CDC/IDSA COVID-19 Clinician Call

October 9, 2021

Welcome & Introductions

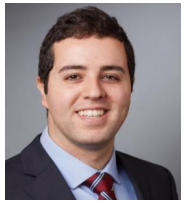
Dana Wollins, DrPH, MGC
Vice President, Clinical Affairs & Guidelines
IDSA

- 76th in a series of weekly calls, initiated by CDC as a forum for information sharing among frontline clinicians caring for patients with COVID-19
- The views and opinions expressed here are those of the presenters and do not necessarily reflect the official policy or position of the CDC or IDSA. Involvement of CDC and IDSA should not be viewed as endorsement of any entity or individual involved.
- This webinar is being recorded and can be found online at www.idsociety.org/cliniciancalls.

Diagnosis & Treatment of Respiratory Illness This Winter Season

How CDC Is Preparing for Possible Co-Circulation of Influenza & SARS-CoV-2 for the Upcoming Flu Season

Shikha Garg, MD, MPH
Medical Officer, Influenza Division
COVID-19 Epidemiology Task Force
U.S. Centers for Disease Control and Prevention



Diagnosis & Testing Update

Marwan Mikheal Azar, MD, FAST
Infectious Diseases Fellowship Program Director
Assistant Professor, Infectious Diseases
Yale School of Medicine

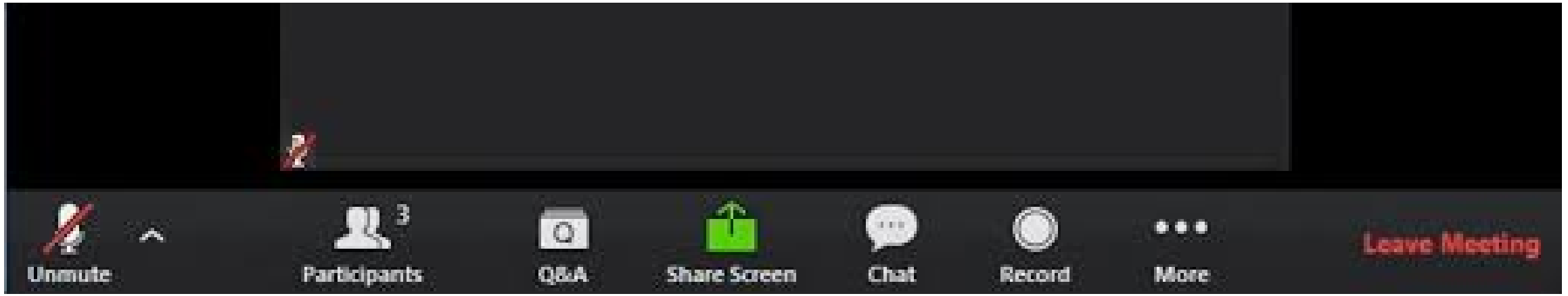
Treatment Update & Clinical Considerations

Sankar Swaminathan, MD
Don Merrill Rees Presidential Endowed Chair
Chief of Infectious Diseases
Department of Medicine
University of Utah School of Medicine

Drs. Azar, Garg and Swaminathan have no disclosures

Question?
Use the “Q&A” Button

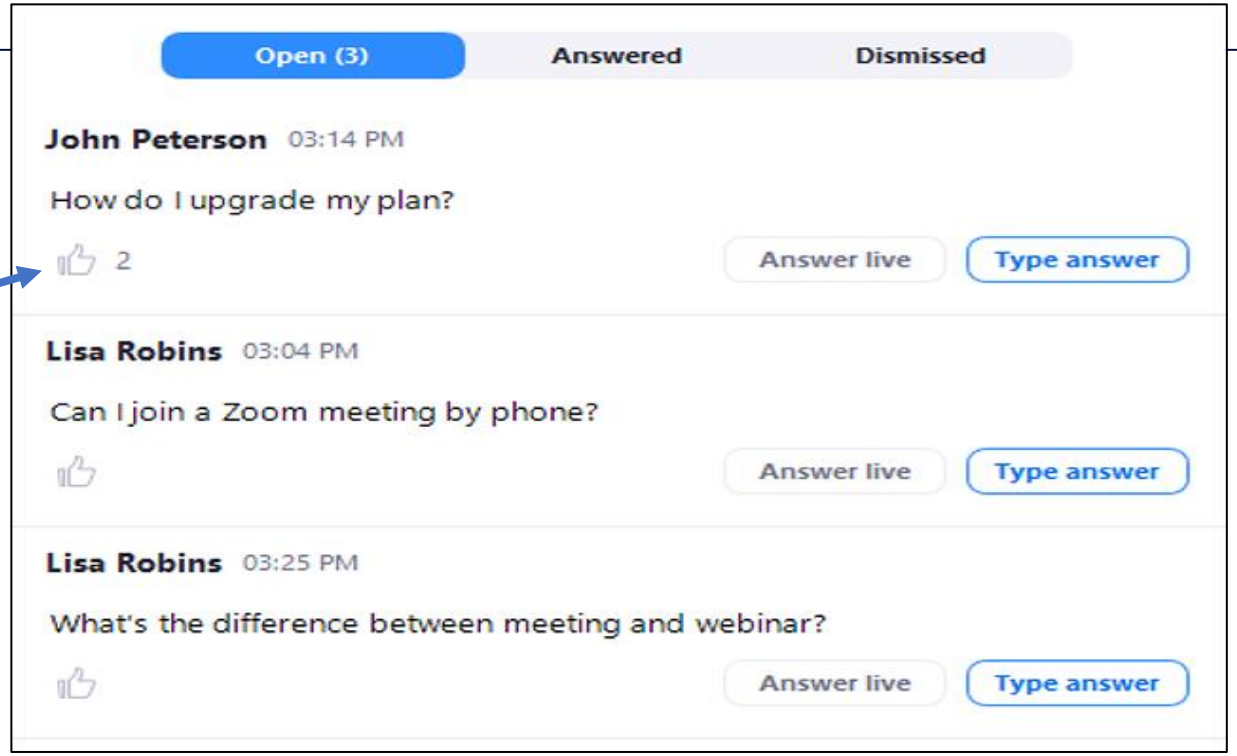
Comment?
Use the “Chat” Button



Survey Questions & Comments:

Q: How do I upvote a question?

A: Questions that have been upvoted will automatically be sorted by number of upvotes. You can upvote a question by clicking the thumbs up icon.



Survey Questions & Comments:

Q: It would be helpful to have people send questions in advance.

A: We welcome questions in advance. Please send to dlewis@idsociety.org. Questions are shared with the moderator and panelists in advance of the call.

Q: Can you send out the slides afterwards, once available?

A: The slides are posted with a recording of the call on Monday at www.idsociety.org/cliniciancalls

Diagnosis and Treatment of Respiratory Illness This Winter Season

How CDC Is Preparing for Possible Co-Circulation of Influenza & SARS-CoV-2 for the Upcoming Flu Season

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How CDC is preparing for possible cocirculation of influenza and SARS-CoV-2 for the upcoming flu season

Shikha Garg, MD, MPH

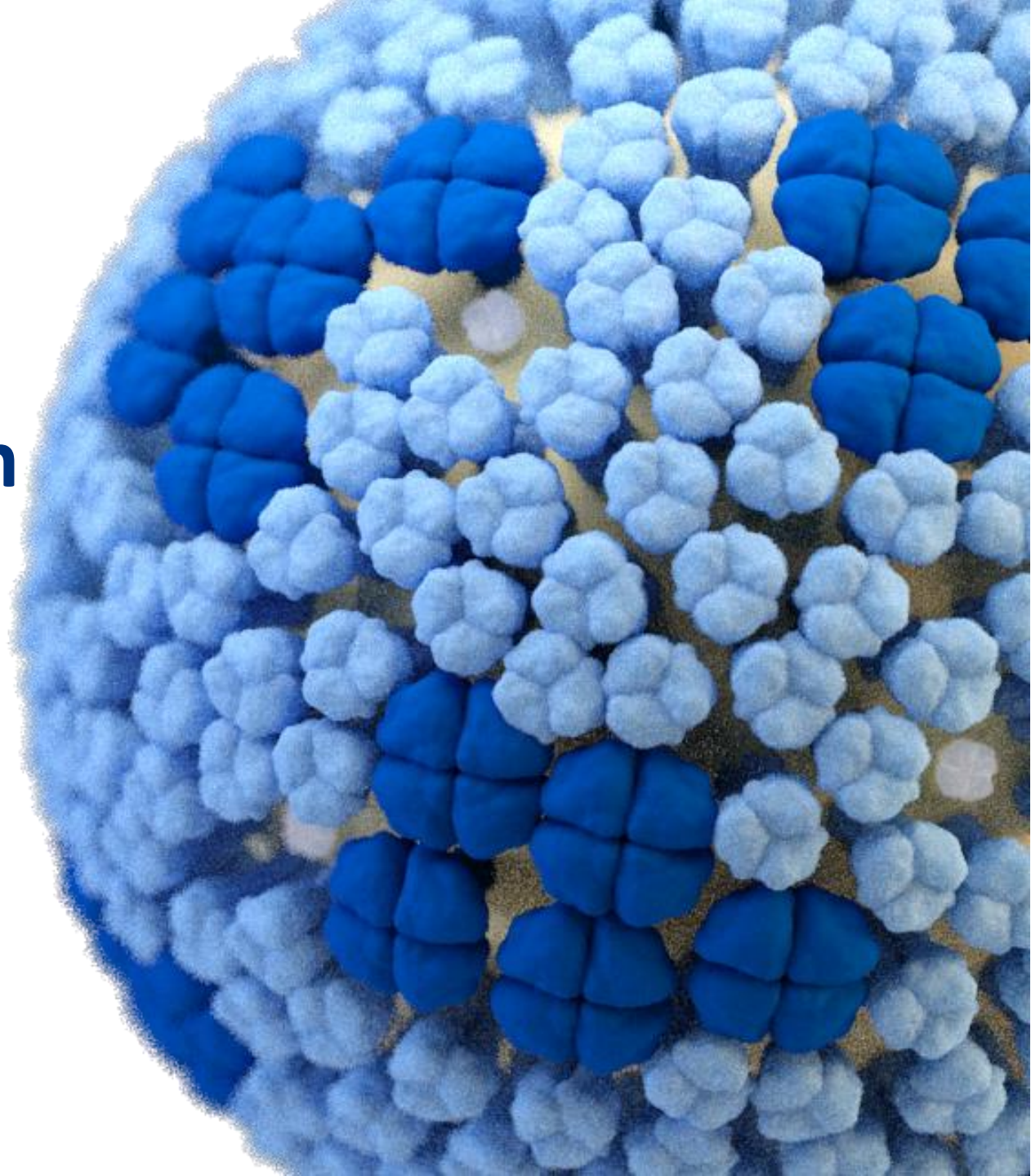
Medical Officer

Influenza Division

COVID-19 Epidemiology Task Force

Centers For Disease Control and Prevention

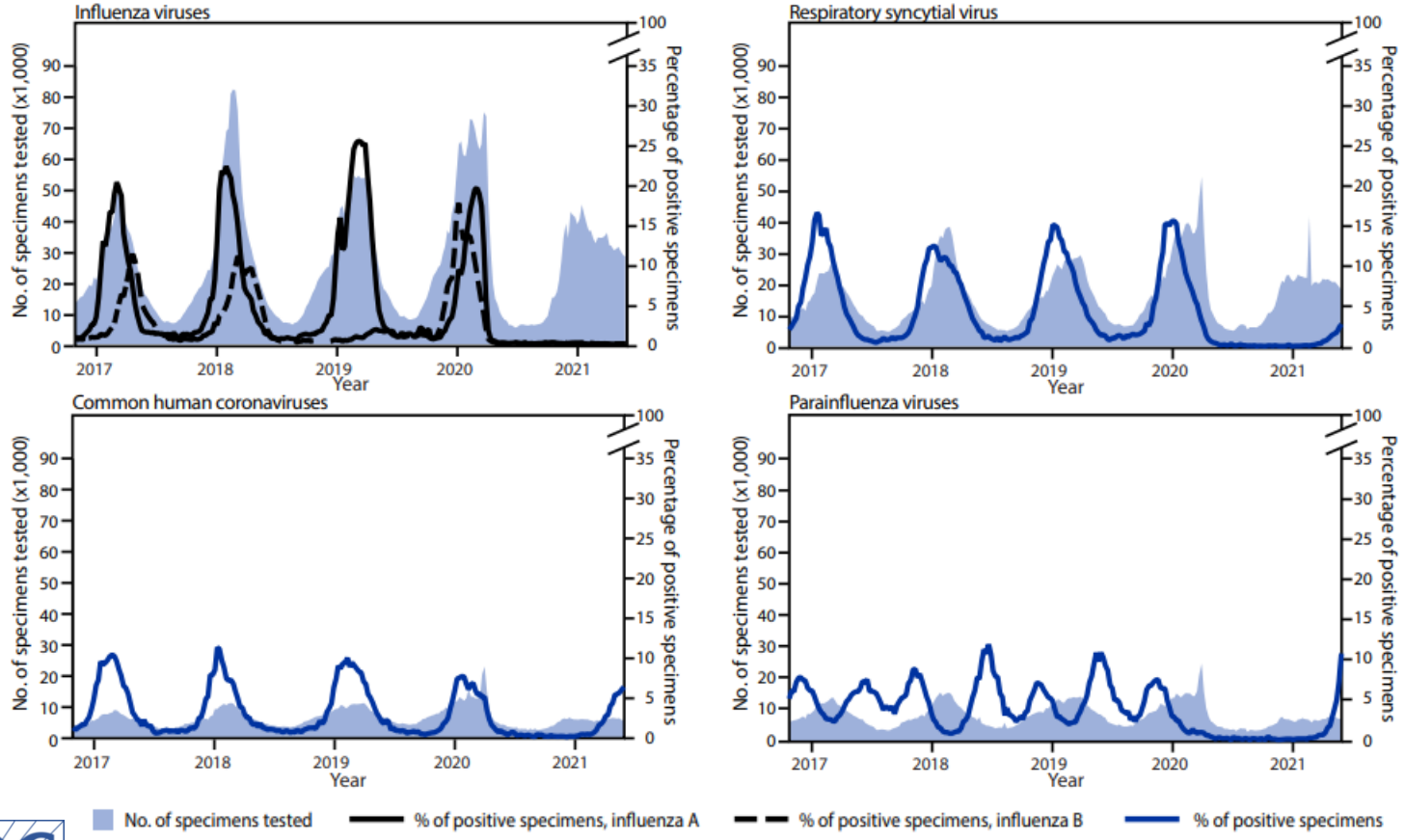
October 9, 2021



CDC Influenza

Flu activity was unusually low during the 2020-2021 season

FIGURE 1. Number of specimens tested and the percentage of positive tests for influenza viruses, respiratory syncytial virus, common human coronaviruses, parainfluenza viruses, human metapneumovirus, respiratory adenoviruses, and rhinoviruses/enteroviruses, by year — United States, 2016–2021



Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 70 / No. 29
July 23, 2021

Changes in Influenza and Other Respiratory Virus Activity During the COVID-19 Pandemic — United States, 2020–2021

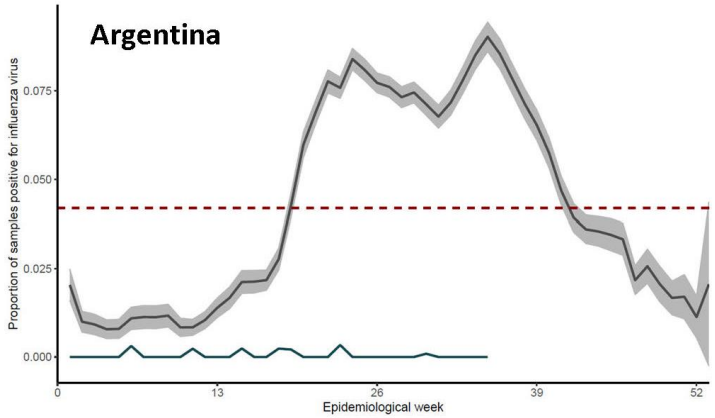
Sonja J. Olsen, PhD[1]; Amber K. Winn, MPH[2]; Alicia P. Budd, MPH[1]; Mila M. Prill, MSPH[2]; John Steel, PhD[1]; Claire M. Midgley, PhD[2]; Krista Kniss, MPH[1]; Erin Burns[1]; Thomas Rowe, MS[1]; Angela Foust[1]; Gabriela Jasso[1]; Angiezel Merced-Morales, MPH[1]; C. Todd Davis, PhD[1]; Yunho Jang, PhD[1]; Joyce Jones, MS[1]; Peter Daly, MPH[1]; Larisa Gubareva, PhD[1]; John Barnes, PhD[1]; Rebecca Kondor, PhD[1]; Wendy Sessions, MPH[1]; Catherine Smith, MS[1]; David E. Wentworth, PhD[1]; Shikha Garg, MD[1]; Fiona P. Havers, MD[2]; Alicia M. Fry, MD[1]; Aron J. Hall, DVM[2]; Lynnette Brammer, MPH[1]; Benjamin J. Silk, PhD[2]

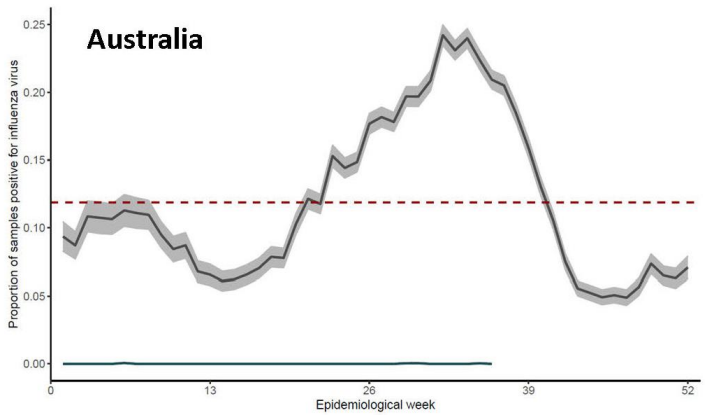
During October 2020-May 2021, only 0.2% of submitted specimens tested positive for flu (peak positivity 26-30% for 3 prior seasons)

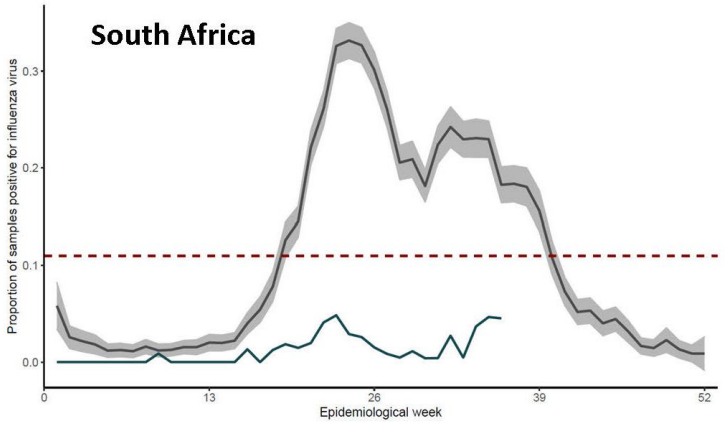
CDC Influenza

Virologic data from U.S. World Health Organization Collaborating Laboratories System and CDC's National Respiratory and Enteric Viruses Surveillance System (NREVSS)

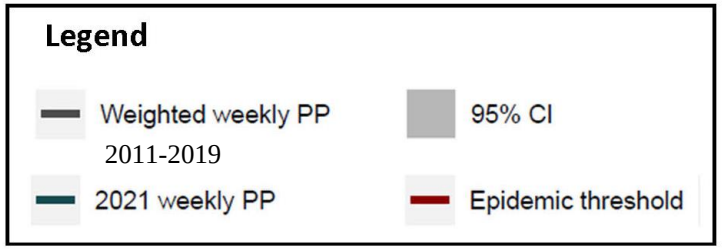
Flu activity in the Southern Hemisphere during 2021 has also remained low







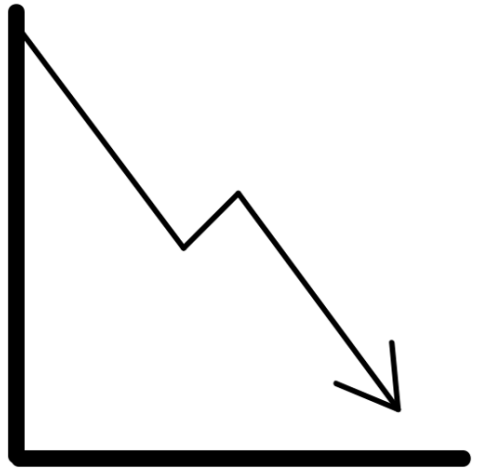
Argentina, Australia, and South Africa, three countries which CDC tracks as sentinels for Southern Hemisphere activity, still have few influenza detections. Activity remains below the historical mean activity for 2011–2019



CDC Influenza

Why was flu activity so low during 2020-2021?

