Influenza and other Respiratory Viruses Update--2017

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and

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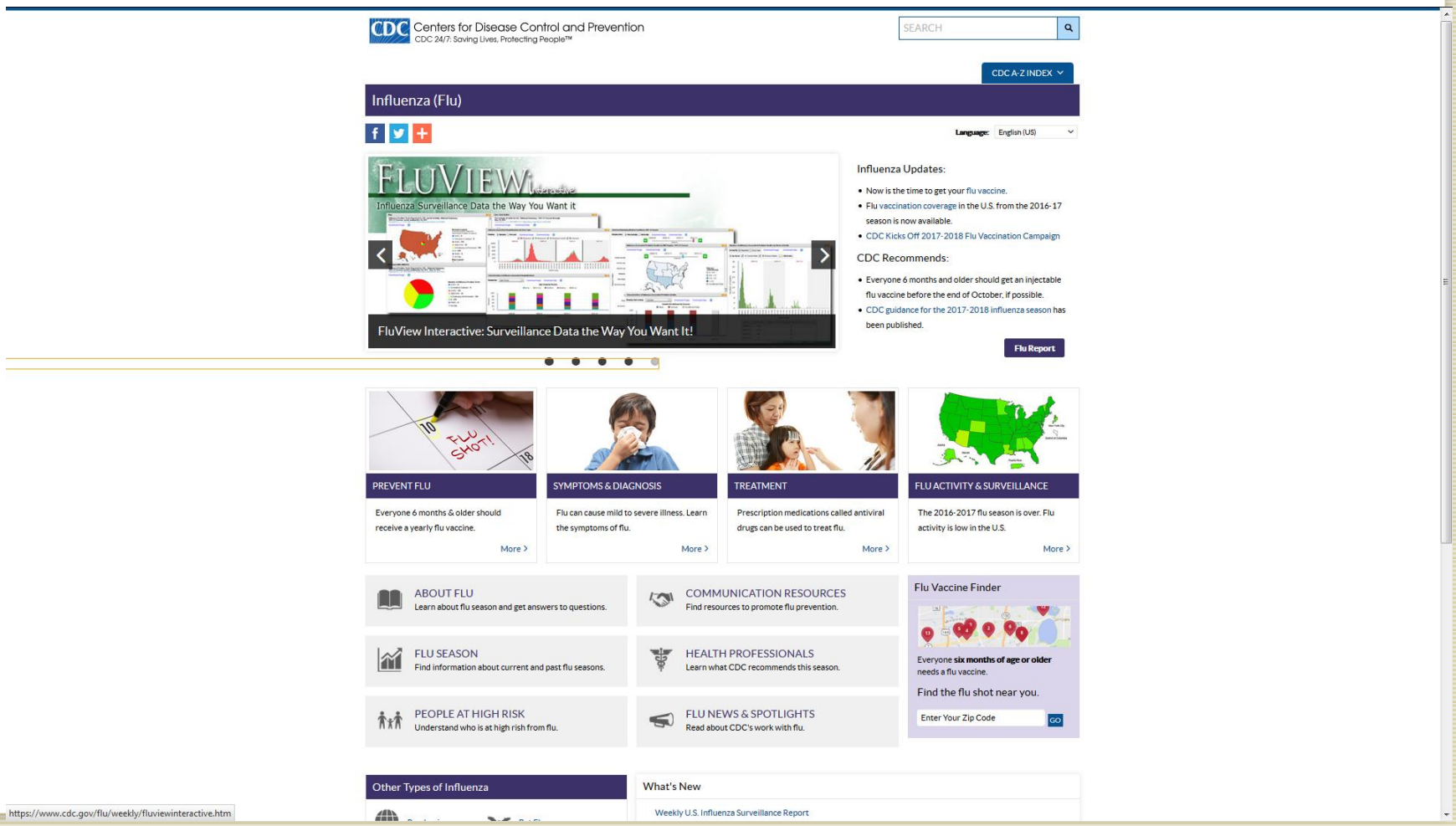
Learning Objectives

- Review of influenza basics
- Review of the 2016-2017 influenza season.
- Influenza A H7N9 and “variant” virus update.
- RIDT update.
- Discuss surveillance strategy for 2017-2018

