Upcoming Respiratory Season: Update and Trends for Flu, RSV, and COVID-19

Rodney E. Rohde

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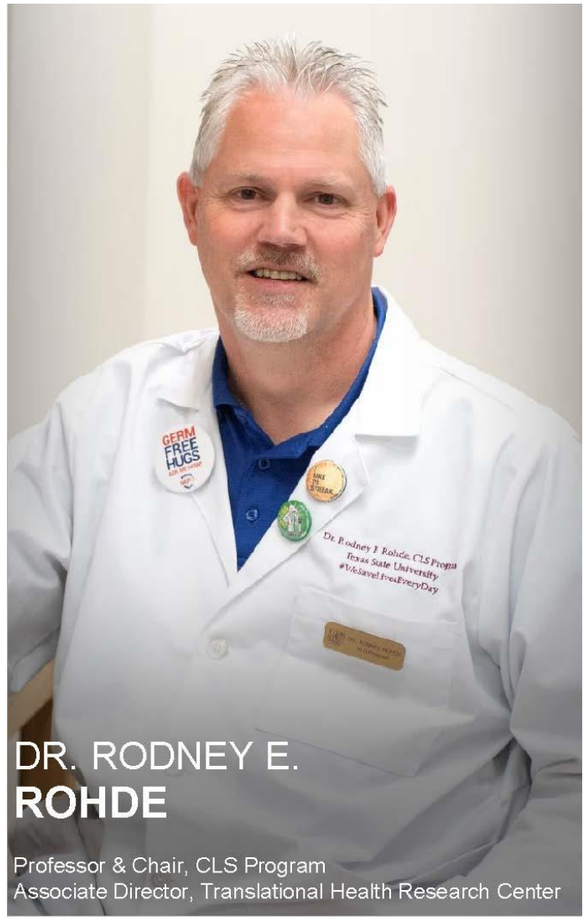

Overview

In the 2022-23 season, the world witnessed a “tripledemic” of flu, COVID, and RSV. In this presentation, I will discuss the primary microbiology, epidemiology, control, and prevention of these three primary respiratory season microbes. The 2023-24 landscape is already different, with new vaccines and treatments, like the game-changing antibody that protects kids from RSV. The healthcare and public health community has also learned some valuable lessons going forward with the ever-evolving respiratory agents. How can we all best prepare for the upcoming season?

Learning Objectives

After attending this webinar, participants will be able to:

- Describe Influenza (flu), Respiratory Syncytial Virus [RSV] and SARS-CoV-2 [COVID-19] history and background.
- Summarize the risk factors associated with each agent.
- Describe the diagnostic microbiology, clinical laboratory role and molecular epidemiology of each agent.
- Review the changing epidemiology of each agent between the community, healthcare setting and occupational health.
- Correlate infection prevention and control in the environment, including the types of PPE to be utilized.
- Summarize the 2023-2024 season, including preparations, for each agent.

Influenza: What can we expect?

The latest National Academy of Sciences report investigating the rising tide of new diseases spoke of myriad factors creating the microbial equivalent of a "perfect storm." "However, unlike a major climactic event where various meteorologic forces converge to produce a tempest," it reads, "this microbial perfect storm will not subside. There will be no calm after the epidemic; rather the forces combining to create the perfect storm will continue to collide and the storm itself will be a recurring event."[1244] And there is no storm like influenza.

From: Bird Flu: A Virus of our own Hatching
http://birdflubook.com/a.php?id=56

Influenza: What can we expect?

World Health Organization

INFORMATION NOTE/2009/2
20 May 2009

Summary report of a High-Level Consultation: new influenza A (H1N1) Geneva, 18 May 2009

KEY UNCERTAINTIES

10. The only thing certain about influenza viruses is that nothing is certain.

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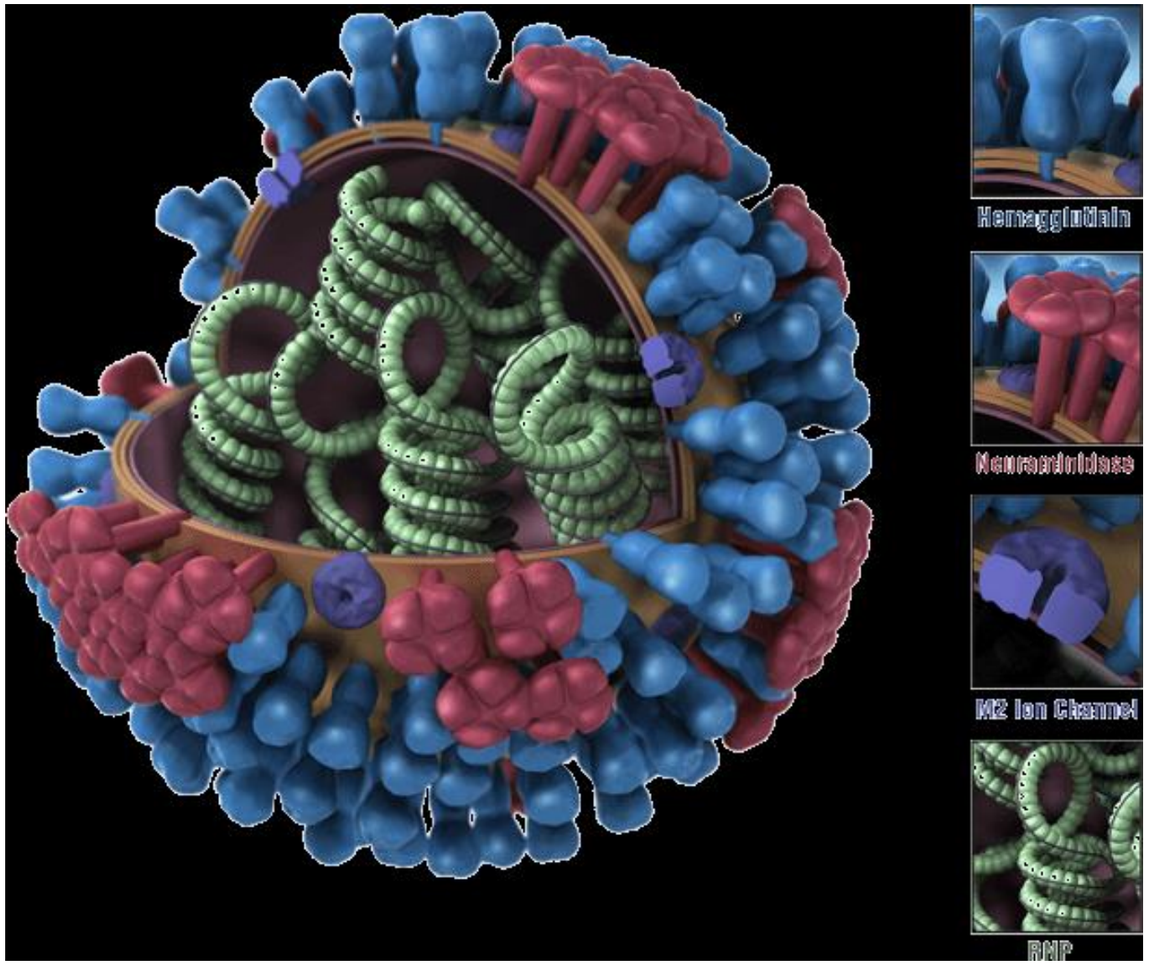
History and Background - Flu

- Influenza (flu) is an RNA virus that is notorious, and some might say diabolical, in its ability to mutate from year to year.
- RNA viruses (like flu and SARS-CoV2) are unfortunately very smart and mischievous in this aspect. Flu, like SARS, also can live as a zoonotic agent.
- The flu virus has long been an inhabitant of swine, fowl, and humans, which continually allow for antigenic drift (small changes in the virus genome) and shift (major changes in the virus genome).

History and Background - Flu

- It is a contagious respiratory illness, which can cause mild to severe illness resulting in hospitalization or death.
- Some people, such as older people, young children, and people with certain health conditions, are at high risk of serious flu complications.
- There are two main types of influenza (flu) virus: Types A and B. Type C is not clinically relevant to humans and Type D is only found in pigs and cattle. The influenza A and B viruses that routinely spread in people (human influenza viruses) are responsible for seasonal flu epidemics each year. Type A = pandemic strains.

History and Background



H

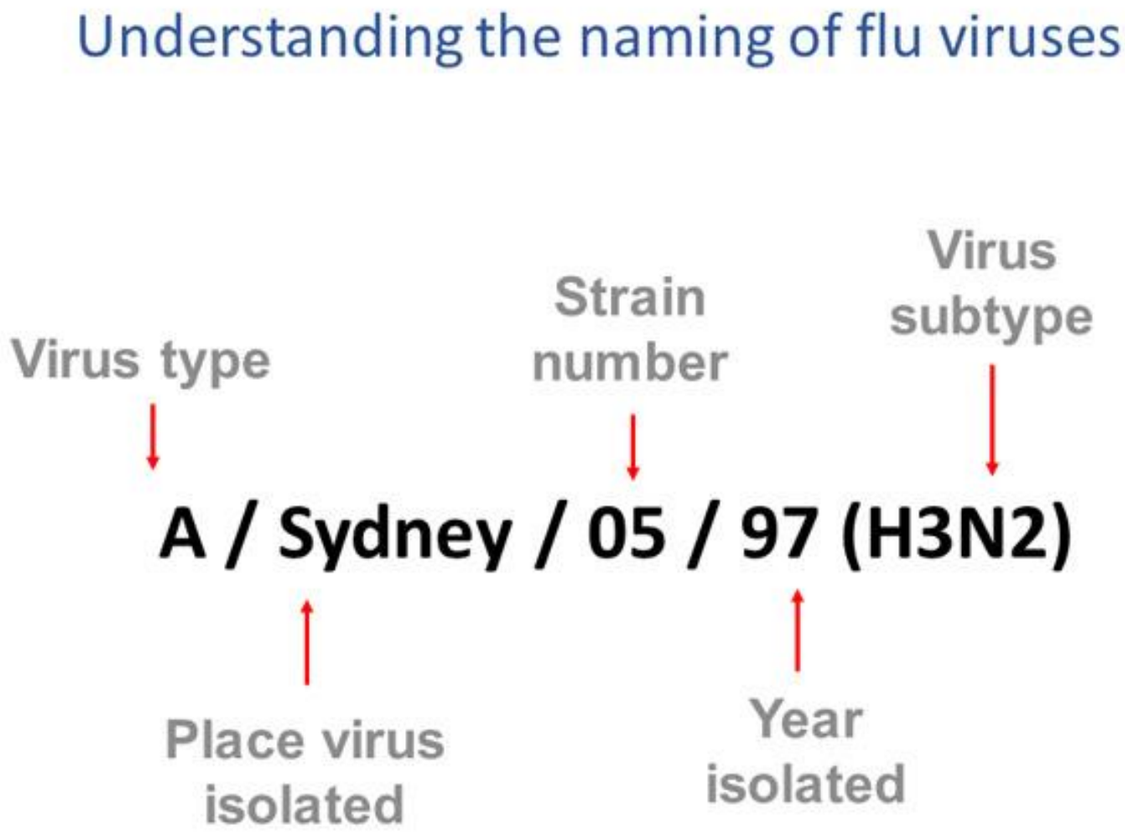
N

M2 Ion Channel

RNP

This is a picture of an influenza virus. Influenza A viruses are classified by subtypes based on the properties of their hemagglutinin (H) and neuraminidase (N) surface proteins. There are 18 different HA subtypes and 11 different NA subtypes. Subtypes are named by combining the H and N numbers – e.g., A(H1N1), A(H3N2). https://www.cdc.gov/flu/about/viruses/types.htm

History and Background



This image shows how influenza viruses are named. The name starts with the virus type, followed by the place the virus was isolated, followed by the virus strain number, the year isolated, and finally, the virus subtype. https://www.cdc.gov/flu/about/viruses/types.htm

History and Background - Flu

- Person to person – direct transmission
- Indirect via “high-touch” surfaces / fomites
- People with flu are most contagious in the first three to four days after their illness begins. Most healthy adults may be able to infect others beginning 1 day before symptoms develop and up to 5 to 7 days after becoming sick. Children and some people with weakened immune systems may pass the virus for longer than 7 days.
- You may be able to pass on flu to someone else before you know you are sick, as well as while you are sick.