- COVID-19 mitigation measures
  - Physical distancing, staying home
  - Wearing face masks
  - Improved hand hygiene
  - School closures, virtual learning
  - Improved indoor ventilation
- Influenza vaccination



CDC Influenza

While its uncertain what will happen this season, CDC is preparing for seasonal flu viruses to spread this fall and winter

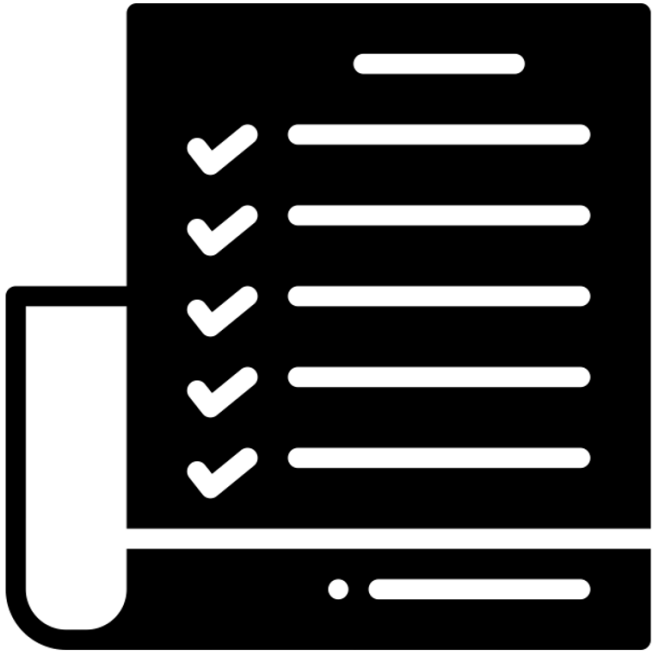
- While flu activity was low in many countries during their past flu season—Southern Hemisphere activity is not always predictive of Northern Hemisphere activity and adherence to COVID-19 mitigation measures may differ
- Reduced population immunity due to lack of flu activity since March 2020 could result in a severe flu season
    - Young children who may not have been previously vaccinated or exposed to natural infection
- As COVID-19 mitigation measures are relaxed, the likelihood that flu will circulate more normally will increase
- If flu and COVID-19 occur at the same time, along with other respiratory viruses such as RSV, could place addition strain on the healthcare system

CDC Influenza

Crystal Ball by Yazmin Alanis from the Noun Project

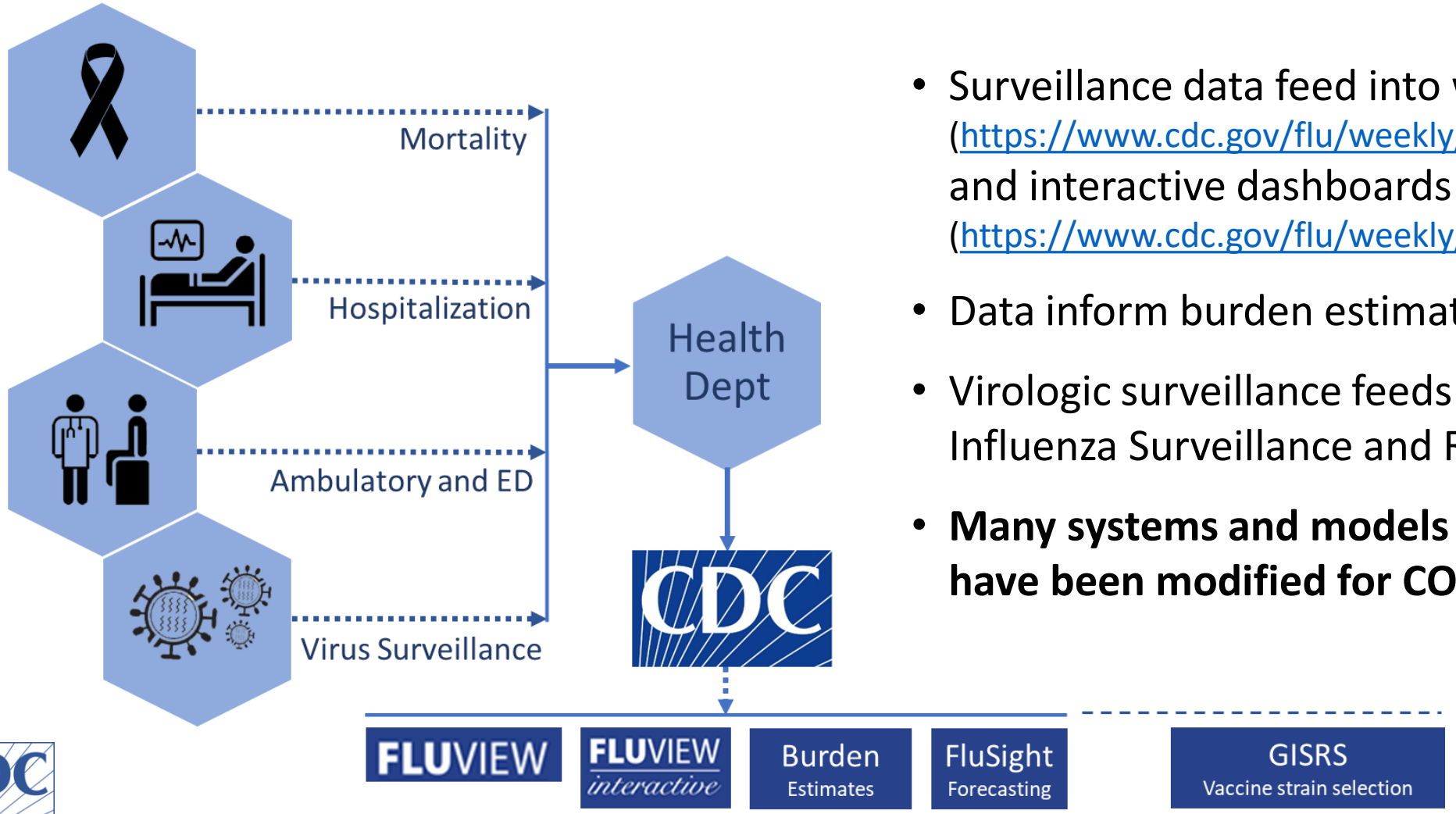
How CDC is preparing for the upcoming flu season

- Surveillance for detection of influenza and other respiratory viruses
- Vaccination
  - Guidance, coverage, effectiveness
  - Communication campaigns
- Healthcare provider education/outreach
  - Clinical guidance on testing and antiviral treatment



Preparation by WEBTECHOPS LLP from the Noun Project

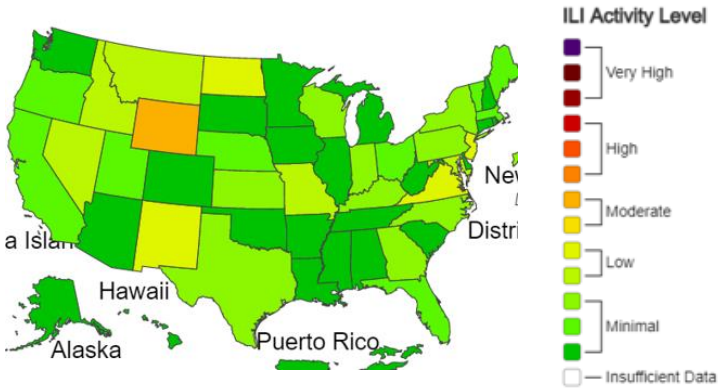
CDC has a comprehensive and layered approach to influenza surveillance

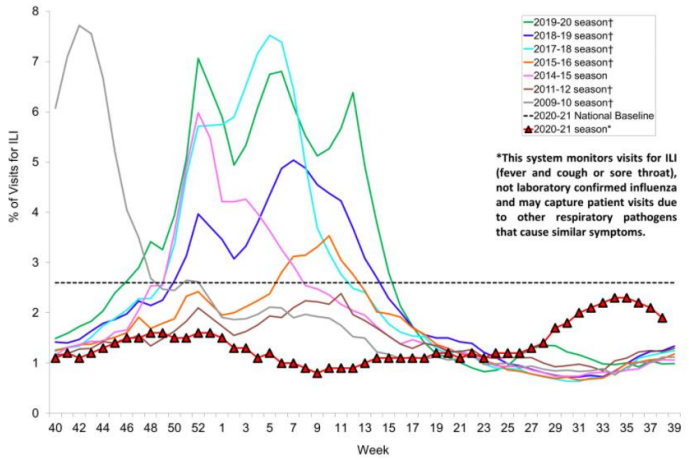


- Surveillance data feed into weekly reports (https://www.cdc.gov/flu/weekly/) and interactive dashboards (https://www.cdc.gov/flu/weekly/fluviewinteractive.htm)
- Data inform burden estimates and forecasting
- Virologic surveillance feeds into GISRS (Global Influenza Surveillance and Response System)
- **Many systems and models are being used or have been modified for COVID-19**

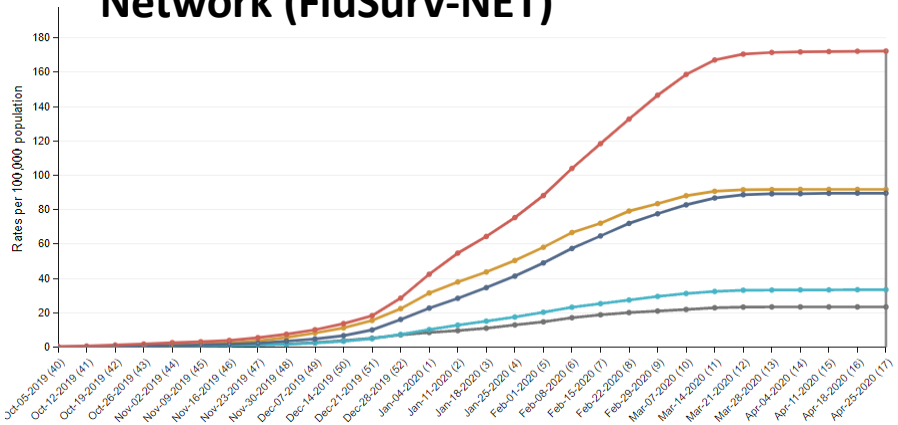
Overview of U.S. Influenza Surveillance

Influenza-Like Illness (ILI) Network

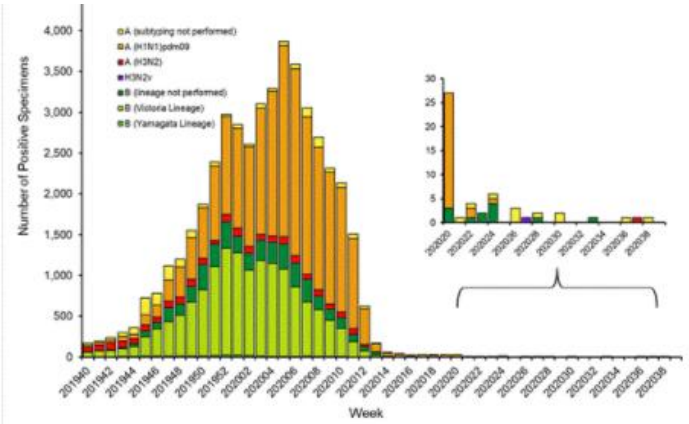




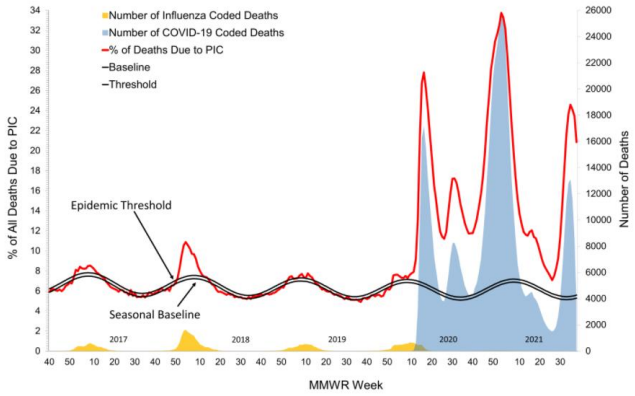
Influenza Hospitalization Surveillance Network (FluSurv-NET)



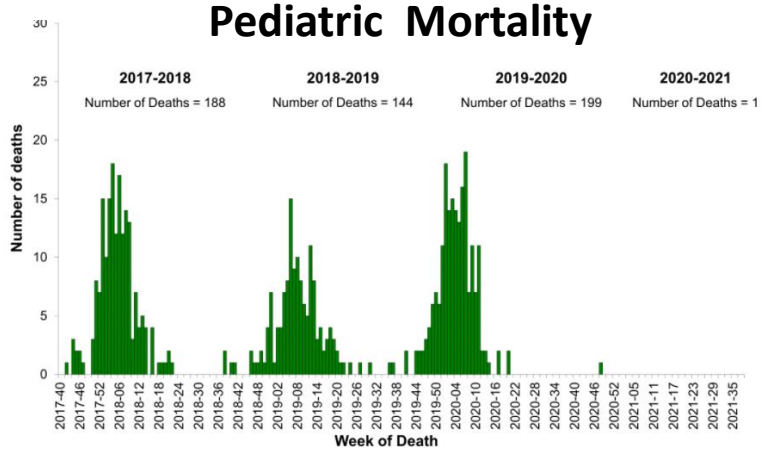
Influenza Virologic Surveillance



NCHS Mortality Surveillance

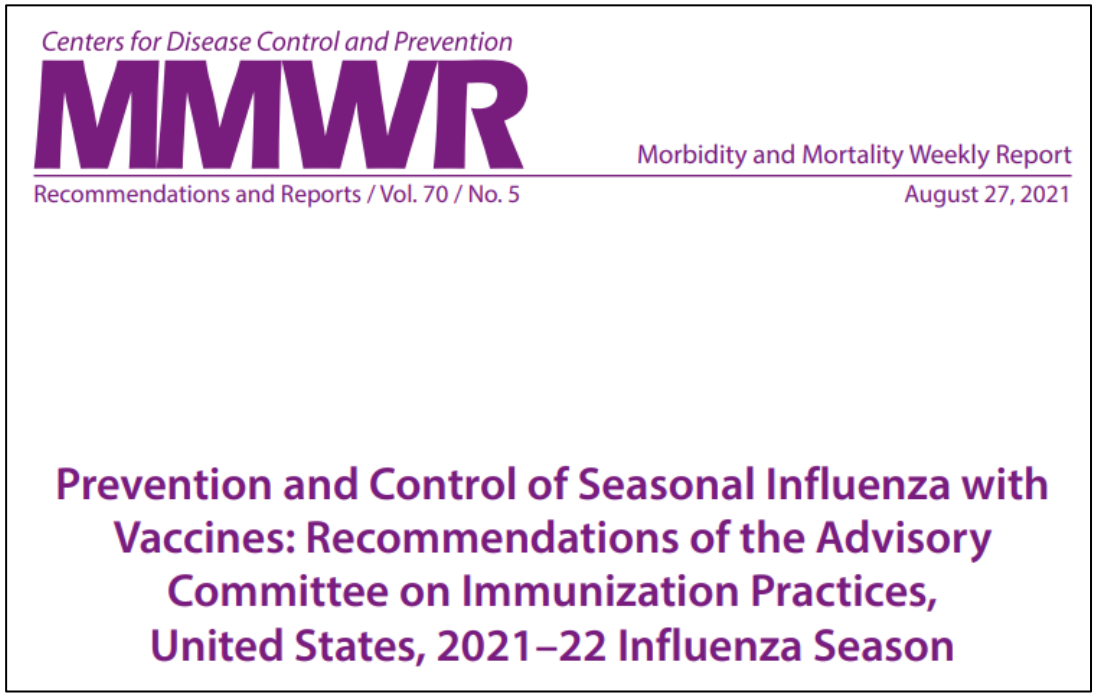


Pediatric Mortality



Flu vaccine recommendations for 2021-2022

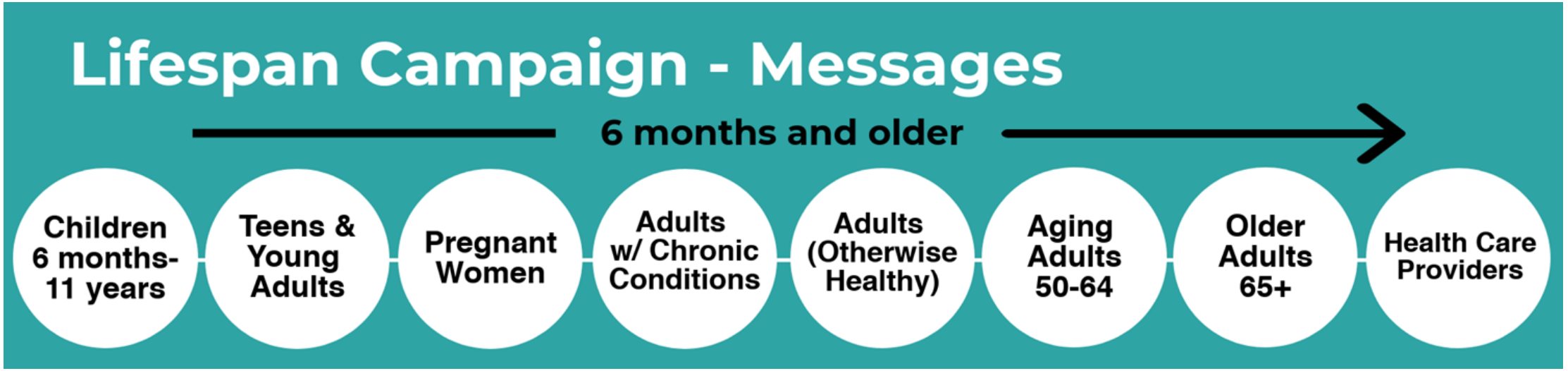
- All seasonal influenza vaccines for the 2020-2021 season are quadrivalent with HA from A(H1N1)pdm09 virus, A(H3N2) virus, B/Victoria lineage, B/Yamagata lineage
- Timing of vaccination in children and pregnant and non-pregnant persons
- Guidance regarding co-administration of influenza and COVID-19 vaccines



[Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices, United States, 2021–22 Influenza Season | MMWR (cdc.gov)]

CDC Influenza

CDC Annual Flu Vaccine Campaigns



Flu vaccines save lives in children

Flu vaccines protect you and your baby

Flu vaccines are an important part of managing chronic illness

Flu vaccines are part of keeping a healthy lifestyle

A strong provider recommendation is crucial to getting patients vaccinated

CDC Influenza

The 2021-2022 Flu Vaccine Campaign

"I Get It" digital media campaign (collaboration with Weber-Shandwick) targeting people ages 40-64 with chronic medical conditions

"No Time For Flu" comprehensive TV, digital, out of home campaign (CDC, AMA, Ad Council collaboration) aimed at the general population, with a focus on non-Hispanic Black and Hispanic adults ages 25-54

CDC Guidance for Health Professionals

Information for Clinicians on Influenza Virus Testing

Español | Other Languages

Testing and treatment of influenza when SARS-CoV-2 and influenza viruses are co-circulating

- **New** Consolidated Clinical Algorithm for Outpatient Clinic or Emergency Department Patients with Acute Respiratory Illness Symptoms (With or Without Fever)
- **New** Clinical Algorithm for Outpatient Clinic or Emergency Department Patients with Acute Respiratory Illness Symptoms (With or Without Fever) Not Requiring Hospital Admission
- **New** Clinical Algorithm for Patients with Acute Respiratory Illness Symptoms Requiring Hospital Admission (With or Without Fever)
- **New** Testing and Management Considerations for Nursing Home Residents

What Influenza Virus Tests Are Available

- Overview of influenza tests
- Influenza Virus Testing Methods
- Table 1: Influenza Virus Testing Methods
- Table 2: FDA-cleared and Available Rapid Influenza Diagnostic Tests
- Table 3: FDA-cleared Nucleic Acid Detection Based Tests for Influenza Viruses
- Table 4. Multiplex Assays Authorized for Simultaneous Detection of Influenza Viruses and SARS-CoV-2
- Information on Rapid Molecular Assays, RT-PCR, and other Molecular Assays for Diagnosis of Influenza Virus Infection
- Information about Rapid Influenza Diagnostic Tests

Seasonal Influenza (Flu)

Information for Health Professionals

Español

Note: "Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2021-2022 Influenza Season" has been published. CDC recommends annual influenza vaccination for everyone 6 months and older with any licensed, age-appropriate flu vaccine (IIV4, RIV4, or LAIV4) with no preference expressed for any one vaccine over another. More information about the 2021-2022 flu season is also available.

Vaccine Dosage & Administration

For Clinicians: Vaccination Summary

For Clinicians: Vaccine Safety

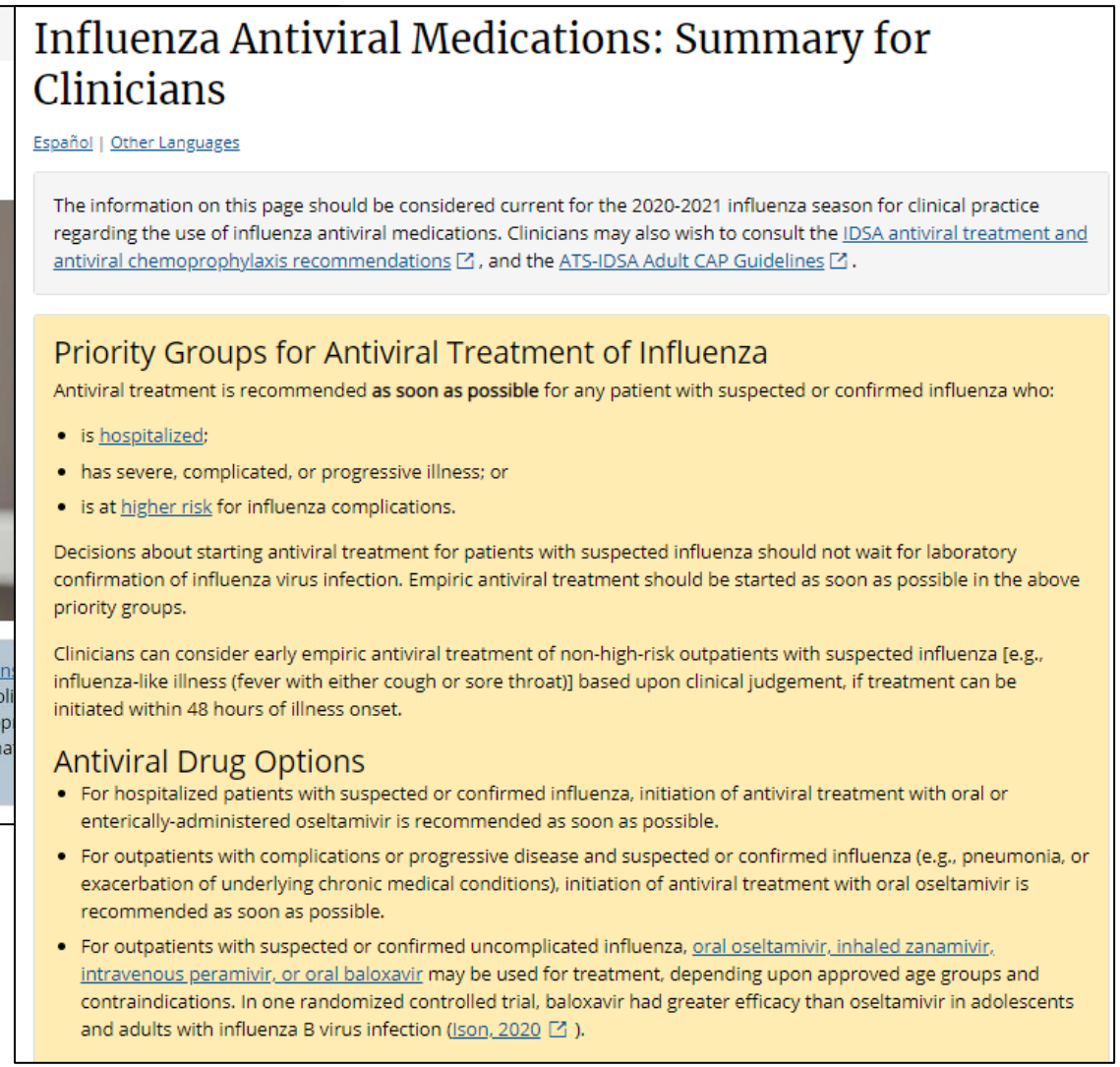
Reallocating Influenza Vaccine

The pages listed below offer public health and health care professionals key information about vaccination, infection control, prevention, treatment, and diagnosis of seasonal influenza.

[Information for Health Professionals | CDC]

CDC Influenza

CDC Guidance for Health Professionals



[Information for Health Professionals | CDC]

CDC Influenza

Frequently Asked Influenza (Flu) Questions: 2021-2022 Season | CDC

Frequently Asked Influenza (Flu) Questions: 2021-2022 Season

Español | Other Languages

What's New for 2021-2022

A few things are different for the 2021-2022 influenza (flu) season, including:

- The composition of flu vaccines has been updated.
- All flu vaccines will be quadrivalent (four component), meaning designed to protect against four different flu viruses. For more information: Quadrivalent Influenza Vaccine | CDC.
- Licensure on one flu vaccine has changed. Flucelvax Quadrivalent is now approved for people 2 years and older.
- Flu vaccines and COVID-19 vaccines can be given at the same time.
- More detailed guidance about the recommended timing of flu vaccination for some groups of people is available.
- Guidance concerning contraindications and precautions for the use of two flu vaccines – Flucevax Quadrivalent and Flublok Quadrivalent – were updated.

