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Seasonal Influenza: Vaccination, Prevention and Control in the COVID-19 Era

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Disclosures

No current disclosures



Objectives

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

1. Discuss the current epidemiology of influenza
2. Contrast the presentation and complication of influenza with SARS-CoV-2
3. Provide updates on vaccination recommendations
4. Summarize testing and treatment guidelines

When you see this icon...



Epidemiology and Clinical Characteristics of influenza

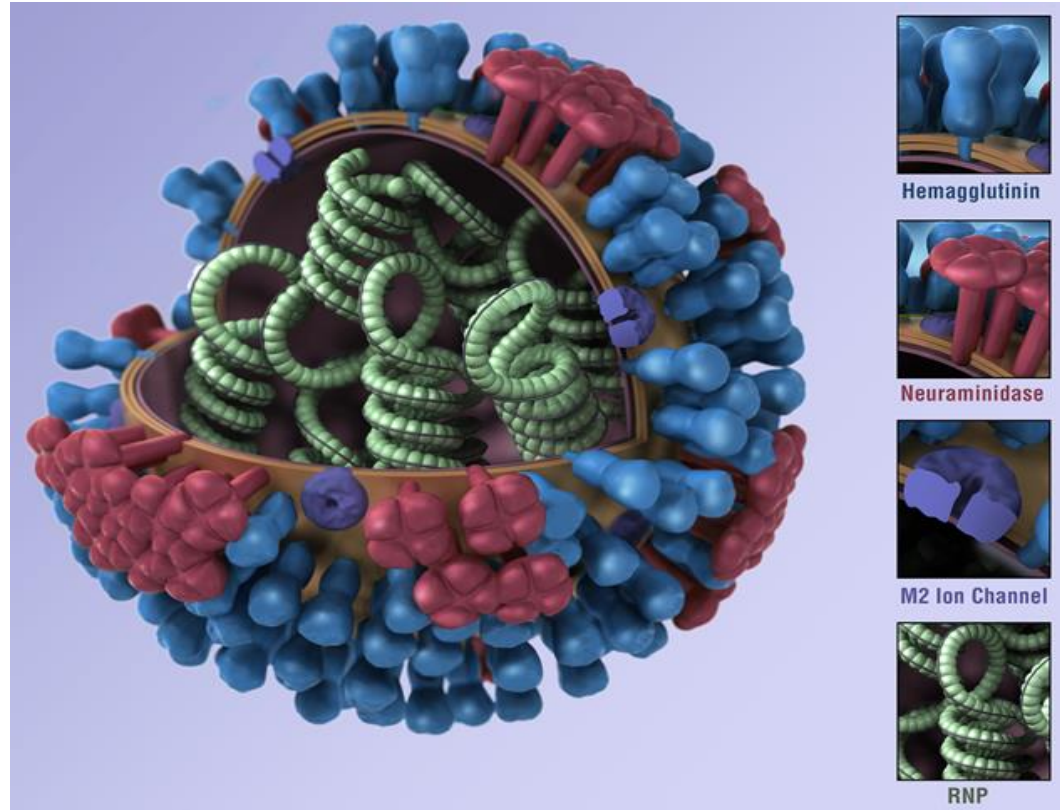


Influenza

Segmented
genome

Hemagglutinin
binds to sialic
acid receptors

Neuraminidase
facilitates
release from
cell

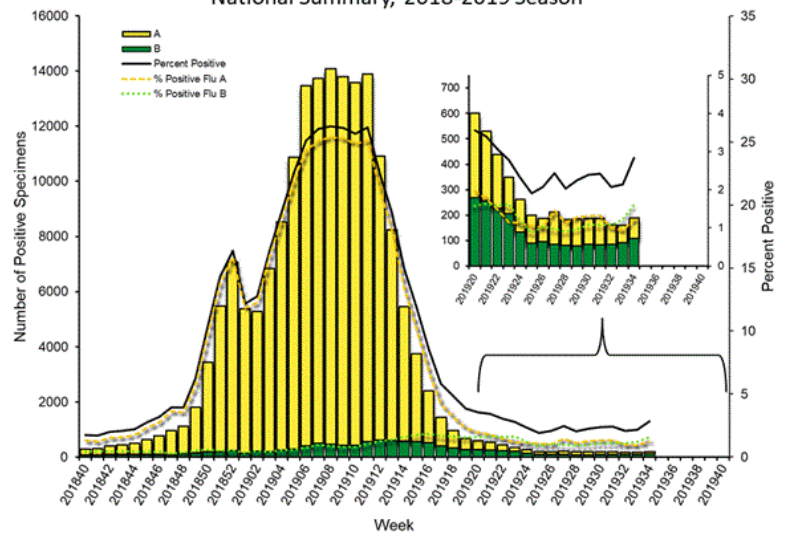




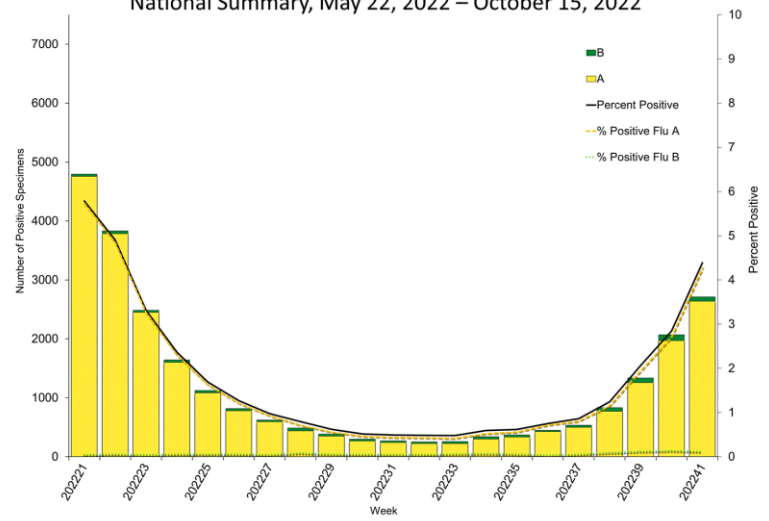
be inFLUential

Influenza cases already emerging in the US

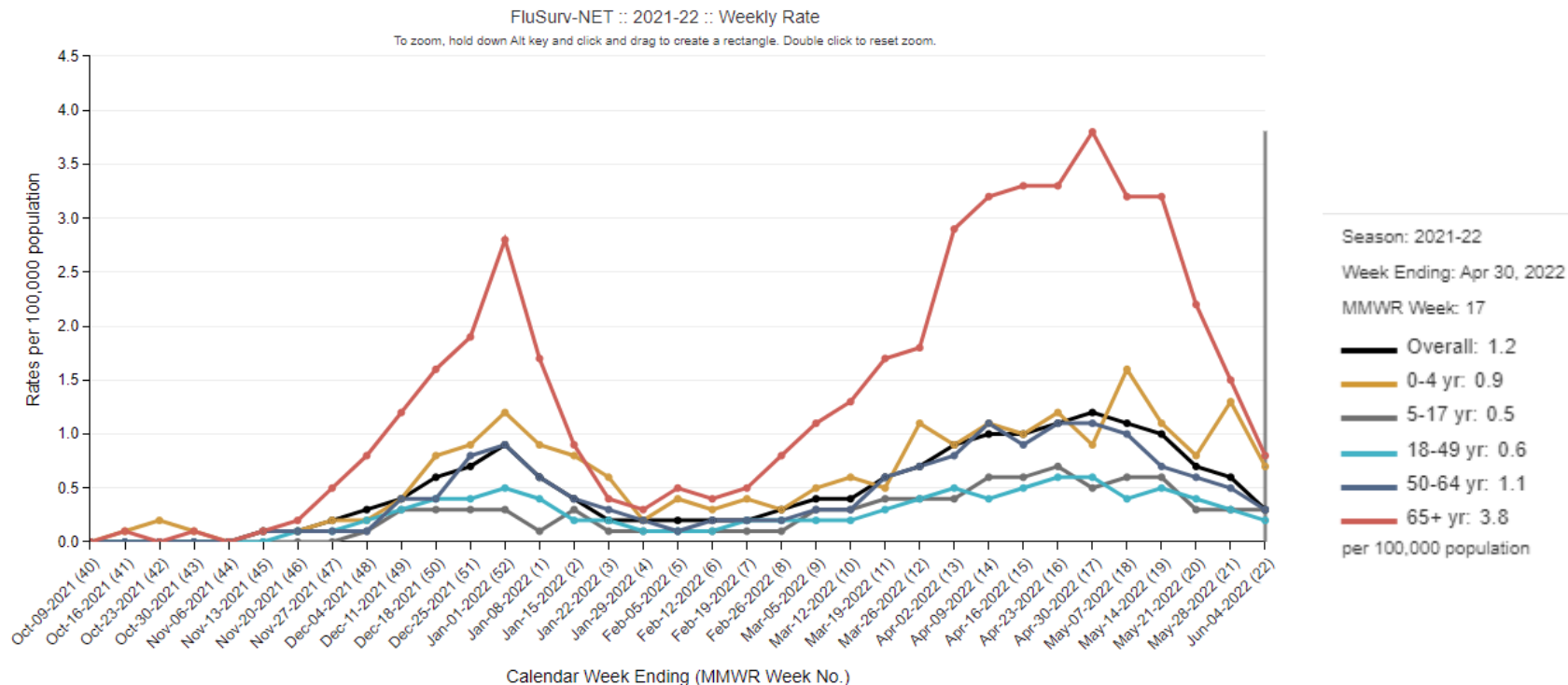
