Influenza and other Respiratory Viruses Update--2019

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and

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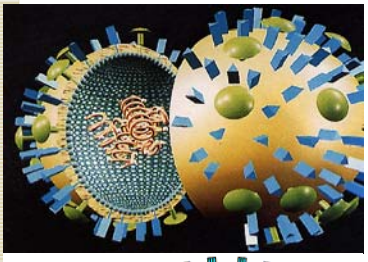
Learning Objectives

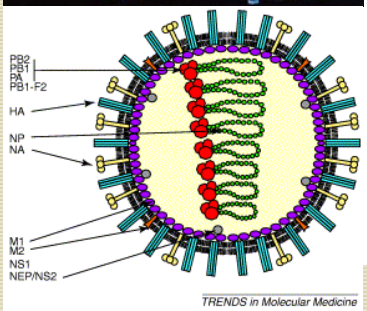
- Review of influenza basics.
- Review of the 2018-2019 influenza season.
- Influenza vaccine updates.
- Review the impact of the FDA reclassification in Wisconsin.
- Describe why specimens and testing data is vital for public health programs.
- Discuss surveillance strategy for 2019-2020.

Influenza
The latest information

www.cdc.gov/flu/index.htm

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**

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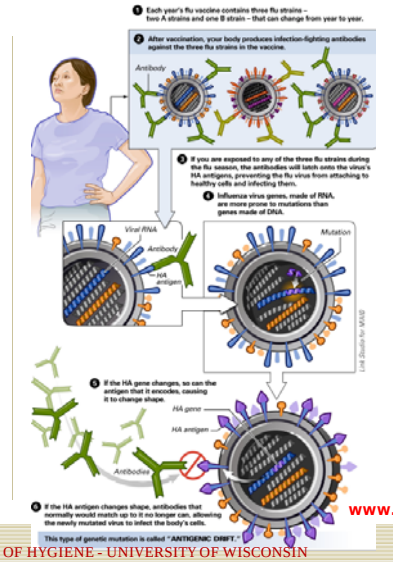
The Changeability of Influenza

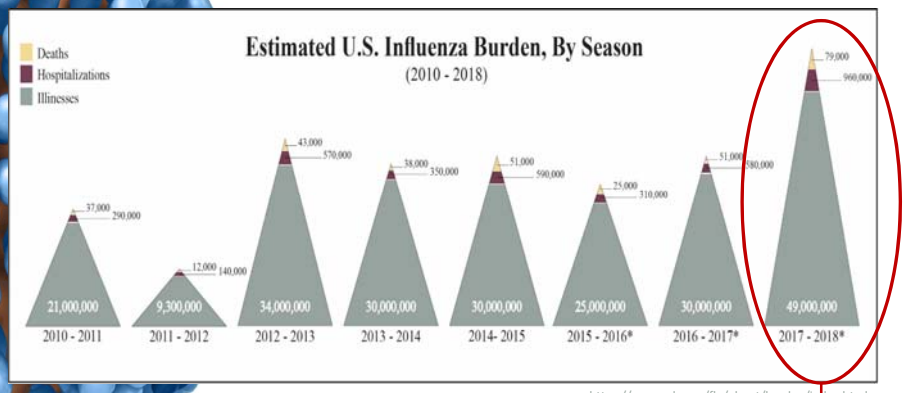
Antigenic Drift → Seasonal Influenza

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

Estimated Influenza Disease Burden, by Season United States, 2010-11 through 2017-18 Influenza Seasons



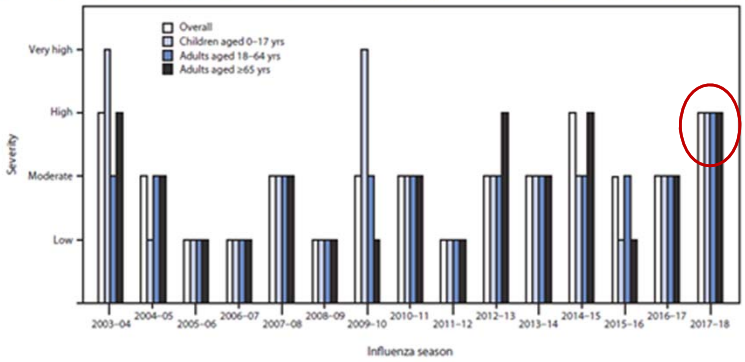
https://www.cdc.gov/flu/about/burden/index.html

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

Historically Severe Year!

