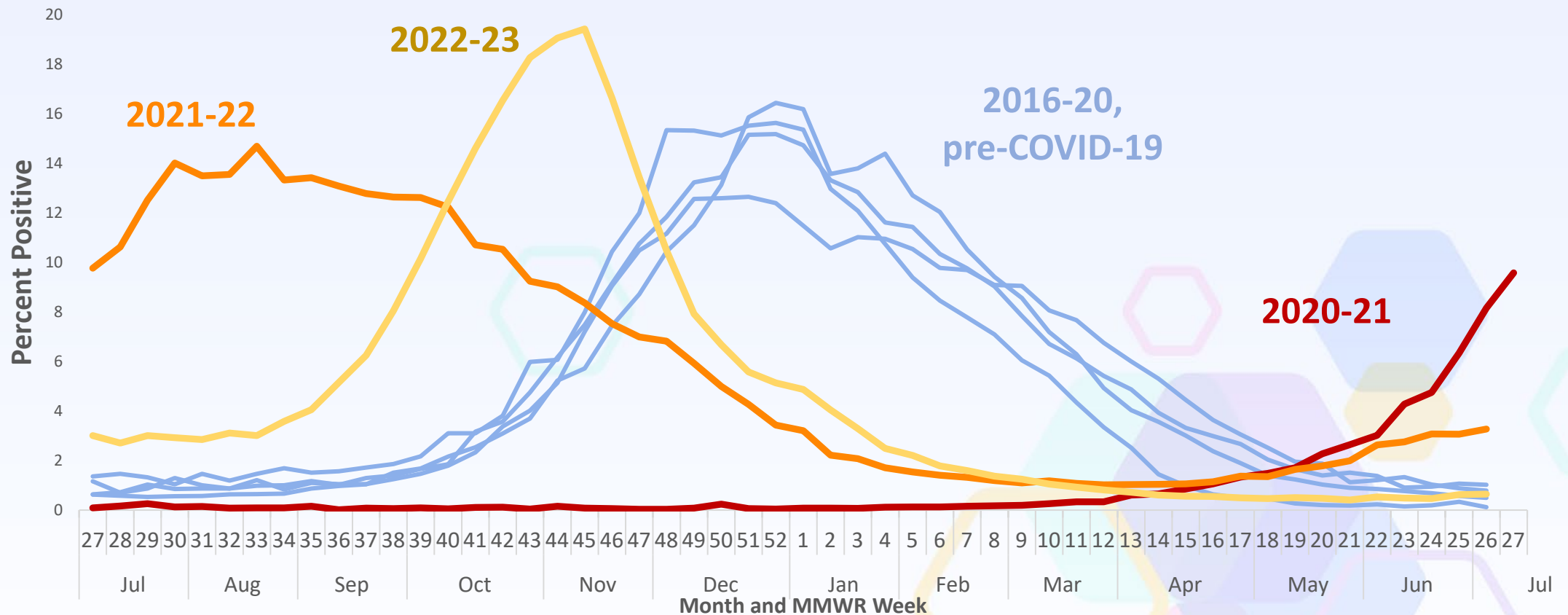
Work Group considerations on timing of RSV vaccination for adults ages 60 years and older

In June 2023, the decision to recommend year-round RSV vaccination was based on 3 considerations:

1. RSV seasonality had been disrupted by the COVID-19 pandemic. Based on the two preceding RSV seasons (2021-2022 and 2022-2023), **it was not clear when RSV circulation might start, peak, and decline.** Therefore, it was also unclear when to time RSV vaccination to optimize benefit to an individual.



