

SARS-CoV-2, Influenza, and other Respiratory Viruses Update - 2021

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Your participation in the Wisconsin surveillance system is **vital** to monitor for emerging novel strains with pandemic potential and other pathogens that impact community health.

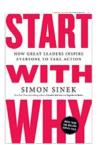
Outline and Learning Objectives

- W
- Review of SARS-CoV-2 circulation and surveillance
- Review of influenza basics
- Review of the 2020-2021 respiratory virus season
- Influenza vaccine updates
- Describe why specimens and testing data are vital for public health programs
- Discuss respiratory virus surveillance strategy for 2021-2022

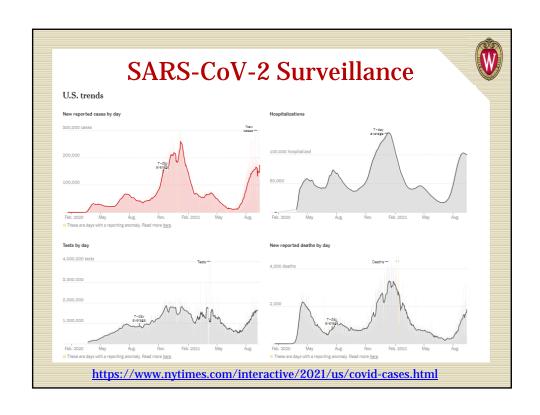
Why Perform Surveillance?

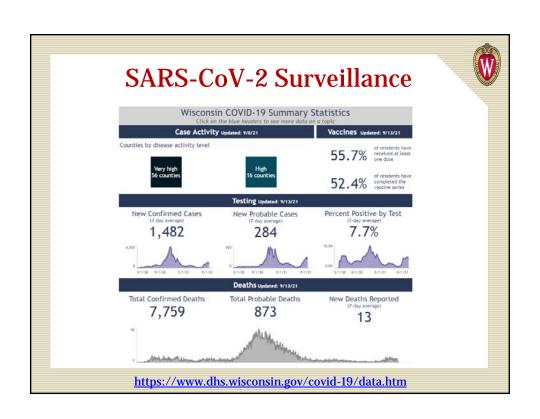


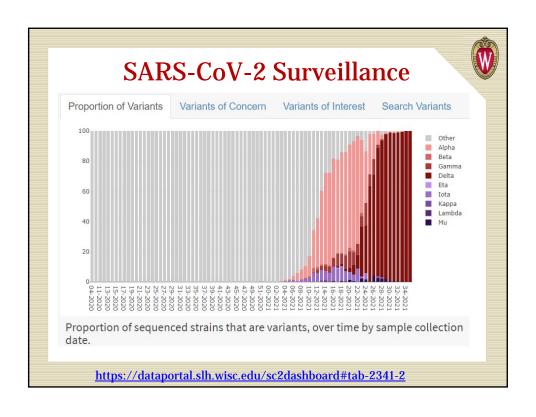
- Depends on the pathogen
- SARS-CoV-2:
 - Number of cases, hospitalizations, deaths
 - Geographic distribution
 - Age/gender distribution
 - Genomic surveillance
 - Track virus lineages/variants of interest and concern
 - · Inform monoclonal antibody use

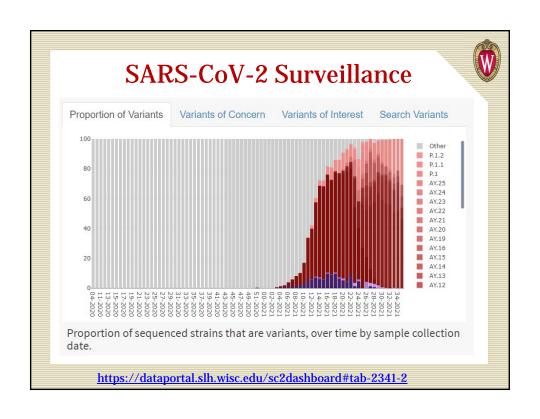












SARS-CoV-2 Whole-genome Sequencing Through the Pandemic

Began May 2020; low volume and used for outbreaks

Morbidity and Mortality Weekly Report

COVID-19 Outbreak at an Overnight Summer School Retreat — Wisconsin, July–August 2020

