

RSV : ARE CHANGES IN THE AIR?

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DISCLOSURES:

Viracor- Research non-monetary grant support

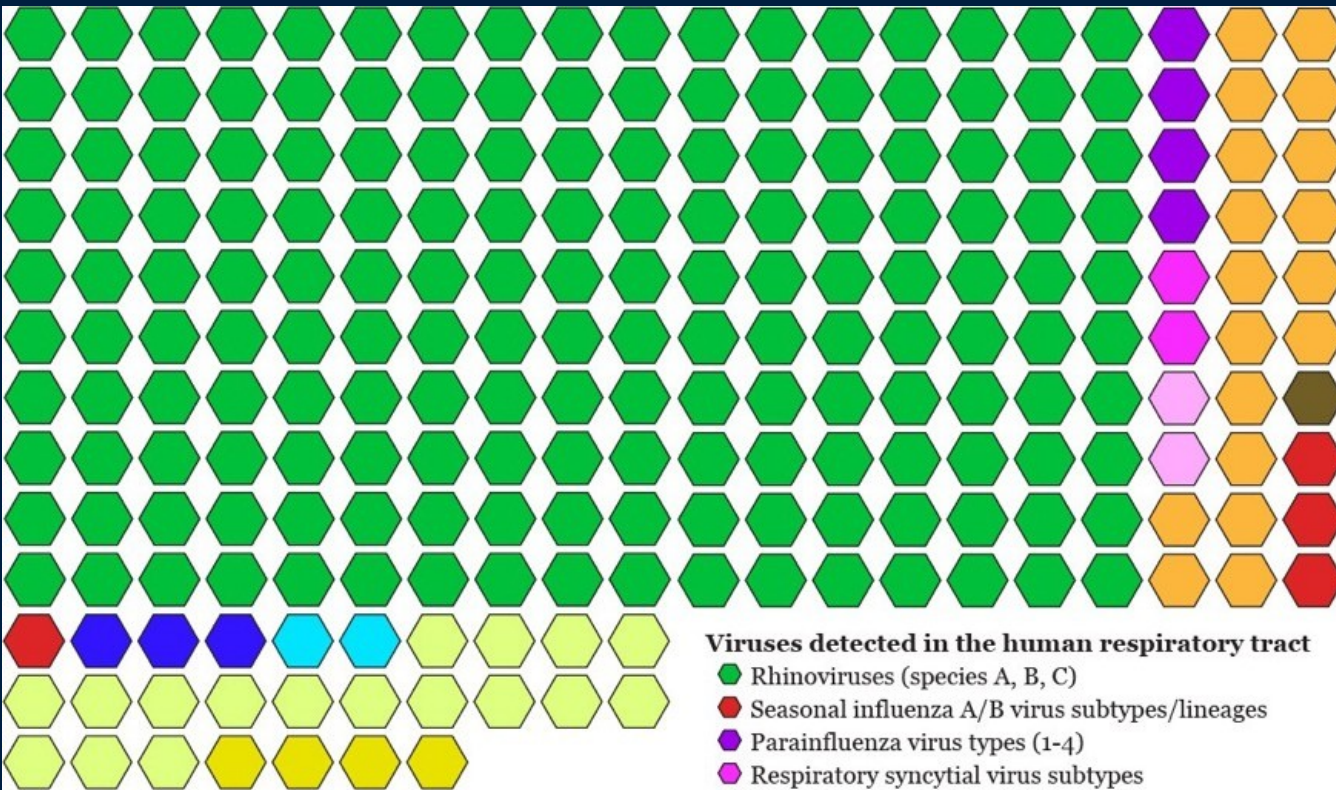
Merck Sharpe Dohme- Research support to institution



Outline

- Respiratory Syncytial Virus
 - The virus and disease
- Pandemic influence on changing patterns
- Mitigation strategies for RSV
 - Maternal immunization
 - Monoclonal antibody for infant





n=227

Viruses detected in the human respiratory tract

- Rhinoviruses (species A, B, C)
- Seasonal influenza A/B virus subtypes/lineages
- Parainfluenza virus types (1-4)
- Respiratory syncytial virus subtypes
- Metapneumovirus subtypes
- Adenoviruses (species B, C, E)
- Human coronaviruses
- Bocavirus 1
- Parechoviruses (types 1, 3, 6)
- Saffold cardioviruses
- Respiratory enteroviruses (species A, B, C, D)

>200
respiratory
viruses

← Tweet



Ian M. Mackay, PhD (he/him)
@MackayIM



RSV number one in children

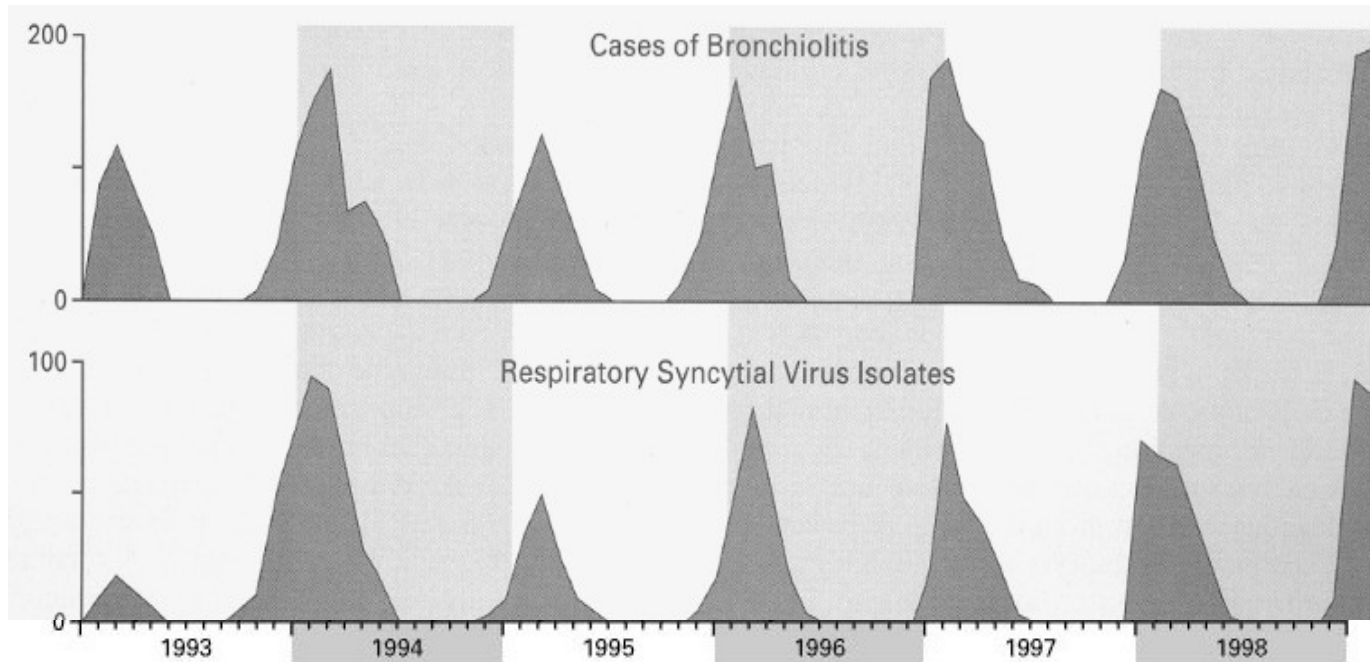
- Leading cause of lung infection in infants and children worldwide
- > 3 million hospitalizations
- ~60,000 deaths worldwide in children < 5 years of age

Shi et al, *Lancet* 2017

Mazur et al, *Lancet ID* 2022

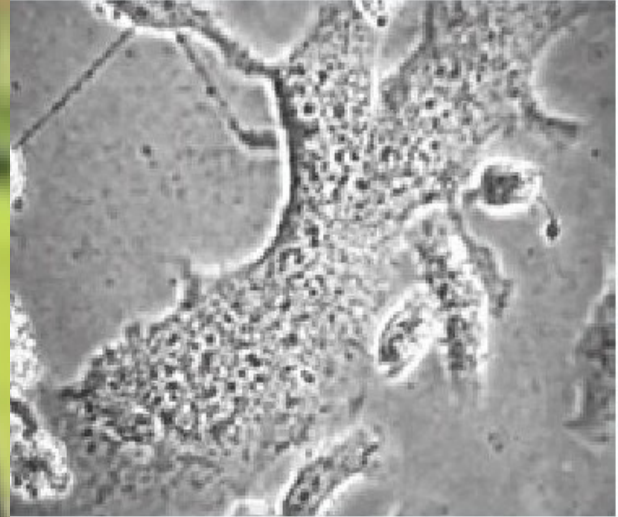
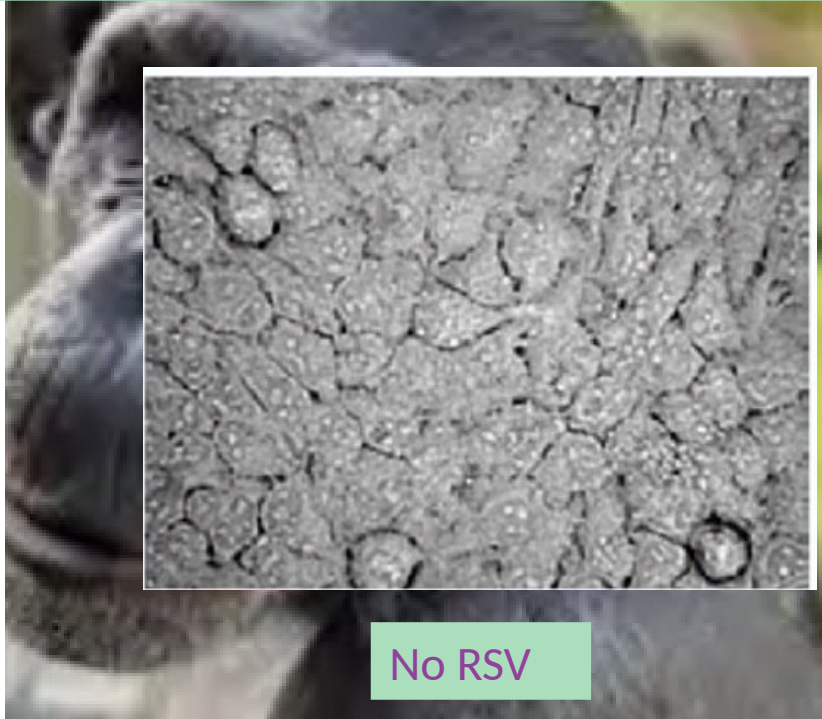