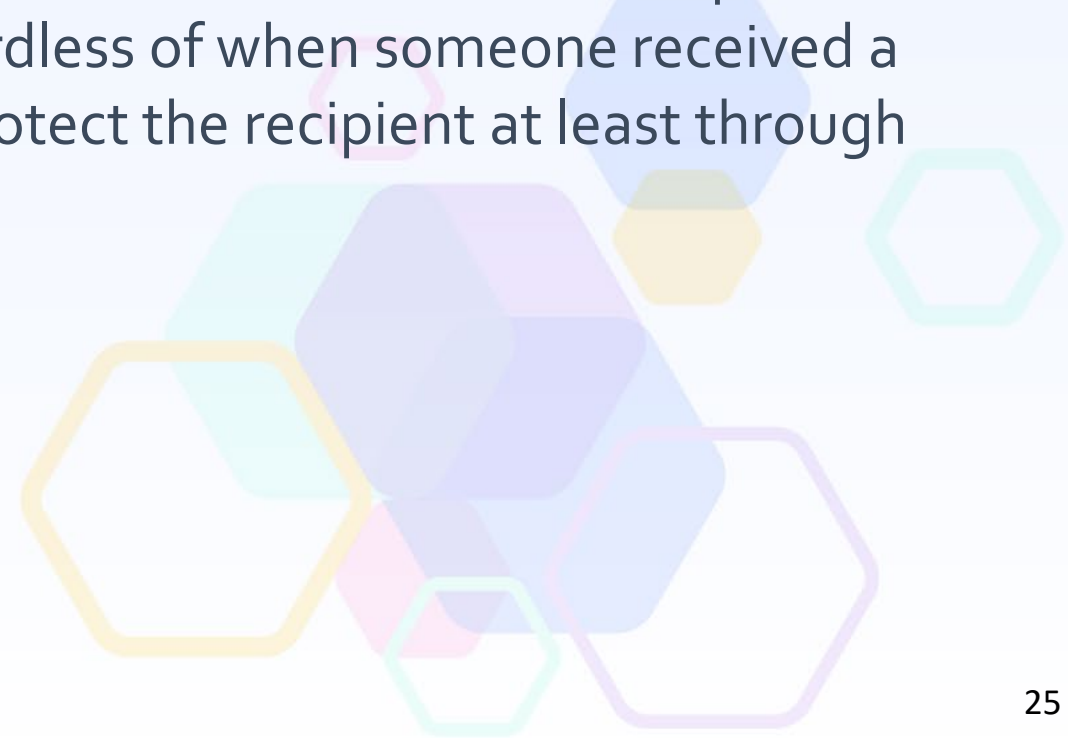
National weekly* RSV percent positivity of PCR results, NREVSS July 2016–June 2023



*All results presented from nucleic acid amplification tests which represent >90% of the diagnostic tests reported to NREVSS. The last three weeks of data may be less complete. NREVSS is an abbreviation for the National Respiratory and Enteric Virus Surveillance System. For more information on NREVSS, please visit www.cdc.gov/surveillance/nrevss. RSV: Respiratory Syncytial Virus. Types A and B are reported but not shown separately in this report. Results are crude, and therefore may differ from smoothed results reported online.

