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IMMUNIZING WITH NIRSEVIMAB: INDICATIONS, EFFICACY, USAGE AND '23-'24 LESSONS LEARNED

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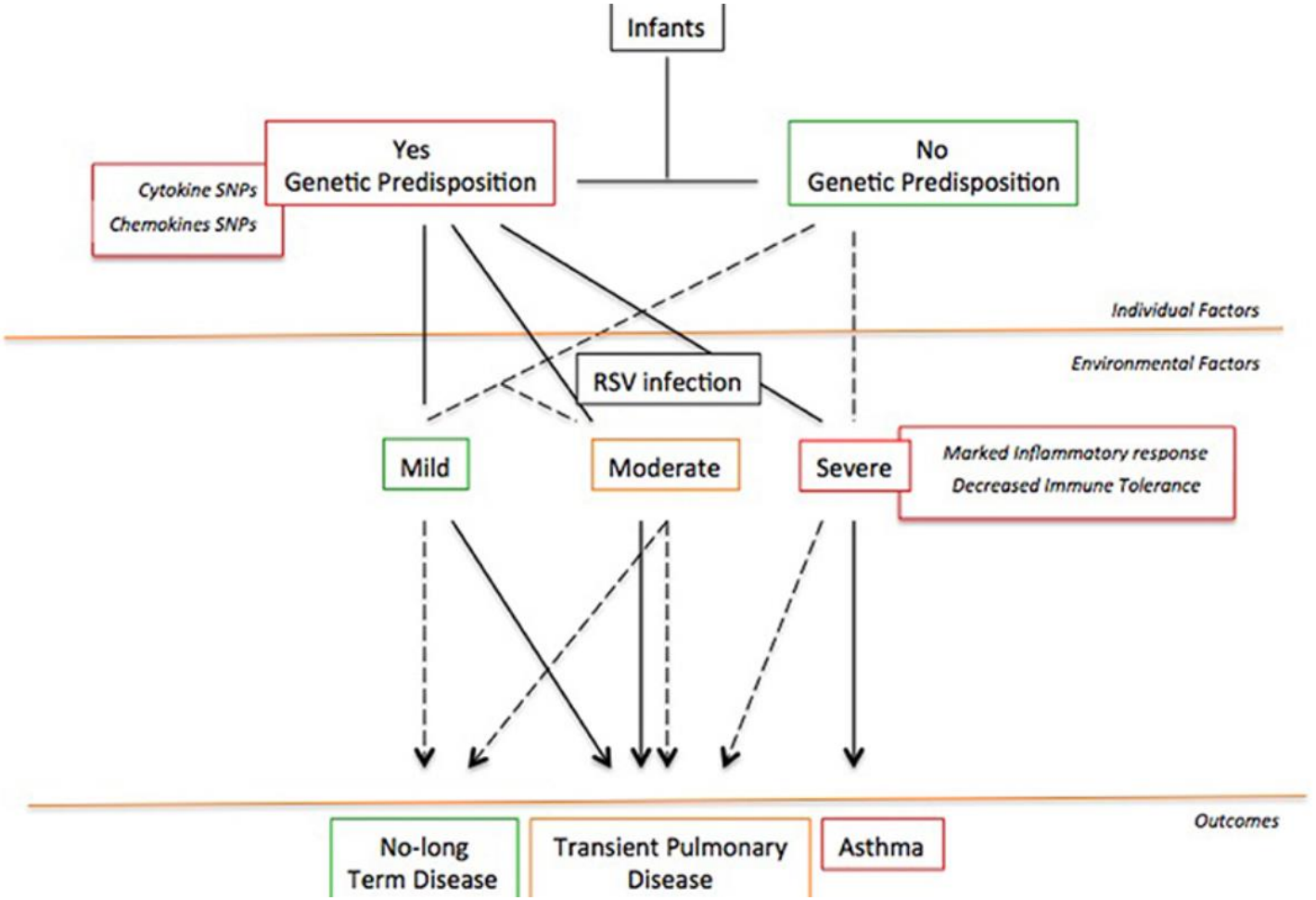
Disclosure

I, Mary Beth Miotto, have been asked to disclose any relevant financial relationships with ACCME-defined commercial entities that are either providing financial support for this program or whose products or services are mentioned during this presentation.

I have no relevant financial relationships to disclose.

Why prevent RSV in infancy?
-Medically attended and severe infections
-Potential for Long-term Sequelae/Asthma



From: Manti, S., & Piedimonte, G. (2022). An overview on the RSV-mediated mechanisms in the onset of non-allergic asthma. Frontiers in Pediatrics, 10, 998296.

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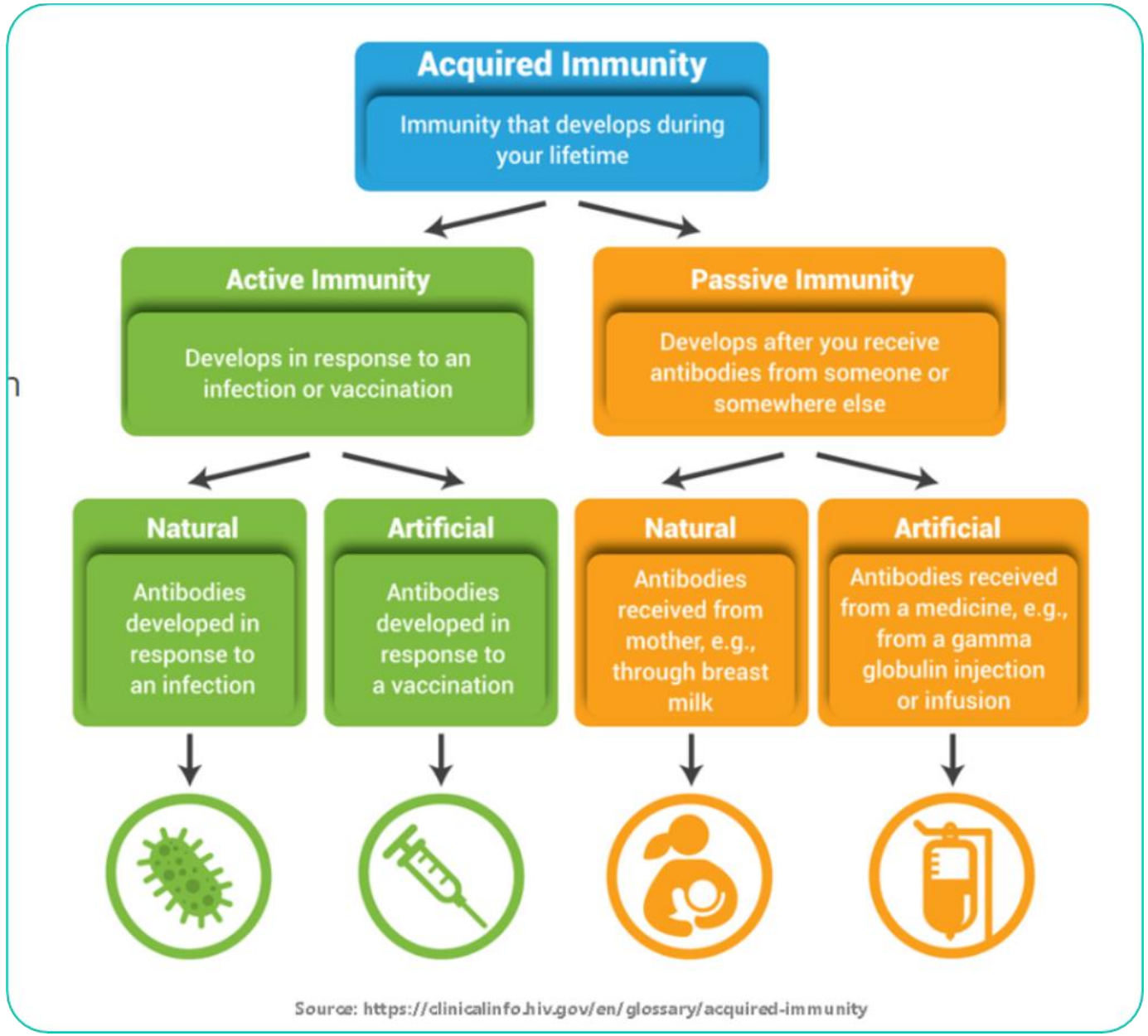
Fundamentals: RSV Prevention in Infants and Toddlers