Influenza

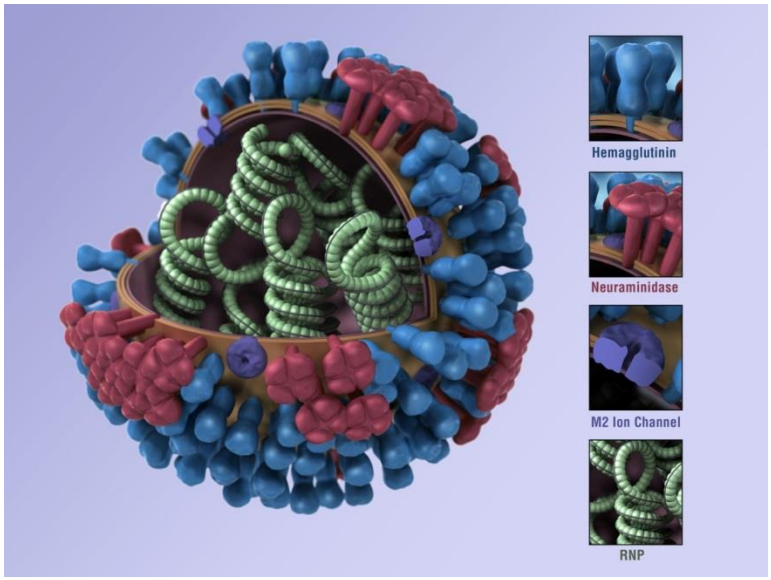
The latest information

www.cdc.gov/flu/index.htm



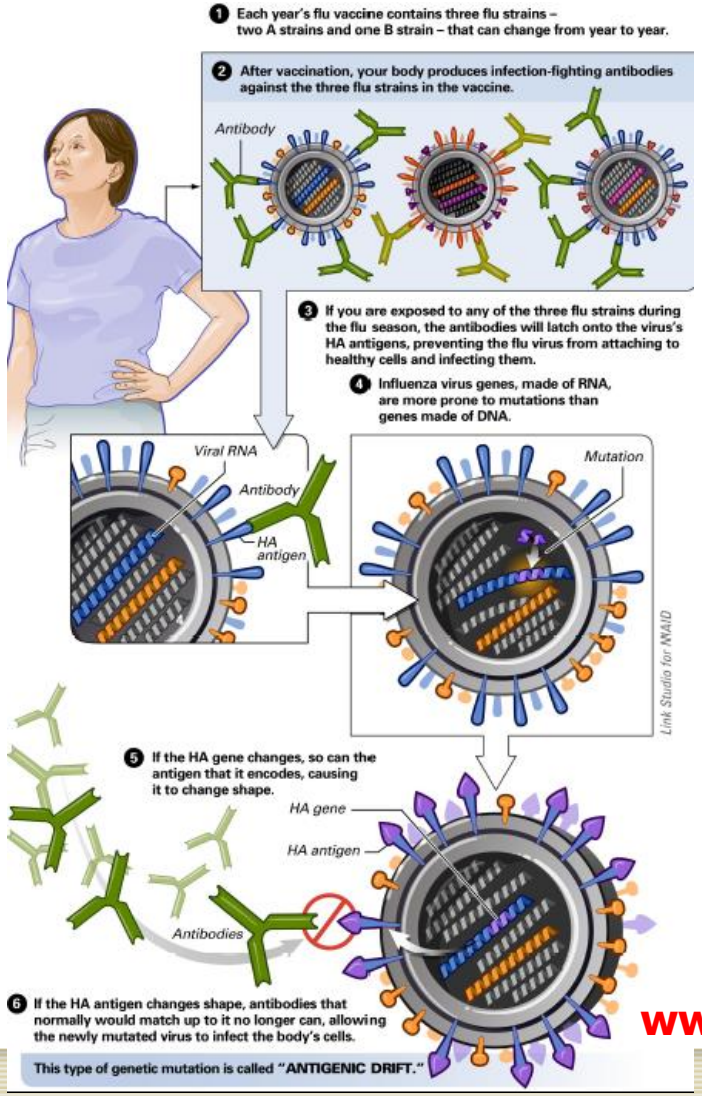
The Changeability of Influenza

Antigenic Drift →Seasonal Influenza



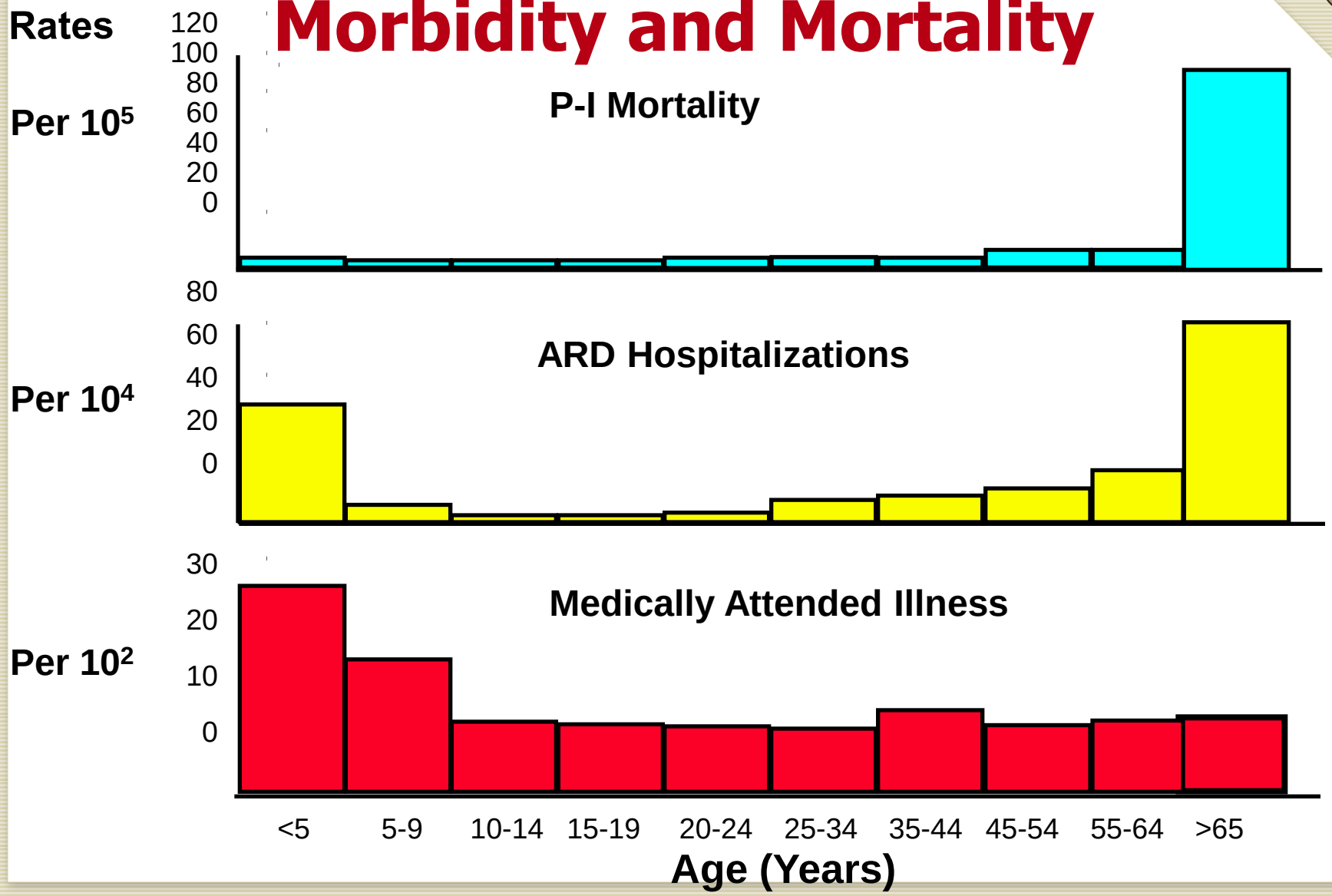
Antigenic Drift

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



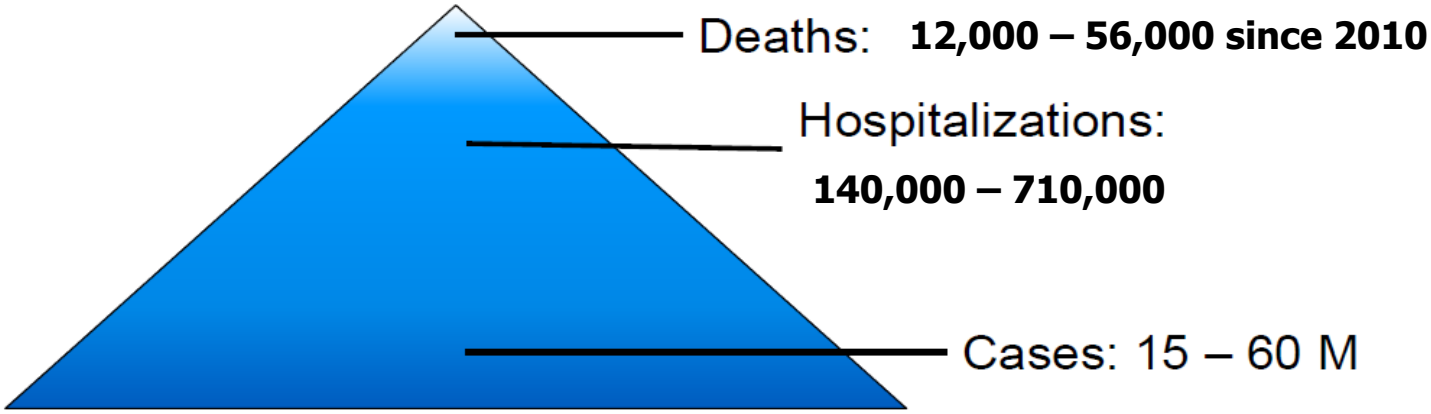
