

I-VAC Pediatric Learning Collaborative for COVID-19 Vaccination



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Disclosures

- No one in a position to control the education content of the activity has any relevant financial disclosures with ineligible companies to disclose
- What gets said here today may change based on new data and recommendations
 - Knowledge is shared more rapidly through ECHO



COVID Update for US

Early Indicators

Test Positivity >

% Test Positivity

9.5%

(October 8 to October 14, 2023)

Trend in % Test Positivity

-0.7% in most recent week



Aug 26, 2023 Oct 14, 2023

Emergency Department Visits >

% Diagnosed as COVID-19

1.3%

(October 8 to October 14, 2023)

Trend in % Emergency Department Visits

-11.9% in most recent week



Aug 26, 2023 Oct 14, 2023

These early indicators represent a portion of national COVID-19 tests and emergency department visits. [Wastewater](#) information also provides early indicators of spread.

Severity Indicators

Hospitalizations >

Hospital Admissions

16,158

(October 8 to October 14, 2023)

Trend in Hospital Admissions

-5% in most recent week



Aug 26, 2023 Oct 14, 2023

Deaths >

% of All Deaths in U.S. Due to COVID-19

2.5%

(October 8 to October 14, 2023)

Trend in % COVID-19 Deaths

+4.2% in most recent week



Aug 26, 2023 Oct 14, 2023

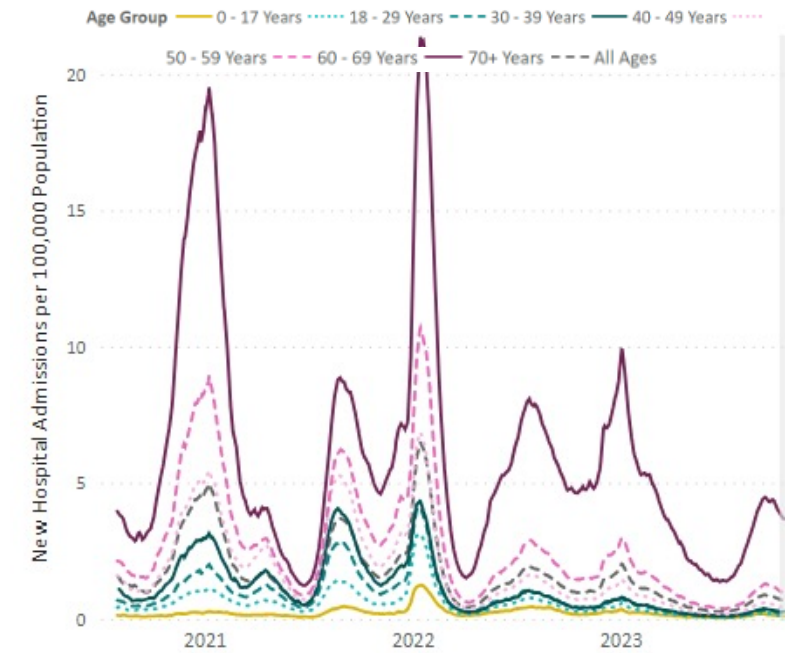
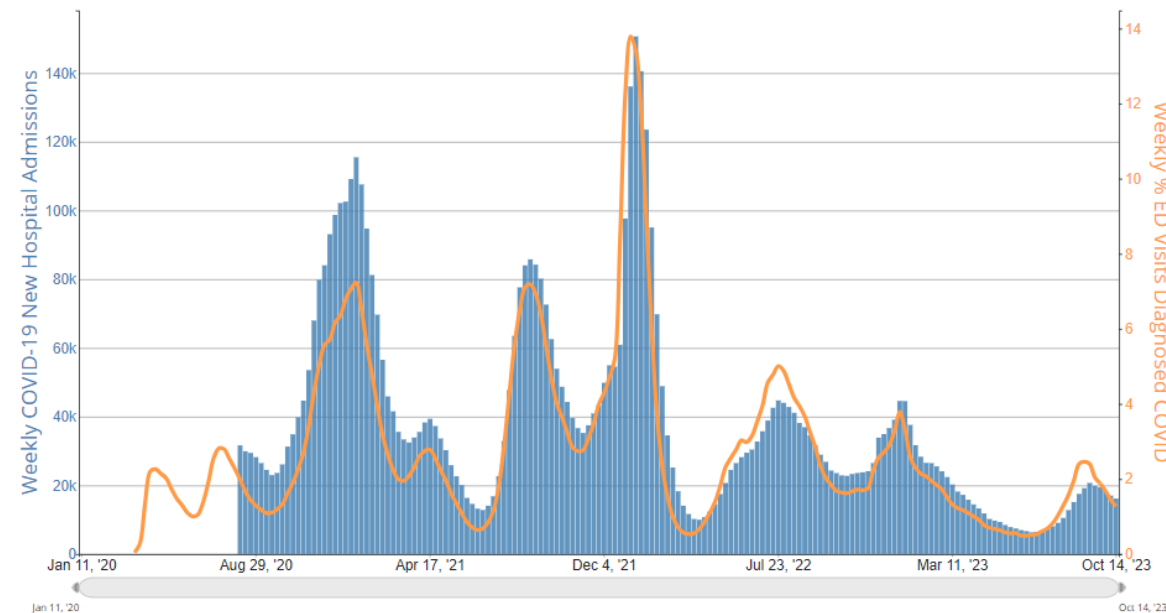
Total Hospitalizations