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Getting a Flu Vaccine During the COVID-19 Pandemic
Information for Healthcare Professionals
Testing and Treatment of Respiratory Illness when SARS-CoV-2 and Influenza Viruses are Co-circulating
2020-21 Flu Burden

Flu Vaccine

- What is CDC's recommendation for getting a flu vaccine for the 2021-2022 flu season? +
- What viruses will the 2021-2022 flu vaccines protect against? +
- Will this season's flu vaccine match be affected by the low levels of flu virus activity last season? +
- Do updates made to the composition of Southern Hemisphere flu vaccines mean that Northern Hemisphere flu vaccines are mismatched to circulating flu viruses? +
- What should someone 65 or older do who is having trouble finding high-dose or adjuvanted flu vaccine? +
- What if my vaccine provider doesn't have my preferred flu vaccine? +
- What is CDC doing to promote flu vaccination for the 2021-2022 flu season? +
- I don't have a primary care provider. Where can I get a flu vaccine? +
- When is the best time to get my influenza vaccine? +

Information for Healthcare Professionals

Administering Flu Vaccine during the COVID-19 Pandemic

- What is CDC's recommendation regarding drive-through influenza vaccination clinics? +
- Should a flu vaccine be given to someone with suspected or confirmed COVID-19? +
- When can someone who recovered from COVID-19 receive a flu vaccine? +
- Is there guidance for safely administering vaccines during the COVID-19 pandemic? +
- Can COVID-19 and flu vaccines be administered at the same time? +
- What are clinical best practices for administering COVID-19 vaccines and influenza vaccines at the same time? +
- Will there be changes in how and where flu vaccines are given this fall and winter? +
- What steps can health care personnel take to safely give flu vaccine during the COVID-19 pandemic? +
- Is there guidance for giving flu vaccine in settings other than a doctor's office (e.g., pharmacies; temporary, off-site, or satellite clinics; and large-scale influenza clinics)? +
- What is CDC's recommendation regarding drive-through influenza vaccination clinics? +
- Does CDC have any information about consumer attitudes related to flu and COVID-19 vaccines and getting them at the same time? +

Testing and Treatment of Respiratory Illness when SARS-CoV-2 and Influenza Viruses are Co-circulating

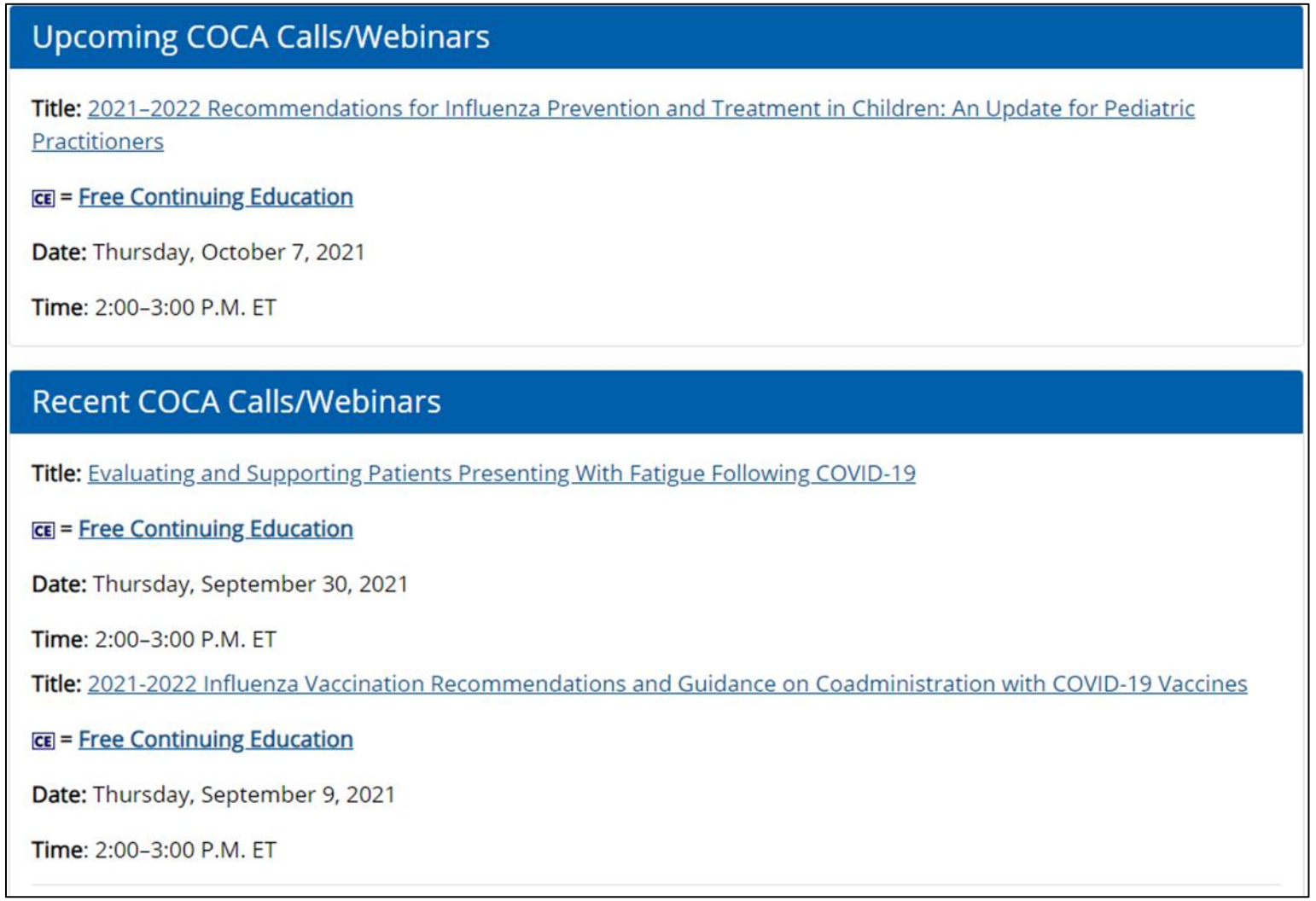
- What should we do if we have a patient who is sick with influenza/COVID-19-like symptoms while waiting for diagnostic test results? +
- I have a patient who has influenza/COVID-19-like symptoms, how should I proceed with testing and treatment? +
- Do antiviral medications for treatment of influenza have any effect on COVID-19? +

2020-21 Flu Burden

- Why aren't there flu burden estimates for the 2020-21 flu season? +
- If there are no burden estimates, how does CDC characterize the 2020-2021 season? +
- Are there other metrics that can be used to compare the 2020-2021 flu season with past seasons? +

CDC Influenza

Clinician Outreach and Community Activity (COCA) Calls



Upcoming COCA Calls/Webinars

Title: 2021–2022 Recommendations for Influenza Prevention and Treatment in Children: An Update for Pediatric Practitioners

CE = Free Continuing Education

Date: Thursday, October 7, 2021

Time: 2:00–3:00 P.M. ET

Recent COCA Calls/Webinars

Title: Evaluating and Supporting Patients Presenting With Fatigue Following COVID-19

CE = Free Continuing Education

Date: Thursday, September 30, 2021

Time: 2:00–3:00 P.M. ET

Title: 2021-2022 Influenza Vaccination Recommendations and Guidance on Coadministration with COVID-19 Vaccines

CE = Free Continuing Education

Date: Thursday, September 9, 2021

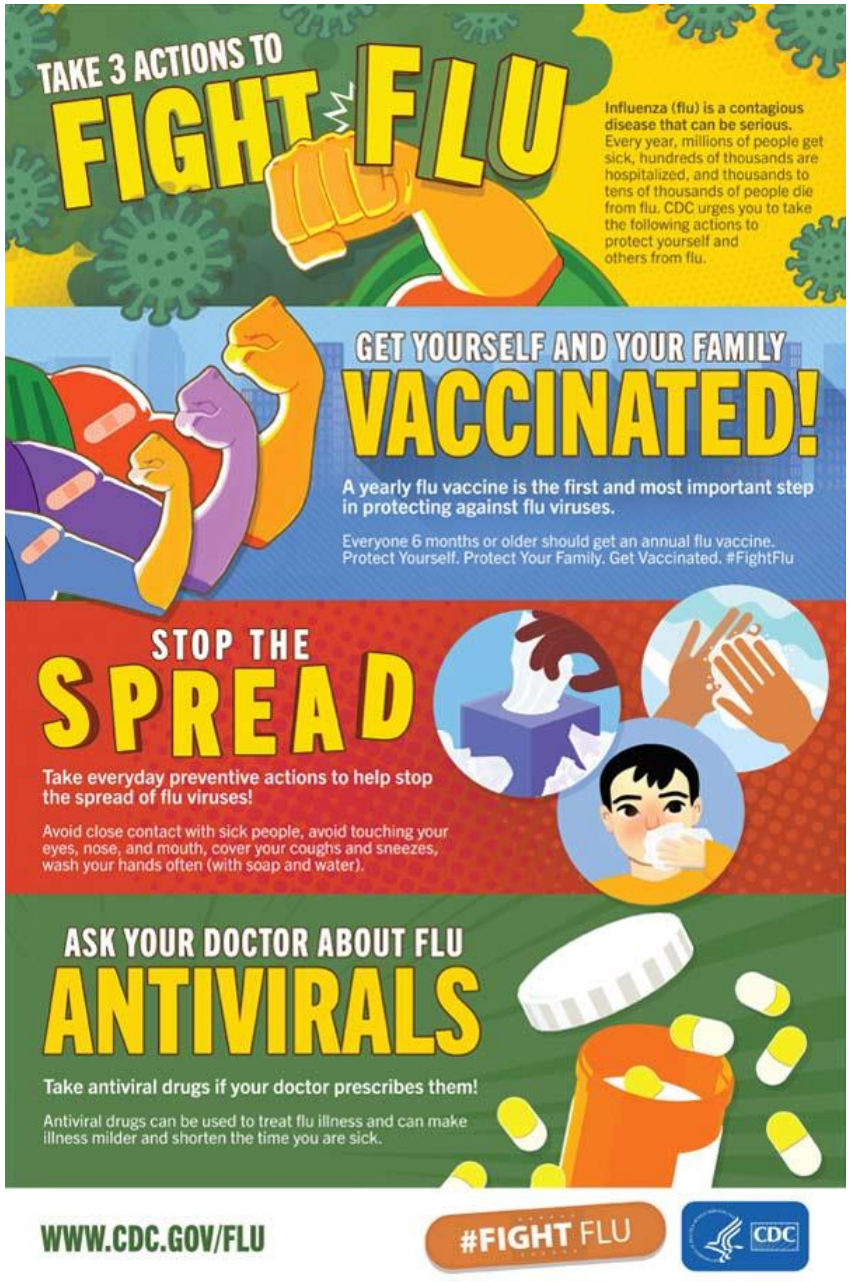
Time: 2:00–3:00 P.M. ET

Calls/Webinars | Clinician Outreach and Communication Activity (COCA) (cdc.gov)

CDC Influenza

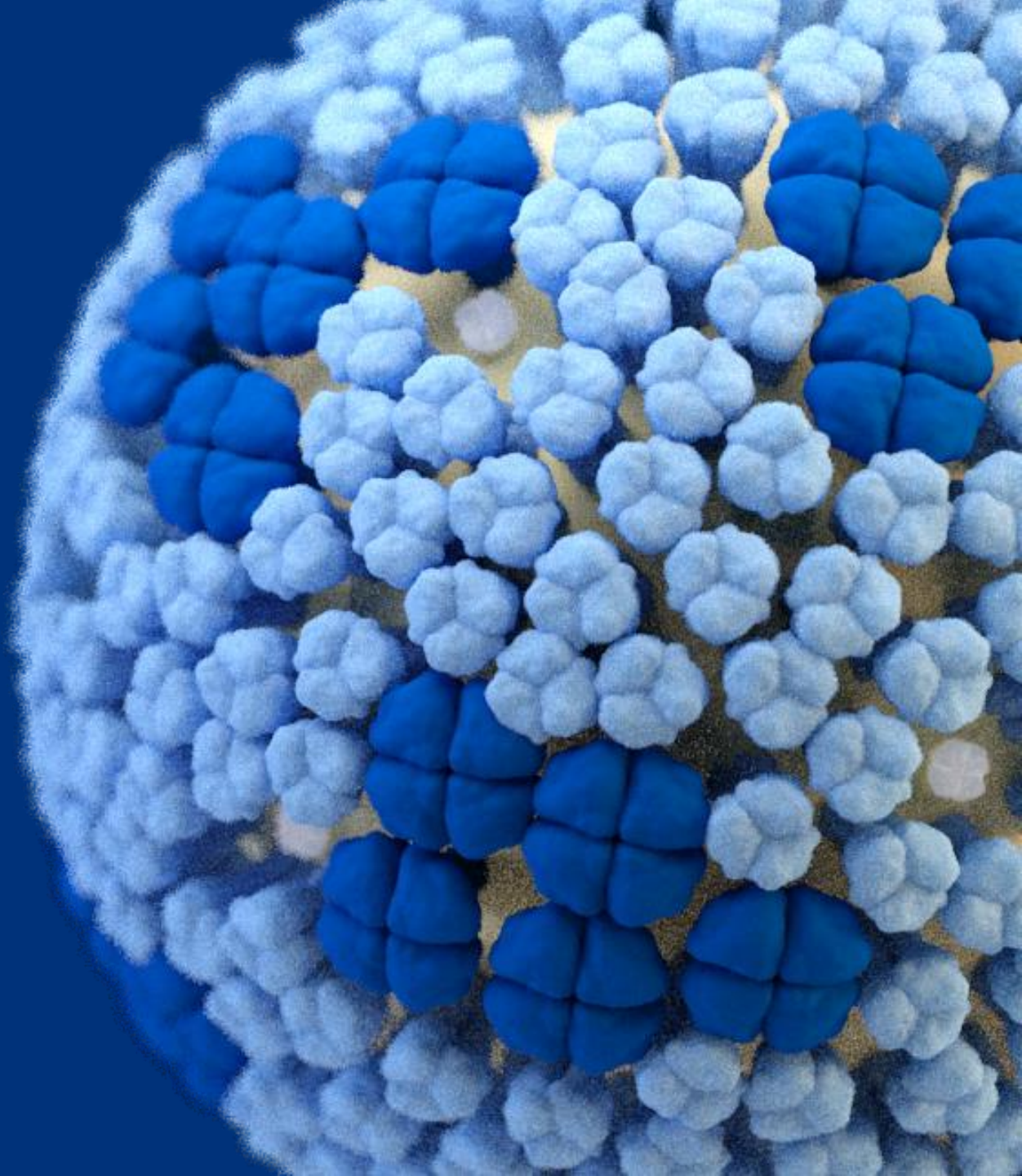
Additional CDC Resources

- CDC Influenza homepage: https://www.cdc.gov/flu/
- Influenza surveillance: https://www.cdc.gov/flu/weekly/fluactivitysurv.htm
- Influenza vaccination coverage: https://www.cdc.gov/flu/fluvaxview/index.htm
- For Healthcare Professionals: https://www.cdc.gov/flu/professionals/index.htm
  - Vaccination homepage: https://www.cdc.gov/flu/professionals/vaccination/index.htm
  - 2019-20 ACIP Influenza Recommendations: https://www.cdc.gov/mmwr/volumes/68/rr/rr6803a1.htm
  - Antiviral homepage: https://www.cdc.gov/flu/professionals/antivirals/index.htm



CDC Influenza

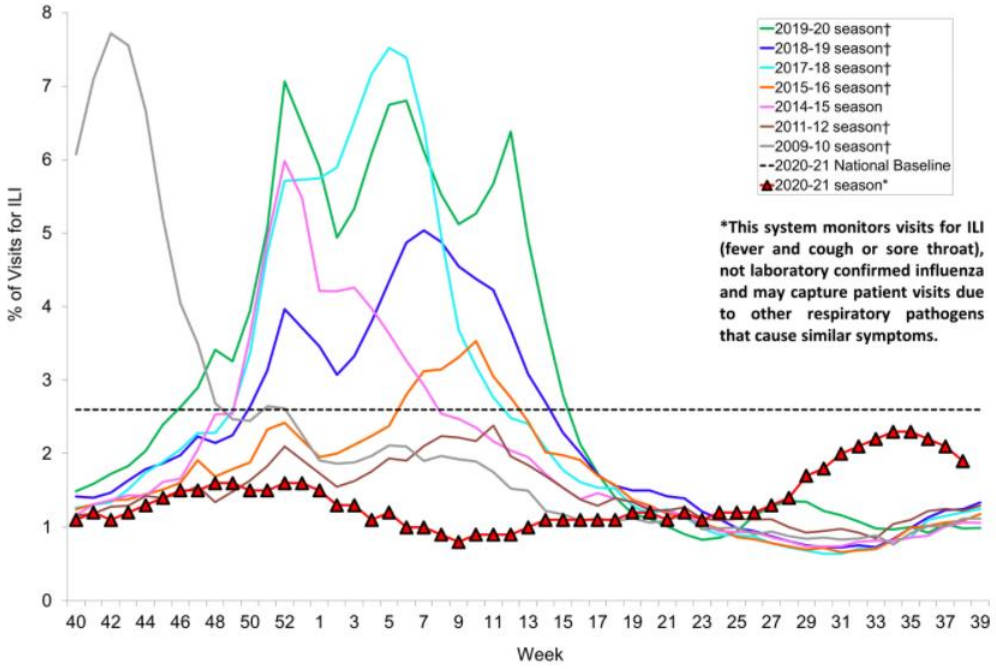
Thank You!

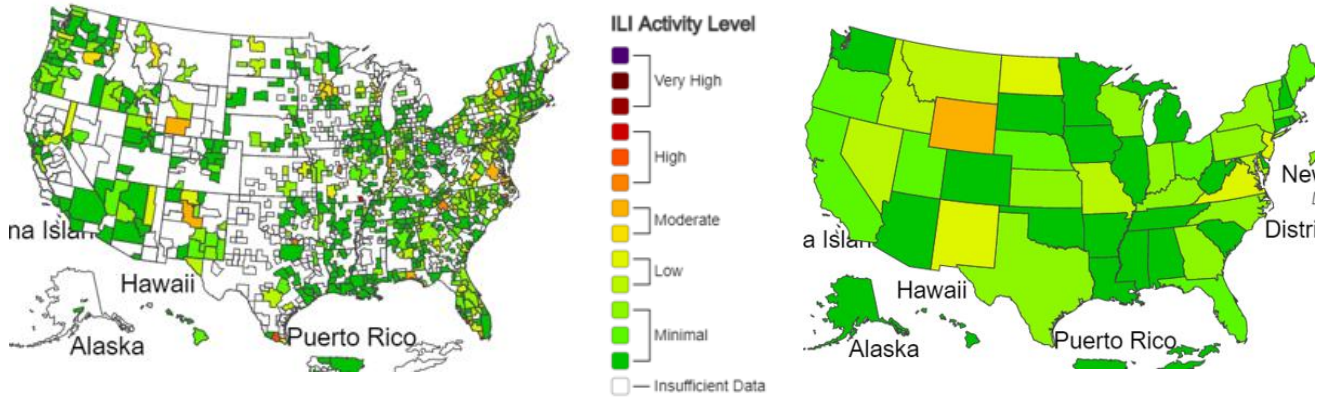


CDC
Influenza

Outpatient Syndromic Surveillance for ILI

- Influenza-Like Illness (ILI) Network
  - System also used for COVID-19 monitoring in ambulatory care centers
  - Each season, ~60 million patient visits under surveillance
  - Over 3,000 ambulatory care centers report each week





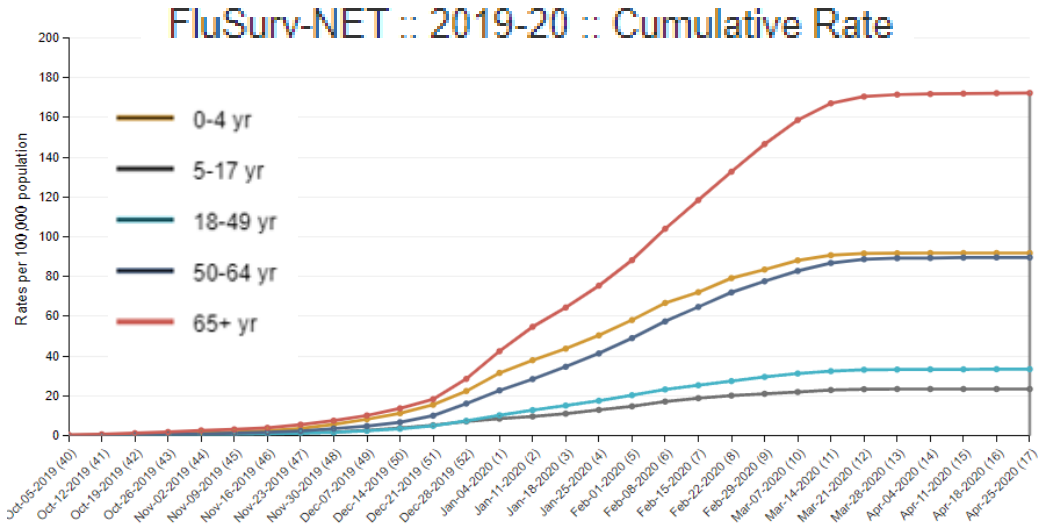
Activity as of week ending September 27, 2021

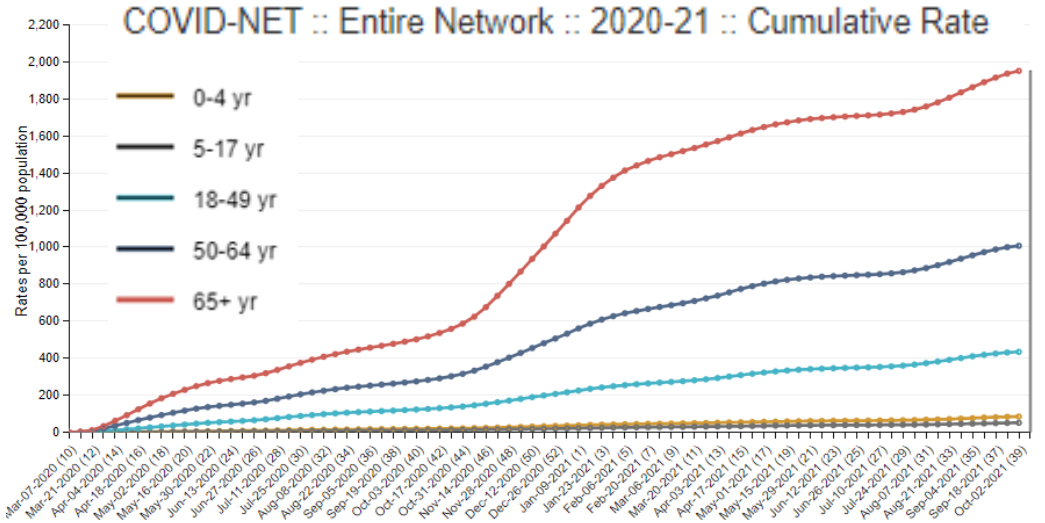
https://www.cdc.gov/flu/weekly/overview.htm

