Influenza and other Respiratory Viruses Update--2020

Pete Shult, PhD
CDD Director & Emergency Laboratory Response

and

Erik Reisdorf, MPH, M(ASCP)^{CM}
Surveillance and Virology Lab-Team Lead

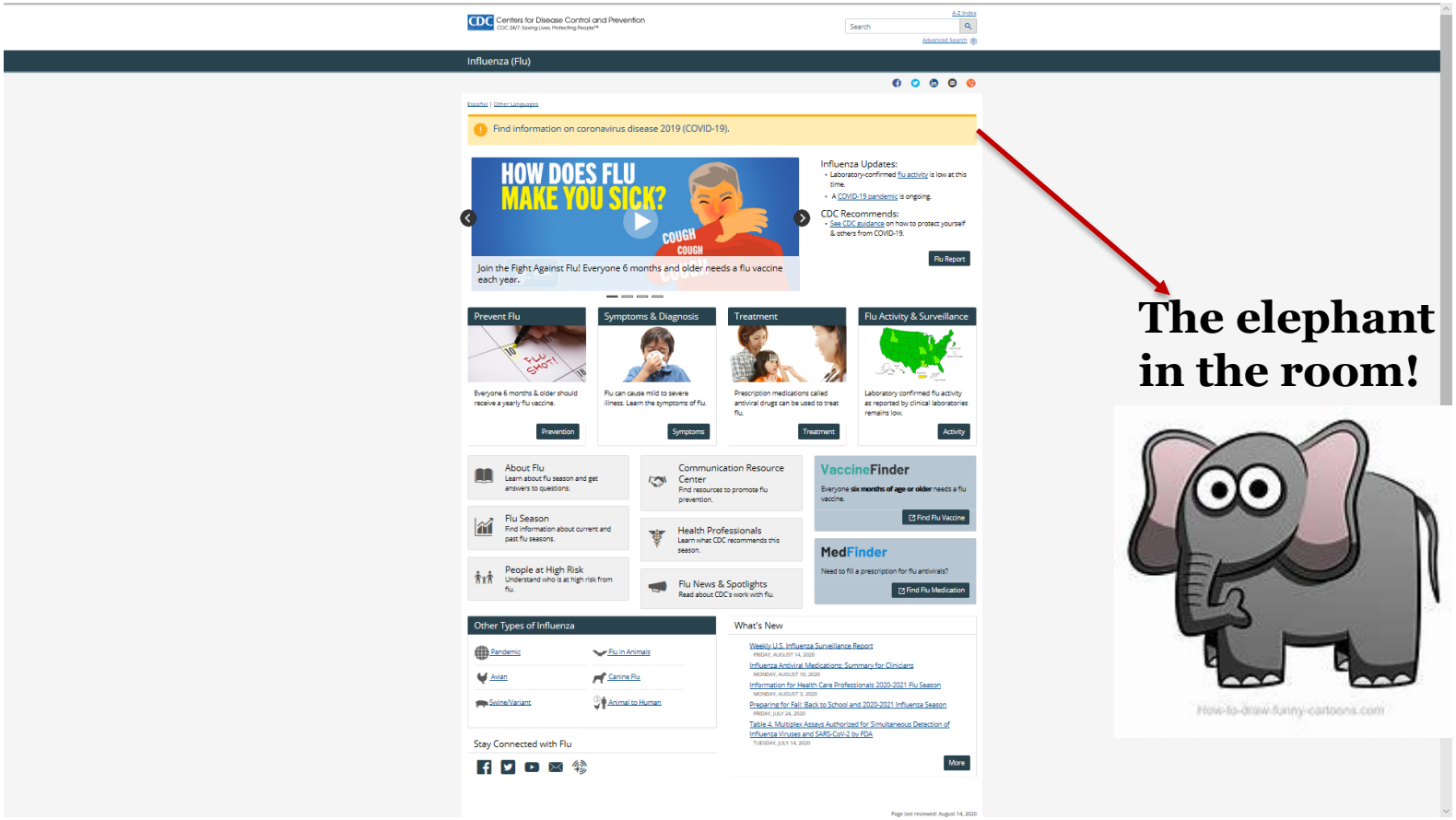
Learning Objectives

- Review of influenza basics.
- Review of the 2019-2020 influenza season.
- Influenza vaccine updates.
- Review laboratory issues related to diagnosis and surveillance.
- Describe why specimens and testing data is vital for public health programs.
- Discuss surveillance strategy for 2020-2021.

Influenza

The latest information

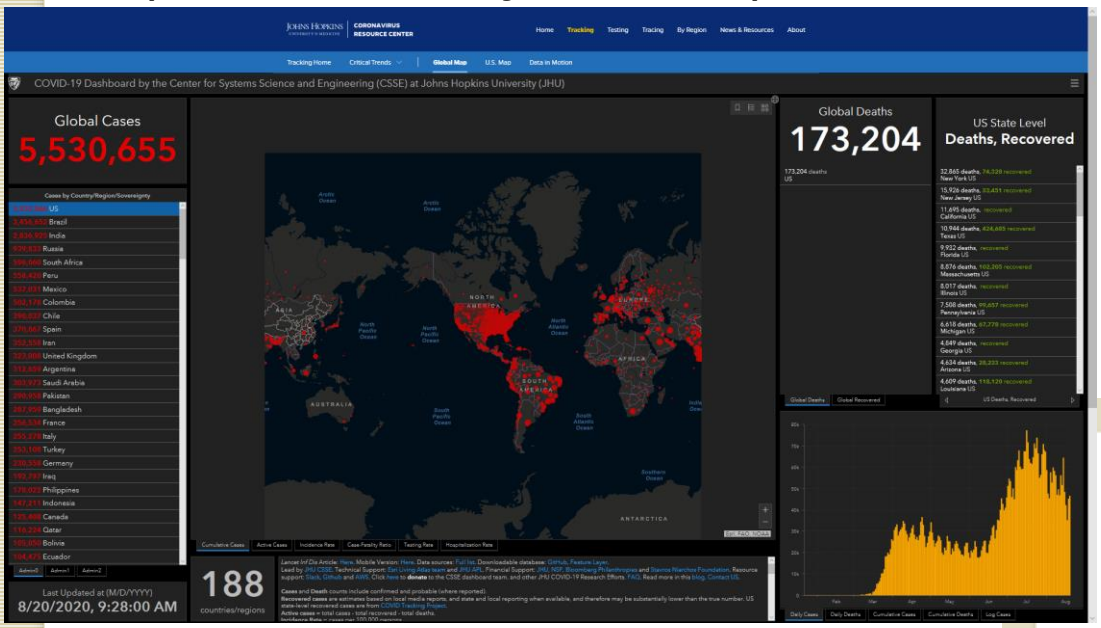
www.cdc.gov/flu/index.htm



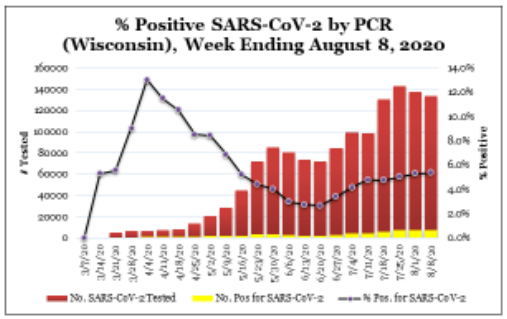
The elephant in the room!

Current SARS-CoV-2 Impact

https://coronavirus.jhu.edu/map.html



http://www.slh.wisc.edu/wcln-surveillance/surveillance/



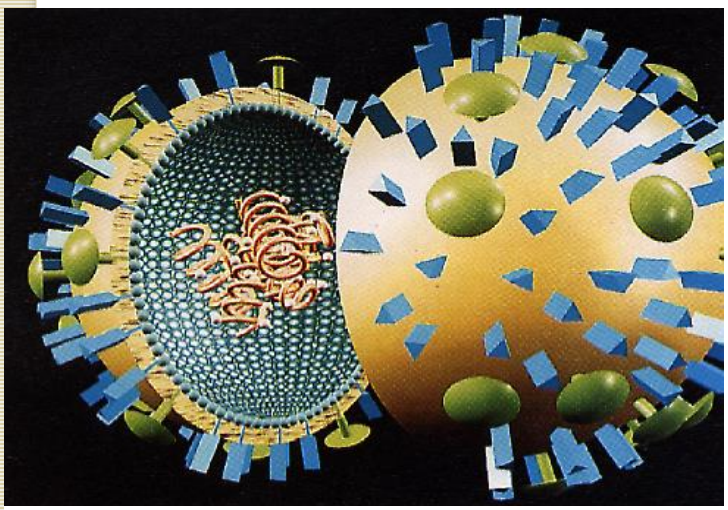
WISCONSIN STATE LABORATORY OF HYGIENE - UNIVERSITY OF WISCONSIN

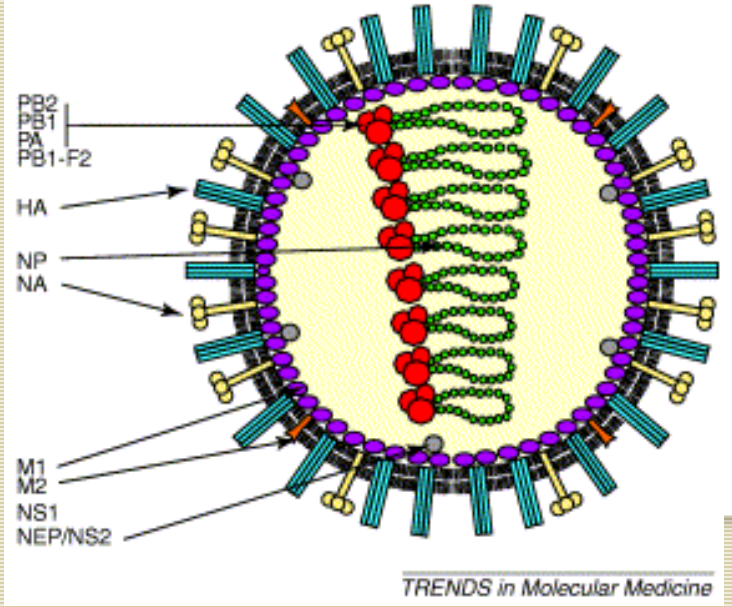
Why should we still worry about flu?

- Significant morbidity and mortality
- Clinical and epidemiological (age, seasonality, risk groups) overlap with COVID-19
- Vaccines and treatments available
- Recent very severe seasonal flu epidemics
- Ongoing threat of novel flu emergence and pandemics.

