



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

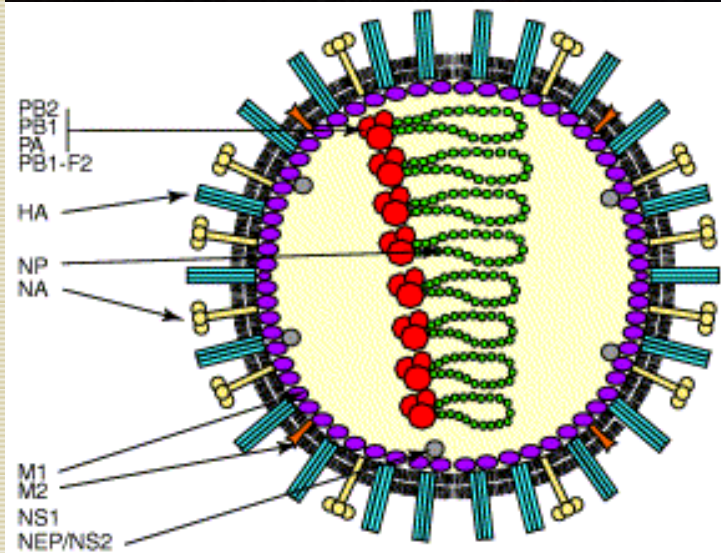
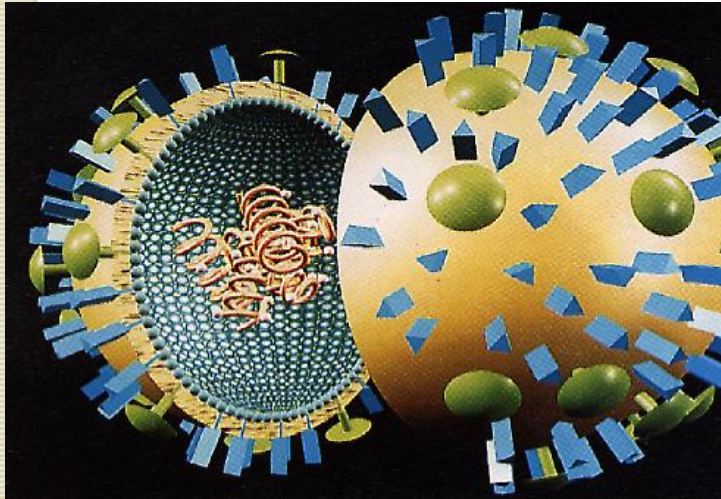
www.cdc.gov/flu/index.htm

The screenshot shows the CDC website for Influenza (Flu). At the top, it features the CDC logo and a search bar. The main heading is "Influenza (Flu)". Below this, there is a featured image titled "CDC Kicks Off 2019-2022 Flu Vaccination Campaign" showing two men in white lab coats. To the right of the image is an "Influenza Updates" section with bullet points: "US flu activity is low, but flu season is approaching.", "Now is the time to get a flu vaccine!", "CDC recommends everyone 6 months and older get a flu vaccine by the end of October.", and "Flu vaccination has important benefits:". Below the updates is a "CDC on Flu Vaccine" section with similar bullet points. The main content area is divided into four columns: "Prevent Flu" (with a "Flu Shot" graphic), "Symptoms & Diagnosis" (with a person coughing), "Treatment" (with a person at a doctor's office), and "Flu Activity & Surveillance" (with a map of the US). Below these columns are several utility boxes: "About Flu", "Flu Season", "People at High Risk", "Communication Resource Center", "Health Professionals", "Flu Vaccine Finder", and "Flu News & Spotlights". At the bottom, there are sections for "Other Types of Influenza" (Pandemic, Avian, Swine/Variant, Flu in Animals, Swine Flu, Animal to Human) and "What's New" (with a "More" button).



Influenza Virus Basics

“Changeability is its hallmark”