Influenza in the U.S. :2003-18
Overall Influenza Season Severity

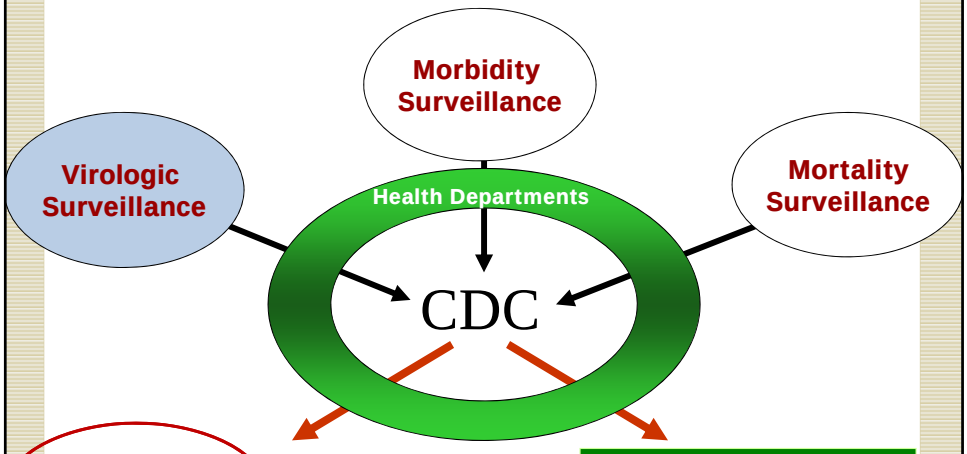
FIGURE 3. Influenza season severity classification,* by age group and season — United States, 2003–04 through 2017–18 seasons†



* 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



Influenza Virologic Surveillance

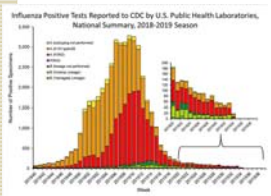
How we monitor the virus

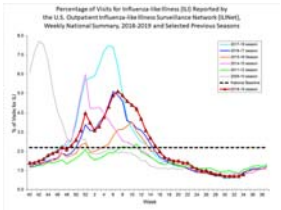
- Provide situational awareness
  - **Clinical lab testing data** → (Via PHL or directly) **CDC**
- **Detect novel or reassortant viruses**
- Inform vaccine strain selection
- Detect and monitor antiviral resistance
  - **Specimens / isolates from clinical labs** → **PHL → NIRC → CDC**

FLUVIEW
A Weekly Influenza Surveillance Report Prepared by the Influenza Division

The 2018-19 Influenza Epidemic

Key Virologic and Epidemiologic Indicators





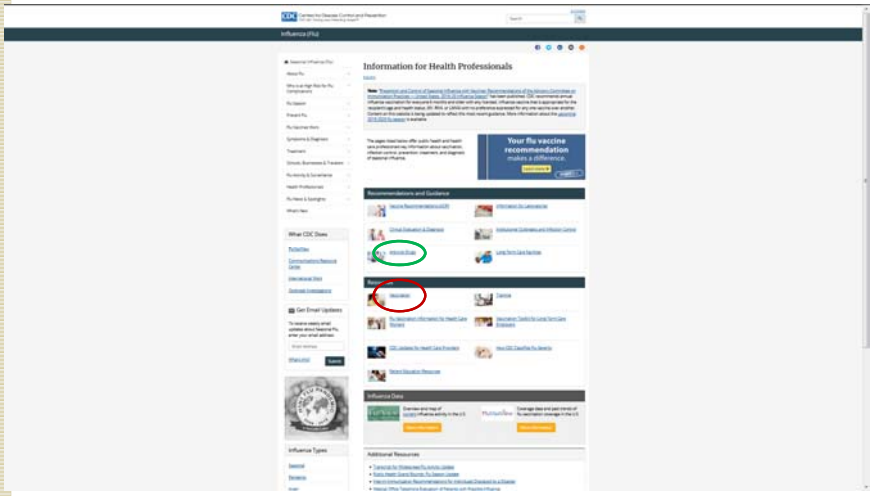
CDC estimates that, from **October 1, 2018**, through **May 4, 2019**, there have been:

37.4 million – 42.9 million flu illnesses	17.3 million – 20.1 million flu medical visits
531,000 – 647,000 flu hospitalizations	36,400 – 61,200 flu deaths

NOTE: This is the last week in-season burden estimates will be provided. CDC's active surveillance for laboratory-confirmed hospitalizations for the 2018-2019 season concluded on April 30, 2018.

Influenza – Prevention and Treatment

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



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Seasonal Influenza

Antivirals

- **Adamantanes (Amantadine & Rimantadine)**
  - No longer effective against influenza type A,
- **Neuraminidase inhibitors**
  [Tamiflu & Zanamivir; Peramivir(i.v.)]
  - Effective against influenza subtypes A and B
  - Both oral, inhalant and i.v. preparations available
    - Differ in age ranges, routes of administration, costs, and adverse events
  - Development of complete resistance by former seasonal H1N1; pdmH1N1 and H3N2 remains susceptible
- **Baloxavir marboxil**

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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
    - 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

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Influenza 2018-19

What was expected…

- **A/Singapore/INFMH-16-0019/2016 A(H3N2)-like**
- A/Michigan/45/2015 A(H1N1)pdm09-like
- B/Phuket/3073/2013-like (B/Yamagata-lineage)
- B/Colorado/06/2017-like (B/Victoria-lineage)

… but a different H3N2 virus snuck in to give our late season H3N2 peak …

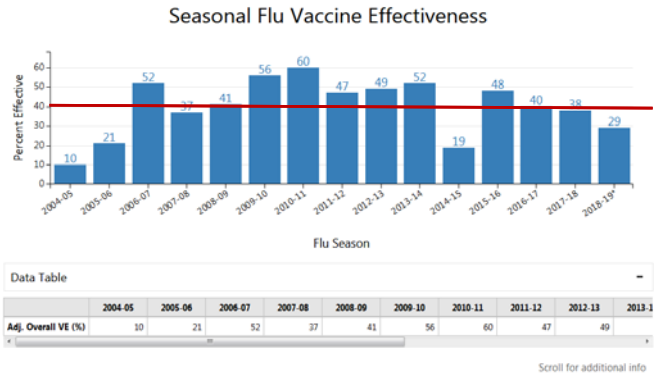
Influenza Vaccine 2019-20

- 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)

Seasonal Influenza Vaccines

How effective?

http://www.cdc.gov/flu/professionals/vaccination/effectiveness-studies.htm



However:

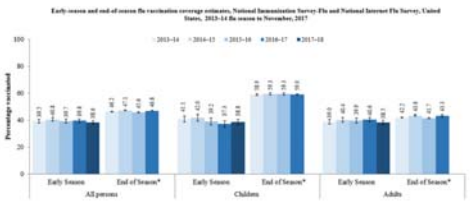
- **Prevents office visits**
- **Prevent hospitalization**
- **Prevents death**

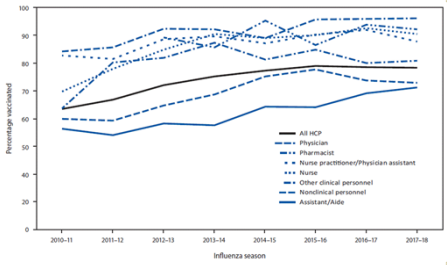
VE= percent reduction of frequency of flu among vaccinated people compared to unvaccinated people

Vaccination Rates---2013-2018

General Population and Healthcare Personnel

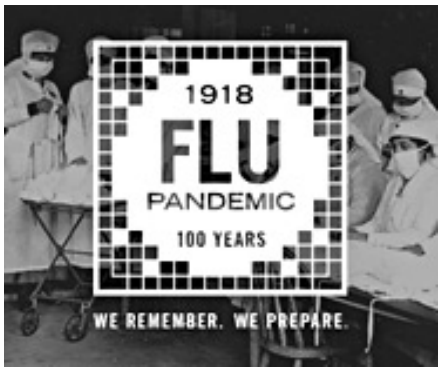
http://www.cdc.gov/flu/professionals/vaccination/





