Punt Away Respiratory Illness

Jason G. Newland MD, Med
Jason.Newland@Nationwidechildrens.org

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

1

Disclosures

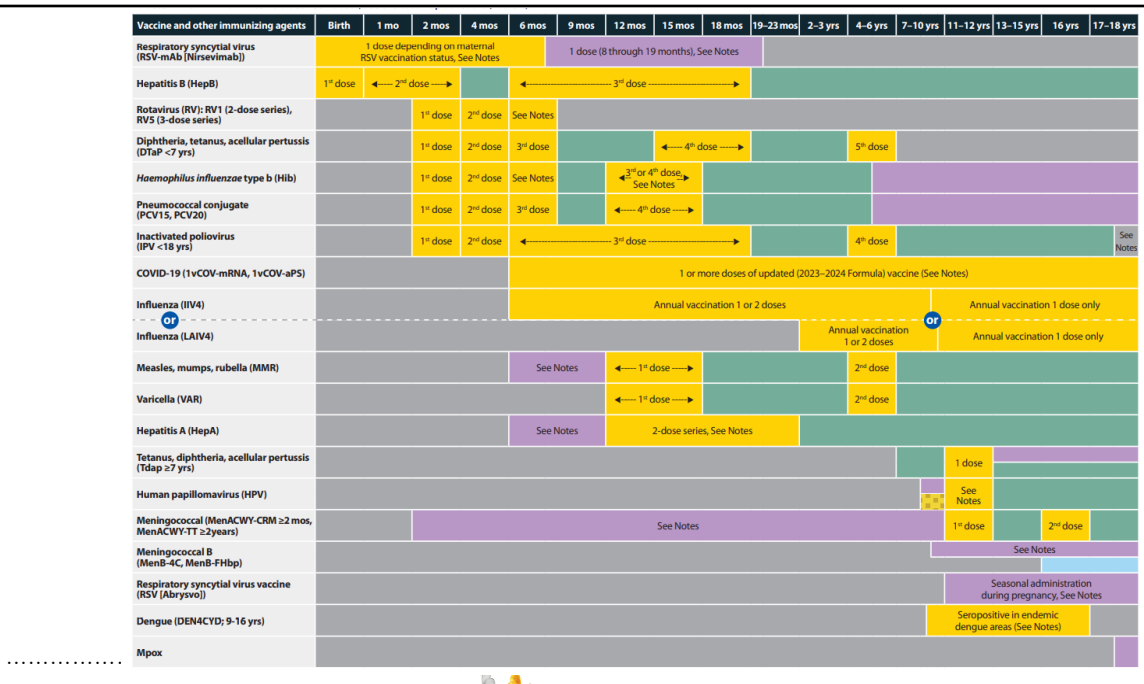
- Pfizer with RSV vaccine study with pregnant women and Sisunatovir
- Merck- antibiotic studies

2

Objectives

- List the immunizations and vaccines available to prevent RSV infections in neonates and adults
- Describe the different vaccines available to for the prevention of *Streptococcus pneumoniae* infections

3

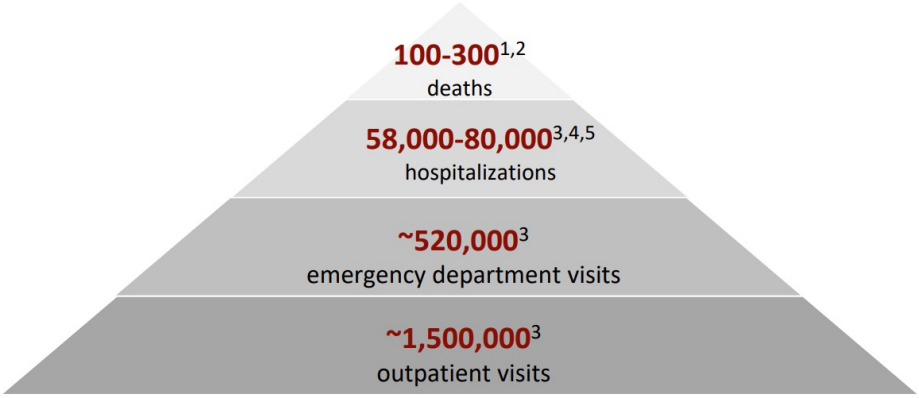


NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.℠

https://www.cdc.gov/vaccines/hcp/imz-schedules/child-adolescent-age.html#table-1

4

Each year among U.S. children aged less than 5 years, RSV is associated with…



[1]Thompson et al, JAMA, 2003; [2]Hansen et al, JAMA Network Open, 2022; [3]Hall et al, NEJM, 2009; [4]Rha et al., Peds, 2020; [5]McLaughlin et al, J Infect Dis, 2022; (*estimate 80,000 hospitalizations in infants <1y)