…and don't forget the impact of a host of other respiratory pathogens

Influenza Virus Basics
"Changeability is its hallmark"





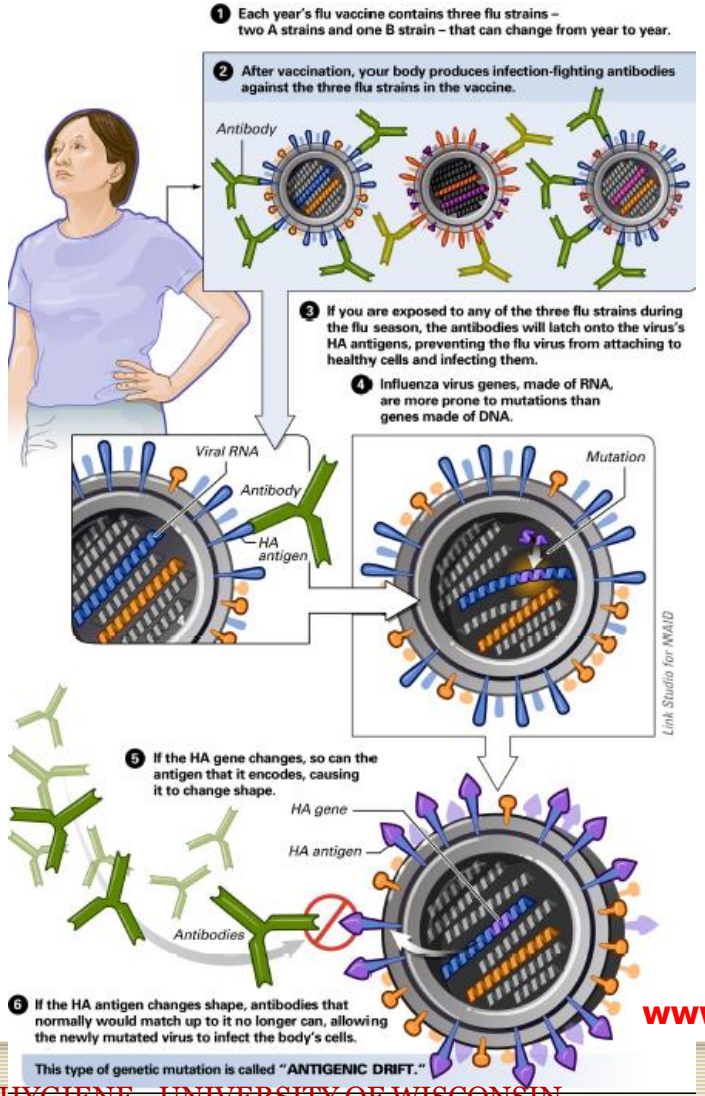
- Influenza **types** A, B, C and D
  - A and B are major human pathogens
- Negative-sense segmented RNA genome
  - 10 major proteins
- Two major surface proteins of A and B viruses: Hemagglutinin (HA) and Neuraminidase (NA)
  - Nomenclature
  - Role in pathogenesis
  - Defines **subtypes**

The Changeability of Influenza

Antigenic Drift →Seasonal Influenza

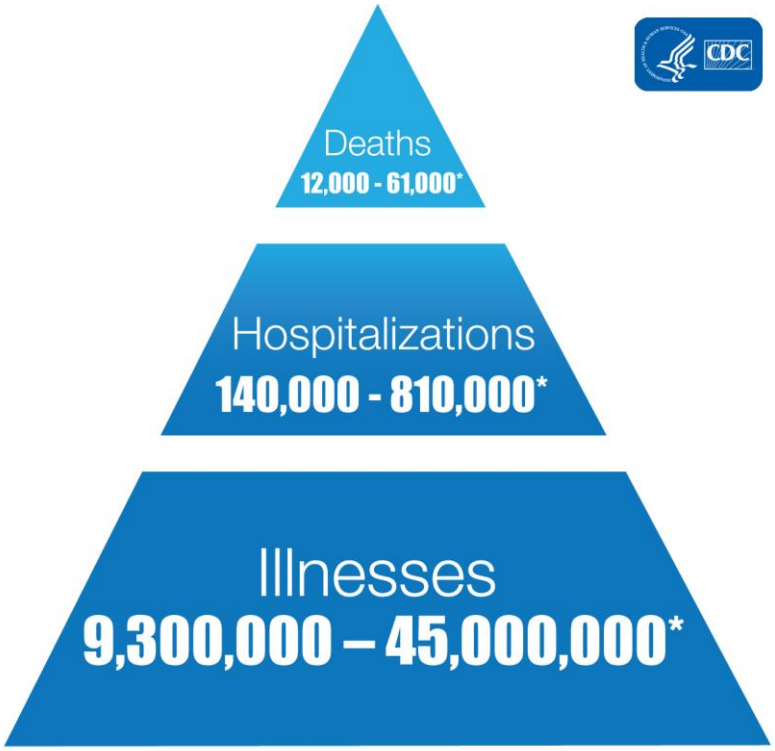
Antigenic Drift

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



www.cdc.gov/flu

The Annual Impact of Seasonal Influenza



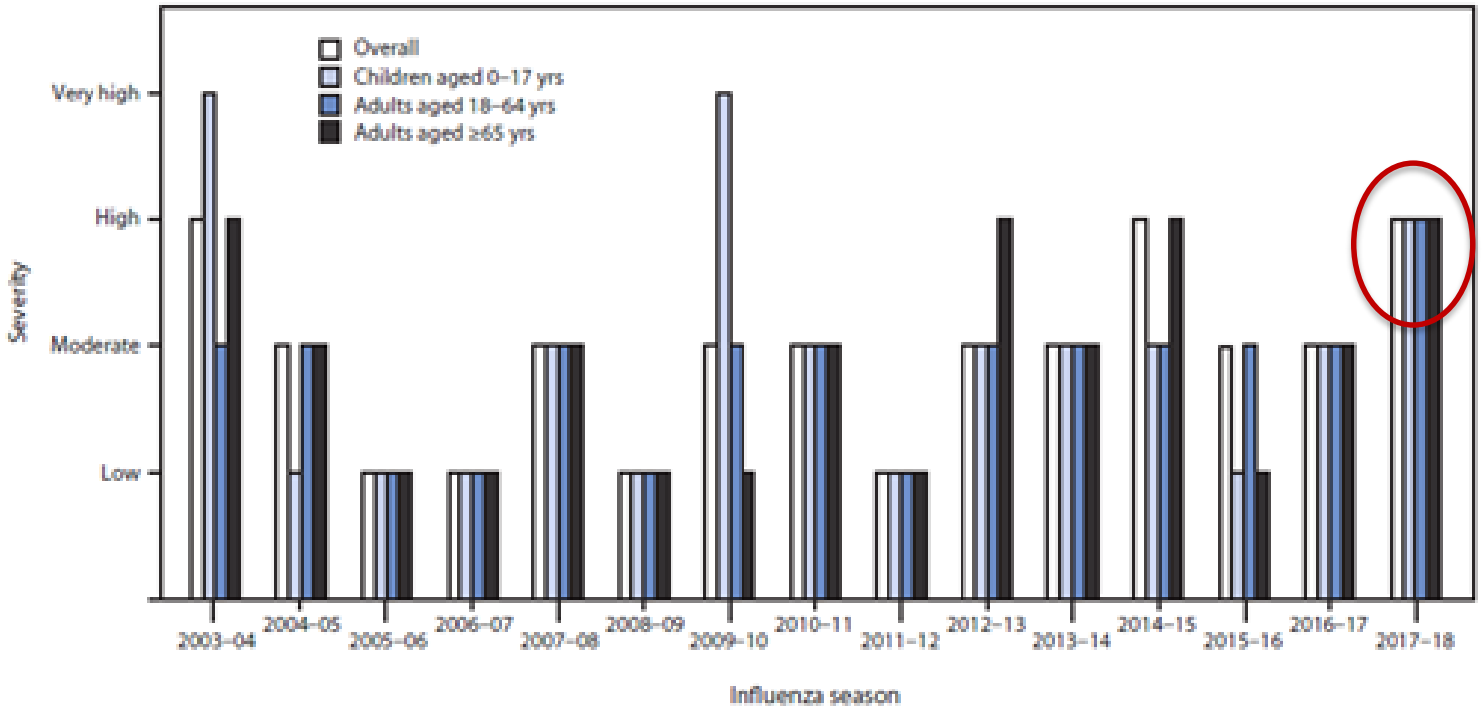
*The top range of these burden estimates are from the 2017-2018 flu season. These are preliminary and may change as data are finalized.

In a given season, 5-20% of community may experience illness

Influenza in the U.S. :2003-18

Overall Influenza Season Severity

FIGURE 3. Influenza season severity classification,* by age group and season — United States, 2003–04 through 2017–18 seasons†



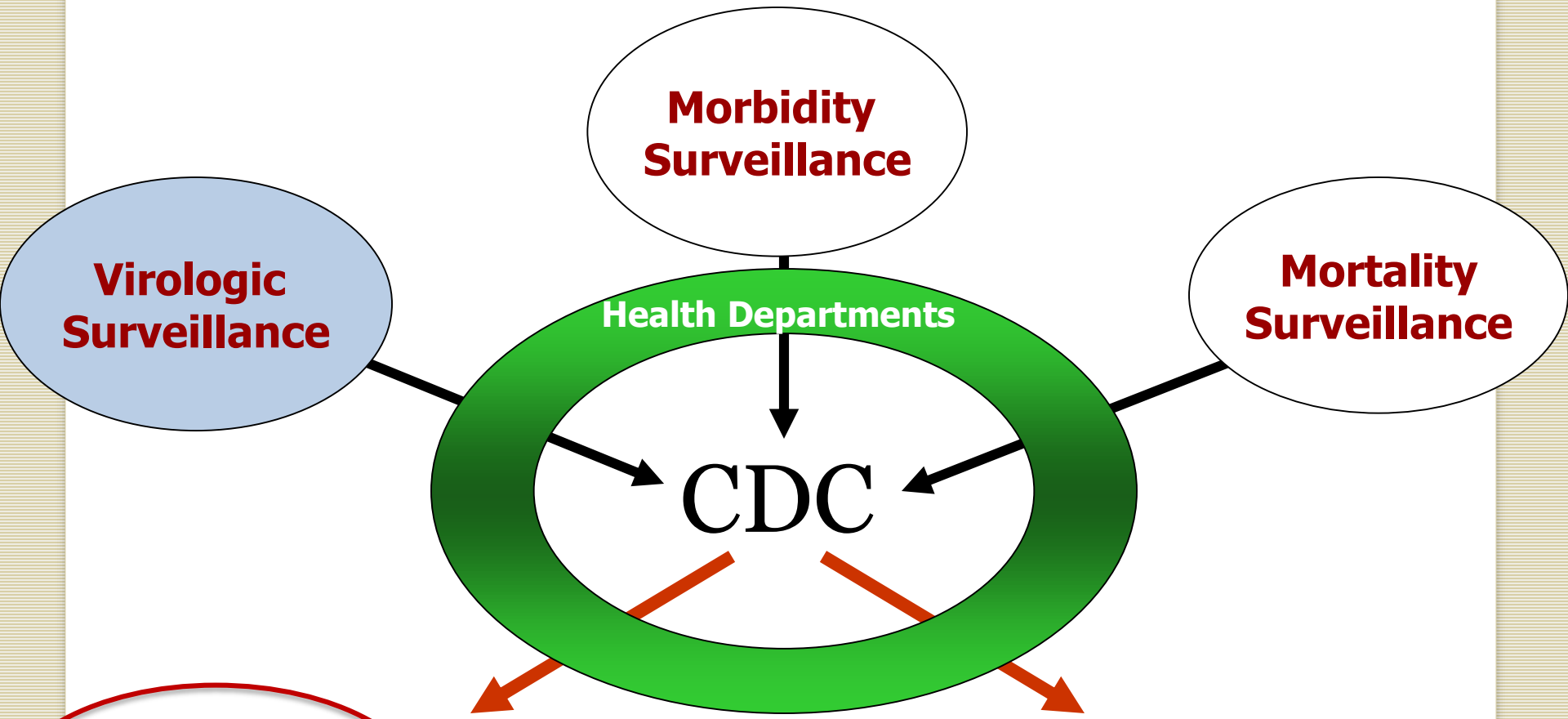
* CDC began using a new method in 2017 to classify influenza season severity using three indicators: the percentage of visits to outpatient clinics for influenza-like illness (ILI) from ILINet, the rates of influenza-associated hospitalizations from FluSurv-Net, and the percentage of deaths resulting from pneumonia or influenza from the National Center for Health Statistics. This method was applied retrospectively, going back to the 2003–04 influenza season. https://www.cdc.gov/flu/professionals/classifies-flu-severity.htm.