TRENDS in Molecular Medicine

- 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**

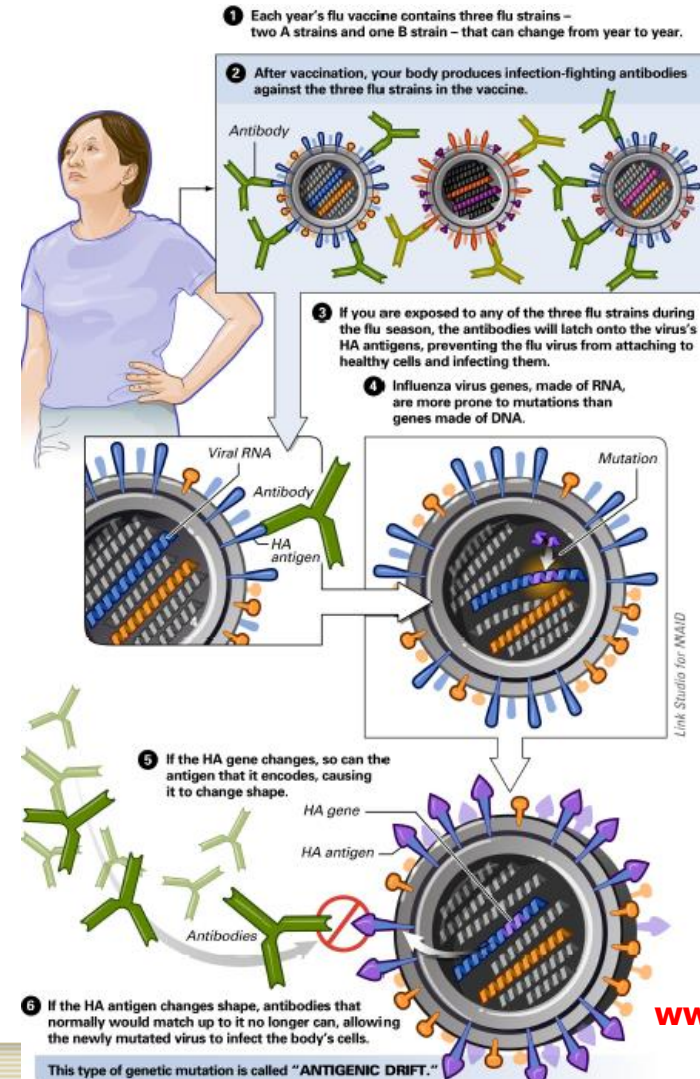


The Changeability of Influenza

Antigenic Drift → *Seasonal Influenza*

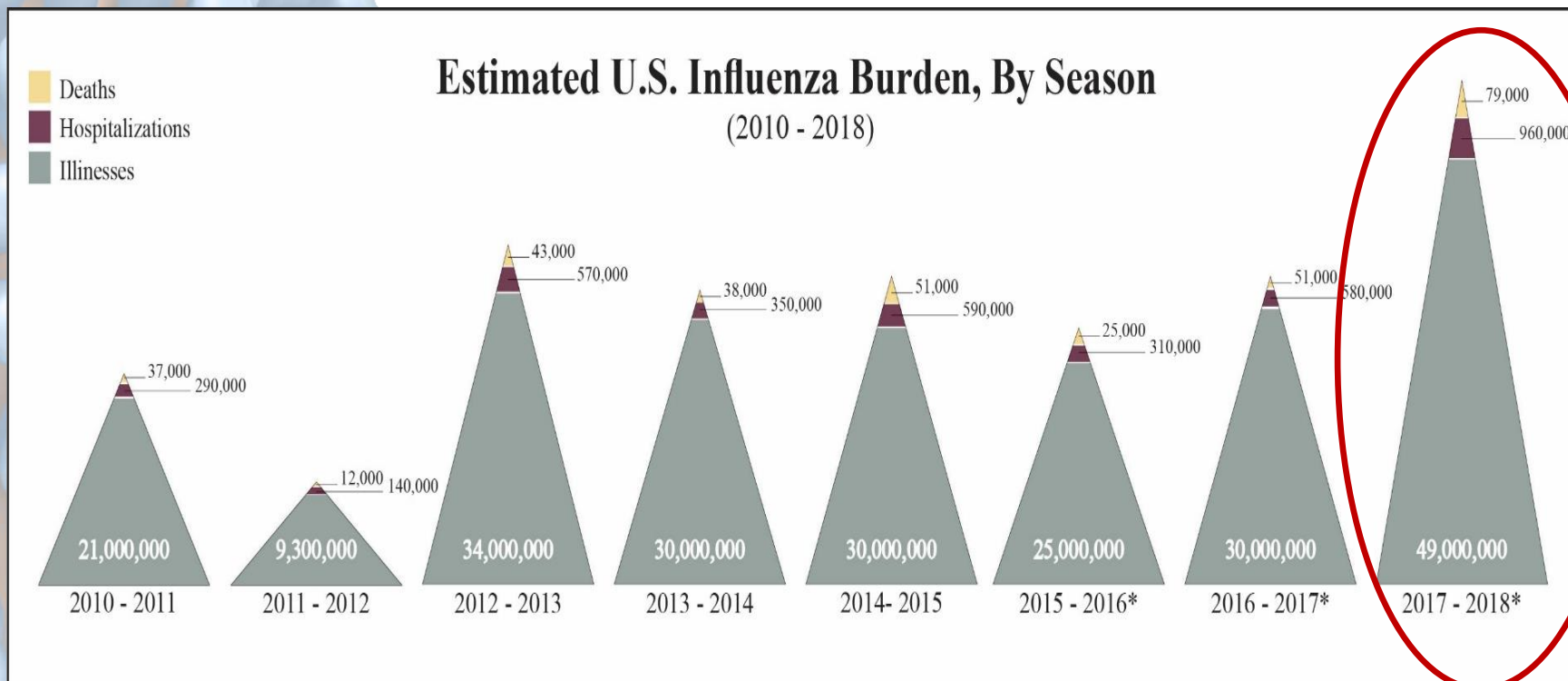
Antigenic Drift

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

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**

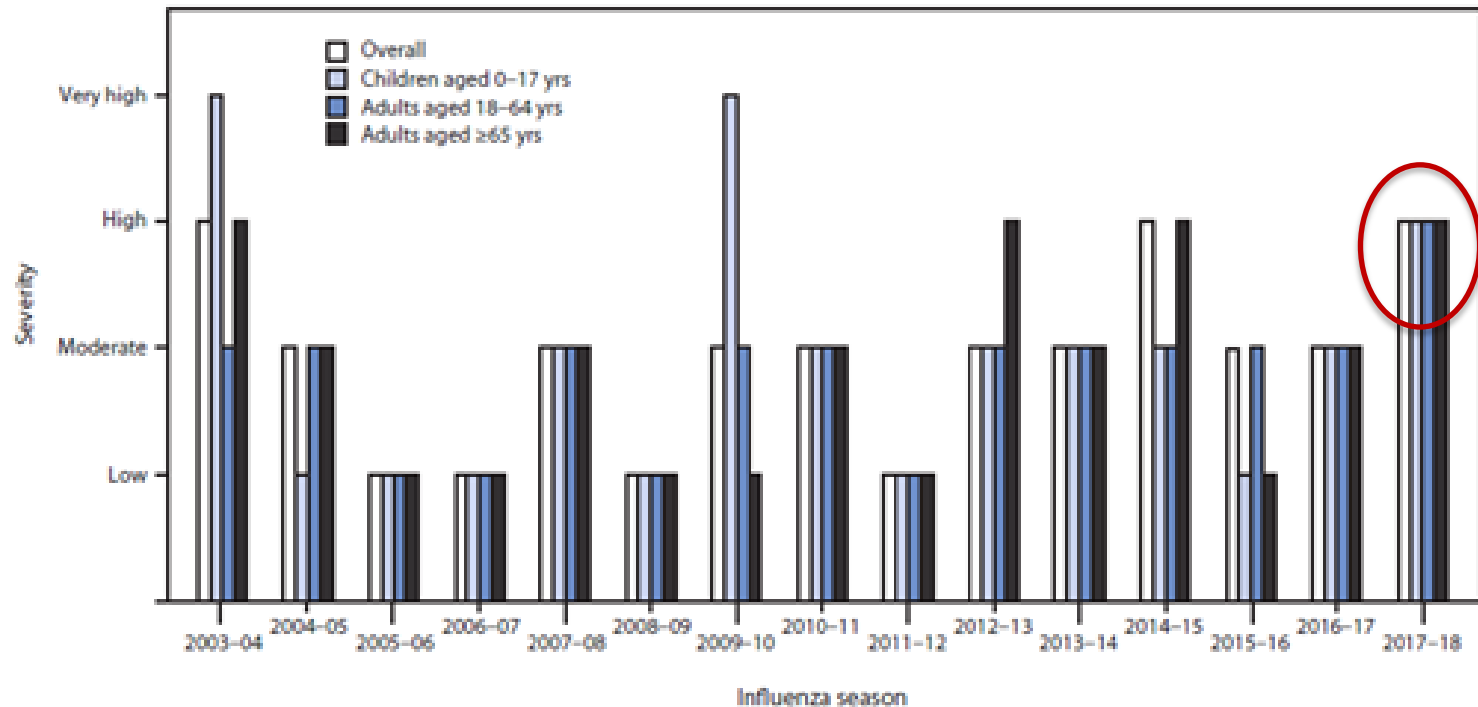
**Historically
Severe
Year!**



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>.

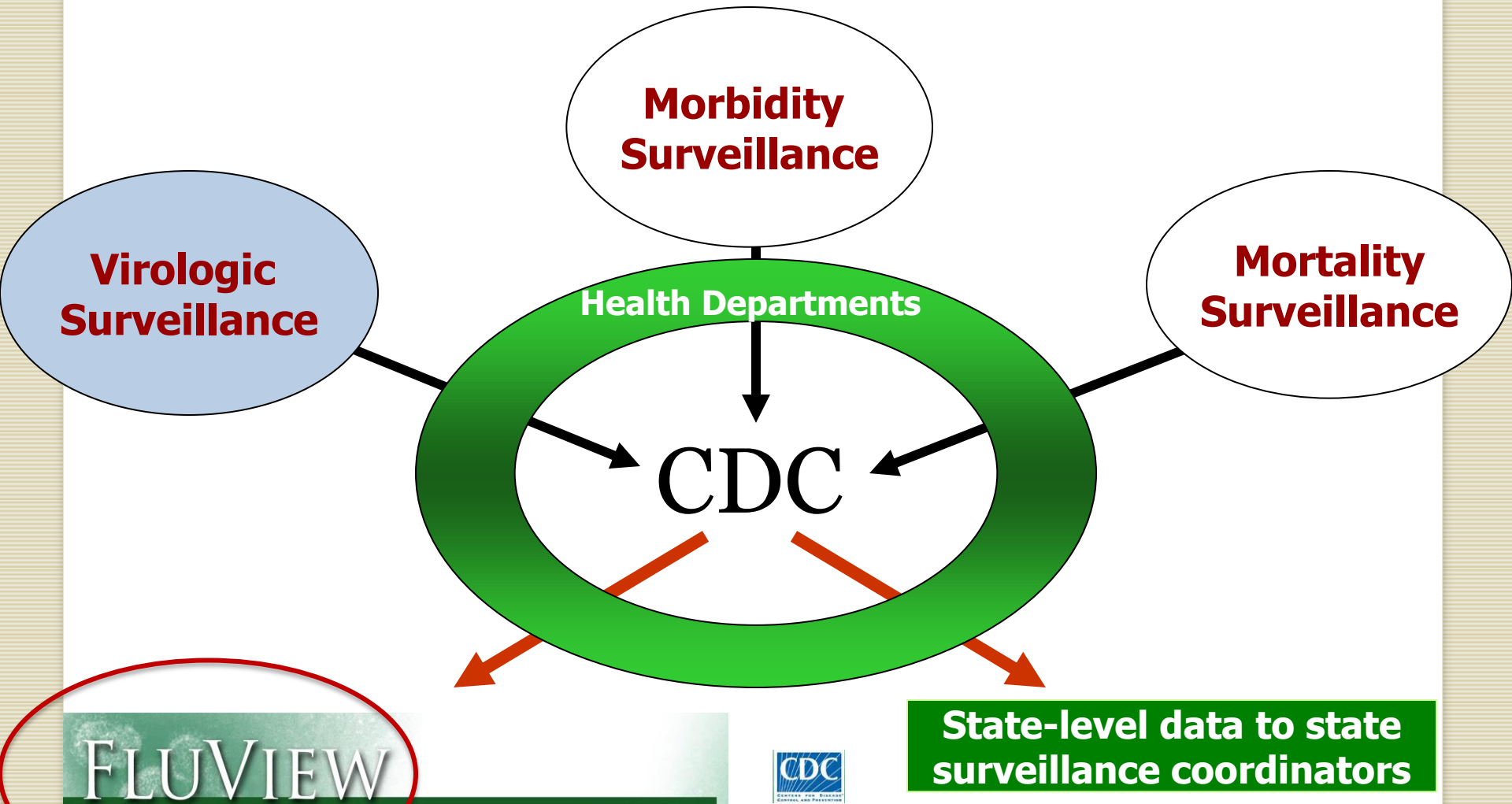
† As of June 1, 2018.