Influenza Positive Tests Reported to CDC by U.S. Clinical Laboratories, National Summary, 2018-2019 Season



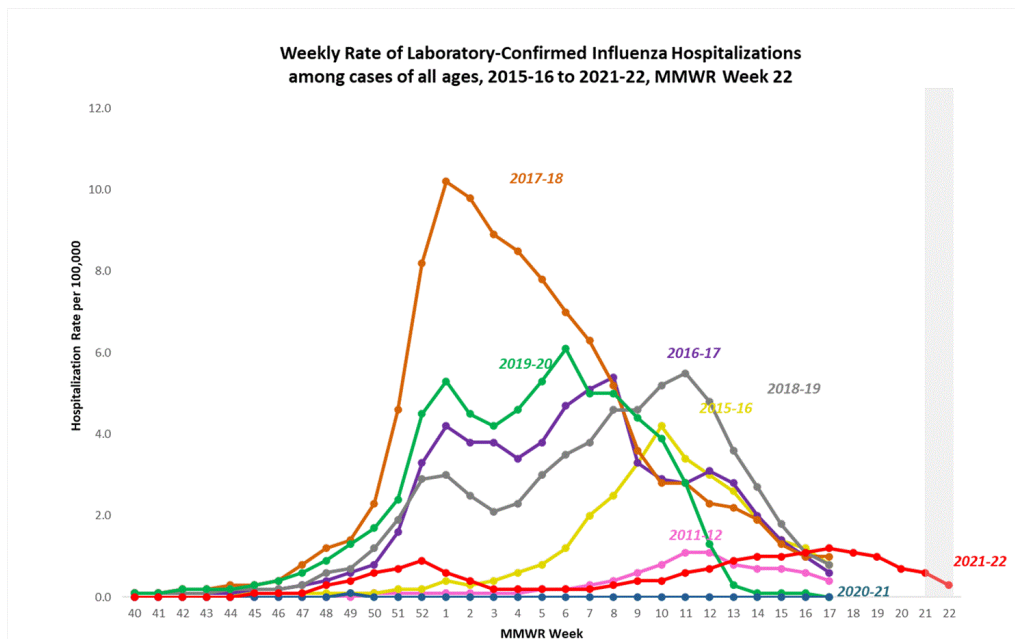
Influenza Positive Tests Reported to CDC by U.S. Clinical Laboratories, National Summary, May 22, 2022 – October 15, 2022



Influenza hospitalization rates in the US

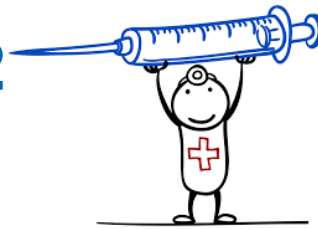


Influenza hospitalization rates, 2011-12 to 2021-22

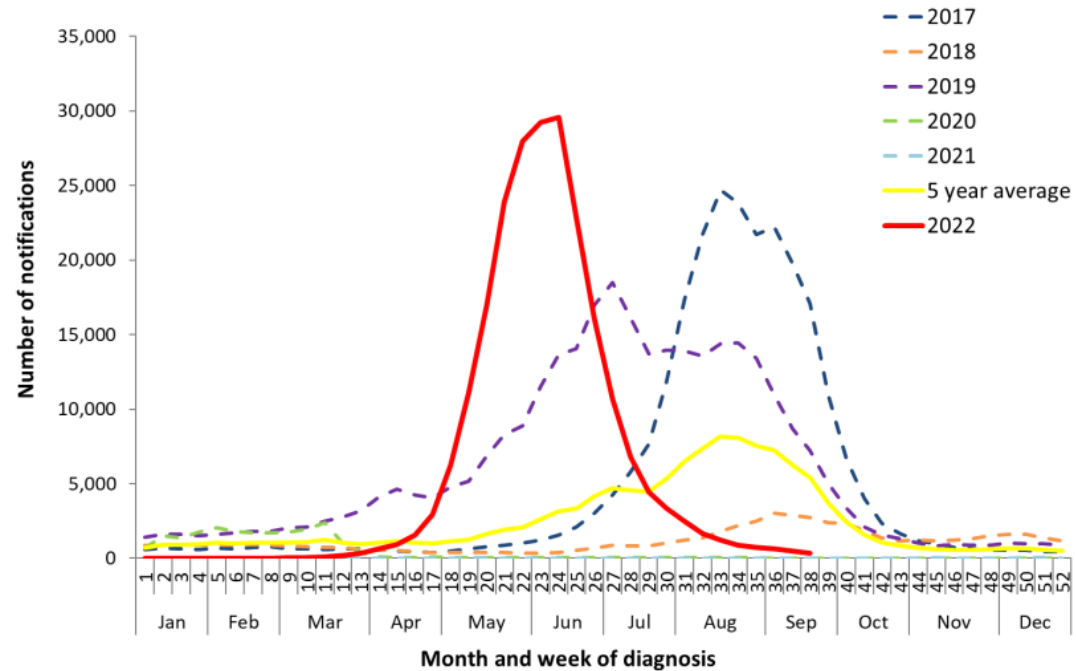


*In this figure, weekly rates for all seasons prior to the 2021-22 season reflect end-of-season rates. For the 2021-22 season, rates for recent hospital admissions are subject to reporting delays. As hospitalization data are received each week, prior case counts and rates are updated accordingly. Due to late season activity during the 2021-2022 season, FluSurv-NET surveillance has been extended beyond the typical end date of April 30 (MMWR week 17).