CDC Influenza

Influenza Hospitalization Surveillance

- **FluSurv-NET: Population-based surveillance for laboratory-confirmed hospitalizations**
  - FluSurv-NET foundation for COVID-NET
  - Same system monitors both influenza and COVID-19-associated hospitalizations
  - Select counties in 14 states (~10% U.S pop)
  - Rates of hospitalization by age, sex and race; interventions and outcomes (Oct—April)
  - Post data once >300 cases reported
- **Tele-tracker Influenza Hospital Admissions**
  - Monitors for daily total number of flu hospitalizations, ICU admissions and deaths
  - >6000 hospitals



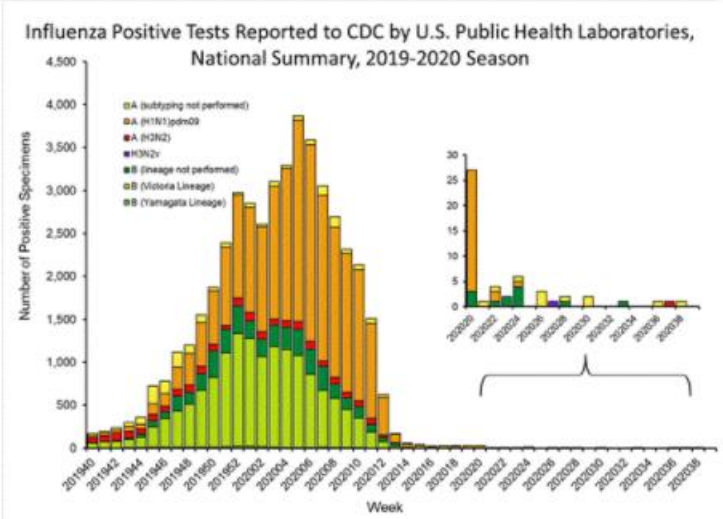


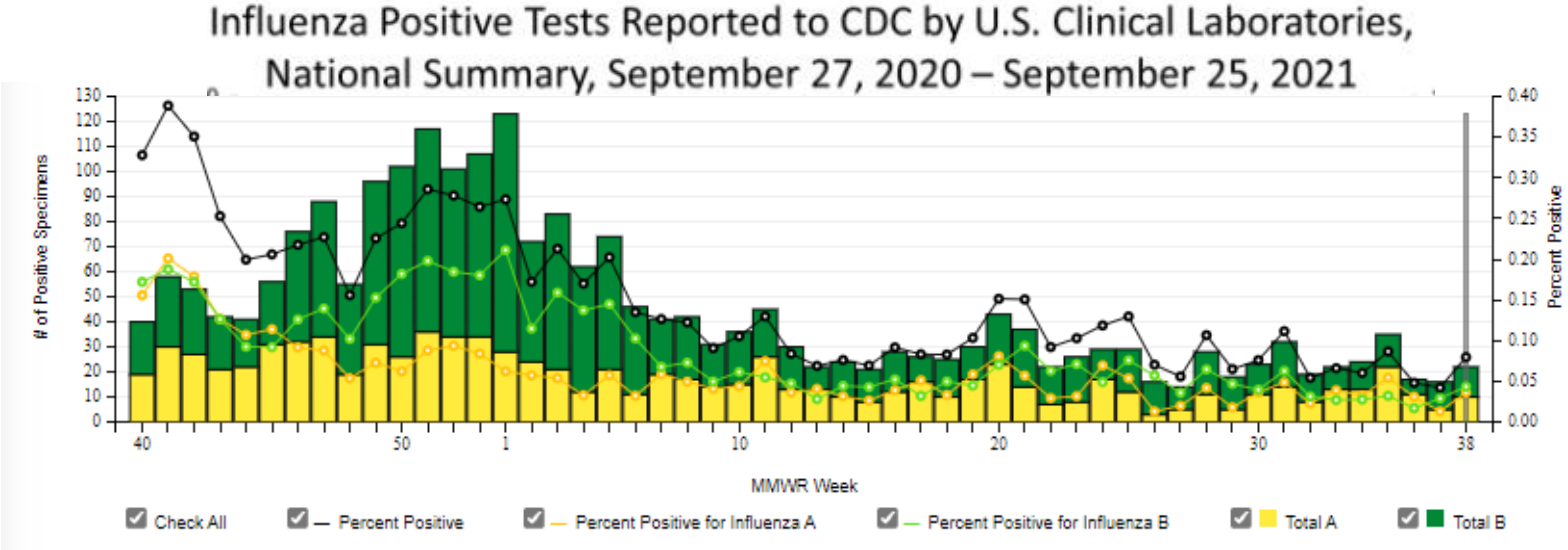
https://www.cdc.gov/flu/weekly/fluviewinteractive.htm

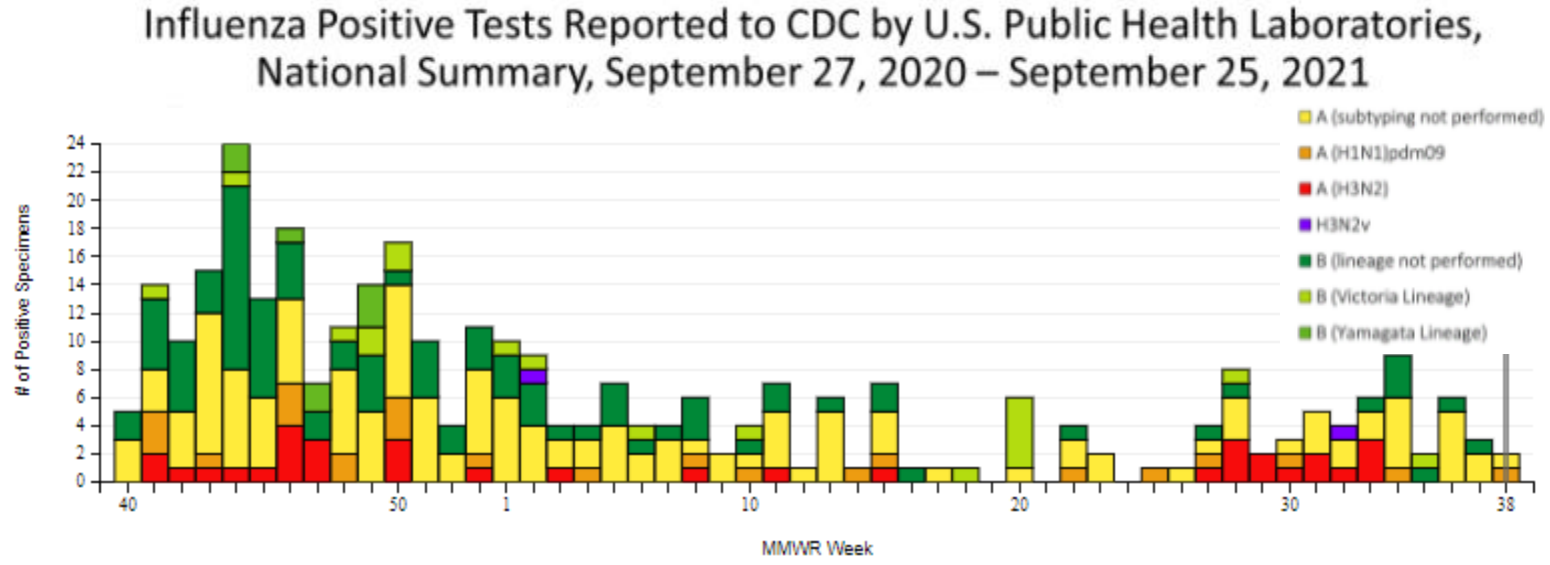
CDC Influenza

Influenza Virus Surveillance

- Network of clinical and public health labs (PHLs) in all 50 states, Puerto Rico, Guam, DC
- Same system monitors testing and characterizes SARS-CoV-2 and influenza at PHLs





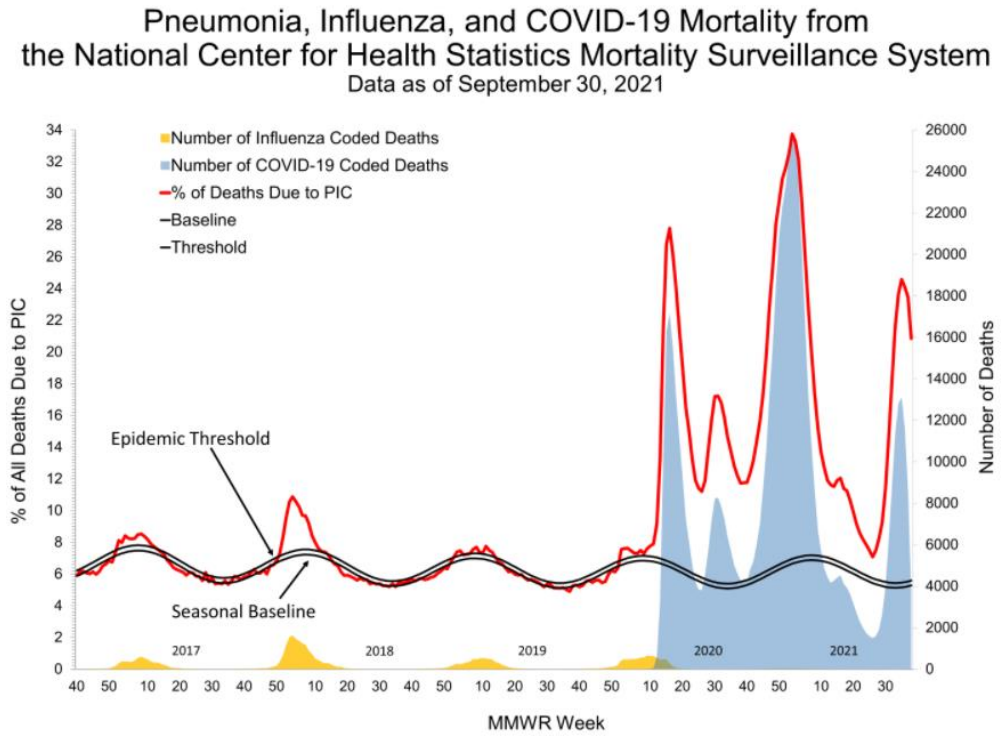


https://www.cdc.gov/flu/weekly/overview.htm

CDC Influenza

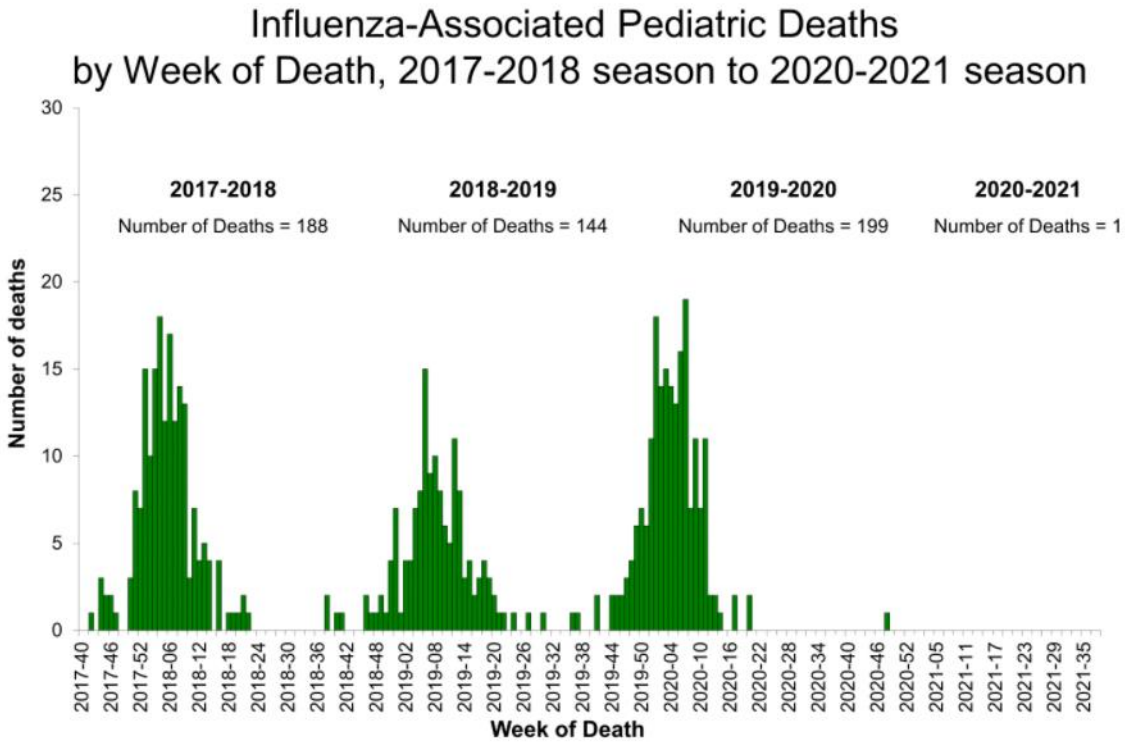
Mortality Surveillance

- **NCHS Mortality Surveillance**
  - Death certificate data for pneumonia, influenza, and COVID-19 for all U.S. deaths
  - Percent of deaths due to pneumonia, influenza, or COVID-19 ICD-10 codes



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

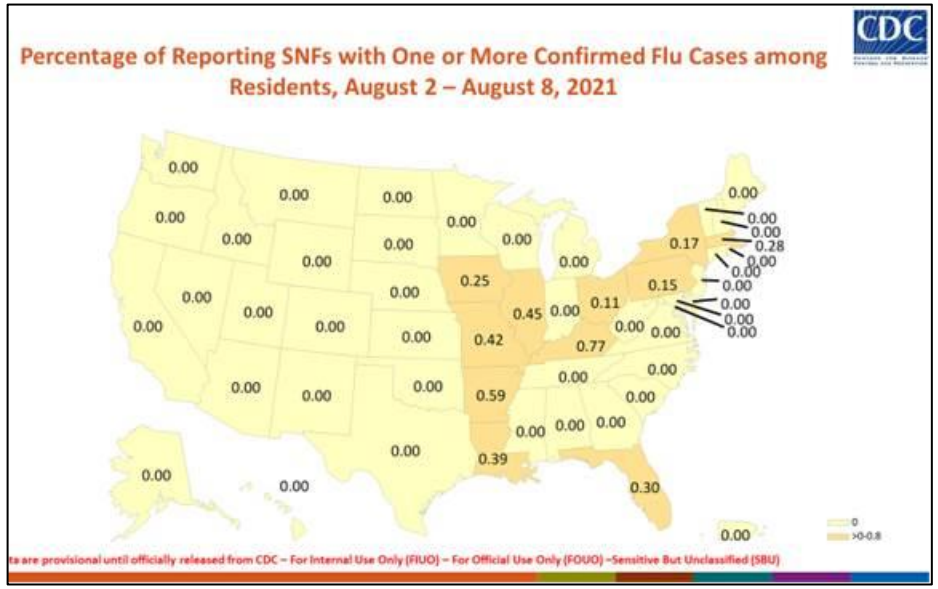
- **Pediatric Mortality**
  - Laboratory-confirmed influenza
  - Nationally notifiable condition
  - Clinical data and pathology



Additional systems that will capture both influenza and COVID-19 during 2021-2022 season

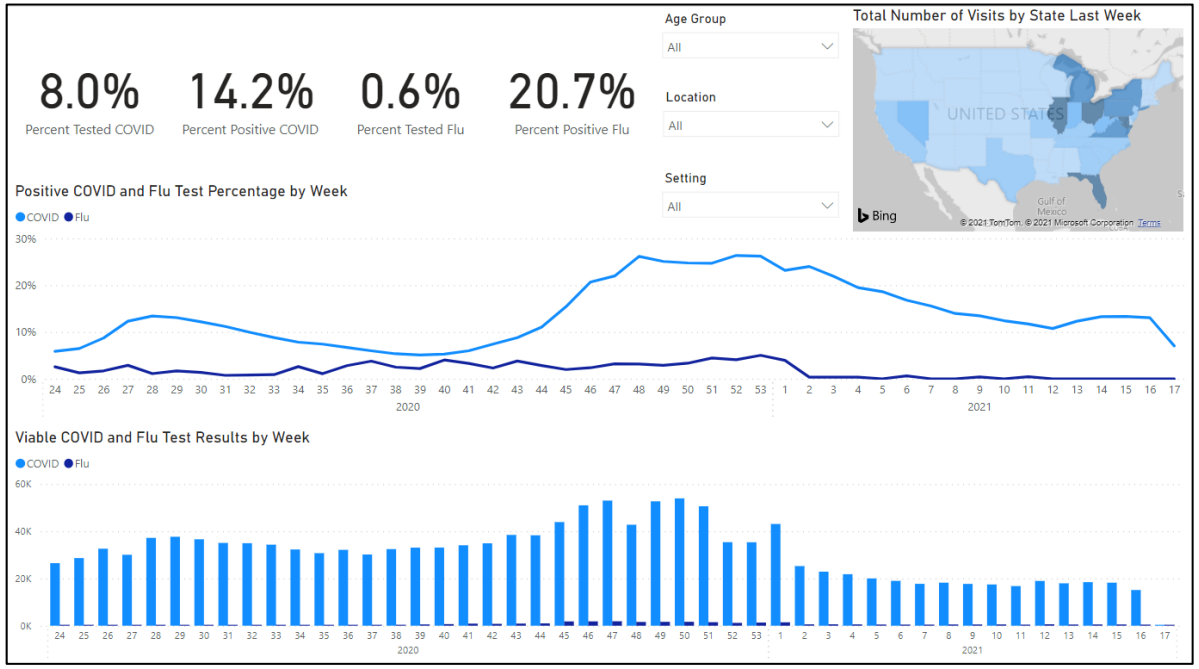
LTCF Surveillance

- National Healthcare Safety Network
- 15,400 facilities



Electronic Health Record Dashboard

- Monitor testing and healthcare seeking
- Multiple healthcare settings
- 40 healthcare systems nationwide



CDC Influenza

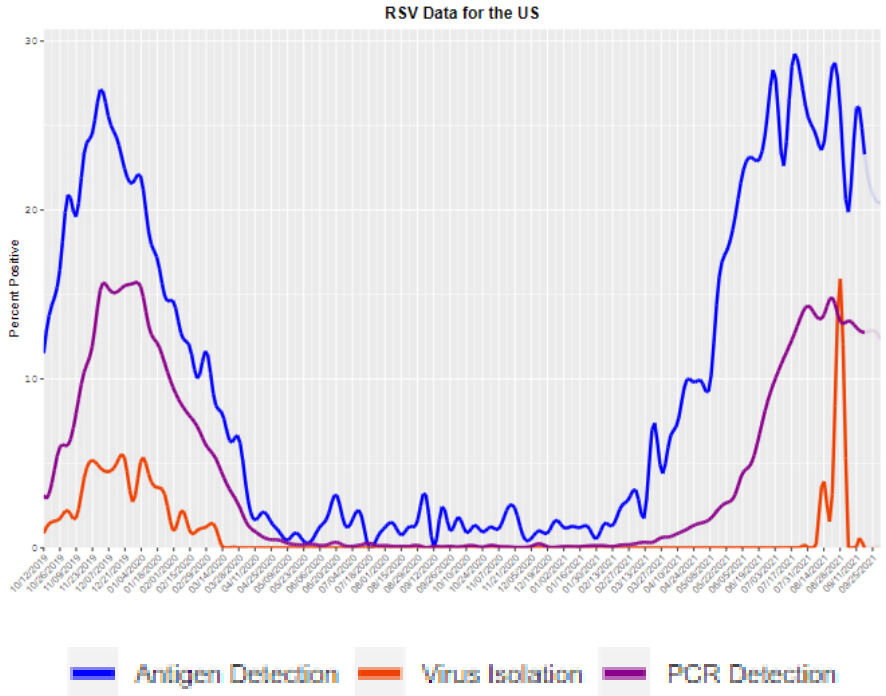
Increased Interseasonal Respiratory Syncytial Virus (RSV) Activity in Parts of the Southern United States

HAN HEALTH ALERT NETWORK

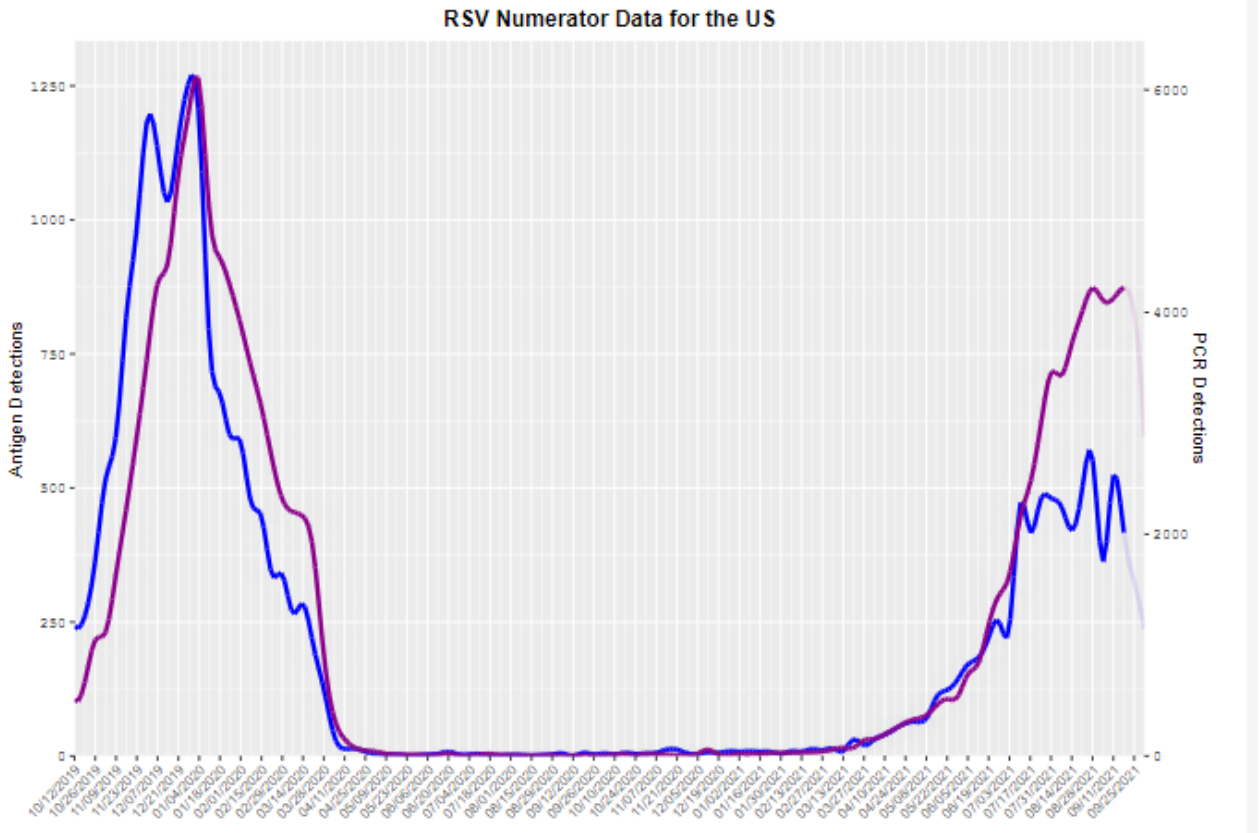
This is an official CDC HEALTH ADVISORY

Distributed via the CDC Health Alert Network
June 10, 2021, 1:30 PM ET
CDCHAN-00443