† As of June 1, 2018.

MMWR June 8, 2018, Vol. 67/No.22

U.S. Influenza Surveillance

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



FLUVIEW
A Weekly Influenza Surveillance Report Prepared by the Influenza Division

State-level data to state surveillance coordinators

Influenza Virologic Surveillance

How we monitor the virus

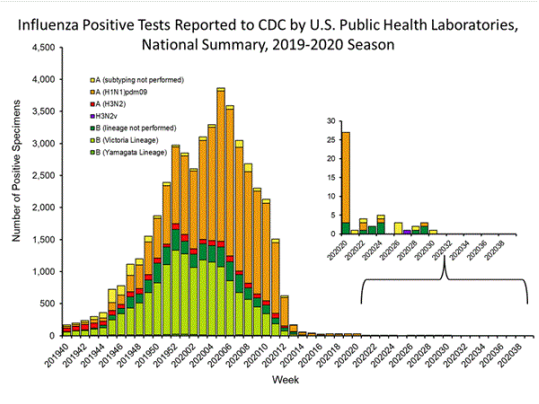
- Provide situational awareness
  - **Clinical lab testing data** → **CDC**
    Via PHL or directly

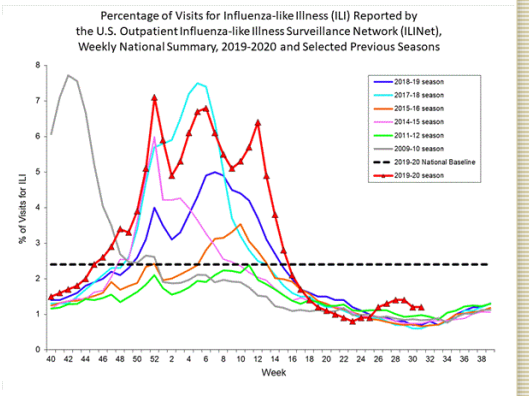
- **Detect novel or reassortant viruses**
- Inform vaccine strain selection
- Detect and monitor antiviral resistance
  - **Specimens/isolates from clinical labs** → **PHL** → **NIRC** → **CDC**

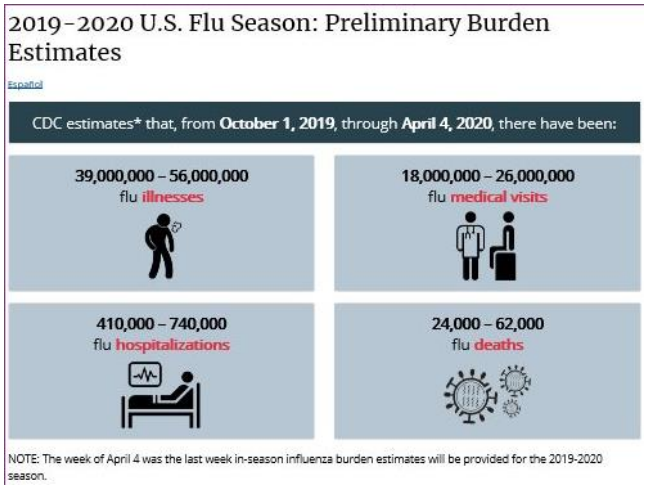
FLUVIEW
A Weekly Influenza Surveillance Report Prepared by the Influenza Division

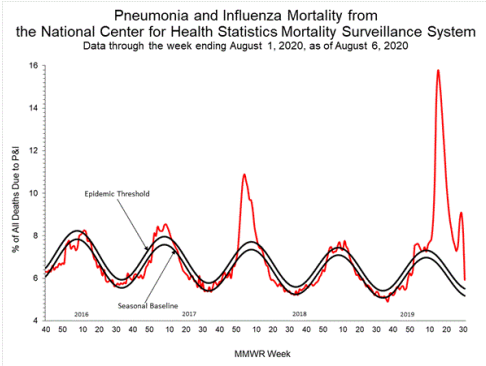
The 2019-20 Influenza Epidemic

Key Virologic and Epidemiologic Indicators

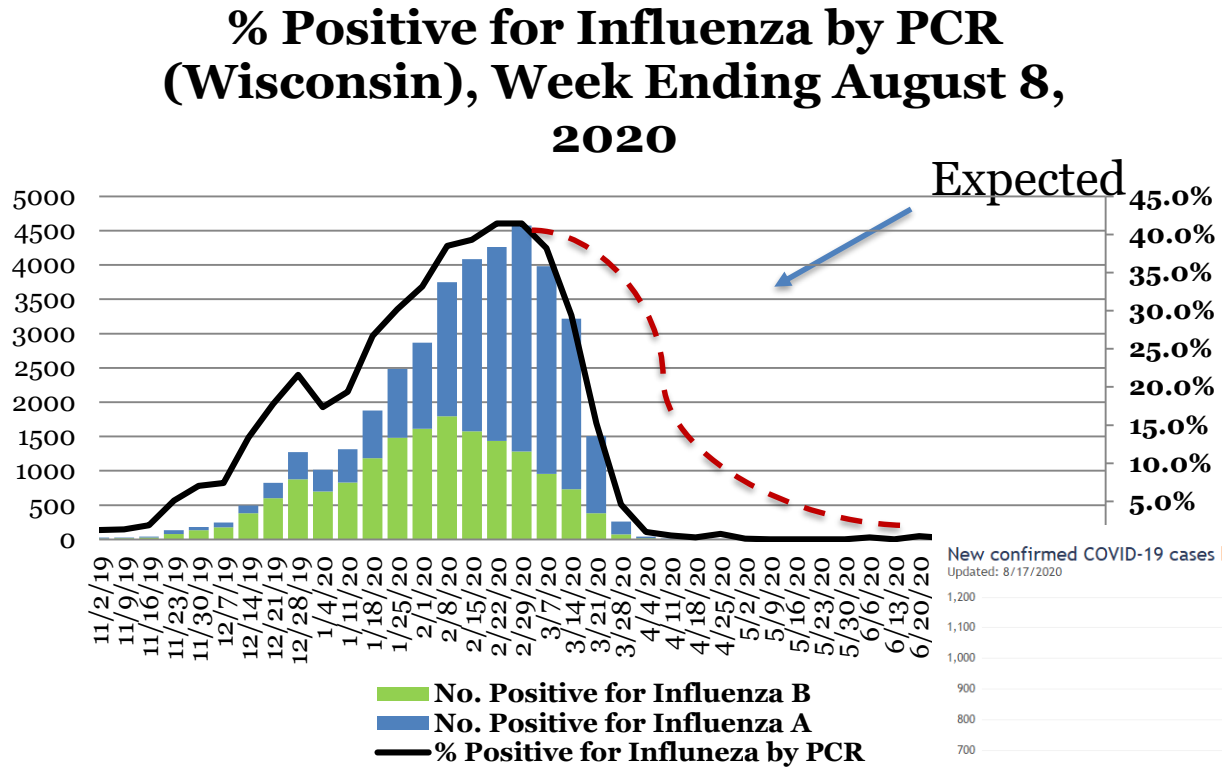


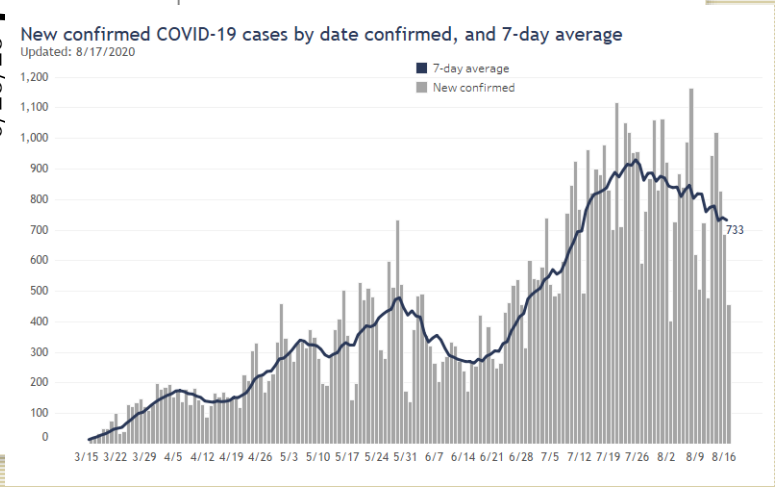






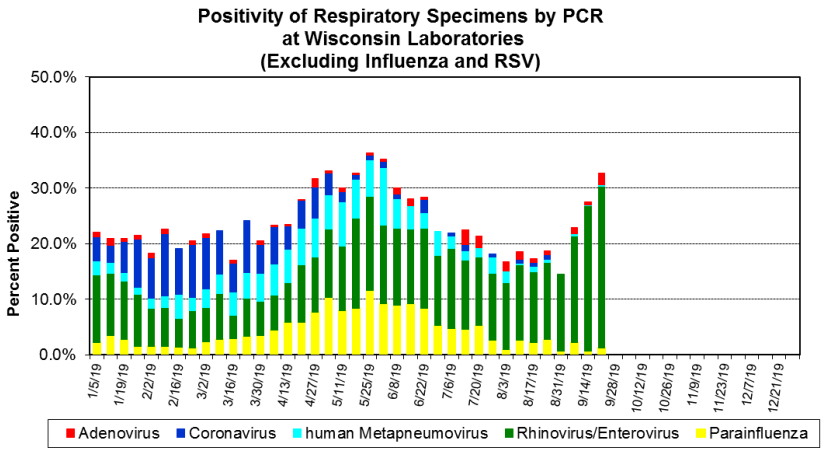
2019-2020 Seasonal Influenza Activity, Wisconsin