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

https://www.cdc.gov/rsv/research/

5

RSV - Epidemiology

- Annual winter epidemics (been summer and fall 2021-2022), lasting approximately 5 months
- Usually all children infected within first 2 years of life
  - Due to pandemic and less viral infection, more children over 2 requiring hospitalization
- Approximately 1% require hospitalization, resulting in 100,000 hospitalizations per year in US
- Reinfections occur frequently
- Transmission by contaminated secretions and large droplets

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

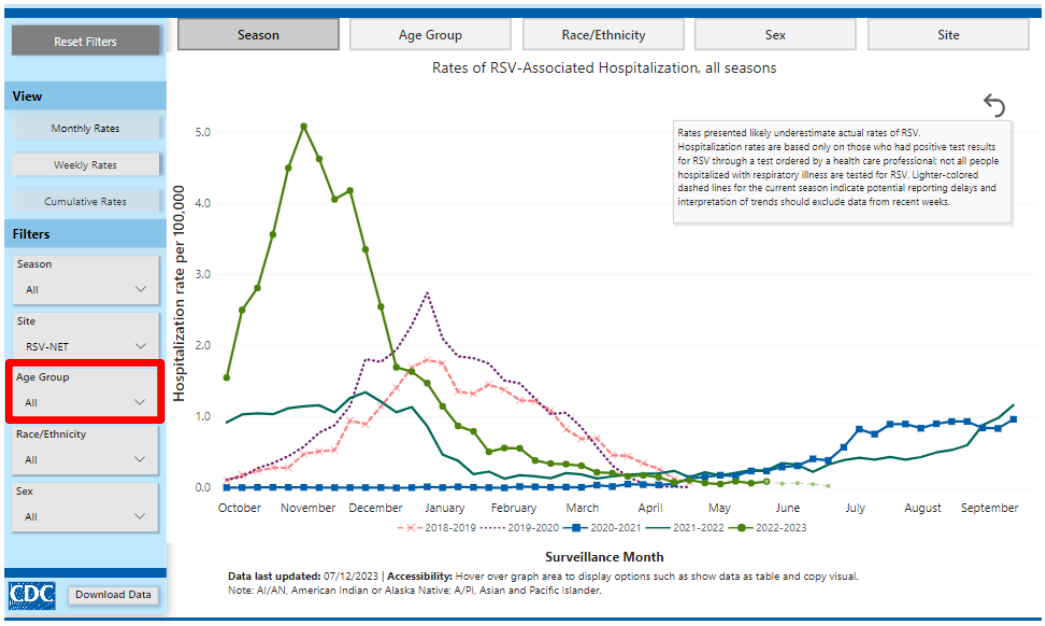
6

RSV – Symptoms & Clinical Manifestations

- Non-specific upper respiratory infection
  - Congestion, runny nose, cough
- Bronchiolitis
  - Fast breathing, copious drainage, tight cough, using extra muscles to breath
  - May or may not have fever
- Apnea (stop breathing) in very young infants
- Severe illness in premature and very young infants and in those with chronic cardiac or pulmonary disease