Influenza (Flu) in Children

- Millions of children in the US get sick with seasonal flu during typical seasons
  - 7,000 to 26,000 estimated flu-related hospitalizations per season in children aged <5 years during 2010-2011 to 2019-2020
  - 37 to 199 reported flu-related deaths in children per season during 2004-2005 to 2019-2020

- Flu vaccination is the ***best*** way to prevent flu in children
  - Studies show that getting vaccinated reduces flu illnesses, doctor's visits, flu-related hospitalizations, life-threatening flu episodes, and death*

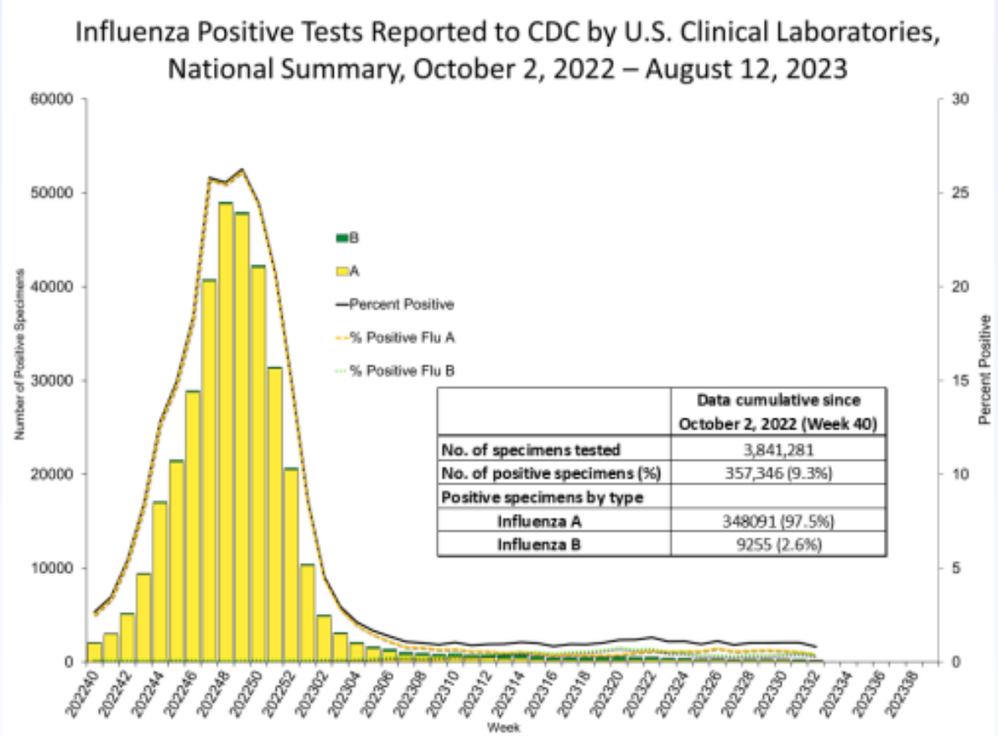
*Key Facts About Seasonal Flu Vaccine | CDC

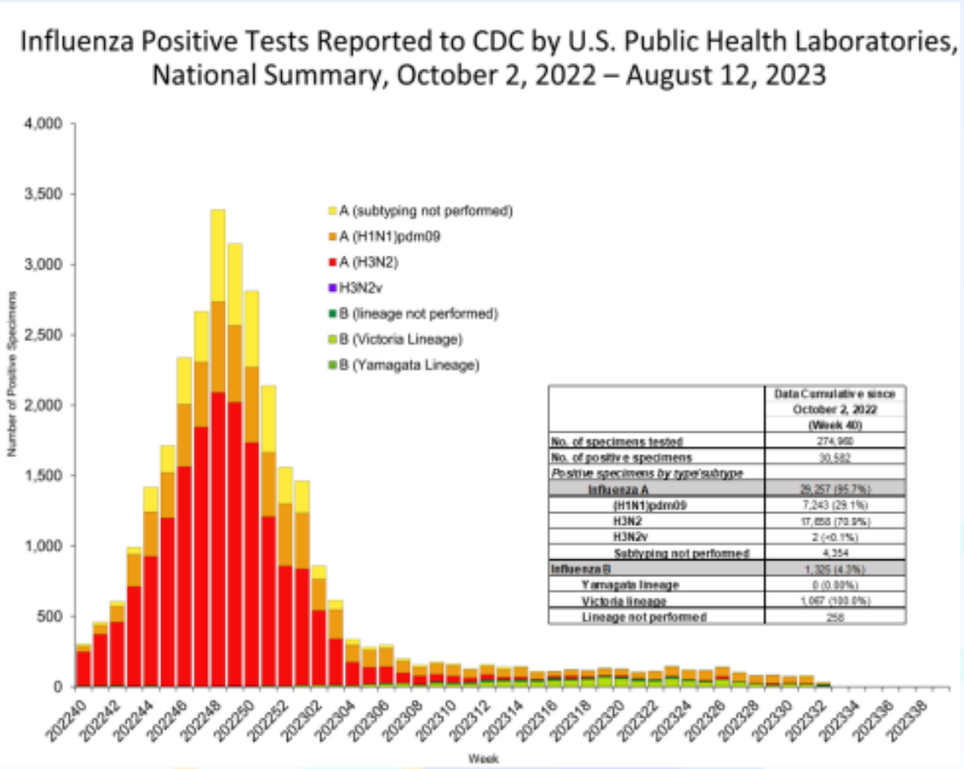
CDC. 2023-2024 Recommendations for Influenza Prevention and Treatment in Children: An Update for Pediatric Providers Clinician Outreach and Communication Activity (COCA) Call Thursday, August 31, 2023. Accessed September 6, 2023, from https://emergency.cdc.gov/coca/ppt/2023/083123_slides.pdf

A Review of Last Influenza Season

- A/H_3N_2 predominant, with some A/H_1N_1 circulation
- Early influenza season
  - Single epidemic wave
  - Activity began to increase in early October and subsided by early January
  - Reports of high pediatric hospitalization rates in some areas
- Influenza virus circulation coincided with other respiratory virus circulation
  - CDC Health Alert Notification issued about early respiratory disease incidence caused by multiple viruses, especially among children

US Clinical Laboratory and Public Health Laboratory Surveillance, October 2022–August 2023

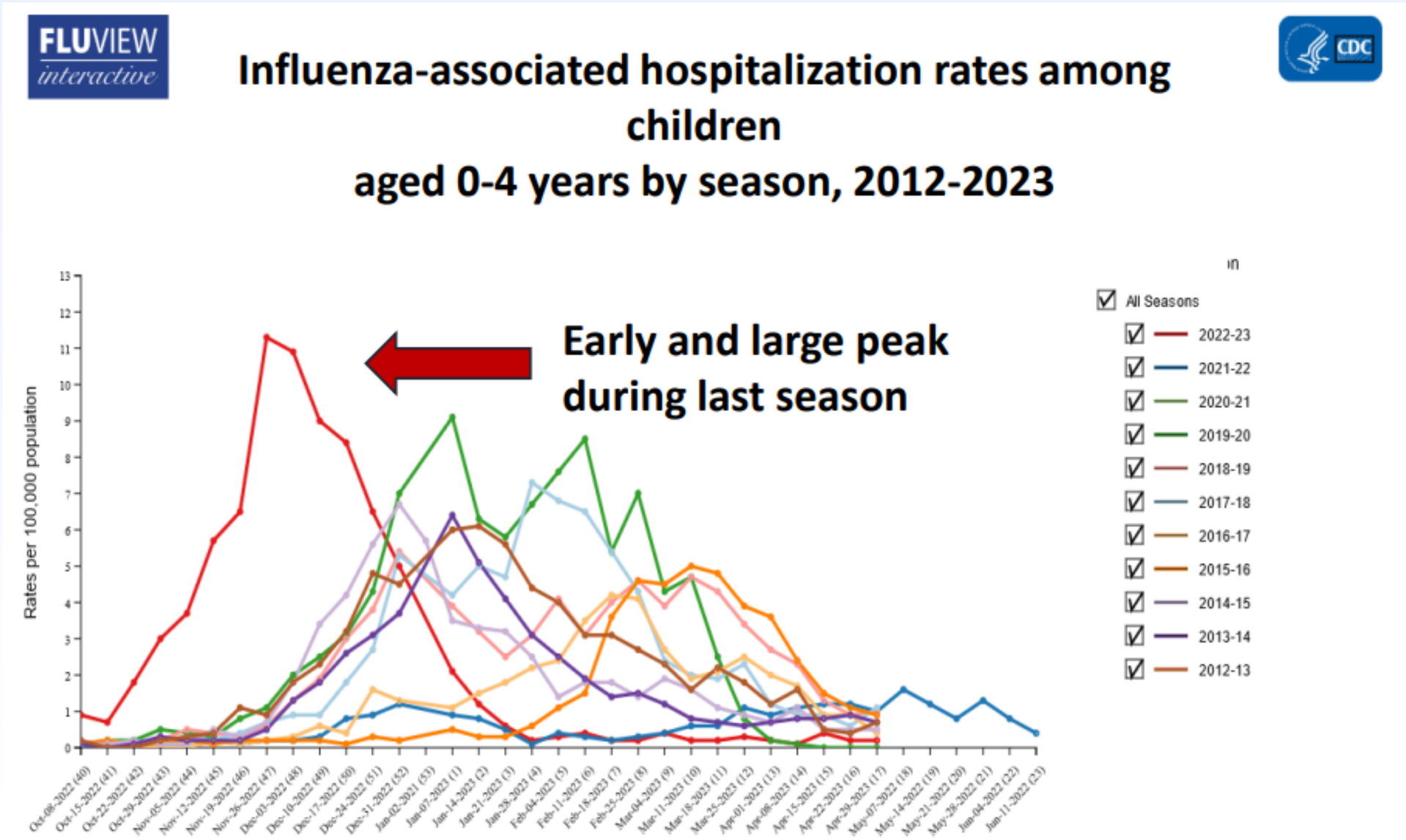




Time Period	Percent Positive at Clinical Labs Median (Range)	Peak Number of Positives at PHLs Median (Range)
Pre-COVID: 2015-16 – 2019-20	26.3 (23.6 – 30.3)	3,482 (3,274 – 4,334)
Early COVID: 2020-21 & 2021-22 *	0.3 – 9.9	24 – 1,528
This Season: 2022-23	26.3	3,387

*NOTE: effect of COVID measures.

Influenza-associated hospitalization rates among children aged 0-4 years by season, 2012-2023



Annual U.S. Influenza Burden Estimates

Estimated Range from
2010 – 2020

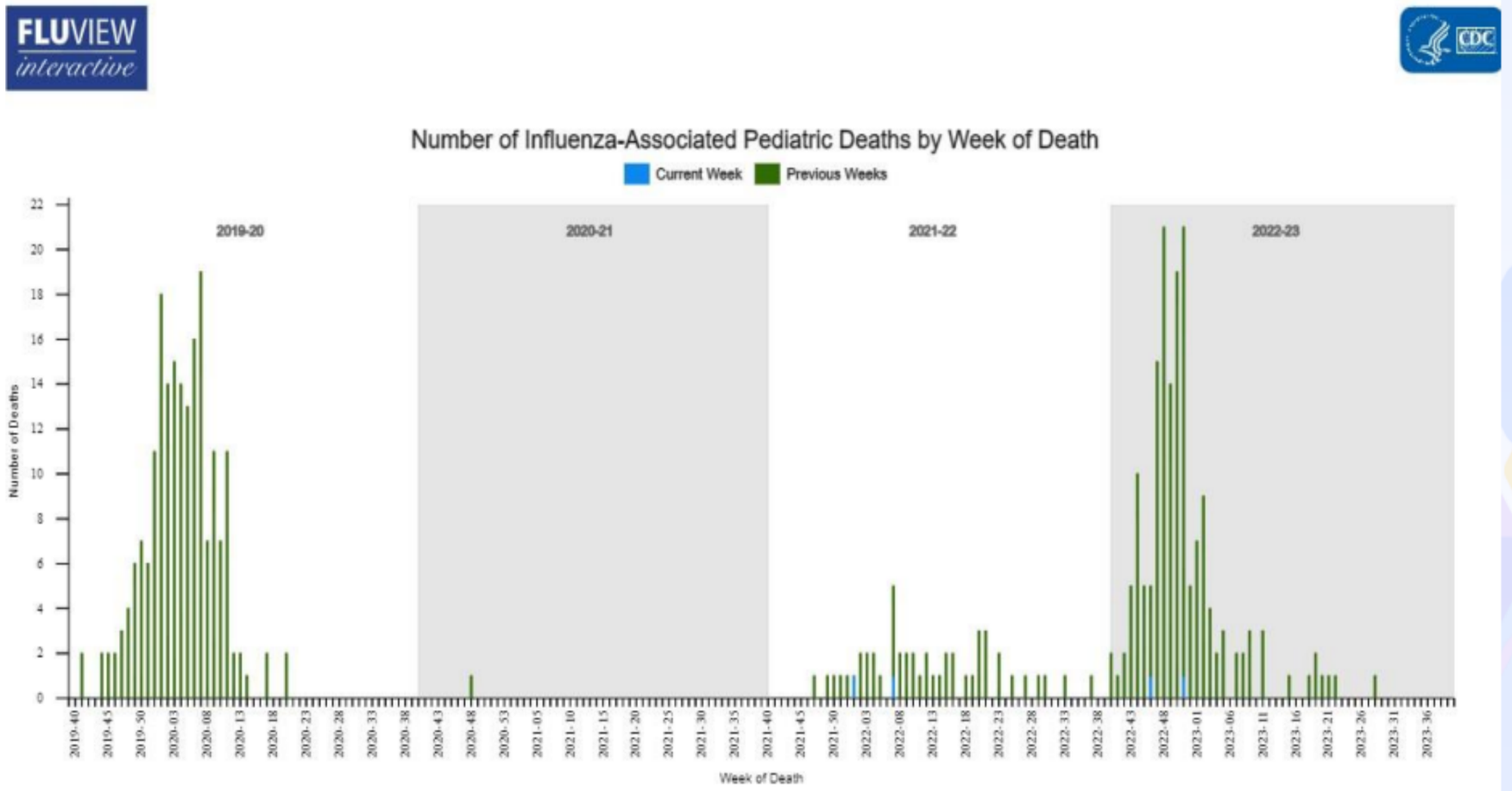
Preliminary
2022 – 2023 Estimates

At least 19,000 deaths

At least 300,000 hospitalizations

At least 27 million illnesses

Influenza-Associated Pediatric Deaths* Reported to CDC



	No. of Pediatric Deaths*
2004-05	47
2005-06	46
2006-07	77
2007-08	88
2008-09	137
2009-10	288
2010-11	124
2011-12	37
2012-13	171
2013-14	111
2014-15	148
2015-16	95
2016-17	110
2017-18	188
2018-19	144
2019-20	199
2020-21	1
2021-22	49
2022-23	**168**

