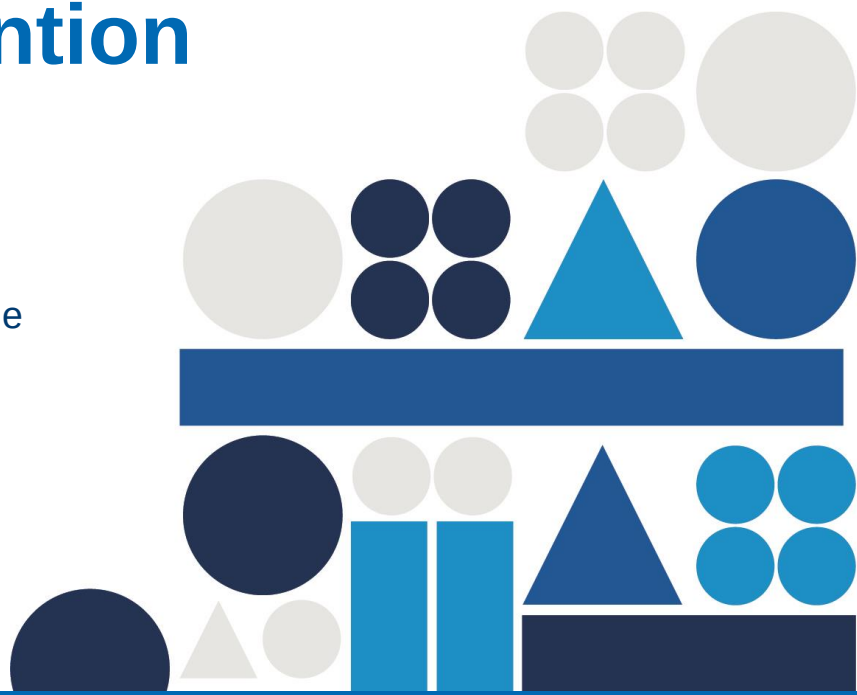
# What's New With the Flu and Updates on RSV Prevention

Suchitra Rao, MBBS, MSCS
Associate Professor of Pediatrics
Infectious Diseases, Epidemiology and Hospital Medicine
University of Colorado School of Medicine
Children's Hospital Colorado



Children's Hospital Colorado
Here, it's different.™

Affiliated with
School of Medicine
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

# Disclosure Slide

Funding: CDC, NHLBI, PCORI, AHRQ

# Objectives

By the end of this talk you should be able to:

1. Discuss the current epidemiology of influenza and RSV in children
2. Summarize influenza testing and treatment guidelines
3. Review influenza vaccination recommendations
4. Understand rationale for current RSV vaccination and monoclonal antibody recommendations

Cullen Family

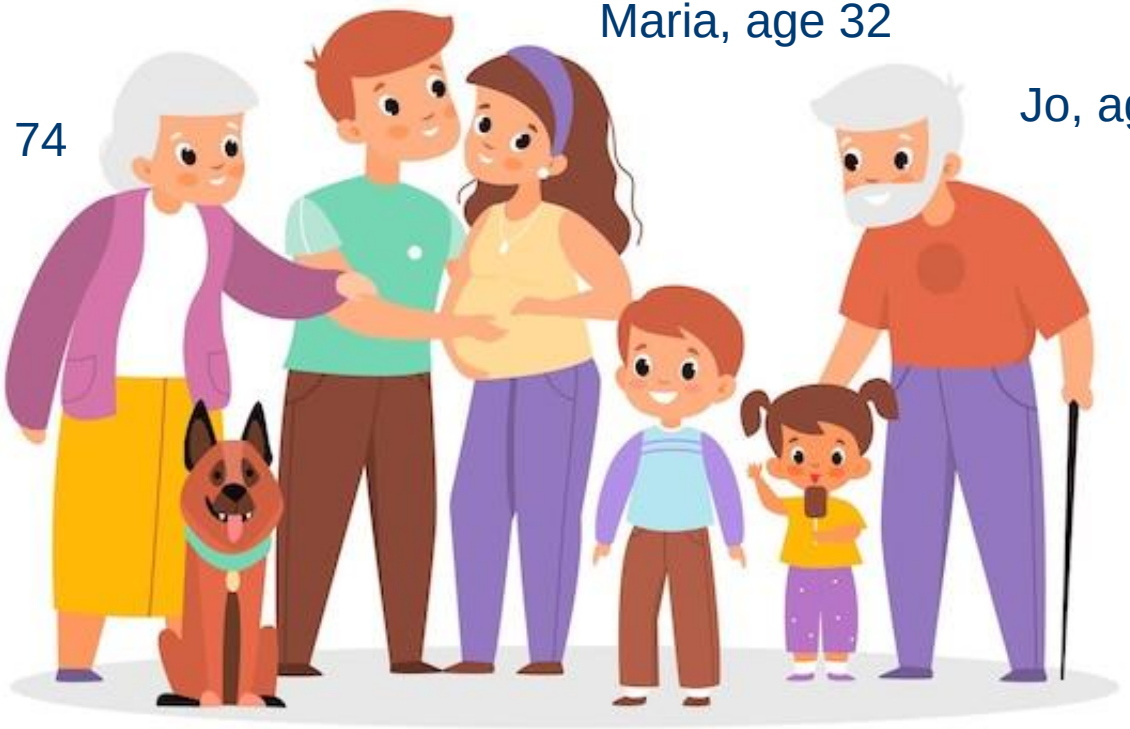
Jeff, age 33

Maria, age 32

Grace, age 74

Jo, age 76

Chase, age 5



Bo, age 4

Miya, age 2


November 2023
SUNDAY
MONDAY
TUESDAY
WEDNESDAY
THURSDAY
FRIDAY
SATURDAY
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30

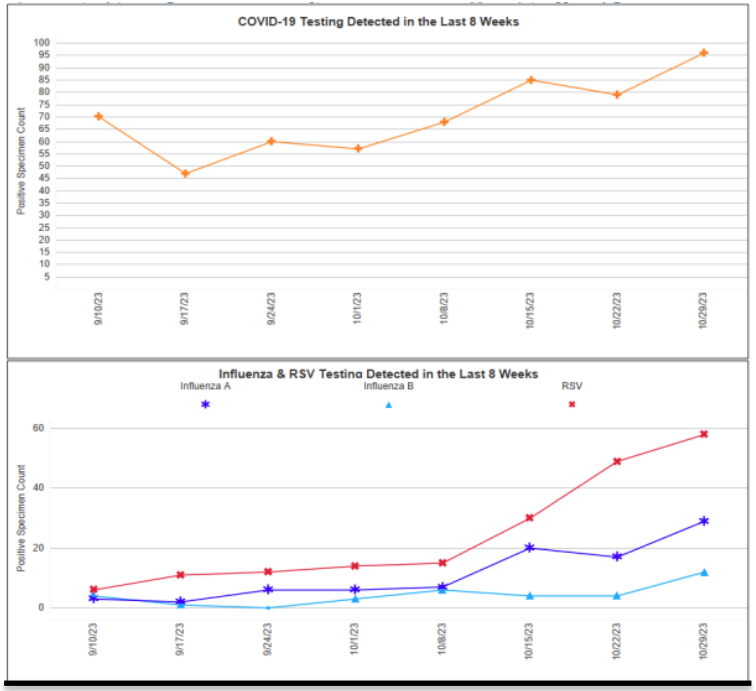
# Chase - 5 year well child check

- Moderate persistent asthma on fluticasone bid
- Allergies to peanuts, eggs (hives and swollen throat)
- Up to date with all pediatric vaccines except 5 year
- Has only received 1 influenza vaccine in his life at 6 months of age

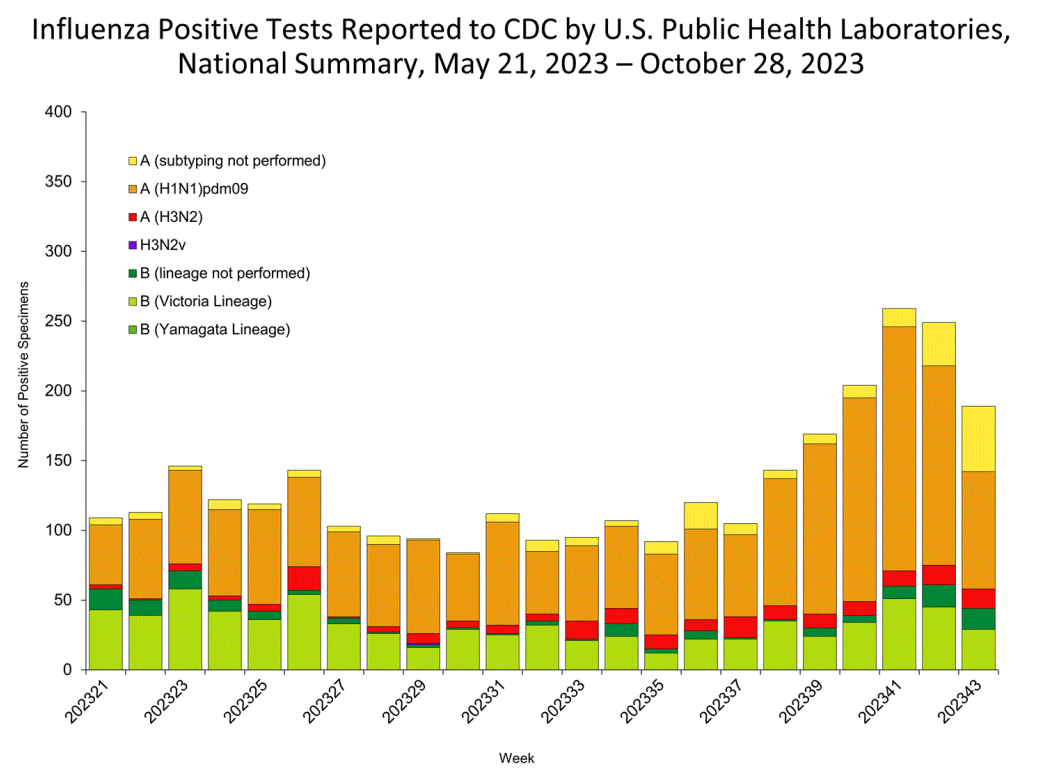
*“I don’t really want to do the flu vaccine for him given his allergy to eggs. Flu vaccines don’t work that well and it hasn’t been much of an issue anyways since the COVID pandemic”*


Influenza is back!