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

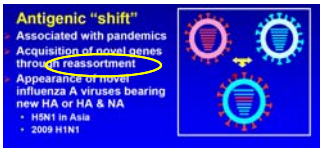
Influenza A
- H1 - H16*
- N1 – N9*

*Bats – H17/18, N10/11

The Changeability of Influenza

Antigenic Shift → Pandemic Influenza

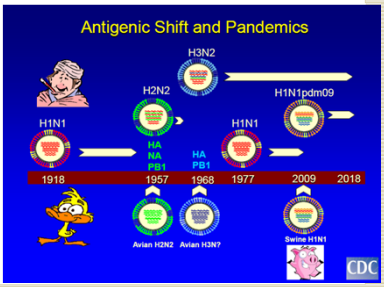
www.cdc.gov/flu



Pandemic Influenza

Replication in Humans

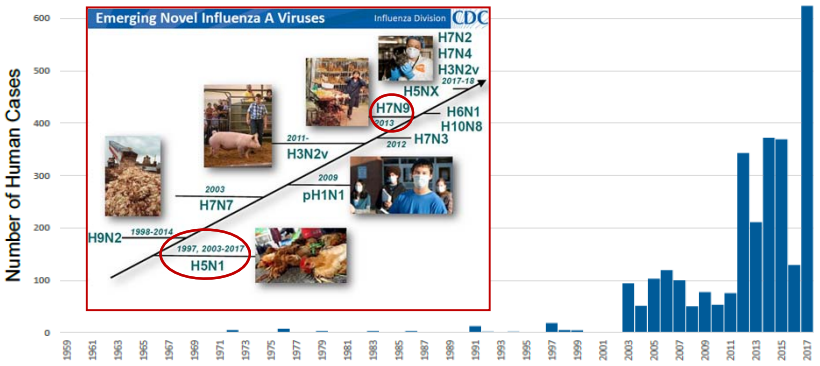
Efficient and sustained human-to-human transmission



Novel Influenza Infection Reports are Increasing

Human Cases of Reported Novel Influenza A Infection, 1959-2017

Includes Avian H4, H5, H6, H7, H9, H10 & Swine H1, H3 (not H1N1pdm09)



Year of Onset 1959 to 2017

>30 fold increase from 1990's to 2000's

Freidl, Meijer, deBruin et al Euro Surveill 2014; Cumulative case counts of H5N1 from WHO and Chinese provincial reports

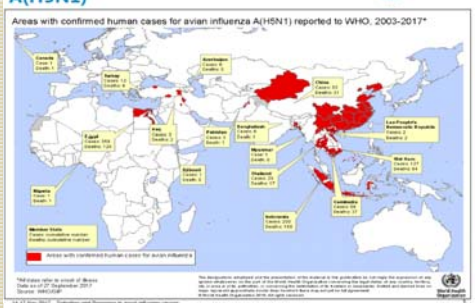
Influenza Division CDC

Defining Event in 2003

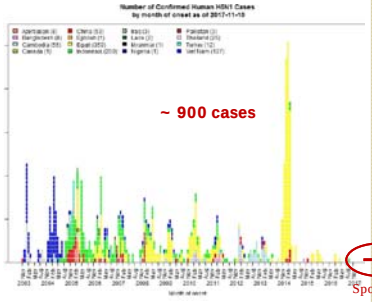
Concerns with Pandemic Influenza

Current zoonotic influenza situation A(H5N1)