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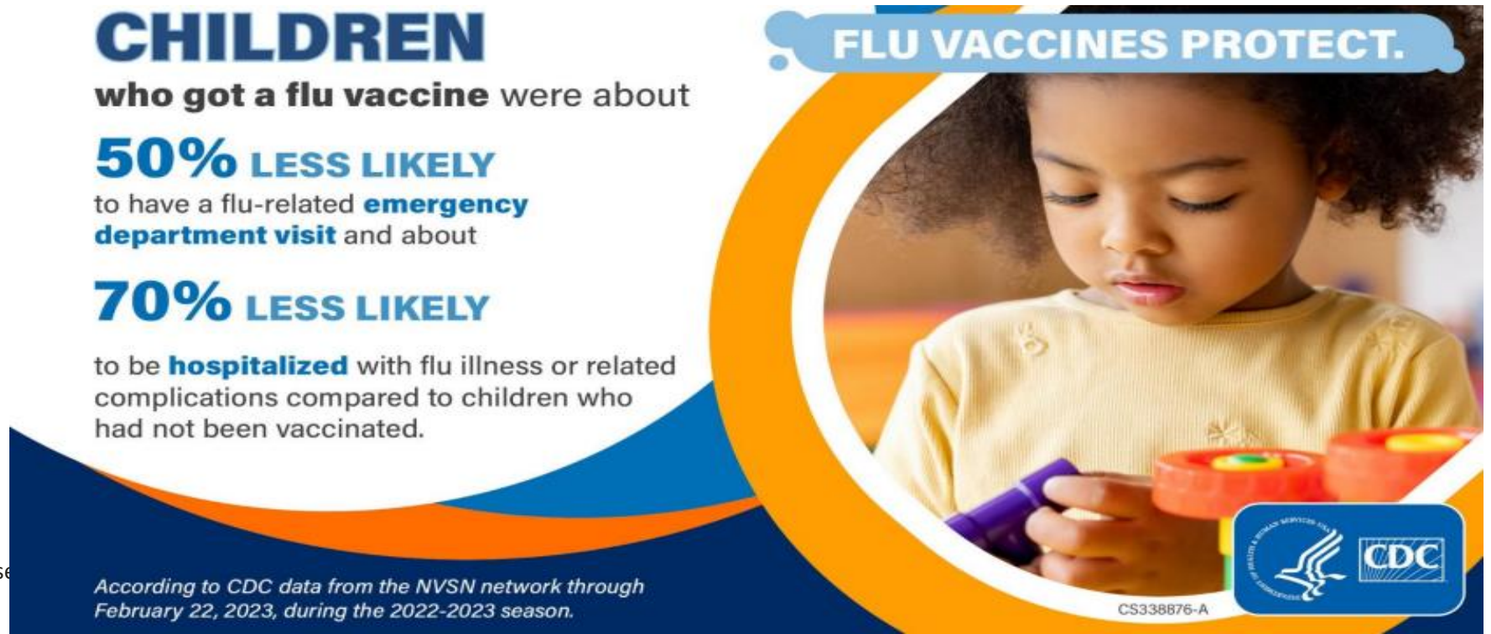
2022-2023 Influenza Vaccine Effectiveness Against Influenza-Associated Emergency Department Visits and Hospitalizations in Children Aged 6 mos–17 years, New Vaccine Surveillance Network (NVSN)

Outcomes	Vaccinated/ Total (%) Influenza positive	Vaccinated/ Total (%) Influenza negative	Effectiveness against laboratory confirmed Influenza A* in hospital and ED settings, 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/H1N1	23/139 (17)	750/2256 (33)	**56 (28 to 72)**

* Of 335 influenza-positive specimens sequenced, 250 were A(H3N2) clade 3C.2a1b.2a.2b and 32 were clade 3C.2a1b.2a.2a.1 and 38 were A(H1N1) clade 6B.1A.5a.2a.1. There were 16 coinfections with Influenza and SARS-CoV-2 that were excluded from the VE estimate.
** Multivariable logistic regression models adjusted for site, age, and calendar time.



CDC Antiviral Treatment Recommendations

- Antiviral treatment is recommended as early as possible for any patient with confirmed or suspected influenza who is:
  - Hospitalized
  - Has severe, complicated, or progressive illness
  - Is at high risk for influenza complications

- Antiviral treatment can be considered for previously healthy, symptomatic outpatient not at high risk with confirmed or suspected influenza, if treatment can be initiated within 48 hours of illness onset

- Clinical benefit is greatest when antiviral treatment is given early

Influenza Antiviral Medication Treatment, Route and Age Indications

Drug	Route	Age Indication for Treatment
Oseltamivir*	Oral	Any age
Zanamivir	Inhaled	≥7 years
Peramivir**	Intravenous	≥6 months
Baloxavir***	Oral	≥5 years

Tamiflu®
Relenza®
Rapivab®
Xofluza®

* Oral oseltamivir phosphate is approved by the FDA for treatment of acute uncomplicated influenza within 2 days of illness onset in people 14 days and older. Although not part of the FDA-approved indications, use of oral oseltamivir for treatment of influenza in infants less than 14 days old is recommended by the CDC and the American Academy of Pediatrics.

** Intravenous peramivir is approved by the FDA for treatment of acute uncomplicated influenza within 2 days of illness onset in people 6 months and older.

*** Oral baloxavir marboxil is approved by the FDA for treatment of acute uncomplicated influenza within 2 days of illness onset in people aged ≥5 years who are otherwise healthy, or in people aged ≥12 years who are high risk of developing influenza-related complications.

2023-2024 Influenza Vaccine Composition

- Egg-based IIVs and LAIV4:
  - An A/Victoria/4897/2022 (H1N1)pdm09-like *(updated)*
  - An A/Darwin/9/2021 (H3N2)-like virus
  - A B/Austria/1359417/2021 (Victoria lineage)-like virus
  - A B/Phuket/3073/2013 (Yamagata lineage)-like virus.
- Cell-culture-based IIV4 and RIV4:
  - An A/Wisconsin/67/2022 (H1N1)pdm09-like virus *(updated)*
  - An A/Darwin/6/2021 (H3N2)-like virus
  - A B/Austria/1359417/2021 (Victoria lineage)-like virus
  - A B/Phuket/3073/2013 (Yamagata lineage)-like virus.

Updates to Guidelines for Influenza Vaccine Administration to People with Egg Allergy

- Most influenza vaccines are produced with an egg-based manufacturing process and contain a small amount of egg proteins
  - Additional safety measures were *previously recommended* for administration of egg-based influenza vaccine to people who had a history of severe allergic reactions to egg

- *UPDATE* People with egg-allergy may receive any influenza vaccine (egg-based or non-egg based) that is otherwise appropriate for their age and health status; additional safety measures are no longer recommended

- All vaccines should be given in settings where allergic reactions can be recognized and treated quickly.

Influenza: What can we expect?

Prevention and treatment.

Different flu vaccines are approved for use in different groups of people – discuss these options with your HCP.

- Flu shots are approved for use in children as young as 6 months old and flu shots approved for use in adults 65 years and older.
- Flu shots also are recommended and approved for use in pregnant women and people with certain chronic health conditions.
- The nasal spray flu vaccine is approved for use in non-pregnant individuals who are 2 years through 49 years of age. People with some certain medical conditions should not receive the nasal spray flu vaccine.

Influenza: What can we expect?

Prevention and treatment.

Make plans to get vaccinated early in fall, before flu season begins. CDC recommends that people get a flu vaccine by the end of October.

However, getting vaccinated early (for example, in July or August) is likely to be associated with reduced protection against flu infection later in the flu season, particularly among older adults.

https://www.cdc.gov/flu/images/prevent/H_PN_CDC-5656.jpg

Influenza: What can we expect?

Flu testing / Diagnosis

Table 1: Influenza Virus Testing Methods

Method[1]	Types Detected	Acceptable Specimens[2]	Test Time	CLIA Waived[3]
Rapid Influenza Diagnostic Tests[4] (antigen detection)	A and B	NP[5] swab, aspirate or wash, nasal swab, aspirate or wash, throat swab	<15 min.	Yes/No
Rapid Molecular Assay [influenza viral RNA or nucleic acid detection]	A and B	NP[5] swab, nasal swab	15-30 minutes[6]	Yes/No[6]
Immunofluorescence, Direct (DFA) or Indirect (IFA) Florescent Antibody Staining [antigen detection]	A and B	NP[4] swab or wash, bronchial wash, nasal or endotracheal aspirate	1-4 hours	No
RT-PCR[7] (singleplex and multiplex; real-time and other RNA-based) and other molecular assays [influenza viral RNA or nucleic acid detection]	A and B	NP[5] swab, throat swab, NP[5] or bronchial wash, nasal or endotracheal aspirate, sputum	Varies (1 to 8 hours, varies by the assay)	No
Rapid cell culture (shell vials; cell mixtures; yields live virus)	A and B	NP[5] swab, throat swab, NP[5] or bronchial wash, nasal or endotracheal aspirate, sputum; (specimens placed in VTM[8])	1-3 days	No
Viral tissue cell culture (conventional; yields live virus)	A and B	NP[5] swab, throat swab, NP[5] or bronchial wash, nasal or endotracheal aspirate, sputum (specimens placed in VTM8)	3-10 days	No

https://www.cdc.gov/flu/professionals/diagnosis/table-testing-methods.htm

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Influenza: What can we expect?

Flu testing / Diagnosis

- The Infectious Diseases Society of America (IDSA) recommends use of rapid influenza molecular assays over rapid influenza diagnostic tests (RIDTs) for detection of influenza viruses in respiratory specimens of **outpatients.**

- IDSA recommends use of RT-PCR or other molecular assays for detection of influenza viruses in respiratory specimens of **hospitalized patients.** Consult the IDSA Influenza Clinical Practice Guidelines for recommendations on influenza testing and information on interpretation of testing results.

Influenza: What can we expect?

Flu testing / Diagnosis

Factors that can affect the outcome of the rapid flu test include:

- **Timing**: Tests are most accurate when specimens are collected within 3-4 days of the onset of symptoms, when influenza viral shedding is highest.
- **Collection**: Each test has its own specifications for specimen collection—nasopharyngeal, nasal, throat swab, or aspirate—which *must be followed for accuracy.*
- **Flu type**: Rapid flu tests are better able to detect influenza A than influenza B.
- **Current flu activity**: False negatives are more likely when flu activity is high but can occur at any time. Similarly, false positives are more common when flu activity is low.

Influenza: What can we expect?

Flu testing / Diagnosis

When interpreting the results of a rapid flu test, your doctor will consider all of this in the context of your symptoms and current flu activity in the community. These tests are available as a tool, but results are not the only deciding factor in making a diagnosis.[2]

False Negative

- You have the flu, but the test did not detect it

False Positive

- The test detected the flu, although you do not have it

****Soapbox statement**: It is CRITICAL for a medical laboratory professional to conduct and interpret all medical laboratory testing.

Risk groups – Flu

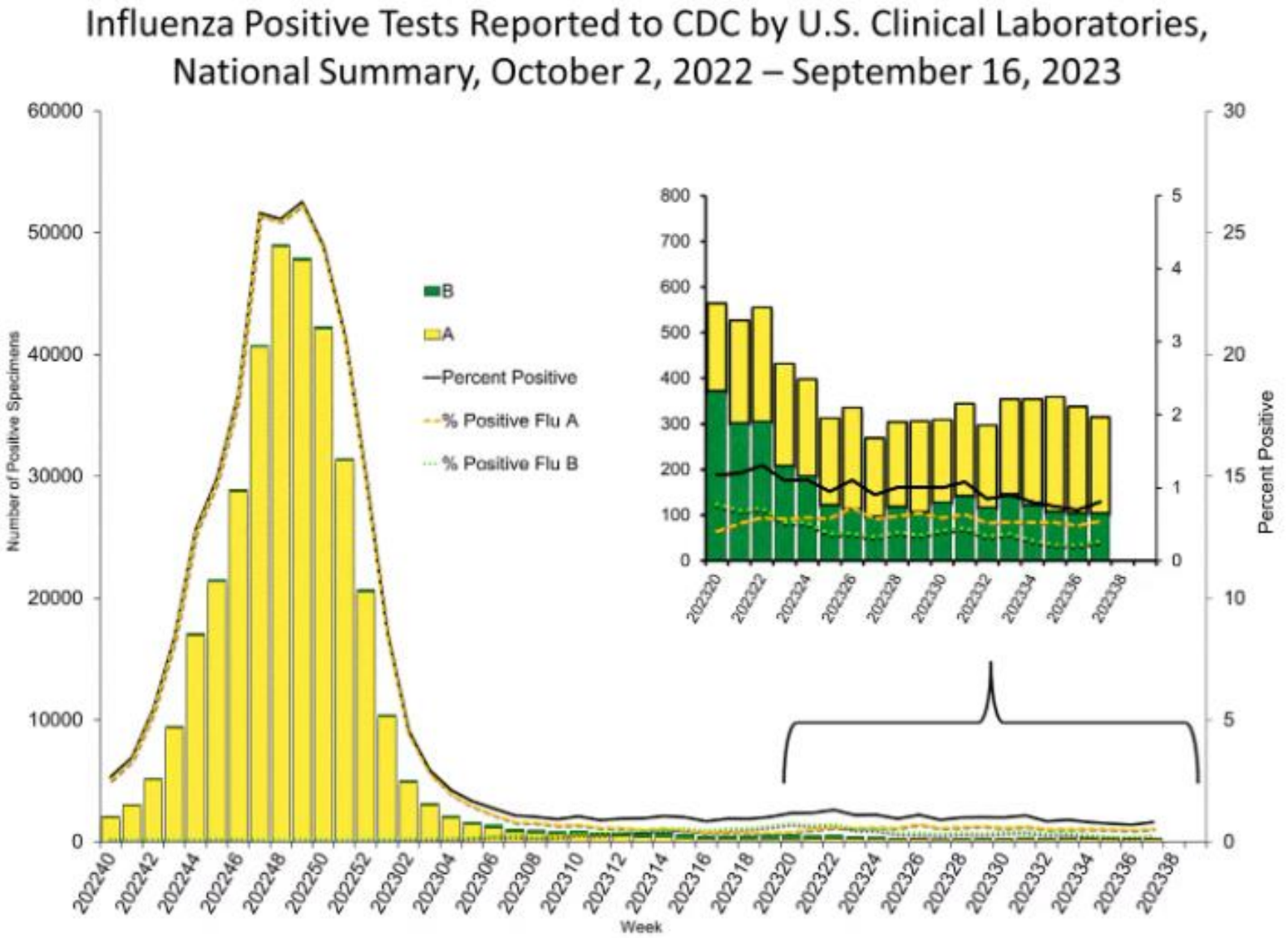
- Adults 65 Years and Older
- Adults with Chronic Health Conditions
- Specific High-Risk Groups
  - HIV / AIDS, Pregnant Women
  - Cancer, Metabolic and Endocrine disorders
  - Young children, Nursing home residents
  - Chronic lung disease, blood disorders, general immunocompromised

Epidemiology – Why is this important?