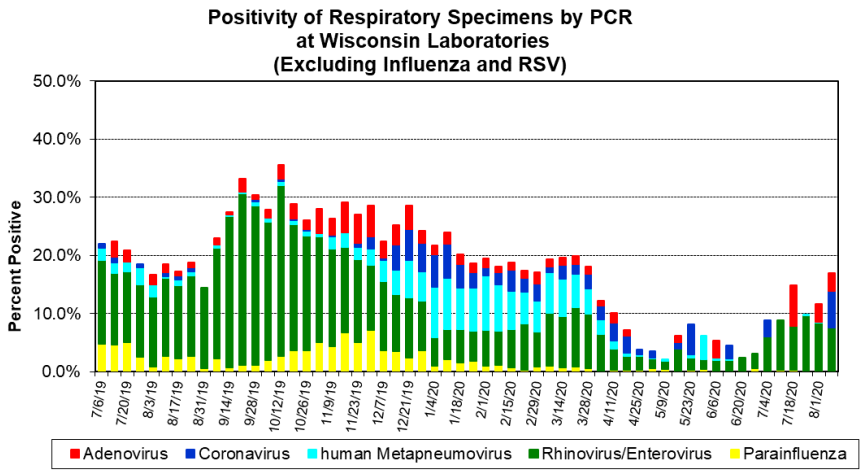


2019-2020 Seasonal Respiratory Virus Activity, Wisconsin

2019



2020



Influenza – Prevention and Treatment

http://www.cdc.gov/flu/professionals/index.htm

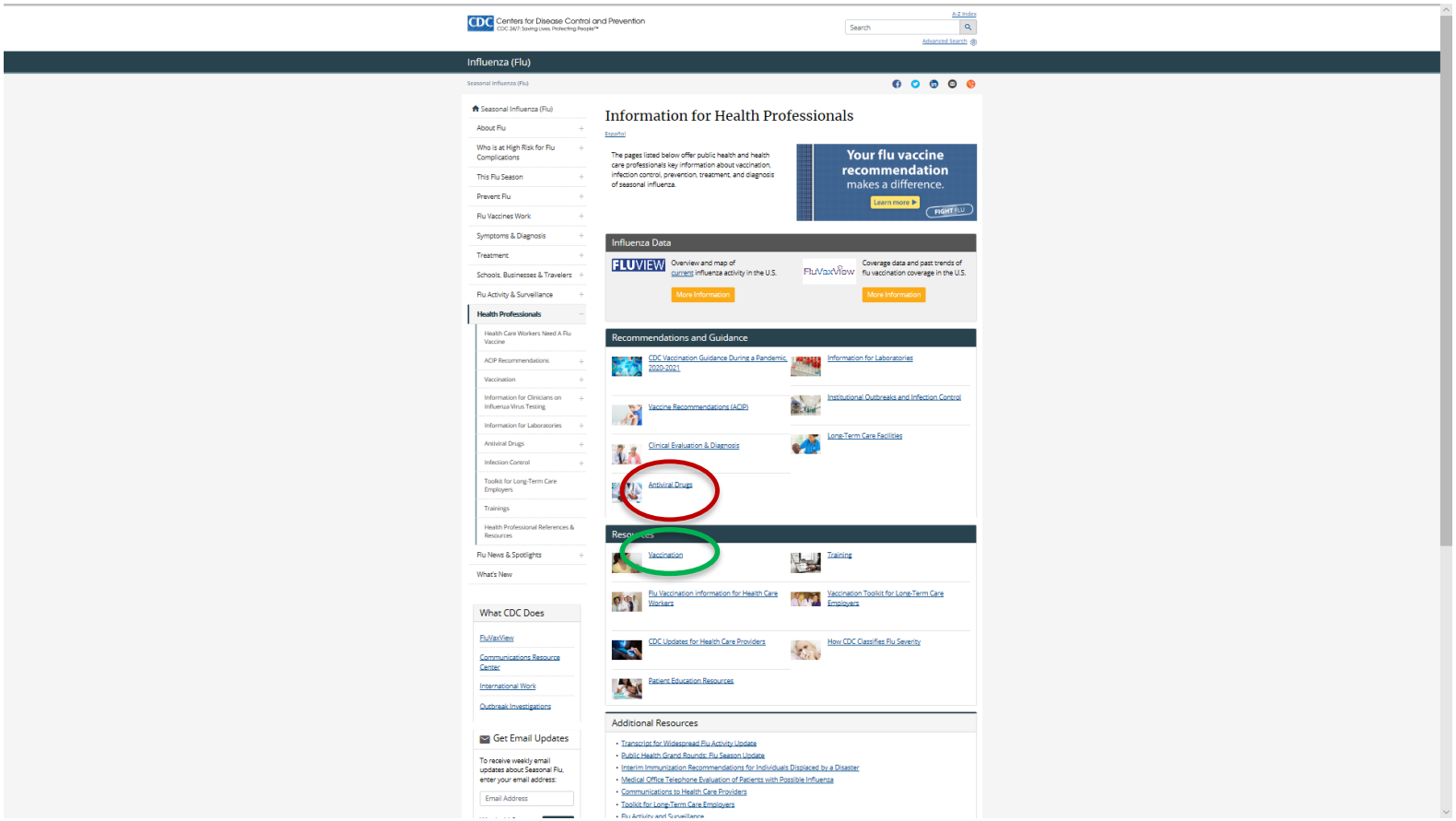


Table 1. Antiviral Medications Recommended for Treatment and Chemoprophylaxis of Influenza

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]	Not recommended	N/A	

Abbreviations: N/A = not applicable, COPD = chronic obstructive pulmonary disease.

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Seasonal Influenza

Vaccine

- **Primary strategy to reduce influenza infections and their complications**
  - Safe and **effective(?);** usage rates **disappointing**
- 2 options:
  - **Inactivated influenza vaccine**
    - Trivalent and quadrivalent
    - Egg or cell culture grown and recombinant
    - For all age groups ≥ 6 months (Universal)
    - Options now include high potency and adjuvanted
  - **Live attenuated influenza vaccine**
    - Licensed for non-pregnant persons aged 2-49 years
- Vaccine is matched to circulating strains of seasonal types A *(2 subtypes)* and B *(2 lineages)* influenza

Influenza Vaccine 2019-20

What was expected….

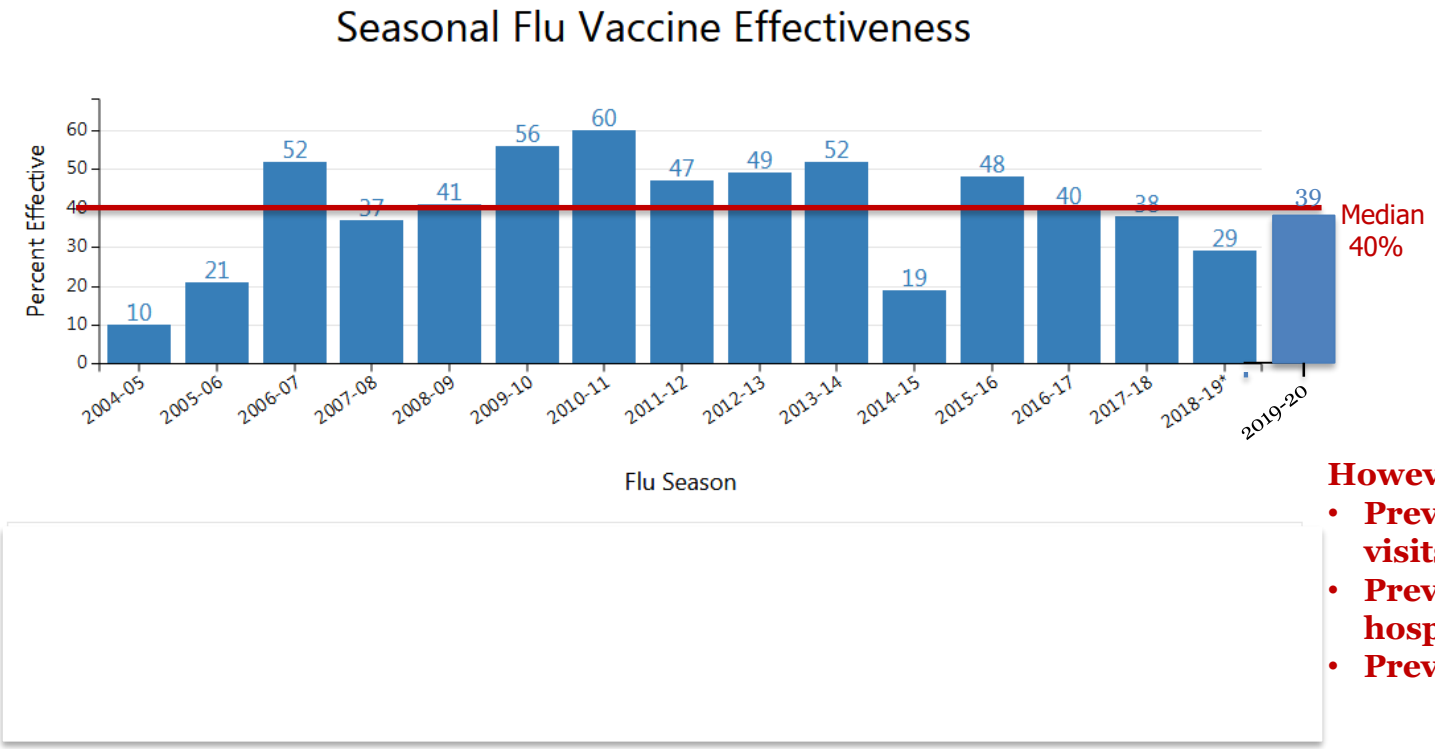
- A/Kansas/14/2017 A(H3N2)-like
- A/Brisbane/02/2018 A(H1N1)pdm09-like
- B/Phuket/3073/2013-like (B/Yamagata-lineage)
- B/Colorado/06/2017-like (B/Victoria-lineage)

…basically what we got

Seasonal Influenza Vaccines

How effective?

https://www.cdc.gov/flu/vaccines-work/effectiveness-studies.htm



However:

- **Prevents office visits**
- **Prevent hospitalization**
- **Prevents death**

VE= percent reduction of frequency of flu among vaccinated people compared to unvaccinated people

Influenza Vaccine 2020-21

https://www.cdc.gov/mmwr/volumes/69/rr/pdfs/rr6908a1-H.pdf

- A/Hong Kong/2671/2019 A(H3N2)-like [egg- based]
- A/Hong Kong/45/2019 A(H3N2) [cell-based and recombinant]

- A/Guangdong-Maonan/SWL1536/2019 A(H1N1)pdm09-like [egg-based]
- A/Hawaii/70/2019 A(H1N1)pdm-09-like [cell-based and recombinant]

- B/Washington/02/2019 (B/Victoria lineage)-like [egg & cell-based]

- B/Phuket/3073/2013 (B/Yamagata-lineage)-like [egg & cell-based]

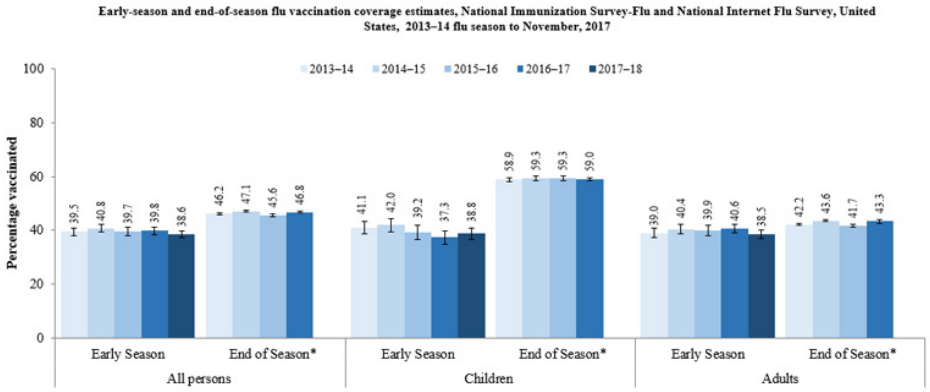
Influenza Vaccine 2020-21

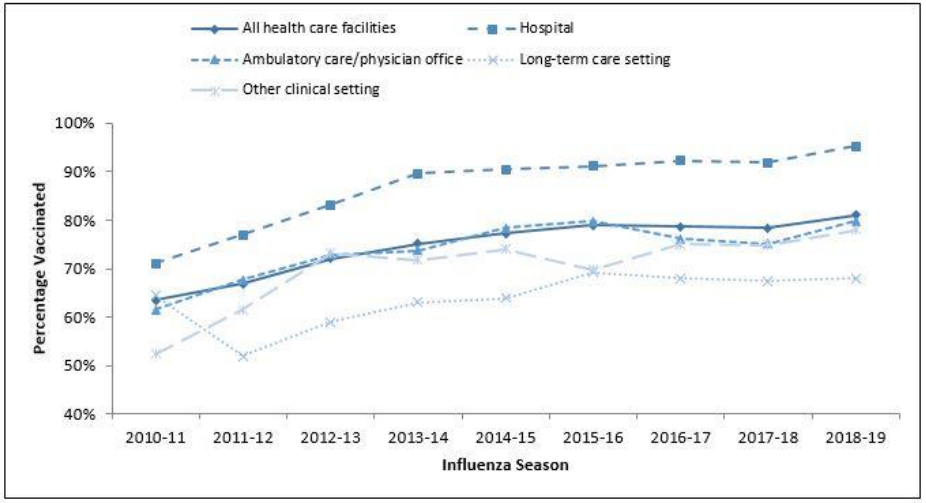
In light of the SARS-CoV-2 pandemic, more important than ever to get your flu vaccine!