www.flu.gov

Seasonal Influenza-Related Morbidity and Mortality



Glezen WP. *Epidemiol Rev.* 1996;18(1):64-76.

Estimated Annual Burden of Seasonal Influenza in the United States



Direct medical costs: $10.4 billion

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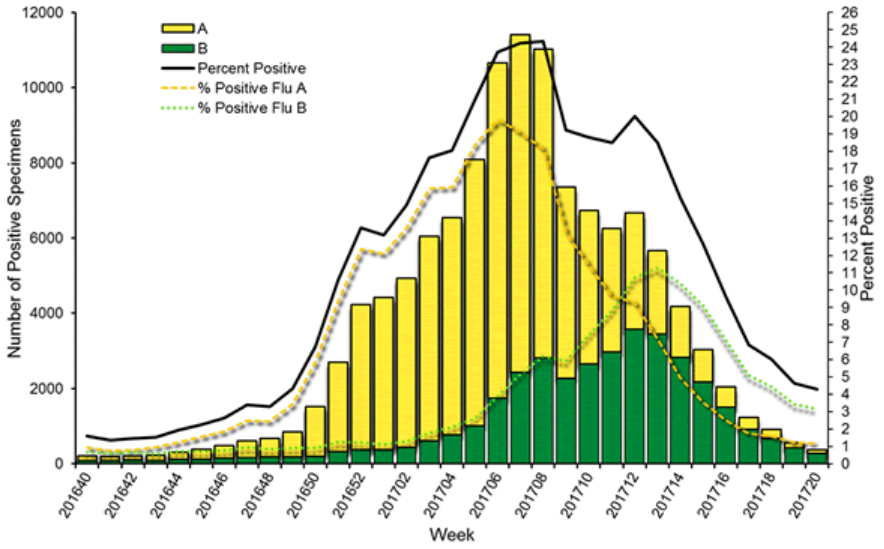
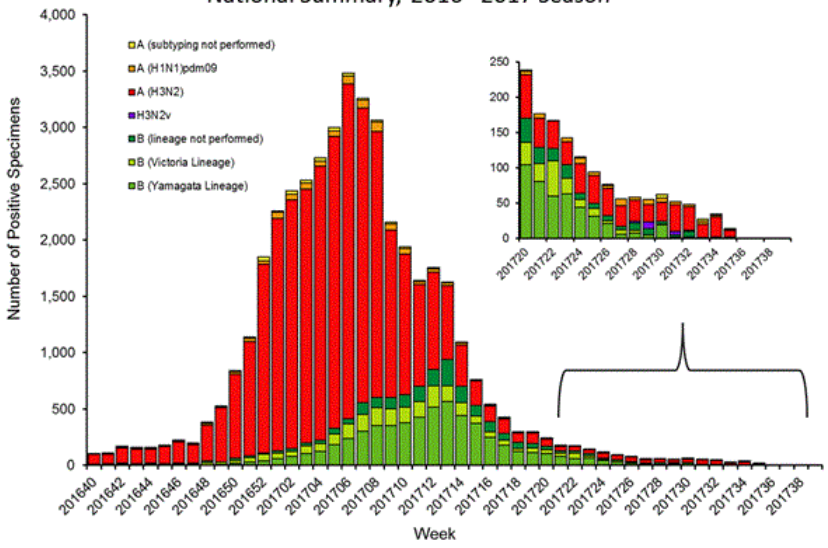
Influenza in the US: 2016-17