- Flu viruses are constantly changing (referred to as antigenic drift).
- Influenza viruses can also undergo an abrupt, major change (referred to as antigenic shift) that results novel viruses.
- Vaccines must be administered annually and are updated regularly based on surveillance findings.
- Flu treatment is guided by laboratory surveillance for antiviral resistance.
- Flu surveillance and targeted research studies are used to monitor the impact of influenza on different segments of the population (e.g. age groups, underlying medical conditions).

*Animal reservoirs allow stealth mode

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



	Week 34	Data Cumulative since October 2, 2022 (Week 40)
No. of specimens tested	33,251	3,929,713
No. of positive specimens (%)	266 (0.8%)	358,134 (9.1%)
Positive specimens by type		
Influenza A	170 (63.9%)	348,600 (97.3%)
Influenza B	96 (36.1%)	9,534 (2.7%)

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

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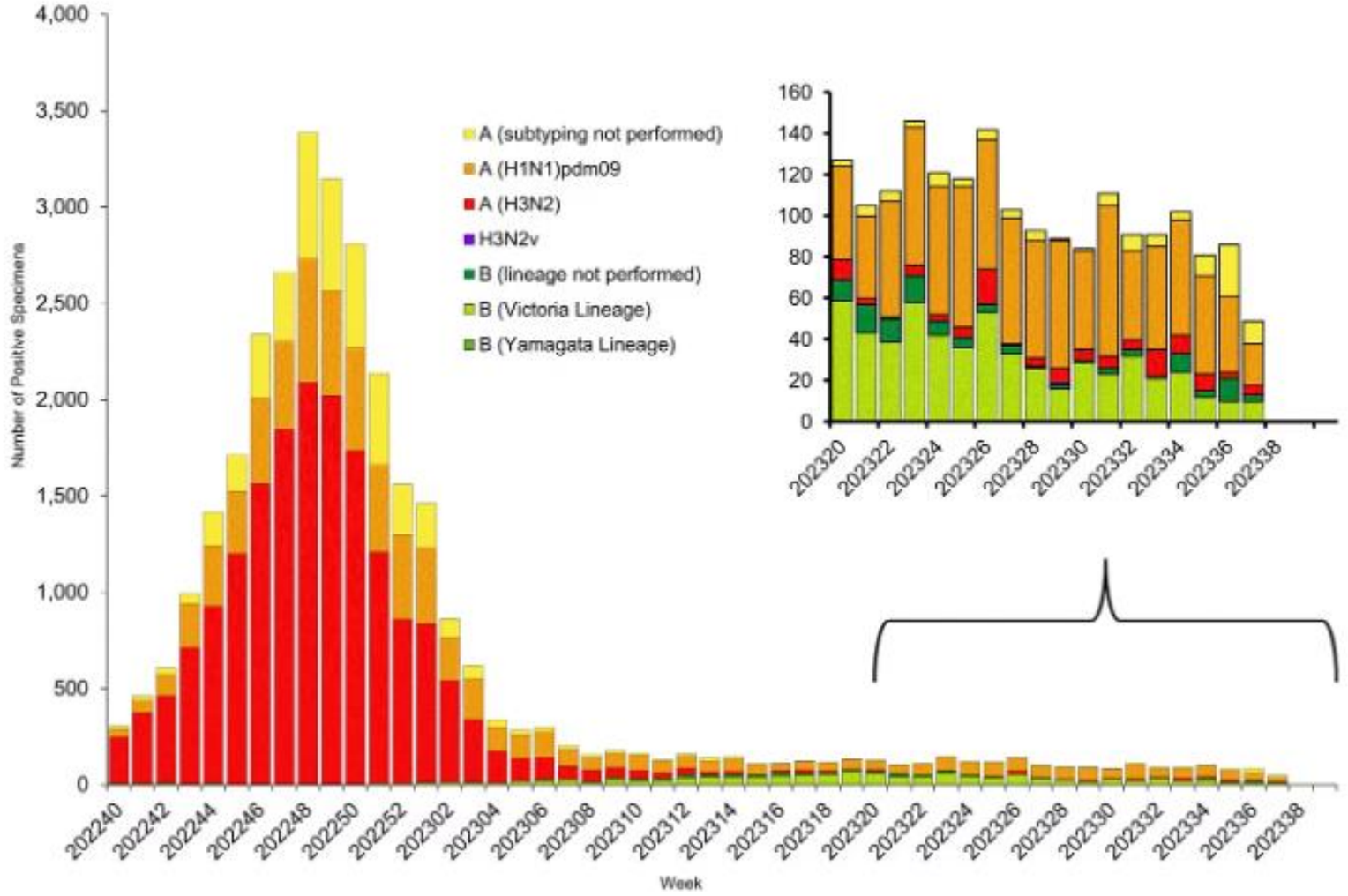
Public Health Laboratories

The results of tests performed by public health laboratories nationwide are summarized below. Data from public health laboratories are used to monitor the proportion of circulating viruses that belong to each influenza virus type/subtype/lineage. Viruses known to be associated with recent live attenuated influenza vaccine (LAIV) receipt or found upon further testing to be a vaccine virus are not included as they are not circulating influenza viruses.

	Week 37	Data Cumulative since October 2, 2022 (Week 40)
No. of specimens tested	2,801	286,709
No. of positive specimens	49	31,107
Positive specimens by type/subtype		
Influenza A	36 (73.5%)	29,641 (95.3%)
(H1N1)pdm09	20 (80.0%)	7,530 (29.8%)
H3N2	5 (20.0%)	17,704 (70.2%)
H3N2v	0	2 (<0.1%)
Subtyping not performed	11	4,405
Influenza B	13 (26.5%)	1,466 (4.7%)
Yamagata lineage	0 (0%)	0 (0%)
Victoria lineage	10 (100%)	1,186 (100%)
Lineage not performed	3	280

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

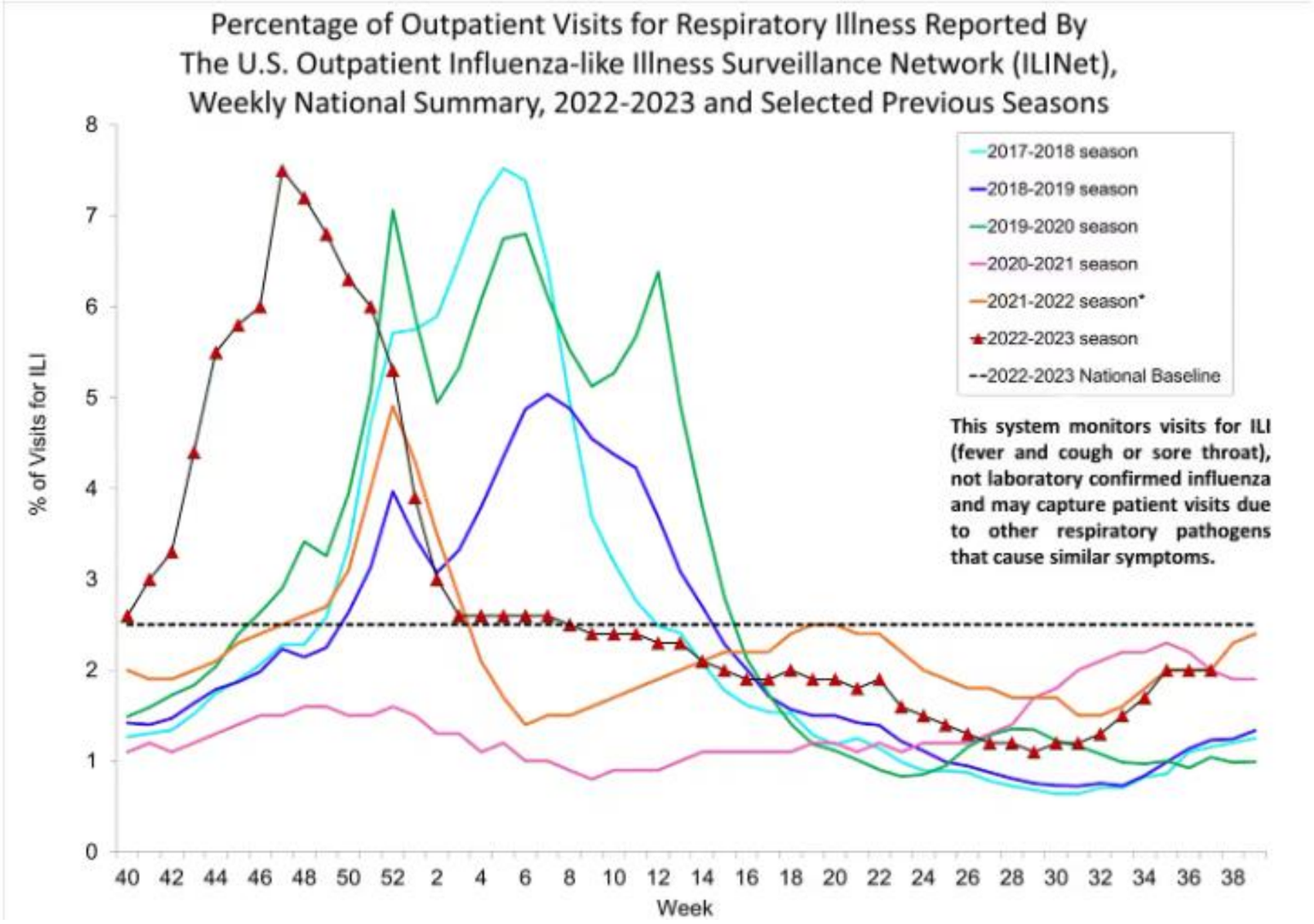
Influenza Positive Tests Reported to CDC by U.S. Public Health Laboratories, National Summary, October 2, 2022 – September 16, 2023



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

Outpatient Respiratory Illness Visits

Nationwide during week 37, 2.0% of patient visits reported through ILINet were due to respiratory illness that included fever plus a cough or sore throat, also referred to as ILI. Multiple respiratory viruses are co-circulating, and the relative contribution of influenza virus infection to ILI varies by location.



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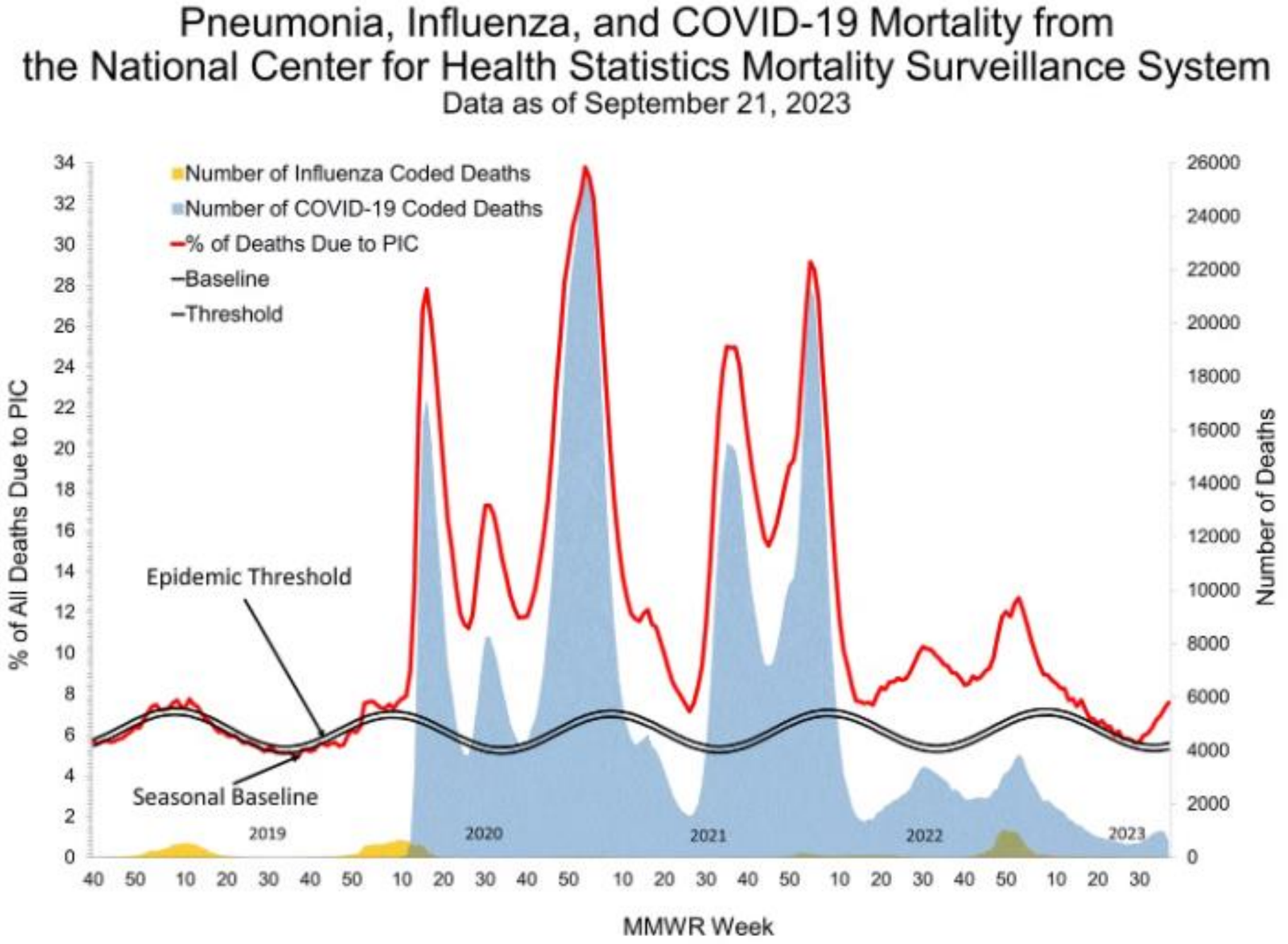

https://www.cdc.gov/flu/weekly/index.htm

Upcoming 2023-2024 U.S. Influenza Season

- Influenza remains unpredictable
- Last season reminded us that influenza viruses can
  - circulate early
  - result in high rates of medically attended illnesses in children
  - co-circulate with other respiratory viruses such as SARS-CoV-2 and respiratory syncytial virus, placing increased strain on healthcare systems

- **Annual influenza vaccination is the most effective way to prevent influenza**

What’s up with RSV?