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

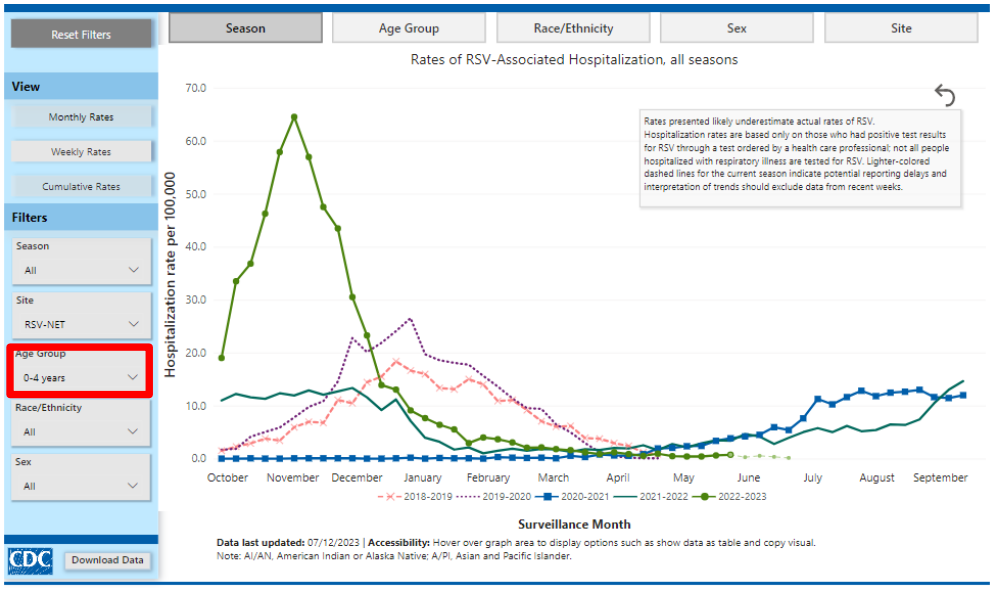
7



NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

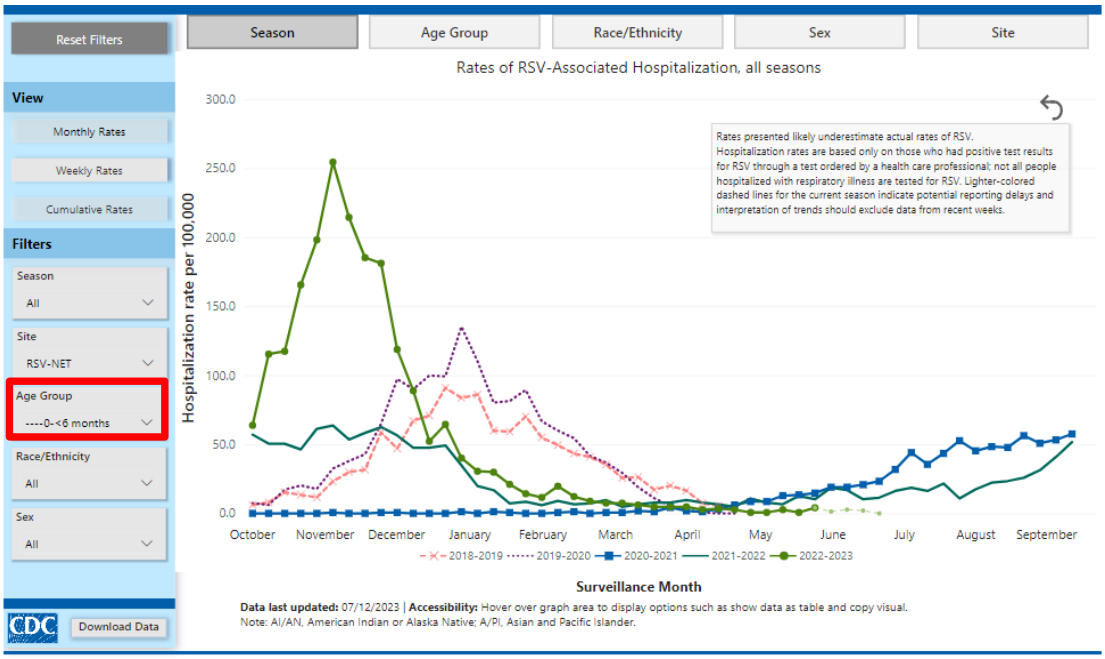
https://www.cdc.gov/rsv/research/rsv-net/dashboard.html

8



NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

9



NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

10

JAMA Network | Open

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 Bline, MD; Melissa L. Cullimore, MD, PhD; Laura Loftis, MD, MS; Vicki L. Montgomery, MD; Asumthia S. Jeyapalan, DO, MHA; Pia S. Pannaraj, MD, MPH; Adam J. Schwarz, MD; Natalie Z. Cvijanovich, MD; Matt S. Zinter, MD; Aline B. Maddux, MD, MSCS; Melania M. Bembea, MD, PhD; Katherine Irby, MD; Danielle M. Zerr, MD, MPH; Joseph D. Kuebler, MD, MBA; Christopher J. Babbitt, MD; Mary Glas Gaspers, MD, MPH; Ryan A. Nofziger, MD, MBA; Michele Kong, MD, MBA; Bria M. Coates, MD; Jennifer E. Schuster, MD, MSCI; Shira J. Gertz, MD; Elizabeth H. Mack, MD, MS; Benjamin R. White, MD, MA; Helen Harvey, MD, MS; Charlotte V. Hobbs, MD; Heda Dapul, MD; Andrew D. Butler, MD; Tamara T. Bradford, MD; Courtney M. Rowan, MD, MScr; Kari Wellnitz, MD; Mary Allen Staat, MD, MPH; Cassyanne L. Aguiar, MD; Saul R. Hymes, MD; Adrienne G. Randolph, MD; Angela P. Campbell, MD, MPH; for the RSV-PIC Investigators