FLUVIEW
A Weekly Influenza Surveillance Report Prepared by the Influenza Division
CDC

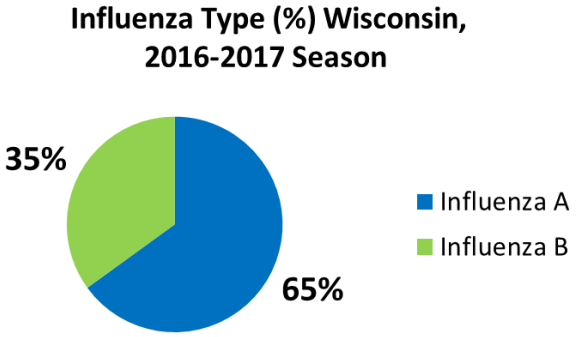
Influenza Positive Tests Reported to CDC by U.S. Clinical Laboratories, National Summary, 2016-2017 Season

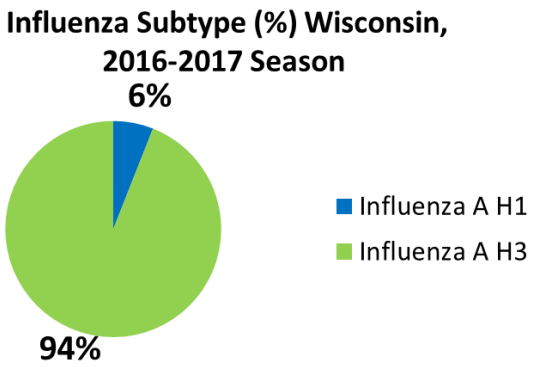


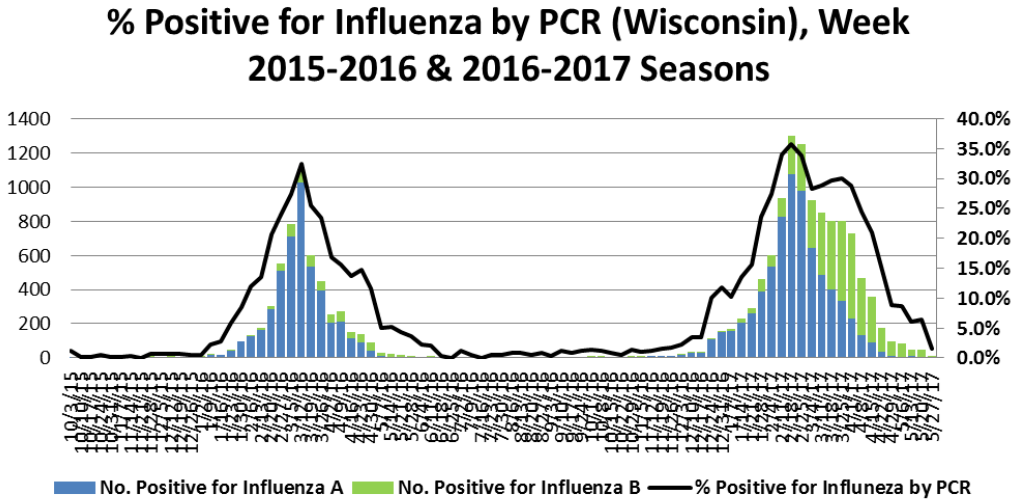
Influenza Positive Tests Reported to CDC by U.S. Public Health Laboratories, National Summary, 2016 –2017 Season