 $\begin{array}{l} \text{Ian W. Pray, PhD}^{1,2}; Suzanne \ N. \ Gibbons-Burgener, DVM, PhD}^1; Avi \ Z. \ Rosenberg, \ MD, PhD}^3; Devlin \ Cole, \ MD^{1,4}; Shmuel \ Borenstein}^5; \\ Allen \ Bateman, PhD}^6; Eric \ Pevzner, PhD}^7; Ryan \ P. \ Westergaard, MD, PhD}^{1,4} \end{array}$

Morbidity and Mortality Weekly Report

Rapid Spread of SARS-CoV-2 in a State Prison After Introduction by Newly Transferred Incarcerated Persons — Wisconsin, August 14–October 22, 2020

Rebecca B. Hershow, PhD^{1,2,4}; Hannah E. Segaloff, PhD^{1,2,5,4}; Abigail C. Shockey, PhD⁴; Kelsey R. Florek, PhD⁴; Sabrina K. Murphy, MD^{3,5}; Weston DuBose, MPH¹; Tammy L. Schaeffer¹; Jo Anna Powell, MPH¹; Krystal Gayle, MPH¹; Lauren Lambert, MPH¹; Amee Schwitters, PhD¹; Kristie E.N. Clarke, MD¹; Ryan Westergaard, MD, PhD^{3,6}

SARS-CoV-2 Whole-genome Sequencing Through the Pandemic

What We Know About The New U.K. Variant Of Coronavirus — And What We Need To Find Out

December 22, 2020 - 3:56 PH ET

MICHAELEEN DOUCLEFF 💖

December 2020:
 B.1.1.7 in the U.K.



https://www.npr.org/sections/goatsandsoda/2020/12/22/948961575/what-we-know-about-the-new-u-k-variant-of-coronavirus-and-what-we-need-to-find-o

SARS-CoV-2 Whole-genome Sequencing Through the Pandemic

SARS-CoV-2 WGS approach in Wisconsin

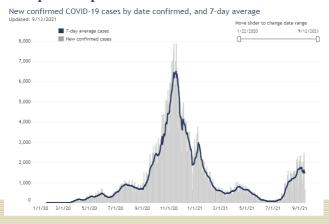
- · Participate in CDC's NS3 program
- Overall approach: general and targeted
 - General
 - · WSLH sequencing all PCR positives from diagnostic testing at WSLH
 - · Request positives from clinical labs statewide
 - Selected clinical labs initially; then broadened to all labs
 - Targeted
 - WI DHS Department of health criteria to enrich for variant identification sent to WSLH: positive samples from individuals with
 - International travel
 - Vaccine failure
 - Prolonged infections
 - Suspected re-infections



SARS-CoV-2 Whole-genome Sequencing Through the Pandemic • June/early July 2021: request all positives New confirmed COVID-19 cases by date confirmed, and 7-day average Updated: 9/13/2021 1-day average cases 1/12/2009 1/100

SARS-CoV-2 Whole-genome Sequencing Through the Pandemic

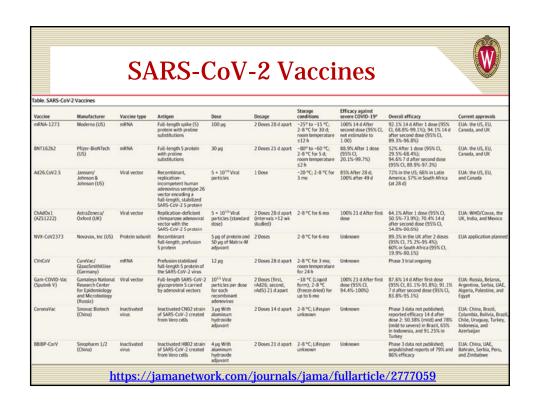
- August 2021: 10 per lab per week
- Now: 5 per lab per week

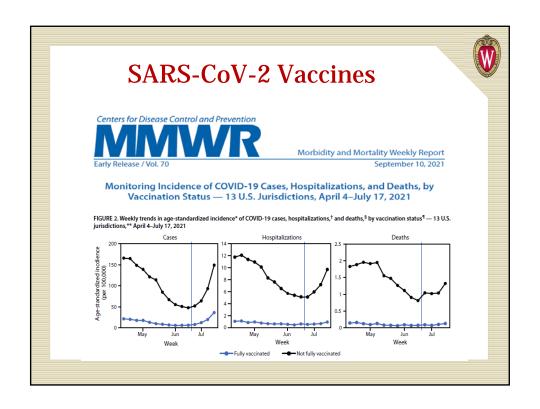


SARS-CoV-2 Whole-genome Sequencing Through the Pandemic

- · 4 other labs in Wisconsin also sequencing
 - City of Milwaukee Health Department Laboratory
 - Marshfield Clinic Research Institute
 - UW-Madison AIDS Vaccine Research Laboratory
 - Medical College of Wisconsin