Bronchiolitis Mirrors RSV Season



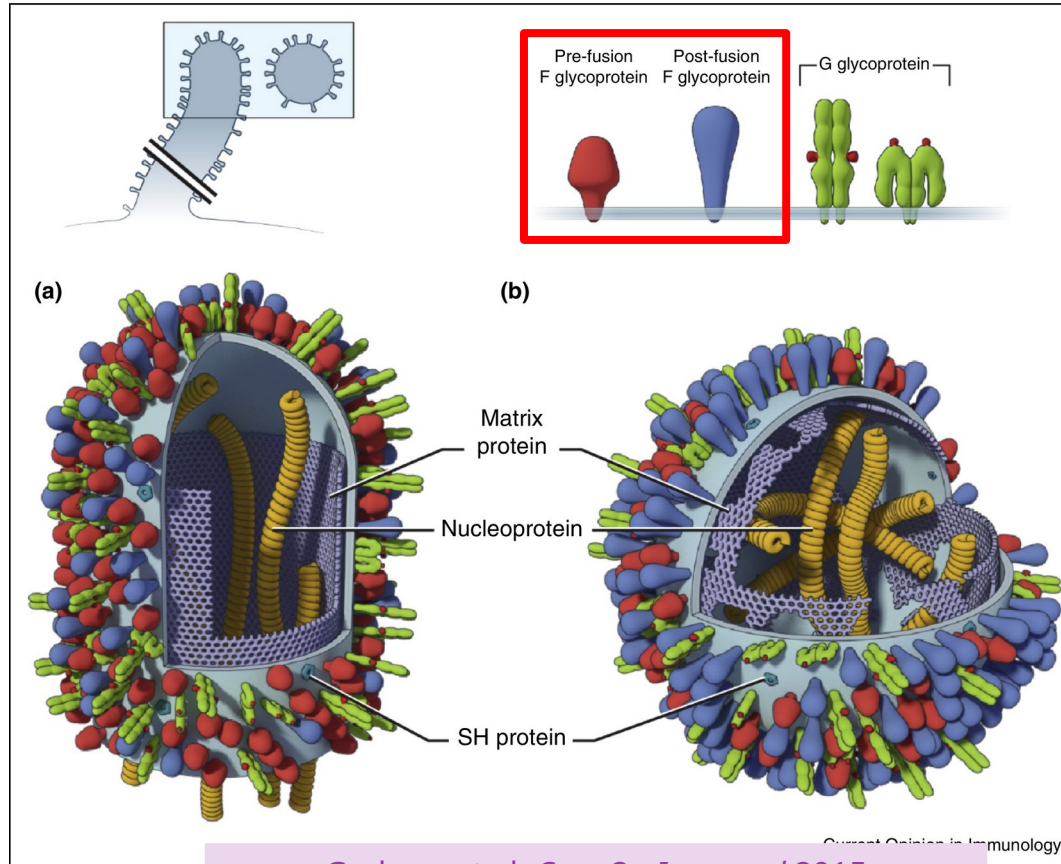
Hall CB, *New Engl J Med* 2001

Respiratory Syncytial Virus RSV



Bitko V et al BMC Microbiology 2003

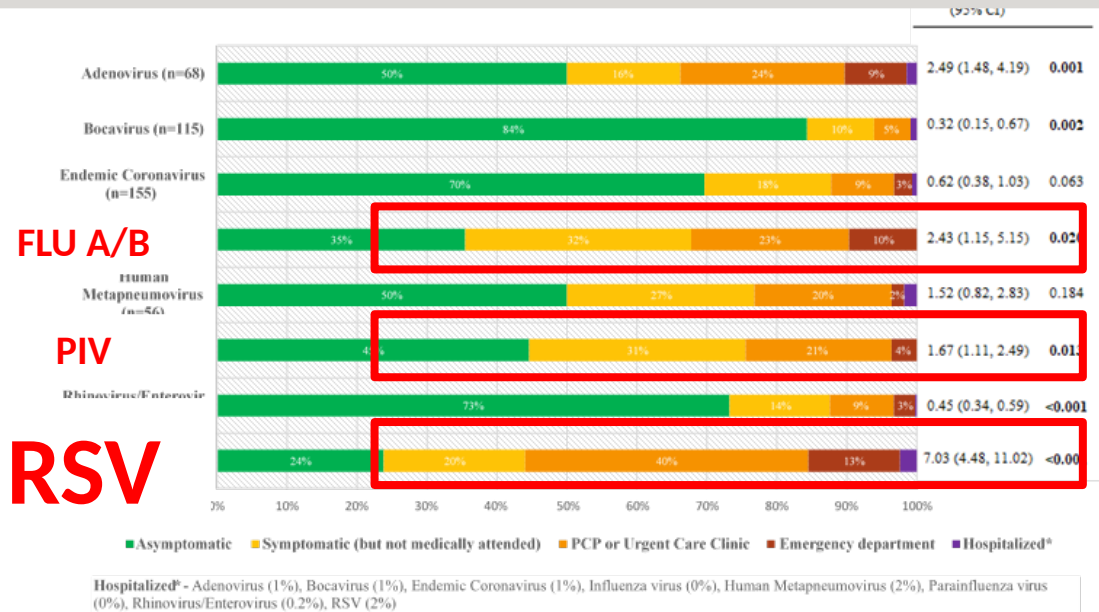
RSV enveloped with negative-sense ssRNA genome



Prevail: Longitudinal Birth Cohort - 2 years

Teoh Z et al CID; 77: 2023

- CDC sponsored Cincinnati study
- 245 Mother-Infant dyads followed longitudinally; >13,700 nasal swabs
- RESULTS: 9.4 respiratory viral infections / child / year
 - Most asymptomatic (green bar)



RSV Immunity:

Reinfection frequent

- Short incubation period
- Nasal IgA incomplete protection and wanes
- Lack of viremia
- Antigenic drift – variants

RSV epidemiology Pre-COVID-19

- ~70-75% of infants infected by 12 months
- Virtually everyone by 2 years *worldwide*
 - ~2% of healthy infants hospitalized
- Transmitted by respiratory droplets (direct contact) and environmental surfaces (indirect contact)
 - 6 hours on hard surfaces; 20-30 min hands
- High attack rate in contacts: family, daycare, *hospital*, etc.

Hall CB et al JID 1980

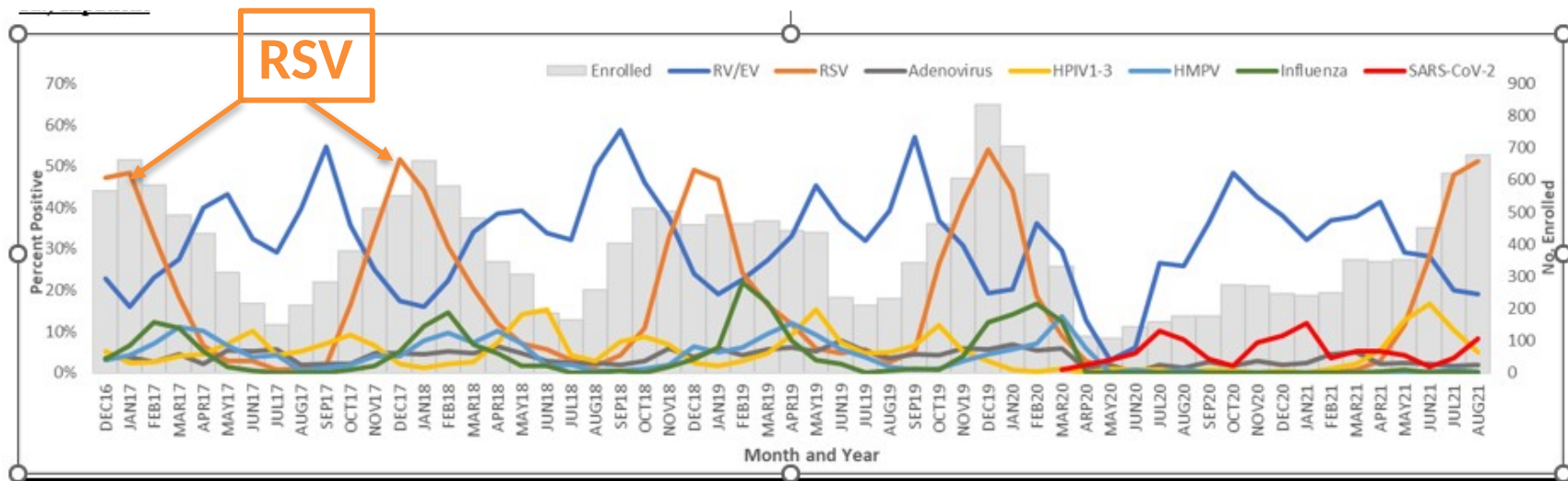


New Vaccine Surveillance Network (NVSN)



Pittsburgh
joined 2016

Respiratory Virus Surveillance Children with ARI- NVSN United States 2016-2021



Perez A et al MMWR/ 71 (40) Oct 7, 2024



NVSN Pediatric Acute Respiratory Illness

Last Updated: 08/05/2024 | Data Presented Through: 09/29/2018

Pathogen

Season

Age

[Return to home page](#)

Viral Detections by Pathogen and Season Among Enrolled Children



Filters

Pathogen

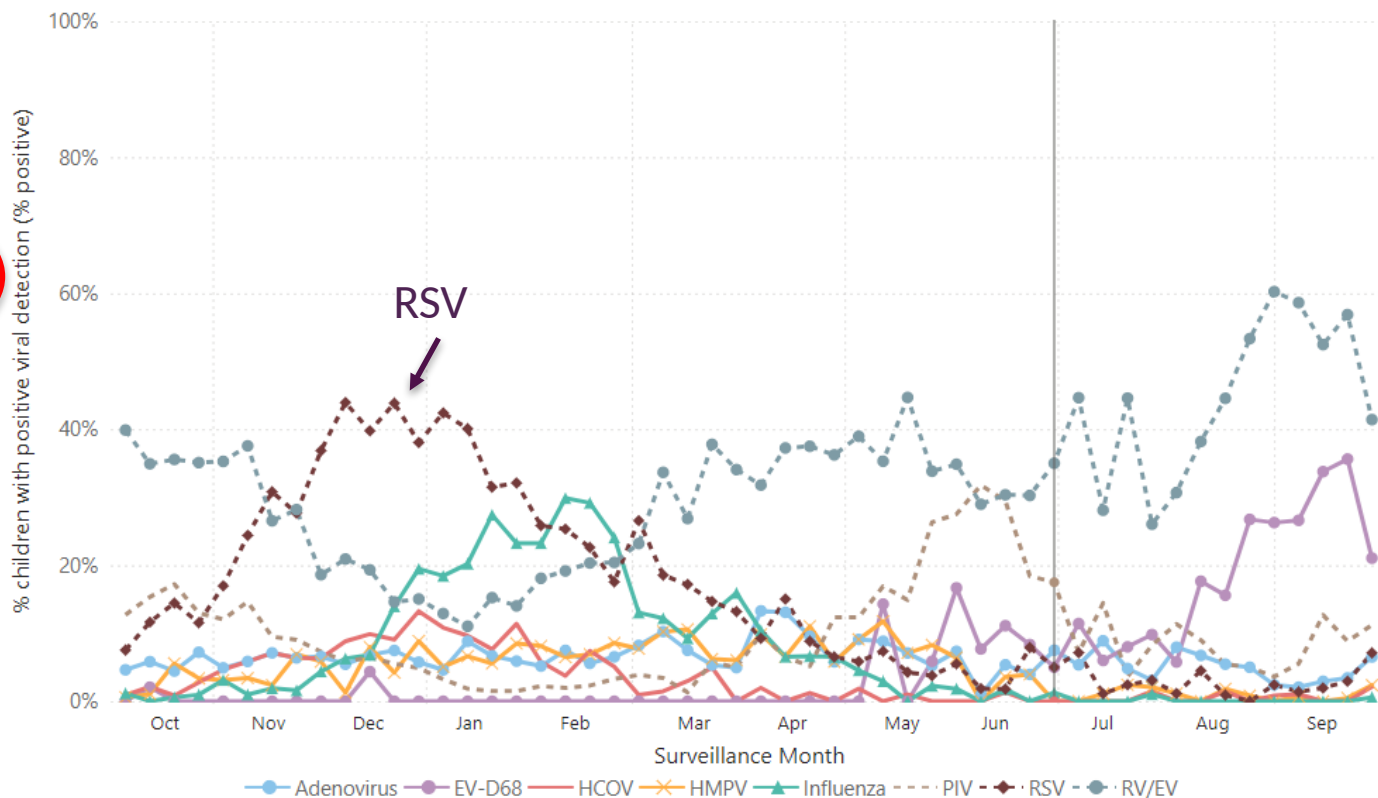
All

Season

2017-2018

Reset Filters

Download Data





NVSN Pediatric Acute Respiratory Illness

Last Updated: 11/05/2024 | Data Presented Through: 10/19/2024

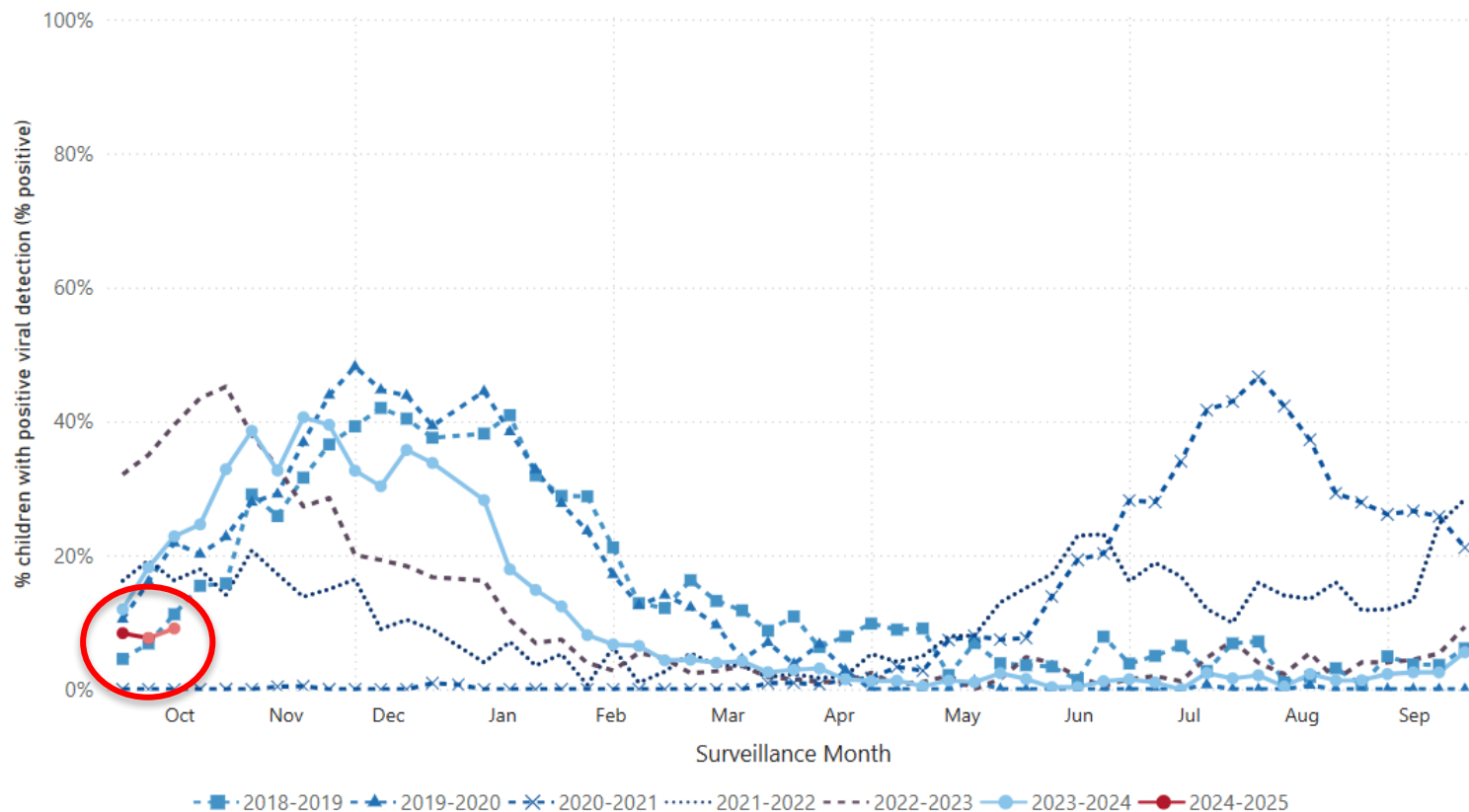
Pathogen

Season

Age

[Return to home page](#)