- Respiratory syncytial (sin-SISH-uhl) virus, or RSV, is a common respiratory virus that usually causes mild, cold-like symptoms.
- Most people recover in a week or two, but RSV can be serious, especially for infants and older adults.
- RSV is the most common cause of bronchiolitis (inflammation of the small airways in the lung) and pneumonia (infection of the lungs) in children younger than 1 year of age in the United States.

Infant and father (source: CDC - https://www.cdc.gov/rsv/index.html)

Overview of RSV Illness

CDC, Centers for Disease Control and Prevention

- Common respiratory virus
  - Fourth most common viral pathogen after influenza A and B, and SARS-CoV-2
- Classified into 2 major subtypes—A and B—based on antigenic and genetic analysis
  - One subtype predominates during one season
- Spreads through air via respiratory droplets or direct contact via surfaces → CDC recommends “contact” precautions
- Contagious for 3 to 8 days but immunosuppressed might shed for up to 4 weeks
- RSV infection does not confer long-term immunity → recurrent infections common

RSV Info

- People of any age can get another RSV infection, but infections later in life are generally less severe. People at highest risk for severe disease include:
  - Premature infants
  - Young children with congenital (from birth) heart or chronic lung disease
  - Young children with compromised (weakened) immune systems due to a medical condition or medical treatment
  - Adults with compromised immune systems
  - Older adults, especially those with underlying heart or lung disease

Children (source: CDC - https://www.cdc.gov/rsv/index.html)

RSV Info

- RSV can survive for many hours on hard surfaces such as tables and crib rails. It typically lives on soft surfaces such as tissues and hands for shorter amounts of time.

- In the United States and other areas with similar climates, RSV infections generally occur during fall, winter, and spring.

Trends and Surveillance

- Each year in the United States, RSV leads, on average, to approximately—
  - 2.1 million outpatient visits among children younger than 5 years old
  - 58,000 hospitalizations among children younger than 5 years old
  - 177,000 hospitalizations among adults 65 years and older
  - 14,000 deaths among adults 65 years and older

Bacterial Superinfections: Common in Patients With RSV

Occur in 12.5% of RSV+ infections[1]

In study of 842 winter hospitalizations (N=771)[2]

- 348 (41%) HAD EVIDENCE OF VIRAL INFECTION
  - OF THESE,
    - 61% INVOLVED VIRAL INFECTION ALONE
    - 18% OF RSV+ PATIENTS HAD CONFIRMED BACTERIAL INFECTION
    - ADDITIONAL 21% OF RSV+ PATIENTS HAD PROCALCITONIN EVIDENCE OF BACTERIAL INFECTION
- 90% RECEIVED ANTIBIOTICS AS PART OF TREATMENT

RSV Is Challenging to Diagnose, Particularly in Older Individuals

Common RSV Clinical Laboratory Tests	Notes
Real-time reverse transcriptase polymerase chain reaction	Most sensitive
Antigen testing	Highly sensitive in children but not in adults
Viral culture	Less commonly used
Serology	Typically used for research purposes

Clinical symptoms of RSV are nonspecific and can overlap with other viral respiratory infections (eg, influenza and COVID-19) and some bacterial infections[1]

- ADULTS WITH REINFECTION SHED VIRUS AT TITERS MUCH LOWER AND FOR SHORTER DURATIONS THAN CHILDREN[2]

Most common RSV clinical laboratory tests[1]:

Making a Diagnosis of RSV: Rapid Molecular PCR Tests

- Now more widely available
- Sensitivity >95% for most platforms
- Usually duplexed with influenza testing and results are available within 1 hour
- Shown to reduce the number of ancillary tests, decrease antibiotic use
- Rapid identification of pathogen also informs infection control measures to prevent nosocomial outbreaks in hospitals and skilled nursing facilities

- Datta S, et al. *J Infect Dis.* 2017;215(11):1706-1710.

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Medical Laboratory Testing Matters!

- A retrospective cohort study on hospitalized adults with RSV infections admitted to 1 of the 3 participating medical units in Hong Kong between 1 January 2009 and 31 December 2011 (i.e., 36 months) (N = 607).
- The mean age of RSV patients was 75 (SD, 16) years; Lower respiratory and cardiovascular complications were diagnosed in 71.9% (pneumonia, 42.3%; acute bronchitis, 21.9%; chronic obstructive pulmonary disease/asthma exacerbation, 27.3%) and 14.3% of patients, respectively; 12.5% had bacterial superinfections
- RSV can cause severe lower respiratory complications in older adults, resulting in respiratory failure, prolonged hospitalization, and high mortality like seasonal influenza.
- Note that the study used a temperature >37.5C as the threshold, a temperature >37.2C is used in the long-term care setting so as to not miss the opportunity for earlier testing (and potential need for intervention/isolation).

Lee N, et al. *Clin Infect Dis.* 2013;57(8):1069-1077. Reproduced by permission of Oxford University Press on behalf of the Infectious Diseases Society of America.

Why Make a Diagnosis?

Low awareness has resulted in delayed diagnosis and intervention, or ability to distinguish RSV from other potential diseases of concern, e.g., COVID

1) Health care utilization associated with RSV for older adults, including antibiotic and diagnostic stewardship
2) Long-term morbidity and mortality associated with RSV infection in this population
3) Risk stratification to inform future vaccine efforts

Health care utilization for older patients hospitalized with RSV has been reported to be similar or higher when compared to patients hospitalized with influenza*

	Influenza	RSV
Hospital length of stay (days)	3. 6	6
Mechanical ventilation (%)	7.2	16.7
Mean adjusted costs	$14,519	$38,828

*Data taken from the Nationwide Inpatient Sample, Healthcare Cost and Utilization Project, and Agency for Healthcare Research and Quality for 1997 to 2012; data did not differentiate among strains.

Recommendations

- In 2023, new prevention tools for RSV have become available.
- Nirsevimab is a long-acting monoclonal antibody approved by the Food and Drug Administration (FDA) to protect infants and some young children at increased risk for severe RSV disease. Nirsevimab is safe and efficacious. In clinical trials, one dose of nirsevimab administered as an intramuscular injection protected infants for at least 5 months (the length of an average RSV season) and reduced the risk of severe RSV disease by about 80%. The incidence of serious adverse events was not increased among nirsevimab recipients compared with placebo recipients in the clinical trials.
- RSVPreF3 and RSVpreF are recombinant protein vaccines that are both approved by FDA for use in adults ages 60 years and older to prevent RSV-associated lower respiratory tract disease. During the first RSV season after vaccination, each vaccine was more than 80% efficacious in preventing RSV-associated lower respiratory tract disease. A small number of participants in clinical trials (6 of 38,177 total participants aged ≥60 years who received either vaccine) developed inflammatory neurologic events within 6 weeks after RSV vaccination, but it was unclear whether these events were related to RSV vaccination.

Nirsevimab (BeyfortusTM, Sanofi and AstraZeneca) & RSVPreF3 (Arexvy, GSK) or RSVpreF (AbrysvoTM, Pfizer)

Recommendations for Clinicians

- Monoclonal antibodies for infants and young children: Clinicians should start to offer nirsevimab when it becomes available (expected by early October) for all infants ages <8 months, and for infants and for children ages 8–19 months who are at increased risk for severe RSV disease.
- RSV vaccines for older adults: CDC recommends that adults ages 60 years and older may receive a single dose of RSV vaccine (either product) using shared clinical decision-making to prevent RSV-associated lower respiratory tract disease. Clinicians should discuss RSV vaccination with adults ages 60 years and older. Vaccination should be prioritized in adults ages 60 years and older who are most likely to benefit, including those with certain chronic medical conditions associated with increased risk of severe RSV disease, such as heart disease (e.g., heart failure, coronary artery disease), lung disease (e.g., chronic obstructive pulmonary disease [COPD], asthma), and immunocompromising conditions. Adults with advanced age and those living in nursing homes or other long-term care facilities are also at increased risk of severe RSV disease and may benefit from RSV vaccination.

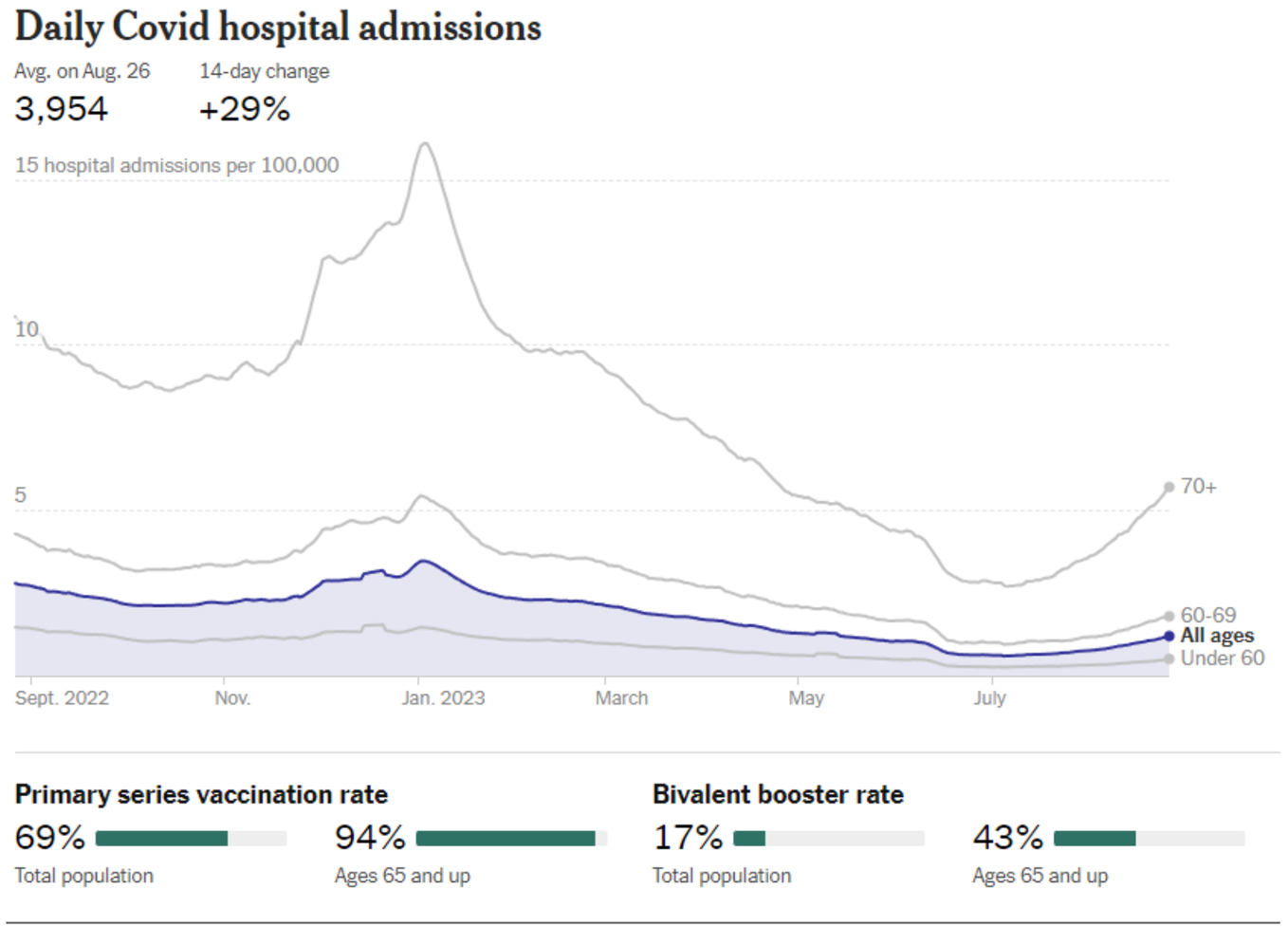
Nirsevimab (BeyfortusTM, Sanofi and AstraZeneca) & RSVPreF3 (Arexvy, GSK) or RSVpreF (AbrysvoTM, Pfizer)

Recommendations for the Public

- Expectant parents, parents of infants under the age of 8 months, and parents with older babies (through age 19 months) at increased risk of severe RSV disease should talk with their healthcare providers about using monoclonal (preventive) antibodies to protect against RSV this season. Infants under the age of 8 months should receive preventive antibodies to protect against RSV this season.
- Adults ages 60 years and older should talk to their healthcare provider about whether RSV vaccination is appropriate for them.
- Stay home and away from others when you are sick. If you are at increased risk of severe illness, contact your healthcare provider to see if you would benefit from early diagnostic testing. Treatments for influenza and COVID-19 are available that, if given within days of symptoms starting, can reduce your risk of hospitalization and death.