Percent Positive



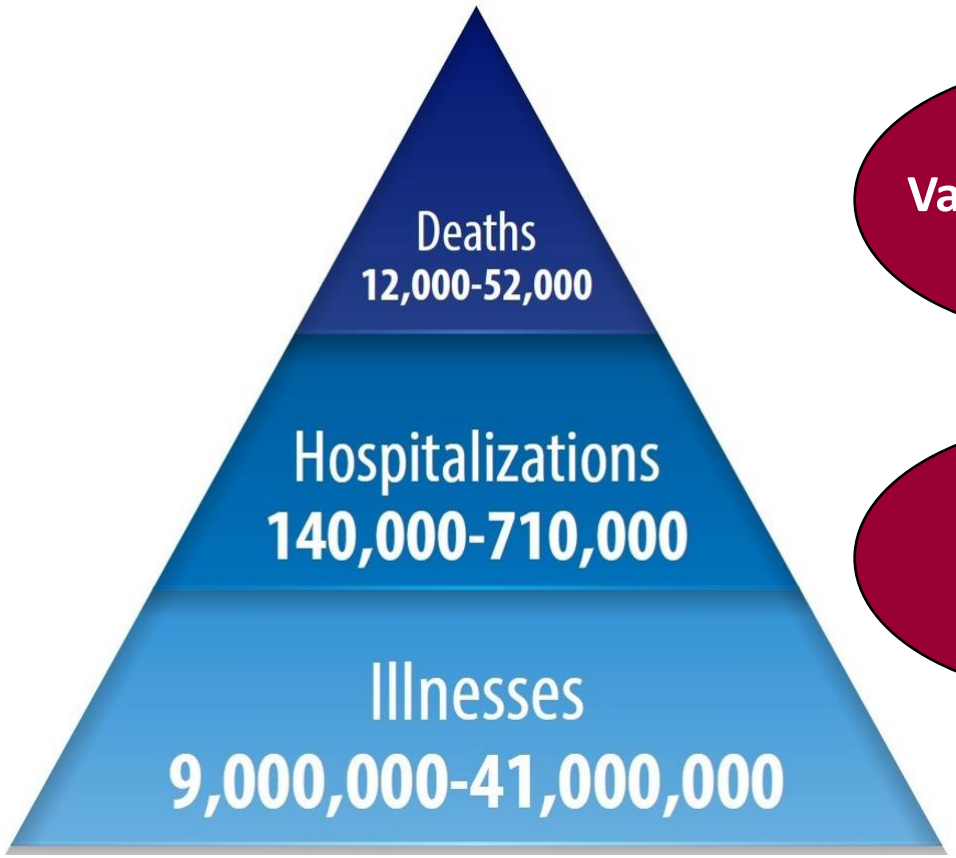
Detections



Data through October 2, 2021

CDC Influenza

Modeling estimated benefits of flu vaccine



Influenza Disease Burden

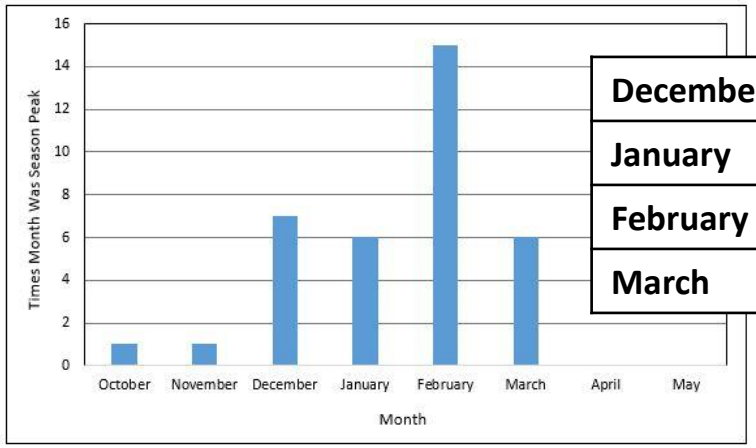
Vaccine Coverage

Vaccine Effectiveness

CDC Influenza

Timing of Flu Seasons and Flu Vaccination

- Timing of the onset and peak of influenza activity varies from season to season.
- Timing of activity onset can also vary geographically.
- In the United States, localized areas of increased activity occur as early as October.
- Over 36 seasons between 1982-83 and 2017-18, peak activity occurred most often in Feb



December	**7 seasons (19%)**
January	**6 seasons (17%)**
February	**15 seasons (42%)**
March	**6 seasons (19%)**

- Ideally vaccinate by the end of October but vaccine should continue to offered as long as flu viruses circulate locally
- Children needing 1 dose can be vaccinated soon after vaccine becomes available
- For children who require 2 doses, first dose should be administered soon after vaccine becomes available, with 2nd dose 4 weeks later
- Pregnant women in 3rd trimester- may consider administration soon after seasonal flu vaccine becomes available
- Non-pregnant adults-vaccination in July or August not recommended even if vaccine is available (unless concern that later vaccination may not be possible)

https://www.cdc.gov/flu/about/season/flu-season.htm

Co-administration of Influenza Vaccines with COVID-19 Vaccines

- ACIP influenza statement cites current Interim Clinical Considerations for Use of COVID-19 vaccines Currently Approved or Authorized in the United States:
  - COVID-19 vaccines may be administered without regard to timing of other vaccines.
  - Includes simultaneous administration of COVID-19 vaccine and other vaccines on the same day
  - Vaccines administered at the same visit should be given at different injection sites (separated by an inch or more, it possible).
  - If COVID-19 vaccines are given with vaccines that might be more likely to cause a local reaction (e.g., high-dose or adjuvanted influenza vaccines), administer in separate limbs, if possible.
- Providers should check current CDC COVID-19 vaccination guidance for updated information concerning co-administration.

  https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fcovid-19%2Finfo-by-product%2Fclinical-considerations.html#Coadministration

Influenza Vaccines Expected to be Available by Age Indication, United States, 2021–22 Influenza Season

Vaccine type		0 through 6 months	6 through 23 months	2 through 17 years	18 through 49 years	50 through 64 years	≥65 years
IIV4s	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			

IIV4=quadrivalent inactivated influenza vaccine **RIV4**=quadrivalent recombinant influenza vaccine **LAIV4**=quadrivalent live attenuated influenza vaccine

Not approved for age group *Egg-based* *Not egg-based*

All vaccines expected for 2021-22 are quadrivalent (i.e., contain hemagglutinin derived from four viruses: one influenza A(H1N1), one influenza A(H3N2), one influenza B/Victoria and one influenza B/Yamagata.

CDC Influenza

Influenza Vaccine Types—2021-22 U.S. Season

Intramuscular Vaccines

Inactivated Influenza Vaccines (IIV4s)

- Contain inactivated virus (split or subunit)
- Most are egg-based (one is cell culture-based—ccIIV4)
- Most contain 15 mcg of hemagglutinin per virus (one contains 60 mcg per virus—HD-IIV4)
- Most are unadjuvanted (one contains the adjuvant MF59—aIIV4)

Recombinant influenza vaccine (RIV4)

- No viruses used in production
- 45 mcg HA per virus
- Contains HA made through recombinant methods

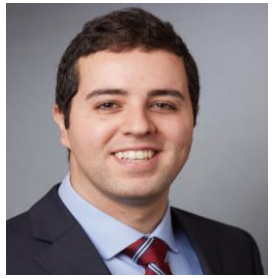
Intranasal Vaccine

Live attenuated influenza vaccine (LAIV4)

- Egg-based
- Contains live, attenuated influenza viruses which must replicate in the nasopharynx in order to promote an immune response
  - Attenuated—to not cause clinical illness
  - Cold adapted—grow best at 25°C
  - Temperature sensitive—growth restricted at 37°-39°C
- For ages 2 through 49 years

Diagnosis and Treatment of Respiratory Illness This Winter Season

Diagnosis & Testing Update



Marwan Mikheal Azar, MD, FAST
Infectious Diseases Fellowship Program Director
Assistant Professor, Infectious Diseases
Yale School of Medicine

Diagnosis of Respiratory Illnesses this Winter Season

Updates and Practical Guidance on Testing

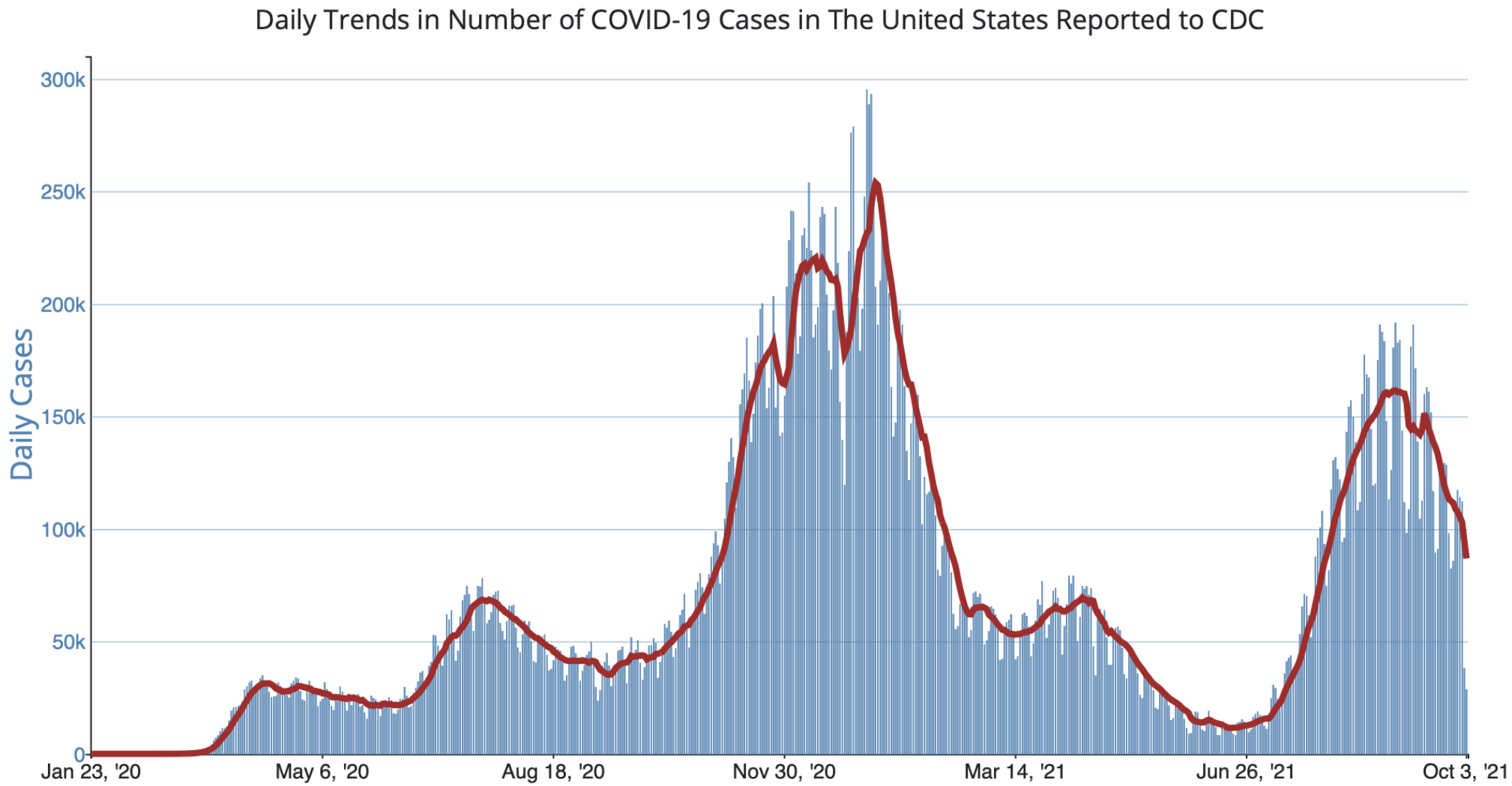
Marwan M. Azar, MD, FAST

Assistant Professor, Infectious Diseases

Infectious Diseases Fellowship Program Director

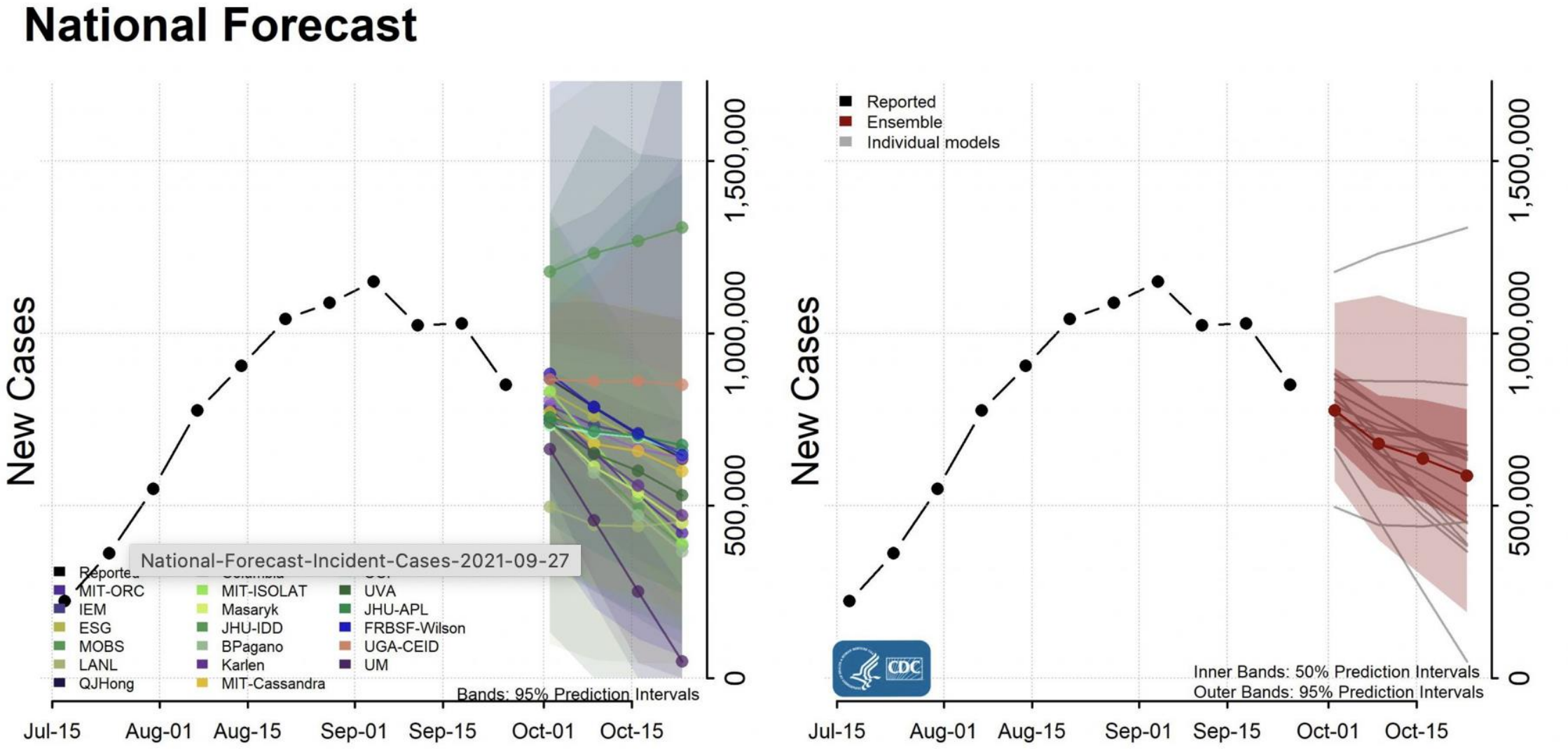
Yale University

COVID-19 Pandemic



https://covid.cdc.gov/covid-data-tracker/#trends_dailycases

COVID-19 Pandemic – CDC Projections

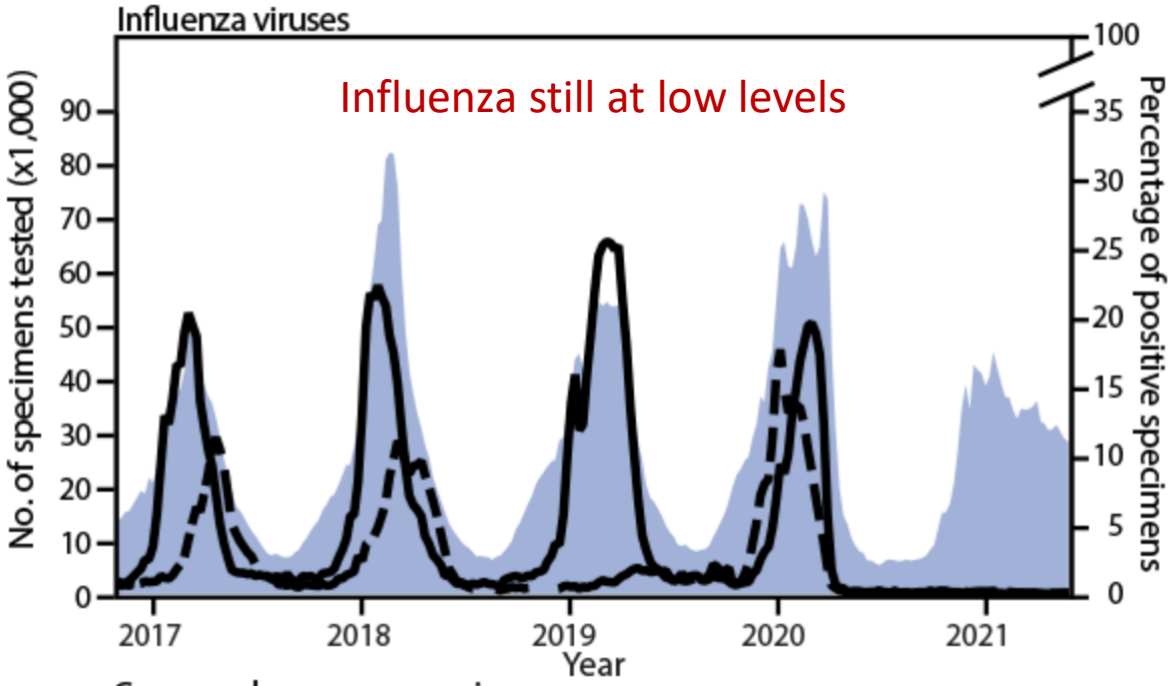


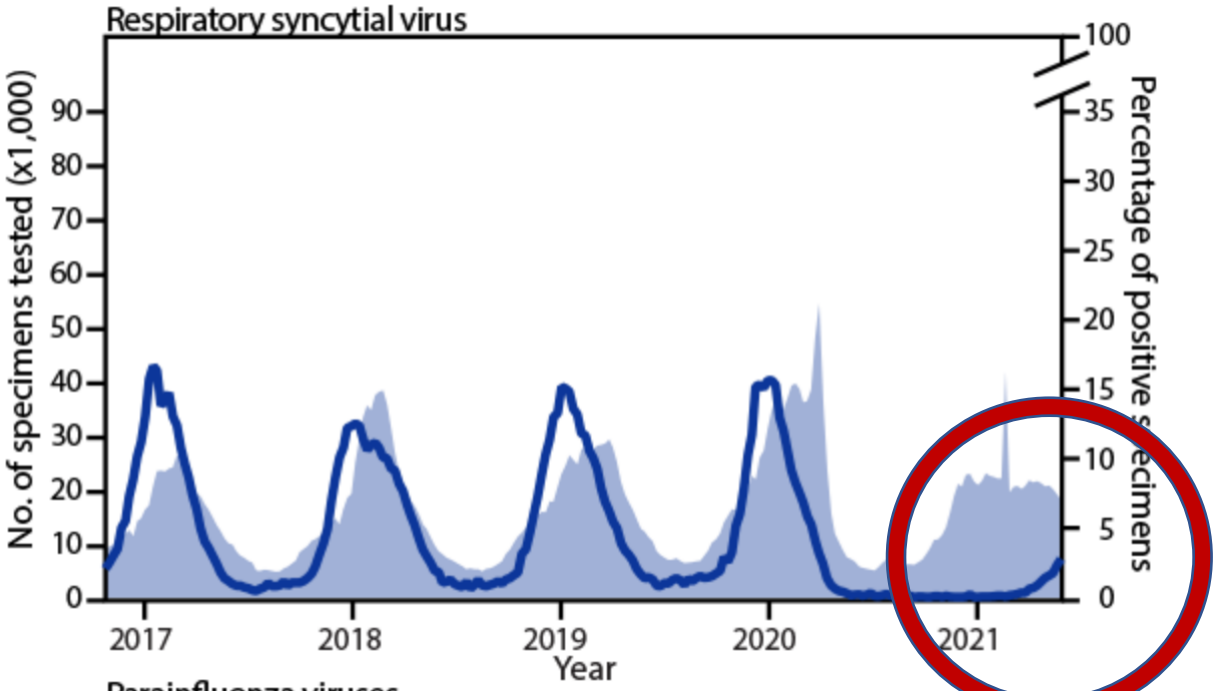
Non-SARS-CoV-2 Respiratory viruses

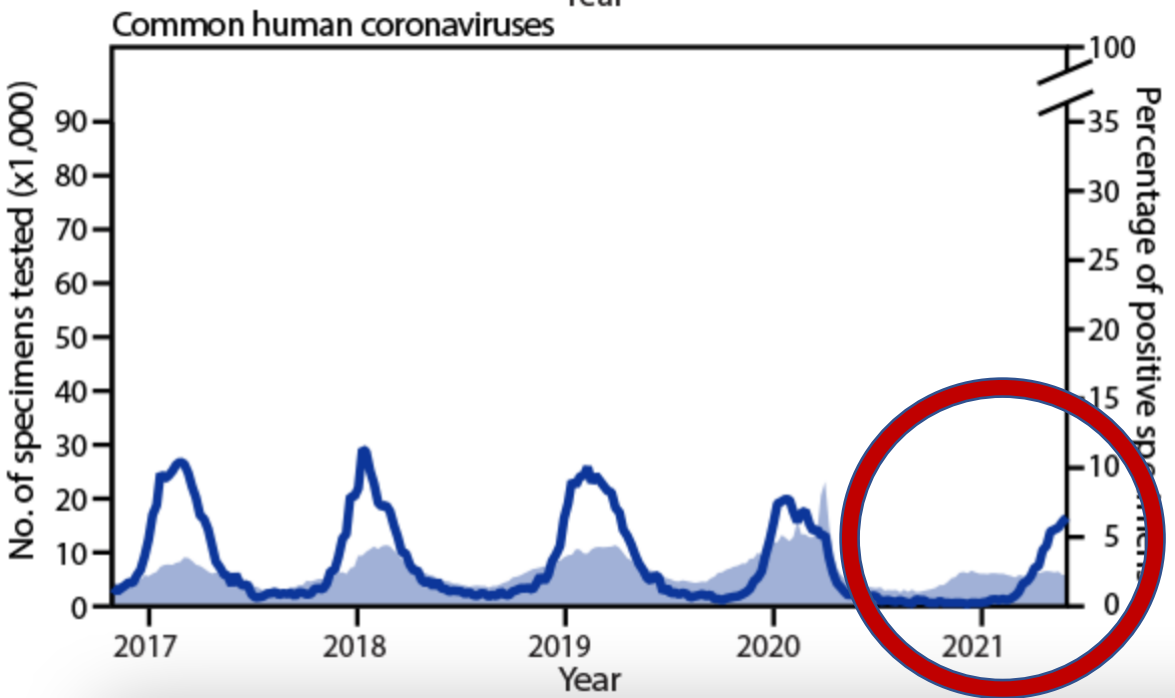
- Non-SARS-CoV-2 respiratory virus activity (Influenza, RSV, HCoV PIV, HMNV, ADV) was historically low from the onset of the COVID-19 pandemic until the Spring of 2021