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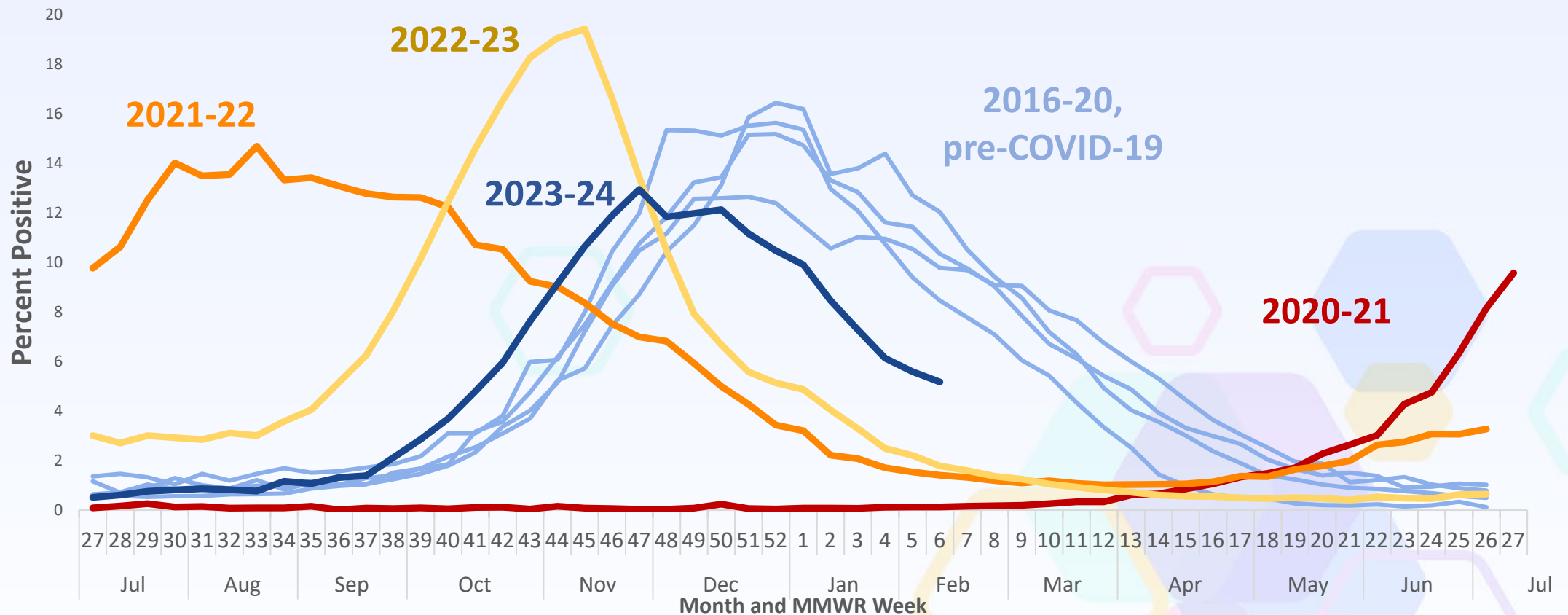
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2. Clinical trial data indicated that both GSK and Pfizer RSV vaccines offered protection **for at least two RSV seasons**. Therefore, regardless of when someone received a dose of RSV vaccine it would be expected to protect the recipient at least through the upcoming RSV season.



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2. Clinical trial data indicated that both GSK and Pfizer RSV vaccines offered protection for at least two RSV seasons. Therefore, regardless of when someone received a dose of RSV vaccine it would be expected to protect the recipient at least through the next upcoming RSV season.
3. There were limited data available to understand if (or when) revaccination would be beneficial. Not having a seasonal end to administration offered maximum flexibility and opportunity for people to receive protection for the next season.

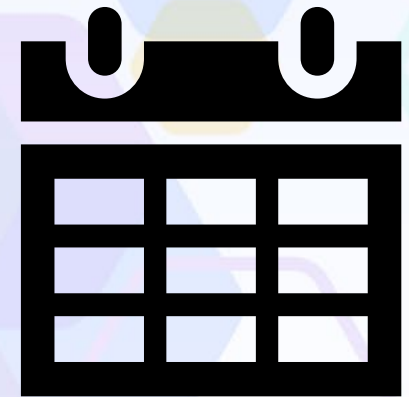
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The Work Group concludes it is now advisable for providers and patients to consider timing of RSV vaccination as part of shared clinical decision-making discussions.

- **Predictable** RSV seasonality makes it possible to anticipate the likely RSV season onset, peak, and offset.
- Maximizing benefits is also desirable as we continue ongoing safety monitoring.
- For most older adults, **benefits will be highest when RSV vaccination is given in the late summer or early fall, just before the onset of RSV season**, so that vaccine recipients experience highest protection during the times of peak RSV transmission over the fall and winter.
- Because clinical trial data suggests that protection will wane over time, vaccinating just before a season starts also maximizes protection for subsequent seasons for which the vaccine offers protection.