Viral Detections by Pathogen and Season Among Enrolled Children



Filters

Pathogen

RSV



Season

All



Reset Filters

Download Data



NVSN Pediatric Acute Respiratory Illness

Last Updated: 11/05/2024 | Data Presented Through: 09/28/2024

Pathogen

Season

Age

[Return to home page](#)

Filters

Pathogen

Multiple selections

Season

2023-2024

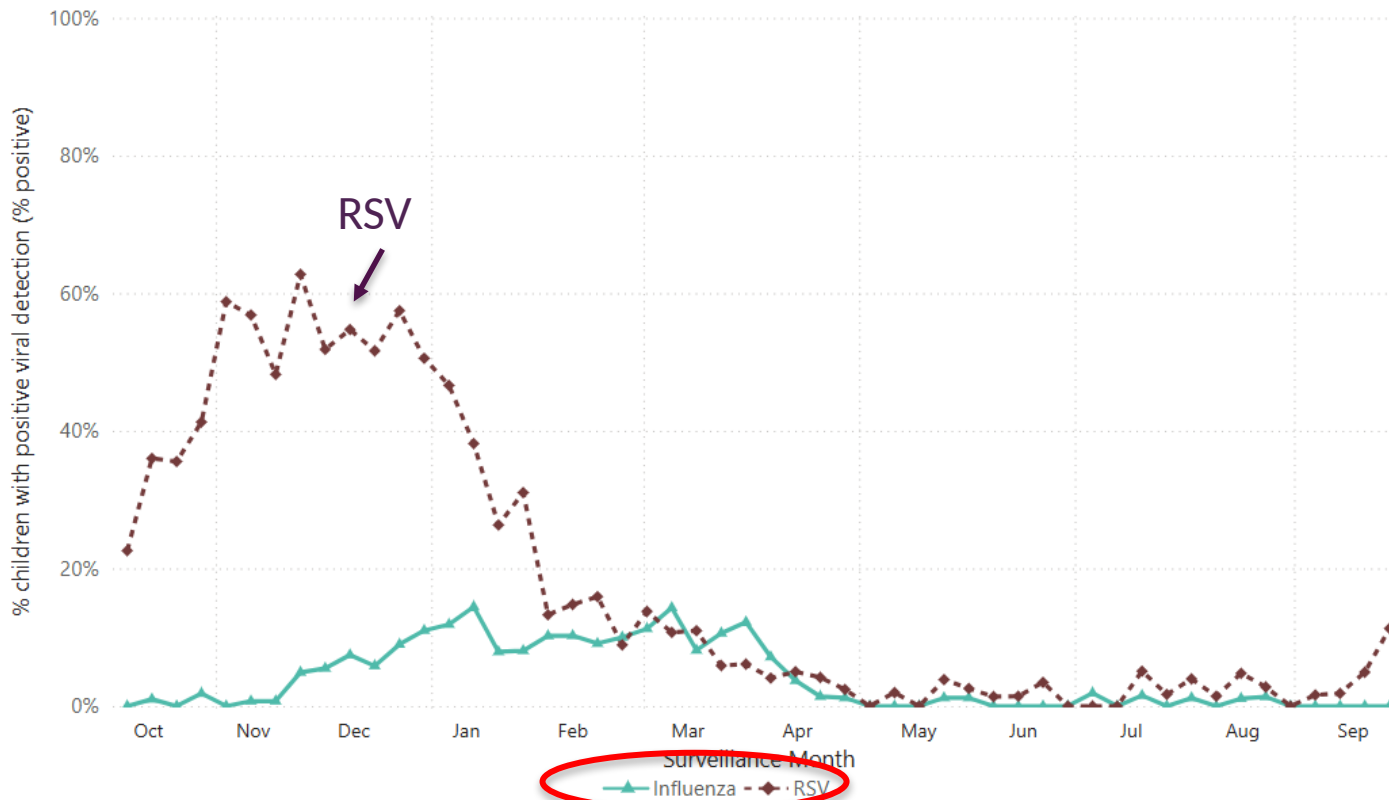
Age

0-11 months

Reset Filters

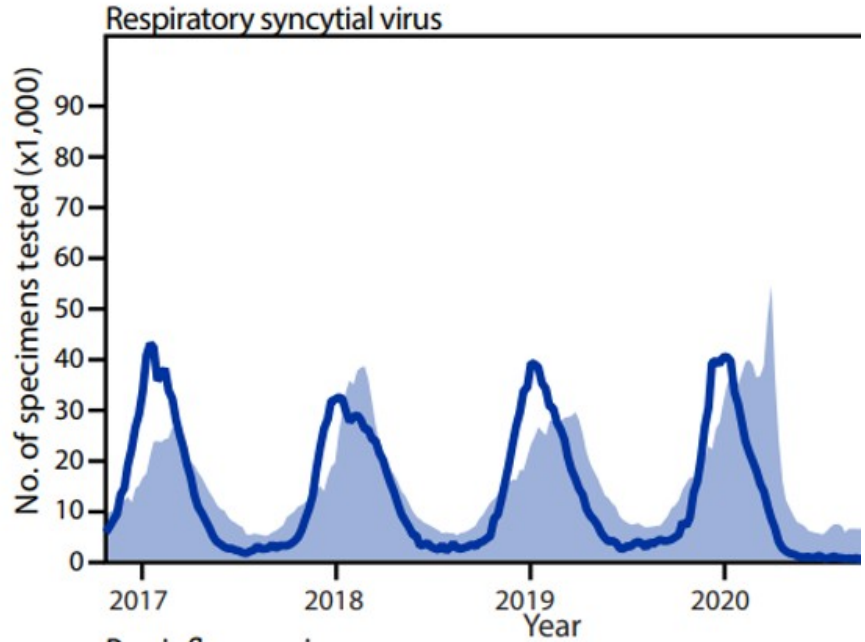
Download Data

Viral Detections by Pathogen and Season Among Enrolled Children



Paradigm of RSV

- RSV circulates annually
- Everyone infected by age 2 years



Olson SJ et al. NVSN surveillance MMWR 2021

NVSN DATA RSV HOSPITALIZATIONS BY AGE

Curns AT et al *Pediatrics* 2024

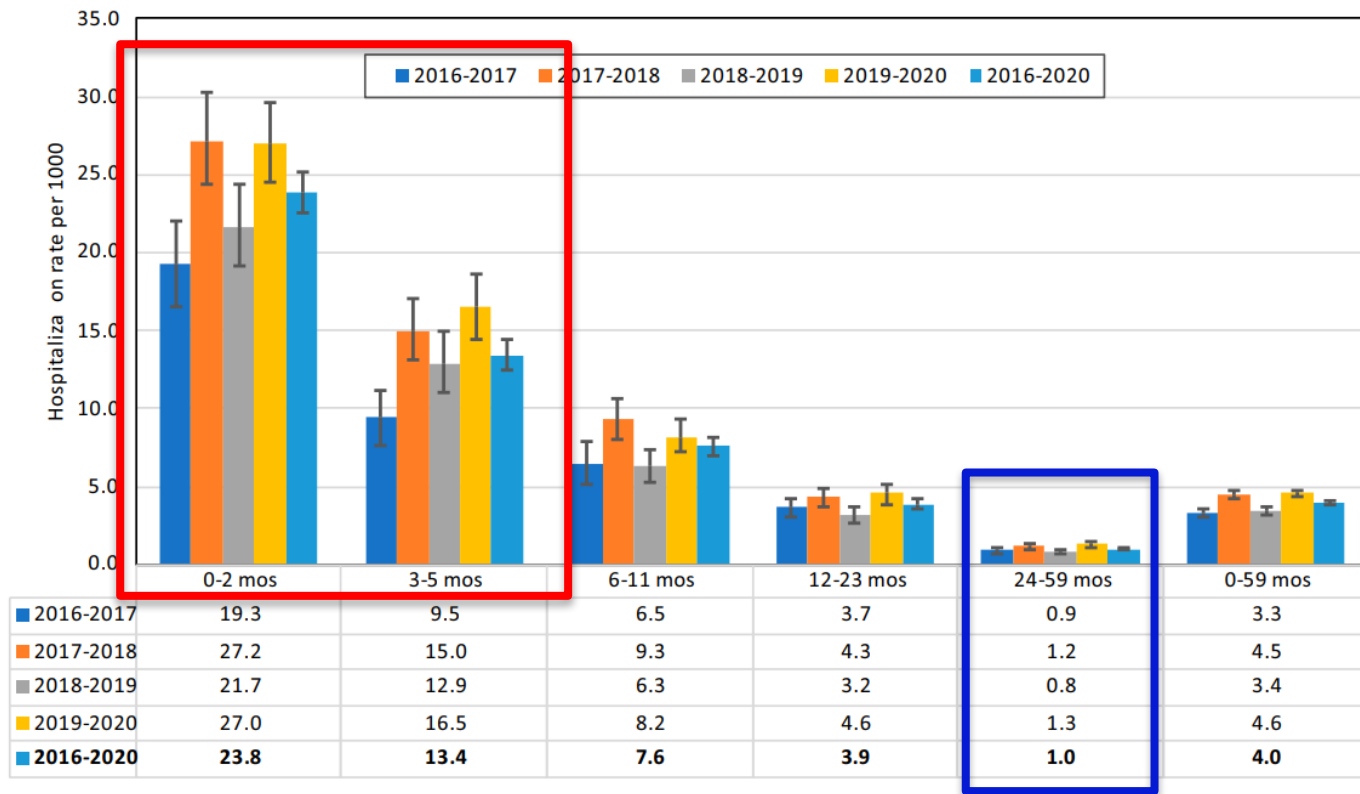


FIGURE 3

RSV-associated hospitalization rate per 1000 children by age group and season among children <5 years old, New Vaccine Surveillance Network, December 2016 through September 2020.



The week that Covid-19 shut the US down – in pictures

The Guardian March 16, 2020

Cities and states across the US, from New York to Washington state, saw empty streets, sporting games cancelled and Disneyland shuttered over the coronavirus pandemic

● [Coronavirus - latest updates](#)



1.

Limit sneezing
& coughing



Into your
elbow



Into a
tissue

PROPER COUGH & SNEEZE ETIQUETTE

AST Power2Save
ONE TRANSPLANT FOR LIFE

2.

Dispose of
tissues



Directly
into
a trashcan

3.