REVIEW
April 2021 Volume 34 Issue 2 e00133-20
https://doi.org/10.1128/CMR.00133-20

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2): a Systemic Infection

Aleksandra Synowiec 💿 ^a, Artur Szczepański 🙃 ^{a,b}, Emilia Barreto-Duran 💿 ^a, Laurensius Kevin Lie 💿 ^a, Krzysztof Pyrc 👩 ^a

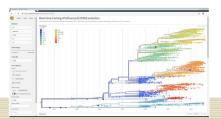
^aVirogenetics Laboratory of Virology, Malopolska Centre of Biotechnology, Jagiellonian University, Krakow, Poland

National Militorbiology Department, Faculty of Biochemistry, Biophysics and Biotechnology, Jagiellonian University, Krakow, Poland

SUMMARY To date, seven identified coronaviruses (CoVs) have been found to infect humans; of these, three highly pathogenic variants have emerged in the 21st century. The newest member of this group, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first detected at the end of 2019 in Hubei province, China. Since then, this novel coronavirus has spread worldwide, causing a pandemic; the respiratory disease caused by the virus is called coronavirus disease 2019 (COVID-19). The clinical presentation ranges from asymptomatic to mild respiratory tract infections and influenza-like illness to severe disease with accompanying lung injury, multiorgan failure, and death. Although the lungs are believed to be the site at which SARS-CoV-2 replicates, infected patients often report other symptoms, suggesting the involvement of the gastrointestinal tract, heart, cardiovascular system, kidneys, and other organs; therefore, the following question arises: is COVID-19 a respiratory or systemic disease? This review aims to summarize existing data on the replication of SARS-CoV-2 in different tissues in both patients and ex vivo models.

Why Perform Surveillance?

- Influenza and other respiratory viruses
 - Situational awareness of what is circulating, to inform clinical decision-making and public health response
- Influenza
 - Track circulating strains to estimate vaccine match
 - Detect antiviral resistance
 - Isolate viruses for inclusion into future vaccines
 - · Detect novel influenza viruses with pandemic potential



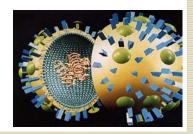
Added Importance of Influenza Surveillance this Year



- Anticipated co-circulation of influenza and SARS-CoV-2
 - Similar presentations to clinicians
 - Need to distinguish for treatment decisions, accurate surveillance and public health decision making
 - Surveillance for SARS-CoV-2 may limit routine influenza testing
- Potential for severe influenza season:
 - Waning immunity in all populations
 - Increased demand on the healthcare system
- · Limited data on influenza and SARS-CoV-2 co-infections
- Influenza vaccine uptake and timing with COVID-19 booster

Influenza virus: Changeability is its hallmark

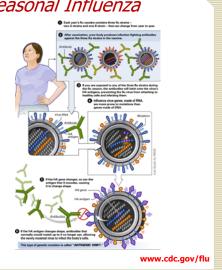
- Influenza types A, B, C and D
 - A and B are major human pathogens
- Negative-sense segmented RNA genome
 - 10 major proteins
- Two major surface proteins of A and B viruses: Hemagglutinin (HA) and Neuraminidase (NA)
 - Nomenclature
 - Role in pathogenesis
 - Defines subtypes



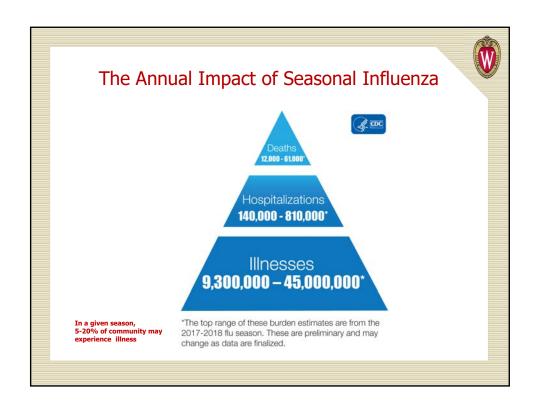
The Changeability of Influenza Antigenic Drift → Seasonal Influenza