6,422,520

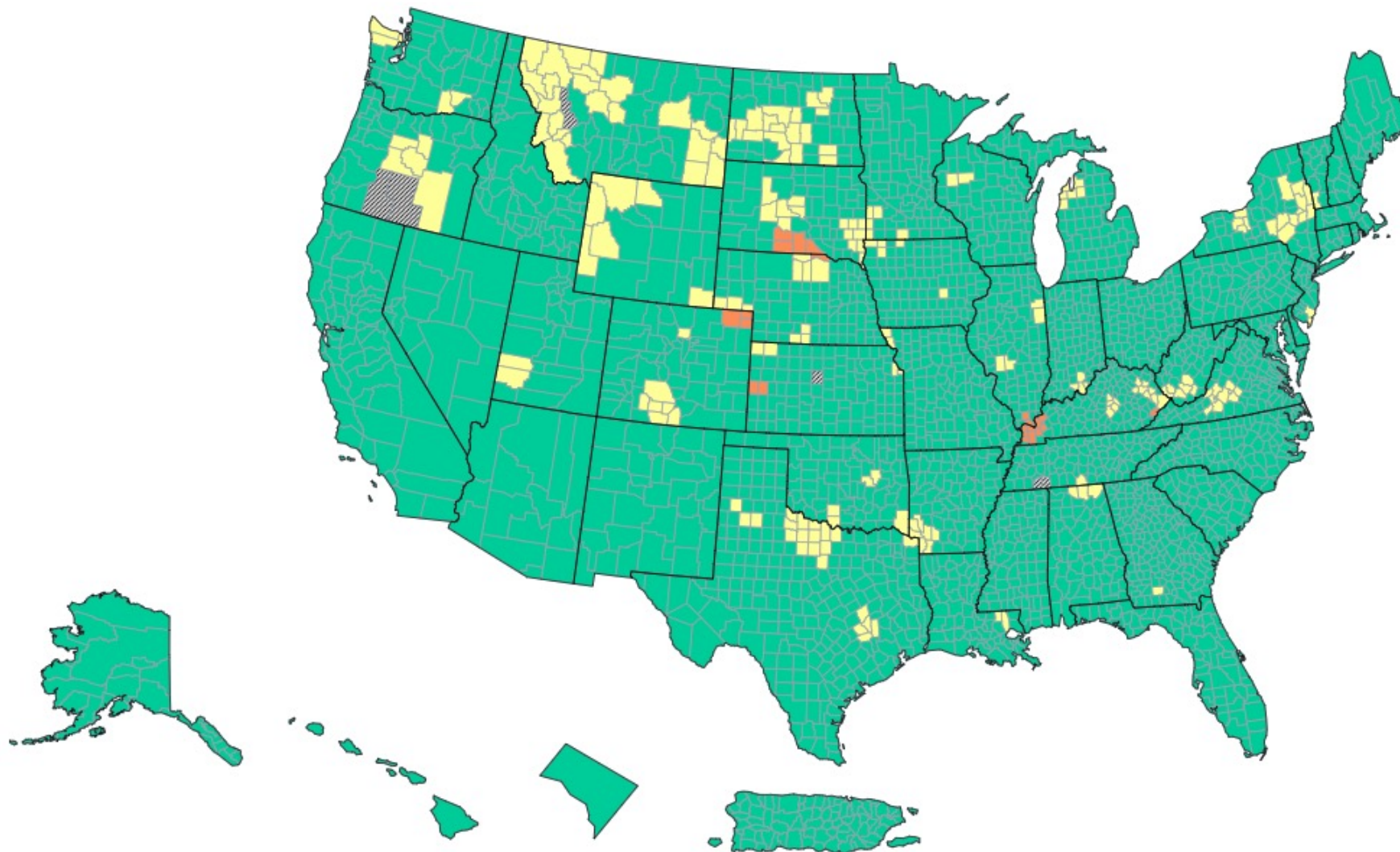
Total Deaths

1,148,691

COVID-19 New Hospital Admissions and Percentage of Emergency Department (ED) Visits Diagnosed as COVID-19, by Week, in The United States, Reported to CDC