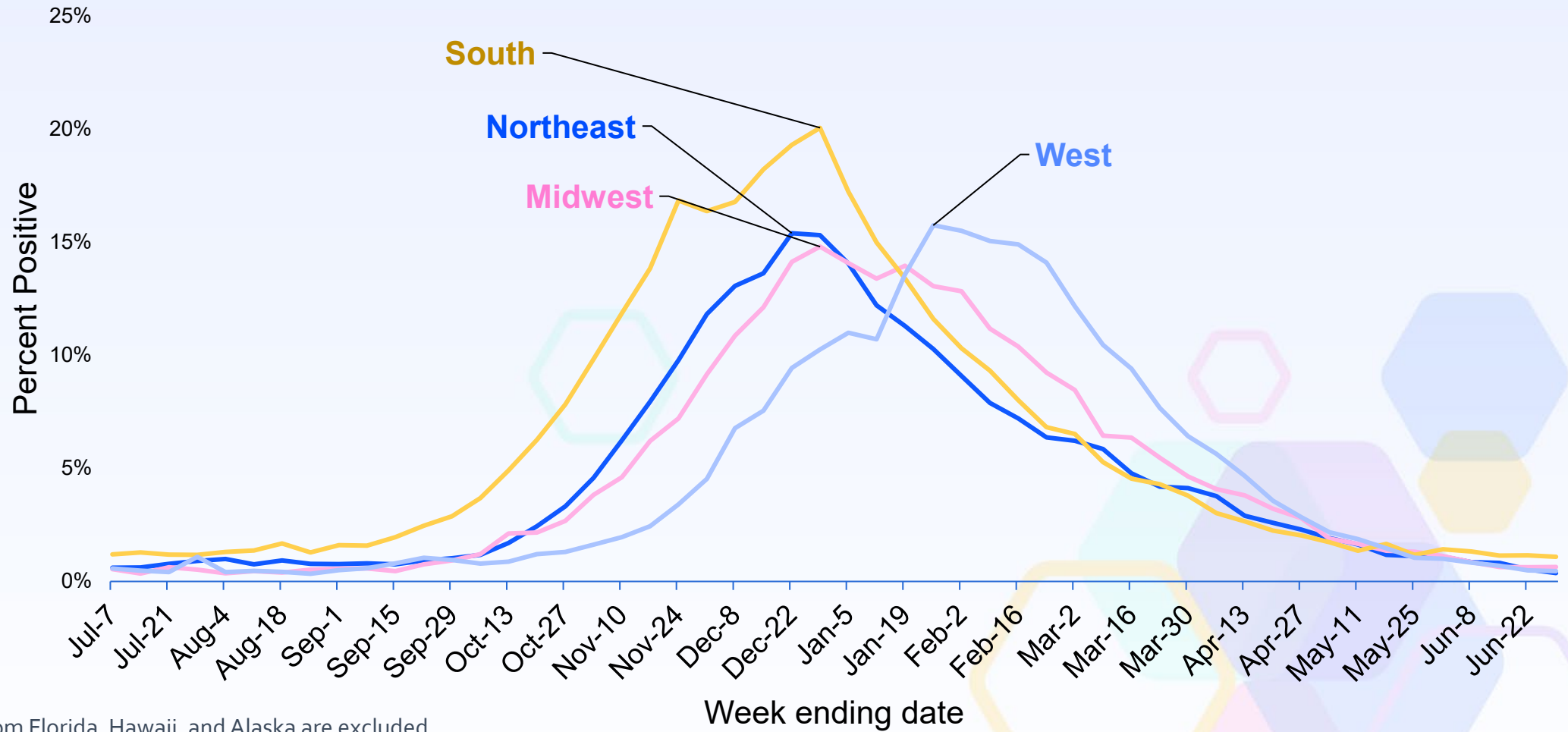


What does it mean to include timing of vaccination in shared clinical decision-making?

In most of the United States, RSV vaccination will have the most benefit if given in late summer or early fall.

- For adults ages 60 years and older who remain unvaccinated and who decide with their healthcare provider to get RSV vaccination, the **best time for vaccination is just before the start of the next RSV season** to maximize the benefits of the vaccine.
- **NOT** a transition to a formal seasonal recommendation for RSV vaccination.
 - Older adults **may continue to receive RSV vaccination year-round**, using shared clinical decision-making.
 - Intent is to allow providers and patients maximum flexibility. Patients with infrequent healthcare contact may benefit from every opportunity to vaccinate.
- **NOT** a recommendation for annual re-vaccination.
 - RSV vaccine for adults 60 and older is currently still recommended as a one-time vaccine.

Mean weekly RSV percent positivity of PCR results by census region, NREVSS*, 2015–2019



*Data from Florida, Hawaii, and Alaska are excluded.

All results presented from nucleic acid amplification tests which represent >90% of the diagnostic tests reported to NREVSS.