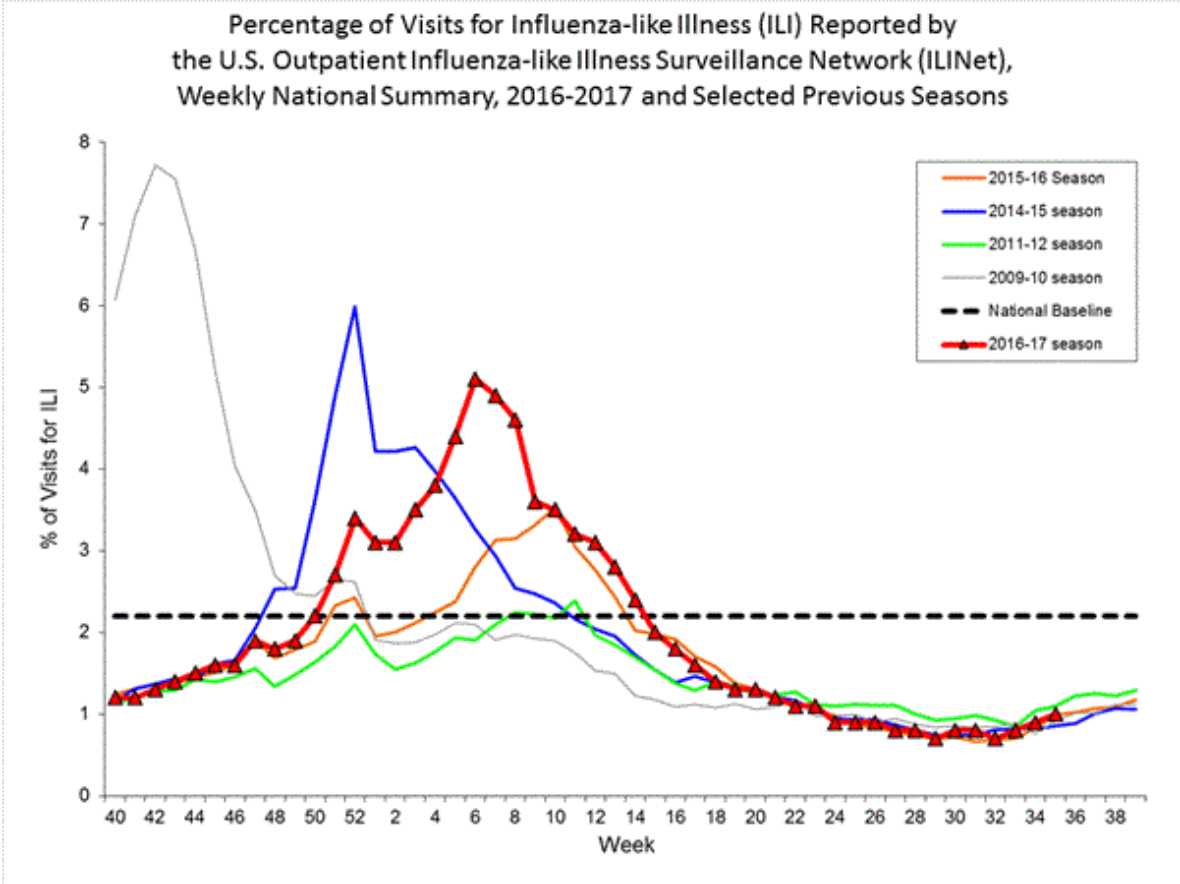
Influenza in WI, 2016-2017



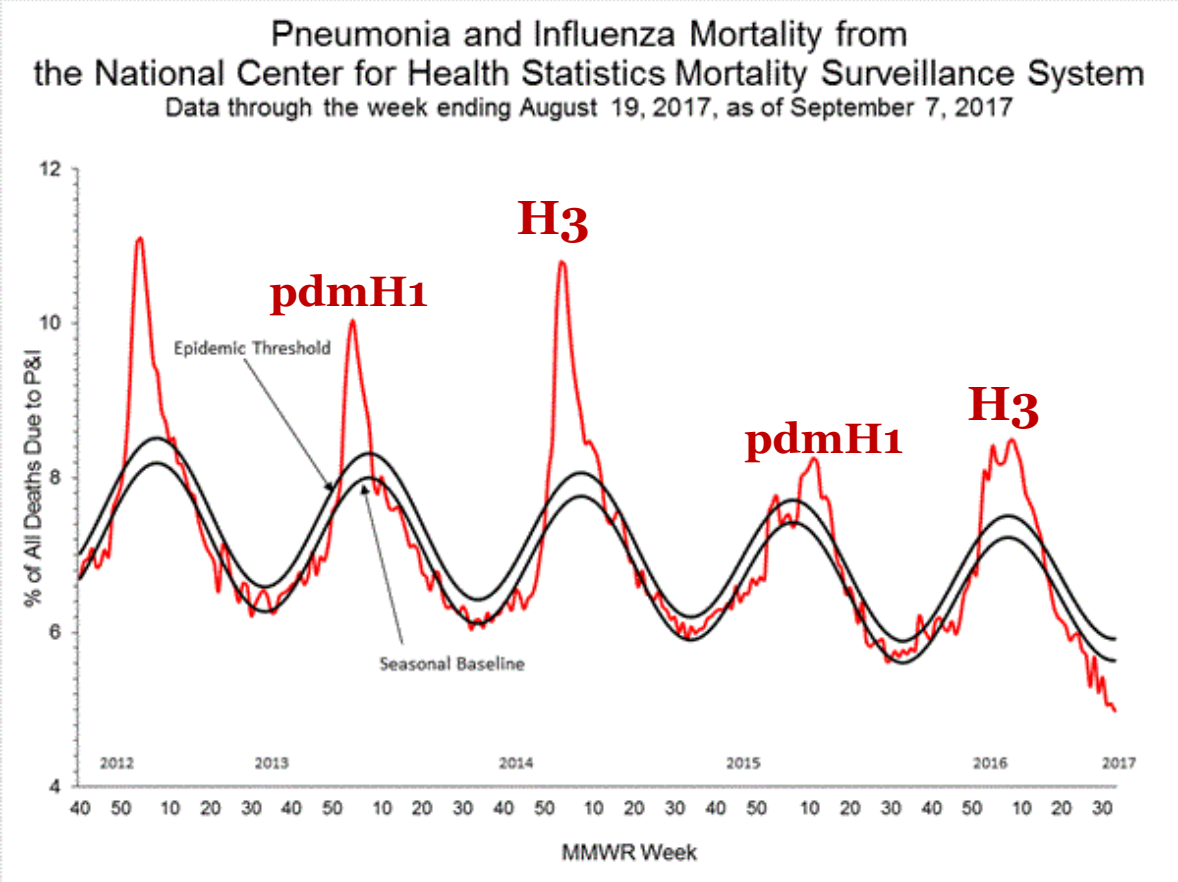




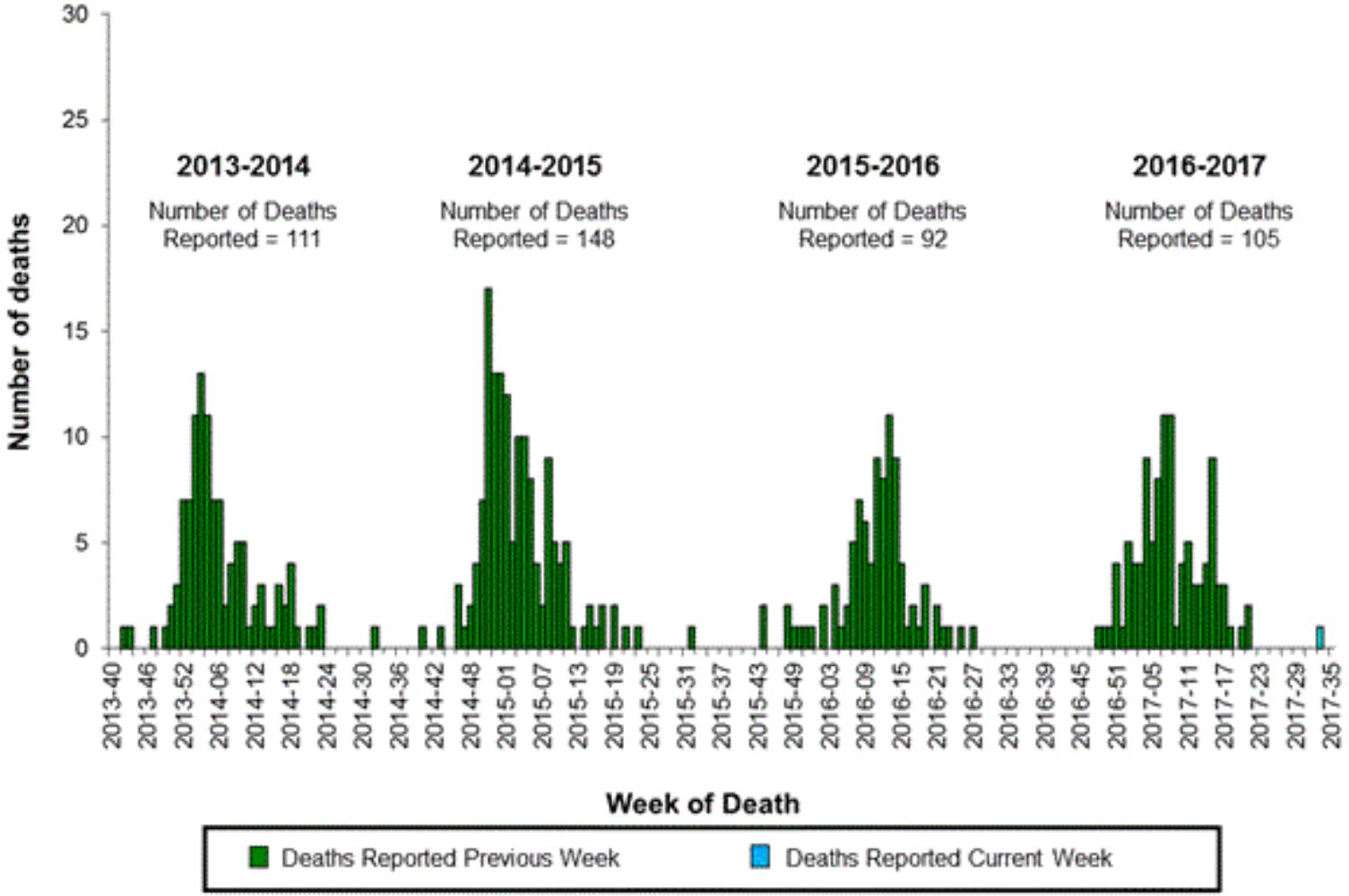
Influenza in the U.S. 2016-17



Influenza in the U.S. 2016-17



Number of Influenza-Associated Pediatric Deaths