# Children's Hospital Colorado Data- Bug Watch



# Influenza circulation in the US, 2023

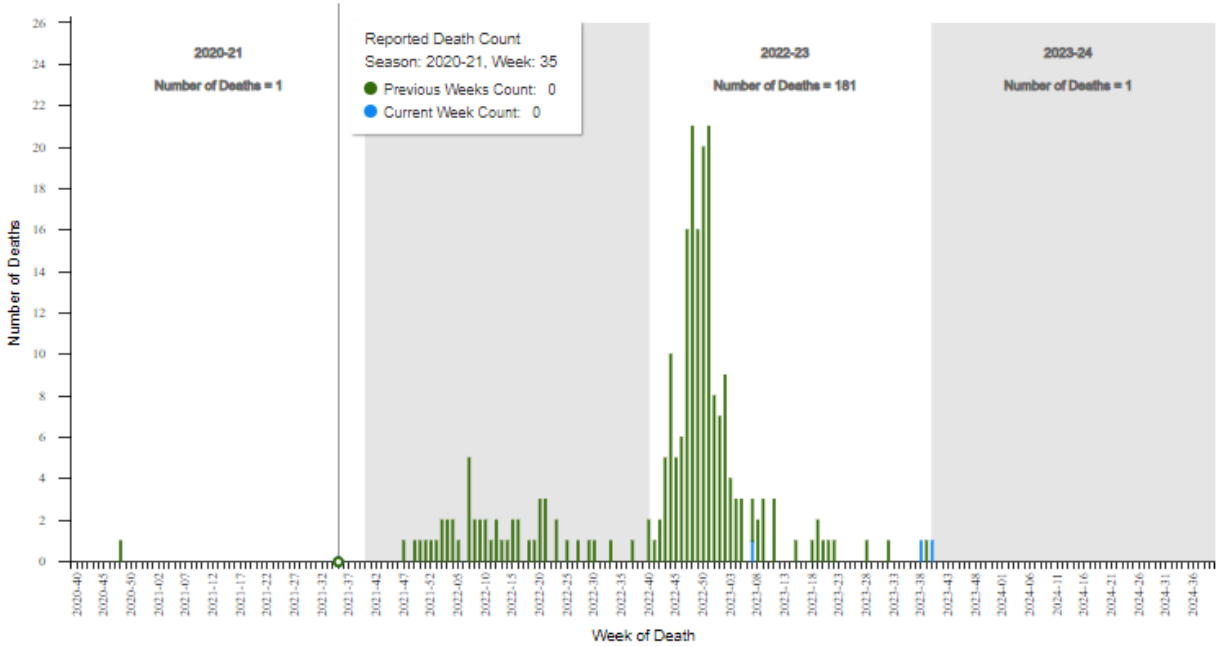



Children's Hospital Colorado
Here, it's different.™

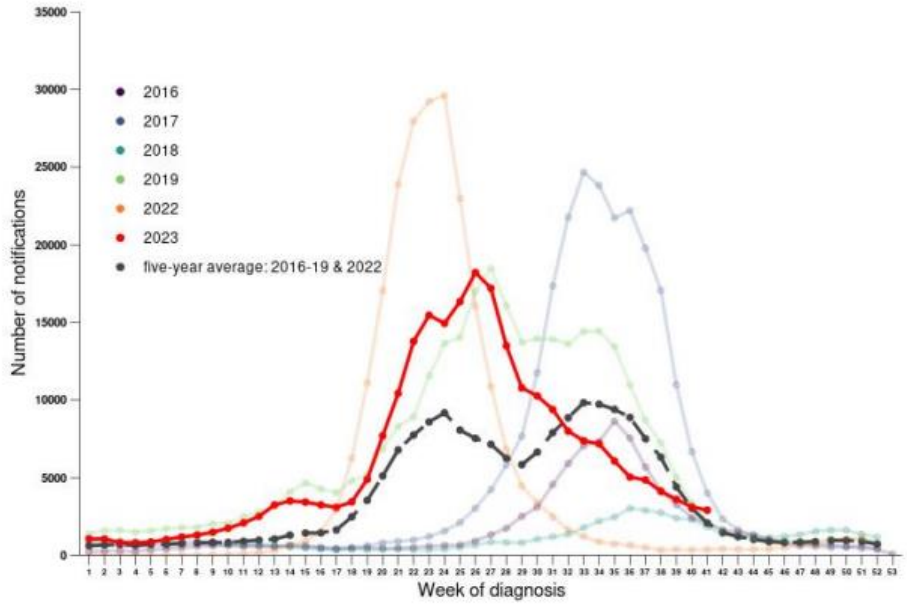
Affiliated with
School of Medicine
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

https://www.cdc.gov/flu/weekly/index.htm

# Pediatric Influenza mortality over 4 seasons



# Influenza circulation in Southern Hemisphere




**Source:** NNDSS

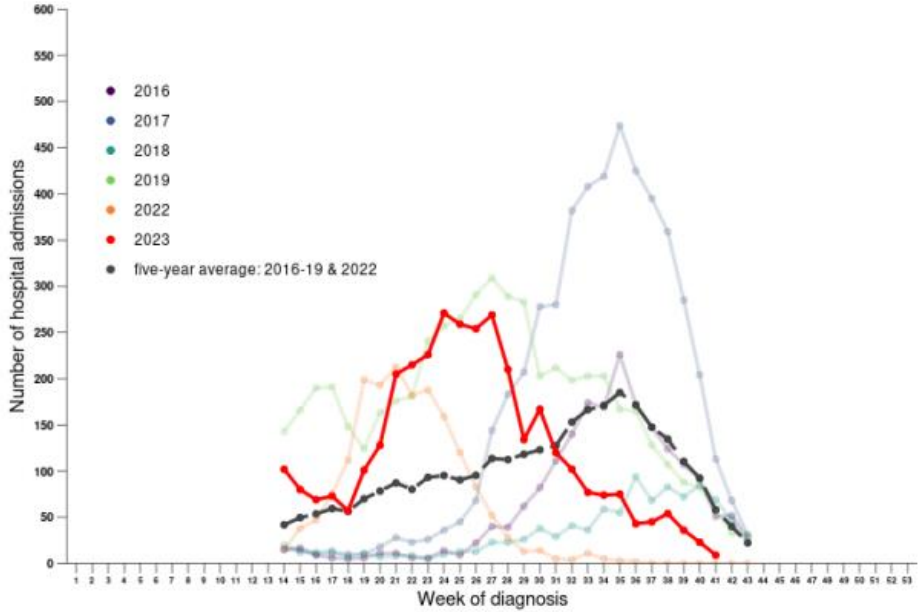
Earlier peak during April to May, compared to typical peaks in June to July.

Of the specimens that tested positive for Influenza, approximately 90% of the viruses were Influenza Type A and 10% were Influenza Type B

Children's Hospital Colorado
Here, it's different.™

Affiliated with
School of Medicine
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

# Influenza circulation in Southern Hemisphere




**Source:** FluCAN

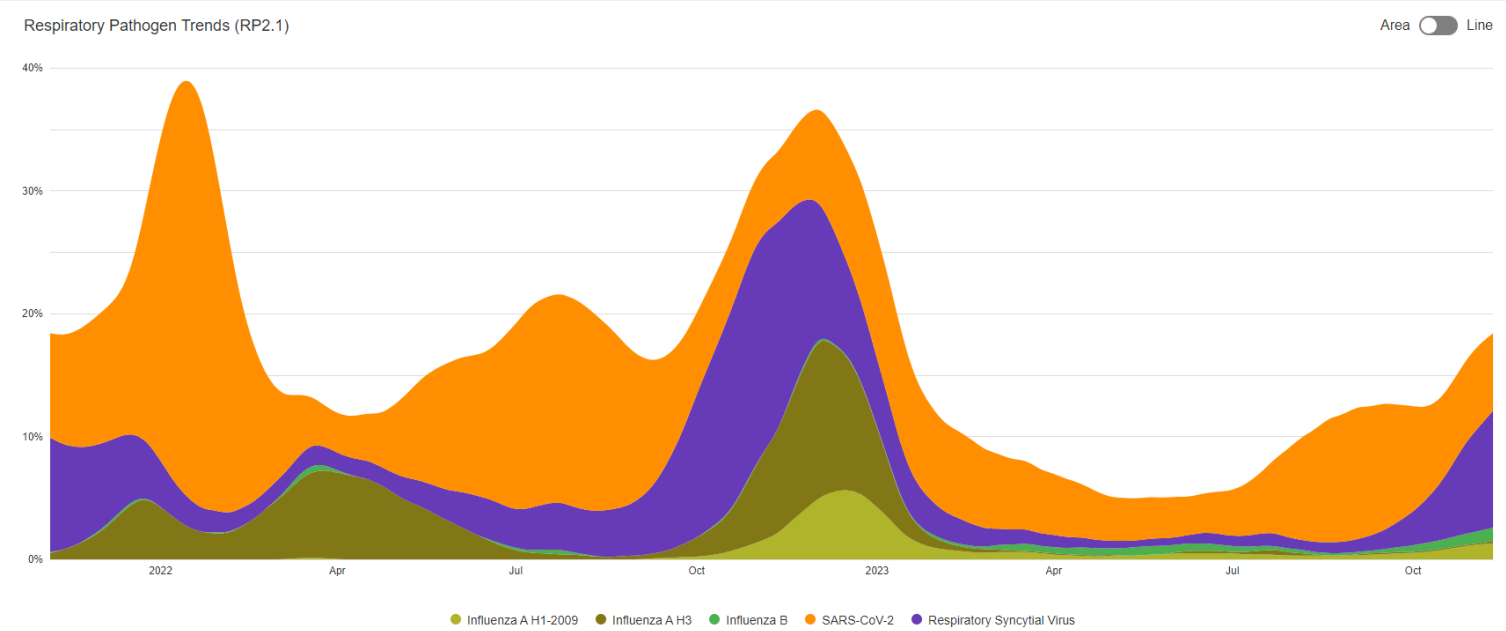
75% of hospitalizations in Australia were in children < 5 years of age

Vaccine uptake decreased by 50% in children during the 2023 season

Children's Hospital Colorado
Here, it's different.™

Affiliated with
School of Medicine
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

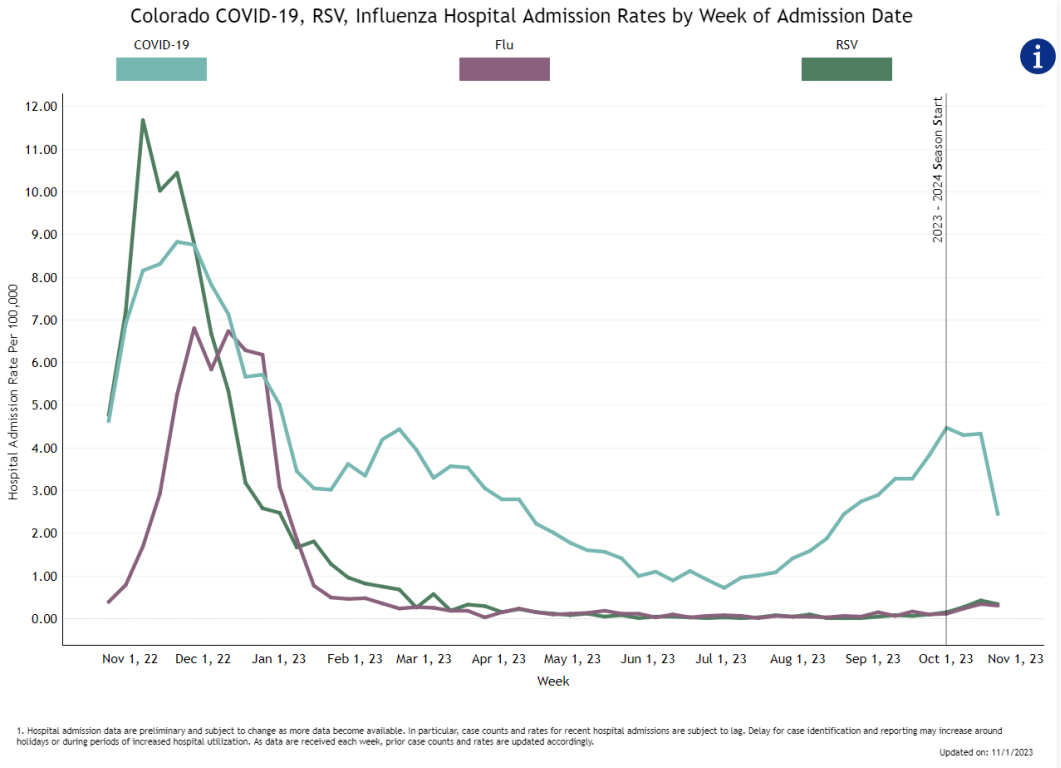
# Influenza, RSV and COVID Co-circulation- 2022-2023