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



U.S. Influenza Surveillance

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



State-level data to state surveillance coordinators



Influenza Virologic Surveillance

How we monitor the virus

- Provide situational awareness

- **Clinical lab testing data** $\xrightarrow{\text{Via PHL or directly}}$ **CDC**

- **Detect novel or reassortant viruses**

- Inform vaccine strain selection

- Detect and monitor antiviral resistance

- **Specimens/isolates from clinical labs** \rightarrow **PHL** \rightarrow **NIRC** \rightarrow **CDC**

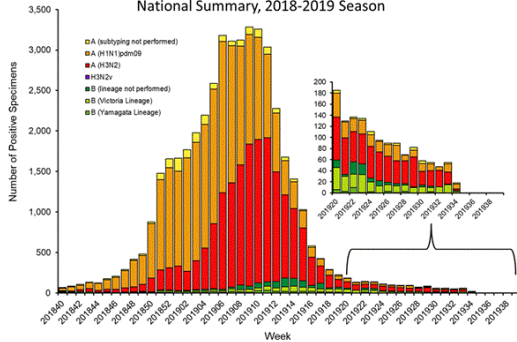




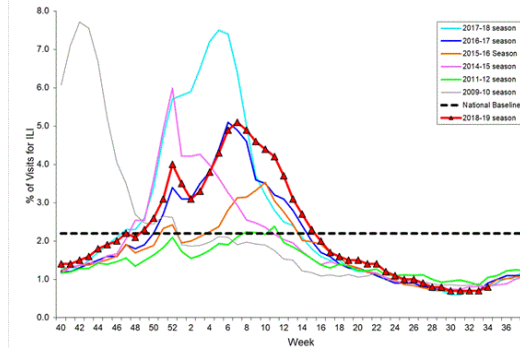
The 2018-19 Influenza Epidemic

Key Virologic and Epidemiologic Indicators

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



Percentage of Visits for Influenza-like Illness (ILI) Reported by the U.S. Outpatient Influenza-like Illness Surveillance Network (ILINet), Weekly National Summary, 2018-2019 and Selected Previous Seasons



FLUVIEW

A Weekly Influenza Surveillance Report Prepared by the Influenza Division
Weekly Influenza Activity Estimates Reported by State and Territorial Epidemiologists*
Week Ending Feb 23, 2019 - Week 8



*This map indicates geographic spread and does not measure the severity of influenza activity.

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>



The screenshot shows the CDC website page for Influenza (Flu) Information for Health Professionals. The page is organized into several sections:

- Seasonal Influenza (Flu)**: A sidebar menu with links to About Flu, Who is at High Risk for Flu Complications, Flu Season, Prevent Flu, Flu Vaccines Work, Symptoms & Diagnosis, Treatment, Schools, Businesses & Travelers, Flu Activity & Surveillance, Health Professionals, Flu News & Spotlights, and What's New.
- What CDC Does**: A section with links to FluNetView, Communications Resource Center, International Work, and Outbreak Investigations.
- Get Email Updates**: A form to receive weekly email updates about Seasonal Flu.
- FluView**: A circular graphic with the text "FLU VIEW 2009 - 2019 A Decade Later".
- Influenza Types**: A section with links to Seasonal, Pandemic, and Avian.
- Information for Health Professionals**: The main content area, featuring a "Note" about the 2019-2020 flu season, a "Your flu vaccine recommendation makes a difference" banner, and a grid of links under "Recommendations and Guidance" and "Resources".
- Recommendations and Guidance**: A grid of links including Vaccine Recommendations (ACIP), Information for Laboratories, Clinical Evaluation & Diagnosis, Institutional Outbreaks and Infection Control, Antiviral Drugs (circled in green), and Long-Term Care Facilities.
- Resources**: A grid of links including Vaccination (circled in red), Training, Flu Vaccination Information for Health Care Workers, Vaccination Toolkit for Long-Term Care Employers, CDC Updates for Health Care Providers, and How CDC Classifies Flu Severity.
- Additional Resources**: A list of links including Transcripts for Widespread Flu Activity Update, Public Health Grand Rounds: Flu Season Update, Interim Immunization Recommendations for Individuals Displaced by a Disaster, and Medical Office Telephone Evaluation of Patients with Possible Influenza.



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**



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



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)

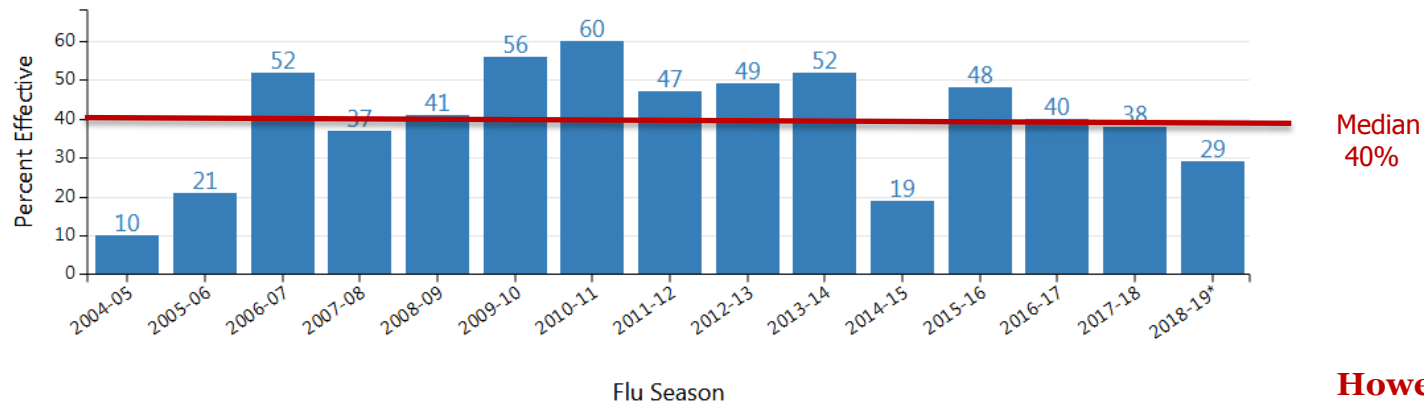


Seasonal Influenza Vaccines

How effective?

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

Seasonal Flu Vaccine Effectiveness



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

Data Table

	2004-05	2005-06	2006-07	2007-08	2008-09	2009-10	2010-11	2011-12	2012-13	2013-14
Adj. Overall VE (%)	10	21	52	37	41	56	60	47	49	52

Scroll for additional info

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

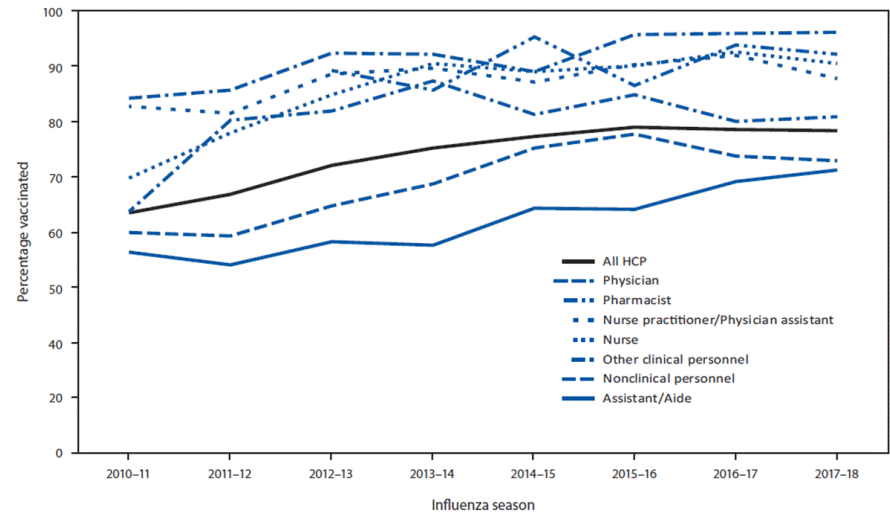
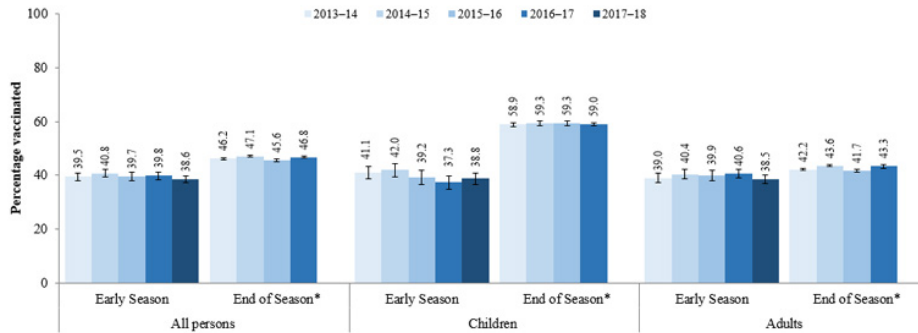