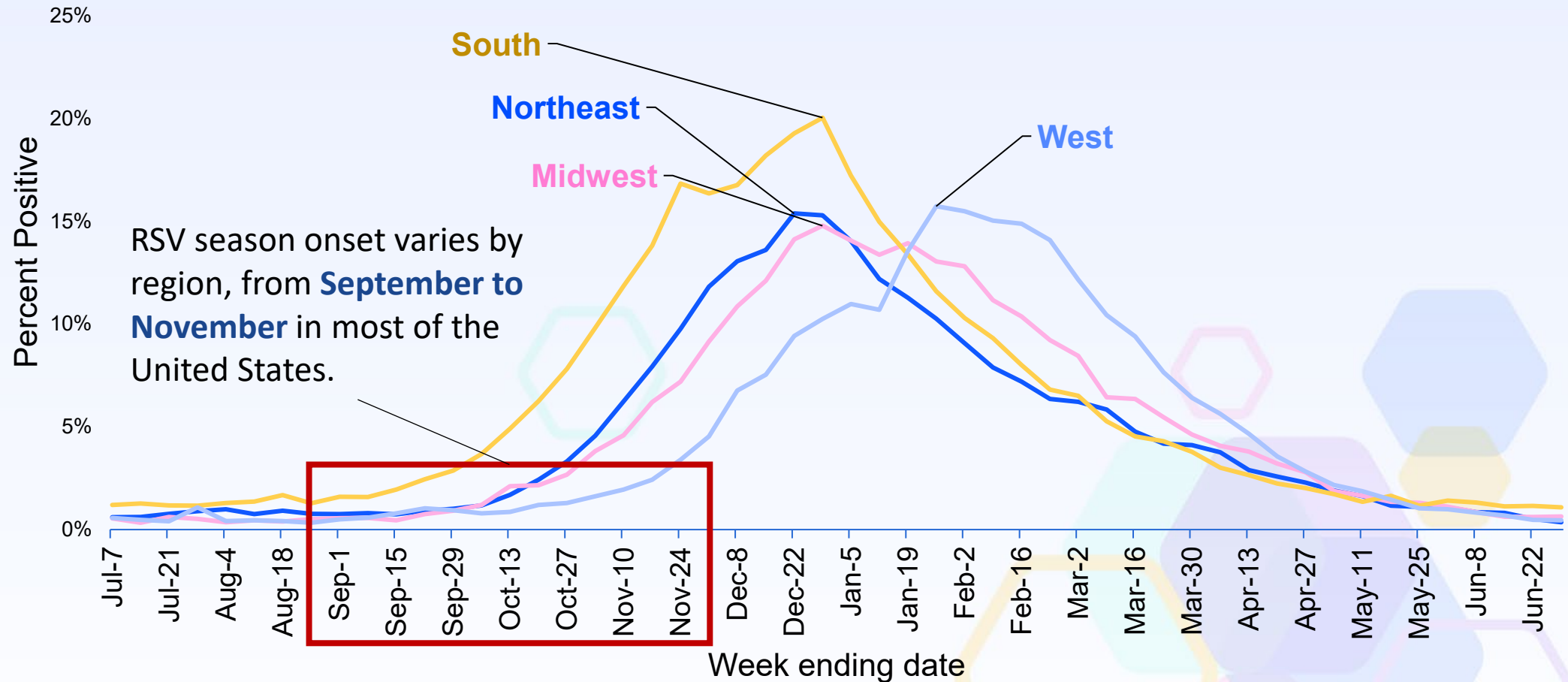
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For more information on NREVSS, please visit www.cdc.gov/surveillance/nrevss.