Children's Hospital Colorado
Here, it's different.™

Affiliated with
School of Medicine
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

# Influenza, RSV and COVID circulation in Colorado, 2023

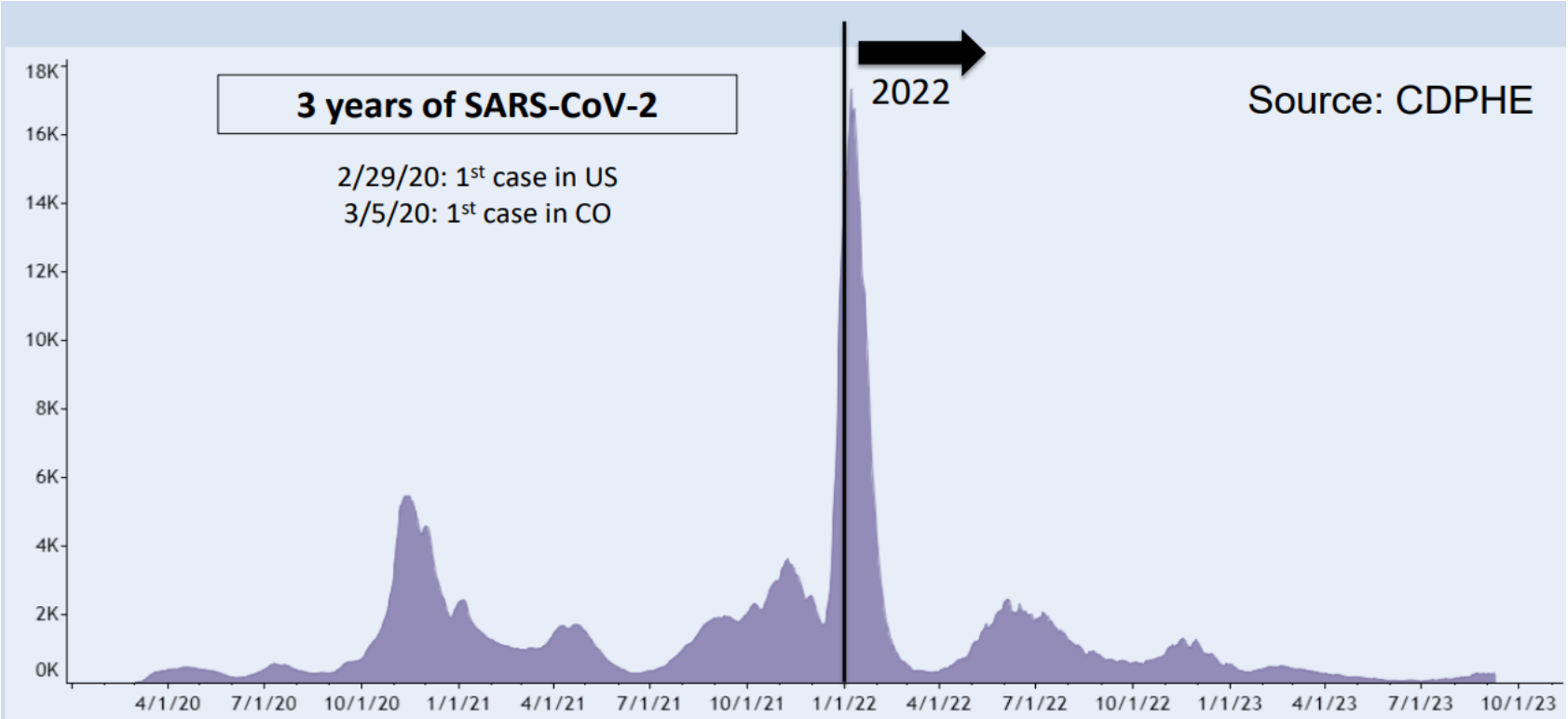



Children's Hospital Colorado
Here, it's different.™

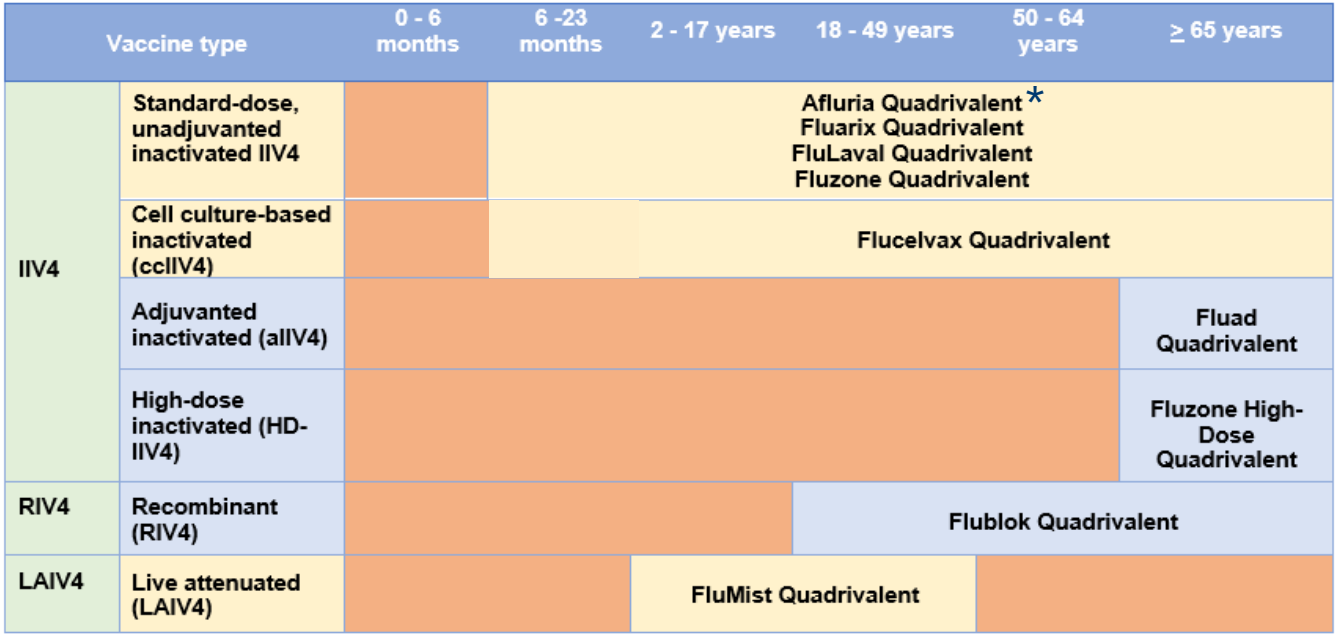
Affiliated with
School of Medicine
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

https://cdphe.colorado.gov/viral-respiratory-diseases-report

# RSV circulation since SARS-CoV-2 in Colorado



# Influenza vaccines by age indication 2023-24 season




Indicated for pediatric population

* Afluria 6-36 months 0.25 mL dosing, all others 0.5 mL

# Pediatric vaccines – IIV4, ccIIV4, LAIV4

| Vaccine type | | 0 - 6 months | 6 -23 months | 2 - 17 years | 18 - 49 years | 50 - 64 years | ≥ 65 years |
|---|---|---|---|---|---|---|---|
| IIV4 | Standard-dose, unadjuvanted inactivated IIV4 | | Afluria Quadrivalent * Fluarix Quadrivalent FluLaval Quadrivalent Fluzone Quadrivalent | | | | |
| | Cell culture-based inactivated (ccIIV4) | | Flucelvax Quadrivalent | | | | |
| | Adjuvanted inactivated (aIIV4) | | | | | | Fluad Quadrivalent |
| | High-dose inactivated (HD-IIV4) | | | | | | Fluzone High-Dose Quadrivalent |
| RIV4 | Recombinant (RIV4) | | | | Flublok Quadrivalent | | |
| LAIV4 | Live attenuated (LAIV4) | | | FluMist Quadrivalent | | | |

Indicated for pediatric population

* Afluria 6-36 months 0.25 mL dosing, all others 0.5 mL

# Influenza vaccines and egg allergies

All persons aged ≥6 months with egg allergy should receive influenza vaccine

Any influenza vaccine (egg based or non-egg based) that is otherwise appropriate for the recipient's age and health status can be used

~~Persons who have had an allergic reaction to egg involving symptoms other than urticaria should be vaccinated in an inpatient or outpatient medical setting supervised by a health care provider who is able to recognize and manage severe allergic reactions~~

# Why is it safe?

- Safe administration of injectable influenza vaccine (containing up to 0.7 mcg ovalbumin per 0.5 mL dose) to over 4000 individuals with egg allergy has been reported, even in those who have history of anaphylaxis to eggs
- Amount of egg protein in a flu vaccine - ≤1 mcg per 0.5 mL dose
- Independent investigators found it to be even lower than manufacturer's claims



https://www.cdc.gov/vaccines/acip/recs/grade/influenza-egg-allergy.html
https://www.cdc.gov/flu/prevent/vaccinesafety.htm

# How effective is the influenza vaccine? 2022-2023 data

| | Influenza positive | | Influenza negative[1] | | Adjusted[2] | |
|---|---|---|---|---|---|---|
| | N vaccinated /Total | (%) | N vaccinated /Total | (%) | VE % | 95% CI |
| **Influenza A All 6 mos – 17 years** | 123/640 | 19 | 750/2256 | 33 | **49** | (36 to 60) |
| **Inpatient** | 19/131 | 15 | 288/913 | 32 | **68** | (46 to 81) |
| **ED** | 104/507 | 21 | 461/1330 | 35 | **42** | (25 to 56) |
| **A/H3N2** | 98/478 | 21 | 750/2256 | 33 | **45** | (29 to 58) |
| **A/H1N1pdm09** | 23/139 | 17 | 750/2256 | 33 | **56** | (28 to 72) |

Children's Hospital Colorado
Here, it's different.™

Affiliated with
School of Medicine
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

**Source: NVSN**
**Vaccine effectiveness against laboratory confirmed influenza A in inpatient and emergency department (ED) settings, September 13, 2022-January 25, 2023**

# Vaccine effectiveness in children 2022-23

Southern Hemisphere data:
VE against hospitalization 52%,
55% against A(H1N1)
(MMWR September 15, 2023 / 72(37);1010–1015)

US Data Interim VE 71% for preventing symptomatic influenza A illness among <18 years
(MMWR Morb Mortal Wkly Rep 2023;72:201–205)

US Data: VE 48% against ED/UC and 40% against hospitalization
(Adams et al. 2023 CID in press)