Nirsevimab: is It a Vaccine?



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Nirsevimab is a passive immunization

- Active immunity results from infection or vaccination, which triggers an immune response
- Passive immunity is when a person receives antibodies from an external source
  - From mother to baby through transplacental or breastmilk transfer
  - Direct administration of antibodies, such as IVIG or monoclonal antibodies

CDC/ACIP presentation,
Dr. J Jones, August 3, 2023

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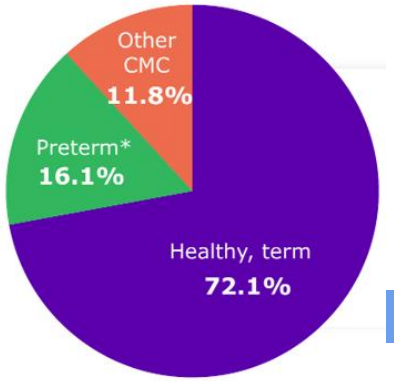
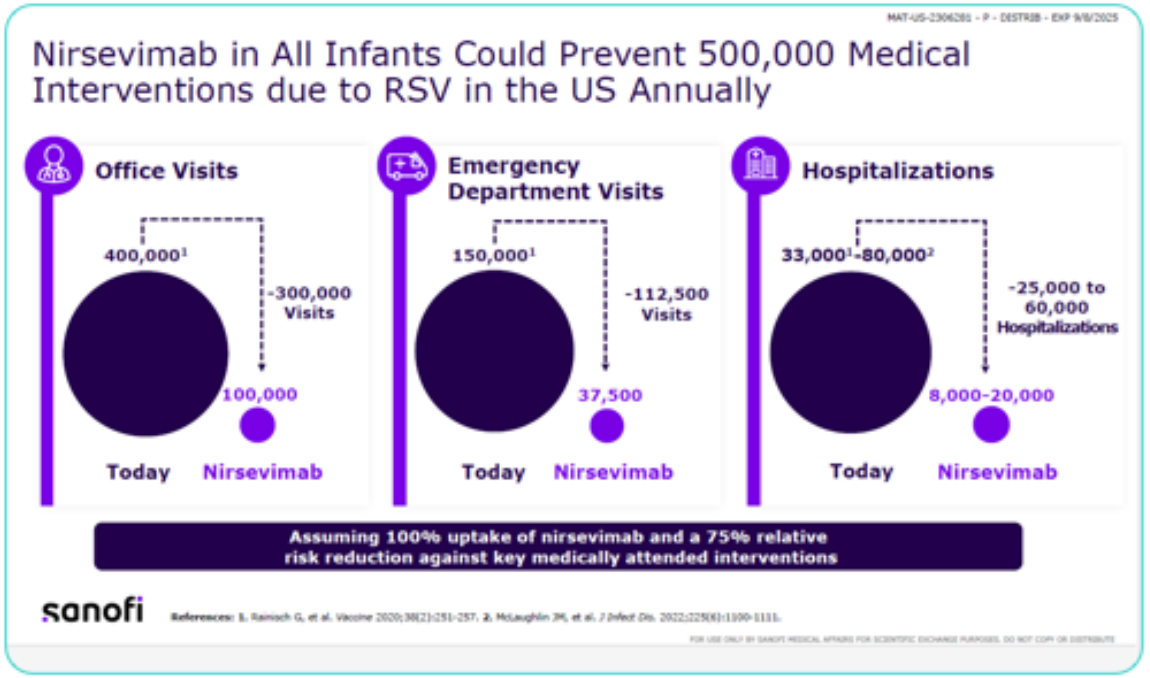
Why did the CDC/ACIP vote to recommend Nirsevimab in all Infants?





How Effective is Nirsevimab in Preventing RSV Disease? "Medically Attended Lower Respiratory Tract Infections"

Efficacy estimates and concerns in certainty of assessment

Outcome	Efficacy estimate*	Concerns in certainty of assessment
Benefits		
Medically attended RSV LRTI	79.0% (95% CI: 68.5%–86.1%)	None
RSV LRTI with hospitalization	80.6% (95% CI: 62.3%–90.1%)	None
RSV LRTI with ICU admission	90.0% (95% CI: 16.4%–98.8%)	Serious (imprecision): Too few events
Death due to RSV respiratory illness	None recorded	N/A
All-cause medically attended-LRTI	34.8% (95% CI: 23.0–44.7%)	None
All-cause LRTI-associated hospitalization	44.9% (95% CI:24.9%–59.6%)	None

*Pooled phase 2b (excluding underdosed) and phase 3 trial estimate comparing nirsevimab arm to placebo arm

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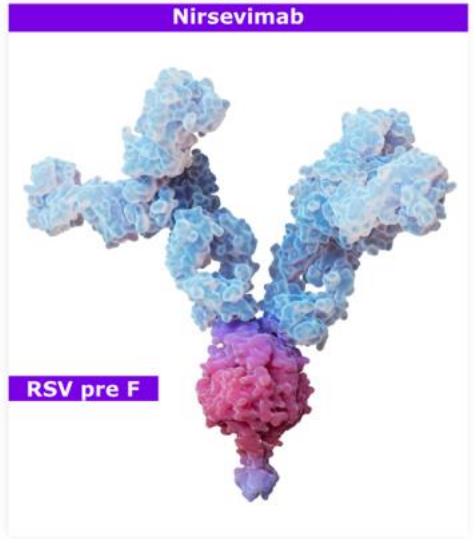
CDC/ACIP presentation, Dr. J Jones, August 3, 2023

What are the 2024-25 Nirsevimab recommendations and how do we give the monoclonal antibody?