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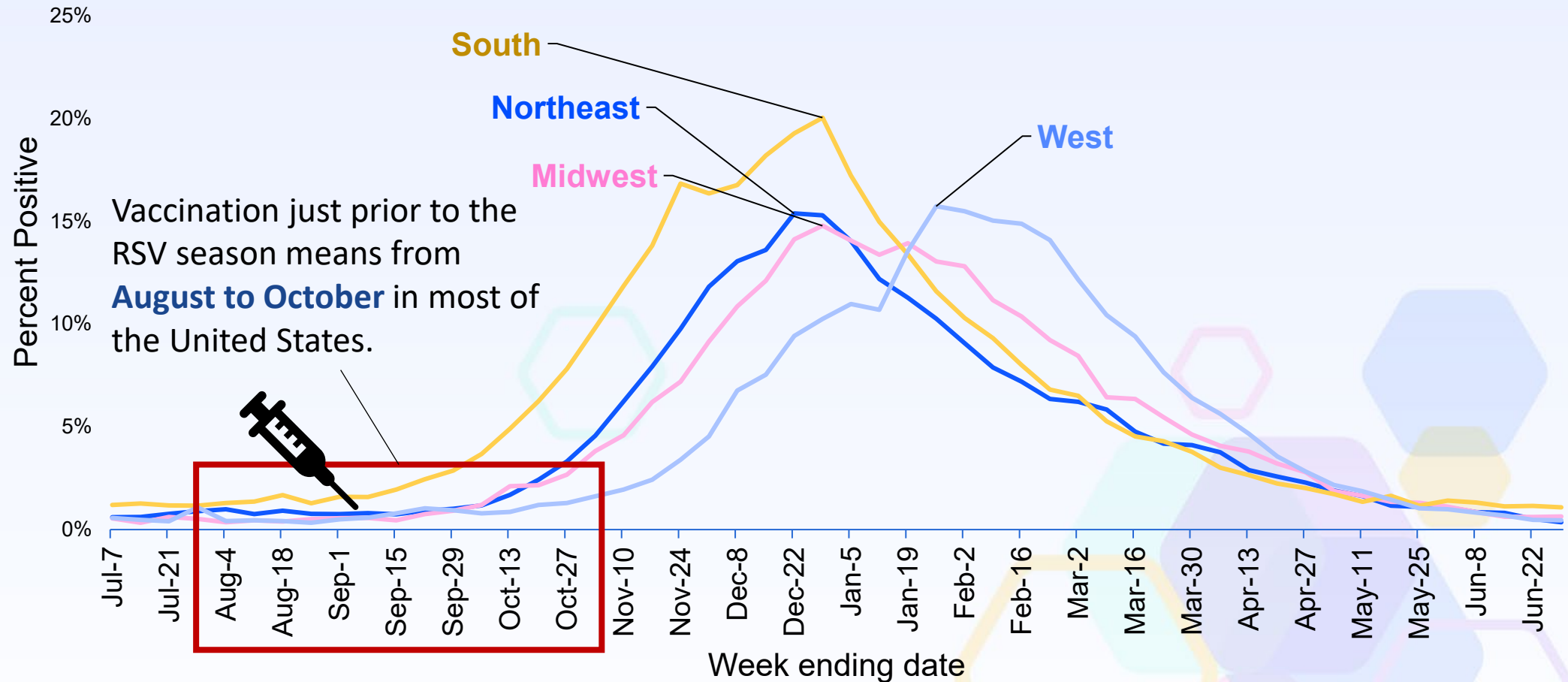
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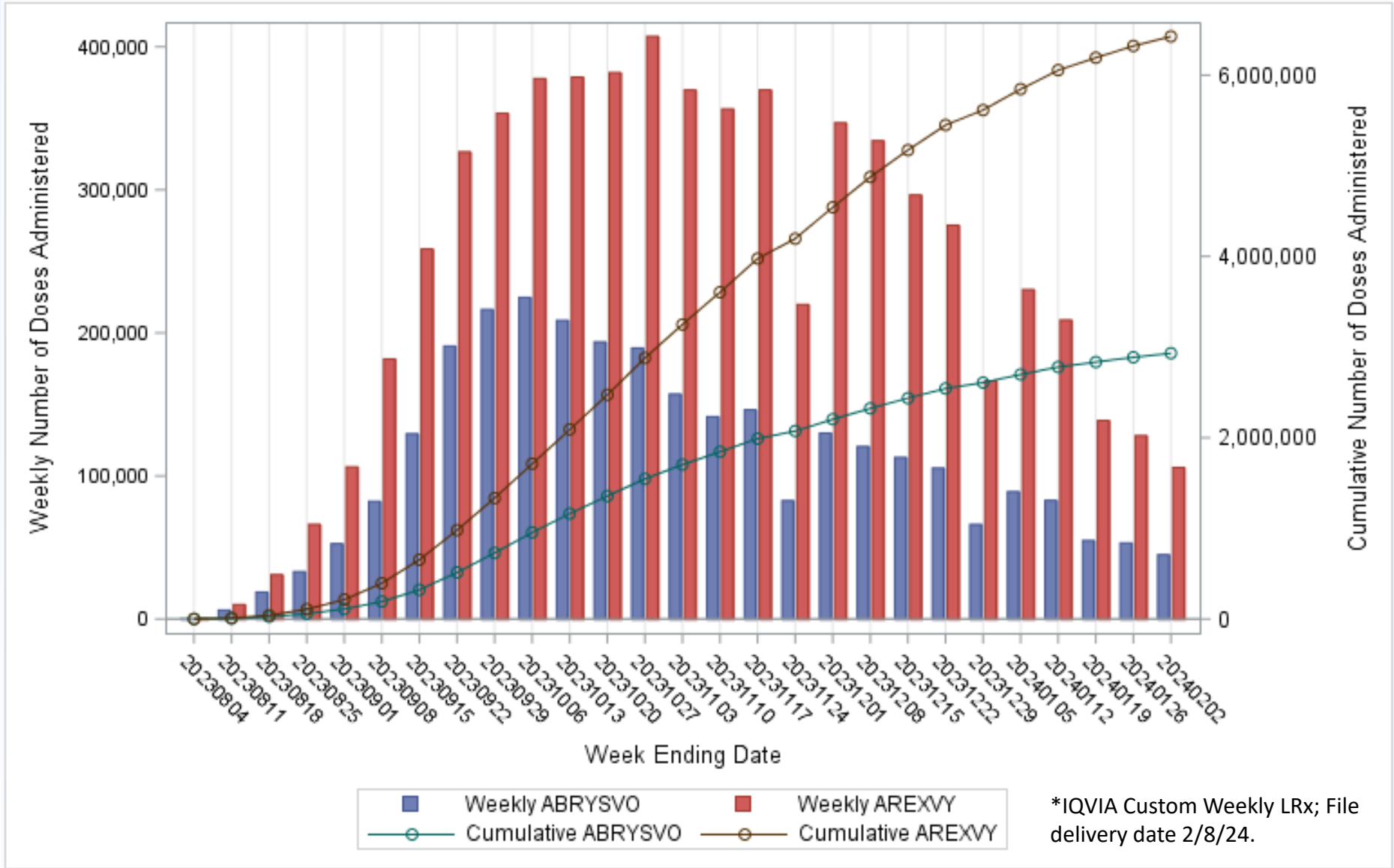
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Weekly and Cumulative Projected RSV Vaccinations Administered in Retail Pharmacies by Product, Adults 60 years and older, August 12, 2024 – February 2, 2024. Data Source: IQVIA*