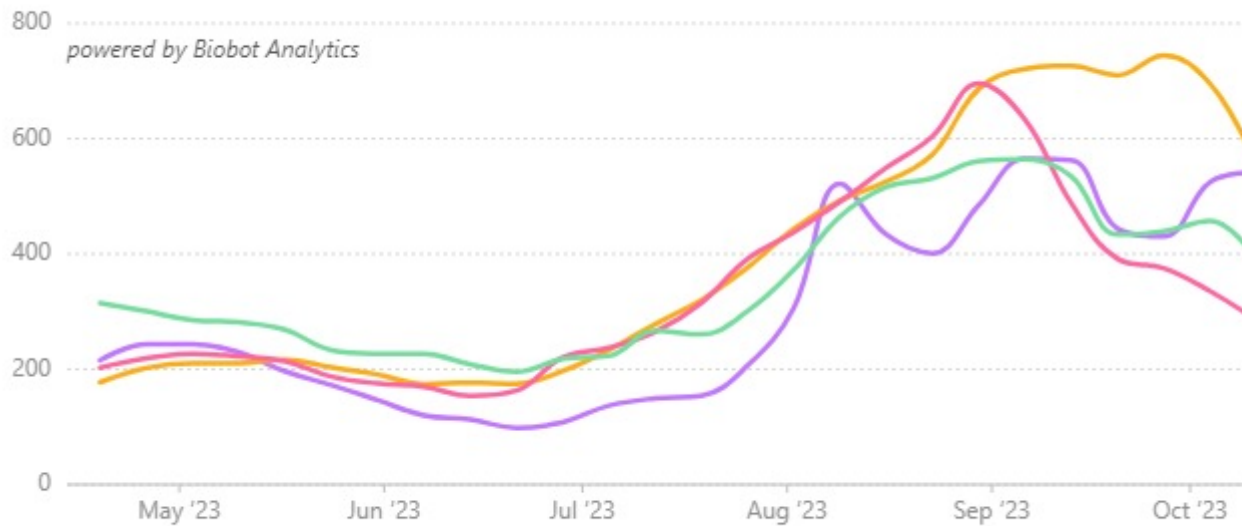


Reported COVID-19 New Hospital Admissions Rate per 100,000 Population in the Past Week, by County - United States

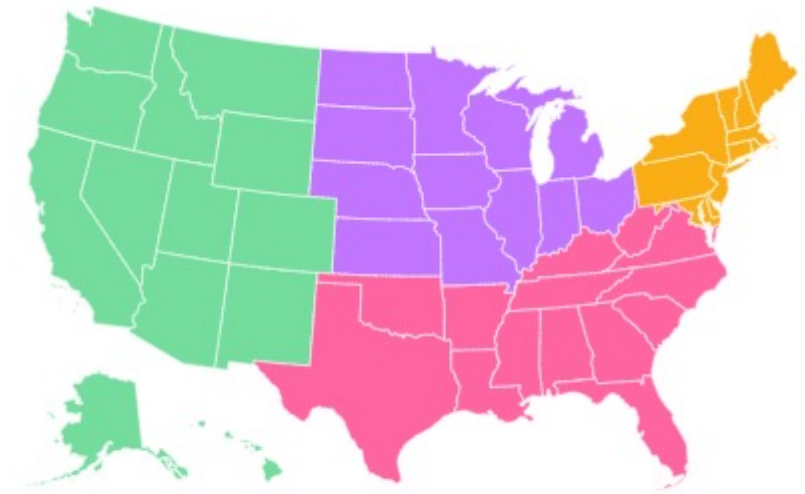


Covid-19 Wastewater Monitoring by Region

Wastewater: Effective SARS-CoV-2 virus concentration (copies / mL of sewage)