The Who, What, and When of Nirsevimab

ACIP Recommendations Published in MMWR

First RSV season[1]

One dose of nirsevimab for all infants aged <8 months born during or entering their first RSV season

- 50 mg for infants weighing <5 kg [<11 lb]
- 100 mg for infants weighing ≥5 kg [≥11 lb]

Second RSV season[1]

One dose of nirsevimab for infants and children aged 8–19 months who are at increased risk for severe RSV disease and entering their second RSV season

- 200 mg, administered as two 100 mg injections given at the same visit

American Indian or Alaska Native children are considered at increased risk in their second season.

The recommendations for nirsevimab apply to infants and children recommended to receive palivizumab by AAP.

Nirsevimab added to the Vaccines for Children program (VFC)[2]

ACIP, Advisory Committee on Immunization Practices

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References: 1. Jones JM, Fleming-Dutra KE, Prill MM, et al. Use of Nirsevimab for the Prevention of Respiratory Syncytial Virus Disease Among Infants and Young Children: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023. MMWR Morb Mortal Wkly Rep 2023;72(34):920–925. DOI: https://dx.doi.org/10.15585/mmwr.mm7234a4. **2.** CDC press release. CDC Recommends a Powerful New Tool to Protect Infants from the Leading Cause of Hospitalization. Available at https://www.cdc.gov/media/releases/2023/p-0803-new-tool-prevent-infant-hospitalization.html. Accessed August 31, 2023.

Clinical Implementation: High-risk children in their 2nd RSV season

Children aged 8–19 months recommended to receive nirsevimab when entering their second RSV season because of increased risk of severe disease

- Children with chronic lung disease of prematurity who required medical support (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) any time during the 6-month period before the start of the second RSV season
- Children with severe immunocompromise
- Children with cystic fibrosis who have manifestations of severe lung disease (previous hospitalization for pulmonary exacerbation in the first year of life or abnormalities on chest imaging that persist when stable) or weight-for-length <10th percentile
- American Indian and Alaska Native children

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Clinical Implementation: When to administer?

Timing of nirsevimab

- Providers should target administration[1]:
  - In the first week of life for infants born shortly before and during the season
  - Shortly before the start of the RSV season for infants aged <8 months
  - Shortly before the start of the RSV season for children aged 8–19 months who are at increased risk of severe RSV disease
- Based on pre-pandemic patterns, this means nirsevimab could be administered in most of the continental United States from October through the end of March
- Because timing of the onset, peak, and decline of RSV activity may vary, providers can adjust administration schedules based on local epidemiology

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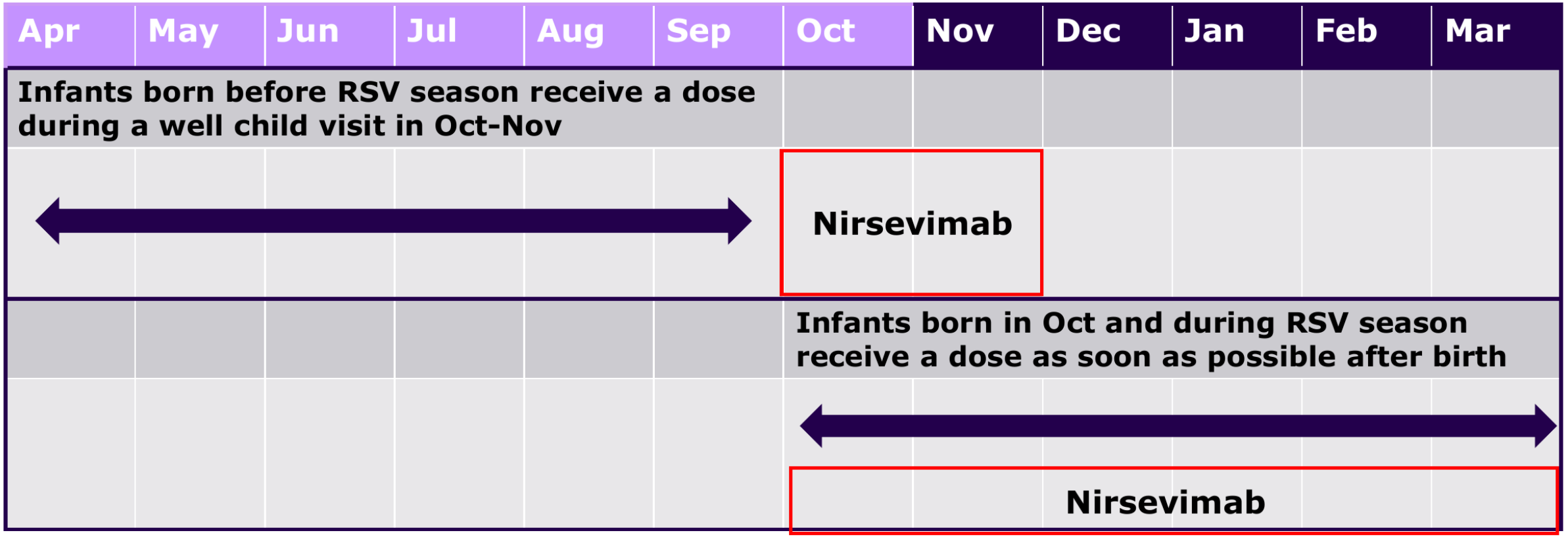
Implementation of Nirsevimab for Infants Entering or Born During First RSV Season

Typical RSV Season*



*Providers in tropical climates (S. Florida, Hawaii, etc.) and Alaska, which may have more unpredictable or longer RSV seasons, should consult local guidance on the timing of nirsevimab administration.

Reference: 1. Jones JM, Fleming-Dutra KE, Prill MM, et al. Use of Nirsevimab for the Prevention of Respiratory Syncytial Virus Disease Among Infants and Young Children: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023. MMWR Morb Mortal Wkly Rep 2023;72(34):920–925. DOI: http://dx.doi.org/10.15585/mmwr.mm7234a4.

What did infant RSV protection in the ‘23-’24 winter season look like?