by Week of Death: 2013-2014 season to present



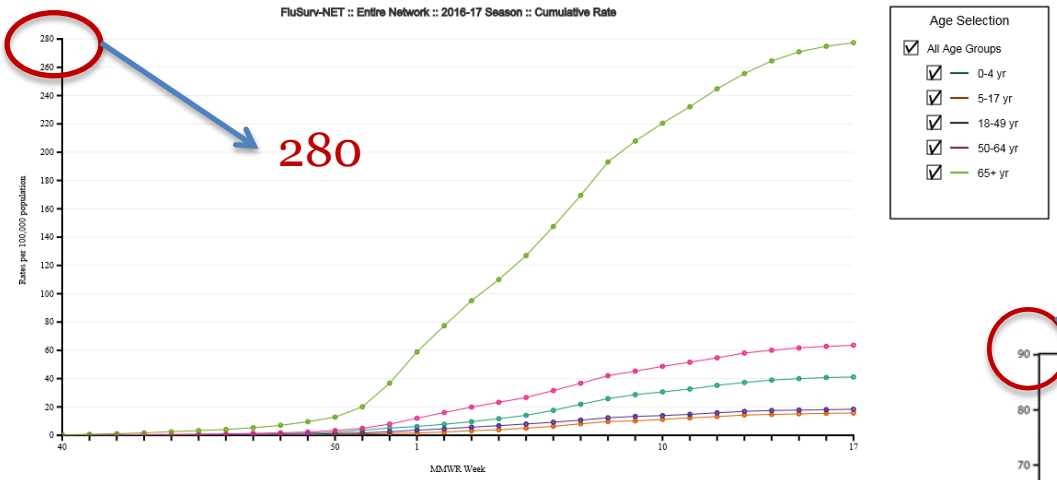
Influenza Hospitalizations

FLUVIEW

CDC

Laboratory-Confirmed Influenza Hospitalizations

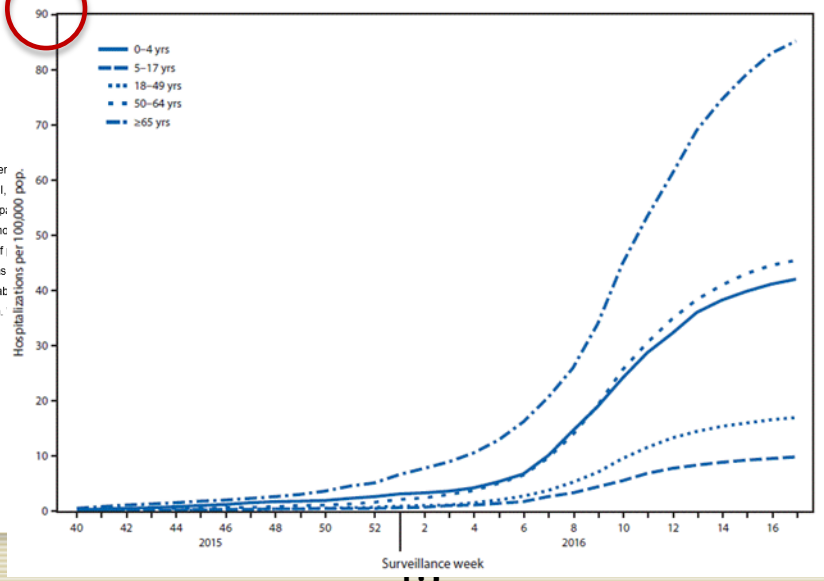
Preliminary cumulative rates as of Sep 02, 2017