Wash your hands



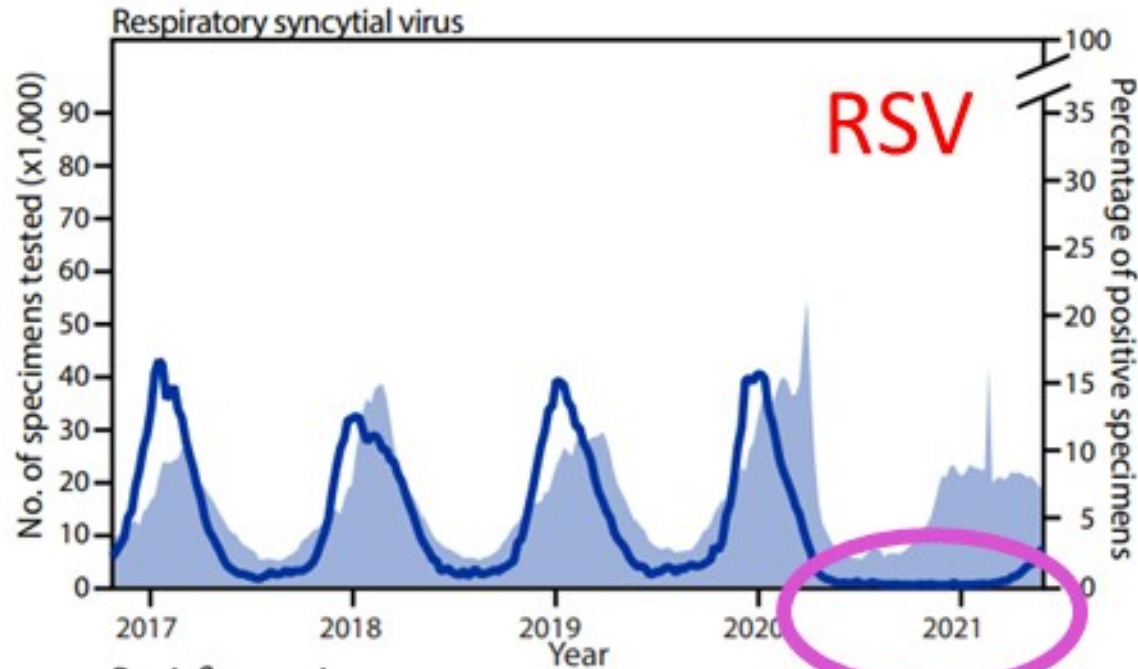
At least 20
seconds



Feb. 27, 2020: Coronavirus scare prompts a
school to shut down

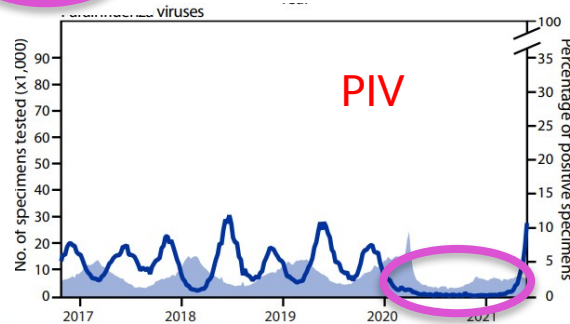
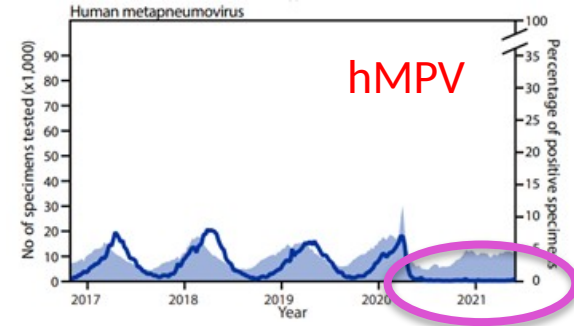
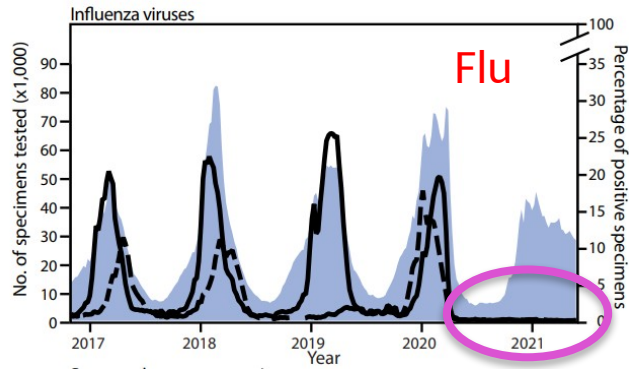


Something happened to RSV during COVID-19 pandemic



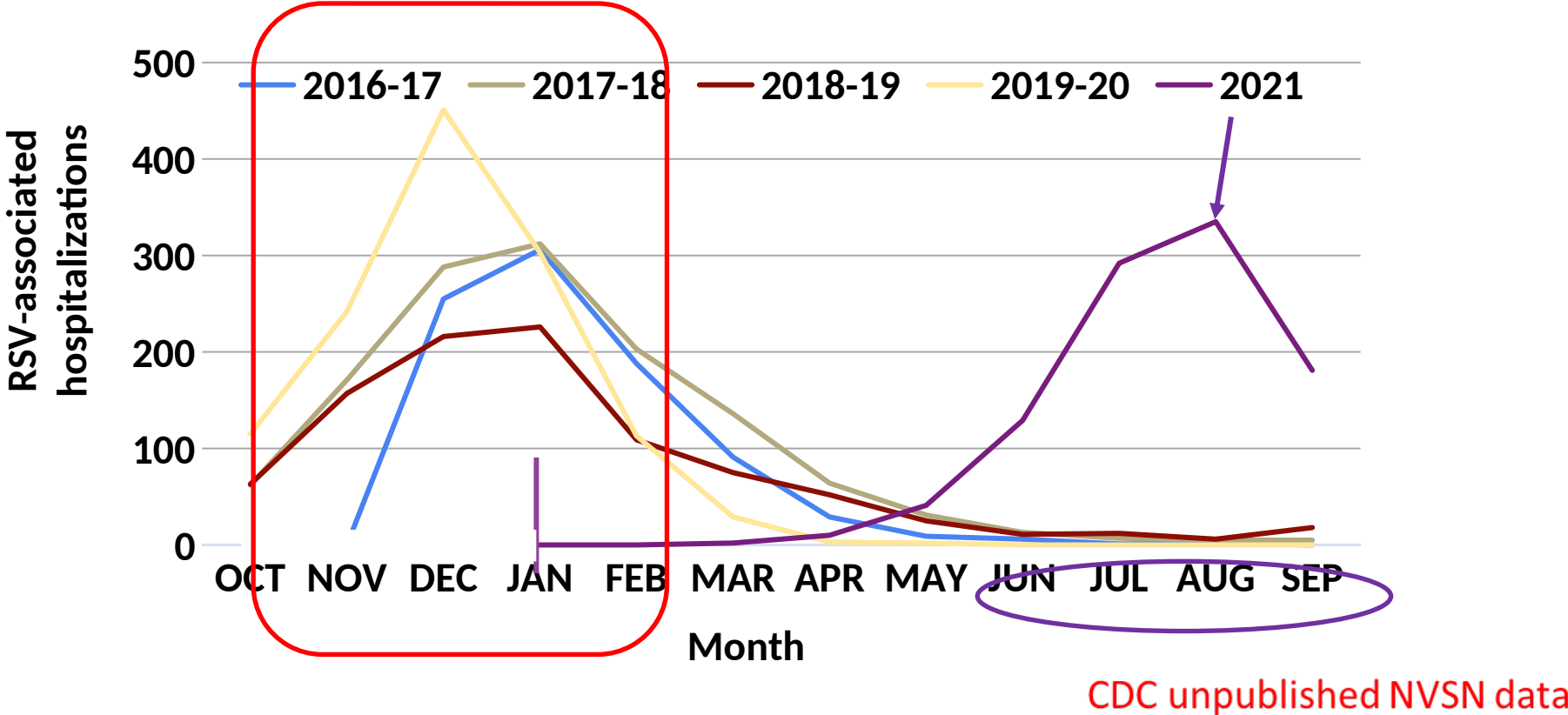
Olson SJ et al.
NVSN
surveillance
MMWR 2021

Something happened to All Respiratory Viruses during COVID-19 pandemic



Olson SJ et al. NVSN
surveillance MMWR 2021

Figure 1. RSV-associated hospitalizations in children aged <5 years by month, New Vaccine Surveillance Network, 2016 - 2021



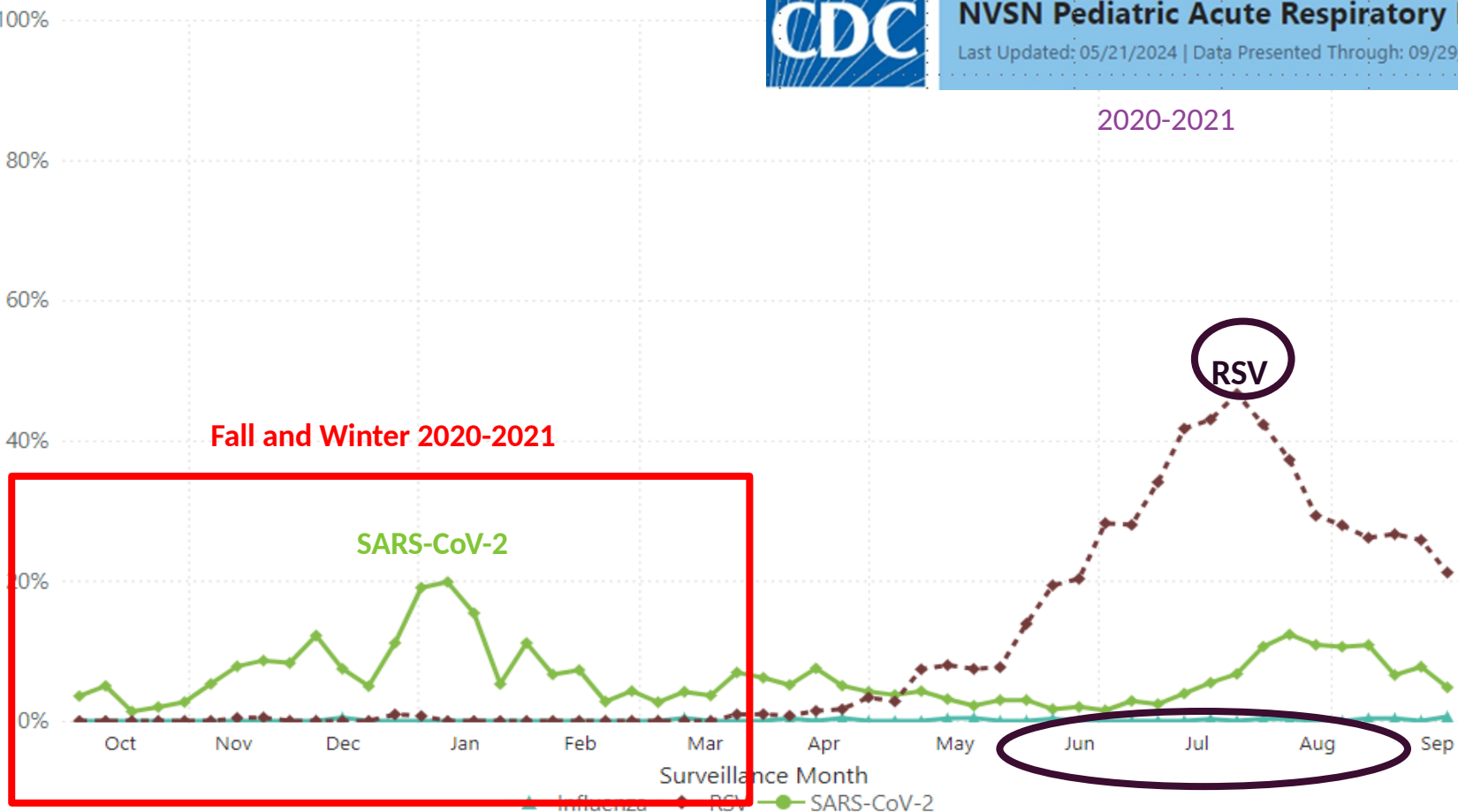
Viral Detections by Pathogen and Season Among Enrolled Children



NVSN Pediatric Acute Respiratory Illness

Last Updated: 05/21/2024 | Data Presented Through: 09/29/2018

% children with positive viral detection (% positive)