Vaccination Rates---2013-2019

General Population and Healthcare Personnel

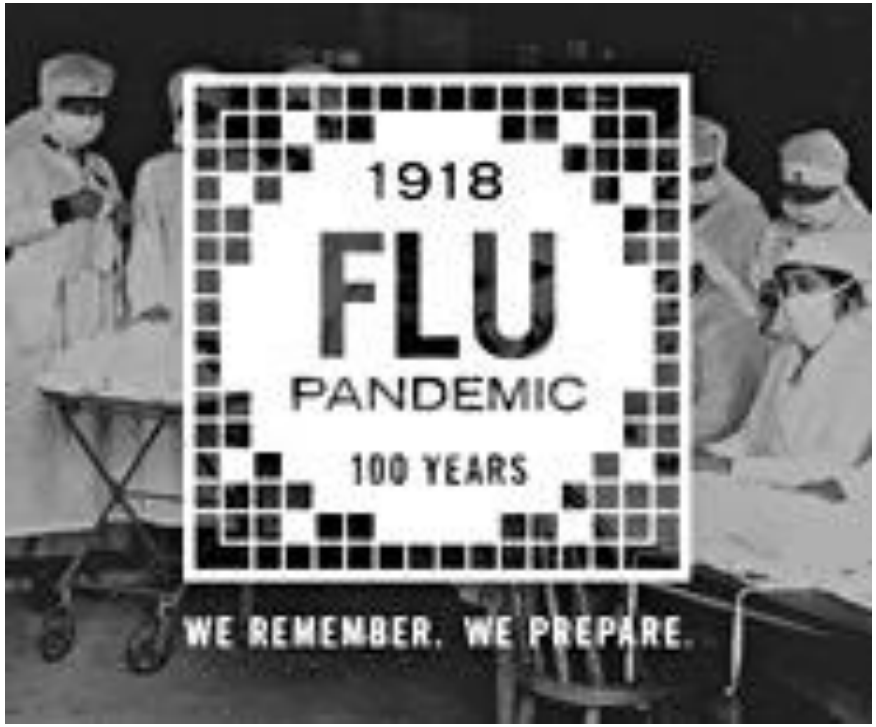
http://www.cdc.gov/flu/professionals/vaccination/





1918 Influenza Pandemic

100 Year Anniversary of the Great Pandemic

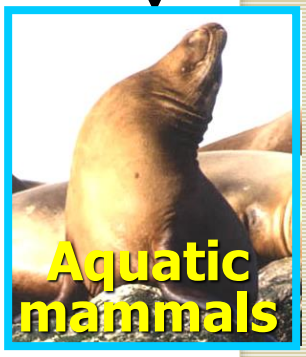


https://www.cdc.gov/flu/pandemic-resources/index.htm

Influenza at the Human-Animal Interface

Influenza A

- **H1 - H16***
- **N1 – N9***

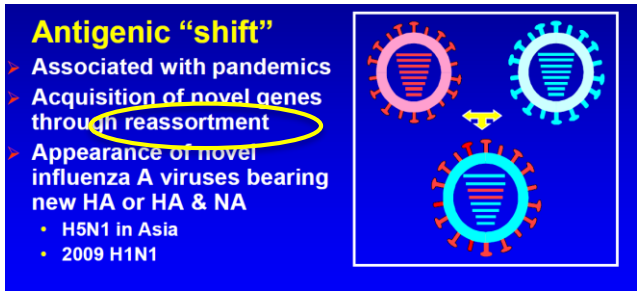


*Bats – H17/18, N10/11

The Changeability of Influenza

Antigenic Shift → Pandemic Influenza

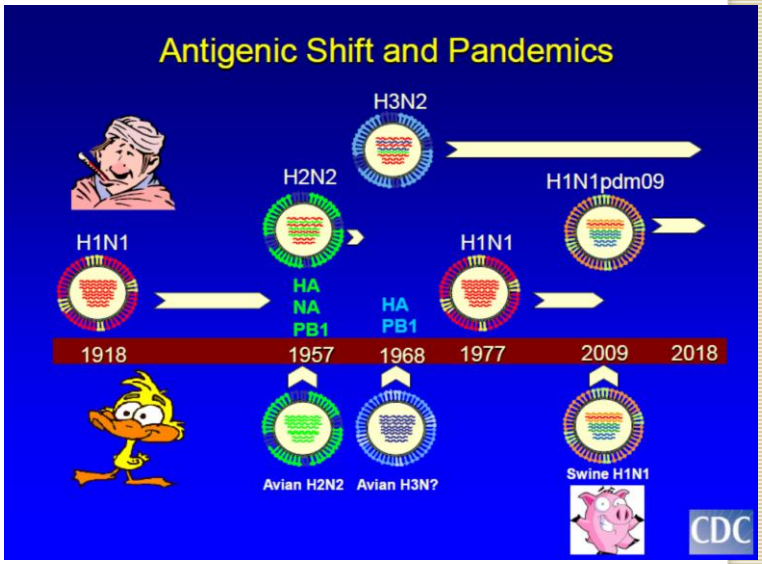
www.cdc.gov/flu



Pandemic Influenza

Replication in Humans

Efficient and sustained human-to-human transmission



A Global Tool for Pandemic Preparedness

Influenza Risk Assessment Tool - IRAT Influenza CDC

- A global public health tool to prioritize pandemic preparedness activities
  - Evaluates risk from novel viruses currently circulating in animals, i.e. in pre-pandemic period
- Assess potential pandemic risk for:
  - Emergence of a novel influenza virus in humans
    - Human-to-human transmission
  - Public health impact
    - Severity
- The IRAT can prioritize readiness activities
  - Diagnostics, reagents, vaccines and antivirals development
  - Stockpiling and deployment
- The IRAT cannot predict the next pandemic strain

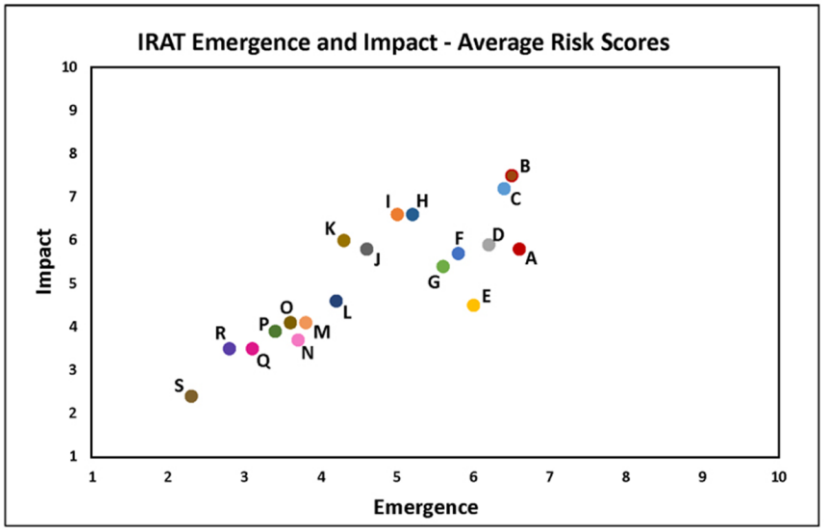
CDC. https://www.cdc.gov/flu/pandemic-resources/monitoring/irat.htm

CDC Influenza Risk Assessment Influenza Division CDC

- CDC Influenza Risk Assessment Tool (IRAT)
  - Ten elements of the virus, population, and animal/human ecology are evaluated to develop a score

Virus	1. Genomic variation 2. Receptor binding 3. Transmission in Laboratory animals 4. Antivirals and Treatment Options
Population	5. Existing Population Immunity 6. Disease Severity and Pathogenesis 7. Antigenic Relationship to Vaccine Candidates
Ecology	8. Global Geographic Distribution 9. Infection in Animals, Human Risk of Infection 10. Human Infections and Transmission

https://www.cdc.gov/flu/pandemic-resources/national-strategy/risk-assessment.htm

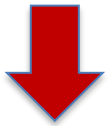


	Virus	Emergence Score	Impact Score
A	A(H3N2) variant [A/Ohio/13/2017]	6.6	5.8
B	A(H7N9) [A/Hong Kong/125/2017]	6.5	7.5
C	A(H7N9) [A/Shanghai/02/2013]	6.4	7.2
D	A(H9N2) Y280 lineage [A/Anhui-Lujiang/13/2018]	6.2	5.9
E	A(H3N2) variant [A/Indiana/08/2011]	6.0	4.5
F	A(H1N2) variant [A/California/62/2018]	5.8	5.7
G	A(H9N2) G1 lineage [A/Bangladesh/0994/2011]	5.6	5.4
H	A(H5N1) Clade 1 [A/Vietnam/1203/2004]	5.2	6.6
I	A(H5N6) [A/Yunnan/14564/2015] – like	5.0	6.6
J	A(H7N7) [A/Netherlands/219/2003]	4.6	5.8
K	A(H10N8) [A/Jiangxi-Donghu/346/2013]	4.3	6.0
L	A(H5N8) [A/gyrfalcon/Washington/41088/2014]	4.2	4.6
M	A(H5N2) [A/Northern pintail/Washington/40964/2014]	3.8	4.1
N	A(H3N2) [A/canine/Illinois/12191/2015]	3.7	3.7
O	A(H5N1) [A/American green-winged teal/Washington/1957050/2014]	3.6	4.1
P	A(H7N8) [A/turkey/Indiana/1573-2/2016]	3.4	3.9
Q	A(H7N9) [A/chicken/Tennessee/17-007431-3/2017]	3.1	3.5
R	A(H7N9) [A/chicken/Tennessee/17-007147-2/2017]	2.8	3.5
S	A(H1N1) [A/duck/New York/1996]	2.3	2.4