Vaccination Rates---2013-2018

General Population and Healthcare Personnel

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

Early-season and end-of-season flu vaccination coverage estimates, National Immunization Survey-Flu and National Internet Flu Survey, United States, 2013-14 flu season to November, 2017





1918 Influenza Pandemic

100 Year Anniversary of the Great Pandemic



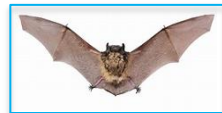
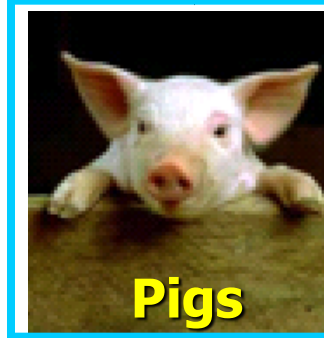
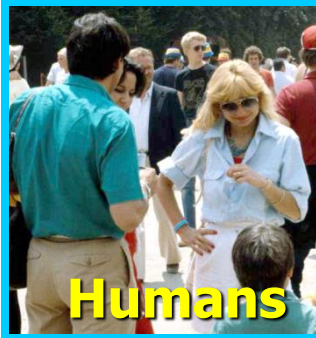
<https://www.cdc.gov/flu/pandemic-resources/index.htm>



Influenza at the Human-Animal Interface

Influenza A

- H1 - H16*
- N1 - N9*



*Bats – H17/18, N10/11





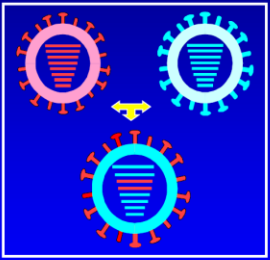
The Changeability of Influenza

Antigenic Shift → *Pandemic Influenza*

www.cdc.gov/flu

Antigenic "shift"

- Associated with pandemics
- Acquisition of novel genes through reassortment
- Appearance of novel influenza A viruses bearing new HA or HA & NA
 - H5N1 in Asia
 - 2009 H1N1