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Let's Talk about the 2023-2024 Nirsevimab Successes

- ❑ The AAP and MCAAP leadership expedited a robust information campaign to educate and prepare pediatricians and birthing hospitals.
- ❑ Public health, pediatricians, and industry established an "all hands on deck" culture.
- ❑ Federal and state agencies expedited the inclusion in Vaccines for Children and in Massachusetts it was included in Universal Purchasing right away.
- ❑ New immunization protocols and training material was disseminated in early autumn even before the product was ready to be ordered on MIIS.
- ❑ Massachusetts neonatologists advocated loudly for all birthing hospitals to enroll immediately in VFC so they could efficiently provide nirsevimab in the nursery and most hospitals did so at breakneck speed.
- ❑ Obstetricians and ACOG here in Massachusetts followed the corresponding FDA and ACIP decisions on RSV preF maternal vaccine and many prepared to offer this product to eligible pregnant individuals between 32 and 36 weeks of pregnancy between September and January.

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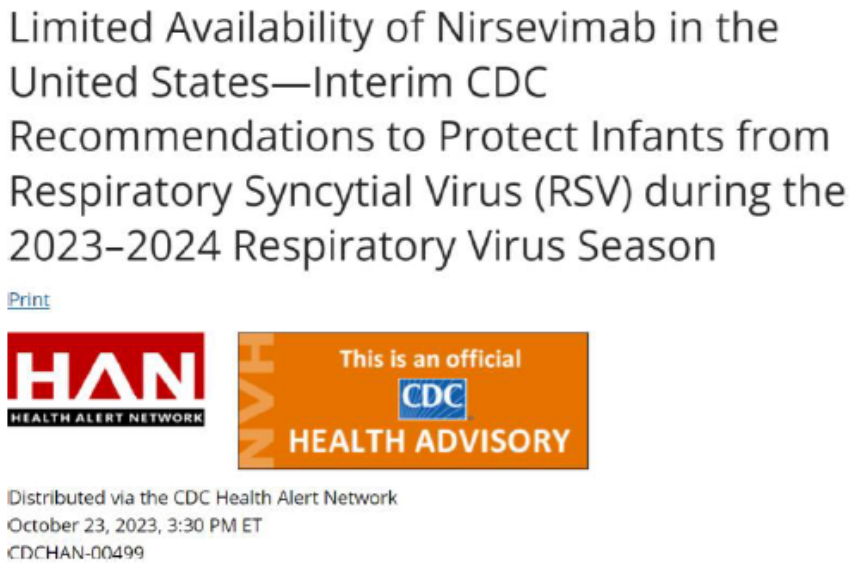
Let's Talk about the 2023-2024 Challenges in Nirsevimab Implementation

- ❑ The prior RSV season ('22-'23) brought the "tripledemic", resulting in increased RSV disease visibility, hospital bed shortages, and new public awareness.
- ❑ FDA (July 17) and ACIP (August 3) 2024 policy decision timelines created a surge of pediatrician and parent demand without a corresponding proportionate supply.
- ❑ Procurement, coding/billing, and payment processes were unwieldy with such a short window for implementation planning.
- ❑ Practices rushed to develop new immunization protocols and trainings for this product and anticipated an imminent distribution.
- ❑ Parents were hearing and seeing direct-to-consumer campaigns before most practices got any supply, creating a parent demand even outside of insurance-paid channels.
- ❑ Supply chain challenges continued for much of the season, resulting in temporary guidelines for triaging and even redistribution of product to prioritize birthing hospital administration of Nirsevimab.

Insufficient supply of nirsevimab to meet demand in 2023-2024 season

- Limited supply of nirsevimab (100mg and 50mg formulations) meant clinicians were uncertain how to ration or prioritize few available doses
- CDC issued an official Health Advisory notice via the Health Alert Network to prioritize available doses to high-risk infants and younger infants
- By January, demand had decreased and additional supply was available allowing return to original recommendations


Limited Availability of Nirsevimab in the United States—Interim CDC Recommendations to Protect Infants from Respiratory Syncytial Virus (RSV) during the 2023–2024 Respiratory Virus Season

Print

HAN HEALTH ALERT NETWORK

This is an official CDC HEALTH ADVISORY

Distributed via the CDC Health Alert Network
October 23, 2023, 3:30 PM ET
CDCHAN-00499

Health Alert Network (HAN) - 00499 | Limited Availability of Nirsevimab in the United States—Interim CDC Recommendations to Protect Infants from Respiratory Syncytial Virus (RSV) during the 2023–2024 Respiratory Virus Season

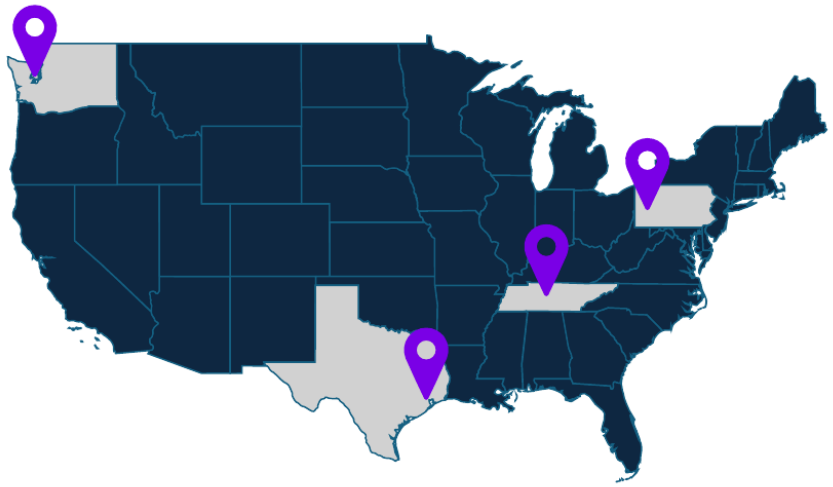
What happened in that small window of RSV prevention?

Nirsevimab Real-World:

Efficacy - performance of nirsevimab under controlled circumstances (intervention included randomization to treatment or no treatment)

Effectiveness - clinical evidence on nirsevimab efficacy from routine healthcare delivery (no intervention such as randomization to a cohort)

Population Impact - measurement and trend of nirsevimab benefit, for example compared to an external control (i.e., A comparison to other years, regions, age groups, etc.)