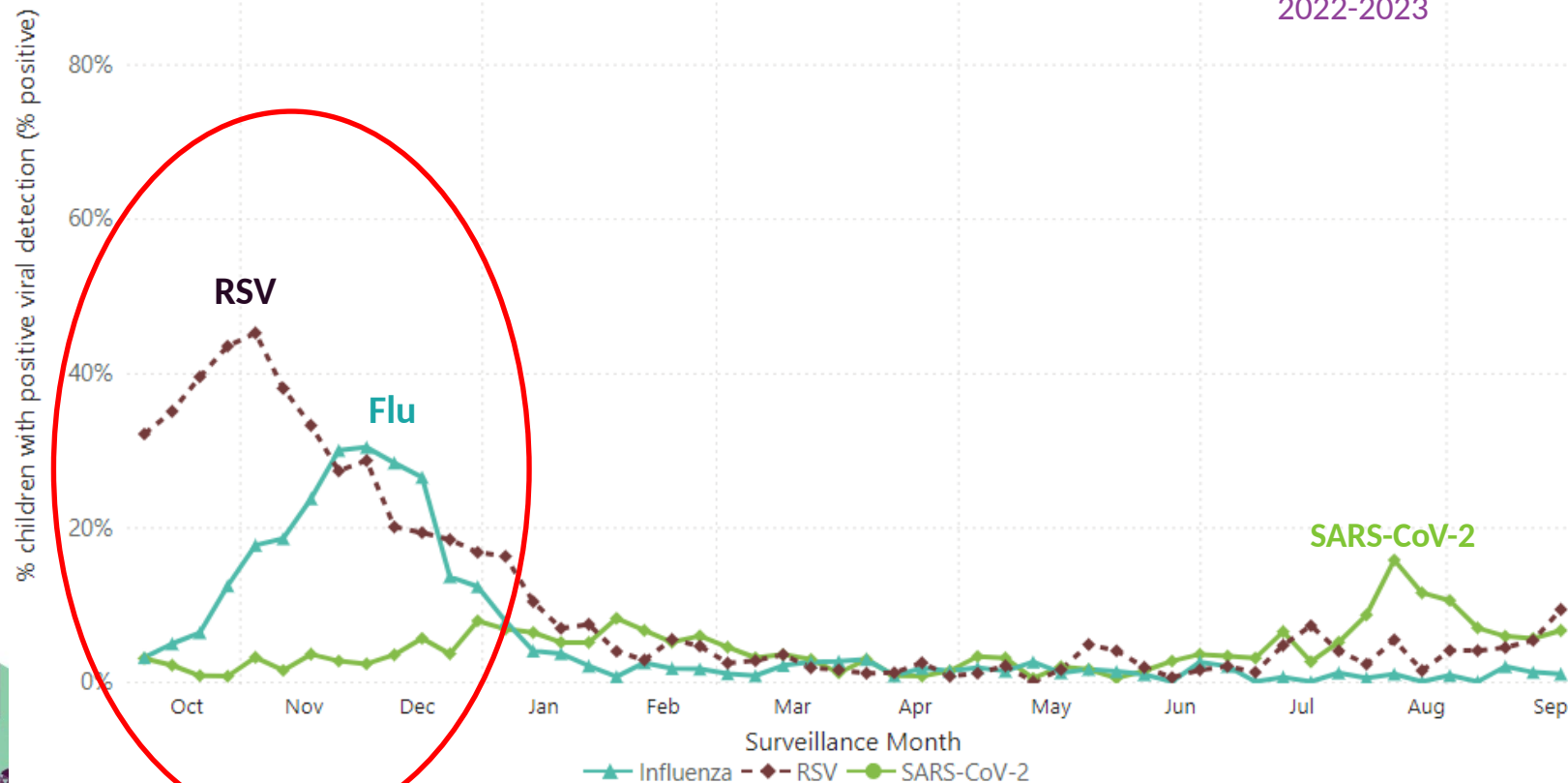
Viral Detections by Pathogen and Season Among Enrolled Children



NVSN Pediatric Acute Respiratory Illness

Last Updated: 05/21/2024 | Data Presented Through: 09/29/2018

2022-2023



RSV in 2022: older age hospitalized and in ICU

Figure. Ages of Children Hospitalized Due to Respiratory Syncytial Virus (RSV) Infection

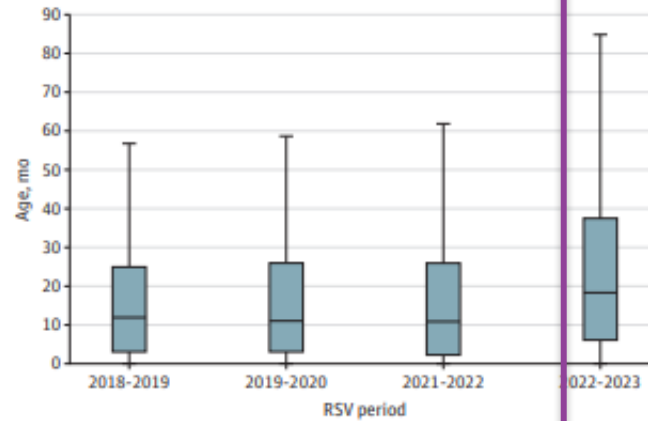


Table. Comparison of Length of Hospital Stay and Intensive Care Unit (ICU) Admission Among Pediatric Hospitalizations Associated With Respiratory Syncytial Virus (RSV) in Colorado During the 2021-2022 and 2022-2023 Periods

	2021-2022 (n = 748)	2022-2023 (n = 637) ^a	P value
Hospital length of stay, median (IQR), d	3.0 (2.0-4.5)	3.8 (2.7-5.5)	<.001
ICU admission, No. (%)	203 (27.1%)	229 (36.0%)	<.001
Age distribution among children admitted to the ICU, % ^b			
0-5 mo	35.3	41.7	<.001
6-11 mo	33.6	33.7	
12-23 mo	20.7	43.0	
24 mo-4 y	21.1	31.1	
5-11 y	10.3	28.3	
12-17 y	16.7	0	

Changed RSV Epidemiology and Seasonality

- Long held beliefs had to be re-examined
- Only infants at risk due to airway size– **WRONG**
- Older infants /children not at risk for severe disease– **WRONG**
- Temperate climates have RSV only in the winter/spring – **WRONG**



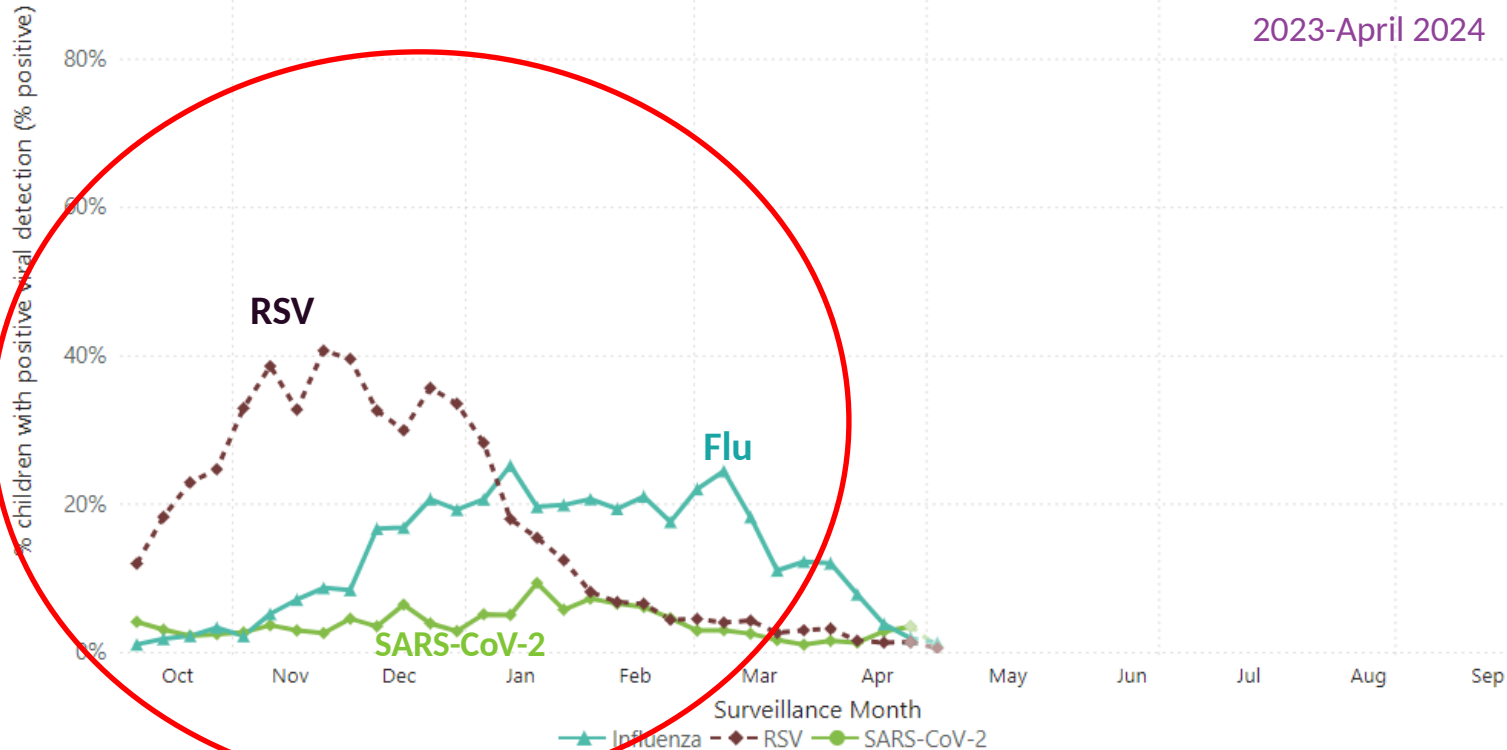
Viral Detections by Pathogen and Season Among Enrolled Children



NVSN Pediatric Acute Respiratory Illness

Last Updated: 05/21/2024 | Data Presented Through: 09/29/2018

2023-April 2024





Original Investigation | Infectious Diseases

Infants Admitted to US Intensive Care Units for RSV Infection During the 2022 Seasonal Peak

Natasha Halasa, MD, MPH; Laura D. Zambrano, PhD, MPH; Justin Z. Amarin, MD; Laura S. Stewart, PhD; Margaret M. Newhams, MPH; Emily R. Levy, MD; Steven L. Shein, MD; Christopher L. Carroll, MD, MS; Julie C. Fitzgerald, MD, PhD, MSCE; Marian G. Michaels, MD, MPH; Katherine Blin, MD; Melissa L. Cullimore, MD, PhD; et al

- 39 PICU in US during 2022 RSV Surge:
 - Cross sectional study 600 infants < 12 months with RSV
 - Evaluate clinical parameters and outcome

Infants in ICU with the 2022 Surge

Table 1. Demographic and Clinical Characteristics of Infants Admitted to the Intensive Care or High Acuity Unit With Respiratory Syncytial Virus Infection

Characteristic	Infants, No. (%)			P value ^a
	All (N = 600)	Nonintubated (n = 457)	Intubated (n = 143)	
Age, median (IQR), mo	2.6 (1.4-6.0)	3.1 (1.6-6.4)	1.9 (1.0-3.2)	<.001
Age group				
0-2 mos	323 (53.8)	221 (48.6)	101 (70.6)	<.001
3-5 mos	127 (21.2)	106 (23.2)	21 (14.7)	
6-11 mos	150 (25.0)	129 (28.2)	21 (14.7)	
Underlying conditions				
None	487 (81.2)	364 (79.6)	123 (86.0)	.07
At least one	113 (18.8)	93 (20.4)	20 (14.0)	

Infants in ICU with the 2022 Surge

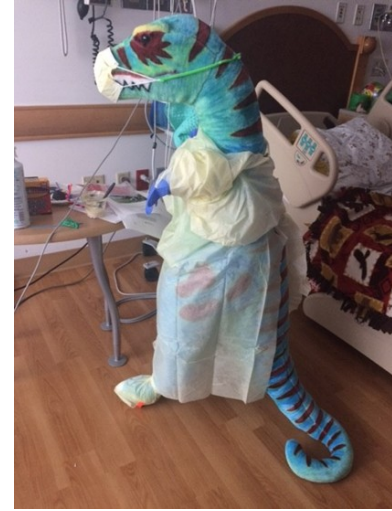
CONCLUSIONS AND RELEVANCE In this cross-sectional study, most US infants who required intensive care for RSV LRTIs were young, healthy, and born at term. These findings highlight the need for RSV preventive interventions targeting all infants to reduce the burden of severe RSV illness.