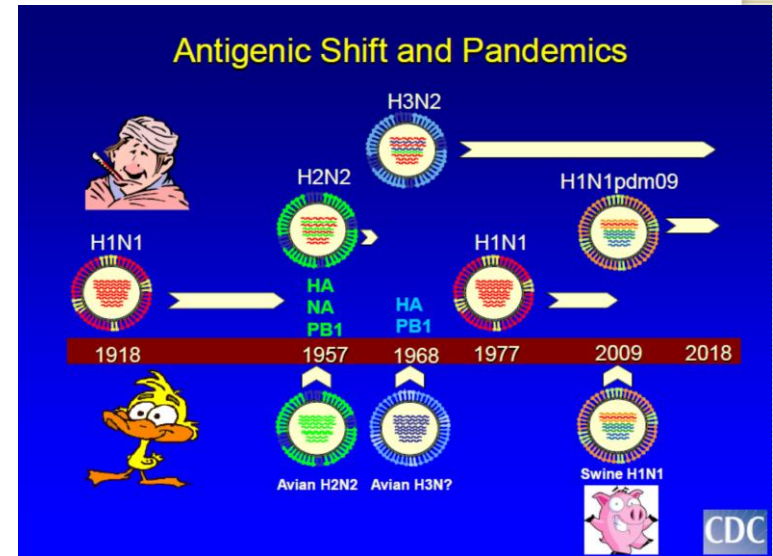


Pandemic Influenza

Replication in Humans



Efficient and sustained human-to-human transmission

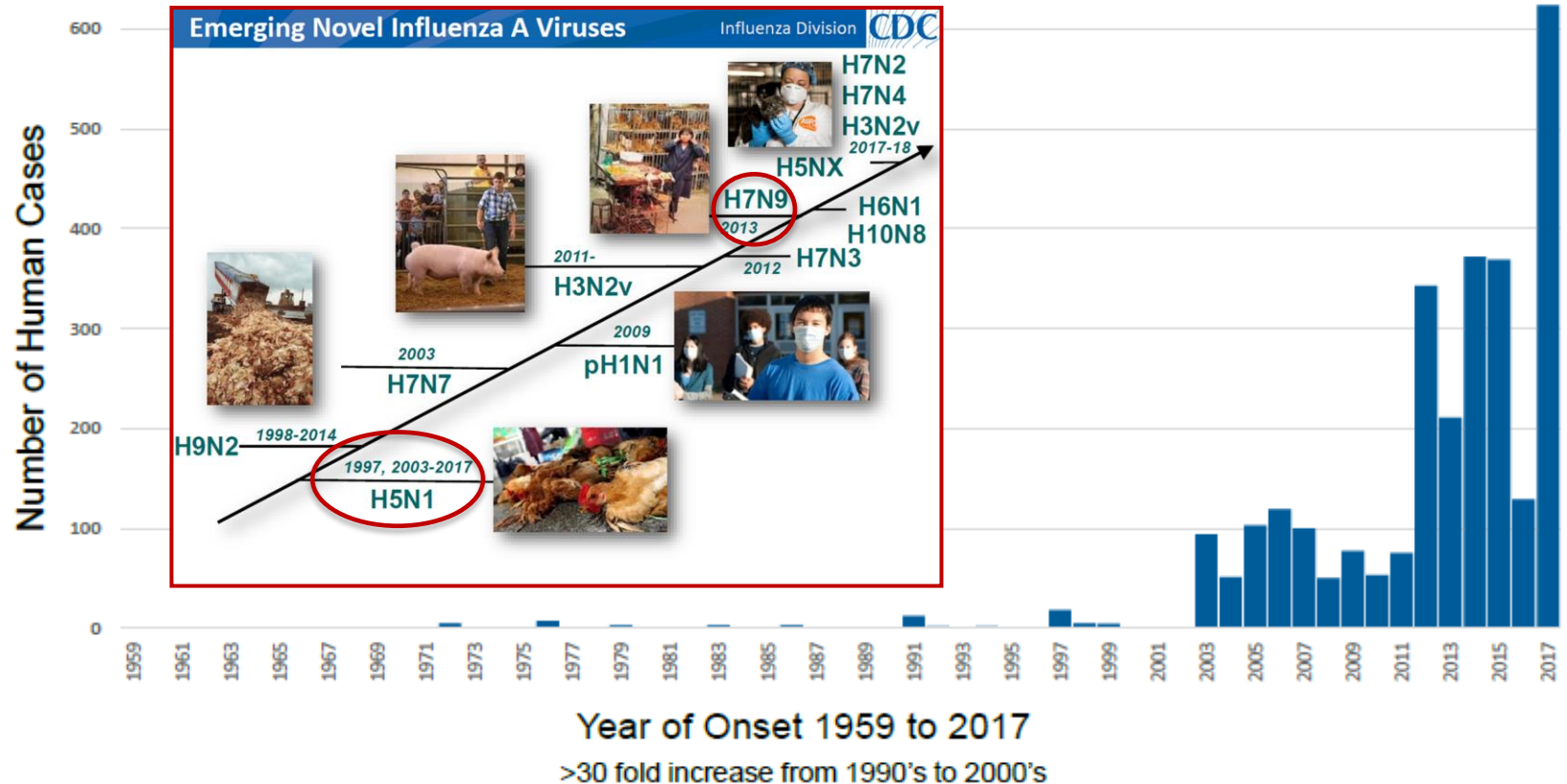




Novel Influenza Infection Reports are Increasing

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

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



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



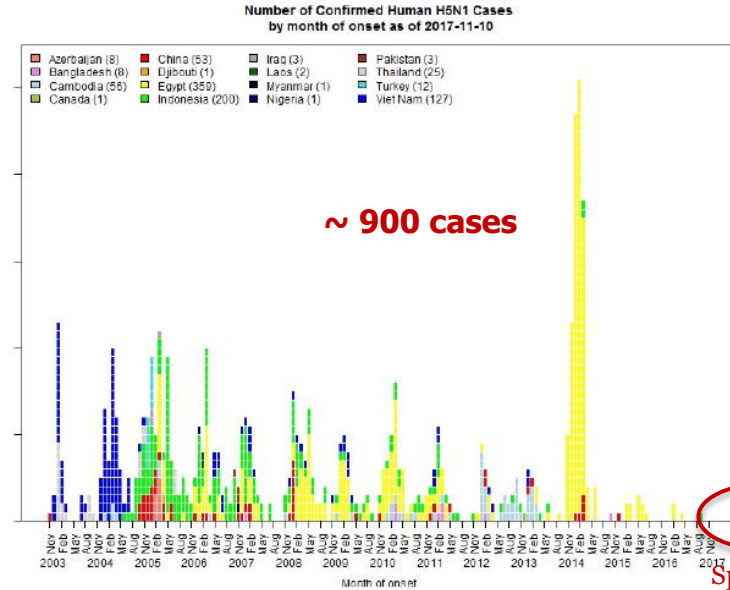
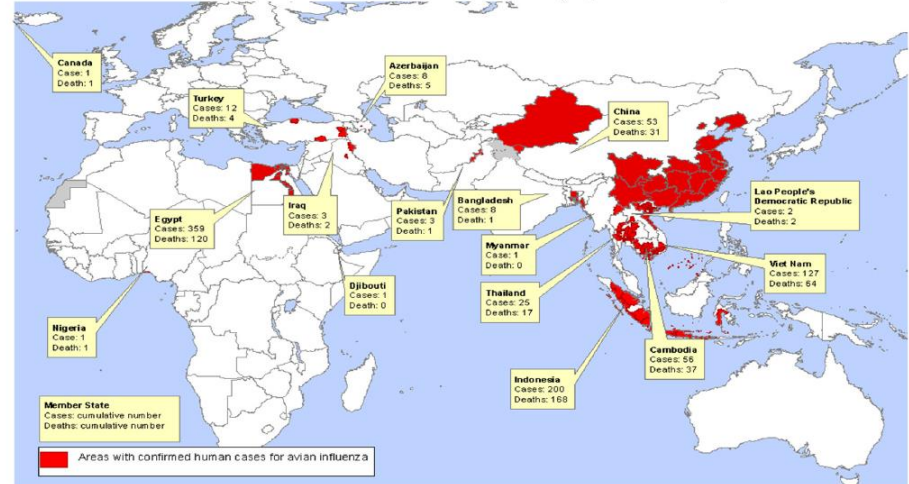
Defining Event in 2003 *Concerns with Pandemic Influenza*

Current zoonotic influenza situation A(H5N1)



The emergence of Influenza A H5N1

Areas with confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2017*



*All dates refer to onset of illness
Data as of 27 September 2017
Source: WHO/GIP

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its borders or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

World Health Organization

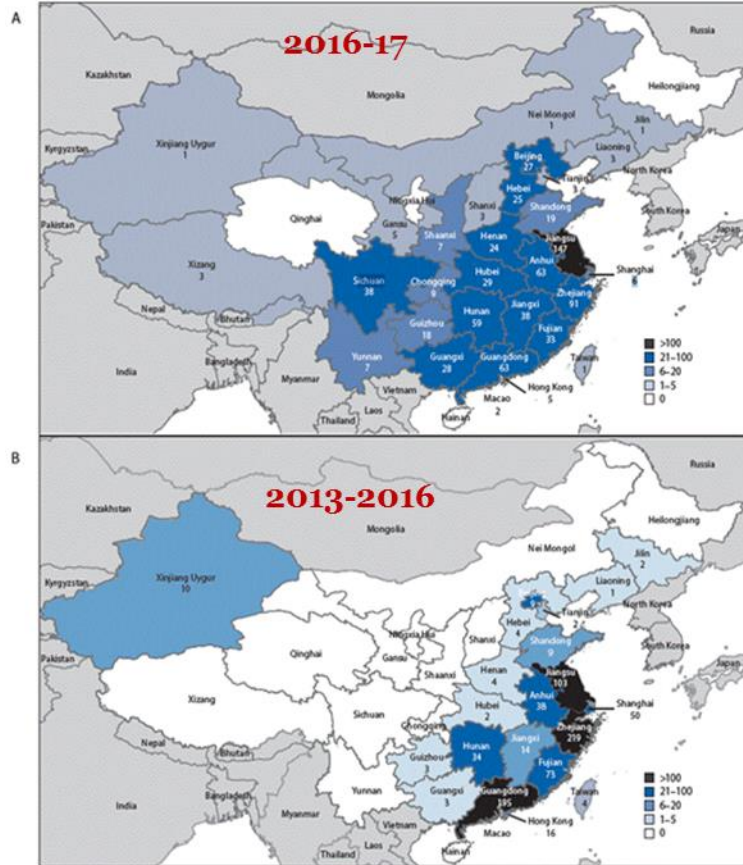


Sporadic cases



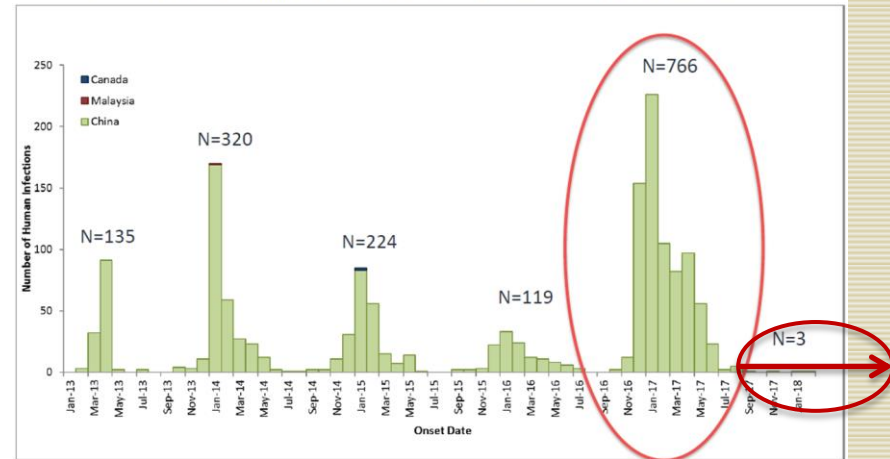
Influenza A H7N9

The latest global concern



Human Infections of A(H7N9) – 6 Waves Influenza **CDC**

Epidemic Curve of Confirmed Avian Influenza A(H7N9) Virus Infections of Humans Reported by WHO or in Chinese Provincial or Hong Kong CHP Press Releases, 18 Feb 2013 – 26 Feb 2018 (N=1,567)



~ 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 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




A Global Tool for Pandemic Preparedness

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

CDC Influenza Risk Assessment


Influenza Division 

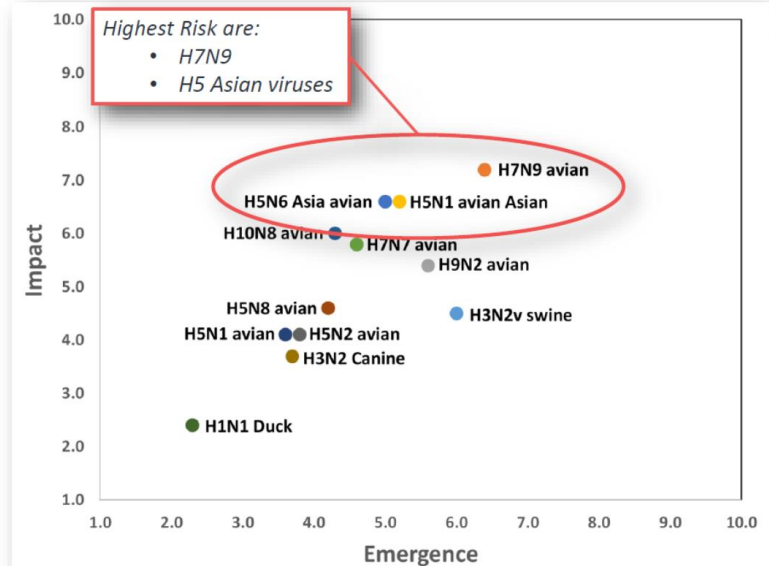
- CDC Influenza Risk Assessment Tool (IRAT)
 - Ten elements of the virus, population, and animal/human ecology are evaluated to develop a score

 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>

Influenza Risk Assessment – H7N9 Highest

Influenza Division 



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

CDC. <https://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.