Harmonie – *UK, France, Germany*

CDC, NVSN - US

Valencia, Murcia, Valladolid - *Spain*

Brault - *France*

Navarre - *Spain*

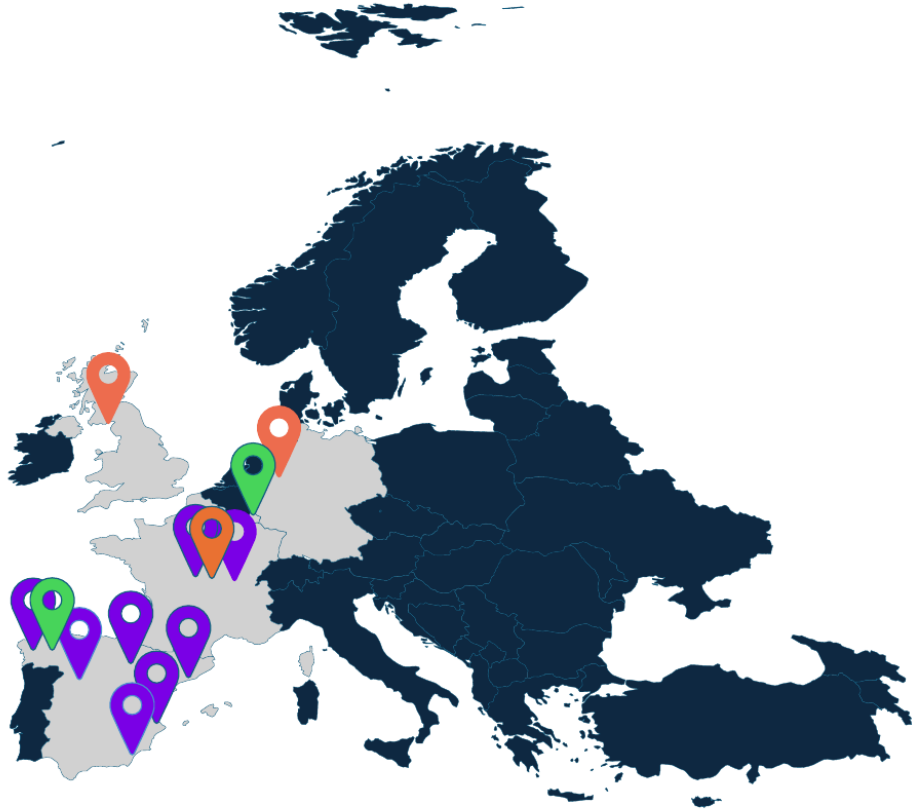
Catalonia - *Spain*

Pairea - *France*

Galicia - *Spain*

Galicia - Spain

Luxembourg



NVSN is a prospective, population-based surveillance network for pediatric acute respiratory illness (ARI) at 7 U.S. medical centers.

Children <18 years of age with ARI are enrolled year-round in the **outpatient, urgent care, emergency department (ED), and hospital** settings.

Surveillance Objectives:

- Determine the **etiology and burden** of laboratory-confirmed acute viral respiratory diseases in children
- Characterize the **clinical and epidemiologic factors** of pediatric ARI and associated syndromes
- Evaluate **vaccine effectiveness (VE)** using a test-negative design (TND) and impact of vaccines and other immunoprophylaxis products.

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Early Estimate of Nirsevimab Effectiveness for Prevention of Respiratory Syncytial Virus–Associated Hospitalization Among Infants Entering Their First Respiratory Syncytial Virus Season — New Vaccine Surveillance Network, October 2023–February 2024

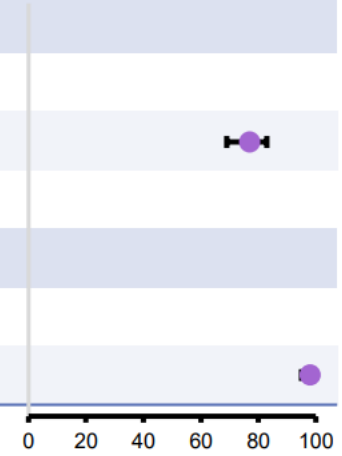
Weekly / March 7, 2024 / 73(9);209–214

- In the first RSV Season in which there was some Nirsevimab available to infants, Nirsevimab effectiveness was 90% against RSV-associated hospitalization in infants in their first RSV season.

- Moline HL, Tannis A, Toepfer AP, et al. Early Estimate of Nirsevimab Effectiveness for Prevention of Respiratory Syncytial Virus–Associated Hospitalization Among Infants Entering Their First Respiratory Syncytial Virus Season — New Vaccine Surveillance Network, October 2023–February 2024. MMWR Morb Mortal Wkly Rep 2024;73:209–214. DOI: http://dx.doi.org/10.15585/mmwr.mm7309a4.

First season nirsevimab product effectiveness (PE) against RSV-associated ED encounters and hospitalization – VISION, October 8, 2023 – March 31, 2024

Outcome | Nirsevimab dosage pattern	Total encounters	RSV-positive encounters N (Row %)	Median days since dose (IQR)	Adjusted PE (95% CI)*
RSV-associated ED encounter				
No nirsevimab doses	4,610	1,988 (43)	N/A	ref
Nirsevimab, ≥7 days prior	442	63 (14)	53 (27-84)	77 (69-83)
RSV-associated hospitalization				
No nirsevimab doses	927	601 (65)	N/A	ref
Nirsevimab, ≥7 days prior	93	4 (4)	48 (25-84)	98 (95-99)



Nirsevimab was effective against RSV-associated ED encounters and hospitalization among infants in their first RSV season.