World Health Organization

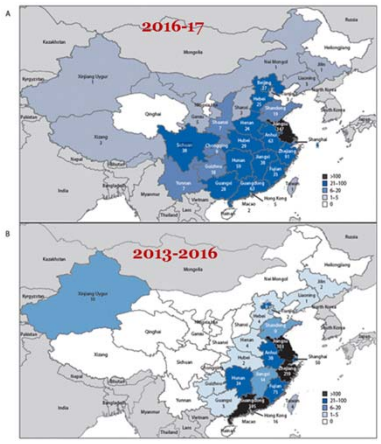


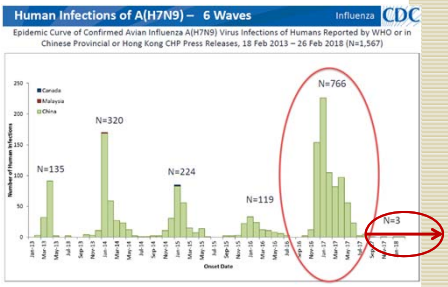
The emergence of Influenza A H5N1



Sporadic cases

Influenza A H7N9
The latest global concern





~ 1600 cases over 5 seasons

Pandemic Influenza:
Public Health's Ongoing Concern

The recipe:

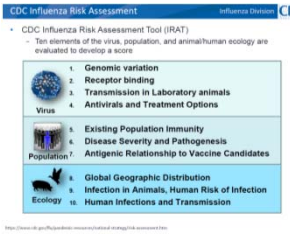
- **Novel influenza A subtype** emerges in humans
- **Virus causes disease** in humans
- **Easily transmitted human-to-human**

A Global Tool for Pandemic Preparedness

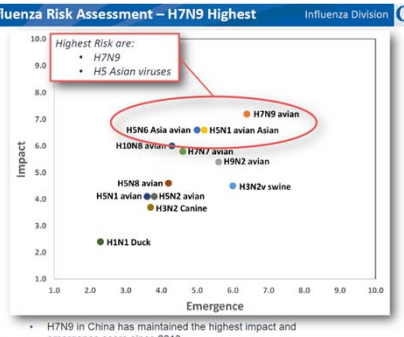
Influenza Risk Assessment Tool - IRAT Influenza CDC

- 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



Influenza Risk Assessment – H7N9 Highest Influenza Division CDC



- H7N9 in China has maintained the highest impact and emergence score since 2013

CDC. http://www.cdc.gov/flu/pandemic-resources/monitoring/irat-virus-summaries.htm

Updates on Lab Testing: RIDT

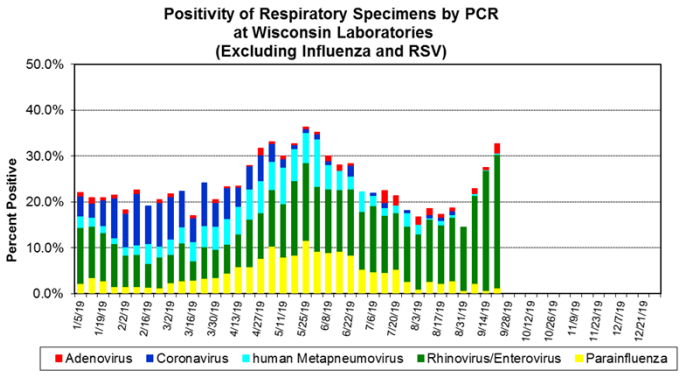
Impact of the FDA Reclassification of RIDTs in WI

- The WSLH collects detailed clinical laboratory testing information on the specimen submission forms that accompany specimens submitted.
- The WSLH RT-PCR results were compared to those provided by the clinical laboratories to assess the "real world" performance characteristics at multiple clinical laboratories pre and post FDA reclassification.

Reclassification Impact

- *Decreasing* the number of RIDTs that were used to primarily two manufacturers.
- The overall performance of the RIDTs assessed by the percent discordant results trended lower, but remained near 10% over the four influenza seasons that were analyzed (pre and post reclassification).
- *Highest* discordant rate from the past three influenza seasons was a rapid molecular assay
- The number of RIDTs performed are similar from year to year.