August 15, 2023

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

11

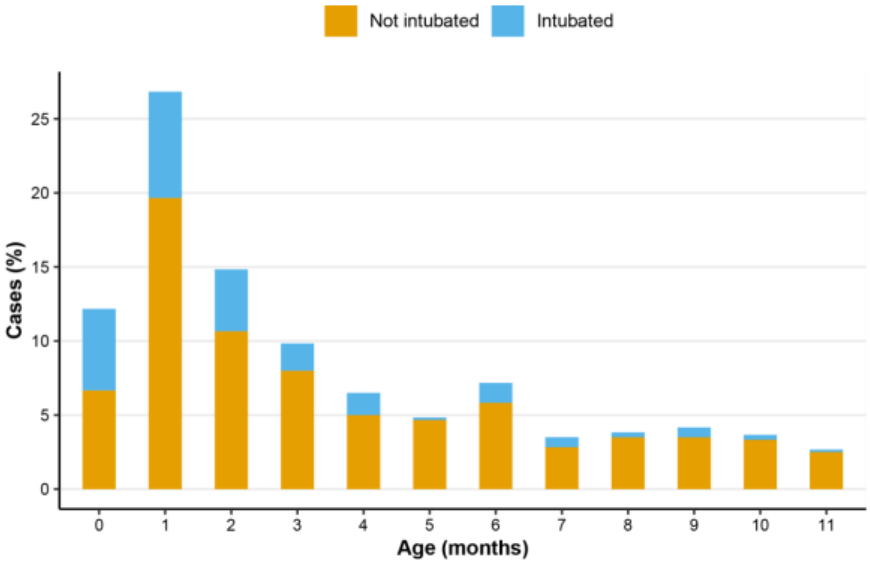
RSV and US Intensive Care Units

- First 15-20 infants less than 1 yo from 39 pediatric hospitals across the United States
- Enrolled October 17 to December 16, 2022
  - Had to be in ICU for greater than 24 hours
  - Symptom onset less than 10 days before hospitalizations
  - Laboratory confirmed RSV within 72 hours of hospitalization
- 600 total infants enrolled

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

12

RSV and US Intensive Care Units- Age distribution



13

Characteristic	Infants, No. (%) All (N = 600)	Nonintubated (n = 457)	Intubated (n = 143)	*P* value[a]
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)	
Sex				
Male	361 (60.2)	277 (60.6)	84 (58.7)	.69
Female	239 (39.8)	180 (39.4)	59 (41.3)	
Race and ethnicity				
Hispanic	135 (22.5)	102 (22.3)	33 (23.1)	NA
Non-Hispanic Asian	13 (2.2)	11 (2.4)	2 (1.4)	
Non-Hispanic Black	95 (15.8)	75 (16.4)	20 (14.0)	
Non-Hispanic White	265 (44.2)	199 (43.5)	66 (46.2)	
Multiple or other[b]	30 (5.0)	21 (4.6)	9 (6.3)	
Unknown	62 (10.3)	49 (10.7)	13 (9.1)	
SVI score, median (IQR)[c]	0.50 (0.39-0.64)	0.50 (0.40-0.64)	0.50 (0.38-0.65)	.98
Insurance				
Public	336 (56.0)	242 (53.0)	94 (65.7)	.050
Private	240 (40.0)	196 (42.9)	44 (30.8)	
Self-pay	11 (1.8)	9 (2.0)	2 (1.4)	
Other or unknown	13 (2.2)	10 (2.2)	3 (2.1)	

- ICU patients are young
- Higher disease severity scores in < 3 months
- Majority with public insurance
- 4 infants required ECMO
- 2 infants died
- 81% had no underlying conditions

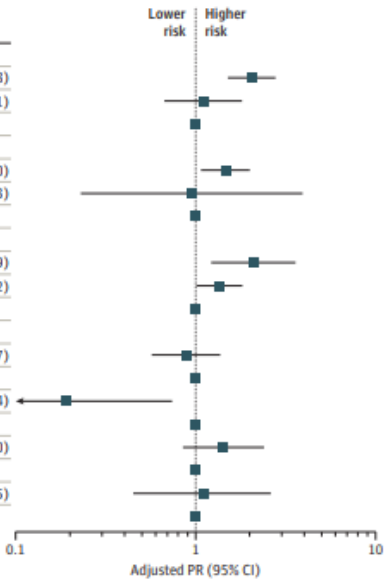
14

Characteristic	Infants, No. (%) All (N = 600)	Nonintubated (n = 457)	Intubated (n = 143)	*P* value[a]
Prematurity	169 (28.9)	116 (26.1)	53 (37.5)	.01
Gestational age, median (IQR)[d]	34.0 (32.0-35.7)	34.0 (32.4-35.7)	34.0 (32.0-35.4)	.91
Multiple pregnancy	28 (4.7)	16 (3.5)	12 (8.4)	.18
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)	
Nonrespiratory, noncardiac	48 (8.0)	46 (10.1)	2 (1.4)	<.001
Cardiac, nonrespiratory	20 (3.3)	15 (3.3)	5 (3.5)	.90
Respiratory	45 (7.5)	32 (7.0)	13 (9.1)	.41
Chronic lung disease	22 (3.7)	14 (3.1)	8 (5.6)	.16
Neurologic	13 (2.2)	9 (2.0)	4 (2.8)	.52
Trisomy 21	8 (1.3)	8 (1.8)	0	.21
Reason for admission				
LRTI	594 (99.0)	453 (99.1)	141 (98.6)	.58
Apnea or bradycardia	77 (12.8)	36 (7.9)	41 (28.7)	<.001
Cardiac arrest at home with CPR	3 (0.5)	1 (0.2)	2 (1.4)	.14
CNS infection	2 (0.3)	0	2 (1.4)	.06
Shock requiring vasopressors	5 (0.8)	0	5 (3.5)	.001

15

Figure 2. Factors Associated With Risk for Intubation in Infants Requiring Intensive Care for Respiratory Syncytial Virus Infection