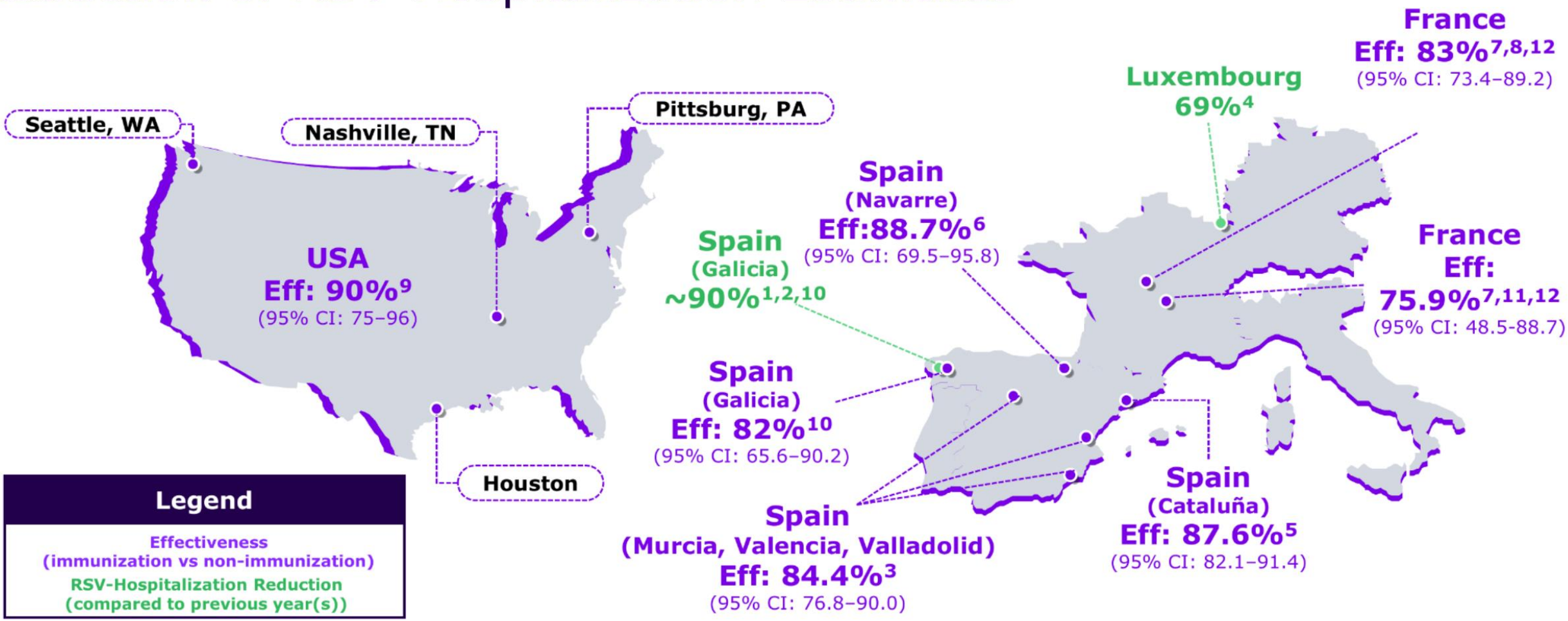
Amanda Payne, PhD, MPH
Coronavirus and Other Respiratory Viruses Division
Centers for Disease Control and Prevention
June 28, 2024; https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2024-06-26-28/04-RSV-Mat-Peds-Payne-508.pdf

Proportion of infants protected from RSV by receipt of nirsevimab or maternal RSV vaccination

- **51.2% of infants are estimated to be protected from RSV by either receipt of nirsevimab or maternal RSV vaccination.**
- Infants eligible for nirsevimab: 3,900,000
  - Those 0–7 months old during October 2023–March 2024
  - Born March 2023–March 2024
  - Assume 300,000 babies born each month
  - 43.0% received nirsevimab (from February NIS-ACM)
- Infants eligible for protection by maternal vaccination (a subset of infants eligible for nirsevimab): 1,800,000
  - Born October 2023–March 2024
  - Born to mothers 32-36 weeks' gestation and eligible for RSV vaccination September 2023–January 2024
  - 17.8% of mothers received RSV vaccination (from VSD data through January 2024)
- Estimated number of infants who received nirsevimab = .430*3,900,000 = 1,677,000
- Estimated number of infants protect by maternal RSV vaccination = .178*1,800,000 = 320,400
- **Percent protected by either = 1,677,000 + 320,400 / 3,900,000 = 51.2%**

Data sources: https://www.cdc.gov/vaccines/imz-managers/coverage/rsvvaxview/nirsevimab-coverage.html, https://www.cdc.gov/vaccines/imz-managers/coverage/rsvvaxview/pregnant-persons-coverage-intent.html, https://wonder.cdc.gov/

Summary of Real-World Effectiveness & Reduction of RSV-Hospitalization Estimates



CI, confidence interval; Cov, coverage; Eff, effectiveness; RSV, respiratory syncytial virus.

References: 1. NIRSE-GAL research team. Results of implementation of Nirsevimab in Galicia. https://www.nirsegal.es/en 2. Martinon-Torres et al. ESWI Respiratory Virus Summit 2024 | ESWI, 5 March 2024. https://eswi.org/cnt/activity/eswi-summit-2024#activity-programme. 3. López-Lacort M. et al Euro Surveill. 2024;29(6):pii=2400046. 4. Ernst C et al. Euro Surveill. 2024;29(4):pii=2400033. 5. Coma E. et al, Preprints with the Lancet, https://ssrn.com/abstract=4749763 6. Ezpeleta G, et al. Vaccines. 2024, 12: 383. 7. Bronchiolite : deux études françaises démontrent l'efficacité du Beyfortus® dans la prévention des cas graves et la réduction des hospitalisations chez les nourrissons (santepubliquefrance.fr) accessed 5th of May 2024 8. Assad Z, et al. N Eng J Med 2024, in press. 9. Moline HL et al., MMWR Morb Mortal Wkly Rep 2024;73:209–214. 10. Ares-Gómez S et al. Lancet Infectious Diseases, May 1st 2024. 11.Paireau J et al.. Nirsevimab effectiveness against cases of respiratory syncytial virus bronchiolitis hospitalised in pediatric intensive care units in France, September 2023 -January 2024. 2024. (pasteur-04501286) 12. Cohen R. et al. Oral presentation; 29th of April 2024, ESCMID 2024; Barcelona, Spain