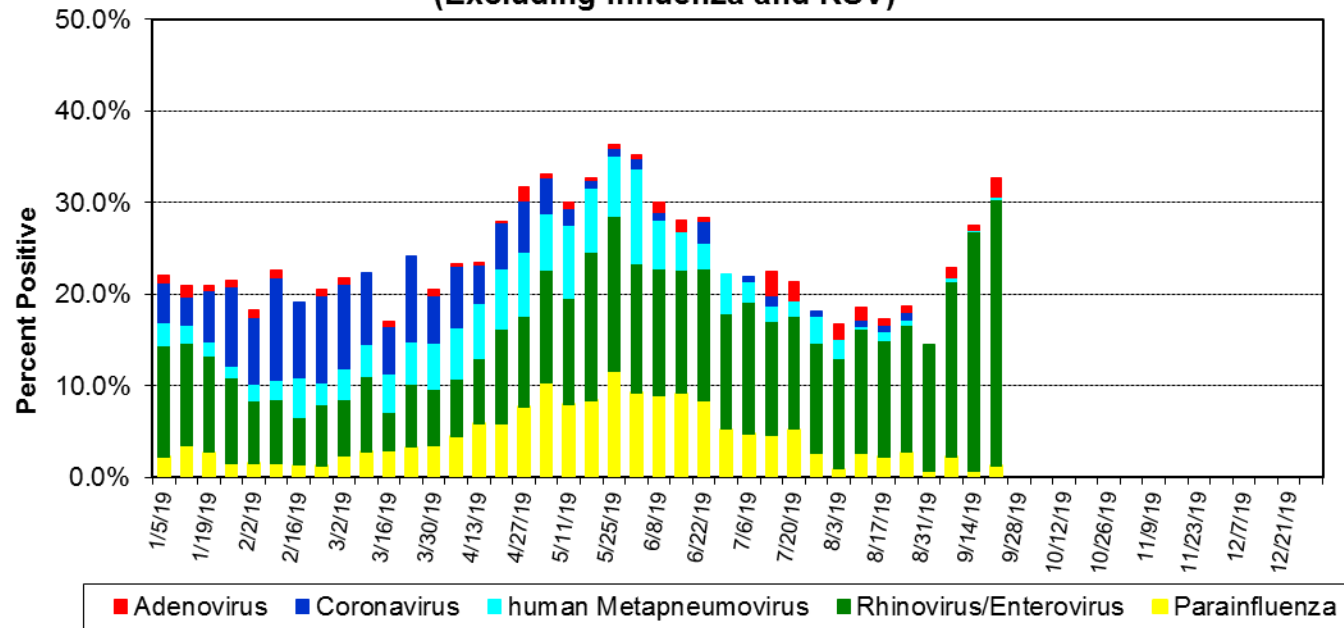
Reclassification Impact

- *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

Positivity of Respiratory Specimens by PCR
at Wisconsin Laboratories
(Excluding Influenza and RSV)





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

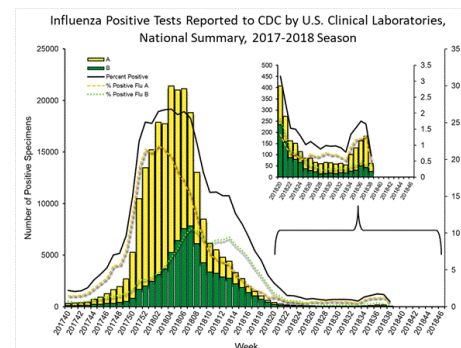
- Virus Activity Graphs

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



National

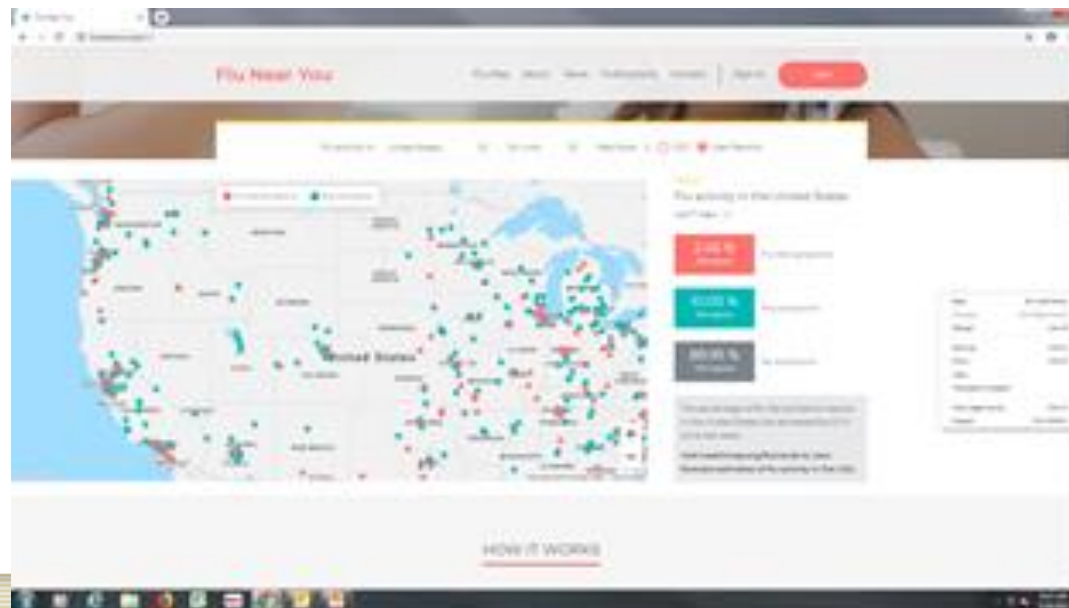
- FluView (CDC)
- NREVSS (CDC)





Flu Near You!

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





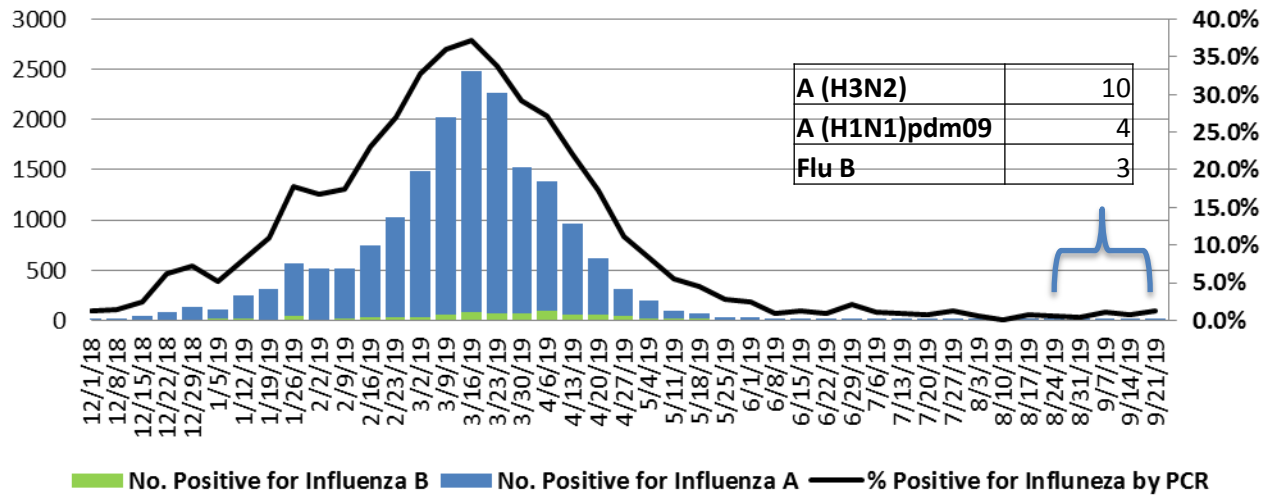
Influenza and non-influenza virus respiratory surveillance