JAMA Network Open. 2023;6(8):e2328950. doi:[10.1001/jamanetworkopen.2023.28950](https://doi.org/10.1001/jamanetworkopen.2023.28950)



Mitigation Strategies

- Shut down the world again and isolate everyone
- OR.....
- Prevention strategies
 - Monoclonal antibody for infants
 - Immunize: pregnant women



RESPIRATORY SYNCYTIAL VIRUS DISEASE IN INFANTS DESPITE PRIOR ADMINISTRATION OF ANTIGENIC INACTIVATED VACCINE

[Get access >](#)

HYUN WHA KIM, JOSE G. CANCHOLA, CARL D. BRANDT, GLORIA PYLES, ROBERT M. CHANOCK,
KEITH JENSEN, ROBERT H. PARROTT ✉

American Journal of Epidemiology, Volume 89, Issue 4, April 1969, Pages 422–434,

- 1960's formalin inactivated RSV Vaccine
- Immunized children exposed to wild type virus had worse disease
- 80% hospitalization rate and 2 deaths



Injected RSV immunoglobulin

- RSV-IGIV prevented serious disease in high-risk babies demonstrated proof of principle that immunoprophylaxis could work
- Led to development of Palivizumab
 - Approved in 1998
 - Humanized mouse monoclonal
 - Required monthly shots
 - \$\$\$\$
 - Used for high risk preemies, ♂disease, IC



Nirsevimab

- Most ICU were previously healthy FT infants
- Optimized from a **human** F mAb D25
- More potent than palivizumab in cells and cotton rats
- Has M252Y/S254T/T256E (YTE) mutations in Fc region

— Increases affinity for FcγR receptor

— Prolongs half-life to months

Zhu Sci Trans Med

2017

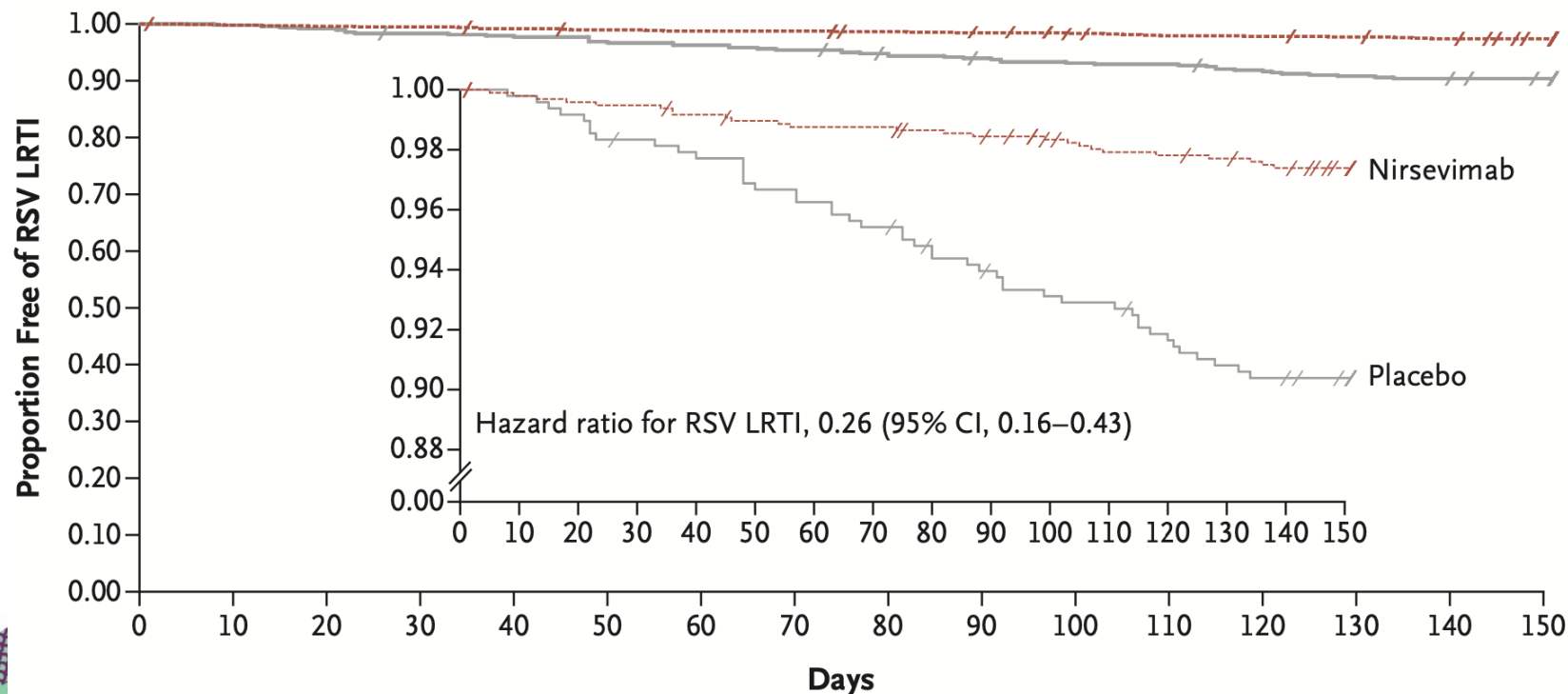
Nirsevimab against RSV LRI in preemies

- 1453 infants 29 wk – 34wk 6d
 - 969 Nirsevimab, 484 placebo
- 164 sites, 23 countries
- Monitored for 150 days through RSV season
 - Every 2 weeks by phone, some in person visits

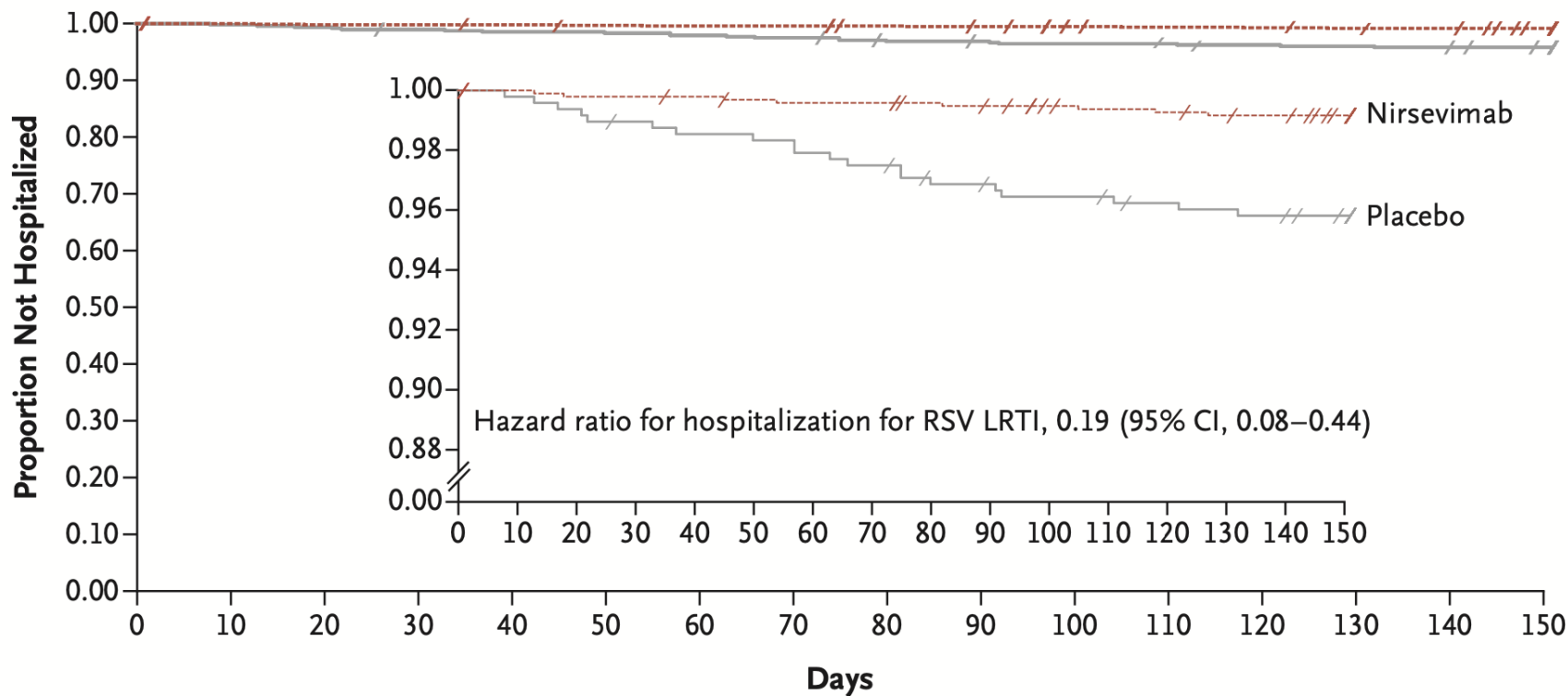
Griffin et al, *NEJM* 2020



Treated infants at reduced risk for medically attended RSV LRI throughout



Treated infants at reduced risk for hospitalized RSV LRI throughout



Nirsevimab against RSV in term infants?

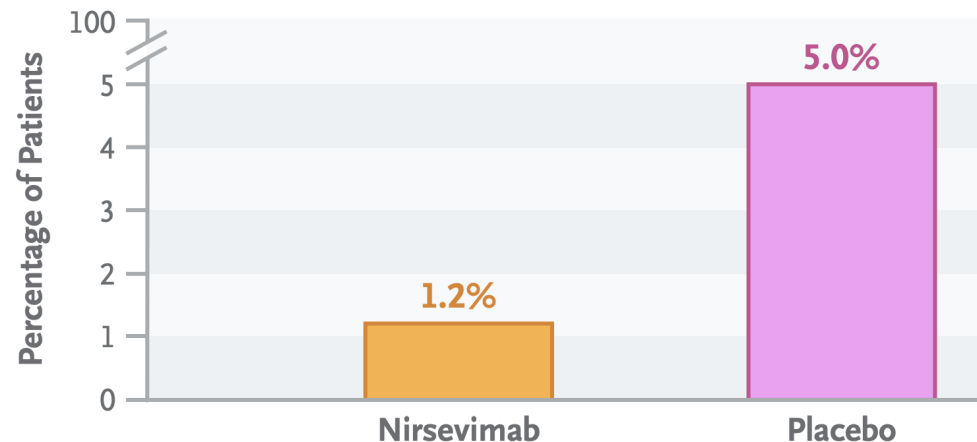
- 1490 infants >35 wks GA
 - 994 Nirsevimab, 496 placebo
- 160 sites, 30 countries
- Monitored for 150 days through RSV season
 - Every 2 weeks by phone, some in person visits

Hammitt et al, *NEJM* 2022

Nirsevimab reduced *medically attended* RSV LRI but not significant for hospitalization

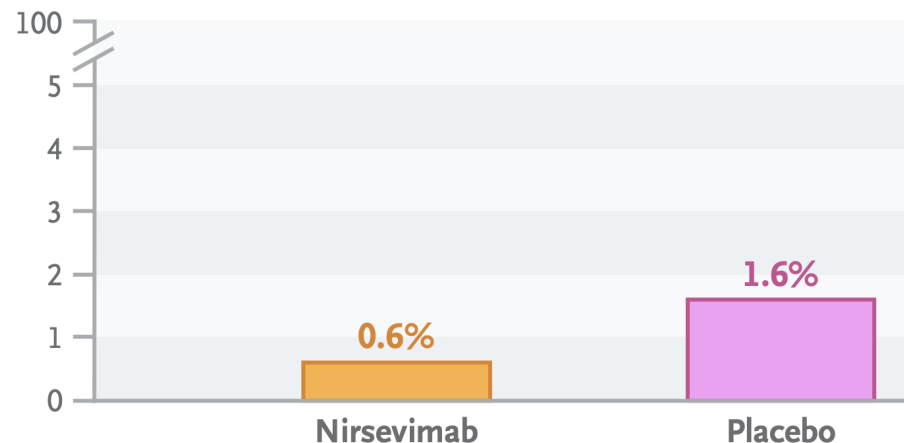
Medically Attended Lower Respiratory Tract Infection
through Day 150

Efficacy, 74.5%; 95% CI, 49.6 to 87.1; $P < 0.001$



Hospitalization for Lower Respiratory Tract Infection
through Day 150

Efficacy, 62.1%; 95% CI, -8.6 to 86.8; $P = 0.07$



Hammitt et al, *NEJM* 2022

Challenges in 2023-2024 season

- Timing is everything:
 - FDA licensed July 17, 2023
 - ACIP met August 3, 2023
 - RSV started Sept 2023
- Limited supply of nirsevimab in the US
 - Especially locally
 - Personal opinion: it is still overpriced
- Despite this nirsevimab appeared to be efficacious

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

Heidi L. Moline, MD¹; Ayzsa Tannis, MPH¹; Ariana P. Toepfer, MPH¹; John V. Williams, MD^{2,3}; Julie A. Boom, MD^{4,5}; Janet A. Englund, MD⁶; Natasha B. Halasa, MD⁷; Mary Allen Staat, MD^{8,9}; Geoffrey A. Weinberg, MD¹⁰; Rangaraj Selvarangan, PhD¹¹; Marian G. Michaels, MD^{2,3}; Leila C. Sahni, PhD^{4,5}; Eileen J. Klein, MD⁶; Laura S. Stewart, PhD⁷; Elizabeth P. Schlaudecker, MD^{8,9}; Peter G. Szilagyi, MD¹⁰; Jennifer E. Schuster, MD¹²; Leah Goldstein, MPH¹; Samar Musa, MPH^{2,3}; Pedro A. Piedra, MD^{4,5}; Danielle M. Zerr, MD⁶; Kristina A. Betters, MD⁷; Chelsea Rohlfs, MBA⁹; Christina Albertin, MPH¹⁰; Dithi Banerjee, PhD¹²; Erin R. McKeever, MPH¹; Casey Kalman, MPH¹; Benjamin R. Clopper, MPH¹; New Vaccine Surveillance Network Product Effectiveness Collaborators; Meredith L. McMorrow, MD^{1,*}; Fatimah S. Dawood, MD^{1,*}

Update to 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>

New Vaccine Surveillance Network (NVSN)

MMWR March 7, 2024. vol 73 No 9

VISION Multi-Site Network of Electronic Health Records (EHRs)