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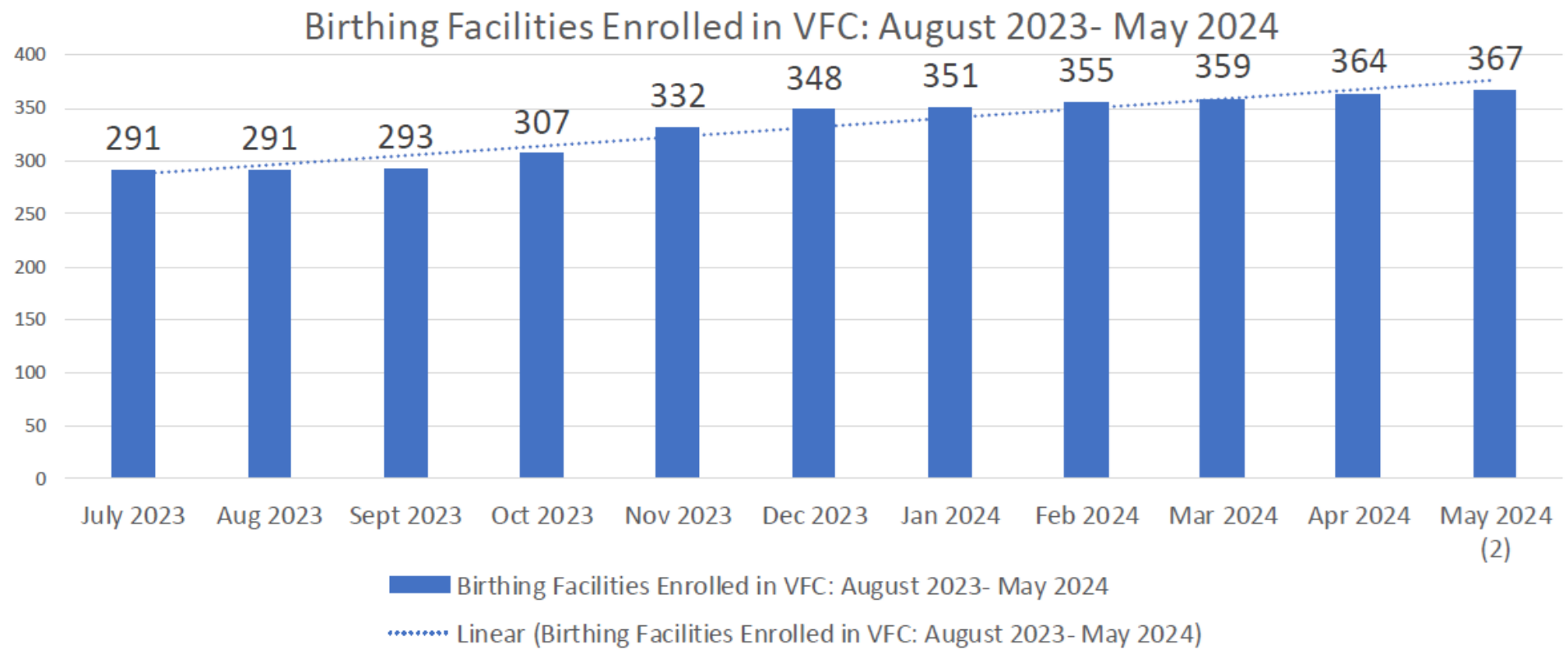
Birthing Hospital Enrollment into VFC: Strategy



(1) These newly enrolled provider counts include 7 providers who were previously enrolled in the VFC program.
(2) Data for May 2024 is through May 8, 2024.

Looking forward

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View from Massachusetts: General

- Ordering of RSV products will open in the MIIS on September 3:
  - Beyfortus 50 mg
  - Beyfortus 100 mg
  - Abrysvo
- Massachusetts is on allocation from the CDC for all RSV products this respiratory season.
  - Due to allocation constraints, sites will NOT be able to order their full season need at the **opening** of MIIS ordering.
  - Sites will be able to receive **all doses** necessary throughout the duration of respiratory season.
  - It is best practice for sites to **order monthly in smaller increments** rather in sporadic large orders.

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View from Massachusetts: Abrysvo

- Abrysvo orders will be capped at 20 doses per order to begin the respiratory season
- Order small increments REGULARLY to keep your supply going
- Use the Updated Adult Availability tables on the Vaccine Management website.
- State- supplied ABRYSVO is only available to pregnant 18-year-olds. Commercial supplied ABRYSVO is ordered independently for other pregnant individuals.
- State-supplied Beyfortus is available universally for all eligible infants.

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View from Massachusetts: Nirsevimab/Beyfortus

- Practice sites that have Beyfortus doses still inventory from last season should use those dose first before replenishing stock with newly ordered additional doses.
- Beyfortus 50 mg doses will be prioritized to enrolled Birthing Hospitals and additional dose distribution will be considered when the autumn supply allocation is clear.
- Beyfortus 100 mg dose orders will be capped at 50 doses per order to begin the respiratory season.
- State-supplied Beyfortus is available universally for all eligible infants and the defined high-risk toddlers.

What do we need to do?