The Influenza Hospitalization Surveillance Network (FluSurv-NET) conducts population-based surveillance for laboratory-confirmed influenza-associated hospitalizations in children (persons younger years) and adults. The current network covers over 70 counties in the 10 Emerging Infections Program (EIP) states (CA, CO, CT, GA, MD, MN, NM, NY, OR, and TN) and three additional states (MI, UT). The network represents approximately 9% of US population (~27 million people). Cases are identified by reviewing hospital, laboratory, and admission databases and infection control logs for p hospitalized during the influenza season with a documented positive influenza test (i.e., viral culture, direct/indirect fluorescent antibody assay (DFA/IFA), rapid influenza diagnostic test (RIDT), or mo assays including reverse transcription-polymerase chain reaction (RT-PCR)). Data gathered are used to estimate age-specific hospitalization rates on a weekly basis, and describe characteristics of hospitalized with associated influenza illness. Laboratory-confirmation is dependent on clinician-ordered influenza testing. Therefore, the unadjusted rates provided are likely to be underestimated as influenza-associated hospitalizations can be missed if influenza is not suspected and tested for. FluSurv-NET hospitalization data are preliminary and subject to change as more data become availab incidence rates are unadjusted. Please use the following citation when referencing these data: "FluView: Influenza Hospitalization Surveillance Network, Centers for Disease Control and Prevention. Accessed on DATE".

80

In contrast, 2015-16



Influenza 2016-17

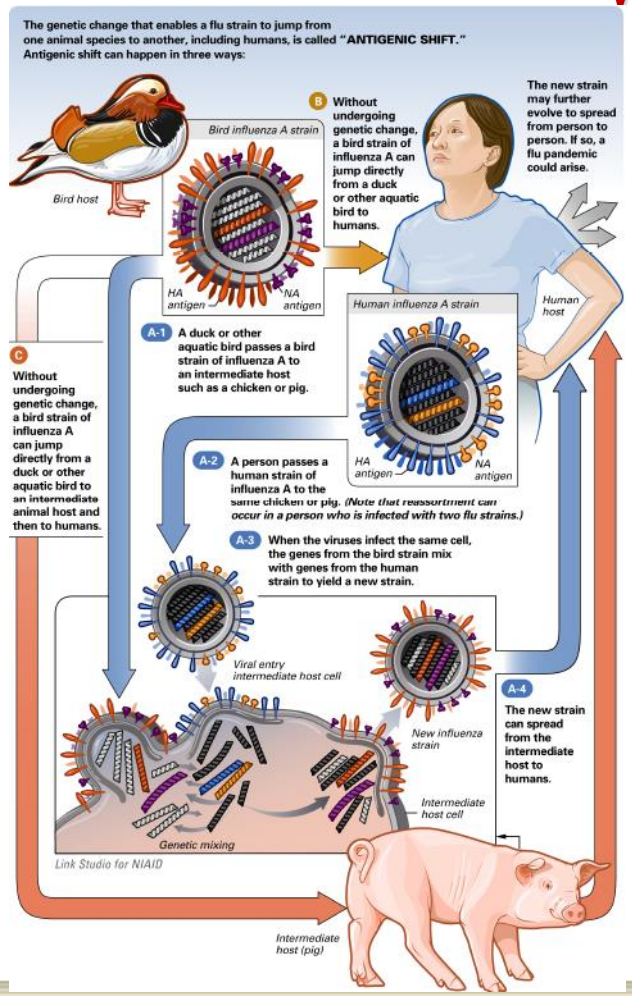
What was expected…

- A/Hong Kong/4801/2014(H3N2)
- A/California/7/2009
- B/Phuket/3073/2013 (B/Yamagata-lineage)
- B/Brisbane/60/2008 (B/Victoria-lineage)