127 emergency rooms and 107 hospitals

- **Population:** Visiting a participating ED for or hospitalized with RSV-like illness (RLI)*
- **Immunization data:** Infant and maternal RSV immunization status documented by electronic health records, state and city registries, and claims data (subset of sites)
- **Covariate data:** Documented in electronic health records
 - Underlying medical conditions: ICD-10 discharge diagnosis codes at time of RLI encounter
 - Patient characteristics
 - Date of birth
 - Census tract of residence
 - Sex



VISION 2.0 partners included in this analysis –

ED: Columbia, HealthPartners Institute, Intermountain Healthcare, KPSC, KPCHR, Regenstrief

Inpatient: Columbia, HealthPartners Institute, Intermountain, KPSC, KPCHR, Regenstrief

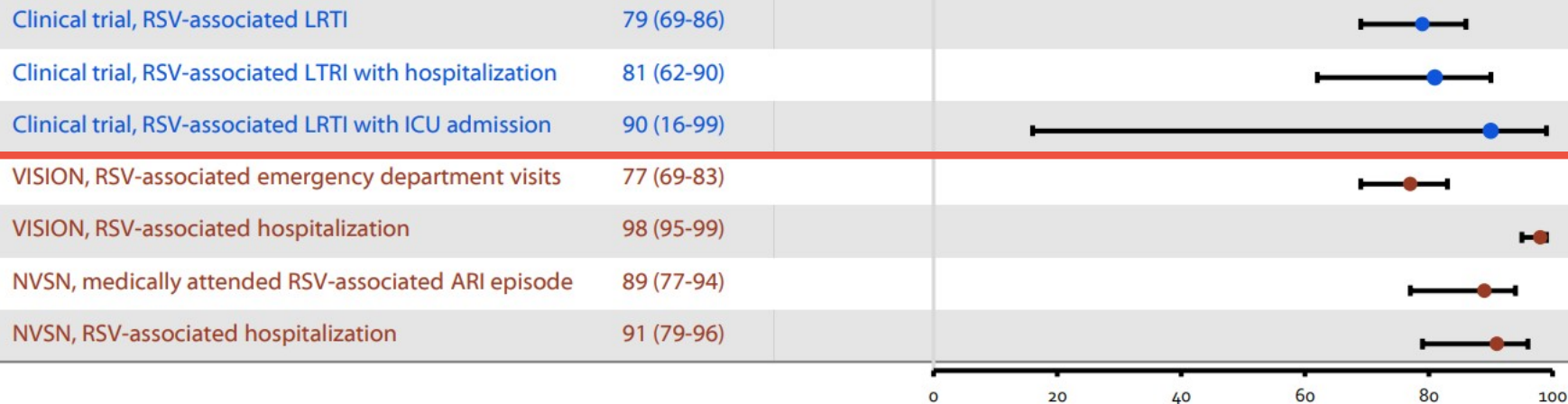
ACIP June 28, 2024

Amanda Payne - CDC

Observational data indicate nirsevimab is working as expected (vs. RCT results) during the first RSV season after approval among infants in their first RSV season

Outcome/Analysis

Vaccine efficacy/effectiveness (%)

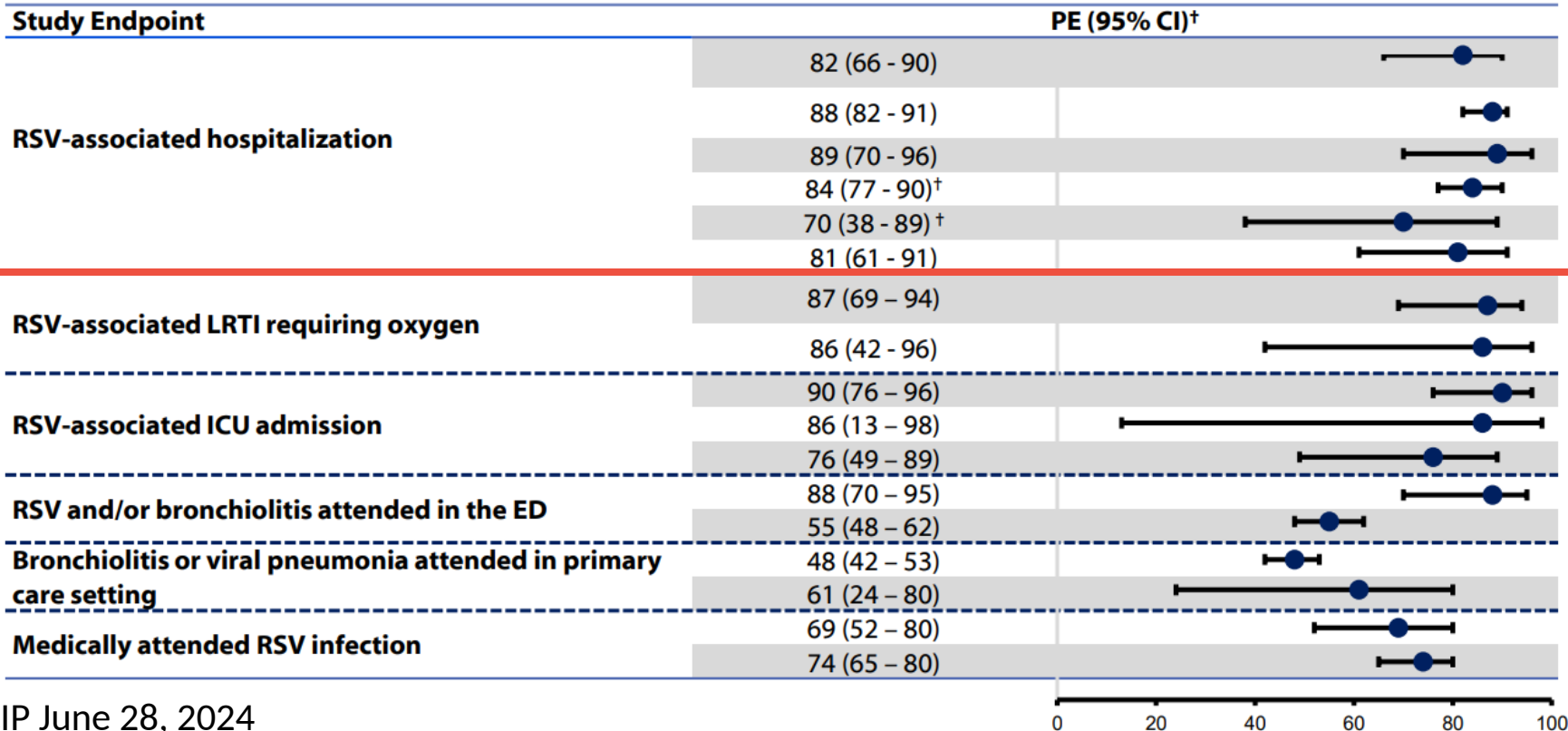


ACIP June 28, 2024
Amanda Payne - CDC

<https://www.cdc.gov/mmwr/volumes/72/wr/mm7234a4.htm>
T = randomized clinical trial | ARI = acute respiratory illness

Results may not be comparable across studies due to differences in outcome definitions, timing, and other factors.

Nirsevimab product effectiveness (PE) among infants in their first RSV season – Data* from Spain and France



ACIP June 28, 2024

Amanda Payne - CDC

*References provided on backup slide 32.

[†]PE estimates generated from the same study, using different methods.

LRTI = lower respiratory tract infection | ICU = intensive care unit

IMMUNIZATIONS FOR PREGNANT PEOPLE

FLU

Pertussis

PROTECTING PARENT & BABY THROUGH VACCINES IN PREGNANCY

- Vaccines before and during pregnancy prevent you from getting very sick from serious diseases.
- The baby gets antibodies (immune protection) that your body creates from vaccines during pregnancy to protect them from serious diseases.

Y = Antibodies = protection from disease



SARS-CoV-2

Tetanus



AAP

Infant Immunization Discussion Guides

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

APRIL 20, 2023

VOL. 388 NO. 16

Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants

B. Kampmann, S.A. Madhi, I. Munjal, E.A.F. Simões, B.A. Pahud, C. Llapur, J. Baker, G. Pérez Marc, D. Radley, E. Shittu, J. Glanternik, H. Snaggs, J. Baber, P. Zachariah, S.L. Barnabas, M. Fausett, T. Adam, N. Perreras, M.A. Van Houten, A. Kantele, L.-M. Huang, L.J. Bont, T. Otsuki, S.L. Vargas, J. Gullam, B. Tapiero, R.T. Stein, F.P. Polack, H.J. Zar, N.B. Staerke, M. Duron Padilla, P.C. Richmond, K. Koury, K. Schneider, E.V. Kalinina, D. Cooper, K.U. Jansen, A.S. Anderson, K.A. Swanson, W.C. Gruber, and A. Gurtman, for the MATISSE Study Group*

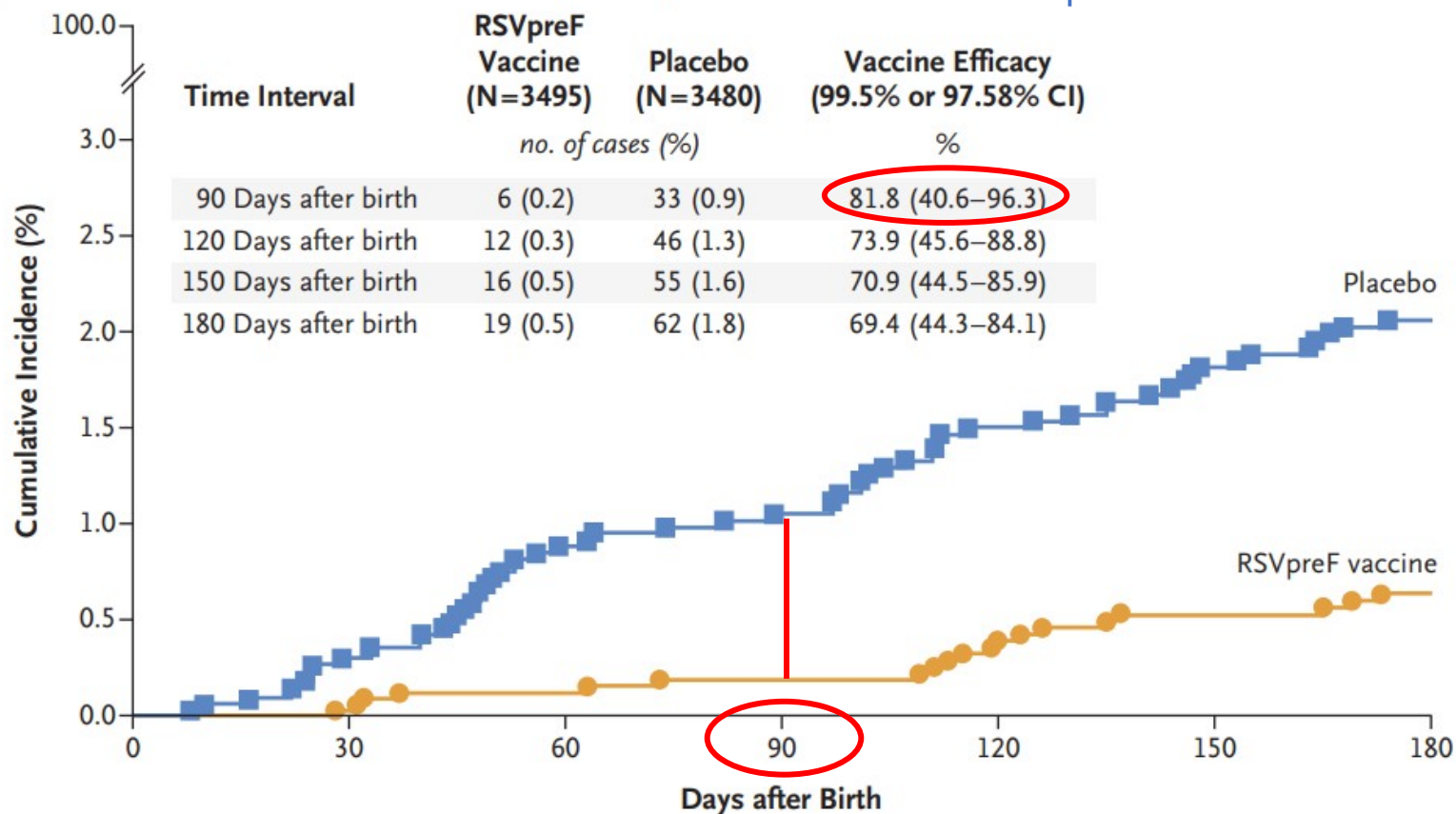
RSV Vaccine Pregnant Women

Kampmann B et al NEJM 2023

- Phase 3 Double blinded trial women 24-36 weeks gestation
- Randomized 1:1
- IM bivalent RSV preF vaccine vs placebo
- Primary efficacy end points medically attended severe RSV associated LRTI within 90, 120, 150 and 180 days of life
- 3,682 Vaccine ■ 3,676 Placebo