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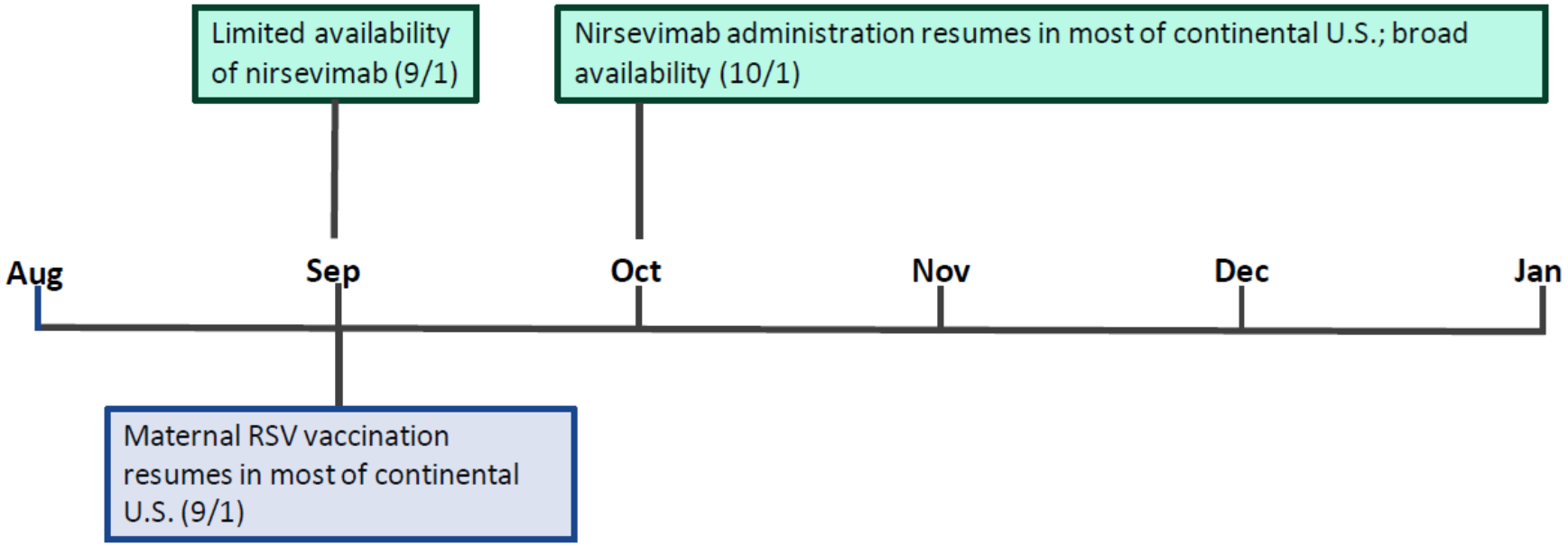
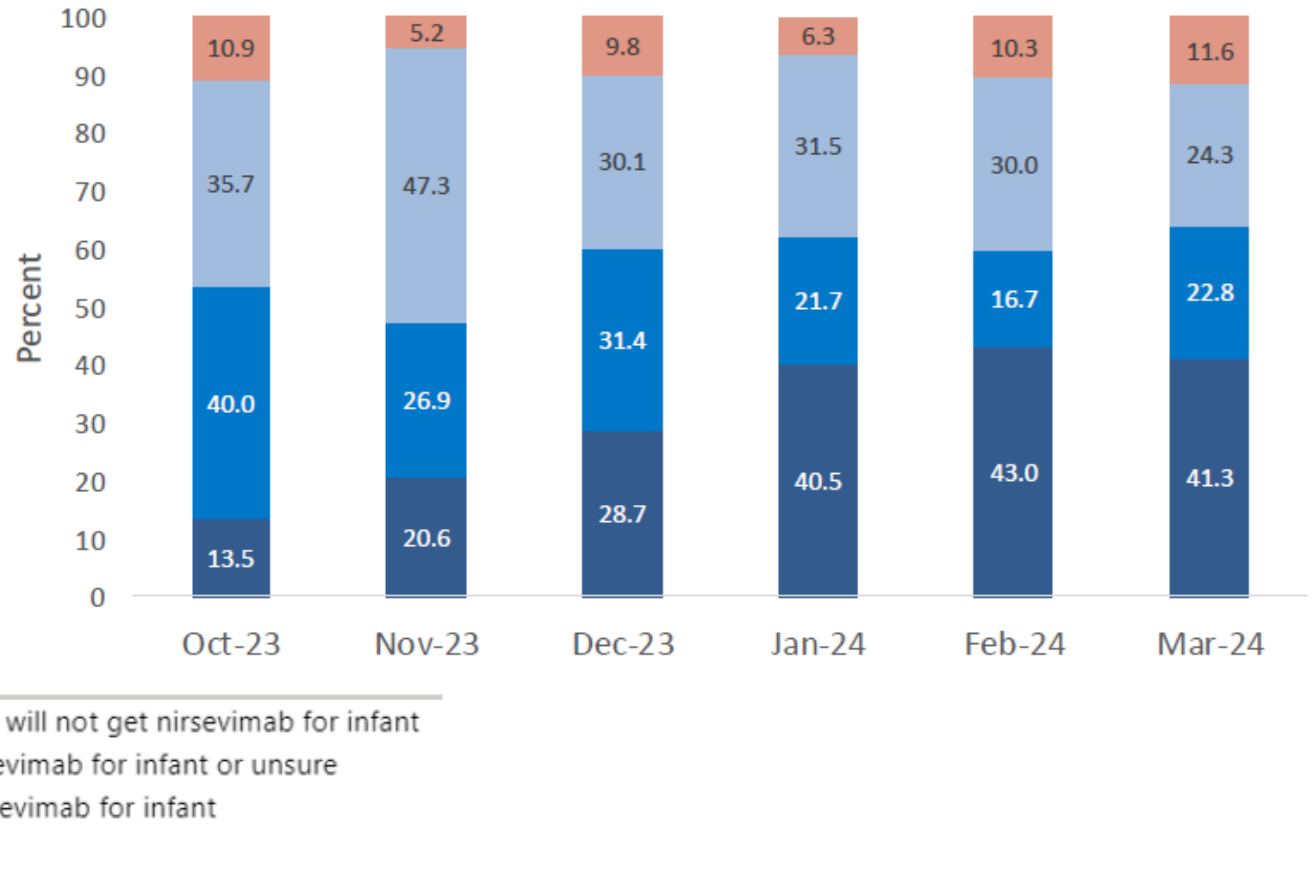
Prospective 2024 RSV immunization timeline



Monthly nirsevimab receipt and intent among women ages 18–49 years who have an infant <8 months, National Immunization Survey-Adult COVID Module (NIS-ACM)



Data source: https://www.cdc.gov/vaccines/imz-managers/coverage/rsvvaxview/nirsevimab-coverage.html

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Take Home Messages on Infant RSV Immunization

- Offer parents both options with shared decision-making. Some parents will prefer maternal vaccine, and some will prefer infant immunization. Keep the offer open throughout the eligible period of infancy to those parents who were previously hesitant.
- Documentation of this vaccine is especially critical because most infants will not need to be immunized with nirsevimab if they are already protected by prenatal vaccination at least 14 days before delivery. Clinicians are urged to clearly document receipt of RSV vaccination in the medical record and the Massachusetts Immunization Information System (IIS).
- Nirsevimab (Beyfortus) can be given concomitantly with childhood vaccines.
- Real-world effectiveness studies have been reassuring despite the first season shortage.

Healthy or With Underlying Conditions

Full Term or Preterm

During or Entering the RSV Season*

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Nirsevimab and Infant RSV Immunization Resources

How Nirsevimab works (American Society for Microbiology): https://youtu.be/f7isAsM2ydI?si=NdyRAWUOy292NtRH

To read the August 25, 2023, edition of the MMWR regarding infant RSV prevention. https://www.cdc.gov/mmwr/volumes/72/wr/pdfs/mm7234a4-H.pdf

Information about the Universal Vaccine Purchasing Program and the Massachusetts Vaccine Purchase Trust Fund: https://malegislature.gov/Laws/GeneralLaws/PartI/TitleXVI/Chapter111/Section24N#:~:text=The%20council%20shall%20recommend%20the,as%20determined%20by%20the%20council.

CDC Page on RSV Prevention (updated frequently): https://www.cdc.gov/vaccines/vpd/rsv/index.html

CDC's Nirsevimab "Immunization Information Sheet" can be found at: https://www.cdc.gov/vaccines/vpd/rsv/downloads/Immunization-Information-Statement.pdf

Red Book RSV https://publications.aap.org/redbook/book/755/chapter/14080939/Respiratory-Syncytial-Virus?searchresult=1

AAP: All you want to know about Nirsevimab and medically attended RSV disease prevention (updated very frequently) :https://www.aap.org/en/patient-care/respiratory-syncytial-virus-rsv-prevention/

AAP: Nirsevimab Readiness Practice Checklist includes coding/billing, ordering, office workflows, and messaging to families and the community. *Invaluable* https://downloads.aap.org/AAP/PDF/Nirsevimab_Readiness_Practice_Checklist_FINAL.pdf

AAP: Nirsevimab Implementation Guide includes recall processes, scheduling in vaccine clinics and well child visits, documentation, eligibility and scheduling, inventory management and more: https://downloads.aap.org/AAP/PDF/Nirsevimab_Implementation_Guide_FINAL.pdf

RSV Prevention Resource Packet on MCAAP Website: https://mcaap.org/2022/wp-content/uploads/MCAAP-Nirsevimab-Resource-Packet-October-26-23.pdf

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Thank you!

Please feel free to contact the Massachusetts Chapter of the AAP Executive Director Cathleen Haggerty at chaggerty@mcaap.org with any additional questions so she can get your question answered by one of our pediatrician leaders.