Nirsevimab (BeyfortusTM, Sanofi and AstraZeneca) & RSVPreF3 (Arexvy, GSK) or RSVpreF (AbrysvoTM, Pfizer)

What's up with SARS-CoV-2 [COVID-19]?



https://www.nytimes.com/interactive/2023/us/covid-cases.html

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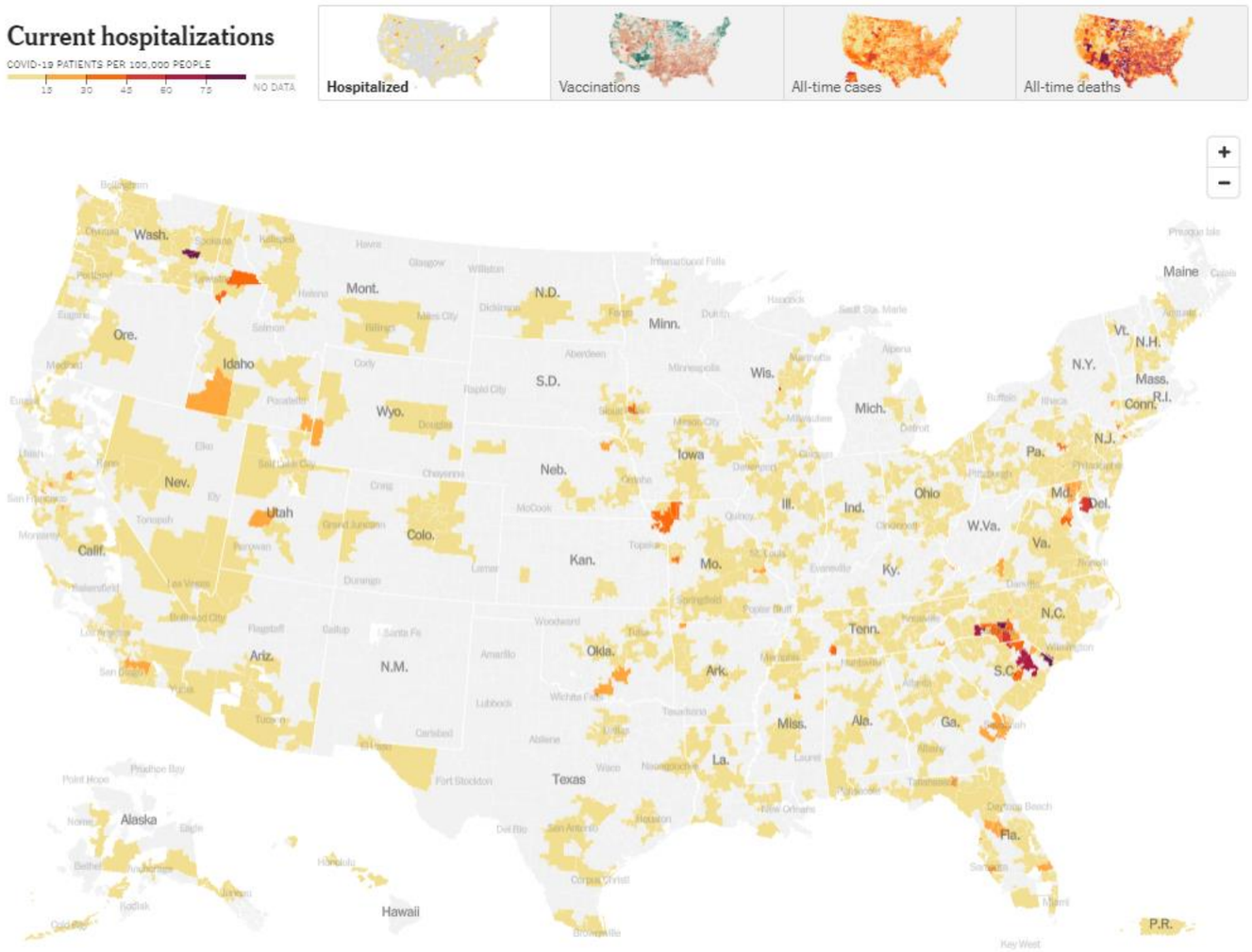

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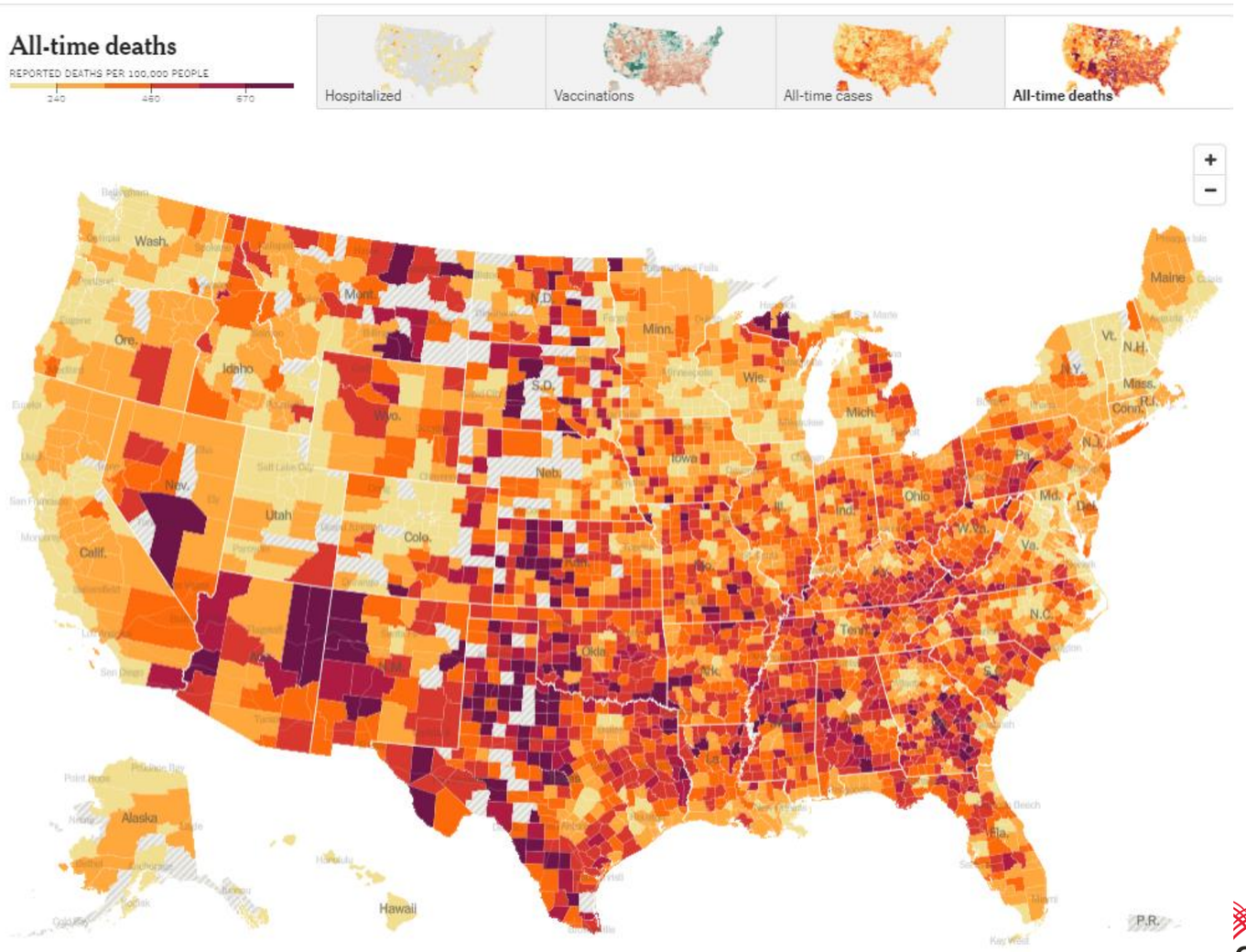

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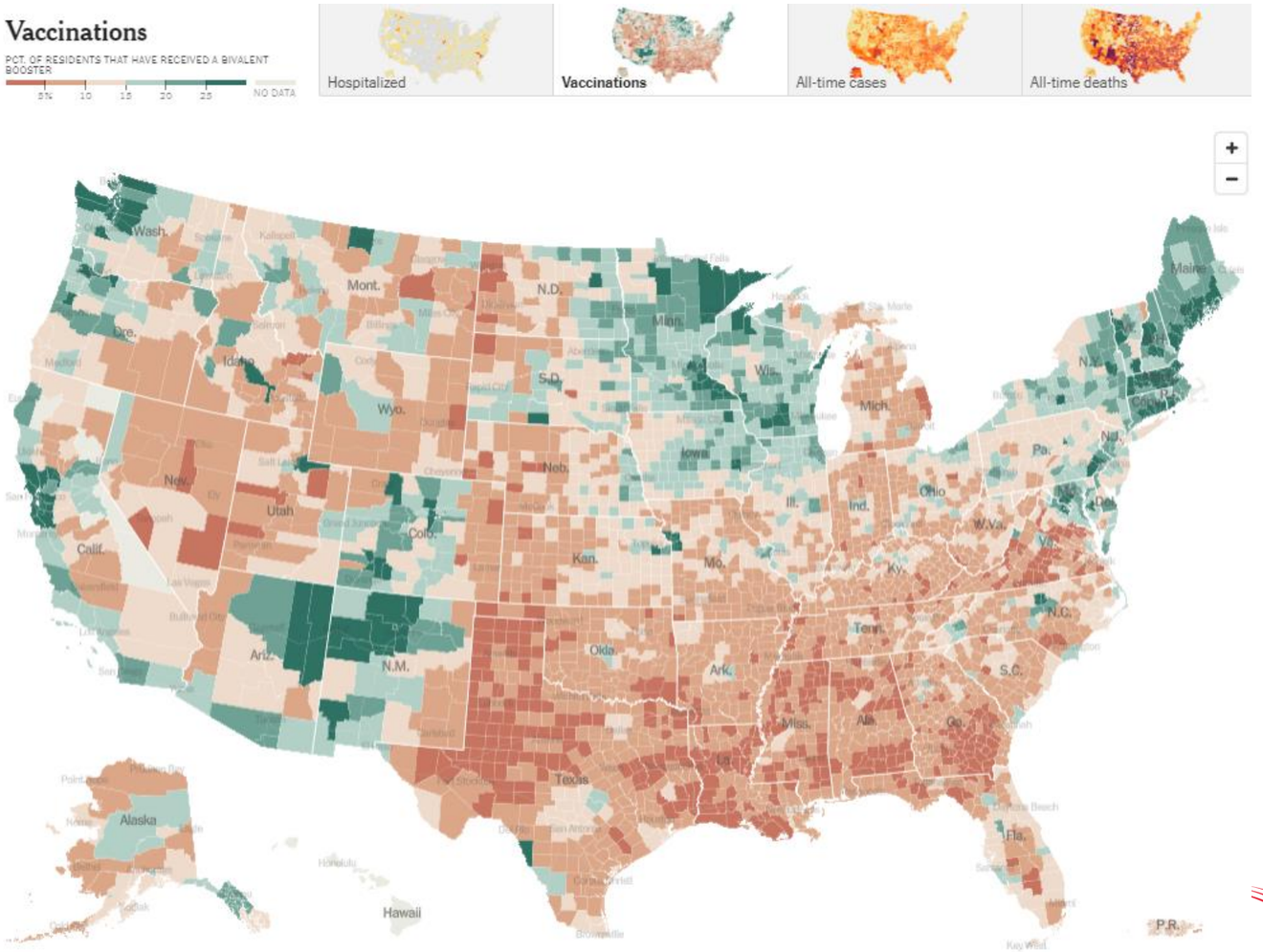

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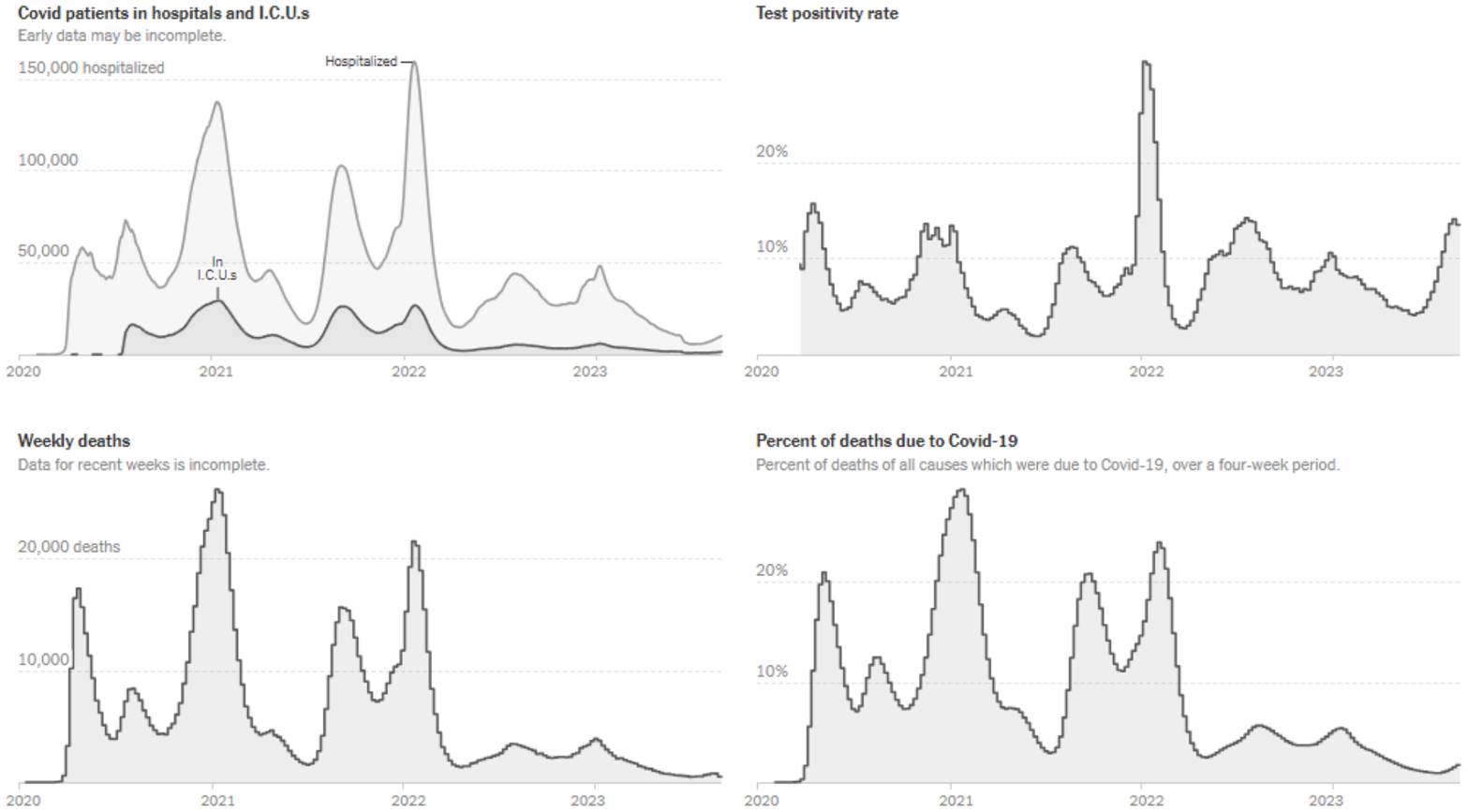