Wisconsin Testing and Surveillance 2020-2021

Possible Impacts of COVID on flu testing

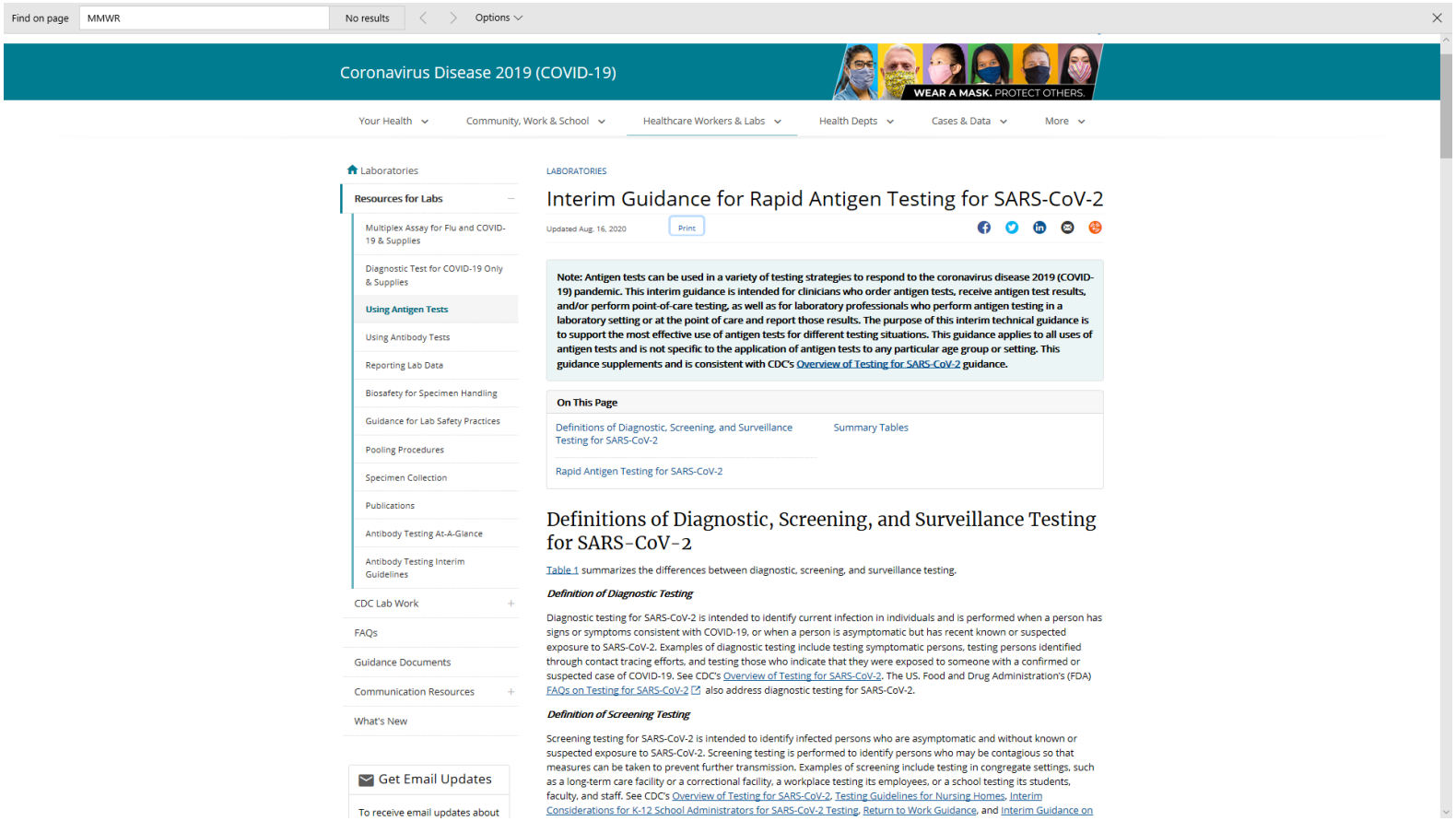
- Lab supply chain shortages and disruptions
- Less staffing resources for flu and other diagnostic testing
- Managing multiple testing platforms
- Coordinating specimen types
- Trend toward testing asymptomatics
- Expanding COVID testing beyond traditional labs
  - "Tack on" flu testing as well



Impacts on surveillance: a PH concern

Excellent Resource

https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html



WSLH Testing Strategy for Influenza and SARS-CoV-2

- Implementing CDC Multiplex PCR assay in September.
- Surveillance testing & outbreak response for suspected influenza or SARS-CoV-2.
- Commercial tests include BioFire, Luminex and Qiagen. Cepheid 4 targets coming soon!
- Many commercial manufacturers developing tests.

CDC Influenza SC2 Multiplex PCR

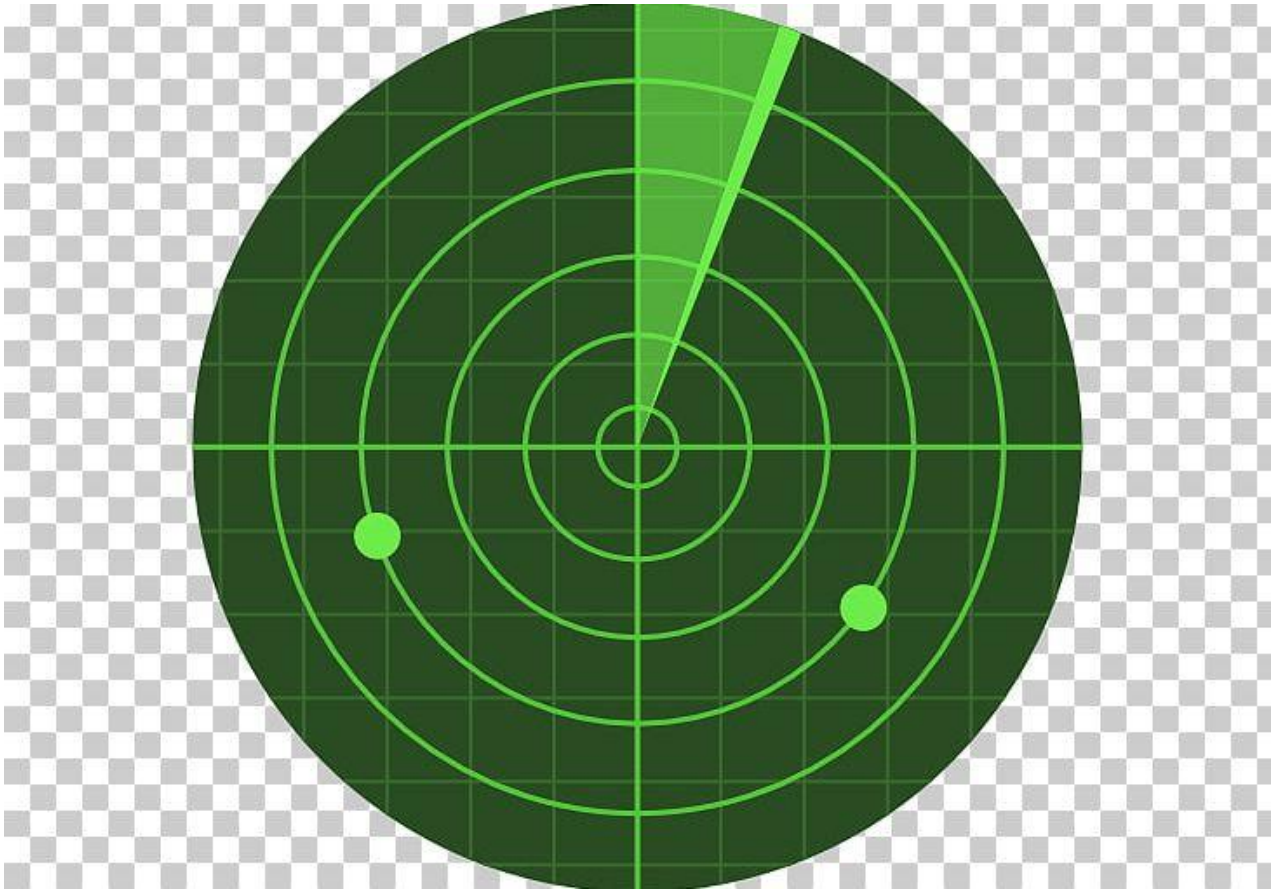
- Targets include InfA, InfB, SC2 and RP
- Equipment needed: real-time PCR instrument (96well) and NA extraction platform.
- Sensitivity for SC2 improved. Similar for influenza viruses.
- PCR sequences available at: https://www.cdc.gov/coronavirus/2019-ncov/lab/multiplex-primer-probes.html

Influenza subtyping changes

2020-2021 Strategy

- Characterize H1 and H3 subtypes.
- Select samples based upon CDC criteria.
- Reduced number.
- Reporting to labs will be RUO.

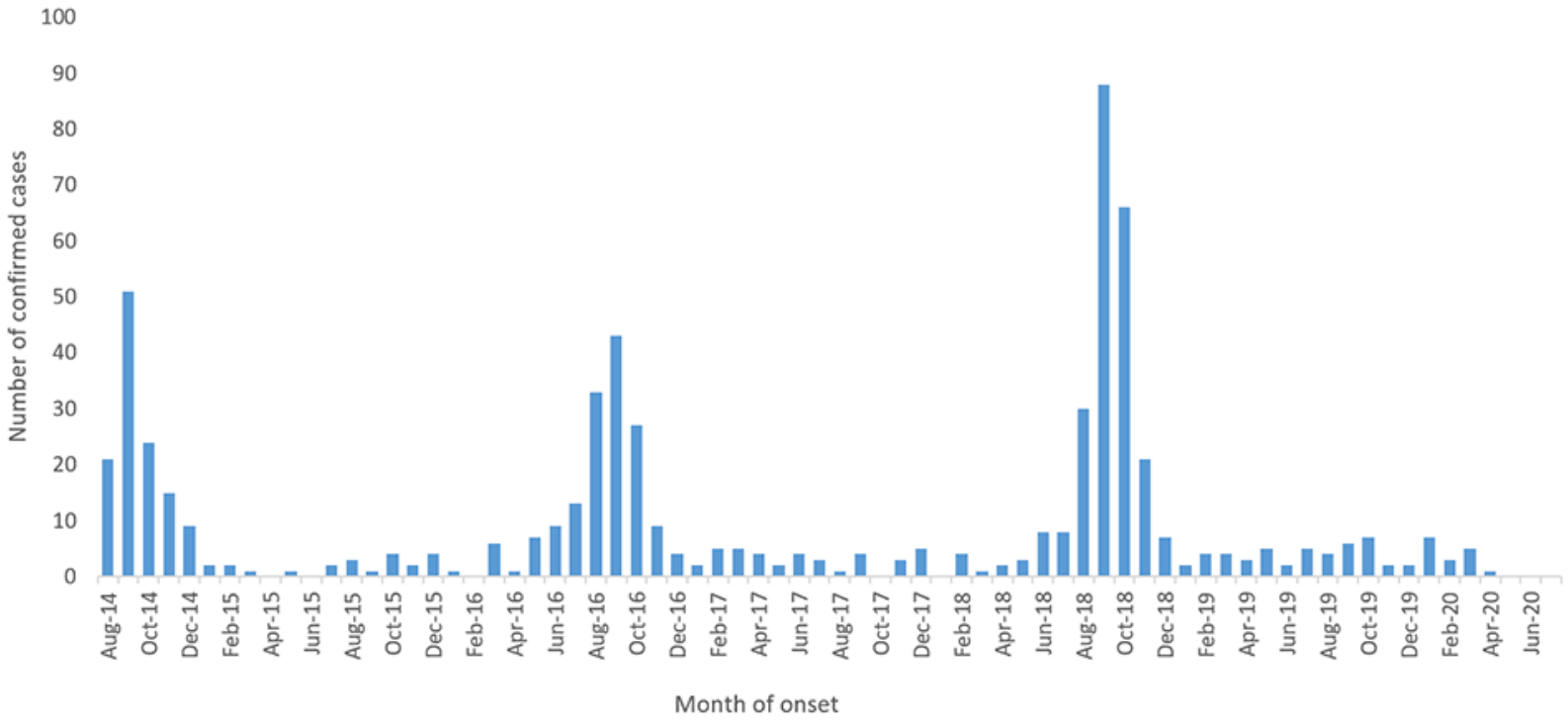
Viral Monitoring Activities (other than Flu)