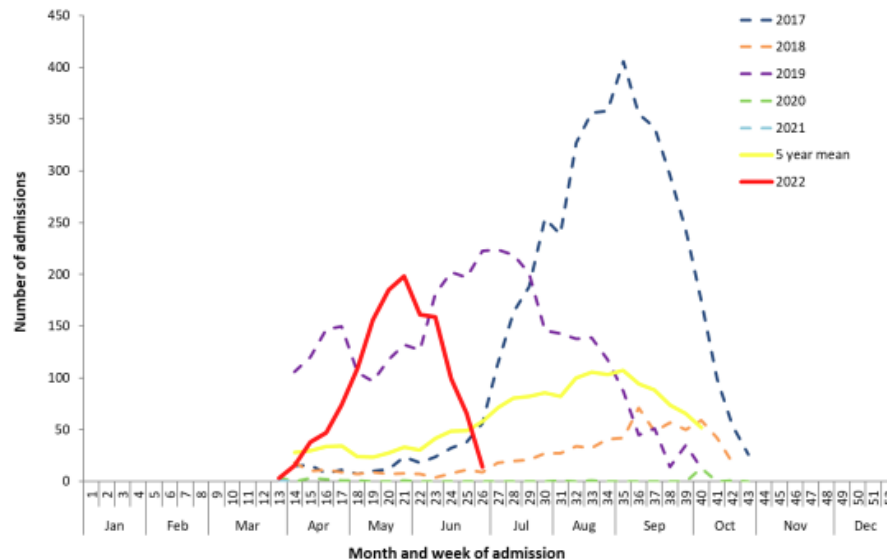
Influenza cases in Southern Hemisphere- 2022



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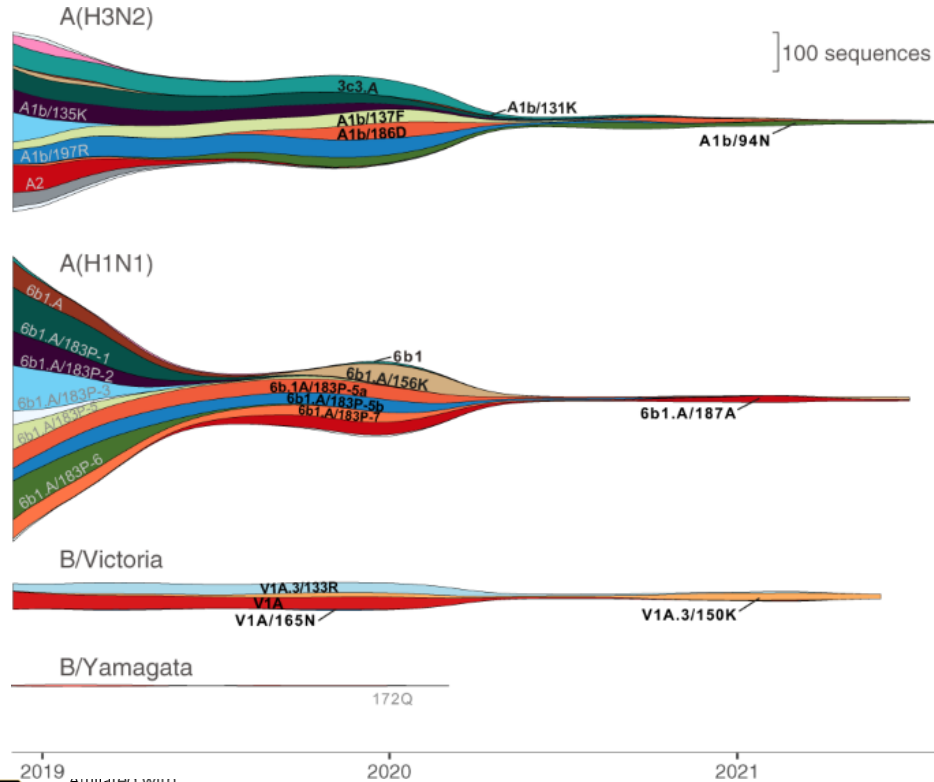
Influenza hospitalizations Southern Hemisphere- 2022



Source: FluCAN

*All data are preliminary and subject to change as updates are received, with most recent weeks considered particularly subject to revisions.

Influenza lineage circulation, 2019-2021










Clinical Characteristics



Limited distinctive clinical characteristics- influenza vs COVID-19

	COVID-19	Influenza
Common symptoms	Fever (50%), non-productive cough (38%) most common	Fever, cough, rhinorrhea most common
Other symptoms	Muscle aches, nasal congestion, headache, loss of appetite, shortness of breath	Muscle aches, nasal congestion, headache, loss of appetite, shortness of breath
Loss of taste and smell	Loss of smell/Loss of taste highly associated	Loss of smell reported in influenza
Gastrointestinal symptoms	Abdominal pain, diarrhea, vomiting more common than flu	Nausea, vomiting and diarrhea more common in pre-school aged children

High Risk Medical Conditions – influenza vs COVID-19

	Influenza	COVID-19
Age	< 5, ≥ 65 years	> 65 years
	Chronic pulmonary including asthma	Asthma, ILD, PE, bronchiectasis, pulmonary hypertension, bronchiectasis, COPD, CF, TB
	Cardiovascular	e.g. heart failure, coronary artery disease, or cardiomyopathies
	Renal, hepatic, hematologic	Cirrhosis, non-alcoholic fatty liver disease, alcoholic liver disease, autoimmune hepatitis, chronic kidney disease
	Metabolic disorders including Diabetes mellitus, obesity	Diabetes type 1 and 2, obesity
	Neurologic and neurodevelopmental conditions	ADHD, CP, Congenital malformations, developmental disabilities, learning disabilities, spinal cord injuries, dementia, cerebrovascular disease
	Immunosuppression	Primary immunodeficiencies, malignancy, SOT, HSCT HIV , immunosuppressive medications
	Pregnancy and within 2 weeks post partum	Pregnancy and recent pregnancy