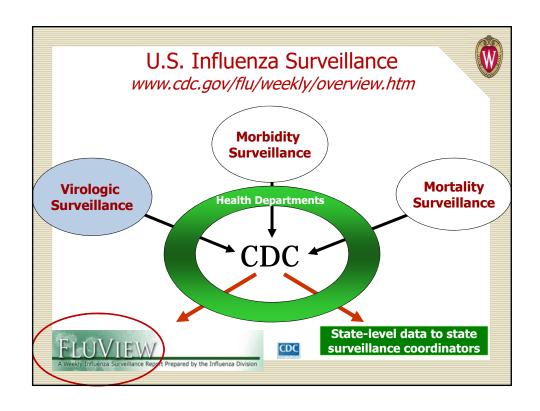
Antigenic Drift

Manifests in HA and NA as a result of continuous and gradual accumulation of point mutations in the HA and NA genes within a subtype



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Influenza Virologic Surveillance

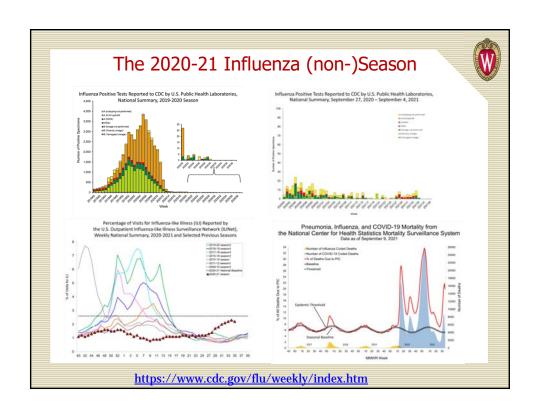


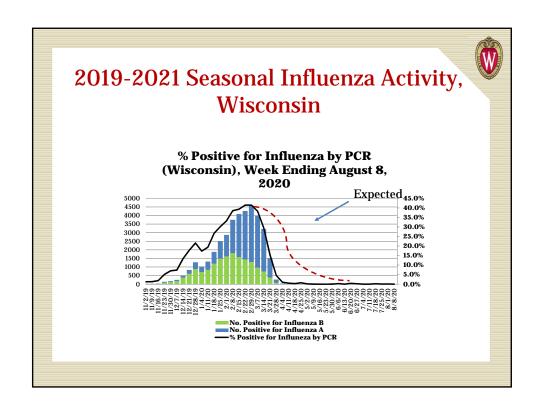
- Provide situational awareness
 - Clinical lab testing data ——> CDC Via PHL or directly

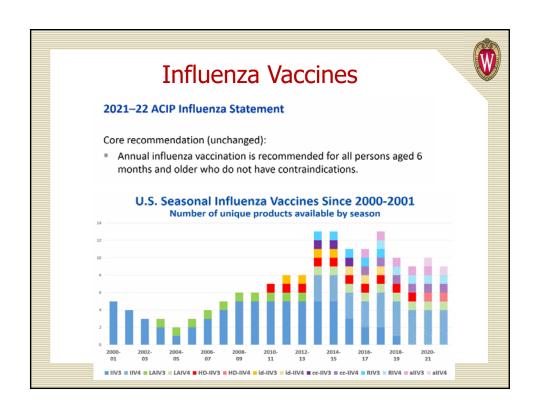
Detect novel or reassortant viruses

- Inform vaccine strain selection
 Detect and monitor antiviral resistance
 - Specimens from clinical labs \rightarrow PHL \rightarrow NIRC \rightarrow CDC