Characteristic	Intubated, No./total No. (%)	Crude PR (95% CI)	Adjusted PR (95% CI)
Age group, mo			
0 to <3	101/323 (31.3)	2.23 (1.46-3.43)	2.05 (1.51-2.78)
3 to <6	21/127 (16.5)	1.18 (0.68-2.06)	1.10 (0.67-1.81)
6 to <12	21/150 (14.0)	1 [Reference]	1 [Reference]
Insurance status (n = 587)			
Public	94/336 (28.0)	1.53 (1.11-2.10)	1.47 (1.07-2.00)
Self-pay	2/11 (18.2)	0.99 (0.28-3.57)	0.95 (0.23-3.93)
Private	44/240 (18.3)	1 [Reference]	1 [Reference]
Gestational age, wk			
23 to <29	8/24 (33.3)	1.60 (0.88-2.89)	2.09 (1.22-3.59)
29 to 36	45/145 (31.0)	1.49 (1.10-2.02)	1.36 (1.01-1.82)
≥37	90/431 (20.9)	1 [Reference]	1 [Reference]
Underlying medical conditions			
≥1 Underlying	20/113 (17.7)	0.70 (0.46-1.07)	0.89 (0.57-1.37)
No	123/487 (25.3)	1 [Reference]	1 [Reference]
Nonrespiratory noncardiac disease	2/48 (4.2)	0.16 (0.04-0.66)	0.19 (0.05-0.74)
No	141/552 (25.5)	1 [Reference]	1 [Reference]
Respiratory	13/45 (28.9)	1.23 (0.76-2.00)	1.43 (0.85-2.40)
No	130/555 (23.4)	1 [Reference]	1 [Reference]
Nonrespiratory cardiac disease	5/20 (25.0)	1.05 (0.49-2.28)	1.10 (0.45-2.65)
No	138/580 (23.8)	1 [Reference]	1 [Reference]



16

RSV and US Intensive Care Units- Palivizumab

- 15 of 17 infants born less than 29 weeks- no documentation of receiving Palivizumab
- 3 infants received palivizumab, none with in previous 30 days

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

17

Palivizumab in <= 35 weeks GA or BPD (N=1502)

TABLE 2. Summary of Analysis of RSV Hospitalization

	Placebo	Palivizumab	% Reduction (95% CI)	*P* Value
Primary analysis (incidence of RSV hospitalizations)*	53/500 (10.6%)	48/1002 (4.8%)	55% (38, 72)	<.001
Alternative analysis (Kaplan-Meier†)	53/500 (10.6%)	48/1002 (4.8%)	55% (38, 72)	<.001
Sensitivity analyses				
Dropout before 150 days and no endpoint‡	53/500 (10.6%)	49/1002 (4.9%)	55% (38, 72)	<.001
Respiratory hospitalization but no RSV test done§	56/500 (11.2%)	54/1002 (5.4%)	52% (35, 69)	<.001
Primary inclusion populations				
Premature (no BPD)	19/234 (8.1%)	9/506 (1.8%)	78% (66, 90)	<.001
BPD	34/266 (12.8%)	39/496 (7.9%)	39% (20, 58)	.038

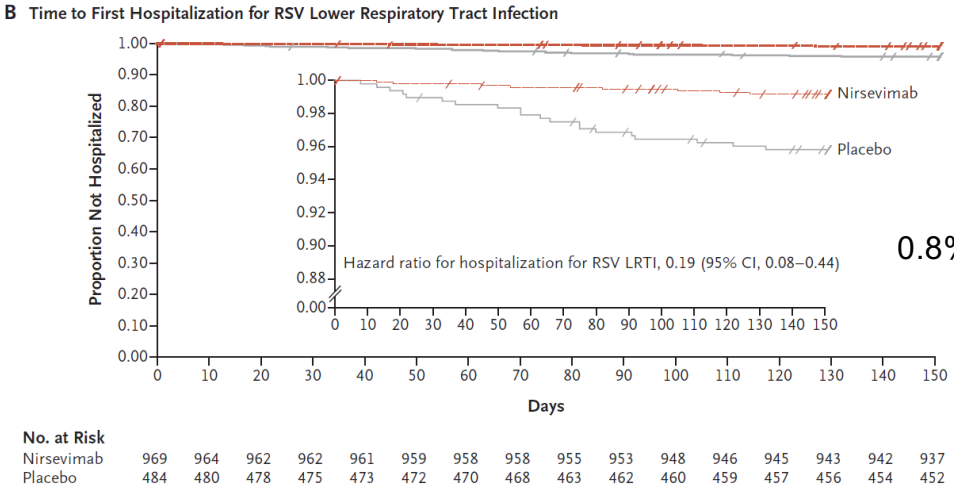
- Fewer days of hospitalization (-0.33 days, p<0.001)
- Fewer ICU admissions (3% vs. 1.3%, p = 0.026)
- NNT to prevent one hospitalization = 17

$3400 per vial;
$20,000 per course

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

18

Nirsevimab in 29 – 35 weeks GA (N=1453)