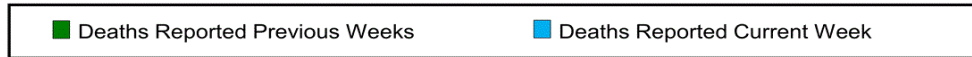
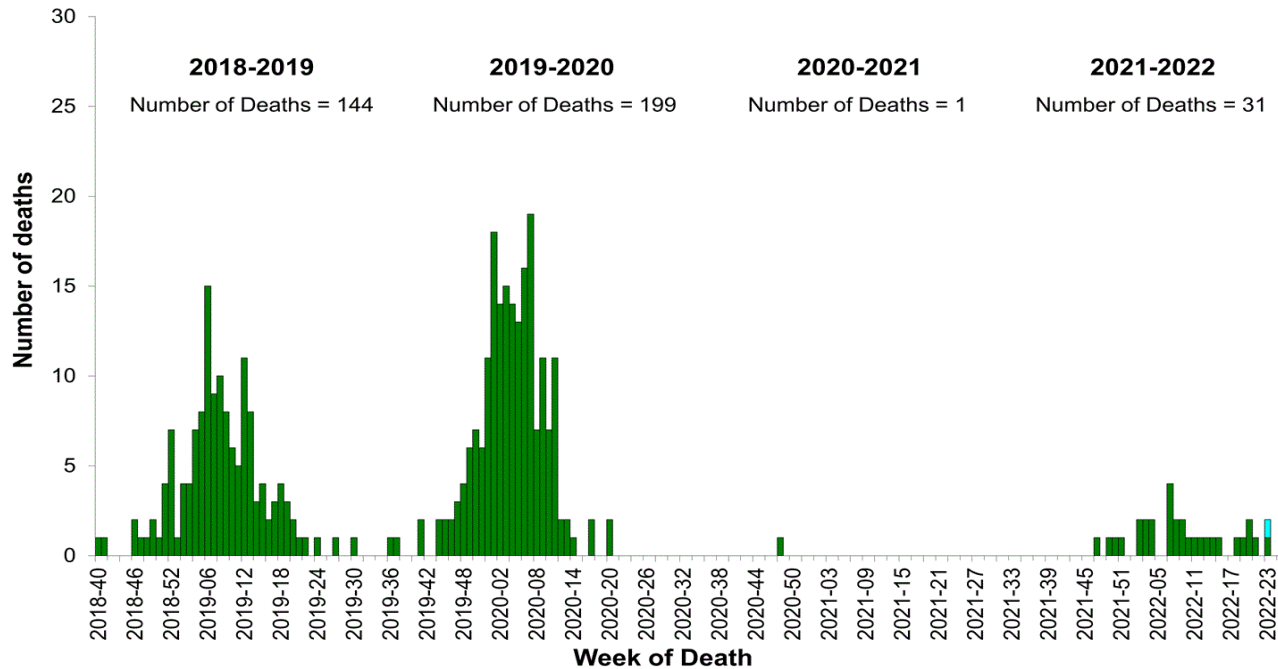
Source: <https://www.cdc.gov/coronavirus/2019-15ncov/hcp/clinical-care/underlyingconditions.html>



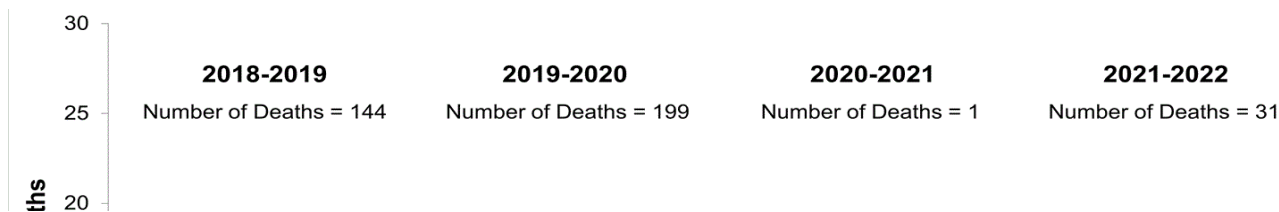
High Risk Medical Conditions- Influenza vs COVID-19

	Influenza	COVID-19
Race/ethnicity	American Indians/Alaska Natives	Black/African American, American Indian/Alaska Native, Hispanic/Latinx
Medications	Long term aspirin therapy	
Mental Health Disorders		Mood disorders including depression, schizophrenia spectrum disorders
Behavioral factors		Physical inactivity Smoking, current and former
Medical complexity		Medical complexity with technology dependence

Influenza deaths in children

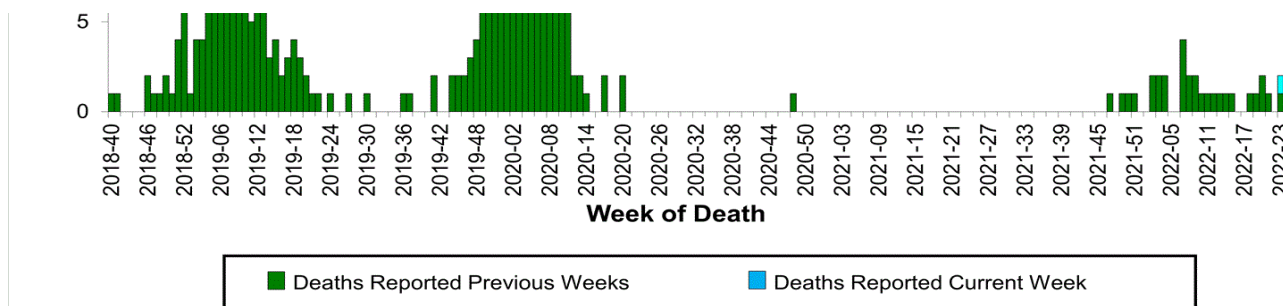


Influenza deaths in children



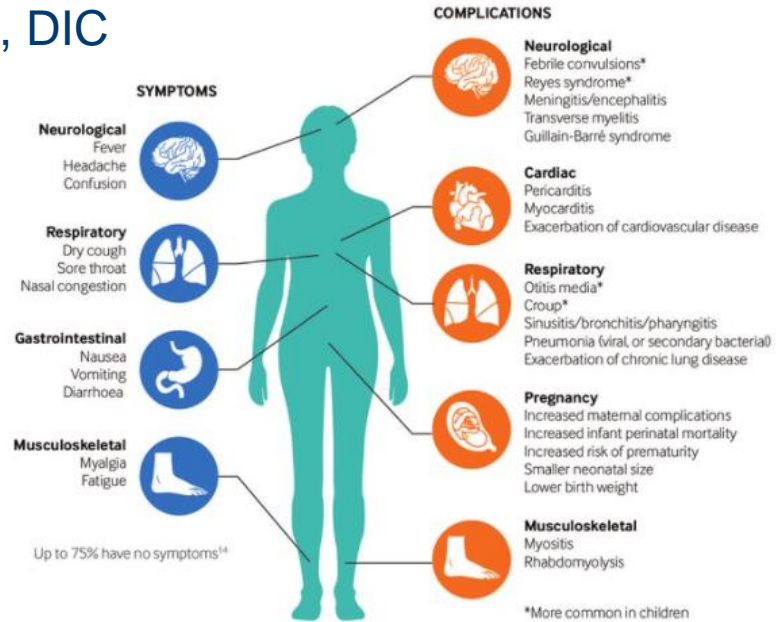
Up to 50% of pediatric deaths from influenza occur in otherwise healthy children

Up to 80% of influenza-associated pediatric deaths have occurred in unvaccinated children 6 months and older