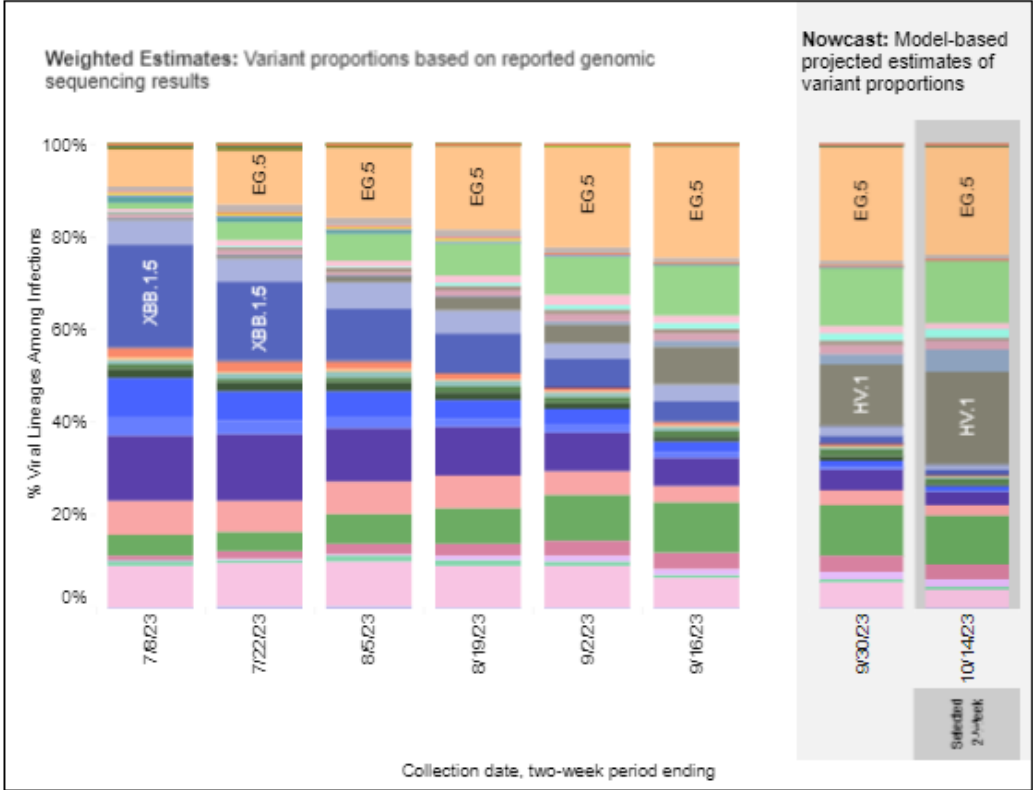


Source: Wastewater data from Biobot Analytics



Weighted and Nowcast Estimates in United States for 2-Week Periods in 6/25/2023 – 10/14/2023

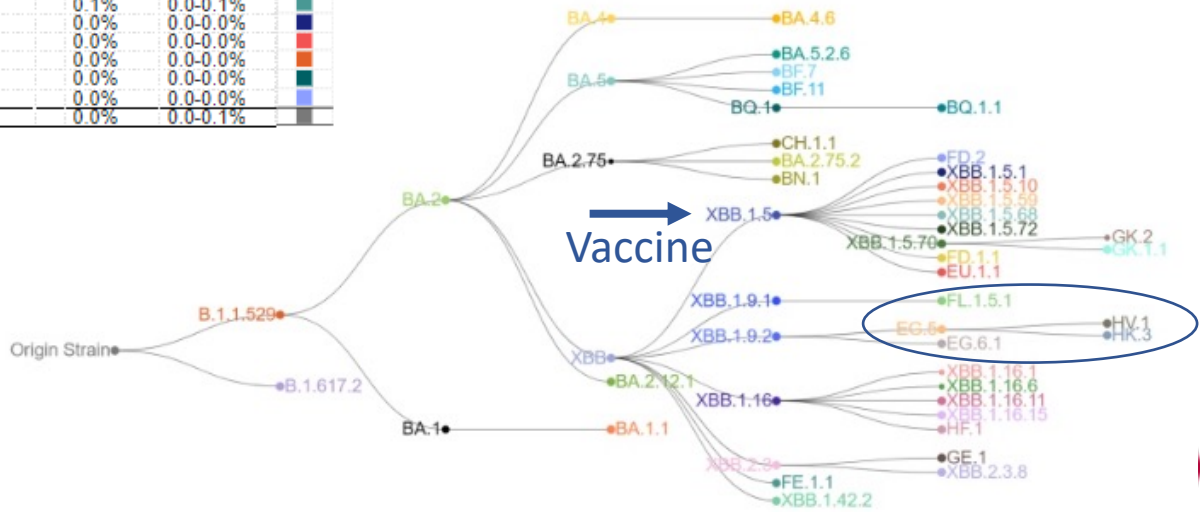
Hover over (or tap in mobile) any lineage of interest to see the amount of uncertainty in that lineage's estimate.