Severe Adenovirus

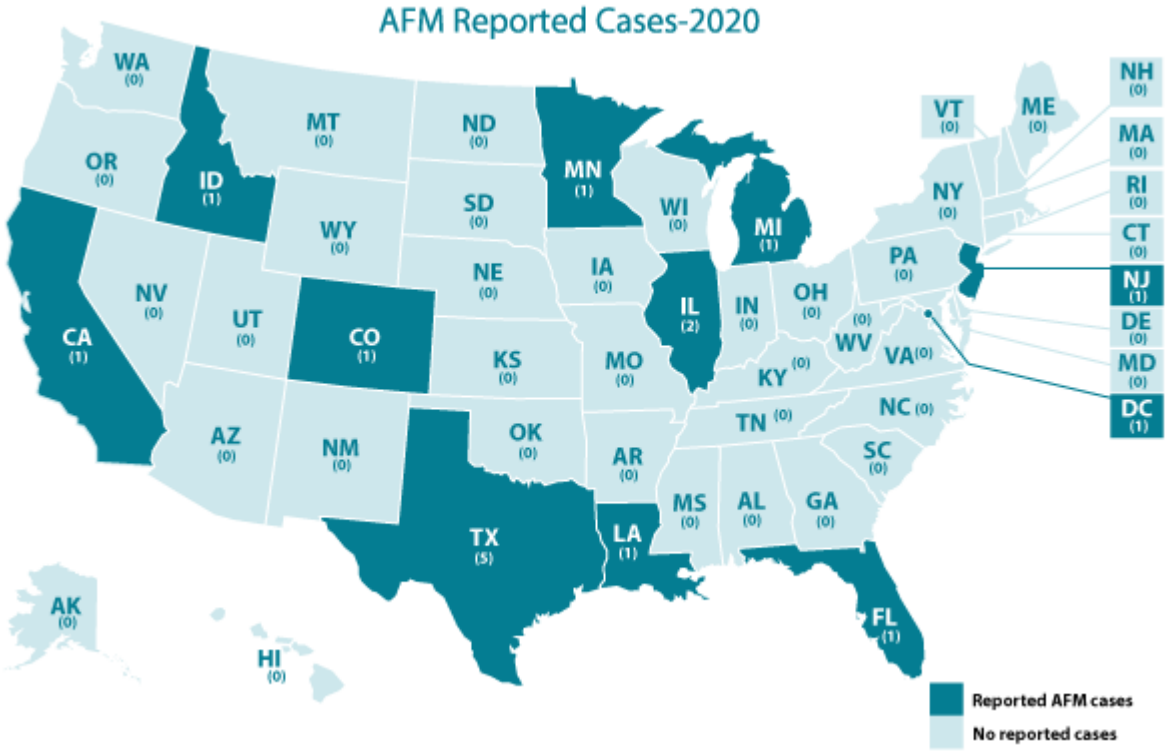
- Adenovirus outbreak occurred in NJ
  - >24 severe illnesses and 11 deaths
  - Children with compromised immune systems
- University of Maryland
  - Freshman death
- University of Wisconsin

Acute Flaccid Myelitis (AFM)



Source: https://www.cdc.gov/acute-flaccid-myelitis/cases-in-us.html

Acute Flacid Myelits (AFM)



Source: https://www.cdc.gov/acute-flaccid-myelitis/cases-in-us.html

Virus Activity Resources

Wisconsin

- Bi-weekly Laboratory Surveillance Report

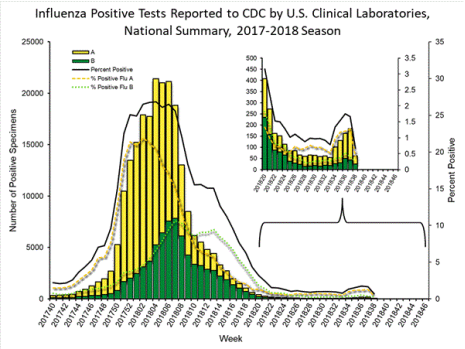
  Subscribe at: wcln@slh.wisc.edu

- Virus Activity Graphs

  http://www.slh.wisc.edu/wcln-surveillance/surveillance/virology-surveillance/

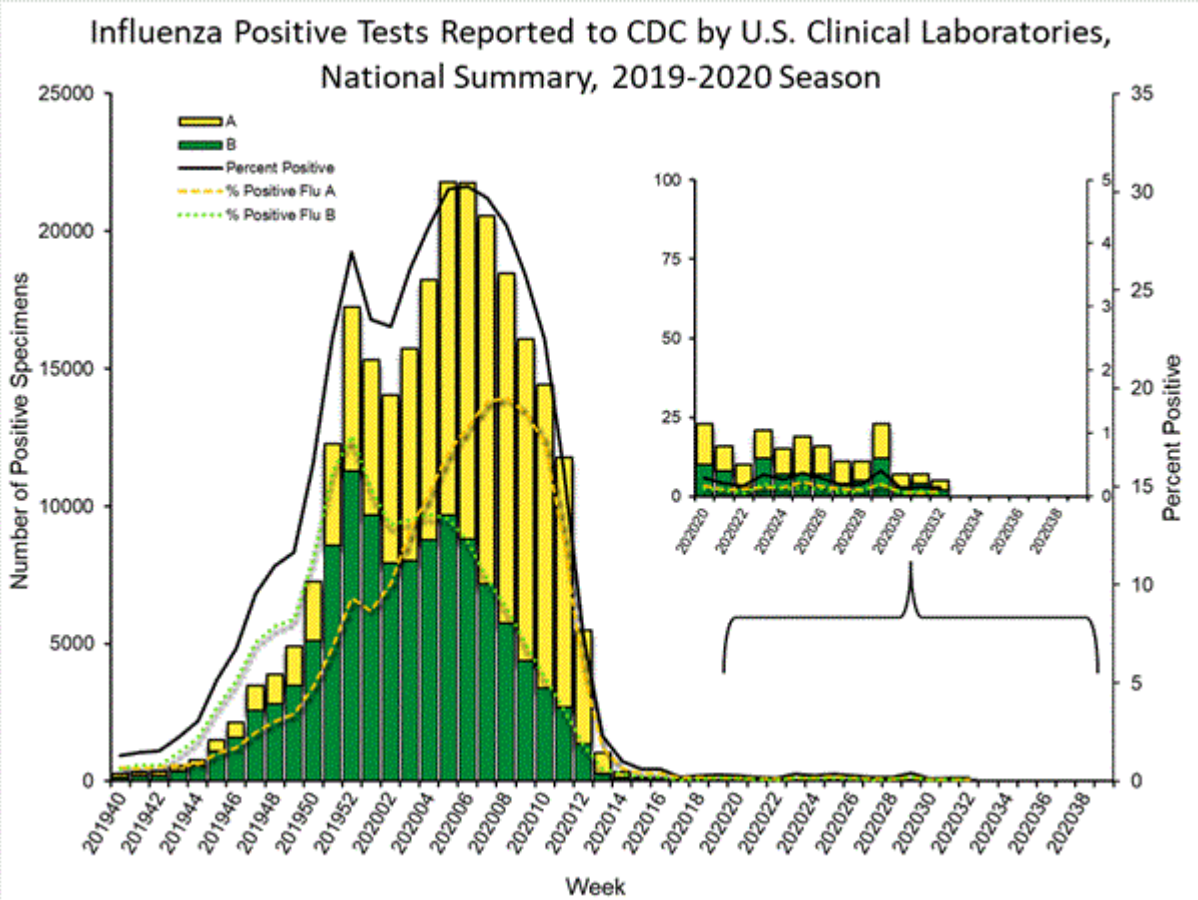
National

- FluView (CDC)
- COVID View (CDC) NEW!
- NREVSS (CDC)



Influenza and non-influenza virus respiratory surveillance

Early……
Influenza season, 2020-2021

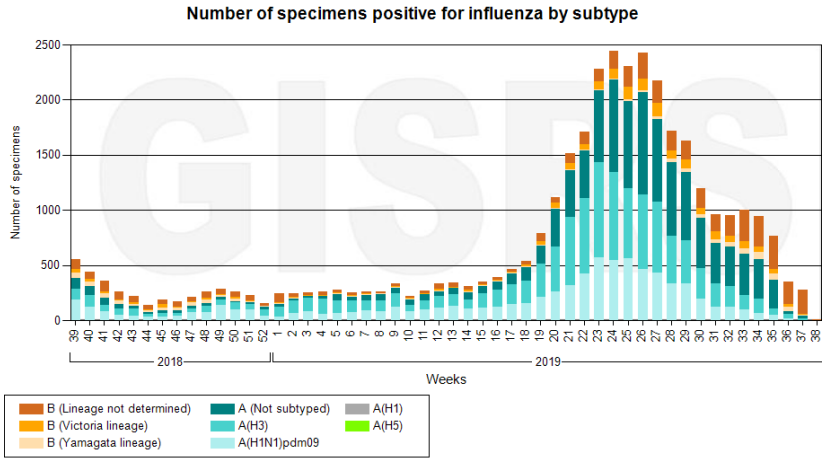


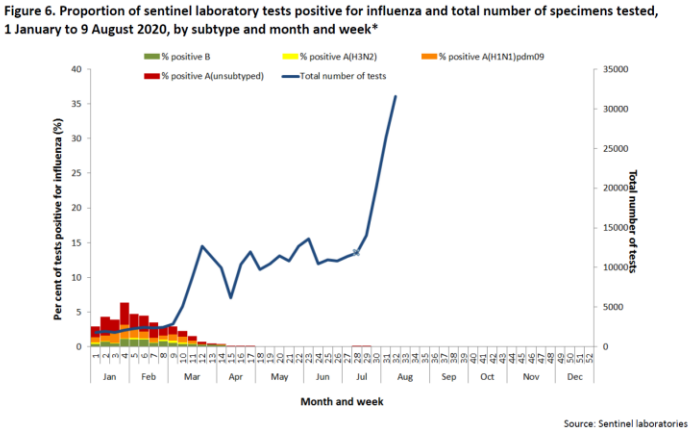
Source: https://www.cdc.gov/flu/weekly/index.htm