Influenza Vaccines 2021-2022



TABLE 1. Influenza vaccines — United States, 2021–22 influenza season*

Trade name (manufacturer)	Presentations	Age indication	μg HA (IIV4s and RIV4) or virus count (LAIV4) for each vaccine virus (per dose)	Route	Mercury (from thimerosal if present), μg/0.5 mL
IIV4 (standard-dose, egg-based vacci	ines†)				
Afluria Quadrivalent (Seqirus)	0.25-mL PFS ⁵	6 through 35 mos [§]	7.5 μg/0.25 mL	IM ⁹	_
	0.5-mL PFS [§]	≥3 vrs [§]	15 µa/0.5 mL	IM [¶]	_
	5.0-mL MDV ⁶	≥6 mos ⁵ (needle/syringe) 18 through 64 yrs (jet injector)	15 μg/0.5 mL	IM [¶]	24.5
Fluarix Quadrivalent (GlaxoSmithKline)	0.5-mL PFS	≥6 mos	15 μg/0.5 mL	IM¶	_
FluLaval Quadrivalent (GlaxoSmithKline)	0.5-mL PFS	≥6 mos	15 μg/0.5 mL	IM [¶]	_
Fluzone Quadrivalent	0.5-mL PFS**	≥6 mos**	15 µg/0.5 mL	IM [¶]	_
(Sanofi Pasteur)	0.5-mL SDV**	≥6 mos**	15 µg/0.5 mL	IM [¶]	_
	5.0-mL MDV**	≥6 mos**	15 μg/0.5 mL 7.5 μg/0.25 mL	IM¶	25
ccllV4 (standard-dose, cell culture-ba	ased vaccine)				
Flucelvax Quadrivalent	0.5-mL PFS	≥2 yrs	15 µa/0.5 mL	IM [¶]	_
(Segirus)	5.0-mL MDV	≥2 yrs	15 µg/0.5 mL	IM [¶]	25
HD-IIV4 (high-dose, egg-based vaccir	ne†)				
Fluzone High-Dose Quadrivalent (Sanofi Pasteur)	0.7-mL PFS	≥65 yrs	60 μg/0.7 mL	IM [¶]	_
allV4 (standard-dose, egg-based† vac	ccine with MF59 adjuvant)				
Fluad Quadrivalent (Segirus)	0.5-mL PFS	≥65 yrs	15 μg/0.5 mL	IM [¶]	_
RIV4 (recombinant HA vaccine)					
Flublok Quadrivalent (Sanofi Pasteur)	0.5-mL PFS	≥18 yrs	45 μg/0.5 mL	IM [¶]	-
LAIV4 (egg-based vaccine†)					
FluMist Quadrivalent (AstraZeneca)	0.2-mL prefilled single-use intranasal sprayer	2 through 49 yrs	10 ^{6.5–7.5} fluorescent focus units/0.2 mL	NAS	_

IIV: inactivated influenza vaccine (many)

LAIV: live-attenuated influenza vaccine (one)

RIV: recombinant influenza vaccine (one)

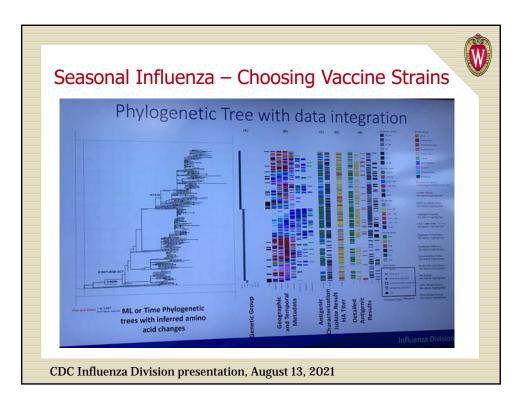


2021–22 Influenza Vaccine Composition

- Egg-based IIV4s and LAIV4:
 - An A/Victoria/2570/2019 (H1N1)pdm09-like virus;
 - An A/Cambodia/e0826360/2020 (H3N2)-like virus;
 - A B/Washington/02/2019 (Victoria lineage)-like virus; and
 - A B/Phuket/3073/2013 (Yamagata lineage)-like virus.
- Cell-culture-based IIV4 and RIV4:
 - An A/Wisconsin/588/2019 (H2N1)pdm09-like virus;
 - An A/Cambodia/e0826360/2020 (H3N2)-like virus;
 - A B/Washington/02/2019 (Victoria lineage)-like virus; and
 - A B/Phuket/3073/2013 (Yamagata lineage)-like virus.

IIV: inactivated influenza vaccine (many) LAIV: live-attenuated influenza vaccine (one)

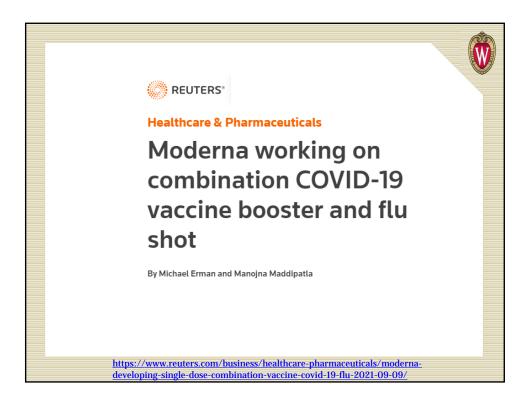
RIV: recombinant influenza vaccine (one)