Nowcast Estimates in United States for 10/1/2023 – 10/14/2023

USA			
WHO label	Lineage #	%Total	95%PI
Omicron	EG.5	23.6%	21.2-26.3%
	HV.1	19.5%	16.8-22.6%
	FL.1.5.1	13.5%	10.8-16.7%
	XBB.1.16.6	10.3%	9.1-11.8%
	HK.3	4.9%	3.6-6.7%
	XBB.2.3	4.1%	3.4-4.9%
	XBB.1.16.11	3.1%	2.5-3.9%
	XBB.1.16	2.8%	2.4-3.3%
	XBB.1.16.1	2.2%	1.7-2.7%
	XBB.1.16.15	1.8%	1.3-2.4%
	HF.1	1.7%	1.2-2.4%
	GK.1.1	1.6%	1.3-2.1%
	XBB	1.4%	1.2-1.7%
	GE.1	1.4%	1.0-1.9%
	XBB.1.5.70	1.2%	0.8-1.8%
	GK.2	0.9%	0.7-1.2%
	XBB.1.5	0.9%	0.7-1.0%
	EG.6.1	0.8%	0.6-1.2%
	XBB.1.9.1	0.8%	0.6-1.0%
	XBB.1.5.72	0.6%	0.4-0.8%
	XBB.1.5.68	0.5%	0.3-0.8%
	XBB.1.9.2	0.5%	0.4-0.7%
	XBB.1.42.2	0.5%	0.3-0.8%
	BA.2	0.3%	0.1-0.8%
	XBB.1.5.10	0.3%	0.2-0.4%
	CH.1.1	0.2%	0.1-0.3%
	XBB.2.3.8	0.2%	0.1-0.3%
	XBB.1.5.59	0.1%	0.1-0.2%
	FD.1.1	0.1%	0.1-0.1%
	FE.1.1	0.1%	0.0-0.1%
	XBB.1.5.1	0.0%	0.0-0.0%
	EU.1.1	0.0%	0.0-0.0%
	B.1.1.529	0.0%	0.0-0.0%
	BQ.1	0.0%	0.0-0.0%
	FD.2	0.0%	0.0-0.0%
Other	Other*	0.0%	0.0-0.1%

- The prevalence of HV.1 in hospitalized patients is similar to the prevalence in non-hospitalized patients
- The same is true for EG.5 and FL.1.5.1, estimated to be the third-most prevalent variant at this time.



COVID booster uptake hindered by prior infections, fear of side effects

- Only 20% of Americans eligible for COVID-19 boosters get them
- Recent study looking at data through March 2023 in Arizona
- The most commonly reported reason for not having been boosted was a prior SARS-CoV-2 infection (39.5%), followed by concern about vaccine side effects (31.5%), believing that the booster would not provide additional protection over the vaccines already received (28.6%), and concern about booster safety (23.4%) or that it would not protect from SARS-CoV-2 infection (23.1%).

Nirsevimab (Beyfortus™) for Prevention of Respiratory Syncytial Virus Disease

Slides in this presentation are used, with some modification, with permission of Sameer Patel, MD, MPH and Tonya Scardina, PharmD, BCPS, BCIDP

Burden of RSV Disease

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- Most common cause of hospitalization in U.S. infants
- 58,000-80,000 hospitalizations among children <5 years old
- 100–300 deaths in children <5 years old
- 2.1 million outpatient visits
- Risk declines by increasing age throughout infancy and early childhood
- Prematurity and other chronic diseases increase risk of RSV-associated hospitalization, but most hospitalizations are in healthy, term infants

CDC Respiratory Syncytial Virus Infection.2023 <https://www.cdc.gov/rsv/index.html>; Hall CB. *New Engl J Med*. 2009; Rha B. *Pediatrics* 2020

Nirsevimab-alip (Beyfortus™)

Monoclonal antibody FDA approved July 2023

Mechanism of Action

- Recombinant human immune globulin G1 kappa monoclonal antibody, binds the highly conserved site Ø epitope present on the prefusion conformation of the respiratory syncytial virus (RSV) fusion protein
- Neutralizes RSV by inhibiting changes of the F protein needed for viral entry via fusion of viral and cellular membranes
- Triple amino acid substitution in the Fc region ↑ binding to the Fc receptor → extending half-life



Pharmacokinetics

Absorption:

- Bioavailability: 84-85%
- Median time to maximum concentration is 6 days (range 1-28 days)

Metabolism:

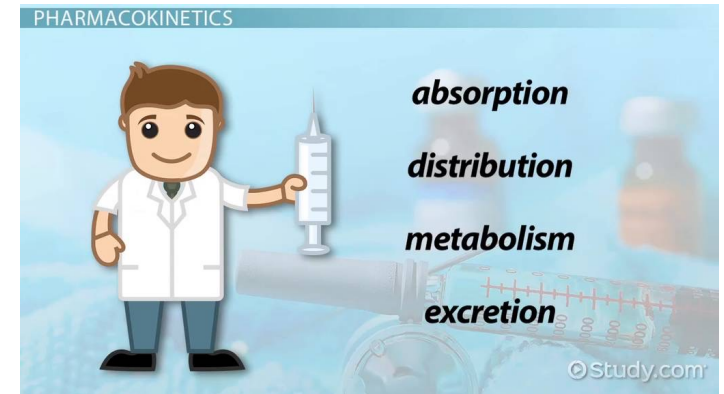
- Degraded into small peptides by catabolic pathways via lysosomal degradation
 - Effects of renal and hepatic impairment on nirsevimab pharmacokinetics are not expected