# Decreased risk of hospitalization, death and ICU admission

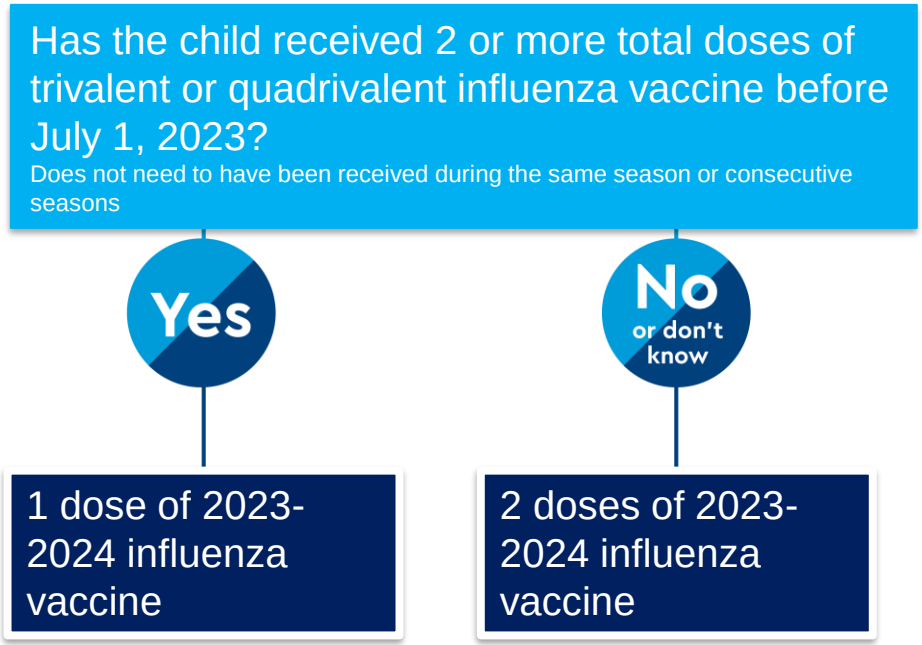
- Influenza vaccination can decrease your risk of being hospitalized by 68%
- Influenza vaccination can decrease the risk of a child being admitted to the ICU by 74%, and an adult by 82%
- Influenza vaccination can decrease a child's risk of dying from the flu by 65%

Children's Hospital Colorado
Here, it's different.™

Affiliated with
School of Medicine
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

Flannery et al. Pediatrics May 2017, 139 (5) e20164244
Feldstein JPIDS 2020; Segaloff CID 2019 69(12):2153-2161; Blyth et al. Vaccine 2020;38(13):2779–2787;
Kaalligeros M et al. Vaccine 2020;38(14):2893–2903

# Number of Doses for children < 9 years of age




Children's Hospital Colorado
Here, it's different.™

Affiliated with
School of Medicine
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS


November 2023
SUNDAY
MONDAY
TUESDAY
WEDNESDAY
THURSDAY
FRIDAY
SATURDAY
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30

# Miya- 2 year old sick visit

Born at term, no significant PMH

Up to date with all vaccines except COVID

Has had cough, coryza, congestion for 2 days with fever up to 103

Good po intake, alert

- How reliable is influenza testing in the office?
- If it is positive, should you start oseltamivir?
- Is there anyone in the family who would benefit from prophylaxis?
- Can she still get her COVID vaccines this visit?

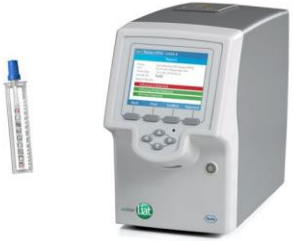
# Whom to test depends on how results will affect clinical management

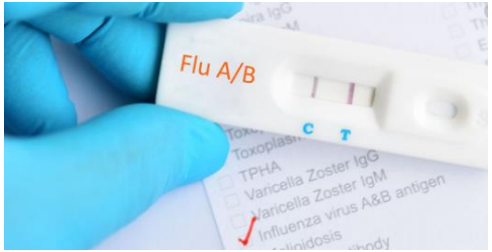
- Turnaround time of tests
- Patient's illness severity
- Disease prevalence
- Availability of other ancillary test results
- Co-morbidities, risk factors
- Public health and infection control considerations
- Duration of symptoms
- Types of testing available



Hanson et al CID 2020
Rao S. Curr Opin Infect Dis. 2014 Aug;27(4):342-7

# Testing






Point of care tests

PCR | NAAT | DIA | RIDT

Decreasing sensitivity

Children's Hospital Colorado
Here, it's different.™

Affiliated with
School of Medicine
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

Source: Google images

REVIEW

Annals of Internal Medicine

# Diagnostic Accuracy of Novel and Traditional Rapid Tests for Influenza Infection Compared With Reverse Transcriptase Polymerase Chain Reaction

## A Systematic Review and Meta-analysis

Joanna Merckx, MD, MSc; Rehab Wali, BSc, MBBS; Ian Schiller, MSc; Chelsea Caya, MScPH; Genevieve C. Gore, MLIS; Caroline Chartrand, MD, MSc; Nandini Dendukuri, PhD; and Jesse Papenburg, MD, MSc

Increasing sensitivity

| | Influenza A | Influenza B |
|---|---|---|
| RIDT | 54.4% (95% credible interval [CrI], 48.9% to 59.8%) | 53.2% (CrI, 41.7% to 64.4%) |
| DIA | 80.0% (CrI, 73.4% to 85.6%) | 76.8% (CrI, 65.4% to 85.4%) |
| NAATs | 91.6% (CrI, 84.9% to 95.9%) | 95.4% (CrI, 87.3% to 98.7%) |
| PCR | Reference standard | Reference standard |

*Table 2.* Overall and Subgroup Analyses of Pooled Rapid Test Accuracy Estimates for Influenza A and B, by Index Test Type*

| Index Test Type | Influenza A | | Influenza B | |
|---|---|---|---|---|
| | Pooled Sensitivity (95% CrI), % | Pooled Specificity (95% CrI), % | Pooled Sensitivity (95% CrI), % | Pooled Specificity (95% CrI), % |
| **Subgroup analyses†** | | | | |
| Study population (age)‡ | | | | |
| Traditional RIDTs | | | | |
| Children (31 influenza A studies; 9 influenza B studies) | 61.2 (55.0 to 67.2) | 99.2 (98.5 to 99.7) | 65.7 (45.3 to 80.5) | 99.6 (99.2 to 99.8) |
| Adults (23 influenza A studies; 5 influenza B studies) | 42.6 (34.8 to 50.9) | 99.5 (98.6 to 99.8) | 33.2 (19.9 to 50.7) | 99.9 (99.4 to 100) |
| Difference in RIDT sensitivity: children vs. adults | **18.5 (8.4 to 28.3)** | – | **31.8 (6.1 to 52.6)** | – |
| DIAs | | | | |
| Children (11 influenza A studies; 11 influenza B studies) | 87.6 (81.8 to 92.2) | 98.1 (96.4 to 99.1) | 82.5 (71.2 to 90.2) | 98.8 (95.6 to 99.7) |
| Adults (8 influenza A studies; 7 influenza B studies) | 75.4 (66.6 to 82.6) | 96.7 (94.7 to 98.0) | 57.0 (39.5 to 71.6) | 98.8 (97.5 to 99.5) |
| Difference in DIA sensitivity: children vs. adults | **12.1 (3.1 to 22.1)** | – | **25.3 (6.9 to 44.7)** | – |
| Rapid NAATs | | | | |
| Children (4 influenza A studies; 4 influenza B studies) | 90.2 (79.2 to 95.8) | 99.0 (96.8 to 99.8) | 95.9 (82.9 to 99.2) | 99.5 (98.2 to 99.9) |
| Adults (4 influenza A studies; 4 influenza B studies) | 87.4 (71.1 to 95.6) | 98.0 (93.2 to 99.5) | 75.7 (51.8 to 90.7) | 99.3 (97.8 to 99.8) |
| Difference in NAAT sensitivity: children vs. adults | 2.7 (−10.7 to 19.7) | – | **19.5 (1.0 to 43.7)** | – |

# My Take

- Traditional RIDTs being phased out -poor sensitivity
- RIDTs now need to demonstrate sensitivity and specificity of at least 80%
- DIAs are simple, fast and more reliable than RIDTs, but NAAT have highest sensitivity, specificity
- Can diagnose influenza on the basis of a positive RIDT, DIA, or rapid NAAT result during influenza season, less reliable outside season
- Newer testing options including combined SARS-CoV-2/influenza/RSV

# Back to Miya…

You test Miya with the NAAT SARS-CoV-2/RSV/Influenza test

Result: Influenza A positive

Will you treat with oseltamivir?

Is there anyone in the family who would benefit from prophylaxis?

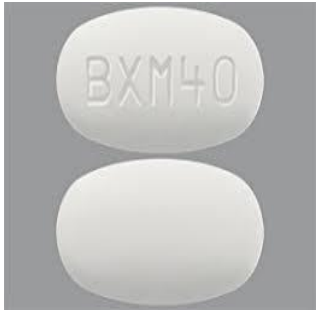
Can she still get her COVID vaccines this visit?

# Influenza Treatment


oseltamivir

zanamivir

peramivir




baloxavir

# Influenza Treatment


## oseltamivir

**14 d-3 mo** 3 mg/kg/dose bid X 5 days

**3-12 months:** 3 mg/kg/dose bid

**Children 1-12 years:**

≤ 15 kg: 30 mg/dose bid

> 15-23 kg: 45 mg/dose bid

>23-40 kg: 60 mg/dose bid

>40 kg: 75 mg/dose bid

**Children > 13 years and adults:**

75 mg/dose bid

SE: nausea, vomiting, behavioral change

## zanamivir

Two inhalations (10 mg) twice daily X 5 days

7 years of age and older

Not recommended in patients with underlying airway disease due to risk of bronchospasm. Contraindicated in those with milk-protein allergy

## peramivir

Children 6 months-12 years: 12 mg/kg once daily IV

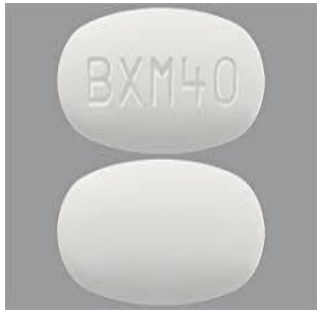
13 years and older: 600 mg once daily IV

Treat for 5-10 days (ID consult)

Monitor renal function

Diarrhea, behavioral changes, neutropenia

Not superior to oseltamivir, so given if unable to provide enteral oseltamivir




## baloxavir

Children 5 years of age and older:

<20kg: 2mg/kg as a single dose using the suspension formulation

20 to <80 kg: 40 mg as a single dose

>80 kg: 80 mg as a single dose

Well tolerated

Avoid administration with dairy, calcium fortified drinks or polyvalent cations

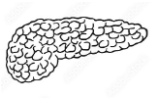
# Which patients should be treated with influenza antivirals?