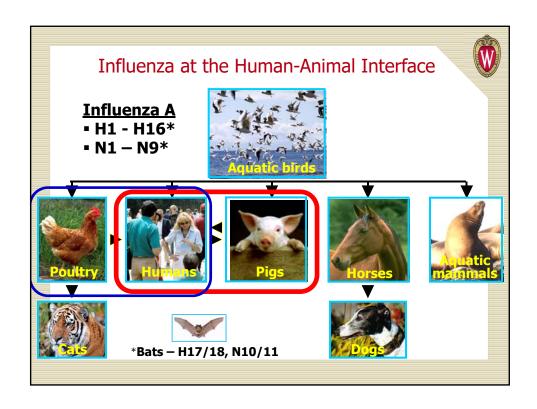
Coadministration of Influenza Vaccines with COVID-19 Vaccines

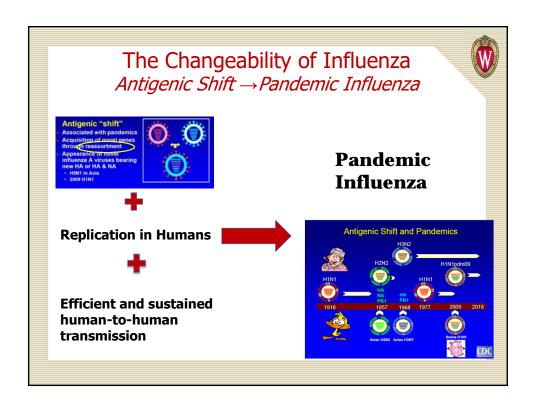
- ACIP influenza statement cites current Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Approved or Authorized in the United States:
 - States that COVID-19 vaccines may be administered without regard to timing of other vaccines.
 - Vaccines administered at the same visit should be given at different sites (separated by an inch or more, if 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.

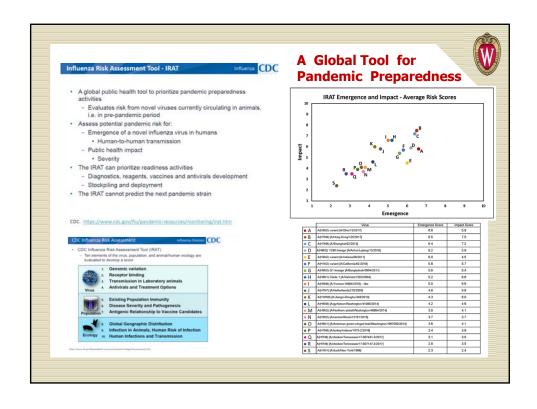


Influenza Vaccine 2021-22

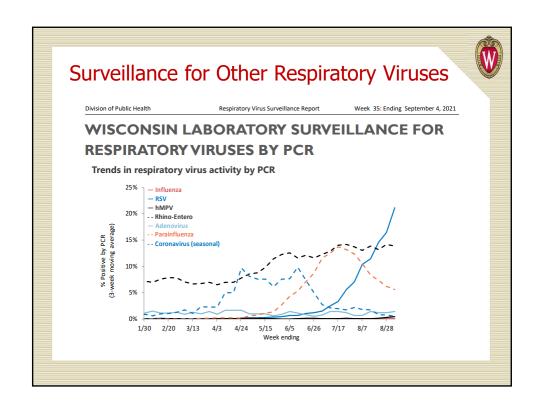
In light of the ongoing SARS-CoV-2 pandemic, more important than ever to get your flu vaccine!