Excretion:

- Half-life: 63-73 days

Duration of protection:

- 5-6 months



Efficacy and Adverse Reactions

- ▶ Preterm 29 week-35 week gestation babies:
 - ▶ 70% reduction in LRTI medical visits for RSV
 - ▶ 78% reduction in hospitalization
- ▶ Babies \geq 35 week gestation
 - ▶ 75-76% reduction in LRTI medical visits for RSV
 - ▶ 62%-77% reduction in hospitalization
- ▶ Adverse events were minimal - site reactions of mild pain and rash

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

Griffin MP *et al.* *N Engl J Med* 2020; Hammitt LL *et al.* *N Engl J Med* 2022; Muller WJ *et al.* *N Engl J Med* 2023; Package Insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761328s000lbl.pdf

Recommended Dose

Age	Body Weight	Recommended dose
Infants aged < 8 months born during or entering their 1st RSV season	< 5 kg*	Nirsevimab 50 mg IM as a single dose
	≥ 5 kg	Nirsevimab 100 mg IM as a single dose
Children aged 8-19 months who are at increased risk of severe RSV disease and entering their 2nd RSV season**	N/A	Nirsevimab 200 mg (2 x 100mg) IM as two simultaneous IM injections

*Exposure in infants < 1 kg may lead to higher exposure. The benefits and risks of nirsevimab use in infants < 1 kg should be carefully considered.

**Increased risk defined as:

- Children with chronic lung disease of prematurity who required medical support (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) any time during 6-months before start of second RSV season
- Children with severe immunocompromised
- Children with cystic fibrosis who have manifestations of severe lung disease (previous hospitalization for pulmonary exacerbation in 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

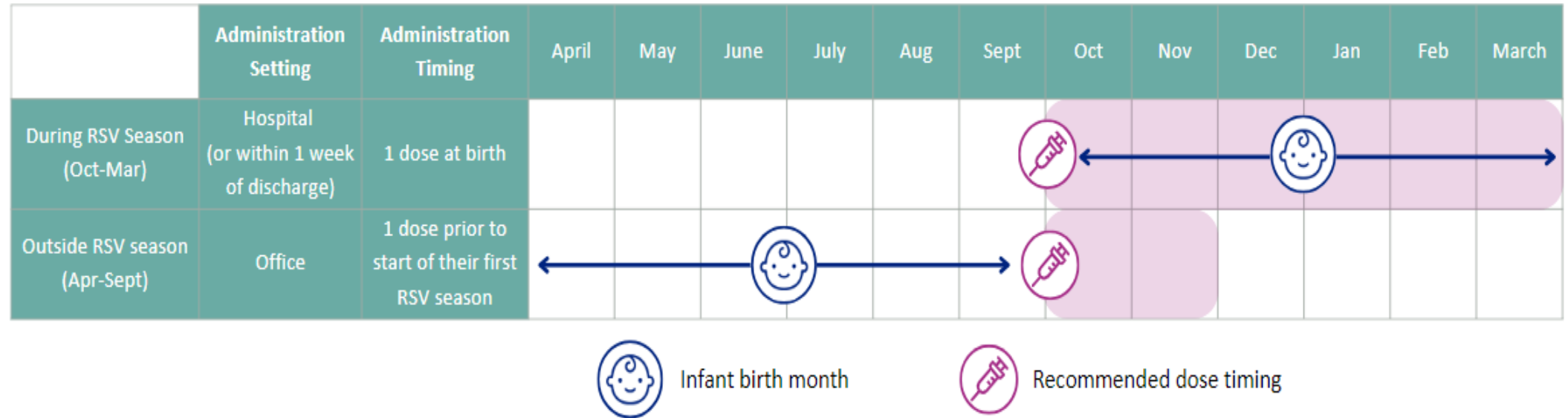
Beyfortus (nirsevimab-alip) [package insert]. AstraZeneca AB; 2023

ACIP and AAP Recommendations for nirsevimab. Red Book: 2021–2024 Report of the Committee on Infectious Diseases (32nd edition)

Beyfortus. Product information. AstraZeneca AB. Accessed August 10, 2023.

https://www.ema.europa.eu/en/documents/product-information/beyfortus-epar-product-information_en.pdf

ACIP Recommendation: All infants aged < 8 months born during or entering their first RSV season.



- ▶ Infants with prolonged birth hospitalizations should receive nirsevimab shortly before or promptly after hospital discharge
 - ▶ No evidence is available to support use of nirsevimab for prevention of hospital-acquired RSV infection and it is not recommended for this indication

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;72:920–925. DOI: <http://dx.doi.org/10.15585/mmwr.mm7234a4>.