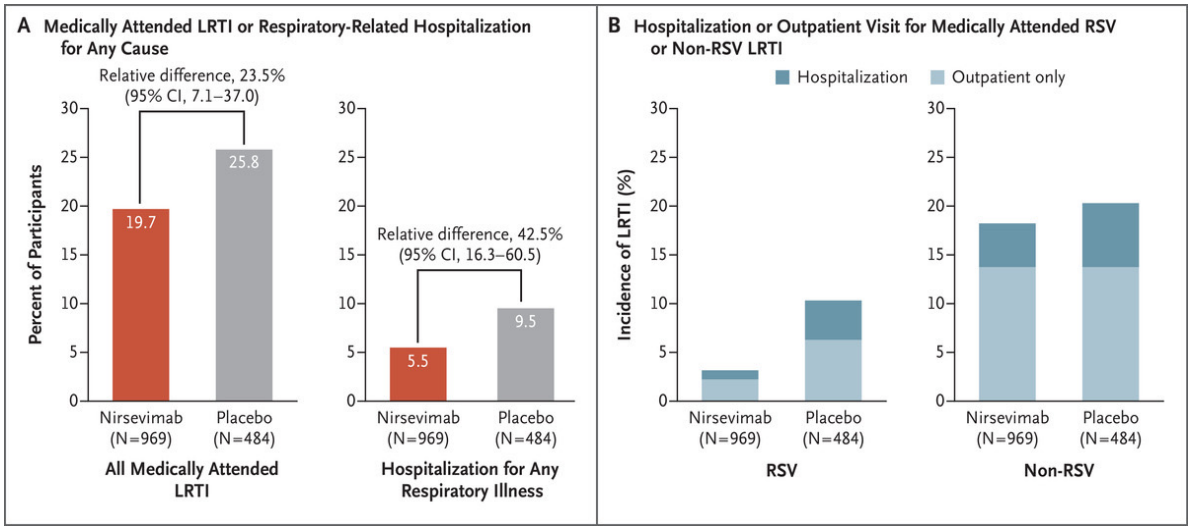


0.8% vs. 4.1%

- NNT to prevent one hospitalization = 33

Griffin et al. N Engl J Med 2020; 383: 415-25.

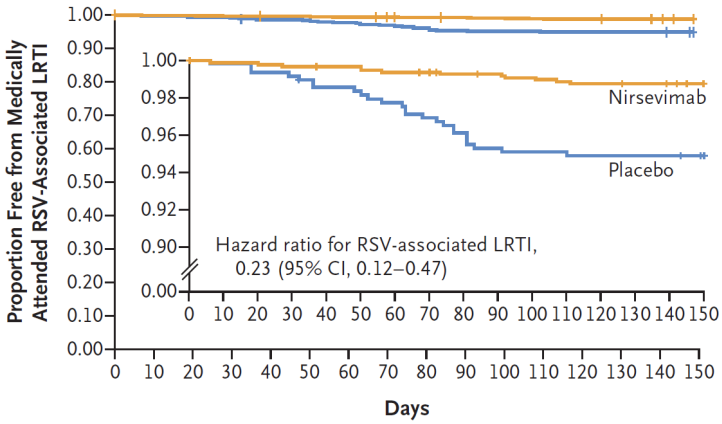
19



Griffin MP et al N Engl J Med July 2020

20

Nirsevimab in late-preterm and term infants (N=1490)



No. at Risk

Nirsevimab	994	984	980	975	970	966
Placebo	496	488	479	467	465	464

- NNT to prevent one inpatient or outpatient visit = 12

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

Hammitt et al. N Engl J Med 2022; 386: 837-46.

21

Nirsevimab in late-preterm and term infants (N=1490)

Table 3. Outcomes through 150 Days after the Injection.*

Outcome	Nirsevimab (N=686)	Placebo (N=342)	Efficacy (95% CI)†	Cases Averted per 1000 Infants Treated (95% CI)‡	Number Needed to Treat (95% CI)§
	no. (%)				
Medically attended RSV-associated lower respiratory tract infection on any test result¶	17 (2.5)	37 (10.8)	77.0 (59.8 to 86.8)	83.4 (62.0 to 105.0)	12 (10 to 17)
Medically attended RSV-associated lower respiratory tract infection on central test result¶	15 (2.2)	33 (9.6)	77.2 (58.7 to 87.5)	74.7 (53.0 to 95.0)	14 (11 to 19)
Medically attended lower respiratory tract infection of any cause¶	60 (8.7)	62 (18.1)	51.5 (32.6 to 65.2)	93.6 (63.0 to 124.0)	11 (9 to 16)
Hospitalization for any respiratory illness due to RSV on any test result	9 (1.3)	11 (3.2)	59.0 (2.1 to 82.9)	19.0 (5.5 to 32.0)	53 (32 to 182)
Hospitalization for any respiratory illness due to RSV on central test result	7 (1.0)	9 (2.6)	61.1 (–3.7 to 85.4)	16.1 (4.5 to 28.0)	62 (36 to 223)
Hospitalization for any respiratory illness of any cause	16 (2.3)	14 (4.1)	42.8 (–15.8 to 71.7)	17.7 (2.0 to 33.0)	57 (31 to 500)

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

Hammitt et al. N Engl J Med 2022; 386: 837-46.