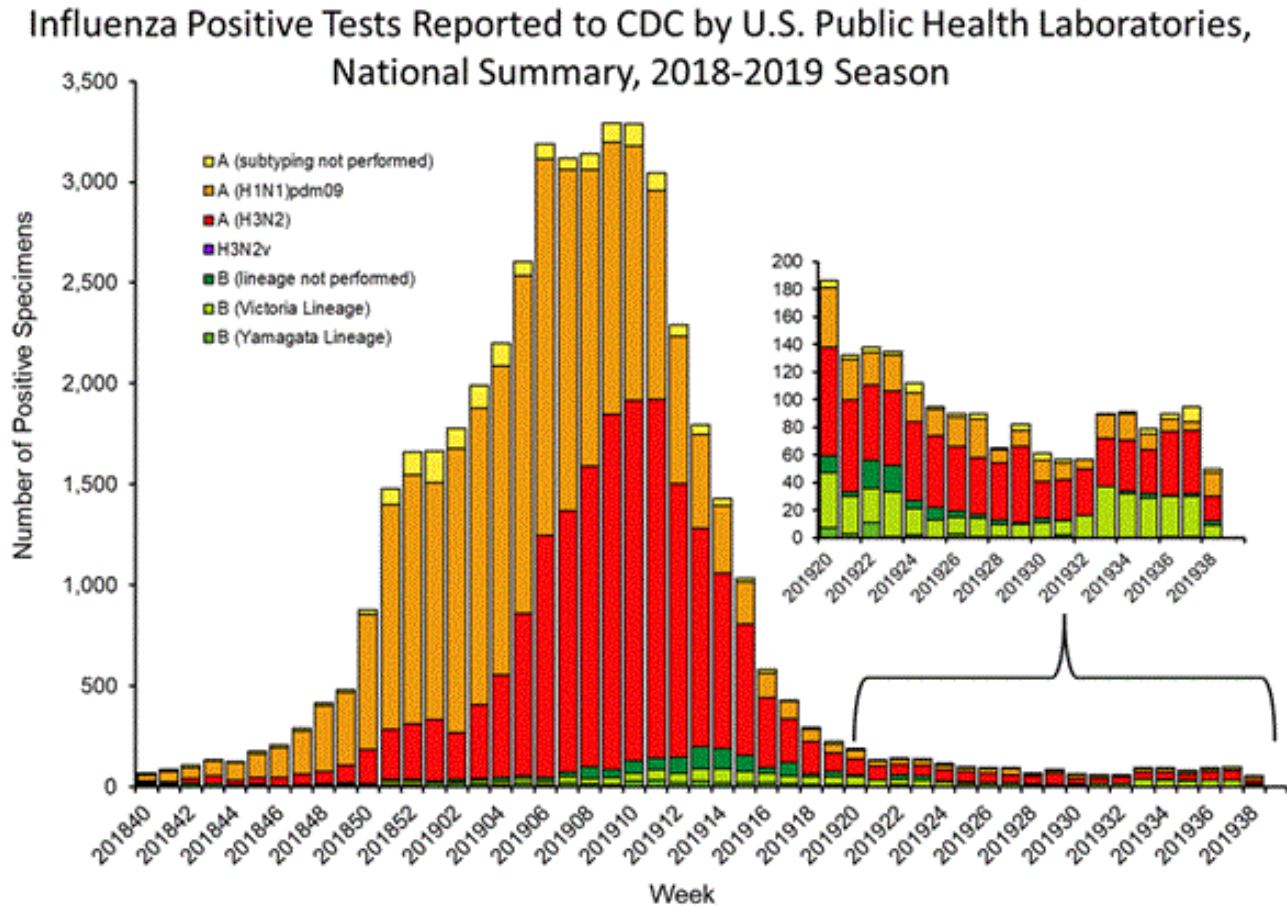
Early..... Influenza season, 2019-2020

**% Positive for Influenza by PCR (Wisconsin), Week
Ending September 21, 2019**





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

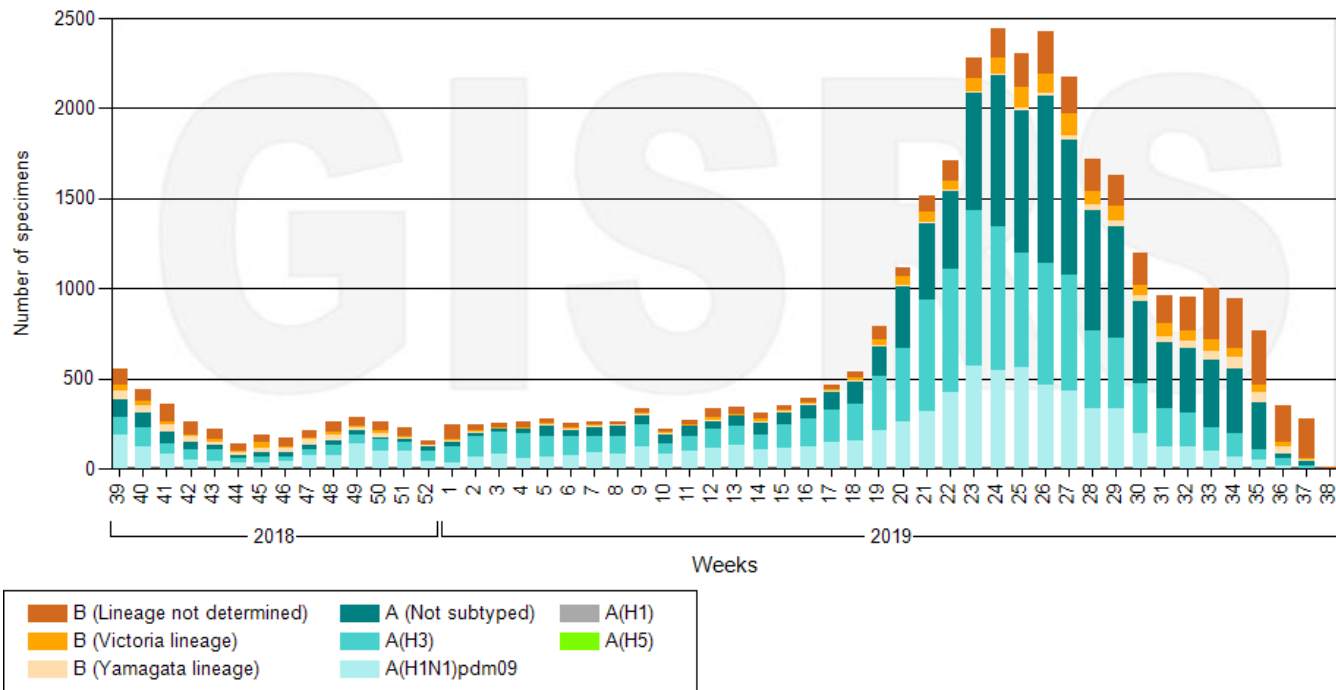


Data source: CDC Flu View



WHO Global Influenza Surveillance and Response System (GISRS)— Southern hemisphere, 2019

Number of specimens positive for influenza by subtype





Influenza Severity, Southern Hemisphere

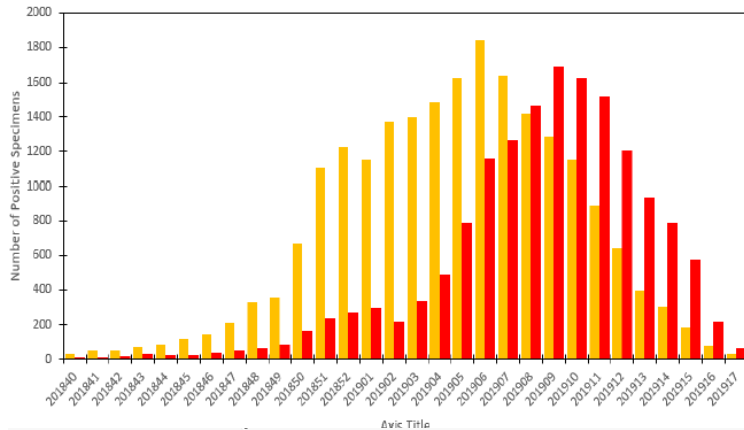
- Clinical severity was low.
- The number of deaths was low.
- VE was expected to be 40-60%