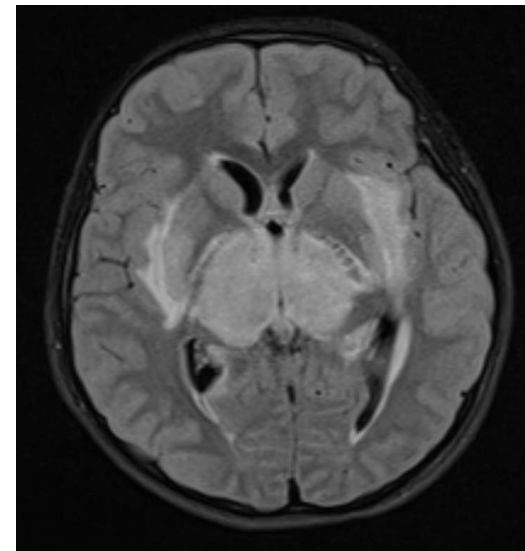
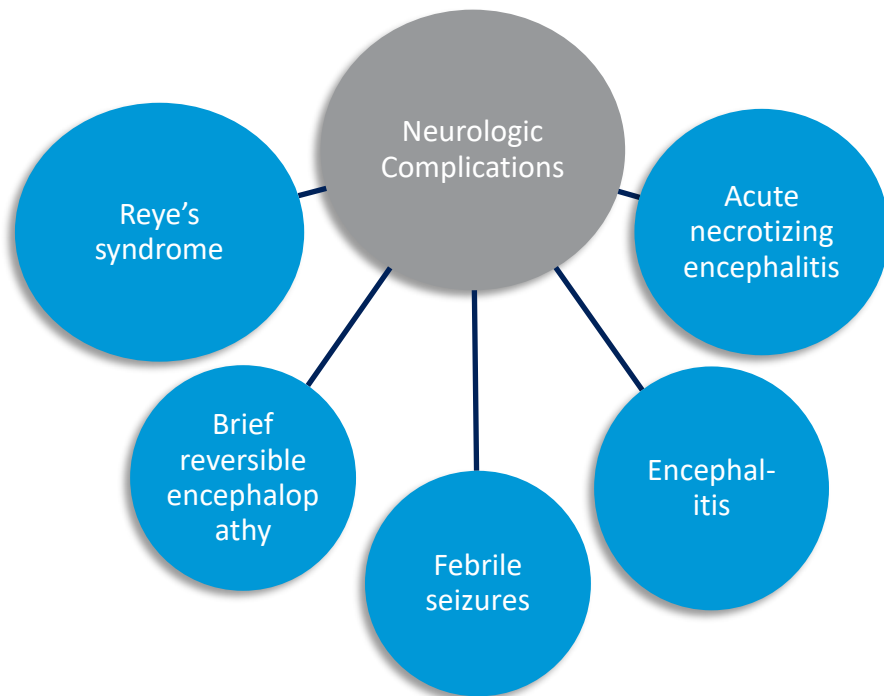
Complications of influenza

- Viral sepsis, cardiorespiratory failure, ARDS, DIC
- Secondary bacterial infections
 - *MRSA*
 - *Streptococcus pneumoniae*
 - Other bacterial pathogens
- Myocarditis
- Neurologic complications
- Hepatitis, AKI



Rao S et al. "Influenza" P, in: Kendig and Chernick's Disorders of the Respiratory Tract in Children, 9th Edition

Neurologic complications of influenza



Acute necrotizing encephalitis. Coronal FLAIR magnetic resonance image of a 7-year-old patient with influenza-associated encephalopathy demonstrating bilateral confluent signal hyperintensity in the white matter and thalami.



Influenza vaccination updates

2022-2023 season

Deciding on which influenza vaccine to use

You are seeing an 18-month-old patient with a history of egg allergy and a 6-month history of wheezing in clinic who has never been vaccinated for influenza in the past. On further questioning, he had hives with eggs 1 year ago, and mother is asking about the flu vaccine. What do you suggest?

1. Offer IIV4 – inactivated influenza vaccine
2. Offer LAIV4- live attenuated influenza vaccine
3. Offer RIV- recombinant influenza vaccine
4. Contraindicated from receiving flu vaccines

Vaccine updates for 2022-23 season

- Recommended for all persons 6 months of age and older who do not have any contraindications during all healthcare seeking opportunities
- No preference of IIV over LAIV

Vaccine composition

Contraindications vs precautions

Age indications

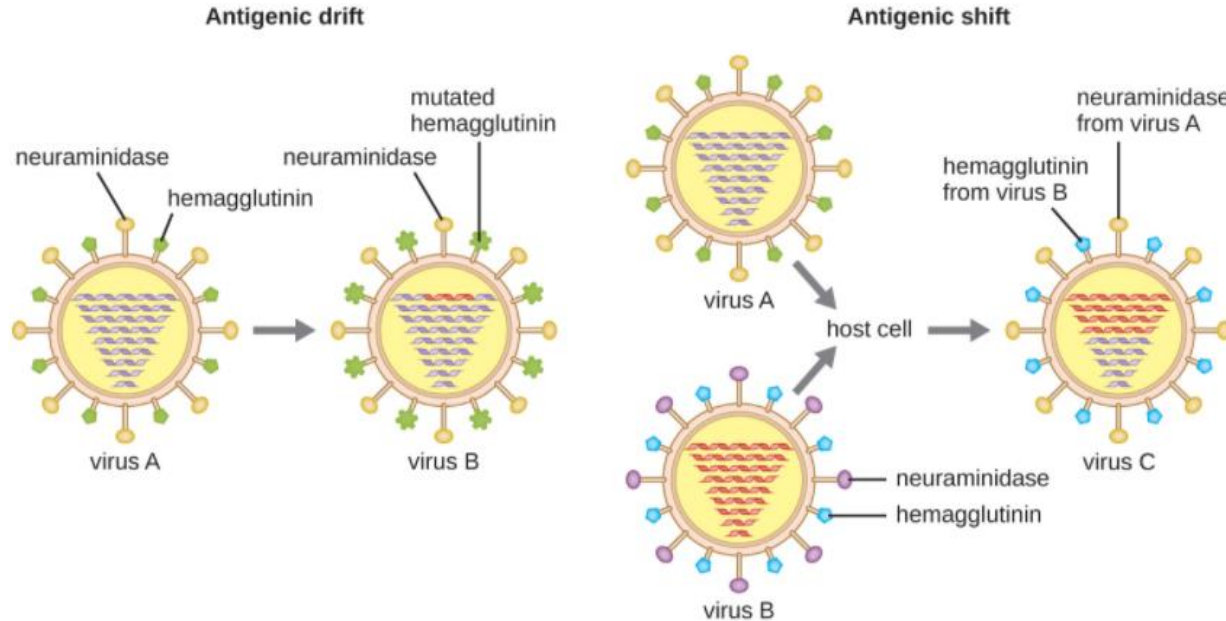
Quadrivalent vs Trivalent

Dosing considerations

Timing of vaccination

Co-administration with COVID-19 vaccines

Why do we have to change influenza vaccines every year?



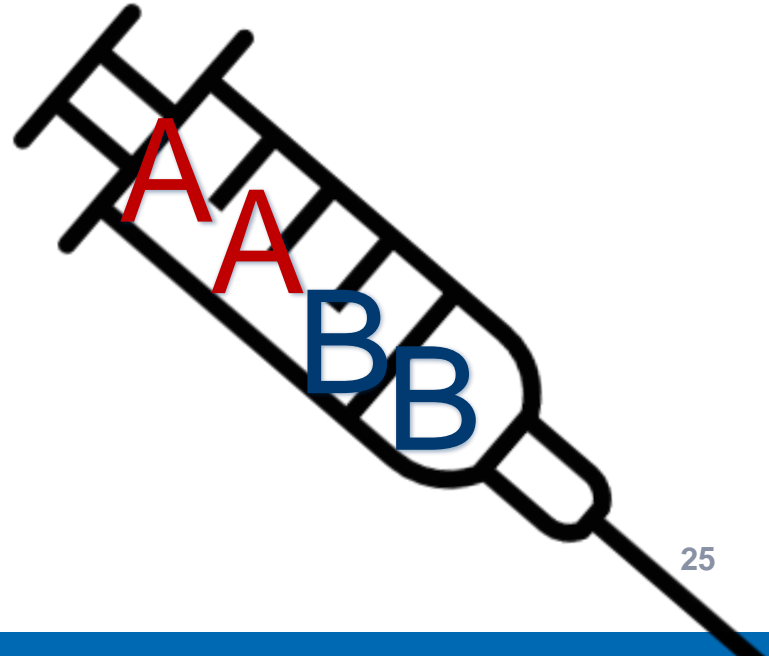
What is in this year's composition of the flu vaccine?