22

Nirsevimab safety

Table 2 **Adverse Reactions Reported at an Incidence Higher Than Placebo in the Safety Population* (Trials 03 and 04)**

Adverse Reaction	BEYFORTUS N=2,570 %	Placebo N=1,284 %
Rash† (occurring within 14 days post-dose)	0.9	0.6
Injection site reaction† (occurring within 7 days post-dose)	0.3	0

Number needed to harm = 333

Package insert

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

23

Nirsevimab Eligibility

- Will start administering Oct 1, 2024 at NCH
- Eligibility- First season
  - All infants <8 months as 11/1/2024 if mom did not receive RSV vaccine > 14 days prior to delivery
  - Some infants born to mom's that received RSV vaccine can get nirsevimab
    - HIV infected mom
    - Immunocompromised mom
    - Substantial risk for severe RSV dises (e.g. congenital heart disease)
- Can be given with other vaccines

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

24

Nirsevimab Eligibility

- Eligibility- Second season
  - Chronic Lung Disease (CLD) of Prematurity during the 6-month period before the start of the RSV season (since 5/1/2024).
  - Cystic fibrosis: previous hospitalization for pulmonary exacerbation in the 1st year of age, persistent abnormalities on chest radiograph/CT scan, or weight for length <10th percentile
  - Prolonged intensive care birth hospitalization due to prematurity/other causes at discharge
  - Severe immunocompromised (e.g., SCID): e-mail HostDefense@nationwidechildrens.org
- Questions- Pablo.Sanchez@nationwidechildrens.org

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

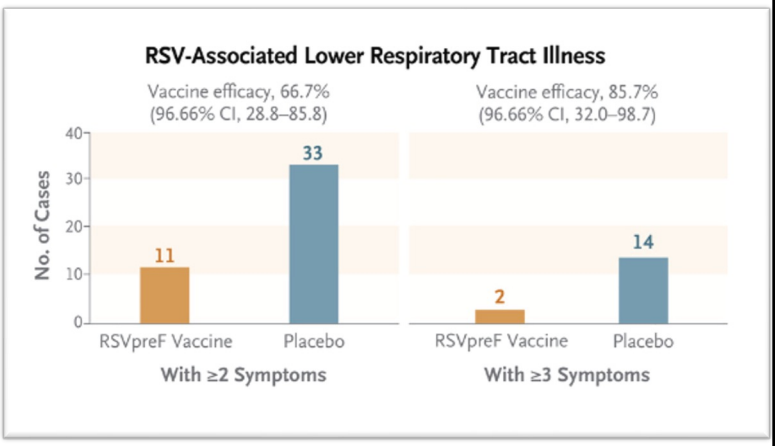
25

RSV Prevention

- **Vaccination**
  - **Age ≥ 60 years**
    - **Pfizer (Abrysvo)**
    - **GSK (Arexvy)**
    - **Moderna (mREsvia)**

FDA APPROVED

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

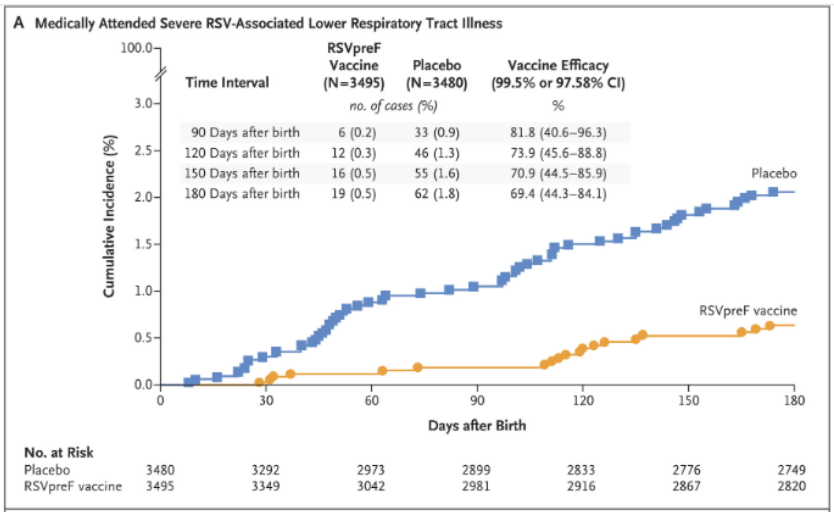


Walsh EE, et al. RENOIR Clinical Trial Group. Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults. N Engl J Med. 2023 Apr 20;388(16):1465-1477. doi: 10.1056/NEJMoa2213836. Epub 2023 Apr 5. PMID: 37018468.