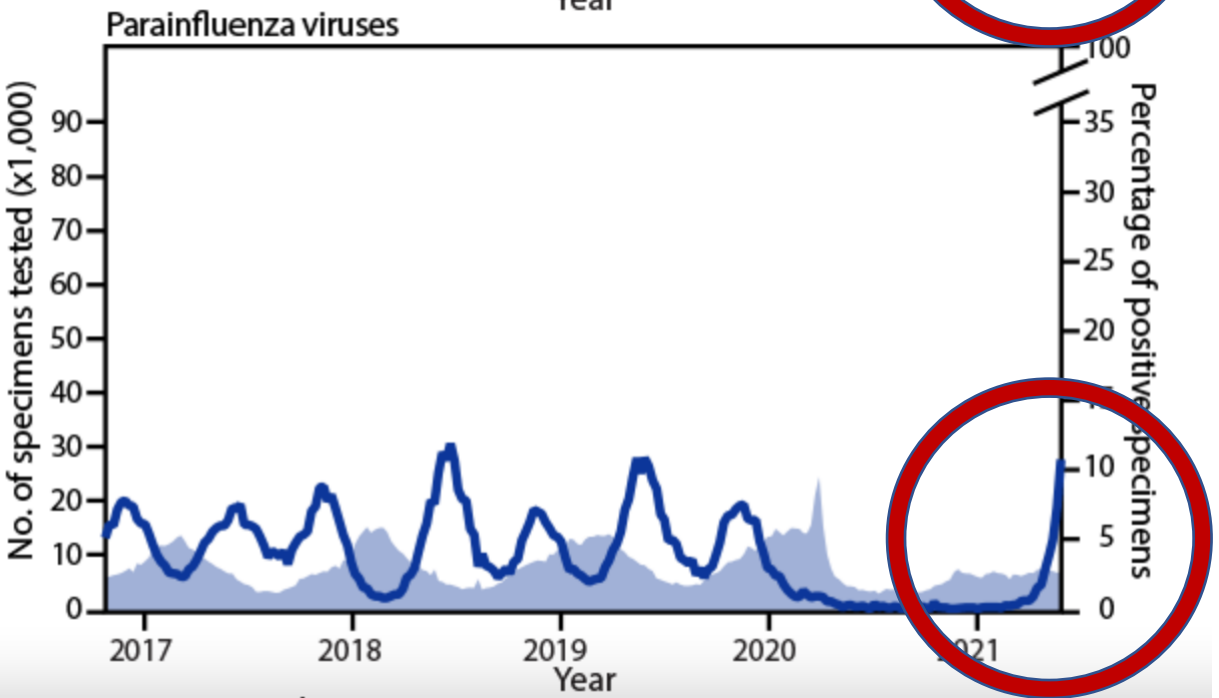
- **In May 2021, circulation of some respiratory viruses began to increase (RSV, HCoV and PIV)**
  - Between April 17–May 22, 2021, the **RSV** weekly percentage of positive results increased **from 1.1% to 2.8%** (mostly in Southeastern USA)
  - Between February 27 -May 22, 2021, **HCoV** weekly percentage of positive results increased **from <1% to 6.6%** (led by types OC43 and NL63)
  - Between April 11–May 22, 2021, the **PIV** weekly percentage of positive results increased **from <1% to 10.9%**

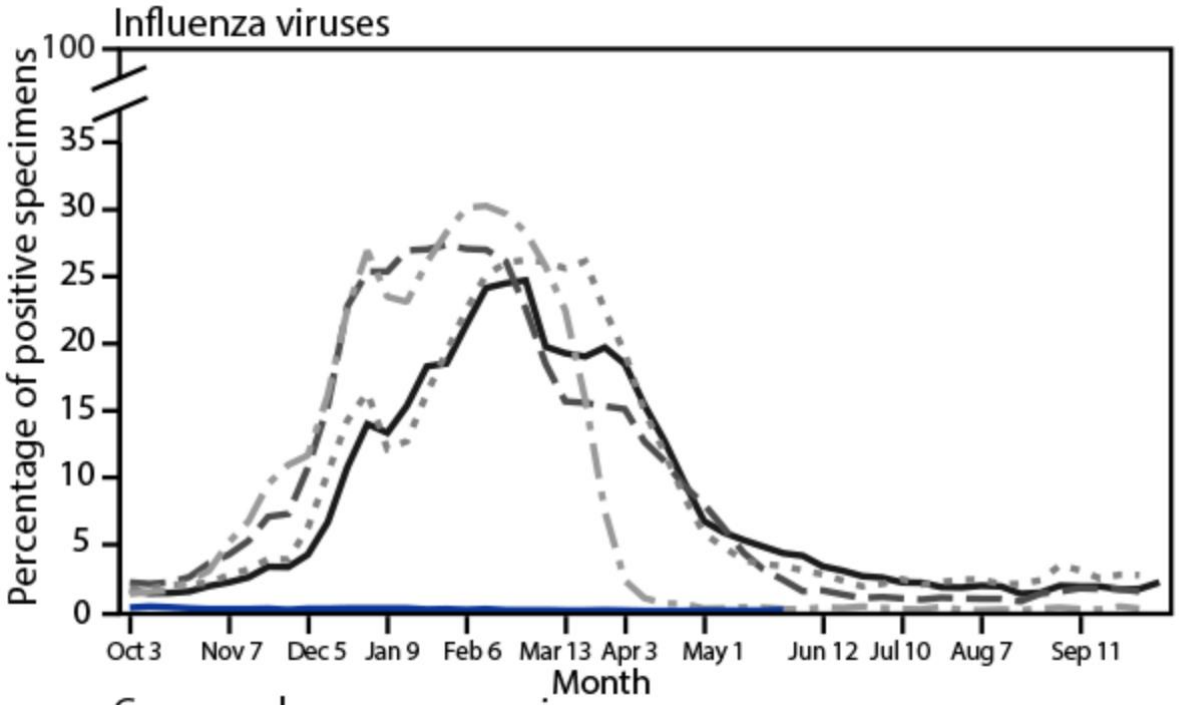
Olsen SJ, et al. Changes in Influenza and Other Respiratory Virus Activity During the COVID-19 Pandemic - United States, 2020-2021. MMWR Morb Mortal Wkly Rep. 2021 Jul 23;70(29):1013-1019. doi: 10.15585/mmwr.mm7029a1. PMID: 34292924; PMCID: PMC8297694.

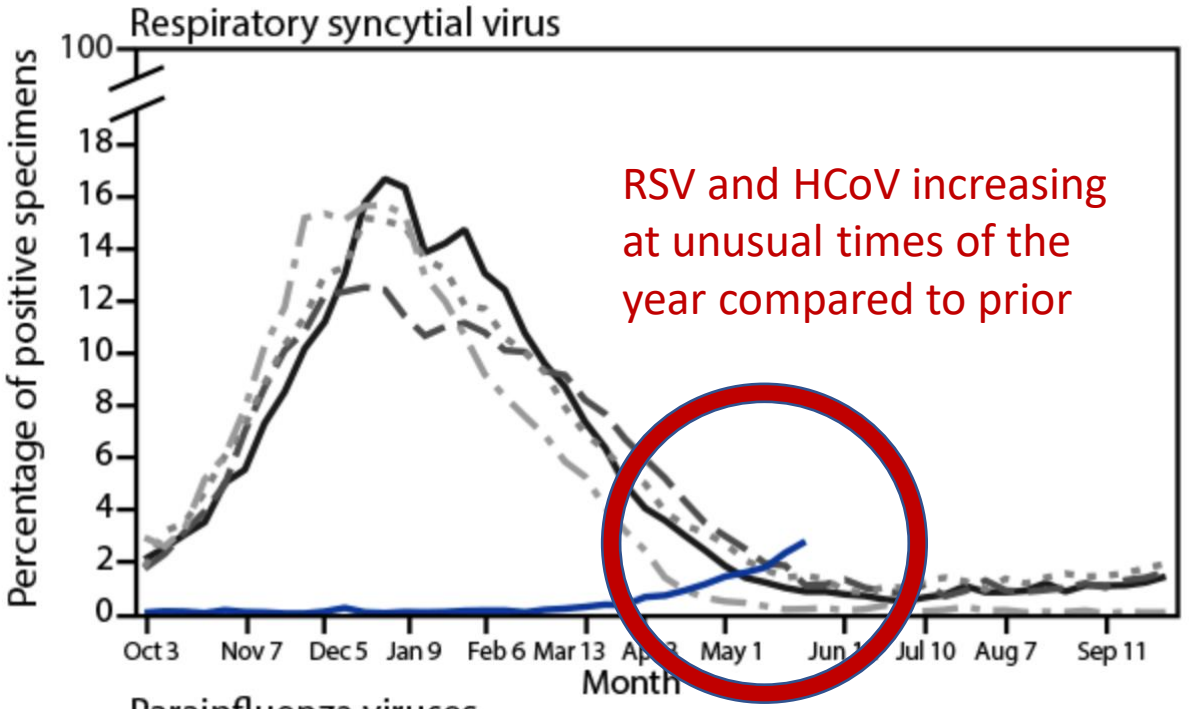

Influenza viruses
Influenza still at low levels
No. of specimens tested (x1,000)
Percentage of positive specimens
Year
2017
2018
2019
2020
2021


Respiratory syncytial virus
No. of specimens tested (x1,000)
Percentage of positive specimens
Year
2017
2018
2019
2020
2021

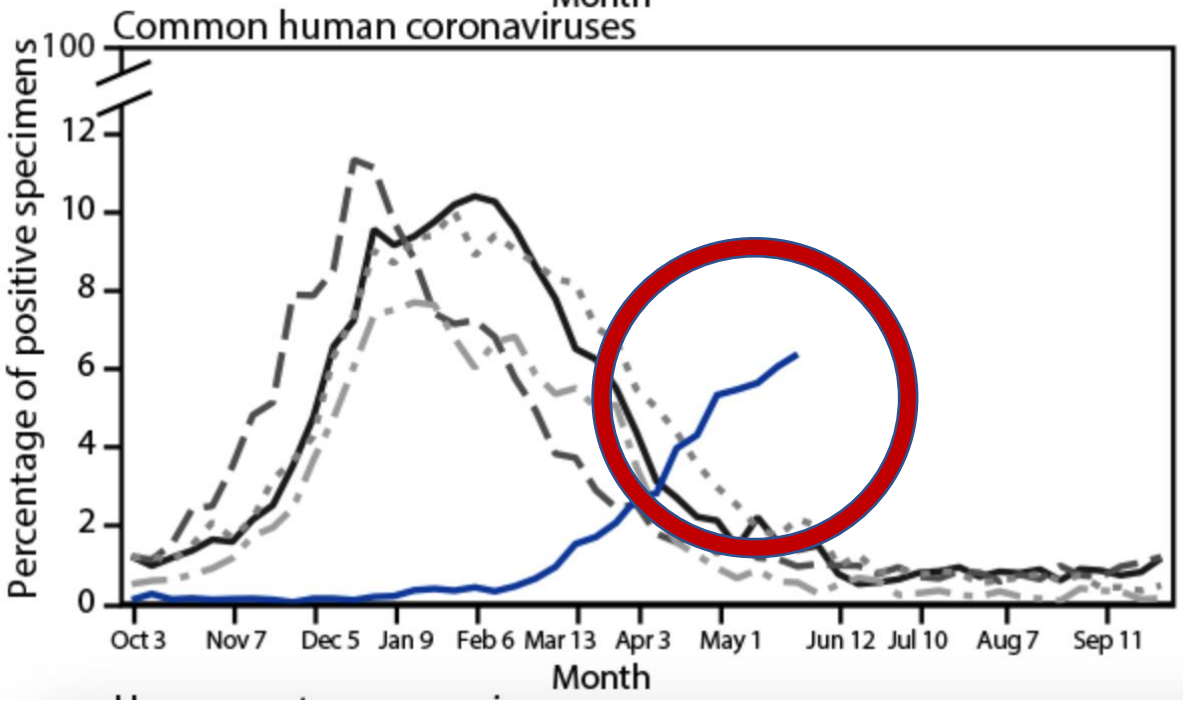

Common human coronaviruses
No. of specimens tested (x1,000)
Year
2017
2018
2019
2020
2021

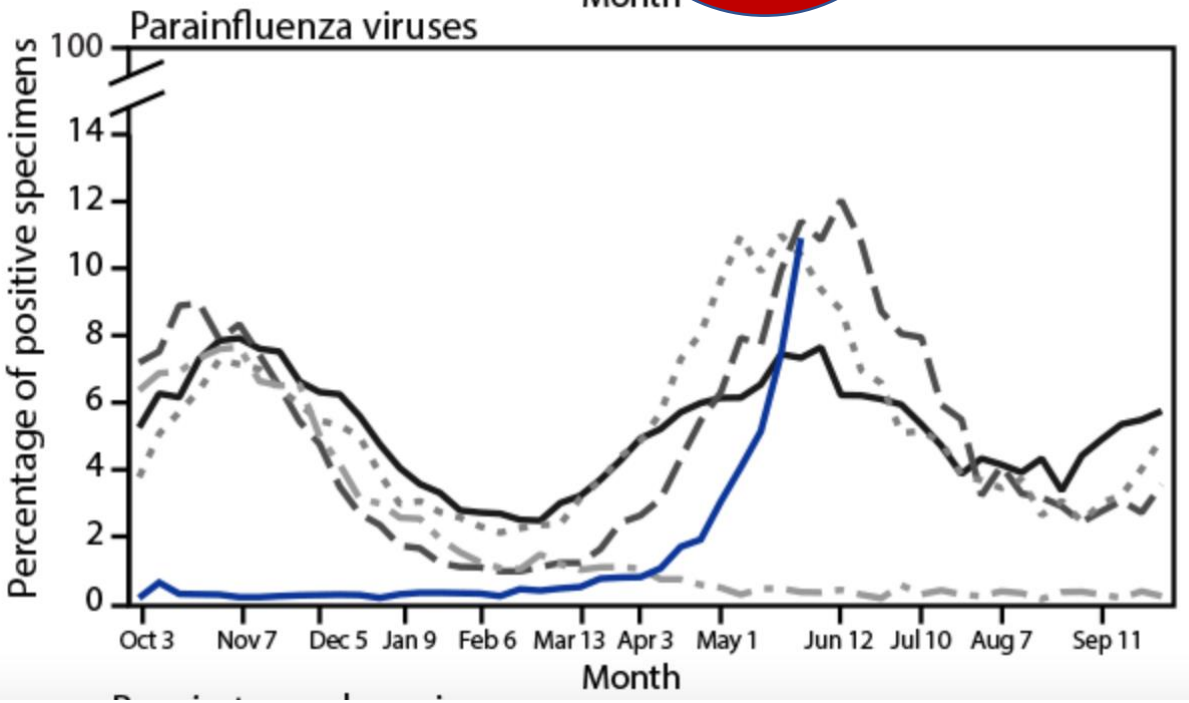

Parainfluenza viruses
No. of specimens tested (x1,000)
Percentage of positive specimens
Year
2017
2018
2019
2020





RSV and HCoV increasing at unusual times of the year compared to prior





Respiratory illnesses to expect this Winter season

- **SARS-CoV-2** pandemic could again worsen during the cold season with more indoor crowding, suboptimal vaccination rates
- **RSV, PIV, HCoV** already on the rise
- Not much **influenza** activity until now but some concern for a severe influenza pandemic this flu season (October to May)
  - Influenza continued to circulate outside the USA (tropics) though Southern Hemisphere has low activity currently
  - Increasing travel, decreased restrictions
  - Low exposure to influenza last year leading to lower levels of population immunity
- **Grp A Streptococcus** infections also most common in the winter and spring.

Clinical presentation

- SARS-CoV-2, Influenza, RSV and other respiratory viruses may present as **Influenza Like Illnesses (ILIs)**
- These **cannot be reliably distinguished** from one another based on clinical criteria alone
- Clinical features suggestive of GAS pharyngitis **(some may differ from ILI)**
  - Sore throat
  - Fever
  - Tonsillar, pharyngeal, uvular edema
  - Tonsillar exudates
  - Cervical LAD
  - Scarlatiniform skin rash or strawberry tongue (scarlet fever)
  - Exposure to GAS

Centor criteria

Centor criteria
Tonsillar exudates
Tender anterior cervical lymphadenopathy
Fever
Absence of cough

One point is given for each criterion. The likelihood of GAS pharyngitis increases as total points rise. Patients with <3 points are unlikely to have GAS pharyngitis and generally do not require testing or treatment. Patients with a score ≥3 may benefit from testing.

GAS: group A *Streptococcus*.

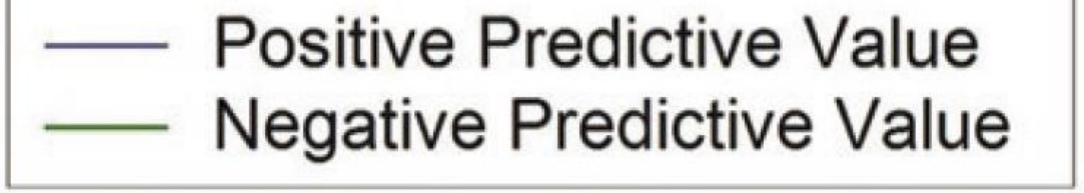
Graphic 116709 Version 2.0

IDSA recommends using clinical judgment to decide who should be tested and treated as empirical treatment of adults having a Centor score of ≥3 is associated with a high rate of unnecessary antibiotic use.

Testing Strategies – Who to Test and What to Test for?

- **Background disease prevalence**
  - Low prevalence = high chance of false positive test
  - Consider not testing for influenza outside of influenza season
- **Clinical severity**
  - Asymptomatic vs. Symptomatic
  - Outpatient vs. Inpatient
  - Consider not testing for viruses other than Influenza/SARS-CoV2 in outpatients with mild disease as unlikely to change management
- **Host status**
  - Normal host vs Immunosuppressed
  - Consider broader testing in immunocompromised hosts who are at higher risk for more severe disease (RSV, ADV)

Prevalence of positive rapid molecular respiratory virus testing in ILI (%)	PPV (%)	NPV (%)
2.5	37.4	99.8
5	55.1	99.5
10	72.1	99.0
15	80.4	98.4
20	85.3	97.7
25	88.5	96.9
30	90.9	96.1



Testing Strategies – Who to Test and What to Test for this Winter season?

- **Asymptomatic patients** (presenting to ED/Inpatient units for care)
  - SARS-CoV-2 testing only → asymptomatic SARS-CoV2 infection/IP implications
- **Symptomatic (ILI) patients with mild-moderate disease**
  - SARS-CoV-2, Influenza +/- RSV testing → antivirals available/IP implications
- **Symptomatic (ILI) patients with severe/critical disease (ICU), structural lung disease and/or significant immunocompromise**
  - SARS-CoV-2, Influenza and RSV + expanded viral/bacterial testing → antivirals available/clinical implications of other viruses like ADV/IP implications
  - Negative URT specimens but high clinical suspicion, test LRT specimen (Influenza, RSV, SARS-CoV2 may be URT -/LRT+ on testing)
- **Symptomatic (pharyngitis syndrome) patients (especially children)**
  - Also test for Grp A Streptococcus (two-tiered approach vs. PCR)

Testing Strategies – Which tests to chose?

- **Molecular (NAAT) testing strongly preferred over Antigen-based testing due to superior sensitivity and specificity especially for SARS-CoV-2 testing**

Testing Guidance for Clinicians When SARS-CoV-2 and Influenza Viruses are Co-circulating

[Based upon local public health surveillance data and testing at local healthcare facilities]

Español | Other Languages

Outpatient Clinic or Emergency Department Patients with Acute Respiratory Illness Symptoms (With or Without Fever)*

Does the Patient Require Hospital Admission?

YES

NO

PATIENT REQUIRES ADMISSION

SARS-CoV-2 and Influenza Testing

a) Order multiplex NAD assay for influenza A/B/SARS-CoV-2

OR

b) If multiplex nucleic acid detection assay is not available, order SARS-CoV-2 NAD assay ***and*** Influenza NAD assay

SARS-CoV-2 Ag testing can be used but negatives requires NAD confirmation

Influenza Ag testing not recommended

If one test is positive, do not assume that the other one will be negative as co-infections can occur

PATIENT DOES NOT REQUIRE ADMISSION

SARS-CoV-2 Testing

Test for SARS-CoV-2 by NAD **OR**
if not available, test by SARS-CoV-2 antigen detection assay

SARS-CoV-2 Ag negative tests requires NAD confirmation

Influenza Testing

Test for influenza if results will change clinical management or for infection control decisions (e.g. returning to a congregate setting) using Influenza NAD assay

If Influenza NAD not available, can use Influenza Ag testing

OR

Empiric Influenza Treatment

For patients with “progressive disease” or at high risk for complications (treatment less likely of benefit if ≥2 days since symptom onset)

Testing and Management Considerations for Nursing Home Residents with Acute Respiratory Illness Symptoms when SARS-CoV-2 and Influenza Viruses are Co-circulating

- **Test any resident with symptoms of COVID-19 or influenza for both viruses with NAD (molecular testing)**
  - If NAD for SARS-CoV-2 or Influenza not available, Ag testing can be used but negatives must be confirmed
- **If SARS-CoV-2 and Influenza testing is negative, test for other respiratory viruses/pathogens**
- Notify Heath Department for:
  - a suspected or confirmed case of either SARS-CoV-2 or influenza in a resident or healthcare personnel (HCP)
  - a resident with severe respiratory infection resulting in hospitalization or death;
  - ≥ 3 residents or HCP with new-onset respiratory symptoms within 72 hours of each other.

Interim Guidance for SARS-CoV-2 Testing in Non-Healthcare Workplaces

Updated Oct. 7, 2021 Languages Print

Summary of Recent Changes

Updates as of October 6, 2021

- Updated descriptions of test types.
- Updated to align with new antigen testing algorithms, one for community settings and one for congregate settings .
- Updated testing recommendations for fully vaccinated workers who are close contacts of someone with COVID-19.
- Clarified that screening testing recommendations apply to asymptomatic, unvaccinated workers.