- Hospitalized with influenza
- Outpatients with severe or progressive illness
- Outpatients who are high risk of complications
- Consider: Outpatients within 2 days of illness onset
- Consider: Children with high-risk household contacts, esp. immunocompromised



Source: CDC, IDSA guidelines

# High Risk Conditions – influenza vs COVID-19 vs RSV

| | Influenza | COVID-19 | RSV |
|---|---|---|---|
| Age | < 5 (especially < 2)<br>≥ 65 years | > 65 years | < 12 months especially < 6 months<br>Premature infants<br>> 65 year olds |
|  | Chronic pulmonary including asthma | Asthma, ILD, PE, bronchiectasis, pulmonary hypertension, bronchiectasis, COPD, CF, TB | < 2 years or adults with chronic lung disease |
|  | Cardiovascular | e.g. heart failure, coronary artery disease, or cardiomyopathies | < 2 years with congenital heart disease<br>Adults with chronic heart disease |
|  | Renal, hepatic, hematologic | Cirrhosis, non-alcoholic fatty liver disease, alcoholic liver disease, autoimmune hepatitis, kidney disease | > 60 years renal, hepatic, hematologic |
|  | Metabolic disorders including diabetes mellitus, obesity | Diabetes type 1 and 2, **obesity** | > 60 years diabetes mellitus |
|  | Neurologic and neurodevelopmental conditions | ADHD, CP, Congenital malformations, developmental disabilities, learning disabilities, spinal cord injuries, dementia, cerebrovascular disease | Neuromuscular disorders |

# High Risk Conditions- – influenza vs COVID-19 vs RSV

| | Influenza | COVID-19 | RSV |
|---|---|---|---|
| Immunosuppression | Immunosuppression | Immunosuppression | Immunosuppression |
| Pregnancy | Pregnancy and 2 weeks post-partum | Pregnancy and 2 weeks post-partum | |
| Race/ethnicity | Native Americans/Alaska Natives | Black/African American, Native American/Alaska Native, Hispanic/Latinx | Native American/Alaska Natives |
| Medications | Long term aspirin therapy | | |
| Mental Health Disorders | | Mood disorders including depression, schizophrenia spectrum disorders | |
| Behavioral factors | | Physical inactivity<br>Smoking, current and former | Reside in nursing homes or other long-term care facilities |
| Medical complexity | | Medical complexity with technology dependence | |



https://www.cdc.gov/flu/highrisk/index.htm

https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html

# Treatment – how effective are influenza antivirals?

**Cochrane review – 6 RCT (2356 children) and 5 new RCTs (1598 children)**

Oseltamivir can decrease illness duration by 1.5 days

Oseltamivir can decrease risk of acute otitis media in children 1-5 yrs

Zanamivir can decrease illness duration by 1.3 days

**Reduction in influenza-associated deaths**

If given within 48 hrs of illness onset, aOR 0.37; 95% CI, 0.22 to 0.63
If given within 5 days, of illness onset, aOR 0.5; 95% CI, 0.32 to 0.79

**Reduction in hospital LOS- PHIS data**

If given within 24 hrs of hospitalization, 18% reduction in total hospital days (Time Ratio: 0.82, p=0.02)

**Reduction in transmission**

If given within 48 hrs of illness onset, reduced viral shedding (12% vs 6%, p = 0.0009)

Wang K et al. Cochrane Database Syst Rev. 2012;(4):CD002744;
Jefferson T, et al.. Cochrane Database Syst Rev. 2014;(4):CD008965;
Coffin SE et al. Pediatr Infect Dis J. 2011;30(11):962-6
Domínguez A et al. Epidemiol Infect. 2018;146(7):799–808
Hayden et al. CID July 10 2021; Fry et al. Lancet Infectious Diseases 14 (2) P109-118

# Treatment – how effective are antivirals?

**Cochrane review – 6 RCT (2356 children) and 5 new RCTs (1598 children)**

Oseltamivir can decrease illness duration by 1.5 days

Oseltamivir can decrease risk of acute otitis media in children 1-5 yrs

Zanamivir can decrease illness duration by 1.3 days

**Reduction in influenza-associated deaths**

If given within 48 hrs of illness onset, aOR 0.37; 95% CI, 0.22 to 0.63
If given within 5 days, of illness onset, aOR 0.5; 95% CI, 0.32 to 0.79

**Reduction in hospital LOS**

If given within 24 hrs of hospitalization, 18% reduction in total hospital days (Time Ratio: 0.82, p=0.02)

**Reduction in transmission**

If given within 48 hrs of illness onset, reduced viral shedding (12% vs 6%, p = 0.0009)

Wang K et al. Cochrane Database Syst Rev. 2012;(4):CD002744;
Jefferson T, et al.. Cochrane Database Syst Rev. 2014;(4):CD008965;
Coffin SE et al. Pediatr Infect Dis J. 2011;30(11):962-6
Domínguez A et al. Epidemiol Infect. 2018;146(7):799–808
Hayden et al. CID July 10 2021; Fry et al. Lancet Infectious Diseases 14 (2) P109-118

# Treatment – how effective are antivirals?

**Cochrane review – 6 RCT (2356 children) and 5 new RCTs (1598 children)**

Oseltamivir can decrease illness duration by 1.5 days

Oseltamivir can decrease risk of acute otitis media in children 1-5 yrs

Zanamivir can decrease illness duration by 1.3 days

**Reduction in influenza-associated deaths**

If given within 48 hrs of illness onset, aOR 0.37; 95% CI, 0.22 to 0.63
If given within 5 days, of illness onset, aOR 0.5; 95% CI, 0.32 to 0.79

**Reduction in hospital LOS- PHIS data**

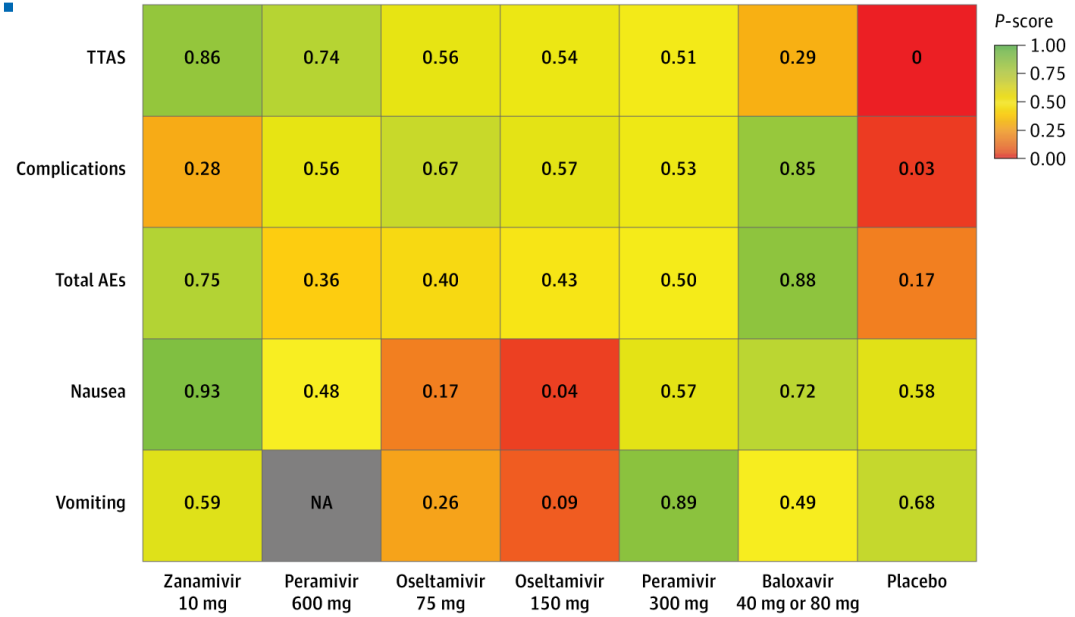
If given within 24 hrs of hospitalization, 18% reduction in total hospital days (Time Ratio: 0.82, p=0.02)

**Reduction in transmission**

If given within 48 hrs of illness onset, reduced viral shedding (12% vs 6%, p = 0.0009)

Wang K et al. Cochrane Database Syst Rev. 2012;(4):CD002744;
Jefferson T, et al.. Cochrane Database Syst Rev. 2014;(4):CD008965;
Coffin SE et al. Pediatr Infect Dis J. 2011;30(11):962-6
Domínguez A et al. Epidemiol Infect. 2018;146(7):799–808
Hayden et al. CID July 10 2021; Fry et al. Lancet Infectious Diseases 14 (2) P109-118

# Which antiviral is associated with the most safety and best outcomes among healthy adults and children?




Children's Hospital Colorado
Here, it's different.

Affiliated with
School of Medicine
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

JAMA Netw Open. 2021;4(8):e2119151.
doi:10.1001/jamanetworkopen.2021.19151

# Which patients should be treated with influenza antivirals?

- Hospitalized with influenza
- Outpatients with severe or progressive illness
- Outpatients who are high risk of complications
- Pregnant women and those within 2 weeks postpartum
- Consider: Outpatients within 2 days of illness onset
- Consider: Children with high-risk household contacts, esp. immunocompromised



Source: CDC, IDSA guidelines

# Influenza Treatment


## oseltamivir

**14 d-3 mo** 3 mg/kg/dose bid X 5 days

**3-12 months:** 3 mg/kg/dose bid

**Children 1-12 years:**

≤ 15 kg: 30 mg/dose bid

> 15-23 kg: 45 mg/dose bid

>23-40 kg: 60 mg/dose bid

>40 kg: 75 mg/dose bid

**Children > 13 years and adults:**

75 mg/dose bid

SE: nausea, vomiting, behavioral change

## zanamivir

Two inhalations (10 mg) twice daily X 5 days

7 years of age and older

Not recommended in patients with underlying airway disease due to risk of bronchospasm. Contraindicated in those with milk-protein allergy

## peramivir

Children 6 months-12 years: 12 mg/kg once daily IV

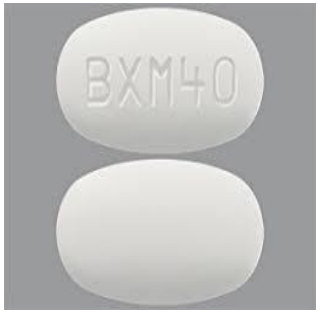
13 years and older: 600 mg once daily IV

Treat for 5-10 days (ID consult)

Monitor renal function

Diarrhea, behavioral changes, neutropenia

Not superior to oseltamivir, so given if unable to provide enteral oseltamivir




## baloxavir

Children 5 years of age and older:

<20kg: 2mg/kg as a single dose using the suspension formulation

20 to <80 kg: 40 mg as a single dose

>80 kg: 80 mg as a single dose

Well tolerated

Avoid administration with dairy, calcium fortified drinks or polyvalent cations

# Influenza chemoprophylaxis

Whom to prophylax?  High risk of influenza complications and exposure:

- during the first two weeks following vaccination after exposure
- cannot receive influenza vaccine due to a contraindication
- severe immune deficiencies or others who might not respond to influenza vaccination

How long to prophylax? 7 days from last exposure

- If not known, then 10 days
- Dosing is once a day compared with bid treatment dosing
- Can use oseltamivir, zanamivir, baloxavir (for those 12 yrs of age and older) within 48 hours of contact with an individual with influenza

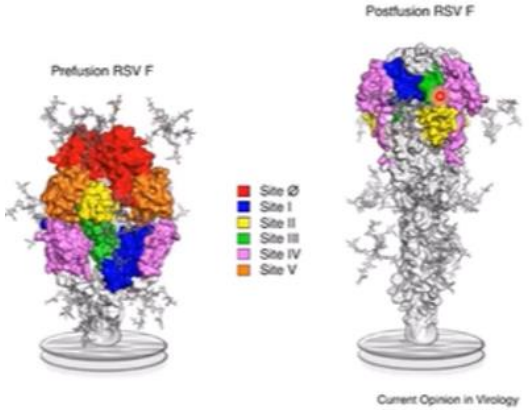
# Vaccination during acute illness

Influenza, RSV and other respiratory illnesses- safe to vaccinate against influenza and COVID-19