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

26

Maternal RSV Vaccine



Safety

- Preterm birth
  - <37 weeks- 5.6% vaccine vs 5.1% placebo
- Congenital malformations
  - 4.9% vaccine vs 5.7% placebo
- Developmental delay
  - 0.3% vaccine vs. 0.3% placebo

B Kampmann et al. N Engl J Med 2023;388:1451-1464.

27

Maternal RSV Vaccine

- RSV maternal vaccine approved by FDA on August 21st, 2023 and ACIP on Sep 22, 2023
  - Give at 32-36 weeks from Sept to January
  - Babies will not need Nirsevimab if maternal vaccine given 2 weeks before birth

https://www.cdc.gov/vaccines/vpd/rsv/public/pregnancy.html

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

28

Influenza Vaccines

- Reduces pregnant women's risk of being hospitalized by an average of 40%
- Reduced children's risk of severe life-threatening influenza by 75%
- Reduced flu-related hospitalizations by 41%
- Being vaccinated protects those around you

https://www.cdc.gov/flu/prevent/flushot.htm

29

Influenza Vaccines

Inactivated Vaccine

- Contains 2 influenza A strains and 2 influenza B strains
- Administered intramuscularly
- NOT INFECTIOUS
- Must receive annually
- When first receiving the flu vaccine between ages 6 months and younger than 9 years, need to receive 2 doses one month apart.
- Given to all ages except < 6 months

30

Influenza Vaccines

Live Attenuated Influenza Vaccine (LAIV)

- Contains 2 A serotypes, 2 B serotypes
- Intranasally administered
- Can produce mild symptoms of influenza:
  - Fever

31

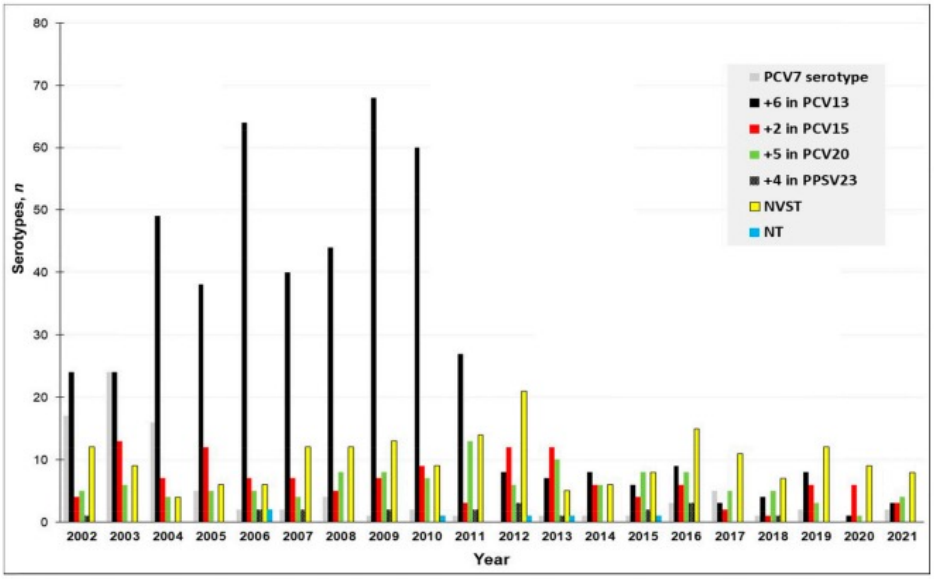
Pneumococcal Vaccines

- PCV15, PCV20, and PPS23
- PCV 15 adds serotypes 22F and 33F to PCV13
- PCV 20 adds serotypes 8, 10A, 11A, 12F, 15B, 22F, 33F
- CDC/ACIP Recommendations
  - Healthy Children- PCV15 or 20
  - High risk individuals- PCV20 is sufficient and don't need PPS23
    - If receive PCV15- need either a PCV20 or PPS23

https://stacks.cdc.gov/view/cdc/133252

32

Invasive Pneumococcal Disease- Massachusetts



PCV15: 2 more Serotypes- 16.9% more IPD

PCV20: 7 more serotypes- 35% more IPD

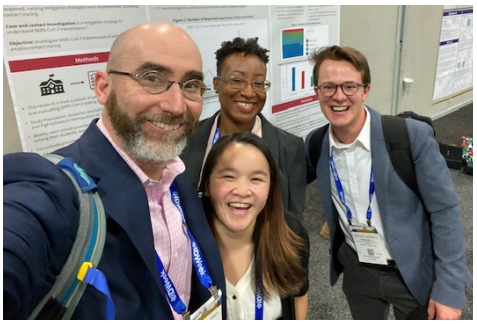
Yildirim I et al Pediatrics Jan 2024

33

Summary

- RSV prevention strategies are available and effective
- Influenza Vaccines important for child health following largest number of deaths in a season
- Pneumococcal vaccines add additional protection though still

34



THANK YOU

When your child needs a hospital, everything matters.

35