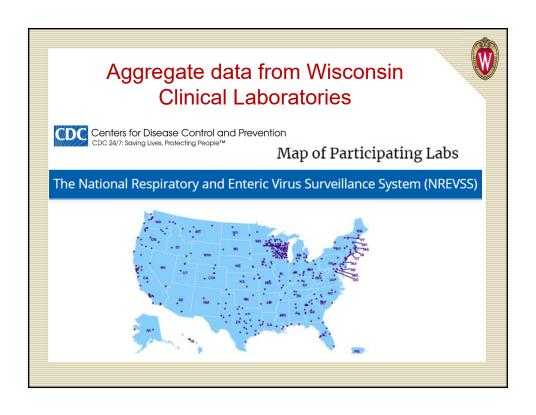


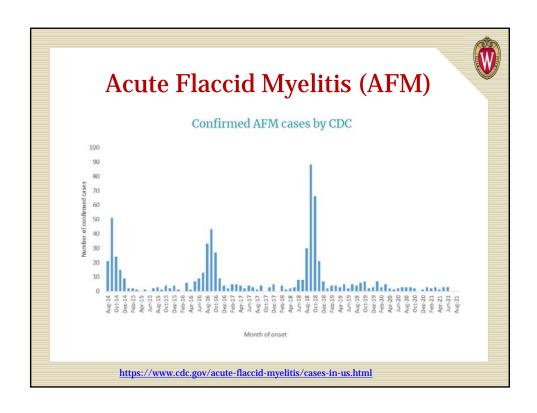


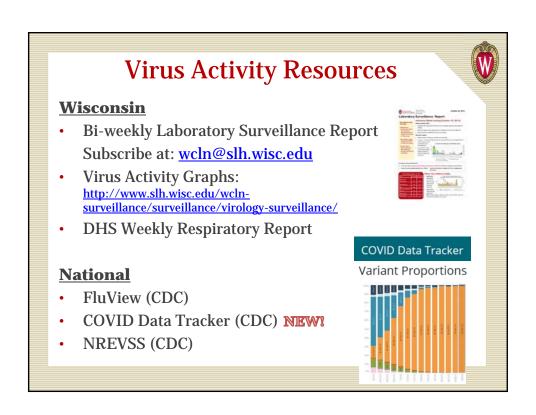














Wisconsin Testing and Surveillance 2021-2022

Possible Impacts of COVID on flu testing



- Lab supply chain shortages and disruptions
- · Managing multiple testing platforms
- Less staffing resources for flu and other diagnostic testing
- Coordinating specimen types
- Trend toward testing asymptomatics



Impacts on surveillance: a public health concern

WSLH Testing Strategy for Influenza and SARS-CoV-2



- Implemented CDC Multiplex PCR assay in September 2020
 - Flu A, Flu B, SARS-CoV-2
- Surveillance testing & outbreak response for suspected influenza or SARS-CoV-2
- Looking to onboard Hologic Panther multiplex test if/when reagents available
- Many commercial manufacturers have developed multiplex tests

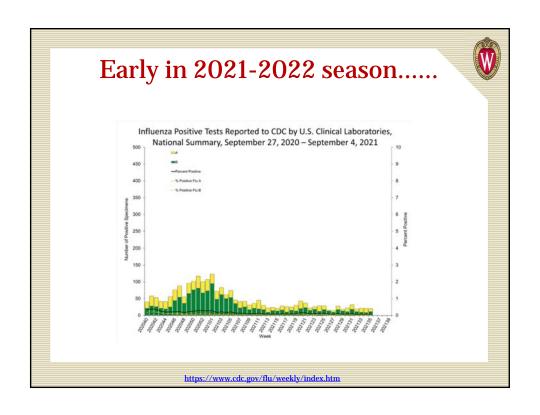
Influenza subtyping

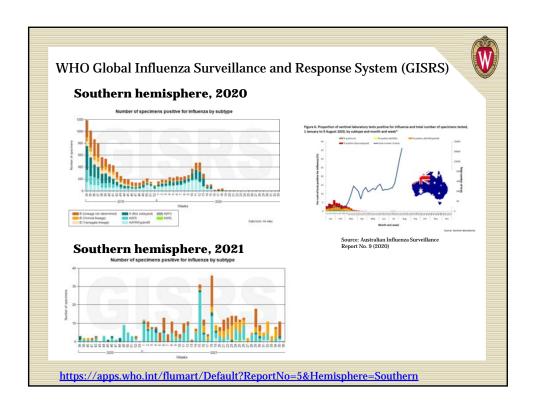


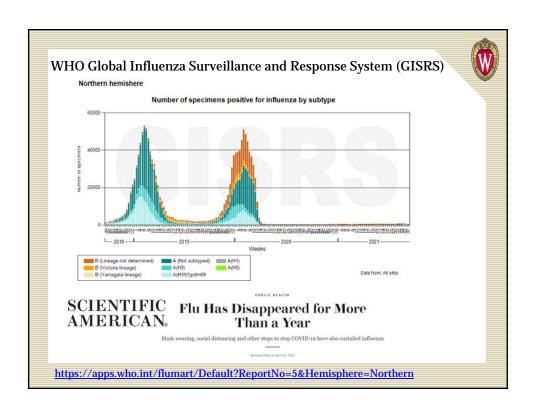
2021-2022 Strategy

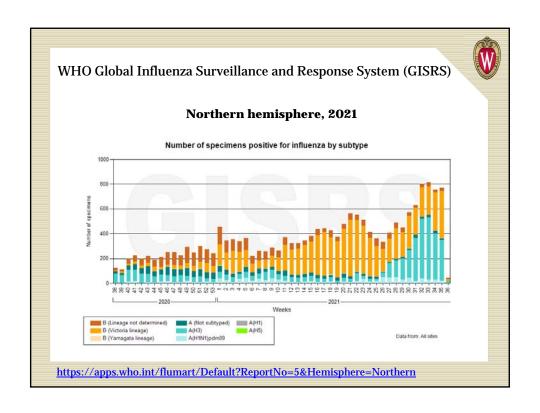
- Characterize H1 and H3 subtypes and B lineage (B/Victoria vs. B/Yamagata)
- Select samples based upon CDC criteria
 - May not be on 100% of positive specimens submitted
- Reporting to labs may be LDT or FDA
 - depends on nucleic acid extraction throughput needed