The weekly number of RSV vaccine doses administered appears to have peaked and now be declining.

*IQVIA Custom Weekly LRx; File delivery date 2/8/24.

The background is a solid blue color with a pattern of semi-transparent hexagons in various shades of blue and purple, some overlapping and some as outlines.

Other upcoming policy considerations for RSV vaccination in adults ages 60 years and older

Additional policy issues Adult RSV Work Group plans to address in June 2024

1. Potential FDA approval of Moderna mRNA-1345 vaccine for use in adults aged ≥ 60 years
2. Potential FDA approval of GSK RSV vaccine for use in adults aged 50–59 years “at increased risk for RSV disease” (*regulatory decision expected June 2024*)
3. Consideration of whether shared clinical decision-making remains the preferred policy option.



Work Group interpretations of initial phase 3 safety and efficacy of Moderna's mRNA-1345 RSV vaccine

- The Work Group notes that safety and efficacy were demonstrated in their phase 3 safety & efficacy trial, most notably:
 - Interim efficacy analysis with median **9 months** follow-up per participant
 - VE against RSV LRTI with ≥ 2 symptoms: 63.3% (95% CI 48.7–73.7%)
 - VE against RSV LRTI with ≥ 3 symptoms: 63.0% (95% CI 37.3–78.2%)
 - Two recorded RSV-associated hospitalizations, both in the placebo arm. Unable to estimate efficacy against hospitalization.
 - No recorded RSV-associated deaths, including in the placebo arm.
 - No reported cases of GBS, ADEM, or other inflammatory neurologic events in clinical trials of mRNA-1345 (N=18,245 vaccine recipients in their pivotal Phase II/III trial).
 - No reported cases of confirmed myocarditis or pericarditis among recipients of mRNA-1345 within 42 days after vaccination.
- If licensed by FDA for use in adults 60 and older, Work Group plans to present full GRADE/EtR to support ACIP deliberations around adding Moderna mRNA-1345 as an option for adults 60 and older to protect against lower respiratory tract disease.

Work Group interpretations of GSK RSV vaccine for use in adults 50–59 at increased risk of RSV disease

- In October 2023, GSK presented data to ACIP demonstrating that the humoral immune response to a **single dose of GSK RSV vaccine in adults 50–59 years is non-inferior to that in adults 60 and older.**
- The Work Group noted that if FDA licensure is granted for use of GSK’s RSV vaccine in adults aged 50–59 years at increased risk of RSV disease, then ACIP will likely need to make a policy recommendation on:
 - Whether RSV vaccination should be recommended in this age group?
 - And if so, how will CDC define populations at increased risk of RSV disease?
- Today we saw data demonstrating the relative risk of severe RSV disease across a range of chronic medical conditions by age group.
- **Work Group members broadly agree that use of RSV vaccine among adults with certain chronic medical conditions aged 50–59 years is likely to have public health benefit, however, upcoming data on safety and effectiveness will be pivotal to determine the preferred policy option in this age group.**

Work Group interpretations on whether shared clinical decision-making will remain the preferred policy option

- Lastly, the Work Group has begun analyzing the experience with shared clinical decision-making this season.
- Feedback from many partners that shared clinical decision-making has been challenging to implement.
- For the time being, the Work Group continues to endorse shared clinical decision-making as we learn more about the estimated benefits and potential risks associated with the currently available RSV vaccines.
- **However, the Work Group has begun reviewing evidence to discuss changing the current recommendation for adults ≥ 60 from shared clinical decision-making to:**
 - ***A universal recommendation among adults older than a specific age cut-off AND***
 - ***A risk-based recommendation in adults 50 years and older up to that age cut-off***

The Work Group is considering a shift away from shared clinical decision-making for multiple reasons.

- A **universal recommendation** among adults over a specific age cut-off may be easier to message and implement.
- A **risk-based recommendation** among adults 50 and older, but below the universal age cut-off may be easier to implement (persons at risk would be more concretely defined) and ensure persons being vaccinated have highest potential to benefit.
- Anticipate presenting additional data on these topics at the June 2024 ACIP meeting

The Work Group emphasizes that future preferred policy options will be contingent on incoming data, including safety analyses and vaccine effectiveness.

Summary

- The first-ever respiratory virus season in which there were vaccines available to protect older adults against RSV disease is coming to a close.
- This is a new vaccine program and remains an evolving landscape with the potential for new products and expansion of current products into new age groups.
- Data from this season is still incoming. Over the coming months CDC and the Work Group will be analyzing these data to inform discussion of future RSV vaccine policy for older adults.
- Data from pre-licensure clinical trials and early findings from post-licensure vaccine safety surveillance suggests the potential for increased risk of GBS after RSV vaccination in older adults; however, these early data are insufficient to confirm if there is an increased risk.
- Assessing the risk for GBS following receipt of the RSV vaccine among older adults in more robust analyses in active vaccine safety surveillance systems will be crucial and is underway.
- Currently, the Work Group continues to endorse the benefits of RSV vaccination for adults 60 and older, especially those at increased risk of severe RSV disease, using shared clinical decision-making.
- Benefits can be maximized by administering RSV vaccine just before the start of RSV season and the Work Group recommends that timing of RSV vaccination should be a part of the shared clinical decision-making discussion.

CDC and the Adult RSV Work Group will continue to transparently share new information with ACIP and the public and incorporate it into future policy recommendations to ensure the greatest benefit and least risk in the RSV vaccine program for older adults.

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

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