Chart adapted from Sanofi's RSV National Expert Program

Interim Recommendations Due to Limited Nirsevimab Availability During the 2023–2024 RSV Season

- For infants weighing <5 kg, no changed, i.e., administer a 50mg dose of nirsevimab in the first week of life
- For infants weighing ≥5 kg, prioritize using 100mg nirsevimab doses for those at highest risk of severe RSV disease:
 - Infants aged <6 months
 - American Indian and Alaska Native infants aged <8 months
 - Infants aged 6 to <8 months with conditions that place them at high risk of severe RSV disease: birth at <29 weeks' gestation, chronic lung disease, hemodynamically significant congenital heart disease, severe immunocompromise, severe cystic fibrosis (either severe lung disease or weight-for-length <10th percentile), neuromuscular disease or congenital pulmonary abnormalities that impair clearing of secretions
- For palivizumab-eligible children aged 8–19 months, suspend using nirsevimab for the 2023–2024 RSV season and give palivizumab (Palivizumab recs can be found here: Pediatrics (2023) 152 (1): e2023061803. <https://publications.aap.org/pediatrics/article/152/1/e2023061803/192153/Palivizumab-Prophylaxis-in-Infants-and-Young?autologincheck=redirected>)
- Continue offering nirsevimab to American Indian and Alaska Native children aged 8–19 months who are not palivizumab-eligible and/or who live in remote regions, or where access to care is an issue or there is a high RSV incidence
- Avoid using two 50mg doses for infants weighing ≥5 kg, because 50mg doses should be reserved for infants <5 kg
- Providers should encourage pregnant people to receive RSVpreF vaccine (Abrysvo, Pfizer) during 32 weeks through 36 weeks and 6 days gestation (not the GSK RSVpreF3 vaccine (Arexvy)) to limit the need for nirsevimab

Preparation and Administration

- Available in 50mg and 100mg pre-filled syringes (single use):
 - 50 mg: purple plunger rod
 - 100mg: light blue plunger rod
- Should not be mixed with any vaccines or medications in the same syringe or vial
- Administered intramuscularly as one or two injections
 - Preferably in the anterolateral aspect of the thigh
 - Gluteal muscle should not be used due to risk of damage to the sciatic nerve



Beyfortus (nirsevimab-alip) [package insert]. AstraZeneca AB; 2023

ACIP Meeting notes (August 2023)- Proposed Clinical Consideration Updates for Nirsevimab

Esposito S, Abu-Raya B, Bonanni P et al. *Frontiers in Immunology* 2021

Beyfortus. Product information. AstraZeneca AB. Accessed August 10, 2023: https://www.ema.europa.eu/en/documents/product-information/beyfortus-epar-product-information_en.pdf

Administration

- May be given concomitantly with childhood vaccines
 - Administer in separate syringes, at different injection sites
- Palivizumab should not be administered if nirsevimab was administered in the same season
- If palivizumab was administered initially for the RSV season and < 5 doses were administered, 1 dose of nirsevimab may be administered
 - No further palivizumab should be administered

Beyfortus (nirsevimab-alip) [package insert]. AstraZeneca AB; 2023

ACIP and AAP Recommendations for nirsevimab. Red Book: 2021–2024 Report of the Committee on Infectious Diseases (32nd edition)

Contraindications/Warnings

- Contraindications
 - Infants and children with a history of serious hypersensitivity reactions, including anaphylaxis, to nirsevimab or to any of its excipients
 - Excipients: arginine hydrochloride, histidine, L-histidine hydrochloride monohydrate, polysorbate 80, sucrose, and water for injection
- Warnings/Precautions:
 - Serious hypersensitivity reactions, including anaphylaxis, have been observed with other human immunoglobulin G1 (IgG1) monoclonal antibodies
 - Initiate appropriate medications and/or supportive therapy if signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur
- As with other IM injections, nirsevimab should be given with caution to infants and children with thrombocytopenia, any coagulation disorder, or to individuals on anticoagulation therapy

Drug Interactions

- Efgartigimod alfa and rozanolixizumab (drugs used to treat myasthenia gravis and perhaps some other autoimmune diseases) – may diminish therapeutic effect of Fc receptor-binding agents
 - Recommended to monitor efficacy of therapy
- Nirsevimab is not predicted to be a substrate of, inhibitor, or inducer of cytochrome P450 enzymes or transporter systems

Nirsevimab. Lexi-Drugs. Hudson, OH: Lexicomp, 2023. <http://online.lexi.com/>. Updated August 1, 2023. Accessed August 8, 2023.