A H1N1

A H3N2

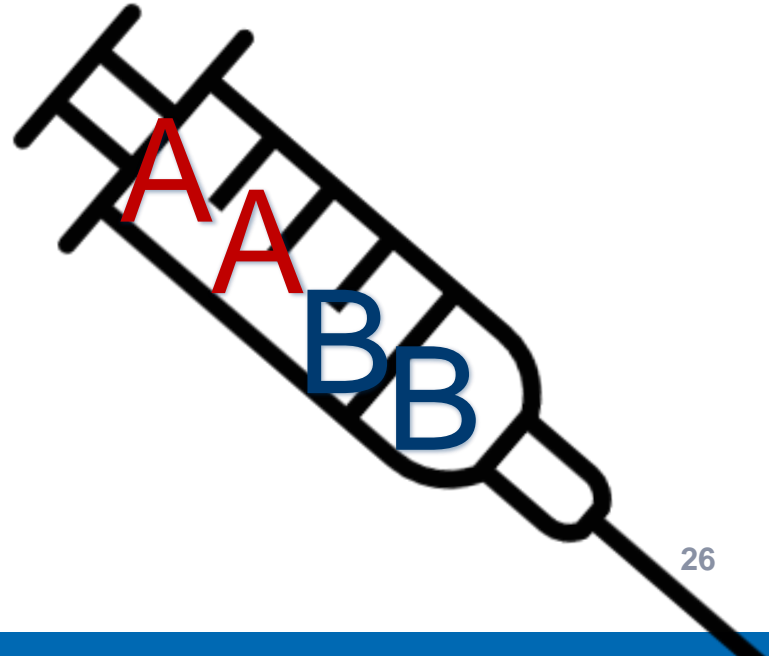
B Victoria lineage

B Yamagata lineage



What is in this year's composition of the flu vaccine? Egg based IIV4 and LAIV

A/Victoria/2570/2019 (H1N1)pdm09-like virus;
A/Darwin/9/2021 (H3N2)-like virus;
B/Austria/1359417/2021 (B/Victoria lineage)-like virus; and
B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.



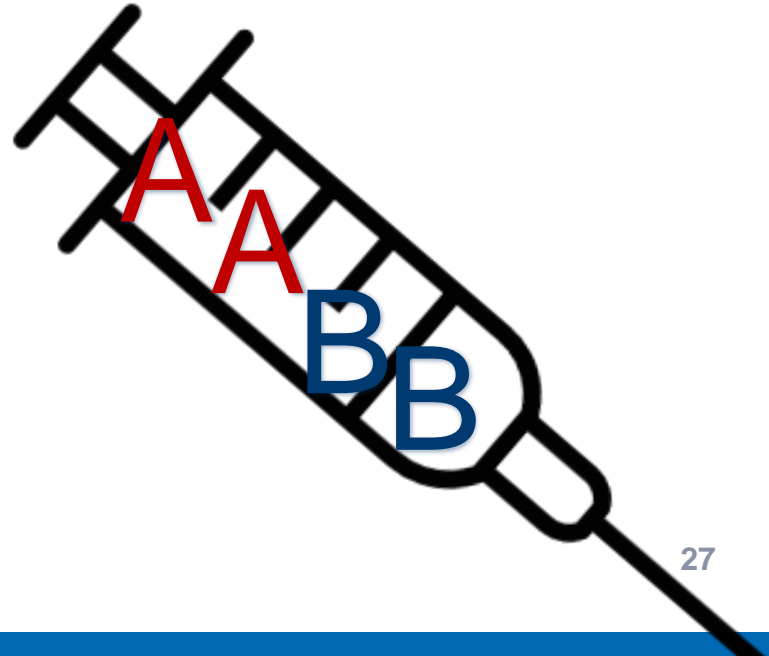
What is in this year's composition of the flu vaccine? Cell-culture IIV4 and RIV

A/Wisconsin/588/2019 (H1N1)pdm09-like virus;

A/Darwin/6/2021 (H3N2)-like virus;


B/Austria/1359417/2021 (B/Victoria lineage)-like virus; and

•B/Phuket/3073/2013 (B/Yamagata lineage)-like virus



Influenza vaccines by age indication 2022-23 season

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

Pediatric vaccines – IIV4, cclIV4, 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 (cclIV4)		Flucelvax Quadrivalent				
	Adjuvanted inactivated (aIIV4)						Flud 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

All vaccines are quadrivalent this season

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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

All pediatric vaccines are 0.5mL except Afluria

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LAIV4	Live attenuated (LAIV4)			FluMist Quadrivalent			

Indicated for pediatric population

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

Inactivated Influenza Vaccine

Contraindications

- History of severe allergic reaction to any component of the vaccine, or to a previous dose of any influenza vaccine
- (for cclIV4, history of severe allergic reaction to cclIV4, clIV3 or to any component of cclIV4)

Precautions

- Moderate or severe acute illness with or without fever
- History of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine
- (for cclIV4 and RIV, history of severe allergic reaction to a previous dose of any other influenza vaccine)

Live Attenuated Influenza Vaccine

Contraindications

- Severe allergic reaction to any component of the vaccine/previous dose
- Aspirin
- Children aged 2 through 4 years with asthma/ wheezing episode has occurred during the preceding 12 months
- Immunocompromised, close contacts and caregivers of severely immunosuppressed persons who require a protected environment
- Pregnancy

Live Attenuated Influenza Vaccine

Contraindications

- Communication b/w cerebrospinal fluid (CSF) and the oropharynx, nasopharynx, nose, or ear or any other cranial CSF leak
- Persons with cochlear implants
- Previous receipt antiviral:
 - 48 hours for oseltamivir and zanamivir
 - 5 days for peramivir
 - 17 days for baloxavir

Live Attenuated Influenza Vaccine

Precautions

- Moderate or severe acute illness with or without fever
- History of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine
- Asthma in persons aged ≥ 5 years
- Other underlying medical conditions that might predispose to complications after wild-type influenza infection (e.g., chronic pulmonary, cardiovascular [except isolated hypertension], renal, hepatic, neurologic, hematologic, or metabolic disorders [including diabetes mellitus])

What are the recommendations for egg allergic patients?

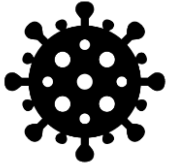
You are seeing an 18 month old patient with a history of egg allergy and a 6-month history of wheezing in clinic who has never been vaccinated for influenza in the past. On further questioning, he had hives with eggs 1 year ago, and mother is asking about the flu vaccine. What do you suggest?