- Acute COVID-19 infection- visits should be deferred until the isolation period has ended
  - COVID + asymptomatic- might consider
  - COVID + mild- might consider deferring
  - moderate or severe COVID-19, vaccination - defer until they have recovered from the acute illness
  - COVID + on IL-6 inhibitors, high-dose steroids- recommend waiting until course completed

# A ‘quick’ question from Maria

*“I heard there are now RSV vaccines available for pregnant moms and other prevention products for babies now, should I wait until after I give birth or just take care of the vaccine now?”*




# RSV prevention

# RSV maternal vaccination

WHAT: RSVpreF vaccine (Abrysvo)

WHEN: 32-36 weeks' gestation so babies are protected against severe RSV disease at birth

WHY: MATISSE Trial phase 3, double-blind, randomized, placebo-controlled trial that was conducted in 18 countries over four RSV seasons (n = 7358), women enrolled at 24-36 weeks gestation

81.8% (99.5% CI, 40.6 to 96.3) against infant medically attended severe lower respiratory tract illness occurred within 90 days after birth (non severe 57.1% (40.6-84.1)

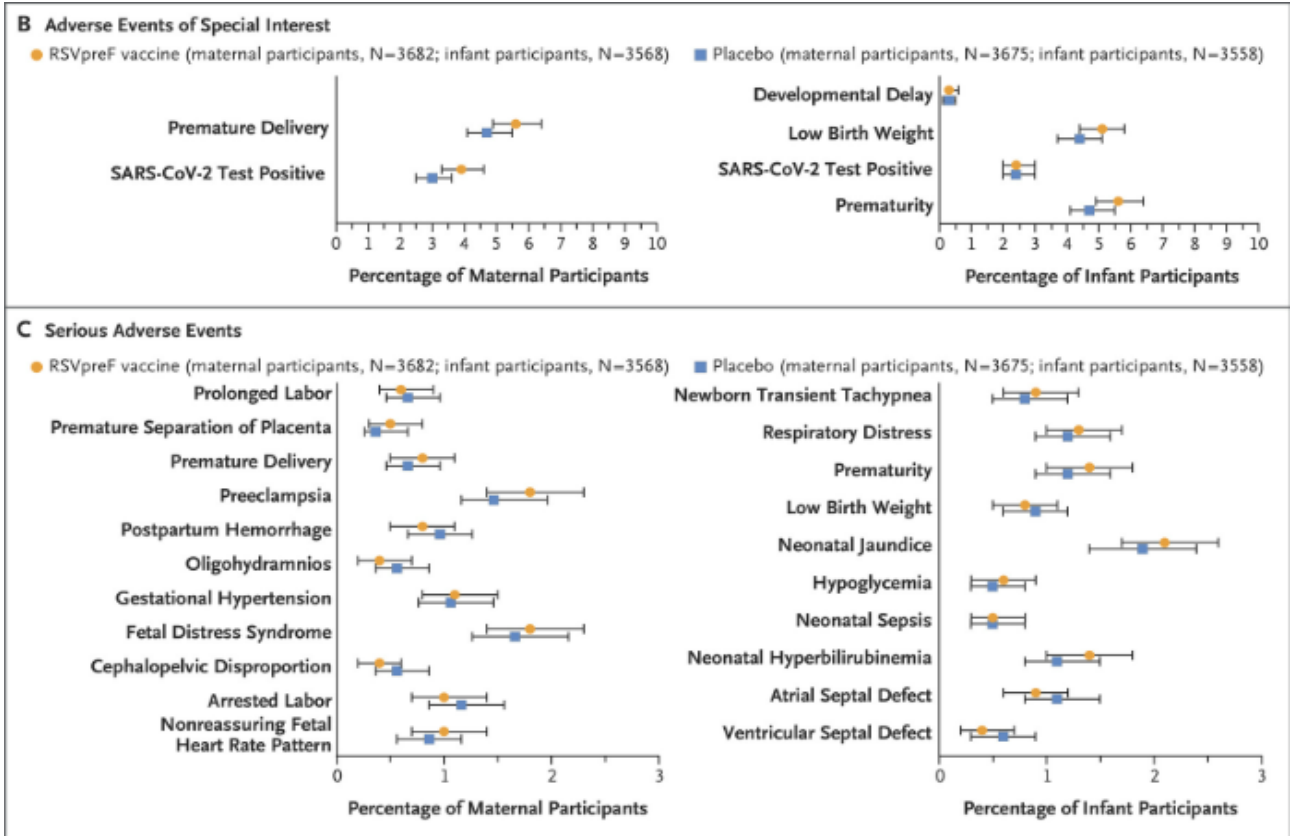
69.4% (97.58% CI, 44.3 to 84.1) against infant medically attended severe lower respiratory tract illness occurred within 6 months after birth (non severe 51.3% (29.4-66.8)

*Severe medically-attended LRTI
Fast breathing, Sats < 93%, high flow nasal cannula or mechanical ventilation, ICU admission for > 4 hours, failure to respond or unconscious

N Engl J Med 2023; 388:1451-1464

# Safety

Maternal vaccination reactogenicity- injection site pain, muscle pain, headache, similar to placebo group






N Engl J Med 2023; 388:1451-1464

# Nirsevimab in infants

WHAT: long-acting monoclonal antibody that locks subunits of the fusion protein, locks in prefusion confirmation to block viral entry

HOW: passive immunization to prevent RSV-associated lower respiratory tract disease among infants and young children

WHO:

NEW UPDATES

HOW MUCH:

- < 5 kg- 50 mg
- ≥5 kg and aged <8 months - 100 mg
- 8-19 months – 100 mg X2 (alternate sites)

WHY: MELODY Trial, phase 3, double-blind, randomized, placebo-controlled trial, 160 sites in 21 countries (n = 1490)

74.5% (99.5% CI, 49.6 to 87.1) against medically attended lower respiratory tract illness

62.1% (99.5% CI, −8.6 to 86.8) against hospitalization for lower respiratory tract illness

Antibodies detected at ~ 1 year in 6.1% of infants

Children's Hospital Colorado
Here, it's different.™

Affiliated with
School of Medicine
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS



N Engl J Med 2022; 386:837-846

# Safety

Low reactogenicity compared with vaccines

Trial safety data: 3.6% experienced side effects, rash within 14 days, injection site reaction within 7 days

CDC Best Practice Guidelines recommend deferring administration for patients with moderate or severe acute illness as a diagnostic precaution

Can be given even if infant had RSV infection this season

# Supply updates

Limited supply of nirsevimab 100 mg (for infants ≥ 5 kg)

Prioritizing available nirsevimab 100 mg doses for infants at the highest risk for severe RSV disease

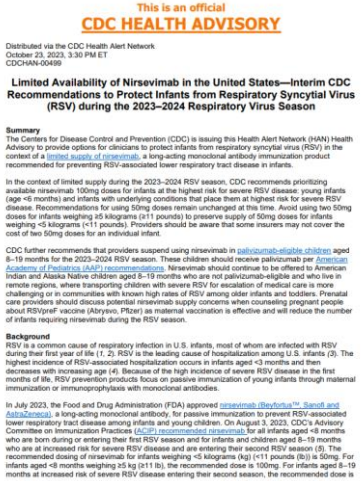
Avoid using 2x 50mg doses for infants ≥ 5 kg

Suspend using nirsevimab in palivizumab-eligible children aged 8–19 months for the 2023–2024 RSV season

Continue to offer Nirsevimab to American Indian and Alaska Native children aged 8–19 months who are not palivizumab eligible

If nirsevimab not available – use palivizumab if eligible in infants < 8 months

Take into account when counseling pregnant people about RSVpreF vaccine



This is an official
CDC HEALTH ADVISORY

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

**Summary**

The Centers for Disease Control and Prevention (CDC) is issuing this Health Alert Network (HAN) Health Advisory to provide options for clinicians to protect infants from respiratory syncytial virus (RSV) in the context of a limited supply of nirsevimab, a long-acting monoclonal antibody immunization product recommended for preventing RSV-associated lower respiratory tract disease in infants.

In the context of limited supply during the 2023–2024 RSV season, CDC recommends prioritizing available nirsevimab 100mg doses for infants at the highest risk for severe RSV disease: young infants (age <6 months) and infants with underlying conditions that place them at highest risk for severe RSV disease. Recommendations for using 50mg doses remain unchanged at this time. Avoid using two 50mg doses for infants weighing ≥5 kilograms (≥11 pounds) to preserve supply of 50mg doses for infants weighing <5 kilograms (<11 pounds). Providers should be aware that some insurers may not cover the cost of two 50mg doses for an individual infant.

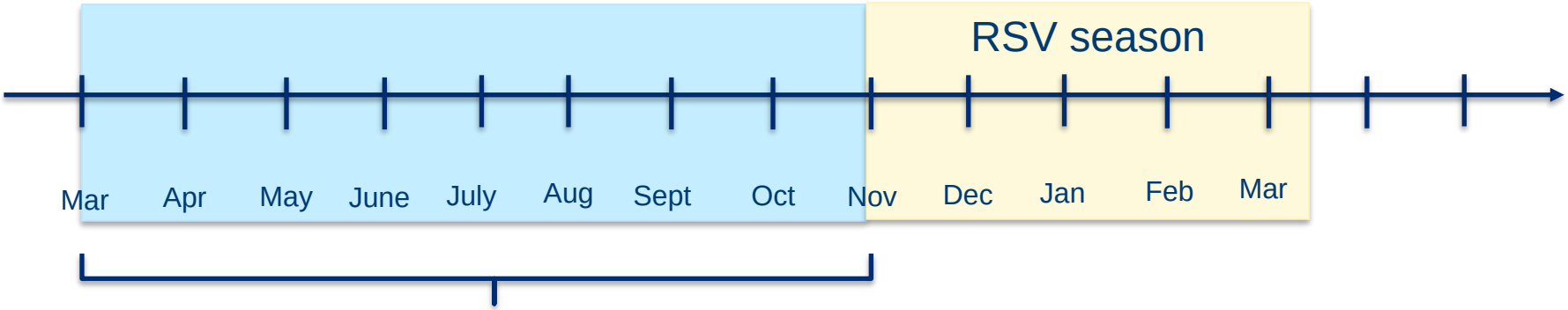
CDC further recommends that providers suspend using nirsevimab in palivizumab-eligible children aged 8–19 months for the 2023–2024 RSV season. These children should receive palivizumab per American Academy of Pediatrics (AAP) recommendations. Nirsevimab should continue to be offered to American Indian and Alaska Native children aged 8–19 months who are not palivizumab-eligible and who live in remote regions, where transporting children with severe RSV for escalation of medical care is more challenging or in communities with known high rates of RSV among older infants and toddlers. Prenatal care providers should discuss potential nirsevimab supply concerns when counseling pregnant people about RSVpreF vaccine (Abrysvo, Pfizer) as maternal vaccination is effective and will reduce the number of infants requiring nirsevimab during the RSV season.

**Background**

RSV is a common cause of respiratory infection in U.S. infants, most of whom are infected with RSV during their first year of life (*1, 2*). RSV is the leading cause of hospitalization among U.S. infants (*3*). The highest incidence of RSV-associated hospitalization occurs in infants aged <3 months and then decreases with increasing age (*4*). Because of the high incidence of severe RSV disease in the first months of life, RSV prevention products focus on passive immunization of young infants through maternal immunization or immunoprophylaxis with monoclonal antibodies.