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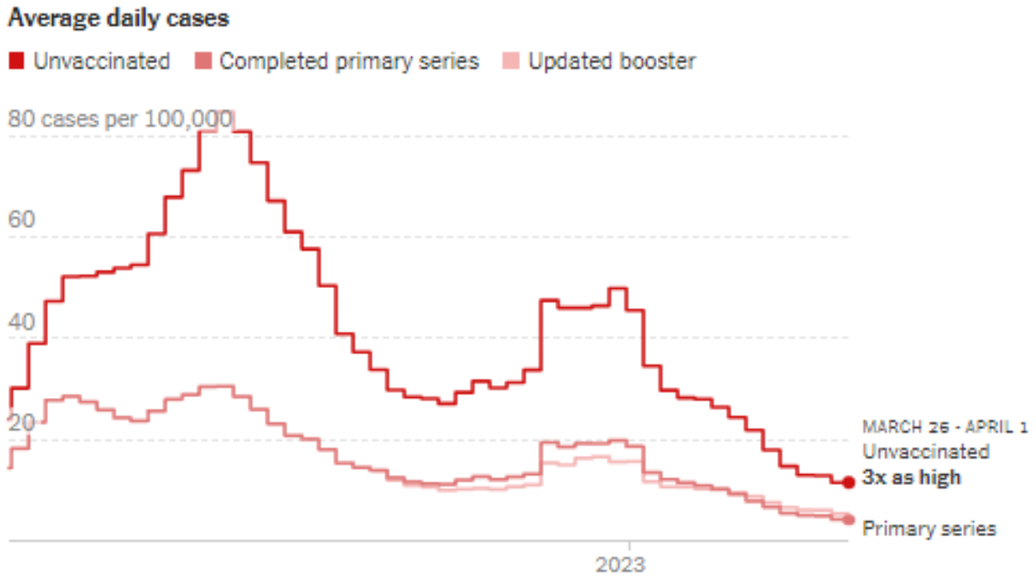
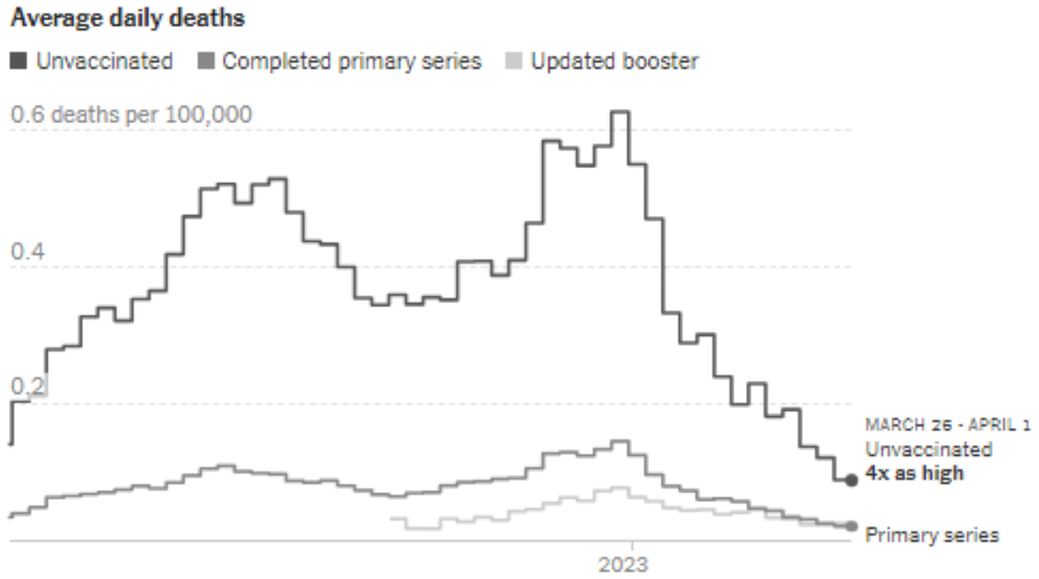
What's up with SARS-CoV-2 [COVID-19]?

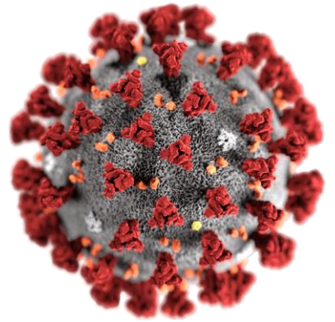


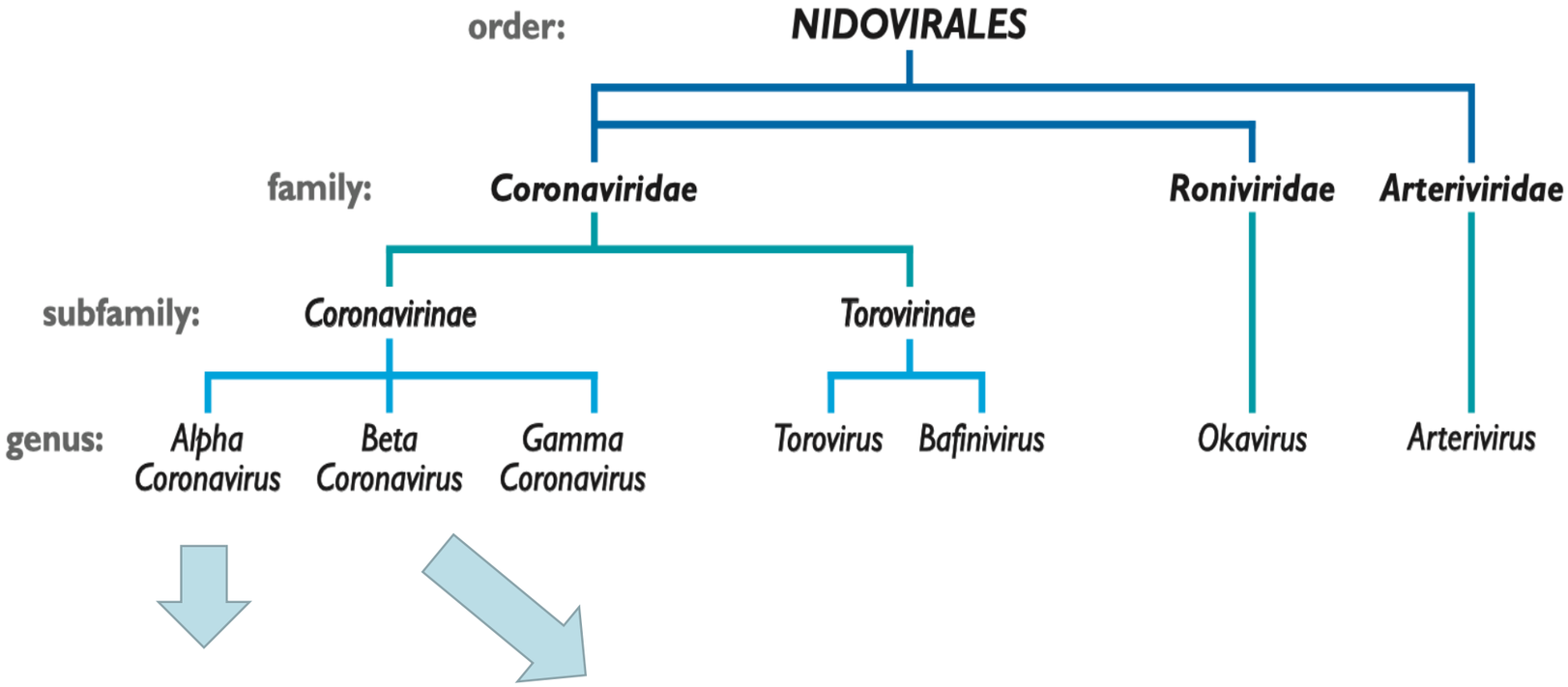


This data shows that people who are unvaccinated are at a much greater risk of dying from Covid-19 than those who have been vaccinated. These charts compare age-adjusted case and death rates for vaccinated and unvaccinated people in the states and cities that provided this data.

https://www.nytimes.com/interactive/2023/us/covid-cases.html

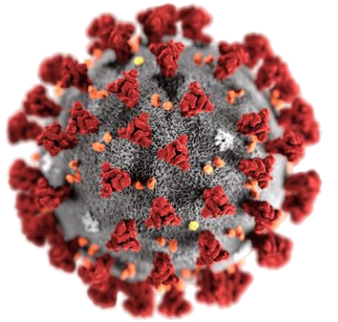
7 Human Coronaviruses: 4 normal; 3 “novel”





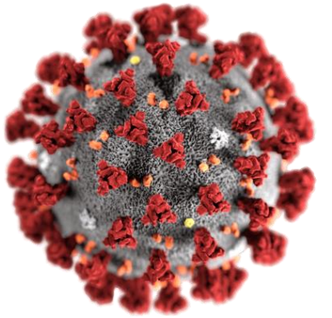
Alpha: **HCoV-229E**, **HCoV-NL63** Beta: **HCoV-HKU1**, **HCoV-OC43**, **MERS-CoV**, **SARS-CoV**, **SARS-CoV-2**

Upper Respiratory Infections



- Normal human coronaviruses cause 5-10% of common cold/URIs, with outbreaks to 30% of common cold
  - **229E** and **NL63 (alpha coronaviruses)**
  - **OC43** and **HKU1 (beta coronaviruses)**
- These four predominately attach to receptors in UPPER airway (receptors: aminopeptidase N, dipeptidyl peptidase 4)
- Seasonality unpredictable (generally winter, but persists year-round), different pattern in tropics than temperate regions
- URI symptoms, croupy or dry cough, rarely pneumonia (except sometimes NL63, but usually just causes croup); Mild diarrhea in infants
  - Don’t forget other URI viruses: Rhinovirus, Influenza A/B, Adenovirus, Parainfluenza, Respiratory syncytial virus, Human metapneumovirus

“Novel” Coronaviruses



- Novel coronaviruses predominantly in LOWER respiratory tract
  - **SARS, MERS, SARS-CoV-2**
  - Don’t forget other LRIs:
    - Viral Pneumonia: Influenza (A/B), Adenovirus, Parainfluenza (Type 1-4), Respiratory syncytial virus, Human metapneumovirus, **NL63**
    - Typical bacteria CAP: Lobar – *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Haemophilus influenzae*, *Moraxella catarrhalis; Gram neg, anaerobic if aspiration*
    - Bacterial bronchitis or atypical CAP: *Bordetella pertussis, Mycoplasma pneumoniae*, and *Chlamydia pneumoniae*
- SARS (2002-2003): Contained. CFR 10%. >50% mortality in >60 years.
- MERS (2012-13): Not Contained. CFR 35%. Linked to direct camel exposure.
- High healthcare worker infection and other nosocomial spread
  - Aerosolization during procedures (intubation, nebs, BiPAP, suctioning)
- SARS-CoV-2 (2019-?): Not Contained. CFR is variable. [see: https://coronavirus.jhu.edu/data/mortality]

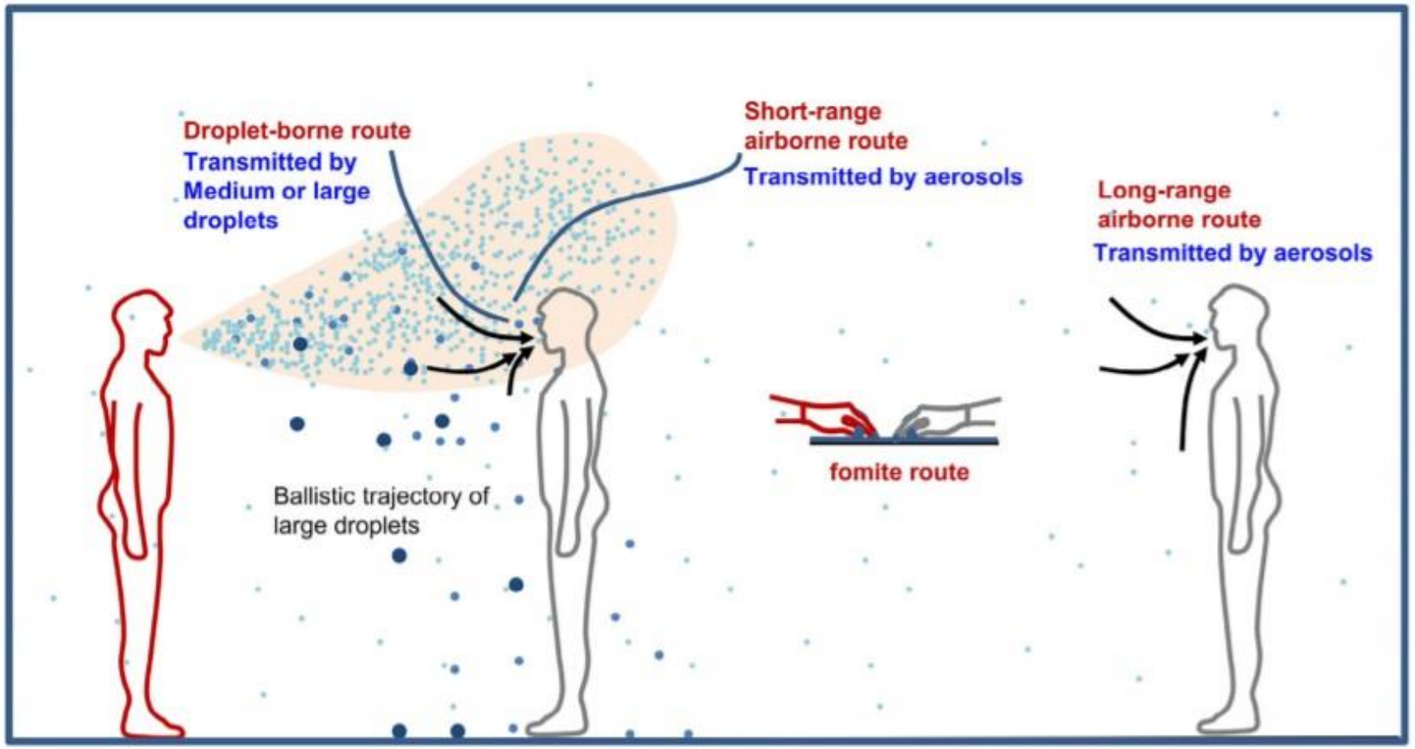


Fig 4. Illustration of different transmission routes. Small droplets (<5 μm), sometimes called aerosols, are responsible for the short-range airborne route, long-range airborne route, and indirect contact route; large droplets are responsible for the direct spray route and indirect contact route.