1. Offer IIV4
2. Offer LAIV4 – *no, given age, and history of wheezing*
3. Offer RIV – *no, age indication is ≥ 18 yrs*
4. Contraindicated from receiving flu vaccines – *egg allergy is not a contraindication to receiving the flu vaccine*

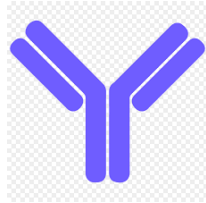
Vaccination of persons with COVID-19 infection

- No data to inform optimal timing of influenza vaccination for persons with COVID-19
- Visits should be deferred until the isolation period has ended
 - COVID + asymptomatic- can receive influenza vaccine
 - COVID + symptomatic- consider deferring
 - COVID + on IL-6 inhibitors, high-dose steroids- recommend waiting until course completed

Timing of vaccination – factors influencing recommendations



Timing of season



Time taken to develop immune response



Time taken for successful vaccine campaign



Time between doses

Waning immunity

- Waning effects have not been observed consistently
- More of an issue with influenza H3N2, which tends to occur earlier in the flu season
- Serologic studies show a modest rather than sharp decline
- Experts concerned about early influenza season this year
- Ideal vaccination Season Sept-October before onset of flu season
- Continue to vaccinate eligible populations before and while flu is circulating
- More of an issue in > 65yrs, can be overcome with high dose or adjuvanted formulations

AAP and CDC Recommendations

- The AAP and CDC recommend vaccination for all individuals 6 months of age and older
- Any licensed vaccine appropriate by age, no product preference
- Can be administered at the same time as COVID-19 vaccines
- Administration at any healthcare seeking visit during influenza season when it is not contraindicated
- Ideally vaccinate before the end of October, but can also continue during the influenza season

Number of Doses for children < 9 years of age

Has the child received 2 or more total doses of trivalent or quadrivalent influenza vaccine before July 1, 2022?

Does not need to have been received during the same season or consecutive seasons