Current Seasonal Respiratory Virus Activity, WI 2019



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

Virus Activity Resources

Wisconsin

- Bi-weekly Laboratory Surveillance Report

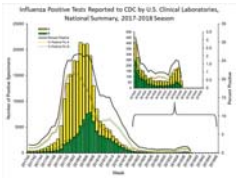
  Subscribe at: wcln@slh.wisc.edu

- Virus Activity Graphs

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

National

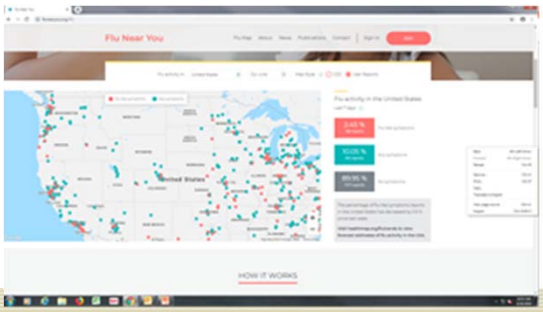
- FluView (CDC)
- NREVSS (CDC)



WISCONSIN STATE LABORATORY OF HYGIENE - UNIVERSITY OF WISCONSIN

Flu Near You!

- Joint research venture.
- Utilizes crowdsourcing data to compile estimates.
- Based on symptom self reporting online
- Anyone can report!



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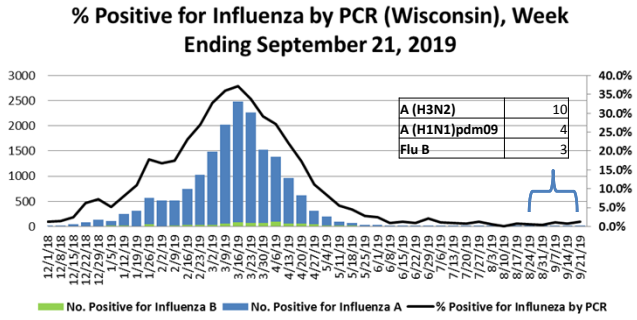
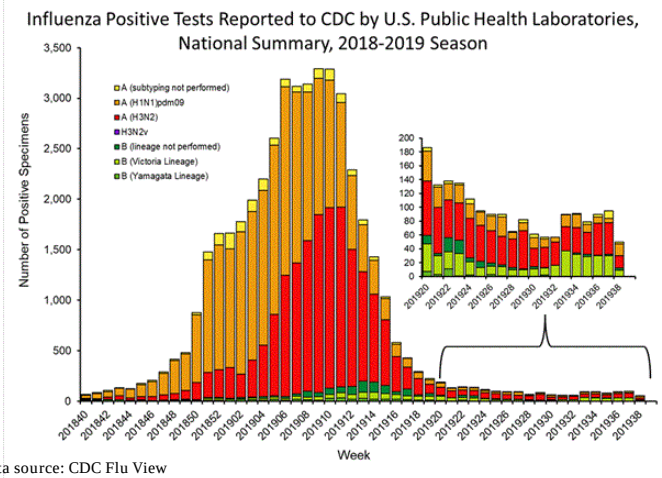
Influenza and non-influenza virus respiratory surveillance