WHO Global Influenza Surveillance and Response System (GISRS)—

https://apps.who.int/flumart/Default?ReportNo=5&Hemisphere=Southern

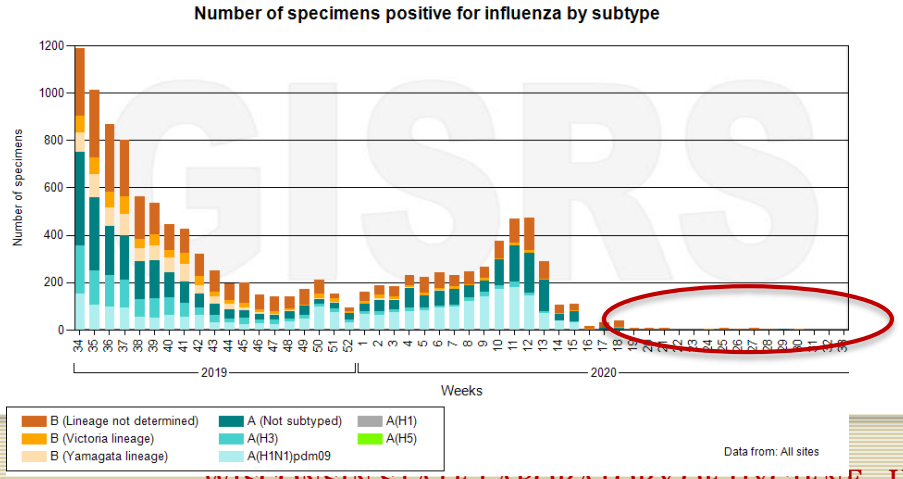
Southern hemisphere, 2019





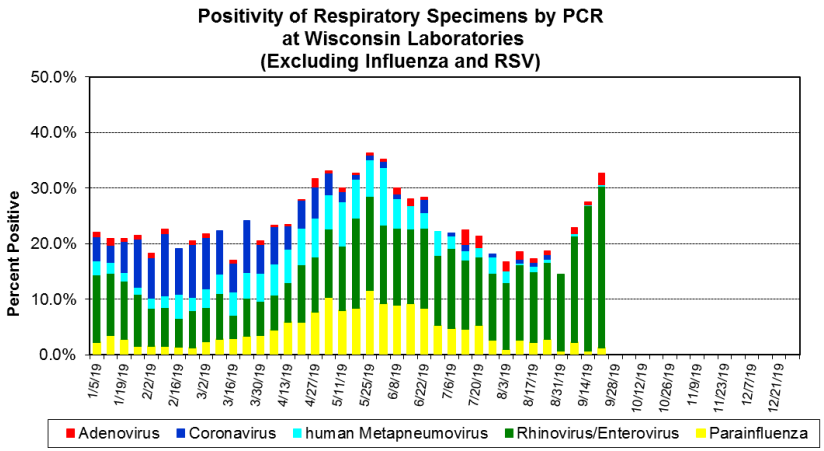
Source: Australian Influenza Surveillance Report No. 9 (2020)

Southern hemisphere, 2020

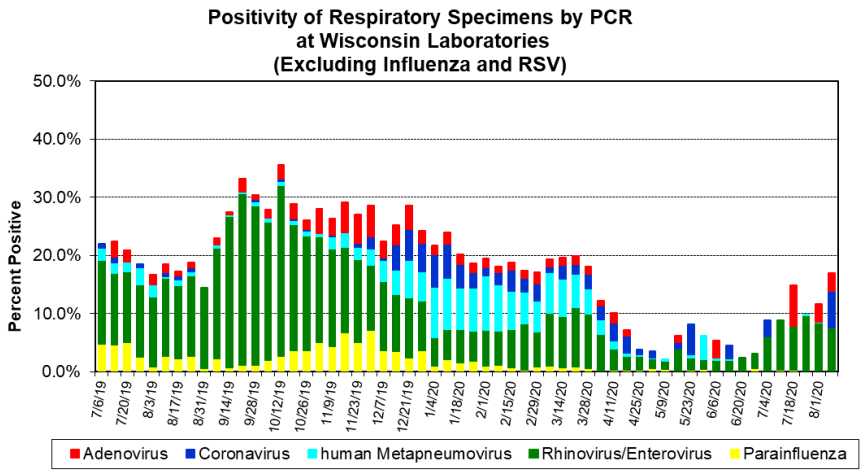


Current Seasonal Respiratory Virus Activity, Wisconsin

2019

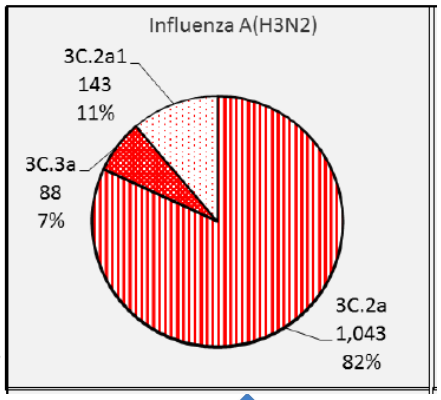


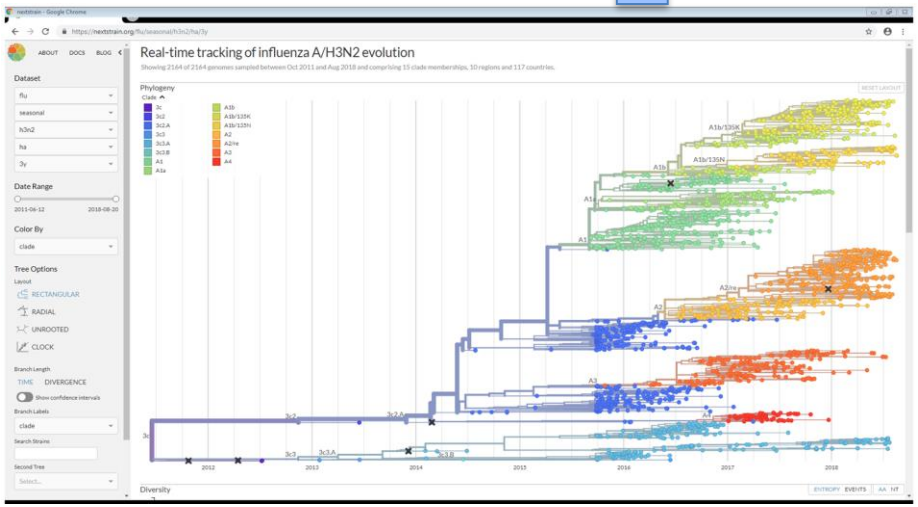
2020



Why is influenza surveillance important?

- Provide specimen/ isolates to characterize and inform vaccine strain selection
- Situational awareness
- Antiviral resistance testing
- Detect novel viruses with pandemic potential





Respiratory Pathogen Surveillance

2020-2021 Season

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 CVV.

Influenza Surveillance in Wisconsin

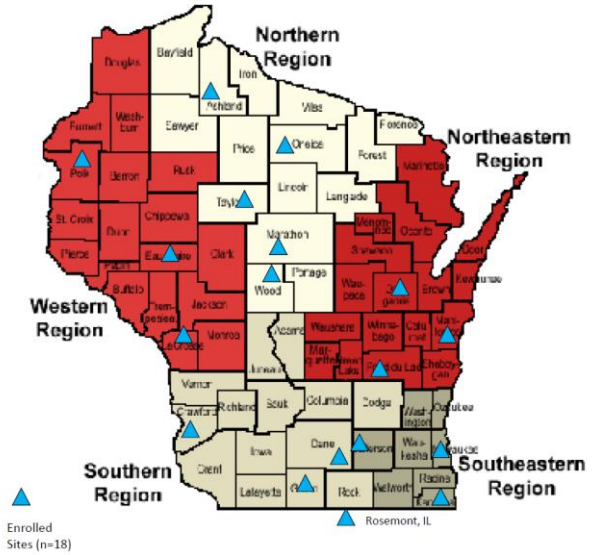
Multi-element approach

1. 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.

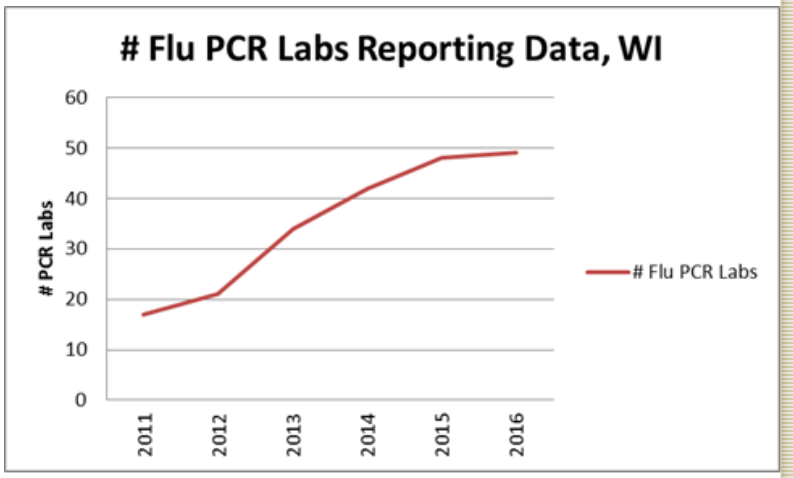


Request to continue to submit the first 2 or 3 specimens per week from symptomatic patients with influenza test requests to WSLH.

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 *number positive* and the *number tested* 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 up to 3 specimens per week for respiratory pathogen testing and characterization.

Laboratory-based Surveillance

All Clinical Laboratories performing influenza diagnostic testing send positives

After activity increases:

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

Summary of Surveillance Activities

PCR Labs & RIDT Sites

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

Enrolled Regional Surveillance & Student Health 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.

WSLH has Influenza Surveillance Supplies!!

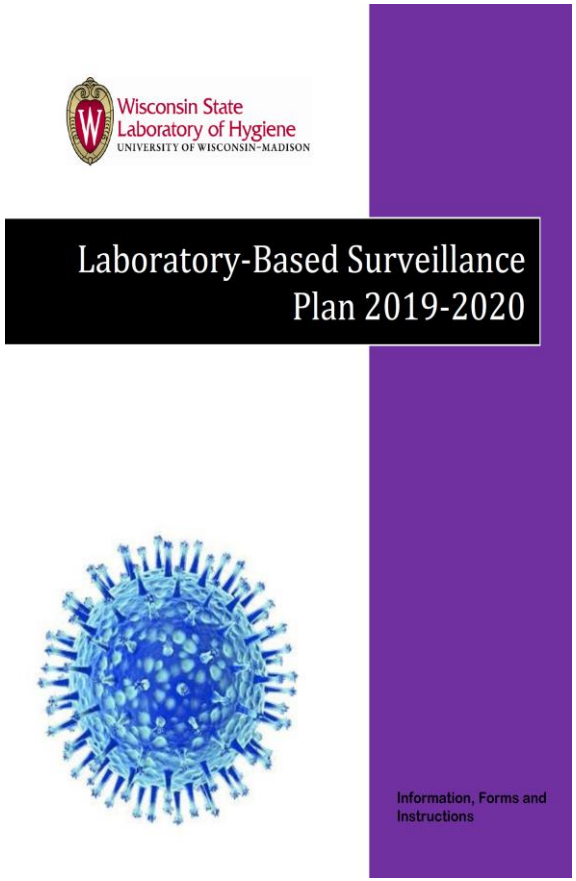
- Specimen collection supplies
  - VTM and swabs
- Shipping supplies
  - Insulated shippers
  - Cold packs
- Specimen submission forms

Contact our Clinical Orders Department at

800-862-1088

Laboratory-based Surveillance Plan

- Detailed instructions
- Description of surveillance requests other than influenza
- Web-based reporting instructions
- SARS-CoV-2 testing criteria



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.

WSLH Surveillance Coordinators

Erik Reisdorf
Virology Lab-Team Lead
erik.reisdorf@slh.wisc.edu

Mary Wedig
Electronic Reporting Coordinator
mary.wedig@slh.wisc.edu

P: 1-800-862-1013