Beyfortus (nirsevimab-alip) [package insert]. AstraZeneca AB; 2023

If Mother Given RSVpreF Vaccine (Abrysvo), No Need for Infant to be Vaccinated Except:

- Receipt of maternal vaccine not confirmed by healthcare record
- Infant born within 14 days of vaccination
- Mother is not anticipated to mount an adequate antibody response to Abrysvo
- Infant born premature (≤ 34 weeks gestation) as passive transfer of antibody may not have fully occurred
- Healthcare provider recommends maximizing protection because infant at high risk of severe disease
 - Especially important if born >3 months prior to peak of RSV season

Storage and Handling

- ▶ Store refrigerated at 36°F to 46°F (2°C to 8°C)
 - ▶ May be kept at room temperature 68°F to 77°F (20°C to 25°C) for a maximum of 8 hours
 - ▶ After removal from refrigerator, must be used within 8 hours or discarded
- ▶ Store in its original carton until time of use
- ▶ Do not freeze, shake, or expose to heat
- ▶ Can be returned after it expires (like other Sanofi products)

Beyfortus (nirsevimab-alip) [package insert]. AstraZeneca AB; 2023

Coding

Proprietary Name	Manufacturer	Unit of Sale NDC11	CVX description	CVX Code	MVX Code	CPT Code
BEYFORTUS	Sanofi Pasteur Inc.	49281-0575-15	RSV, mAb, nirsevimab-alip, 0.5 mL, neonate to 24 months	306	PMC	90380
BEYFORTUS	Sanofi Pasteur Inc.	49281-0574-15	RSV, mAb, nirsevimab-alip, 1 mL, neonate to 24 months	307	PMC	90381
Administration Code: Do not report immunization administration codes 90461-90462 or 90471-90472 for the injection of nirsevimab, as these codes are limited to the administration of vaccine and toxoid products.						96372

- Follow state specifications for reporting the immunization when the immunoglobulin product is provided through the Vaccines for Children program
- Until August 1, 2024, VFC providers are not required to carry a private stock of nirsevimab
- American Medical Association's (AMA's) Current Procedural Terminology (CPT)
- <https://publications.aap.org/aapnews/news/26552/CDC-relaxes-VFC-rules-for-nirsevimab-COVID-19?autologincheck=redirected>

How's It Going So Far?

Sanofi Reports “Unprecedented” Demand For RSV Antibody Therapy

[Reuters](#) (10/20) reported, “French drugmaker Sanofi said on Friday it was seeing an ‘unprecedented level’ of demand for an antibody therapy it co-developed to prevent respiratory syncytial virus (RSV), a leading cause of hospitalizations in infants.” Jointly developed with AstraZeneca, in the US, the drug “was approved in July to prevent RSV in infants and toddlers.” About “1% to 3% of children under 12 months of age in the country are hospitalized each year due to RSV, according to the **American Academy of Pediatrics**.”

Increasing Vaccine Uptake

Using Motivational Interviewing

- ▶ Can help people manage mixed feelings and move toward a healthy behavior change consistent with their values and needs used evidence based and culturally sensitive tactics to speak to the patient about vaccination
- ▶ OARS
 - ▶ Opened ended questions
 - ▶ Offer affirmations
 - ▶ Use reflective listening
 - ▶ Summarize the visit

Resources

- ▶ [Full prescribing information](#)
 - ▶ [AAP's RedBook Online](#)
 - ▶ [AAP's Nirsevimab Frequently Asked Questions](#)
 - ▶ [CDC information](#)
 - ▶ [AAP Page on RSV Prevention Products](#)
- ▶ Handout for patients
 - ▶ [English](#)
 - ▶ [Spanish](#)
 - ▶ [Handout for providers](#)
 - ▶ [CDC HAN 9.5.23](#)

Increased Respiratory Syncytial Virus (RSV) Activity in Parts of the Southeastern United States: New Prevention Tools Available to Protect Patients

[Print](#)



Distributed via the CDC Health Alert Network
September 05, 2023, 2:00 PM ET
CDCHAN-00498

Outreach

PROTECTION FROM RSV IS NOW AVAILABLE!

Your child may be able to receive nirsevimab if they:

- Are born during the RSV season (October - March).
- Are less than 1 year old and are entering their first RSV season.
- Up to 2 years old and at risk of severe RSV disease.

Talk to your child's doctor today!

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Download [here](#)

Nirsevimab = RSV Protection!

A preventative medication that gives immunity from RSV infection!

One dose protects for around 5 months - that's the full RSV season!

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Help Stop the Spread of Germs

- ✓ Cover your cough/sneeze
- ✓ Wash your hands
- ✓ Get vaccinated!

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Download [here](#)



Upcoming Special RSV-focused Session:

Nov. 7th – RSV in Pregnant Populations (led by Drs. Ed Linn & Steve Schrantz)

For any questions, email us at pgower@peds.bsd.uchicago.edu

Funding for this project was made possible by the Office of Disease Control, through the Illinois Department of Public Health.