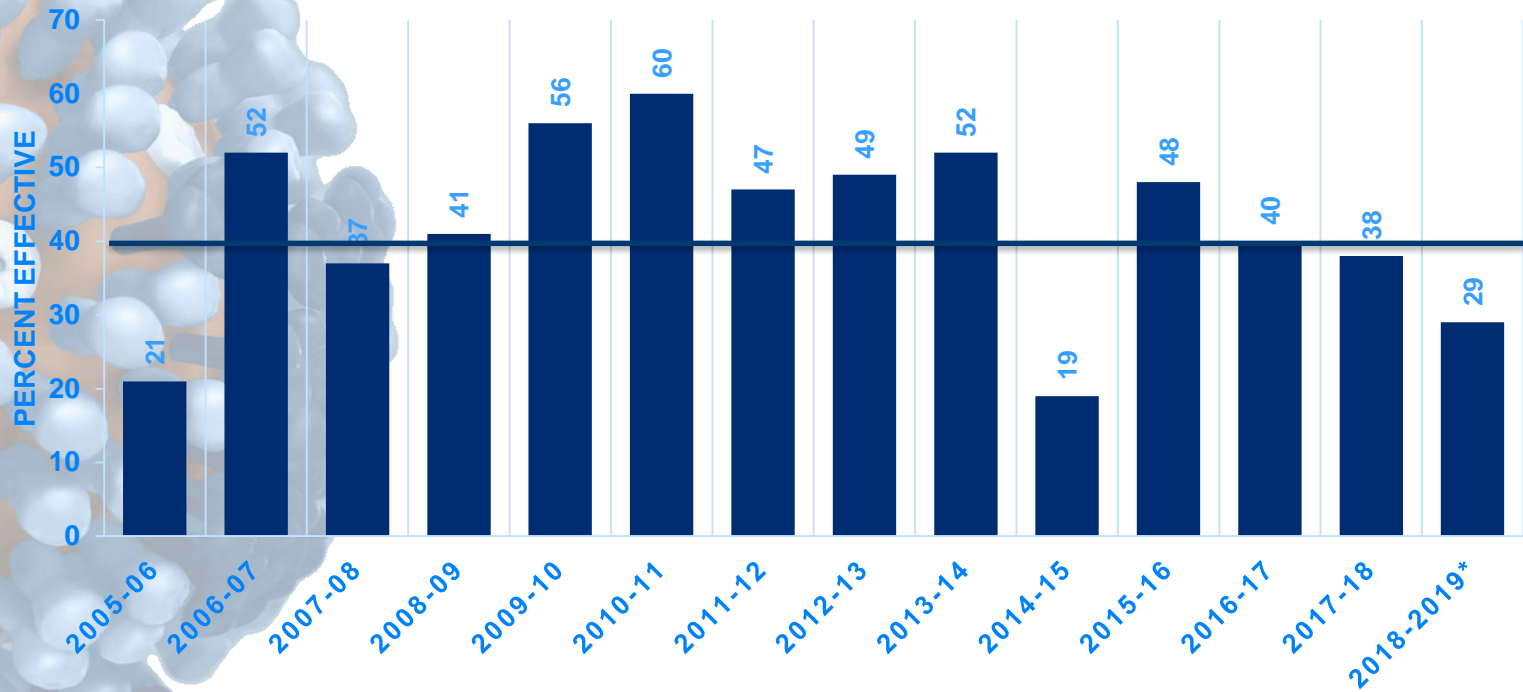
Yes

1 dose of 2022-2023 influenza vaccine

No
or don't know

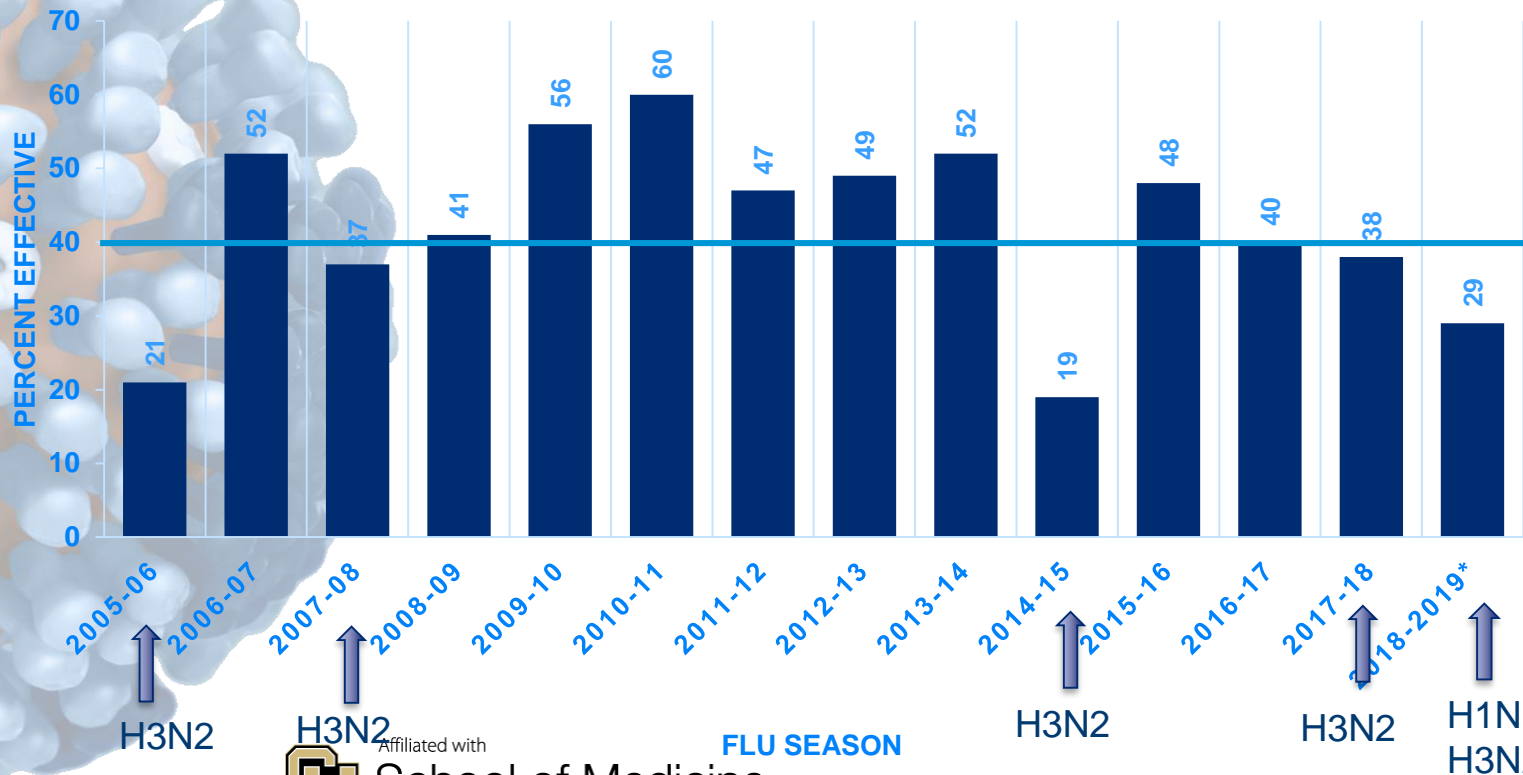
2 doses of 2022-2023 influenza vaccine

Effectiveness of Seasonal Flu Vaccines from the 2005 – 2019 Flu Seasons



*Vaccine effectiveness estimates for 2018-2019 were presented to ACIP on June 27, 2019.
Source: <https://www.cdc.gov/flu/professionals/vaccination/effectiveness-studies.htm>

Effectiveness of Seasonal Influenza Vaccines against medically-attended illness from the 2005 – 2019 Seasons



Disease averted by influenza vaccination 2019-2020

Overall
vaccine
effectiveness
of 39%

the benefits of flu vaccination 2019-2020

Nearly 52% of the U.S. population aged 6 months and older got a flu vaccine during the 2019-2020 flu season, and this prevented an estimated:

7.5
million
flu illnesses

105,000
flu hospitalizations

6,300
flu deaths

More than the
combined population of
Kentucky and Kansas



Enough people to fill
Michigan Stadium at the
University of Michigan



Equivalent to saving
about 17 lives per day
over the course of a year



get vaccinated
www.cdc.gov/flu



Sterilizing immunity versus disease mitigation

- Sterilizing immunity—complete protection from infection, durable over years or a lifetime
- Disease mitigation- for viruses in which a single exposure does not confer long-term immunity from reinfection (RNA viruses)



Decreased risk of hospitalization, death and ICU admission



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- Influenza vaccination can decrease your risk of being hospitalized by **58%**

- 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%**

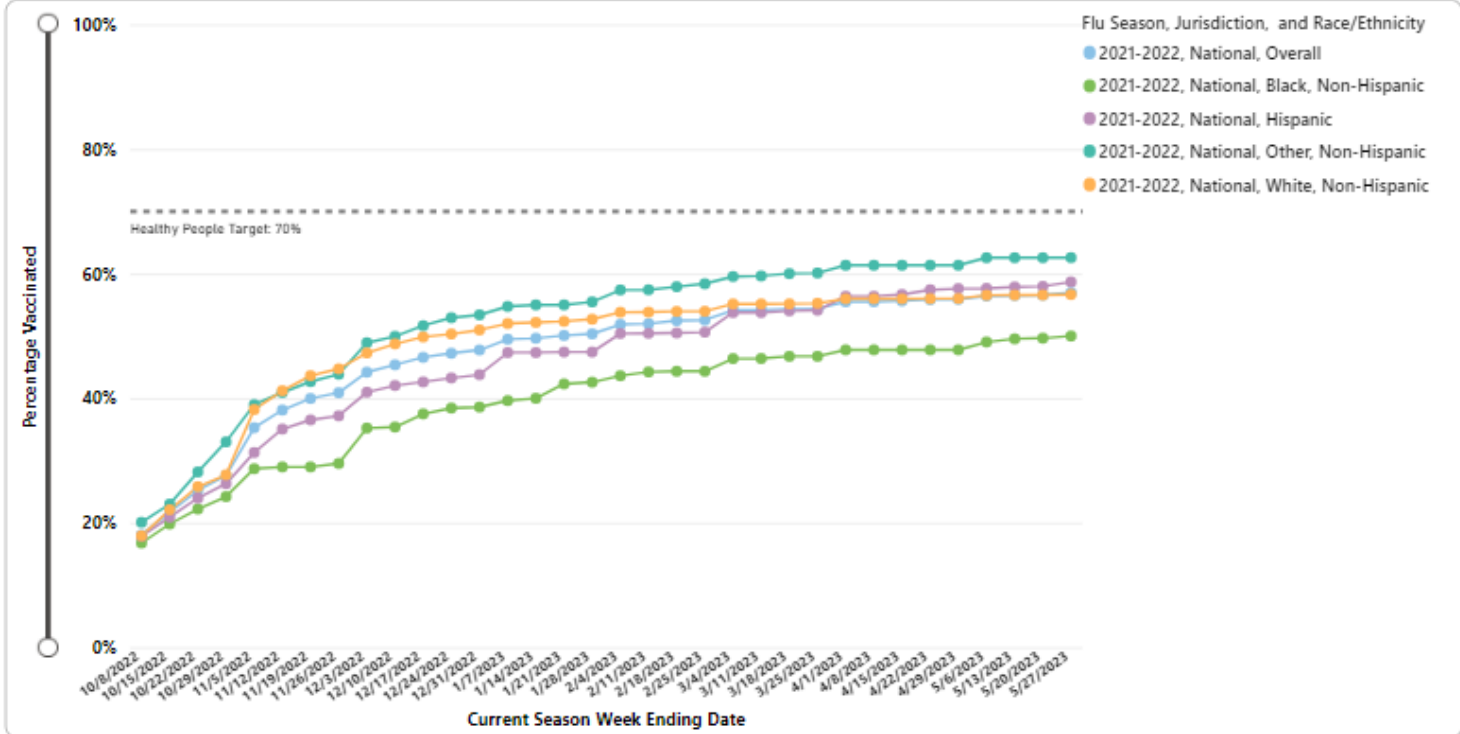
Increasing influenza vaccine effectiveness or increasing coverage?

Increase **effectiveness** by 5% - prevent an additional 1,050,000 illnesses and 25,000 hospitalizations

Increase **coverage** by 5% - prevent an additional 785,000 illnesses and 11,000 hospitalizations

Increase **coverage** to 70% - prevent an additional 3,840,000 illnesses and 39,000 hospitalizations

Vaccination rates are up to 10% lower in certain racial/ethnic groups



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.*

Testing



Testing



PCR



NAAT



DIA



Rapid antigen

Point of care tests

Decreasing sensitivity

Whom to test depends on how results will affect clinical management and public health considerations

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

Influenza Treatment



oseltamivir



zanamivir



peramivir



baloxavir

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

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

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

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Take-home points

- Influenza has already arrived in Colorado, concerns for an early and more severe season
- High risk groups benefit from targeted testing, treatment and require more of an effort for vaccination
- Vaccines unable to provide sterilizing immunity, but can prevent severe complications
- Making a strong provider recommendation – one of the most effective strategies to enhance uptake



Questions?