A Medically Attended Severe RSV-Associated Lower Respiratory Tract Illness

Kampmann B et al NEJM 2023



No. at Risk

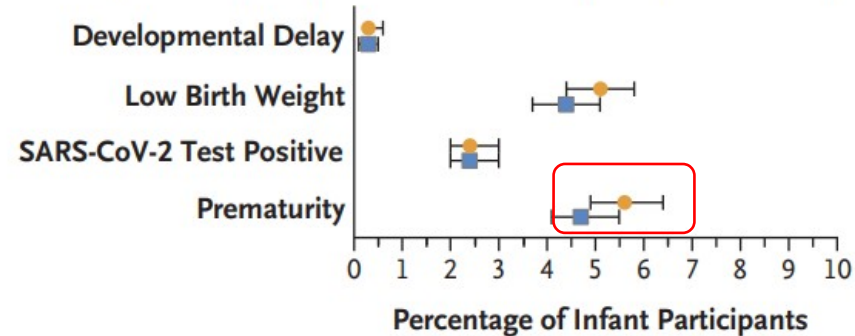
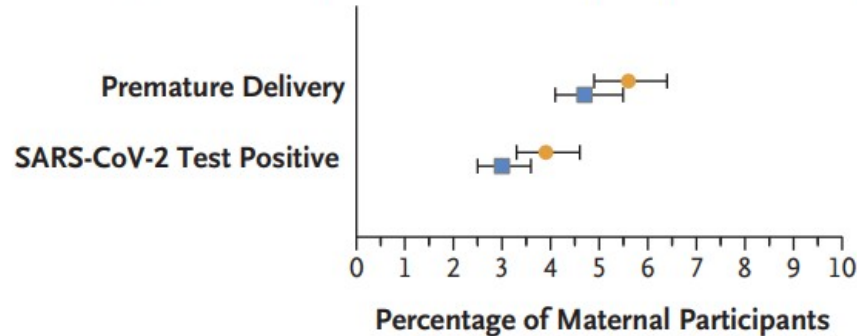
Placebo	3480	3292	2973	2899	2833	2776	2749
RSVpreF vaccine	3495	3349	3042	2981	2916	2867	2820

Safety Signal for Prematurity?

Kampmann B et al NEJM 2023

B Adverse Events of Special Interest

● RSVpreF vaccine (maternal participants, N=3682; infant participants, N=3568) ■ Placebo (maternal participants, N=3675; infant participants, N=3558)



- Not statistically significant
- Found mostly in one site
- But gave pause....
- Recommendations administer 32-36 weeks gestation

RSV Prevention Products

- RSV maternal Vaccination (Abrysvo, Pfizer)
 - Pregnancy 32-36 weeks gestation
- Infant monoclonal antibody Nirsevimab (Beyfortus, Sanofi and AstraZeneca)
 - 0-8 months all infants
 - Second season for high-risk infants (< 19 months)

Timing of RSV vaccine and nirsevimab

ACIP: S Long
June 2024

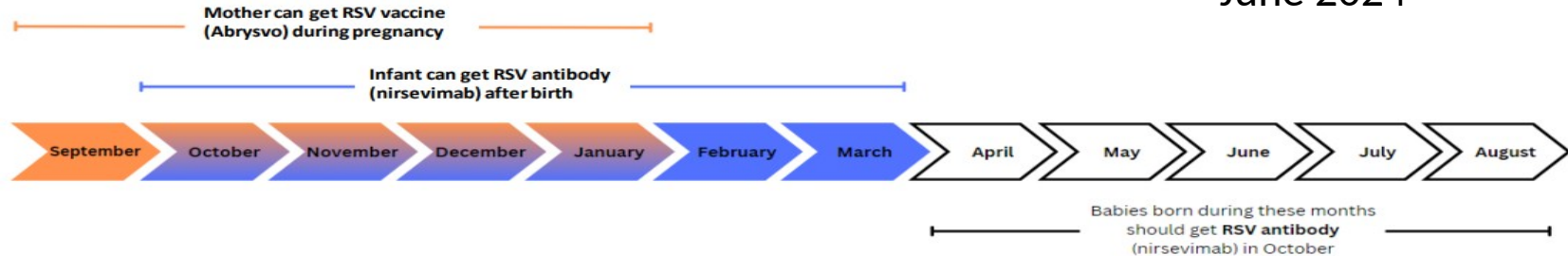
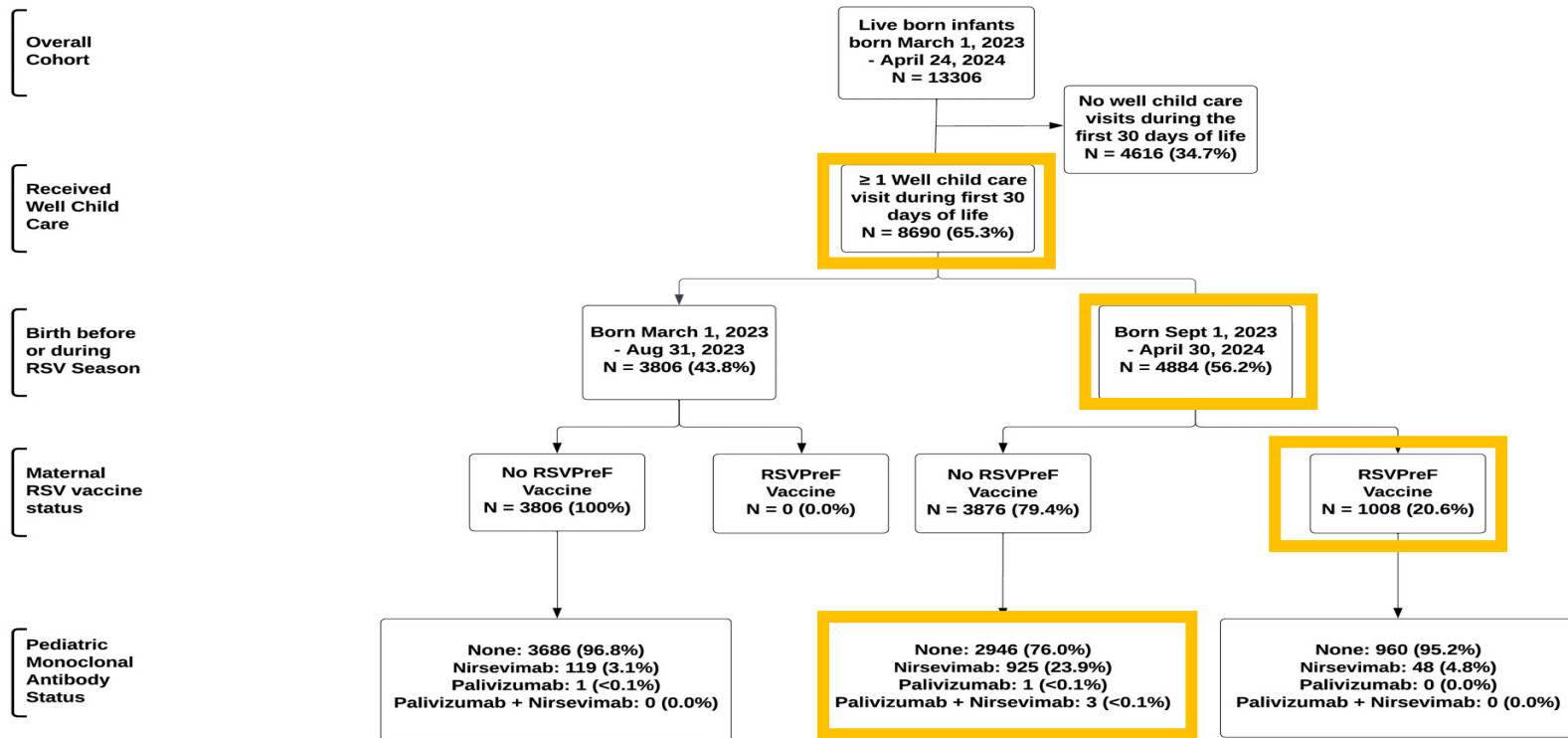


Figure represents recommended timing of immunization product deployment for most of the continental U.S. In jurisdictions with seasonality that differs from most of the continental United States (e.g., Alaska, jurisdictions with tropical climates), providers should follow state, local, or territorial guidance on timing of administration

UPMC Uptake of RSV Prevention Products



Rick et al, unpublished data



University of
Pittsburgh®

Receipt of RSV Prevention by Birth Month

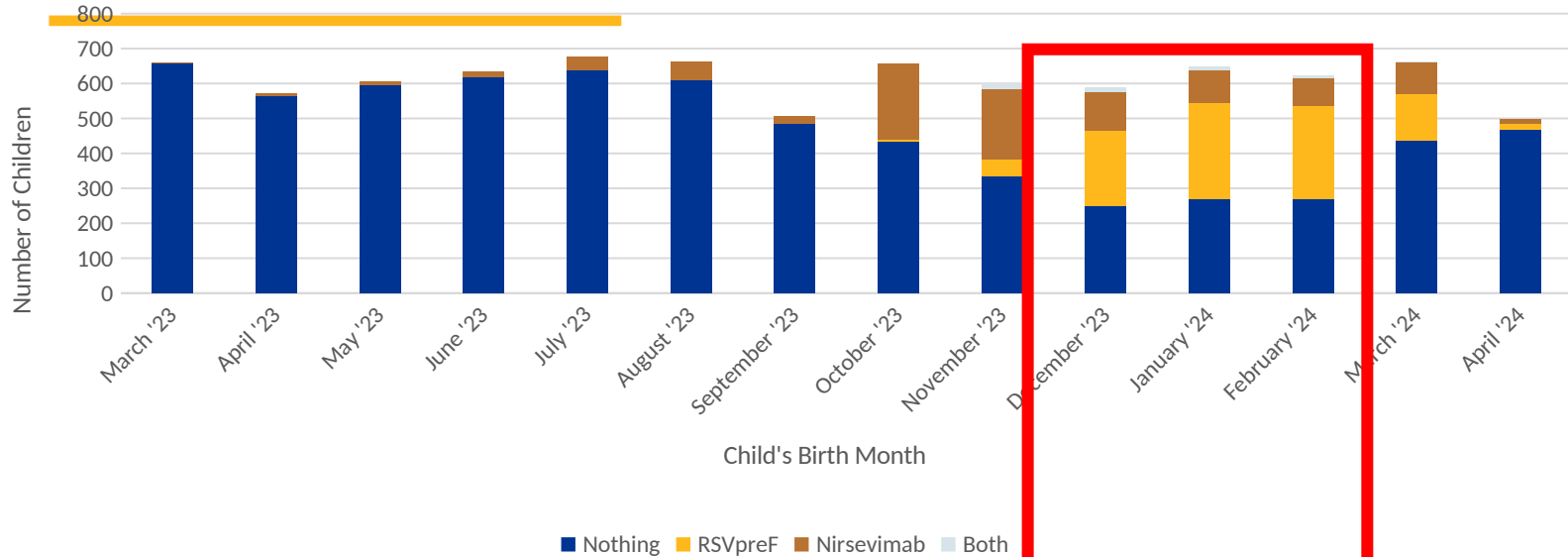


Table 1. Receipt of RSV Prevention Products during 2023-2024 RSV Season by Birth Month among Children with Well Child Care during the first 30 days of life

Birth Year	2023										2024			
Birth Month	March	April	May	June	July	August	September	October	November	December	January	February	March	April
	N=661	N=570	N=606	N=632	N=676	N=661	N=606	N=656	N=599	N=590	N=649	N=624	N=663	N=497
RSVpreF	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.6)	51 (8.5)	214 (36.3)	274 (42.2)	266 (42.6)	136 (20.5)	15 (3.0)
Nirsevimab	2 (0.3)	6 (1.1)	9 (1.5)	15 (2.4)	39 (5.8)	51 (7.7)	20 (3.3)	217 (33.1)	199 (33.2)	111 (18.8)	96 (14.8)	82 (13.1)	91 (13.7)	13 (2.5)
Both	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	16 (2.7)	14 (2.4)	10 (1.5)	7 (1.1)	1 (0.2)	0 (0.0)
Total	2 (0.3)	6 (1.1)	9 (1.5)	15 (2.4)	39 (5.8)	51 (7.7)	20 (3.3)	221 (33.7)	266 (44.4)	339 (57.5)	380 (58.6)	355 (56.9)	228 (34.4)	28 (5.6)

N (%). RSV: respiratory syncytial virus

**“It’s tough to make predictions, especially
about the future”**

- Yogi Berra



RSV coming season

- Prediction 1: RSV is coming this fall
- Prediction 2: Maternal vaccination and infant nirsevimab uptake will continue to improve
 - CDC data from 2023-24 season without increased risk of prematurity
- Prediction 3: RSV hospitalizations will ↓↓↓
- Prediction 4: VE will remain high, albeit likely not as robust as initial study
- Prediction 5: The % of older children hospitalized will increase but not the actual number

Thank you
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