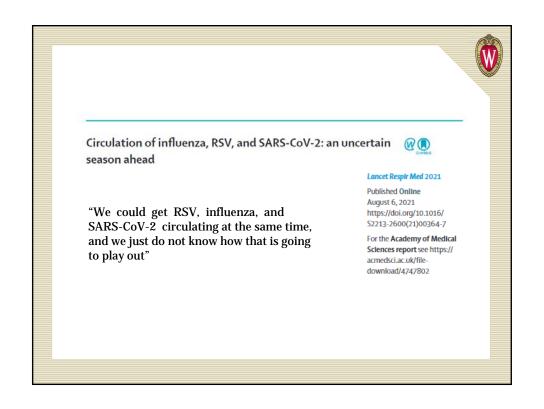














Respiratory Pathogen Surveillance in Wisconsin

2021-2022 Season



SARS-CoV-2 Surveillance in Wisconsin

Multi-element approach

- 1. Reportable disease: all positive and negative results reportable
 - Track cases geographically and over time
- **2.** DHS also tracks hospitalizations and deaths geographically and over time
- **3.** Genomic surveillance: 5 positive samples per week per lab

Influenza Surveillance in Wisconsin



All Clinical Laboratories Performing
Influenza Testing: Please send early
season positive influenza specimens
to WSLH

Early season positives are critical:



- 1. Inform vaccine strain selection.
- 2. Provide samples to make candidate vaccine viruses.

Influenza Surveillance in Wisconsin



Multi-element approach

- Rapid Influenza Diagnostic Testing (RIDT) Sites
 - Now ~50% of influenza testing in WI
 - Confirmatory testing during periods of low prevalence may be warranted
 - Please notify WSLH of suspected performance issues (e.g. False positives/negatives)

Influenza Surveillance in Wisconsin



Multi-element approach

- 2. Enrolled Surveillance Sites
 - 17 labs in 5 public health regions.
 - Provide randomized specimens weekly.
 - Provided a "blue" specimen submission form.



Request to continue to submit the <u>first 2 or 3 specimens</u> <u>per week from symptomatic patients</u> with influenza test requests to WSLH.

Influenza Surveillance in Wisconsin



Multi-element approach

- 3. PCR Labs
 - "Gold Standard" testing.
 - Provide weekly testing data summary reports.
 - Provide early season influenza positive specimens

Request to report both the <u>number positive</u> and the <u>number tested</u> weekly.

**Send Flu A unsubtypable specimens when subtyping for both 2009 H1N1 and seasonal H3 were attempted (Ct<35).

Influenza Surveillance in Wisconsin



Multi-element approach

- 4. University Health Clinics
 - Monitor severe adenovirus infections.
 - Monitor influenza, SCV2 and other respiratory pathogens impacting student health.

Request to <u>up to 3 specimens per week</u> for respiratory pathogen testing and characterization.

Laboratory-based Surveillance



All Clinical Laboratories performing influenza diagnostic testing please send positives

After activity increases:

- Send those with international travel histories
- <u>Up to one</u> influenza-related hospitalization per week
- Unusual presentations/results
- Contact with swine/ sick or dead poultry
- Pediatric deaths

Summary of Influenza Surveillance Activities



PCR Labs & RIDT Sites

- Early season positive influenza specimens
- Continue to report testing data weekly

Enrolled Regional Surveillance Sites

• Send the first 2 to 3 specimens/week University Health Clinics

· Send up to 3 specimens per week

All labs: Please continue to send all positive influenza specimens while influenza transmission is low.

WSLH has Influenza Surveillance Supplies!!



- Specimen collection supplies
 - VTM and swabs
- Shipping supplies
 - Insulated shippers
 - Cold packs
- Specimen submission forms

Contact our Clinical Orders Department at **800-862-1088**

Laboratory-based Surveillance Plan

- Detailed instructions
- Description of surveillance requests
- Web-based reporting instructions