In July 2023, the Food and Drug Administration (FDA) approved nirsevimab (Beyfortus™, Sanofi and AstraZeneca), a long-acting monoclonal antibody, for passive immunization to prevent RSV-associated lower respiratory tract disease among infants and young children. On August 3, 2023, CDC's Advisory Committee on Immunization Practices (ACIP) recommended nirsevimab for all infants aged <8 months who are born during or entering their first RSV season and for infants and children aged 8–19 months who are at increased risk for severe RSV disease and are entering their second RSV season (*5*). The recommended dosing of nirsevimab for infants weighing <5 kilograms (kg) (<11 pounds (lb)) is 50mg. For infants aged <8 months weighing ≥5 kg (≥11 lb), the recommended dose is 100mg. For infants aged 8–19 months at increased risk of severe RSV disease entering their second season, the recommended dose is

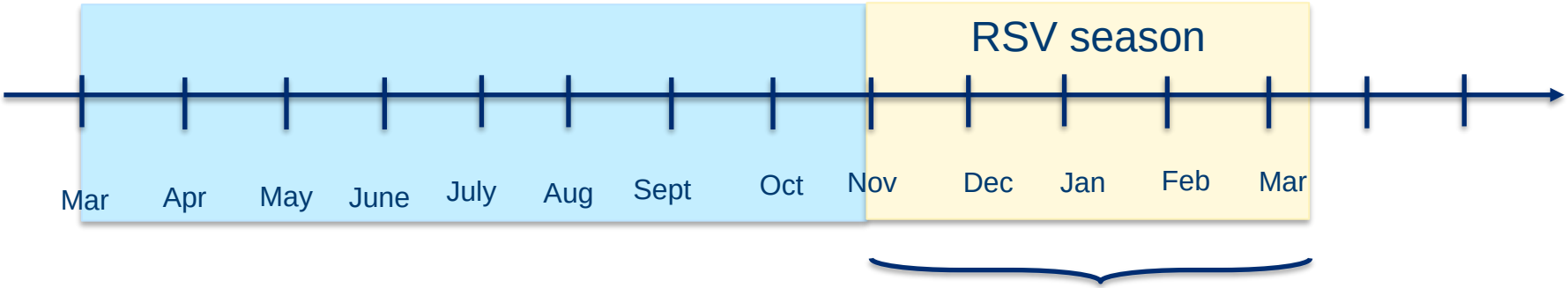
# Nirsevimab




< 8 months
≤ 5 kg

50 mg dose of nirsevimab now

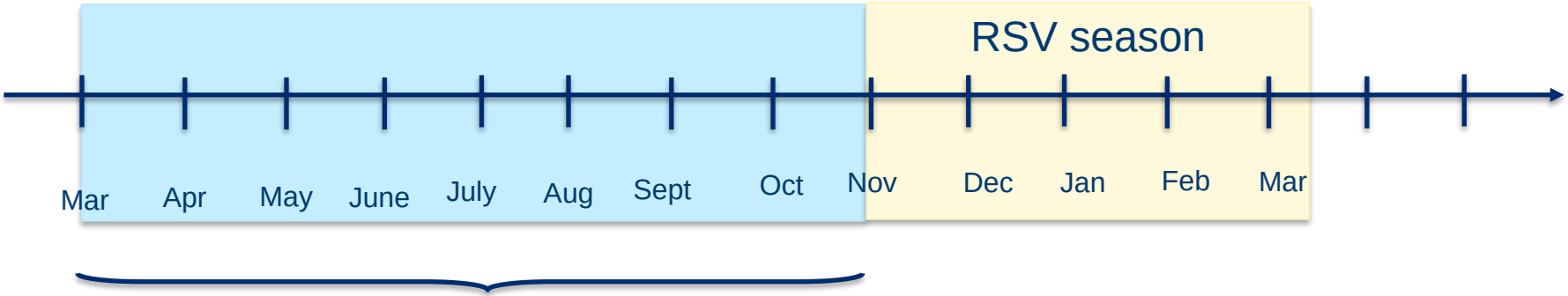
# Nirsevimab




< 8 months
≤ 5 kg

50 mg dose of nirsevimab in first week of life

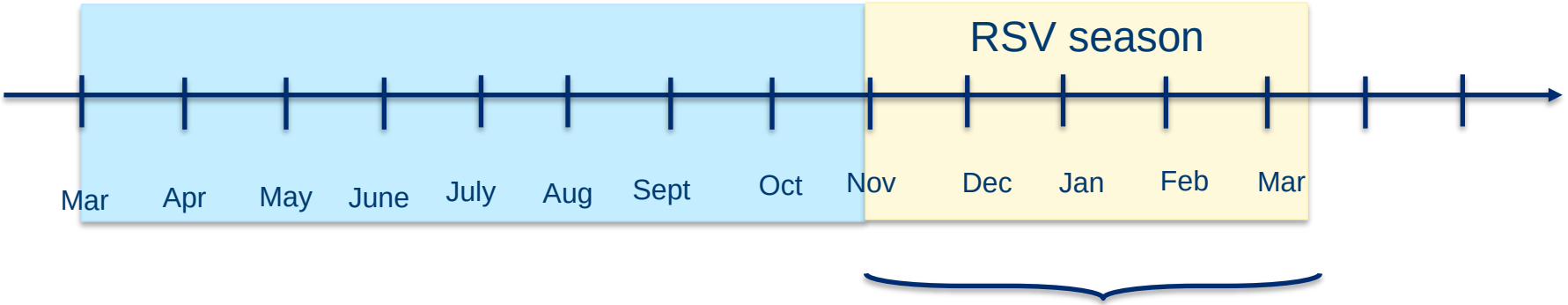
# Nirsevimab




< 8 months
≥ 5 kg

100 mg dose of nirsevimab now for all infants < 6 months and for those at highest risk of severe RSV disease

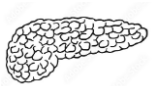
# Nirsevimab




< 8 months
≥ 5 kg

100mg dose of nirsevimab within first week of life for all infants < 6 months and for those at highest risk of severe RSV disease

# Infants at highest risk of severe RSV disease

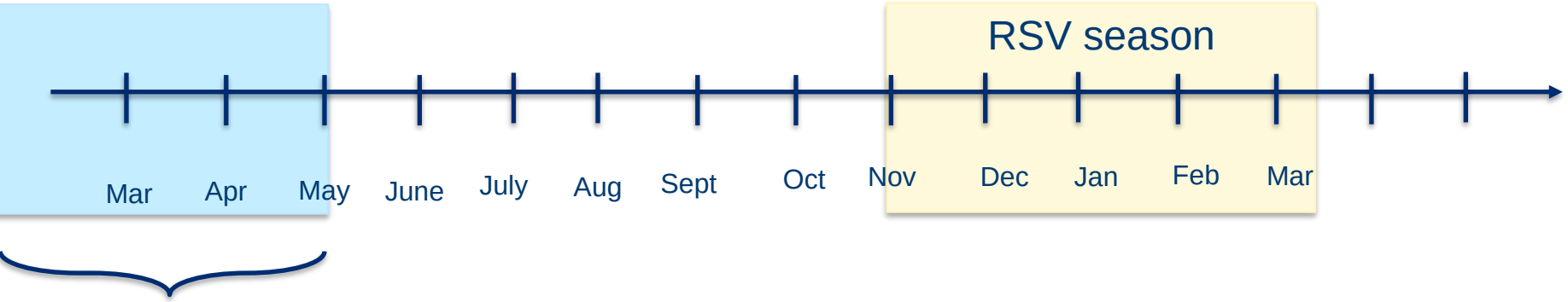
| | RSV |
|---|---|
| Age | **< 6 months** |
| | Premature birth < 29 weeks' gestation |
|  | Chronic lung disease of prematurity |
|  | Hemodynamically significant congenital heart disease |
|  | Severe immunocompromise |
|  | Severe cystic fibrosis (either manifestations of severe lung disease or weight-for-length less than 10th percentile) |
|  | neuromuscular disease or congenital pulmonary abnormalities that impair the ability to clear secretions |

Children's Hospital Colorado
Here, it's different.™

Affiliated with
School of Medicine
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

Source: https://**www.cdc.gov/coronavirus**/2019-ncov/hcp/clinical-care/underlyingconditions.html

# Palivizumab




8-19 months

Palivizumab if eligible

# Palivizumab

**< 1 year of age at time of first dose**

1. Born at less than 29 weeks estimated gestational age
2. Chronic lung disease of prematurity
3. Hemodynamically significant congenital heart disease (requiring medication to control congestive heart failure and/or oxygen therapy)
4. Moderate or severe pulmonary hypertension
5. Pulmonary or neuromuscular abnormalities that impair secretion clearance, not including cystic fibrosis or Down syndrome

**< 2 years of age at time of first dose**

1. Chronic lung disease of prematurity requiring supplemental oxygen, corticosteroid therapy, and/or regular or intermittent diuretics to treat pulmonary disease within the past six (6) months
2. Profound immune compromise due to one of the following:
   A. Immunosuppressive medications
   B. Disease states with severely impaired immune function

*Pediatrics* (2014) 134 (2): 415–420

# Nirsevimab at CHCO

Available at CHCO

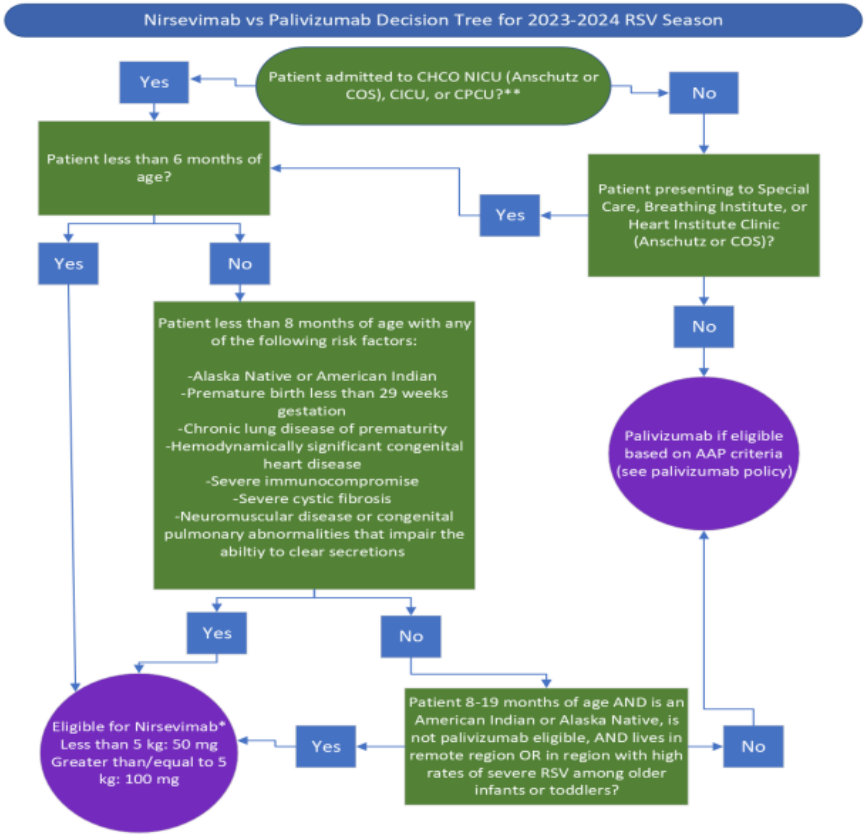
Reserved for infants < 6 months and infants with select underlying conditions