https://www.ajicjournal.org/article/S0196-6553(16)30531-4/pdf

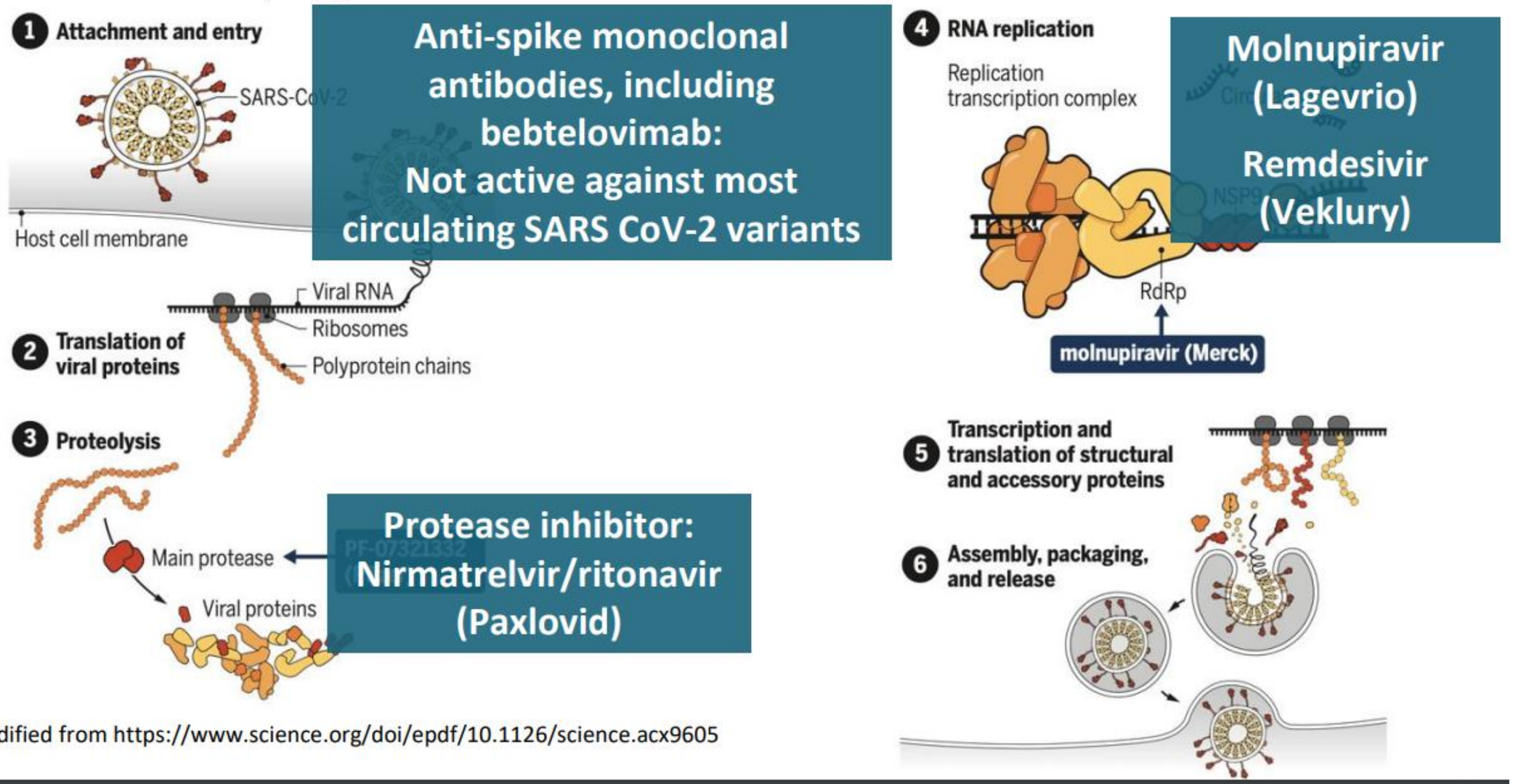
Diagnostic tests are based on nucleic acid or protein

- Nucleic acid amplification tests (NAAT)
  - PCRs, LAMP, CRISPR
  - Often lab-based
  - Highly sensitive and specific
  - Patients often test positive for extended period of time, well beyond infectiousness period

- Rapid antigen tests
  - Detect viral protein
  - May be POC (point-of-care) or at home
  - Less sensitive than NAATs
  - Virus must have replicated enough for protein to be detected
  - Delayed positivity

https://emergency.cdc.gov/coca/ppt/2023/012423_slides.pdf

SARS CoV-2 Antivirals



Modified from https://www.science.org/doi/epdf/10.1126/science.acx9605

https://emergency.cdc.gov/coca/ppt/2023/012423_slides.pdf

Stay Up to Date with COVID-19 Vaccines

Updated July 17, 2023 Español Print

What You Need to Know

- Everyone aged 6 years and older should get **1 updated Pfizer-BioNTech or Moderna COVID-19 vaccine** to be up to date.
- People aged 65 years and older may get a 2nd dose of updated Pfizer-BioNTech or Moderna COVID-19 vaccine.
- People who are moderately or severely immunocompromised may get additional doses of updated Pfizer-BioNTech or Moderna COVID-19 vaccine.
- Children aged 6 months–5 years may need multiple doses of COVID-19 vaccine to be up to date, including at least 1 dose of updated Pfizer-BioNTech or Moderna COVID-19 vaccine, depending on the number of doses they've previously received and their age.
- COVID-19 vaccine recommendations will be updated as needed.

Updated (Bivalent) and Original (Monovalent) COVID-19 Vaccines

Updated vaccines, sometimes called "bivalent" vaccines

The updated vaccines are called "updated" because they protect against **both** the original virus that causes COVID-19 **and** the Omicron variant BA.4 and BA.5. Two COVID-19 vaccine manufacturers, Pfizer-BioNTech and Moderna, have developed updated COVID-19 vaccines.

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html

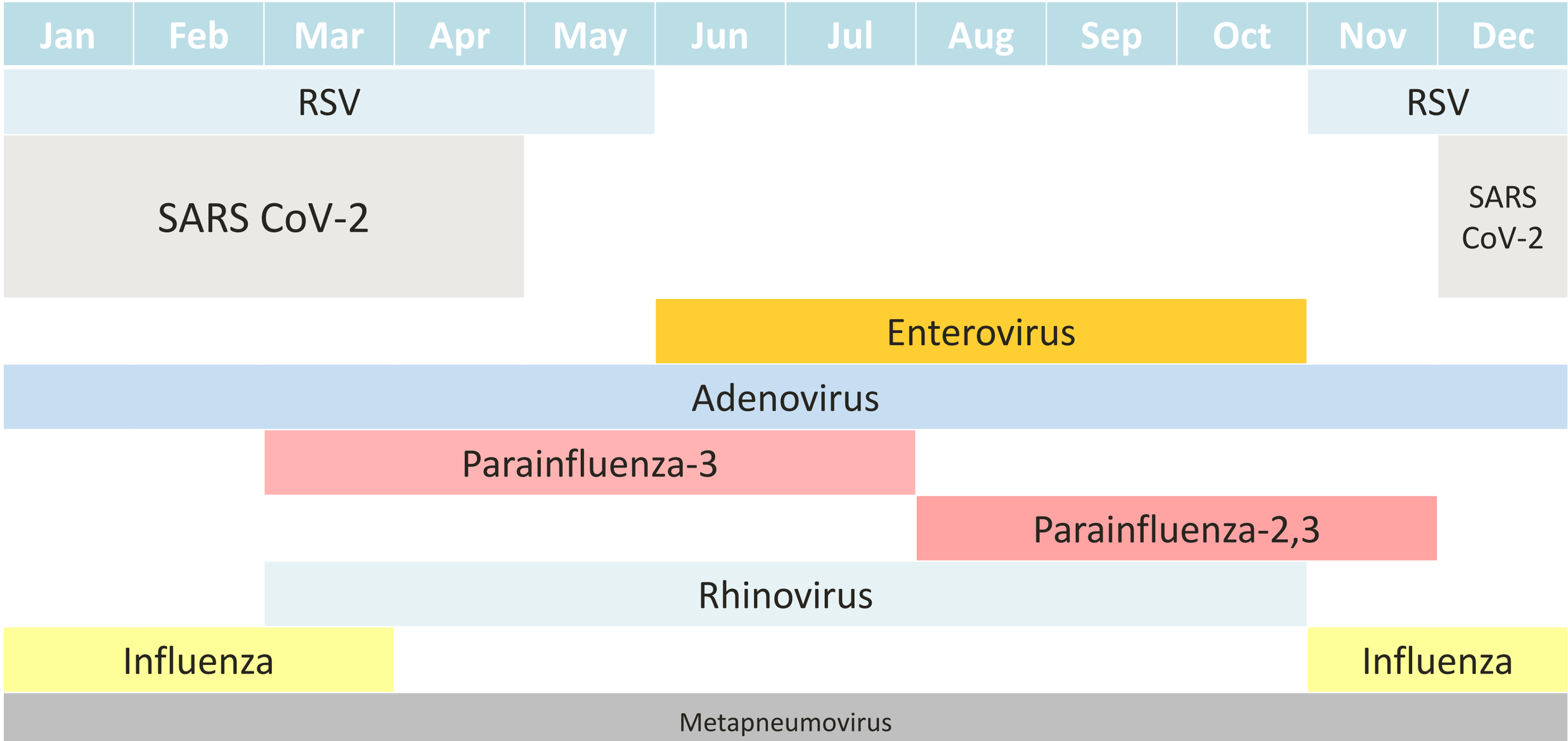
How are the new booster shots different?

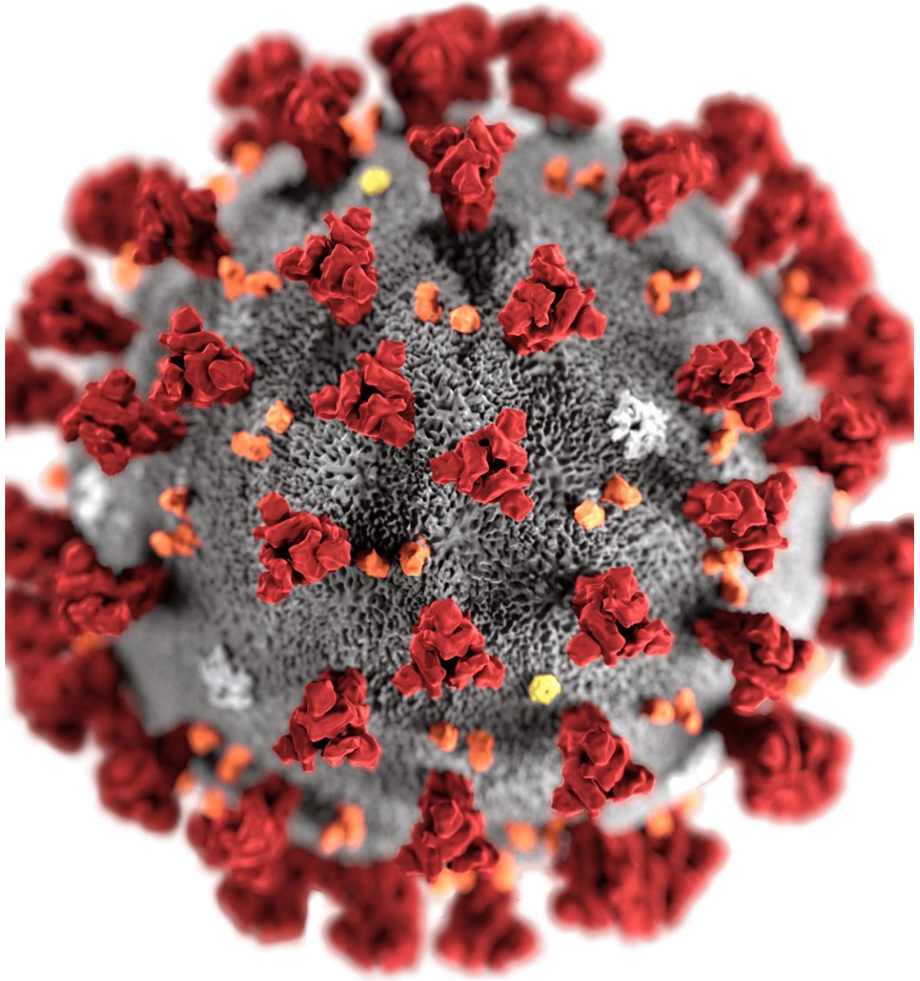
Pfizer, Moderna, and Novavax have all made updated bivalent booster shots which have been reformulated to target the XBB.1.5 Omicron subvariant, which was the predominant new strain when the reformulation decisions were made by U.S. public health officials earlier this year. Last fall, the U.S. rolled out, for the first time, bivalent COVID boosters from Pfizer and Moderna which targeted both the original Wuhan strain of the coronavirus as well as the BA.4 and BA.5 Omicron lineages which had become dominant in 2022. This year's updated boosters also target the newer XBB.1.5 Omicron lineage.

XBB.1.5 is no longer the dominant COVID variant in the U.S., but the ones that have since taken over — including the still rising EG.5 subvariant — are in the same family tree and the updated boosters are expected to offer increased protection against them as well.

https://nymag.com/intelligencer/article/what-to-know-about-the-2023-covid-booster-shots.html

Final Thoughts: Overlapping Seasonality of RSV with Other Respiratory Viruses





“EVERYTHING WE DO BEFORE A PANDEMIC WILL SEEM ALARMIST. EVERYTHING WE DO AFTER WILL SEEM INADEQUATE”

~ Michael Leavitt

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Thanks / Questions

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