Respiratory virus testing in the COVID-19 pandemic

- Single and multiplexed molecular Assays that include **SARS-CoV-2** are under FDA **Emergency Use Authorization (EUA)** status
  - EUA: Temporary authorization of a product during a state of emergency based on a more limited evidence that would be required for full authorization
- Molecular assays that target SARS-CoV-2 include:
  - **Single target assays, Small panels and Expanded panels**
- Some of these assays are designed for Point-of-care (POC) testing
  - Testing is performed at or near the patient setting
- Many POC tests in the United States are Clinical Laboratory Improvement Amendments of 1988 (**CLIA)-waived**, indicating:
  - Low complexity
  - Requirement of little operator expertise
  - Having a low potential for incorrect results

SARS-CoV-2 molecular panels

- Single virus (SARS-CoV2)
  - **Cepheid Xpert® Xpress SARS-CoV-2 (W)**
  - **Mesa BioTech Accula SARS-CoV-2 (W)**
  - **Quidel® Lyra® SARS-CoV-2 Assay (H)**
  - **DiaSorin Simplexa™ COVID-19 Direct (H/M)**
  - **Hologic® Panther Fusion® SARS-CoV-2 (H)**
  - **GenMark Dx® ePlex® SARS-CoV-2 Test (H/M)**
  - **Cue COVID-19 (W)**
  - **Abbott ID Now (W)**

- Small panels (SARS-CoV2 + Flu +/- RSV)
  - **Cepheid Xpert® SARS-CoV-2/Flu/RSV (W)**
  - **Cobas ® SARS-CoV-2 & Influenza A/B (W)**
  - **CDC influenza SARS-CoV-2 multiplex assay (Flu SC2) (H)**

- Extended panels (SARS-CoV2 + other respiratory viruses)
  - **BioMérieux BioFire® FilmArray® Respiratory 2.1 (H/M) and 2.1 EZ (W)**
  - **GenMark Dx® ePlex® RP2 (H/M)**
  - **QIAstat-Dx Respiratory SARS-CoV-2 Panel (H/M)**
  - **Luminex NxTAG® Respiratory Pathogen Panel + SARS-CoV-2 (H/M)**

Assay (Developer)	Method	Specimen	TAT	Viral Targets	Sensitivity(PPA)/ Specificity(NPA)	LOD
Xpert® Xpress SARS-CoV-2 (Cepheid)	rRT-PCR	NS, NPS, OPS, MTS, NA, NW	45 minutes	**Single virus** SARS-CoV-2 (E, N2)	97.8% 98.6%	5400 NDU/mL (FDA)
Xpert® SARS-CoV-2/Flu/RSV (Cepheid)	rRT-PCR	NS, NPS, OPS, MTS, NA, NW	45 minutes	**Small panel** SARS-CoV-2 (E, N2) Influenza A/B RSV	97.9% 100%	131 GCE/mL (FDA LOD under review)
Accula SARS-CoV-2 Test (Mesa Biotech)	RT-PCR	NS, MTS	30 minutes	**Single virus** SARS-CoV-2 (N)	95.8% 100%	150 copies/mL (FDA LOD under review)
Cobas ® SARS-CoV-2 & Influenza A/B: cobas Liat System (Roche)	rRT-PCR	NPS, NS	20 minutes	**Small panel** SARS-CoV-2 (Orf1ab, N) Influenza A/B	100% 97.4%	5400 NDU/mL (FDA)
BioFire ® Respiratory Panel 2.1-EZ (BioFire Diagnostics)	Endpoint melt curve analysis	NPS	45 minutes	**Extended panel** AdV. HCoV SARS-CoV-2 (S, M) Influenza A/B HMPV PIV 1-4 RSV RV/EV	98% 100%	6000 NDU/mL (FDA)

Group A Strep testing

- Traditional laboratory workflows relied on two-tiered testing approach
  - Insensitive RADTs → sensitive bacterial culture reported at 24 or 48 hours
- Recently **GAS Nucleic Acid Detection assays** have been approved by FDA
  - High sensitivity (>97%) eliminating need for culture
  - Requires workflow optimization in order to reduce TAT
- Several POC/CLIA waived commercial rapid PCR assays:
  - Cobas Strep A test of the Liat system (~15 minutes TAT)
  - ID NOW Strep A 2 test (~6 minutes TAT)
  - Xpert Xpress Strep A assay (~18 minutes TAT)

A Guide to Utilization of the Microbiology Laboratory for Diagnosis of Infectious Diseases: 2018 Update by the Infectious Diseases Society of America and the American Society for Microbiologya **J. Michael Miller et al**

Testing Strategies – Micro Lab perspective

- On the back end, microbiology laboratories **must make decisions on testing priority** based on:
  - Clinical severity
  - Host risk factors
  - Infection control implications
  - Patient disposition
- Testing for patients with severe disease, immunocompromise and those being admitted or discharged to congregate settings are often **prioritized for rapid NAD**
- Testing for other populations is often **batched** (longer TAT)

Thank you!

Cepheid Xpert® SARS-CoV-2/Flu/RSV

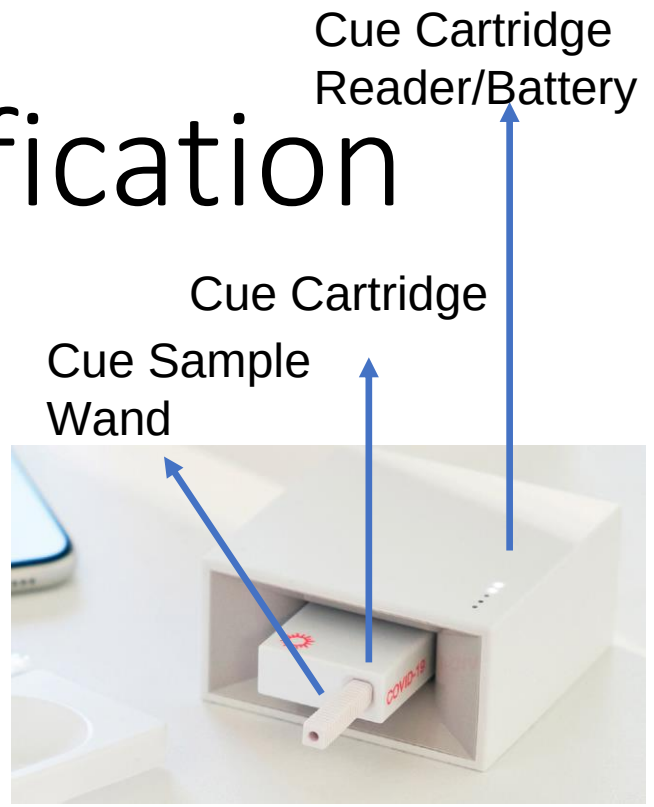
- Multiplexed real-time RT-PCR test designed for use on GeneXpert systems
- Available as **CLIA-waived** and high-throughput-format platforms
  - First CLIA waived assay for SARS-CoV-2 on FDA EUA on 20 March 2020
- Approved on NPS, NS, NW, NA but performance has only been established in NPS specimens
- **Detects SARS-CoV-2, Influenza A, Influenza B and RSV**
  - SARS-CoV-2 targets E and N2
  - SARS-CoV2 LOD is 131 copies/mL
- Only quadriplex panel with above targets
- Turnaround time is around 35 minutes
- Provides Ct value (combined for both analytes)

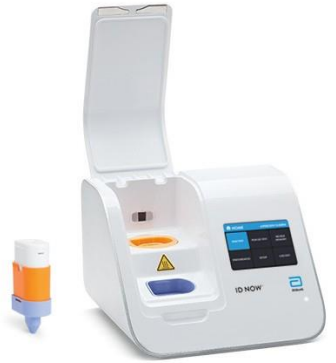
BioFire® FilmArray® Respiratory 2.1 and 2.1 EZ

- Multiplexed real-time RT-PCR test intended for use with the BioFire® FilmArray® 2.0 or BioFire® FilmArray® Torch Systems
- EZ 2.1 is **CLIA-waived**
- Approved on NPS
- **Respiratory viruses + atypical bacteria + SARS-CoV-2**
  - SARS-CoV-2 targets S and M
  - SARS-CoV2 LOD is 160 copies/mL
- Turnaround time is 45 minutes
- Does not provide Ct values
- Does not detect or differentiate the influenza A neuraminidase (N) subtypes

Isothermal Nucleic Acid Amplification

- Enzymatic amplification is achieved using a constant temperature
  - Eliminates need for thermal cyclers for the high-temperature DNA denaturation cycle required for PCR
  - **Decreases the device footprint -> more amenable to highly portable devices and POC testing**
- **Cue COVID-19 test (W):** Isothermal Nicking Enzyme Amplification Reaction (NEAR)
  - Self-collected NS specimen (or collected by adults for children)
  - N gene; Results in 25 minutes
  - **Excellent agreement with reference NAAT (PPA 92-95%)**
- **Abbott ID Now (W):** Isothermal NAAT
  - NS, NPS, TS
  - RdRp gene; Results in up to 13 minutes
  - **Low agreement with reference NAAT (PPA 54.8%)**





Donato LJ, et al. Evaluation of the Cue Health point-of-care COVID-19 (SARS-CoV-2 nucleic acid amplification) test at a community drive through collection center. Diagn Microbiol Infect Dis. 2021 PMID: 33571863

Basu A et al. Performance of Abbott ID Now COVID-19 Rapid Nucleic Acid Amplification Test Using Nasopharyngeal Swabs Transported in Viral Transport Media and Dry Nasal Swabs in a New York City Academic Institution. J Clin Microbiol. 2020 PMID: 32471894

Testing Strategies – Why Test?

- Reduce unnecessary antibiotic use
- Improve antiviral prescribing for treatable viruses
- Limit additional ancillary testing and other interventions
- Shorten hospital or emergency department lengths of stay
- Optimize infection-control practices
- Improve resource utilization
- Reduce community transmission
- Improve epidemiologic surveillance

Diagnosis and Treatment of Respiratory Illness This Winter Season

Treatment Update & Clinical Considerations

Sankar Swaminathan, MD
Don Merrill Rees Presidential Endowed Chair
Chief of Infectious Diseases
Department of Medicine
University of Utah School of Medicine

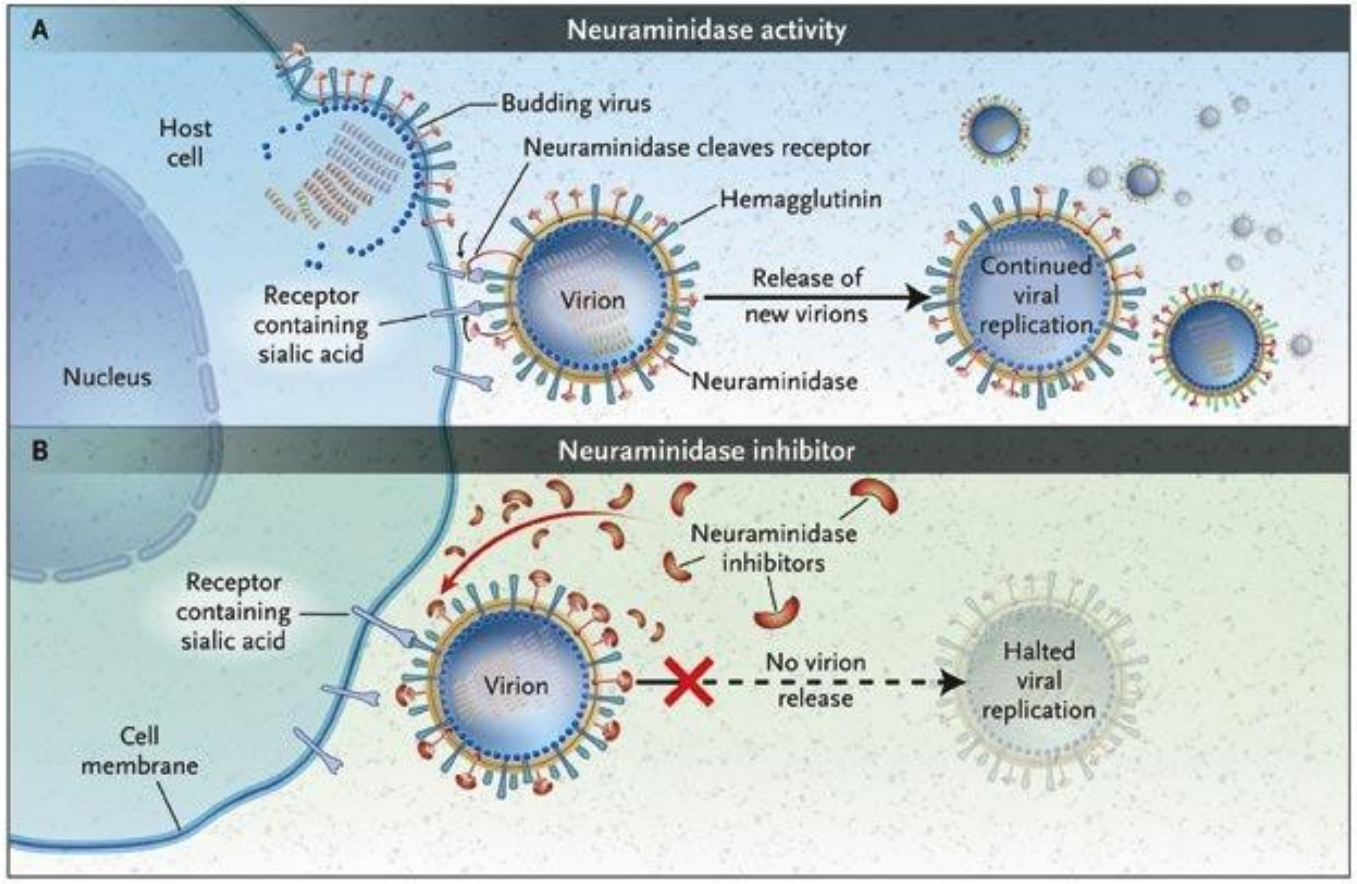
Treatment of COVID and influenza
CDC IDSA conference October 2021

Sankar Swaminathan
Departments of Medicine and Experimental Pathology
University of Utah School of Medicine

Neuraminidase inhibitors

- Oseltamivir, peramivir, and zanamivir
- Active against influenza A and B
- Indicated for treatment as well as prophylaxis (except peramivir)
- Toxicity:
  - Very well tolerated
  - Neuropsychiatric side effects (rare)

Mechanism of Action



Moscona A. N Engl J Med 2005;353:1363-73.

Neuraminidase inhibitor formulations

- Oseltamivir
  - Capsules and oral solution
- Zanamivir
  - Dry-powder inhaler
  - Difficult to inhale with moderate to severe disease
  - Bronchospasm, throat irritation
- Peramivir
  - IV only, given as one-time IV dose

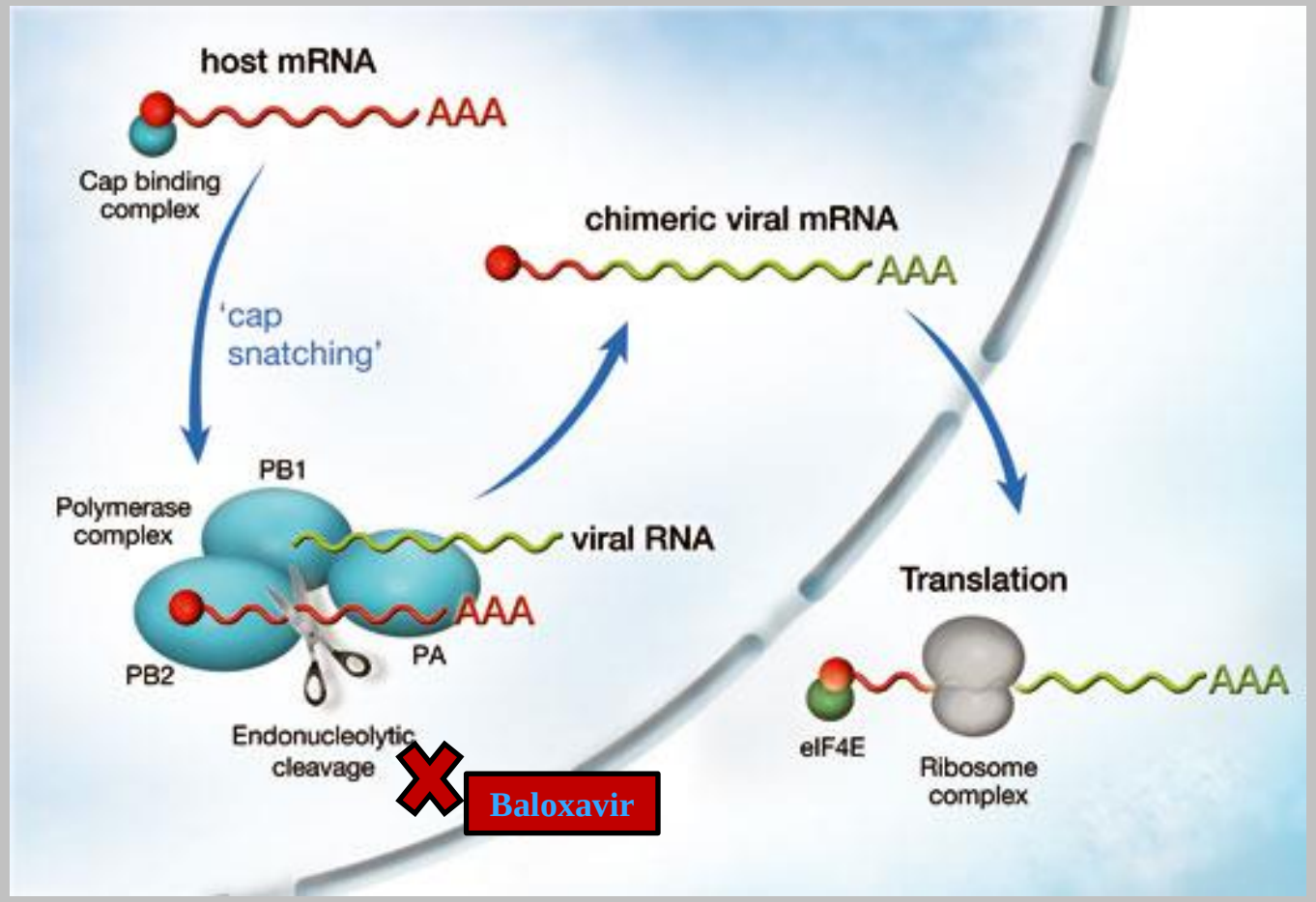
Oseltamivir Resistance (Uncommon)

- Several mutations possible that reduce NA drug binding affinity
- Depending on mutation, can have resistance to one but not all neuraminidase inhibitors
- Of the neuraminidase inhibitors, zanamivir most likely to retain activity if oseltamivir resistance
- Role for baloxavir

Baloxavir

- FDA approved October 2018
- Active against influenza A and B
- Resistance
  - **Low barrier to resistance
  - Due to mutations in PA subunit of RNA polymerase
- Very well tolerated overall
- Oral formulation only

Influenza mRNA “Cap Snatching”



Antiviral drugs work better when given earlier

- In the past, empiric treatment of influenza when ILI was widespread was a clear approach
- Influenza virus load in the upper respiratory tract is highest approximately 2–3 days after infection
- There is a narrow therapeutic window for influenza drugs
- Earlier initiation of oral oseltamivir therapy increased its therapeutic effects, which were seen at every time point of intervention and were progressive.

Outpatient Clinic or Emergency Department Patients with Acute Respiratory Illness Symptoms (With or Without Fever)

Does the Patient Require Hospital Admission?

YES

1. Specimen collection

Implement recommended infection prevention and control measures and collect respiratory specimens for influenza and SARS-CoV-2 testing.

2. SARS-CoV-2 and Influenza Testing

a) Order multiplex nucleic acid detection assay for influenza A/B/SARS-CoV-2. ***OR***

b) If multiplex nucleic acid detection assay is not available, order SARS-CoV-2 nucleic acid detection assay ***and*** Influenza nucleic acid detection assay. (If SARS-CoV-2 nucleic acid detection assay is not available on-site and SARS-CoV-2 antigen detection assay is used confirm negative SARS-CoV-2 antigen detection results by SARS-CoV-2 nucleic acid detection assay at an outside laboratory).

3. Treatment

If bacterial pneumonia or sepsis is suspected, consider testing recommendations and empiric antibiotic treatment per ATS-IDSA Adult Community-acquired Pneumonia Guidelines, and **administer supportive care and treatment for suspected**

Start empiric oseltamivir treatment for suspected influenza as soon as possible regardless of illness duration, without waiting for influenza testing results, per Infectious Diseases Society of America Influenza Clinical Practice Guidelines, and administer supportive care.

NO

Follow recommended infection prevention and control measures

1. SARS-CoV-2 Testing

Test for SARS-CoV-2 by nucleic acid detection; *OR* if not available, by SARS-CoV-2 antigen detection assay.

2. Influenza Testing and Treatment

a) Test for influenza if results will change clinical management or for infection control decisions (e.g. long-term care facility resident returning to a facility, or a person of any age returning to a congregate setting): order rapid influenza nucleic acid detection assay; if rapid influenza nucleic acid detection assay is not available on-site, order rapid influenza antigen assay; prescribe antiviral treatment if positive. ***OR***

b) Prescribe empiric antiviral treatment as soon as possible without influenza testing based on a clinical diagnosis of influenza for patients of any age with progressive disease of any duration, and for children and adults at high risk for influenza complications.

3. Follow isolation and quarantine recommendations for SARS-CoV-2.

Source: https://www.cdc.gov/flu/professionals/diagnosis/testing-guidance-for-clinicians.htm

Co-circulation of SARS CoV-2 and influenza will complicate management

- If someone comes in with ILI, it might be COVID-19 or influenza
- Empiric treatment of flu is more likely to be incorrect when COVID-19 is co-circulating
- Empiric outpatient treatment of COVID is not possible
- For cases not requiring hospitalization, you basically can wait for testing or treat empirically for influenza.
- If you have point of care testing and molecular testing, great

The decision on empiric treatment of influenza should be data driven

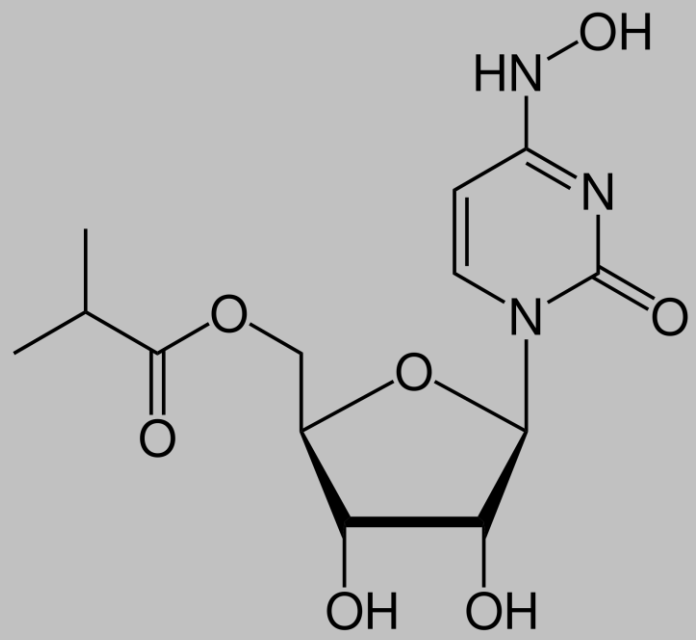
- How much influenza in circulating in your community?
- How much COVID-19 is circulating in your community?
- Has your patient been vaccinated against flu, COVID-19 or both?
- How high risk is your patient even if they do not need to be hospitalized today?
- How long has your patient been symptomatic?