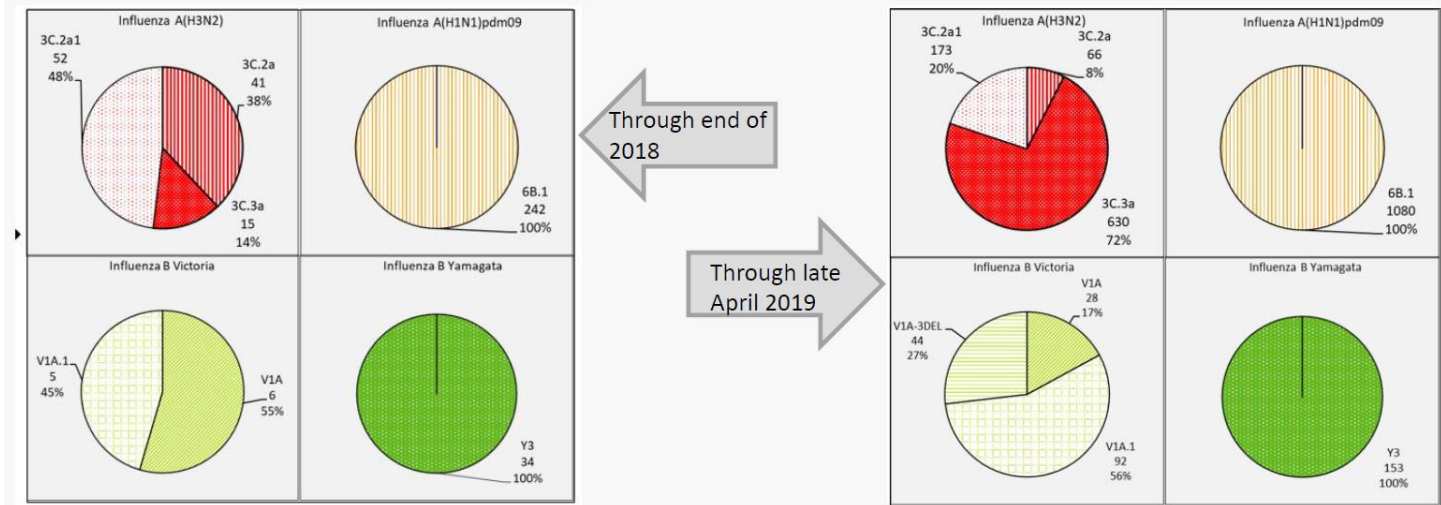
Data source: Dept. of Health, Australia <https://www1.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-ozflu-flucurr.htm#current>



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



H1N1 pdm09 → H3N2

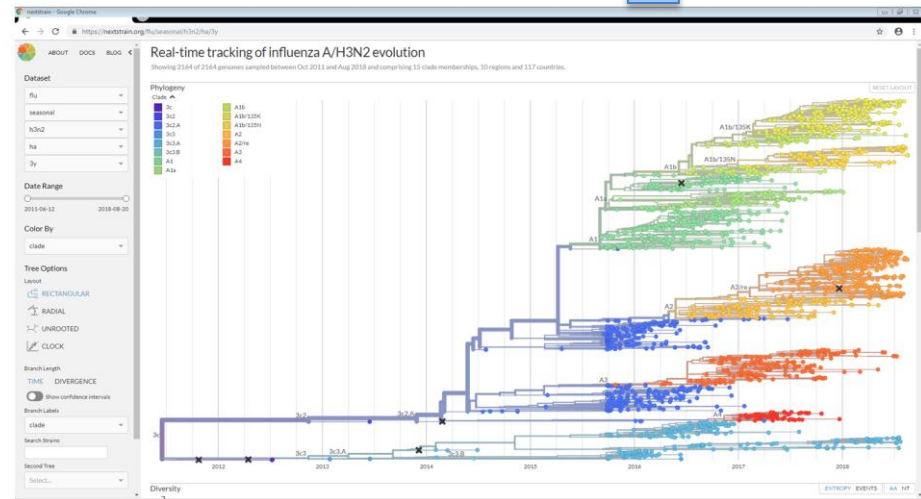
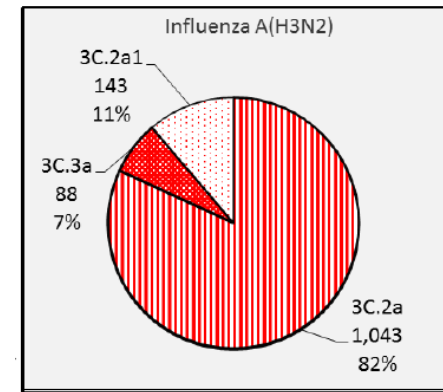


Graphs: Lynette Brammer, CDC



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



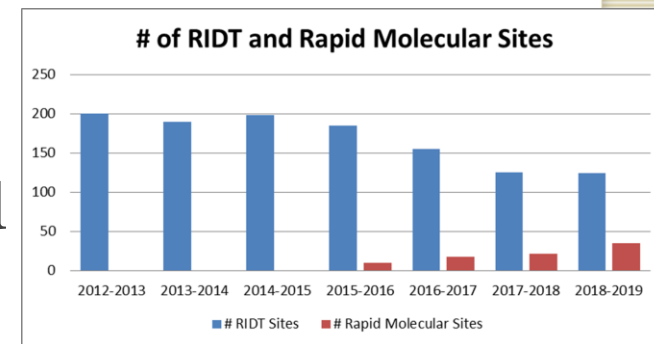


Influenza Surveillance in Wisconsin

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.

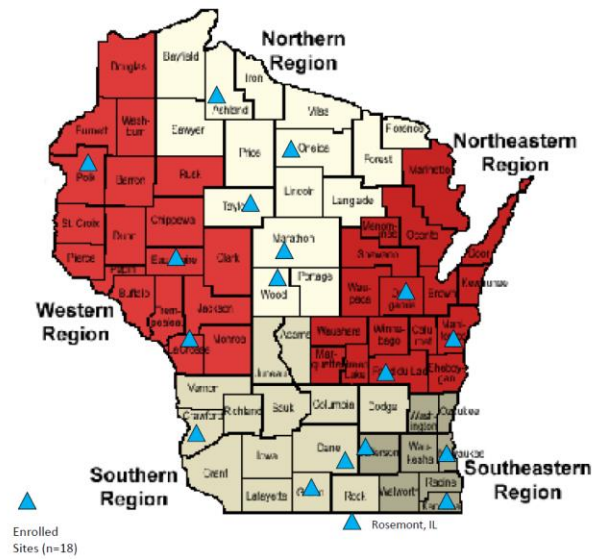


Influenza Surveillance in Wisconsin

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.

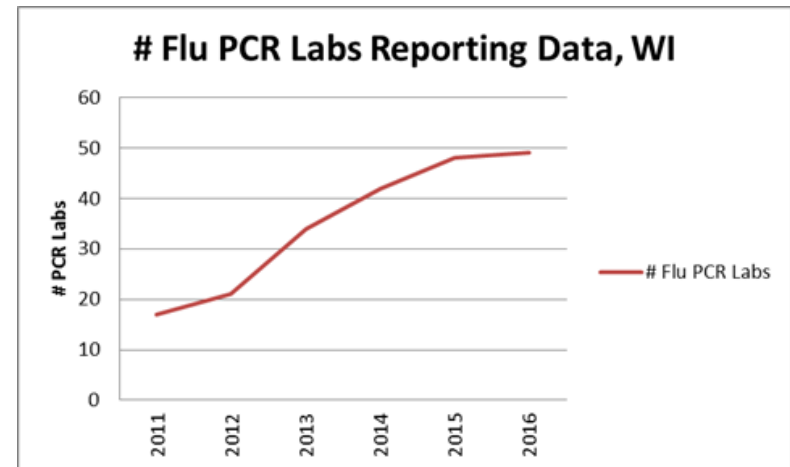


Influenza Surveillance in Wisconsin

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



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.



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