Offered at Anschutz and Colorado Springs

Inpatient: NICU, CICU, CPCU, L&D- ordered at discharge, not during hospital stay

Outpatient: Special Care Clinic, Breathing Institute, Heart Institute

Transplant patients in any areas




Children's Hospital Colorado
Here, it's different.™

Affiliated with
School of Medicine
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

# Another ‘quick’ question from Maria

*“Jeff’s parents are staying with me for the next few months to help out with the baby, should they get the RSV vaccine too?”*

# RSV vaccine in older adults

WHAT:

- RSVPreF3 (Arexvy)- recombinant RSV F protein antigen plus ASO1 adjuvant
- RSVpreF (Abrysvo)- recombinant RSV F protein antigen
- Single dose
- (contraindicated in those with history of anaphylaxis to component of vaccine)

WHO:

- Adults 60 years of age and older
- May receive a single dose of RSV vaccine using shared clinical decision-making
- To help with decision making:
  - Health status (e.g. chronic heart disease, lung disease)
  - Risk of severe RSV disease
  - Exposure risk (living in LTCF, nursing homes)

WHEN:

- Ideally before the onset of RSV season



N Engl J Med 2023; 388:595-608

# RSV vaccine in older adults

WHY:

- **RSVPreF3 -** Decreased symptomatic RSV LRTD by 82.6% in first season and by 56.1% in second season
- More severe (grade 3) reactions in 4% of recipients

- **RSVpreF -** Decreased symptomatic RSV LRTD by 88.9% in first season and by 78.6% in partial second season
- Underpowered to demonstrate efficacy in those > 80 years of age
- More severe (grade 3) reactions in 1% of recipients

- Duration of vaccine efficacy beyond two RSV seasons is unknown



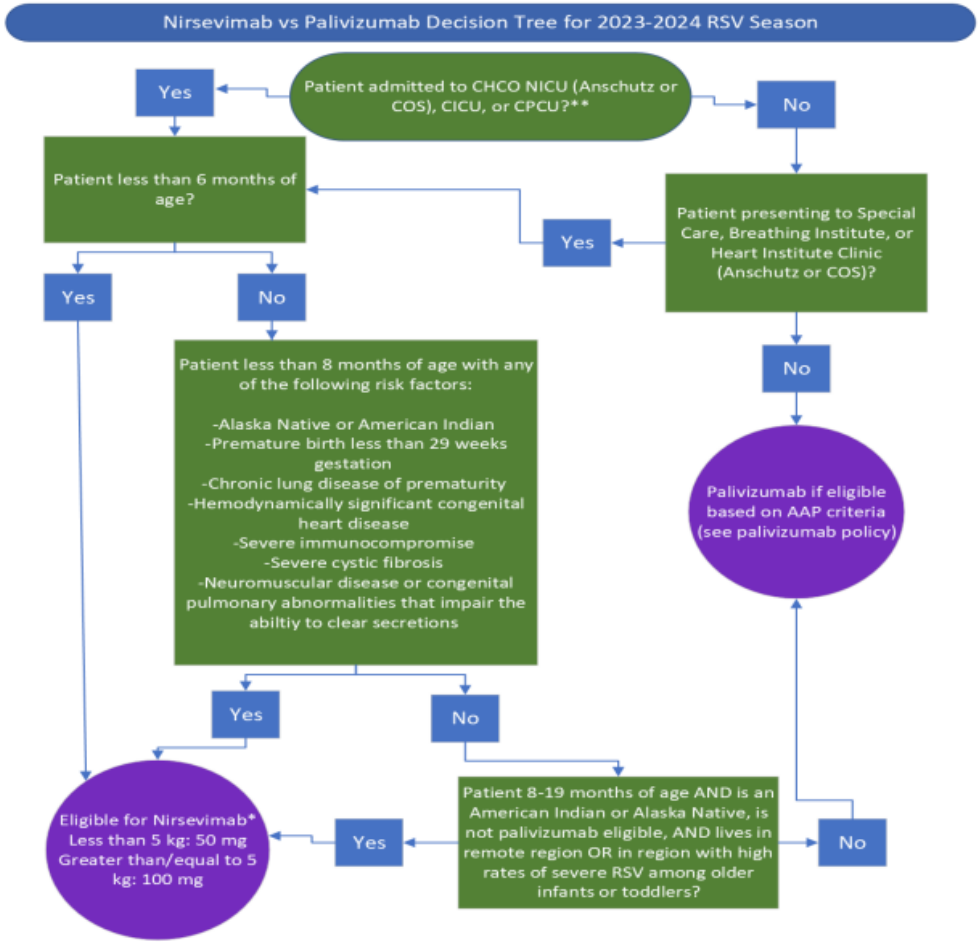
N Engl J Med 2023; 388:595-608

# Main points

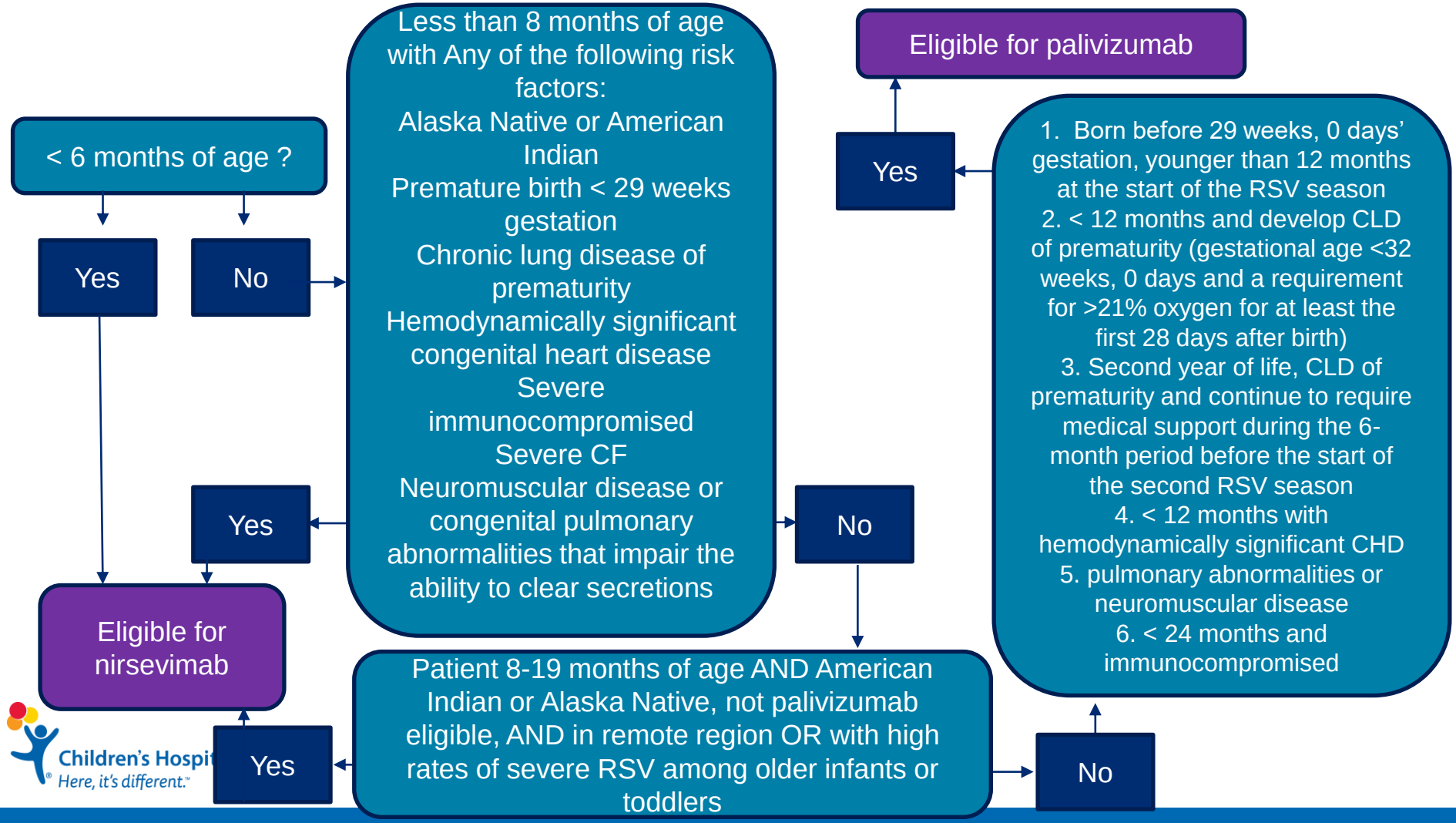
- Influenza, RSV and COVID are currently circulating in Colorado
- Optimal time to have conversations about influenza, RSV and COVID-19 vaccines
- Influenza vaccines can be given to children with egg allergy without observation period afterwards or other medical setting restrictions
- RIDT are more reliable due to improved manufacturing standards, and during influenza season, but point of care NAAT have highest sensitivity and specificity
- Influenza treatment – reserve for hospitalized and those of high risk
- Limited supply of 100 mg nirsevimab- reserved for those at highest risk
- Provide a strong recommendation for maternal RSV vaccine especially during time of limited nirsevimab supply

# Questions?

# Extra slides




Children's Hospital Colorado
Here, it's different.™


Eligible for palivizumab
Less than 8 months of age with Any of the following risk factors:
Alaska Native or American Indian
Premature birth < 29 weeks gestation
Chronic lung disease of prematurity
Hemodynamically significant congenital heart disease
Severe immunocompromised
Severe CF
Neuromuscular disease or congenital pulmonary abnormalities that impair the ability to clear secretions
< 6 months of age ?
Yes
No
Yes
1. Born before 29 weeks, 0 days' gestation, younger than 12 months at the start of the RSV season
2. < 12 months and develop CLD of prematurity (gestational age <32 weeks, 0 days and a requirement for >21% oxygen for at least the first 28 days after birth)
3. Second year of life, CLD of prematurity and continue to require medical support during the 6-month period before the start of the second RSV season
4. < 12 months with hemodynamically significant CHD
5. pulmonary abnormalities or neuromuscular disease
6. < 24 months and immunocompromised
Yes
No
Eligible for nirsevimab
Patient 8-19 months of age AND American Indian or Alaska Native, not palivizumab eligible, AND in remote region OR with high rates of severe RSV among older infants or toddlers
Yes
No
Children's Hospital
Here, it's different.

# How to make a strong vaccine recommendation

- Normalize the process - *We routinely provide flu vaccines to our patients in our clinic/hospital*
- Use presumptive language - *We can take care of your child's flu vaccine during this visit/hospital stay.*
- Be respectful of their concerns- *Do you mind if I ask why you are not wanting your child to receive the flu vaccine today?*
- Tailor the discussion to address concerns - *Thanks for letting me know about your concerns. I've been thinking a lot about this and we get a lot of education about influenza vaccines- would it be alright if I shared some of this information with you?*
- Find common ground - *I know you are a wonderful parent, and you want to do what's best for your child. We also want to do everything possible to keep your child as healthy as possible, and vaccination is one of those ways.*