Individualize to the patient

- How important is a day without symptoms?
- What is the patient's individual social/economic situation?
  - Access to health care
  - Social support
  - Family situation

Mjolnir, the hammer of Thor

Molnupiravir



- 5′-isopropylester of N 4-hydroxycytidine
- Incorporated as cytidine into viral RNA by viral RdRNA polymerases.
- Able to base pair with nucleotides other than G, leading to mutations.

Phase 3 MOVE-OUT trial in at risk, non-hospitalized adult patients

- Laboratory-confirmed mild-to-moderate COVID-19, with symptom onset within 5 days of study randomization.
- 800 mg twice daily for five days
- At least one risk factor associated with poor disease outcome
- Reduced the risk of hospitalization or death by approximately 50%; 7.3% of patients who received molnupiravir were either hospitalized or died through Day 29 (28/385), compared with 14.1% of placebo-treated patients (53/377); p=0.0012.
- At day 29, no deaths in molnupiravir recipients, compared to 8 deaths in placebo recipients.
- Any adverse event: molnupiravir (35%) vs placebo (40%), drug related AE: 12% vs 11% respectively
- Possibility that it is mutagenic, incorporated into host DNA?

Additional Reference Slides from CDC

Priority Groups for Antiviral Treatment of Influenza

Antiviral treatment is recommended **as soon as possible** for any patient with suspected or confirmed influenza who:

- is hospitalized;
- has severe, complicated, or progressive illness; or
- is at higher risk for influenza complications.

Decisions about starting antiviral treatment for patients with suspected influenza should not wait for laboratory confirmation of influenza virus infection. Empiric antiviral treatment should be started as soon as possible in the above priority groups.

Clinicians can consider early empiric antiviral treatment of non-high-risk outpatients with suspected influenza [e.g., influenza-like illness (fever with either cough or sore throat)] based upon clinical judgement, if treatment can be initiated within 48 hours of illness onset.

Antiviral Drug Options

- For hospitalized patients with suspected or confirmed influenza, initiation of antiviral treatment with oral or enterically-administered oseltamivir is recommended as soon as possible.
- For outpatients with complications or progressive disease and suspected or confirmed influenza (e.g., pneumonia, or exacerbation of underlying chronic medical conditions), initiation of antiviral treatment with oral oseltamivir is recommended as soon as possible.
- For outpatients with suspected or confirmed uncomplicated influenza, oral oseltamivir, inhaled zanamivir, intravenous peramivir, or oral baloxavir may be used for treatment, depending upon approved age groups and contraindications. In one randomized controlled trial, baloxavir had greater efficacy than oseltamivir in adolescents and adults with influenza B virus infection (Ison, 2020).

Source: https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm

Co-circulation of Influenza Viruses and SARS-CoV-2

During periods of community co-circulation of influenza viruses and SARS-CoV-2, empiric antiviral treatment of influenza is recommended as soon as possible for the following priority groups: a) hospitalized patients with respiratory illness; b) outpatients with severe, complicated, or progressive respiratory illness; and c) outpatients at higher risk for influenza complications who present with any acute respiratory illness symptoms (with or without fever).

- Influenza and COVID-19 have overlapping signs and symptoms. Testing can help distinguish between influenza virus infection and SARS-CoV-2 infection. However, clinicians should not wait for the results of influenza testing (view Table 3), SARS-CoV-2 testing, or multiplex molecular assays that detect influenza A and B viruses and SARS-CoV-2 (view Table 4) to initiate empiric antiviral treatment for influenza in the above priority groups.
- Co-infection with influenza A or B viruses and SARS-CoV-2 can occur and should be considered, particularly in hospitalized patients with severe respiratory disease.
  - Clinicians should be aware that a positive SARS-CoV-2 test result does not preclude influenza virus infection. For hospitalized patients with suspected influenza who are started on empiric antiviral treatment with oseltamivir, use of influenza molecular assays (view Table 3) or multiplex assays that detect both influenza viruses and SARS-CoV-2 (view Table 4) can inform clinical management.
  - Clinicians should be aware that a positive influenza test result does not preclude SARS-CoV-2 infection. For hospitalized patients with a positive influenza test result, antiviral treatment of influenza with oseltamivir should be started as soon as possible, and clinicians should also follow guidelines for diagnosis and treatment of community-acquired pneumonia (view community acquired pneumonia treatment guidance for adults: Metlay, 2019) and other respiratory infections, including SARS-CoV-2 infection (view NIH COVID-19 treatment guidelines and IDSA COVID-19 treatment guidelines) if clinically indicated, while awaiting SARS-CoV-2 testing results. Oseltamivir does not have in-vitro activity against SARS-CoV-2 (Choy, 2020).
- Clinicians can utilize telemedicine in place of office visits for patients with acute respiratory illness. It may be useful for providers to implement phone triage lines to enable high-risk patients to discuss symptoms over the phone. Please see the Algorithm to Assist in Medical Office Telephone Evaluation of Patients with Possible Influenza.
- Patients at higher risk for influenza complications should be advised to call their provider as soon as possible if they have acute respiratory illness symptoms (with or without fever) for consideration of infection with influenza A or B viruses (and early antiviral treatment), SARS-CoV-2, and other respiratory pathogens.
- Clinicians can consider starting early (≤48 hours after illness onset) empiric antiviral treatment of non-high-risk outpatients with suspected influenza [e.g., influenza-like illness (fever with either cough or sore throat)], based upon clinical judgement, including without an office visit. SARS-CoV-2 and other etiologies of influenza-like illness should also be considered.
- National Institutes of Health (NIH) COVID-19 Treatment Guidelines: Influenza and COVID-19 are available .
- Clinical algorithms for the testing and treatment of influenza when SARS-CoV-2 and influenza viruses are circulating are also available.

Source: https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm

Influenza Antiviral Medications: Summary for Clinicians

Influenza Antiviral Medications: Summary for Clinicians | CDC

Overview of Influenza Antiviral Medications

Antiviral medications with activity against influenza viruses are an important adjunct to influenza vaccine in the control of influenza.

- Influenza antiviral prescription drugs can be used to **treat** influenza, and some can be used to **prevent** influenza.
- Six licensed prescription influenza antiviral drugs are approved in the United States.
  - Four influenza antiviral medications approved by the U.S. Food and Drug Administration (FDA) are recommended for use in the United States during the 2020-2021 influenza season.
    - Three drugs are chemically related antiviral medications known as neuraminidase inhibitors that block the viral neuraminidase enzyme and have activity against both influenza A and B viruses: oral **oseltamivir phosphate** (available as a generic version or under the trade name Tamiflu®), inhaled **zanamivir** (trade name Relenza®), and intravenous **peramivir** (trade name Rapivab®).
    - The fourth drug is oral **baloxavir marboxil** (trade name Xofluza®), which is active against both influenza A and B viruses but has a different mechanism of action than neuraminidase inhibitors. Baloxavir is a cap-dependent endonuclease inhibitor that interferes with viral RNA transcription and blocks virus replication.
    - More information regarding the four recommended antiviral medications is available: Table 1.
- Amantadine and rimantadine are antiviral drugs in a class of medications known as adamantanes, which target the M2 ion channel protein of influenza A viruses. Therefore, these medications are active against influenza A viruses, but not influenza B viruses. As in recent past seasons, there continues to be high levels of resistance (>99%) to adamantanes among circulating influenza A(H3N2) and influenza A(H1N1)pdm09 ("2009 H1N1") viruses. Therefore, amantadine and rimantadine are not recommended for antiviral treatment or chemoprophylaxis of currently circulating influenza A viruses.
- Antiviral resistance and reduced susceptibility to the neuraminidase inhibitors and to baloxavir among circulating influenza viruses is currently very low, but this can change.
  - For weekly surveillance data on susceptibility of circulating influenza viruses to antivirals in the U.S. this season, see the FluView Weekly U.S. Influenza Surveillance Report.
- Influenza viruses with reduced susceptibility or resistance to antivirals can occur sporadically or emerge during or after antiviral treatment in some patients (e.g., immunocompromised). Oseltamivir resistance in influenza A(H3N2) and A(H1N1)pdm09 viruses can develop during treatment, particularly in young children (Roosenhoff, 2019 ; Lina, 2018 ;), and immunocompromised persons (Memoli, 2014) . Following treatment with baloxavir, emergence of viruses with molecular markers associated with reduced susceptibility to baloxavir has been observed in clinical trials in immunocompetent children and adults, with higher detection among baloxavir-treated pediatric patients aged <12 years compared with adults (Hayden, 2018 ; Omoto, 2018 ; Hirostu, 2019 ; Uehara, 2019 ; Takashita, 2019).
  - Human-to-human transmission of influenza A(H1N1)pdm09 viruses with an H275Y mutation in viral neuraminidase conferring resistance to oseltamivir has been reported among severely immunocompromised patients in hospital units, (Gooskens, 2009 ; Chen, 2011 ;) and in the community (Hibino, 2017 ; Le, 2008; Hurt, 2011 ; Hurt, 2012 ; Takashita, 2013) , but currently appears to be uncommon.
  - Limited human-to-human transmission of influenza A(H3N2) virus with reduced susceptibility to baloxavir has been reported sporadically in Japanese children (Takashita, 2019 ; Takashita 2019 ; Imai, 2019), but currently appears to be uncommon.
- Clinical trials and observational data show that early antiviral treatment can shorten the duration of fever and illness symptoms, and may reduce the risk of some complications from influenza (e.g., otitis media in young children, pneumonia, and respiratory failure).
  - Early treatment of hospitalized adult influenza patients with oseltamivir has been reported to reduce death in some observational studies.
  - In hospitalized children, early antiviral treatment with oseltamivir has been reported to shorten the duration of hospitalization in observational studies.
  - Clinical benefit is greatest when antiviral treatment is administered early, especially within 48 hours of influenza illness onset in clinical trials and observational studies.

Source: https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm

Table 1. Antiviral Medications Recommended for Treatment and Chemoprophylaxis of Influenza

Antiviral Agent	Activity Against	Use	Recommended For	Not Recommended for Use in	Adverse Events
Oral Oseltamivir	Influenza A and B	Treatment	Any age[1]	N/A	**Adverse events:** nausea, vomiting, headache. Post marketing reports of serious skin reactions and sporadic, transient neuropsychiatric events[2]
		Chemo-prophylaxis	3 months and older[1]	N/A	
Inhaled Zanamivir	Influenza A and B	Treatment	7 yrs and older[3]	people with underlying respiratory disease (e.g., asthma, COPD)[3]	**Adverse events:** risk of bronchospasm, especially in the setting of underlying airways disease; sinusitis, and dizziness. Post marketing reports of serious skin reactions and sporadic, transient neuropsychiatric events[2]
		Chemo-prophylaxis	5 yrs and older[3]	people with underlying respiratory disease (e.g., asthma, COPD)[3]	
Intravenous Peramivir	Influenza A and B[4]	Treatment	2 yrs and older[4]	N/A	**Adverse events:** diarrhea. Post marketing reports of serious skin reactions and sporadic, transient neuropsychiatric events[2]
		Chemo-prophylaxis[5]	Not recommended	N/A	
Oral Baloxavir	Influenza A and B[6]	Treatment	12 yrs and older[6]	N/A	**Adverse events:** none more common than placebo in clinical trials
		Chemo-prophylaxis[5]	Approved for post-exposure prophylaxis in persons 12 yrs and older[5]		

Source: https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm

Table 2. Recommended Dosage and Duration of Influenza Antiviral Medications for Treatment or Chemoprophylaxis

Antiviral Agent	Use	Children	Adults
Oral Oseltamivir	Treatment (5 days)[1]	**If younger than 1 yr old**[2]: 3 mg/kg/dose twice daily[3,4] **If 1 yr or older, dose varies by child's weight:** 15 kg or less, the dose is 30 mg **twice** a day >15 to 23 kg, the dose is 45 mg **twice** a day >23 to 40 kg, the dose is 60 mg **twice** a day >40 kg, the dose is 75 mg **twice** a day	75 mg **twice** daily
	Chemo-prophylaxis (7 days)[5]	If child is younger than 3 months old, use of oseltamivir for chemoprophylaxis is not recommended unless situation is judged critical due to limited data in this age group. **If child is 3 months or older and younger than 1 yr old**[2] 3 mg/kg/dose once daily[3] **If 1 yr or older, dose varies by child's weight:** 15 kg or less, the dose is 30 mg **once** a day >15 to 23 kg, the dose is 45 mg **once** a day >23 to 40 kg, the dose is 60 mg **once** a day >40 kg, the dose is 75 mg **once** a day	75 mg **once** daily
Inhaled Zanamivir[6]	Treatment (5 days)	10 mg (two 5-mg inhalations) **twice** daily (**FDA approved and recommended for use in children 7 yrs or older**)	10 mg (two 5-mg inhalations) **twice** daily
	Chemo-prophylaxis (7 days)[5]	10 mg (two 5-mg inhalations) **once** daily (**FDA approved for and recommended for use in children 5 yrs or older**)	10 mg (two 5-mg inhalations) **once** daily
Intravenous Peramivir[7]	Treatment (1 day)[1]	(2 to 12 yrs of age) One 12 mg/kg dose, up to 600 mg maximum, via intravenous infusion for a minimum of 15 minutes (**FDA approved and recommended for use in children 2 yrs or older**)	(13 yrs and older) One 600 mg dose, via intravenous infusion for a minimum of 15 minutes
	Chemo-prophylaxis[8]	Not recommended	N/A
Oral Baloxavir[9]	Treatment (1 day)[1]	**FDA approved and recommended for use in children 12 yrs or older.** See adult dosage.	(12 yrs and older) weight <80 kg: One 40 mg dose; weight ≥80 kg: One 80 mg dose[9]
	Chemo-prophylaxis[8]	**FDA-approved for post-exposure prophylaxis for persons aged 12 years and older.** See adult dosage."	(12 yrs and older) weight <80 kg: One 40 mg dose; weight ≥80 kg: One 80 mg dose[8]

Source: https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm

Q&A/Discussion

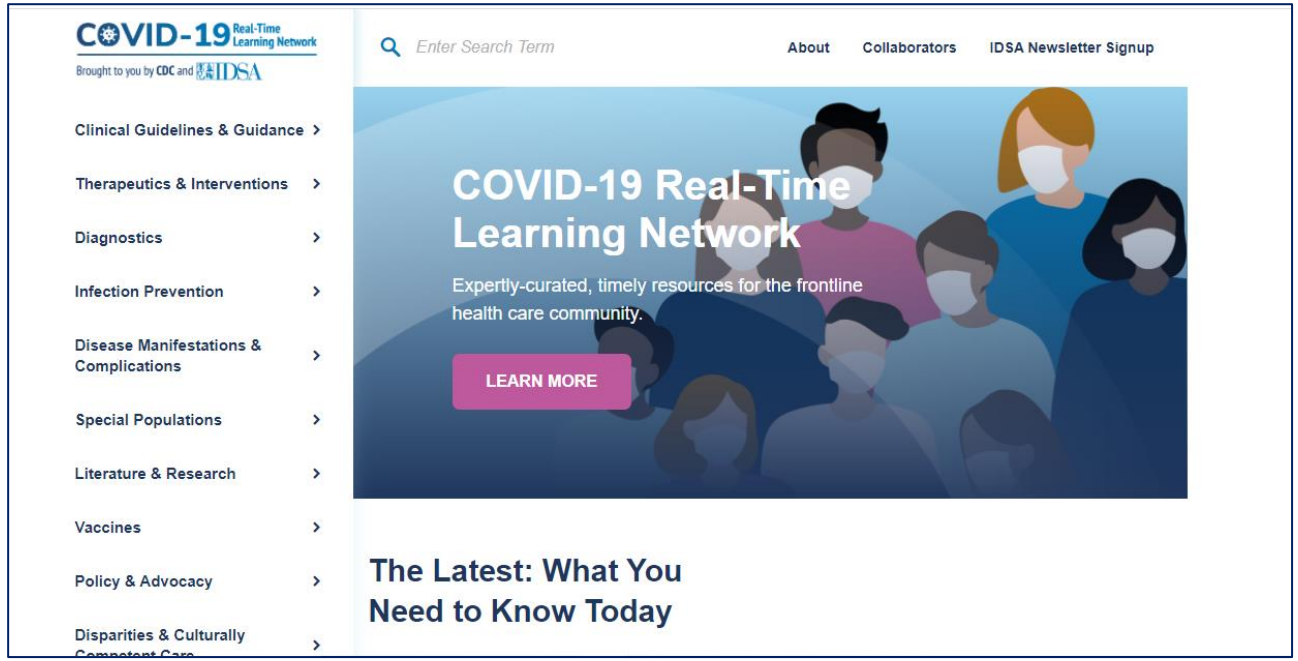
Today's Links

- Slide 1 - This webinar is being recorded and can be found online at www.idsociety.org/cliniciancalls.
- Slide 13 - Surveillance data feed into weekly reports (https://www.cdc.gov/flu/weekly/) and interactive dashboards (https://www.cdc.gov/flu/weekly/fluviewinteractive.htm)
- Slide 15- https://www.cdc.gov/mmwr/volumes/70/rr/rr7005a1.htm
- Slides 18 and 19 - https://www.cdc.gov/flu/professionals/index.htm
- Slide 20 - https://www.cdc.gov/flu/season/faq-flu-season-2021-2022.htm?web=1&wdLOR=c6A1F4966-F336-430D-8E8C-CDA216CD7446
- Slide 21 - https://emergency.cdc.gov/coca/calls/index.asp
- Slide 22: CDC Influenza homepage: https://www.cdc.gov/flu/
  - Influenza surveillance: https://www.cdc.gov/flu/weekly/fluactivitysurv.htm
  - Influenza vaccination coverage: https://www.cdc.gov/flu/fluvaxview/index.htm
  - For Healthcare Professionals: https://www.cdc.gov/flu/professionals/index.htm
  - Vaccination homepage: https://www.cdc.gov/flu/professionals/vaccination/index.htm
  - ACIP Influenza Recommendations: https://www.cdc.gov/mmwr/volumes/68/rr/rr6803a1.htm
  - Antiviral homepage: https://www.cdc.gov/flu/professionals/antivirals/index.htm
- Slide 25 https://www.cdc.gov/flu/weekly/fluviewinteractive.htm
- Slide 26 - https://www.cdc.gov/flu/weekly/overview.htm
- Slide 27 - https://www.cdc.gov/flu/weekly/fluviewinteractive.htm
- Slide 31 - https://www.cdc.gov/flu/about/season/flu-season.htm
- Slide 32 - *https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fcovid-19%2Finfo-by-product%2Fclinical-considerations.html#Coadministration*
- Slide 37 https://covid.cdc.gov/covid-data-tracker/#trends_dailycases
- Slide 70 - https://www.cdc.gov/flu/professionals/diagnosis/testing-guidance-for-clinicians.htm
- Slides 78 -81 - Source: https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm

COVID-19 Real-Time Learning Network

Brought to you by CDC and IDSA

An online community bringing together information and opportunities for discussion on latest research, guidelines, tools and resources from a variety of medical subspecialties around the world.



Specialty Society Collaborators

American Academy of Family Physicians
American Academy of Pediatrics
American College of Emergency Physicians
American College of Physicians
American Geriatrics Society
American Thoracic Society
Pediatric Infectious Diseases Society
Society for Critical Care Medicine
Society for Healthcare Epidemiology of America
Society of Hospital Medicine
Society of Infectious Diseases Pharmacists

www.COVID19LearningNetwork.org
@RealTimeCOVID19
#RealTimeCOVID19

CDC-IDSA Partnership: Clinical Management Call Support

FOR WHOM?

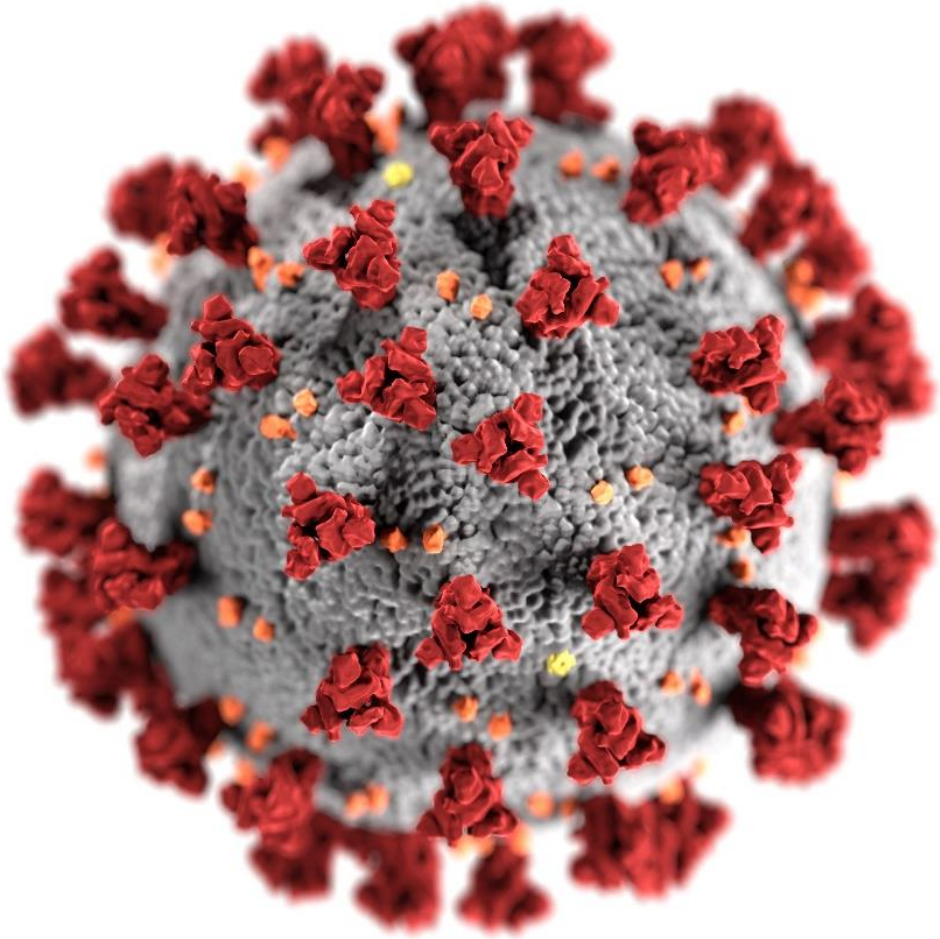
- Clinicians who have questions about the clinical management of COVID-19

WHAT?

- Calls from clinicians will be triaged by CDC to a group of IDSA volunteer clinicians for peer-to-peer support

HOW?

- Clinicians may call the main CDC information line at 800-CDC-INFO (800-232-4636)
- To submit your question in writing, go to www.cdc.gov/cdc-info and click on Contact Form



IDSA
Infectious Diseases Society of America

cdc.gov/coronavirus

Continue the conversation on Twitter

@RealTimeCOVID19
#RealTimeCOVID19

We want to hear from you!

Please complete the post-call survey.

Next Call:

Saturday, Oct. 23th

A recording of this call will be posted at
www.idsociety.org/cliniciancalls

-- library of all past calls now available --

Contact Us:

Dana Wollins (dwollins@idsociety.org)
Deirdre Lewis (dlewis@idsociety.org)