Early..... Influenza season, 2019-2020



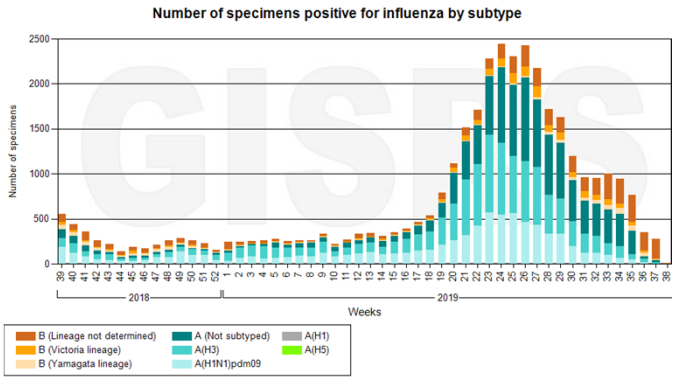
Early.....
Influenza season, 2019-2020



Data source: CDC Flu View

WHO Global Influenza Surveillance and Response System (GISRS)—

Southern hemisphere, 2019

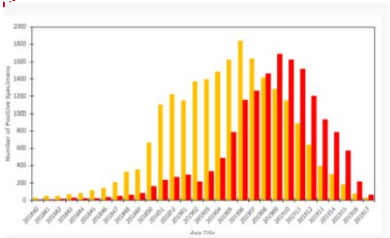


Influenza Severity, Southern Hemisphere

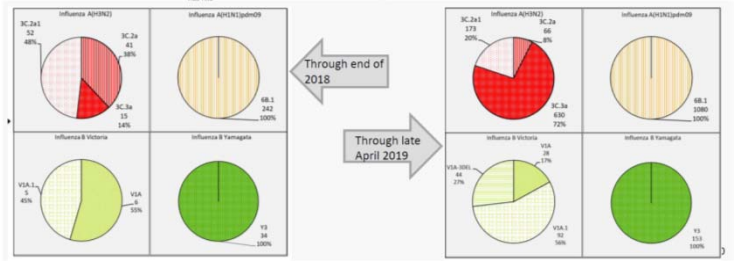
- Clinical severity was low.
- The number of deaths was low.
- VE was expected to be 40-60%

Data source: Dept. of Health, Australia https://www1.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-ozflu-flucurr.htm#current

If you have seen one influenza season, you have seen one influenza season!



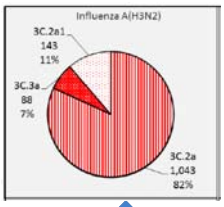
H1N1 pdm09 → H3N2

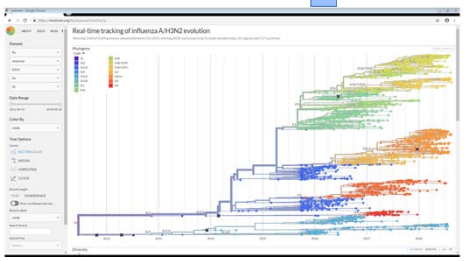


Graphs: Lynette Brammer, CDC

What do we do with the specimens submitted?

- Subtype characterization
- Whole genome sequencing
  - 3c.2a, 3c.2a1, 3c.3a
- Provide specimen/ isolates to CDC
- Provide weekly summaries
- Antiviral resistance testing





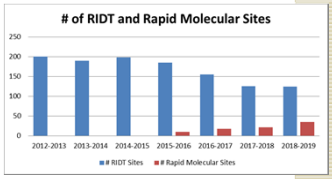
Respiratory Pathogen Surveillance

2019-2020 Season

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 (June to November).
   - Please notify WSLH of suspected performance issues (e.g. False positives/negatives)



WSLH can provide confirmatory testing for the first positive influenza specimen of the season.

Influenza Surveillance in Wisconsin

Multi-element approach

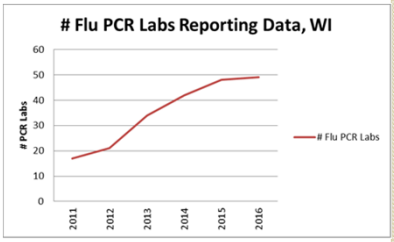
2. Enrolled Surveillance Sites
   - 17 labs in 5 public health regions.
   - Provide randomized specimens weekly.
   - Provided a "blue" specimen submission form.

Request to continue to submit the first 1-2 specimens per week 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.
   - **Do NOT need to send 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
   - Concern with severe adenovirus infections.
   - Monitor and type adenoviruses 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

All Labs:
- Send those with international travel histories
- *Up to one* influenza-related hospitalization per week
- Unusual presentations/results
- Contact with swine/ sick or dead poultry
- Antiviral treatment failure

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NRVESS Reporting

NREVSS was created in the 1980s to monitor seasonal trends in influenza and respiratory syncytial virus (RSV). In 2007, data collection for rhinovirus, enterovirus, and human metapneumovirus began.
https://www.cdc.gov/surveillance/nrevss/index.html

- It is no longer necessary for labs to report testing data to the National Respiratory and Enteric Virus Surveillance System (NRVESS).
- The WSLH is now reporting this data electronically to NREVSS for all labs in Wisconsin that report to WSLH.

Summary of Surveillance Activities

RIDT Sites

- Confirm the first influenza positive specimen if needed.

Hospitalized Patients

- Limit to one specimen per week

Enrolled Regional Surveillance Sites

- Send the first 1 to 2 specimens/week

Student Health

- 3 specimen/week

All labs: Please continue to send all out-of-season positive influenza A specimens (e.g. June-September).

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

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