… and that's what we got☺

The Changeability of Influenza
Antigenic Shift

www.flu.gov

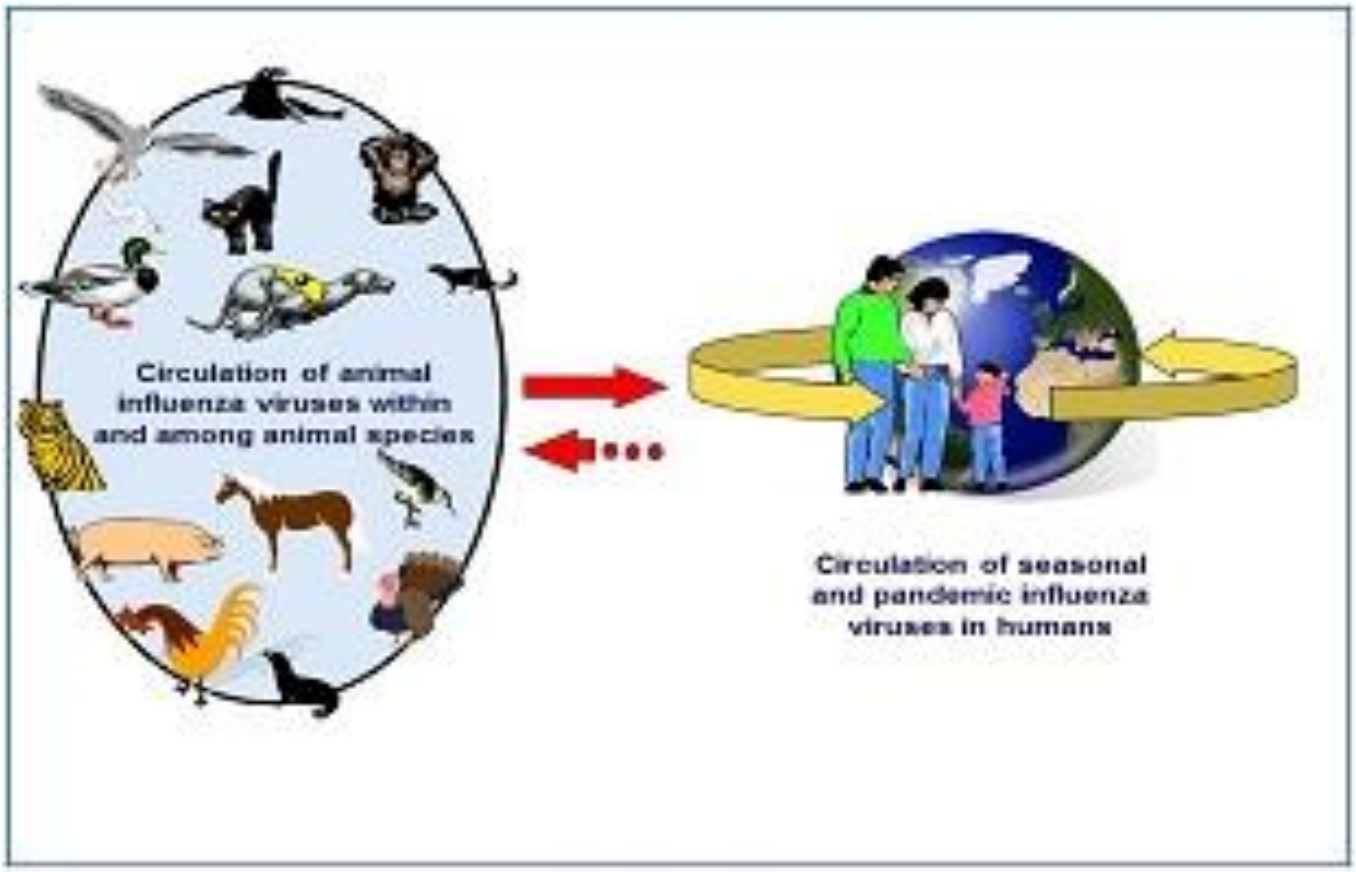


<u>Antigenic Shift</u>

When a new subtype (a novel HA and/or NA) of influenza A emerges in the host (humans)

Infectious Diseases at the Human-Animal Interface

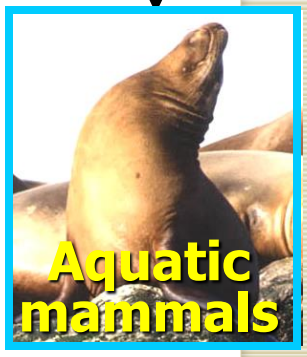
Influenza as an Example



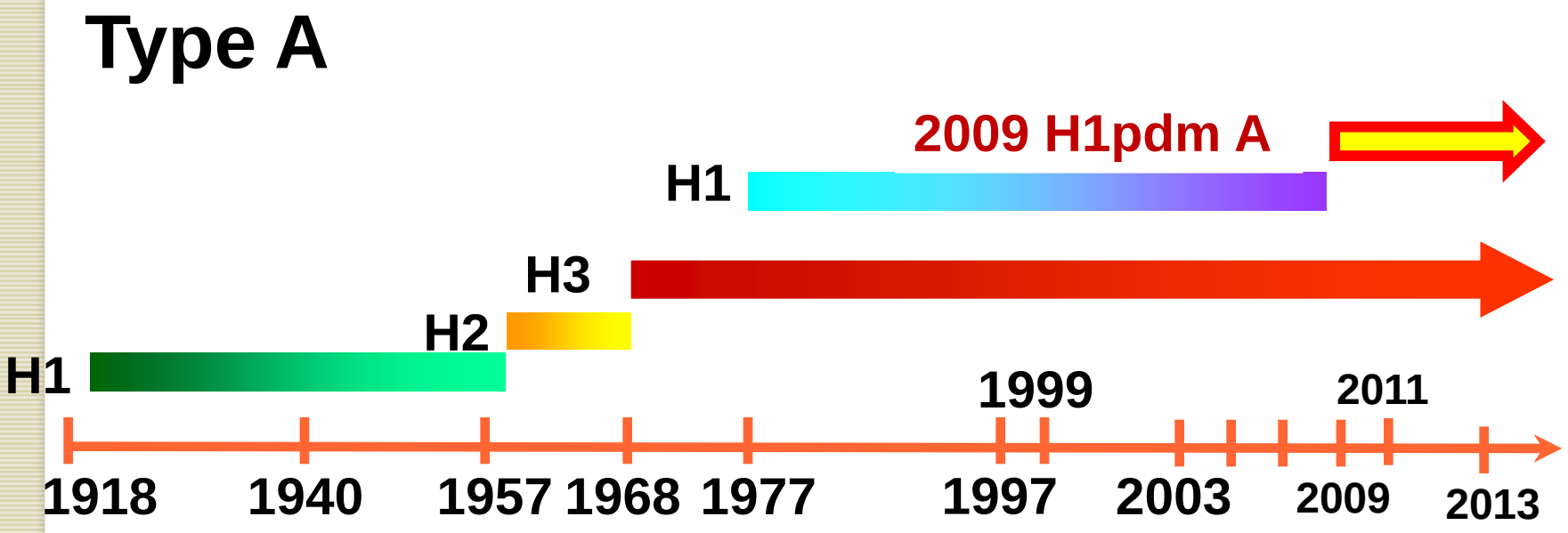
Influenza at the Human-Animal Interface

Influenza A

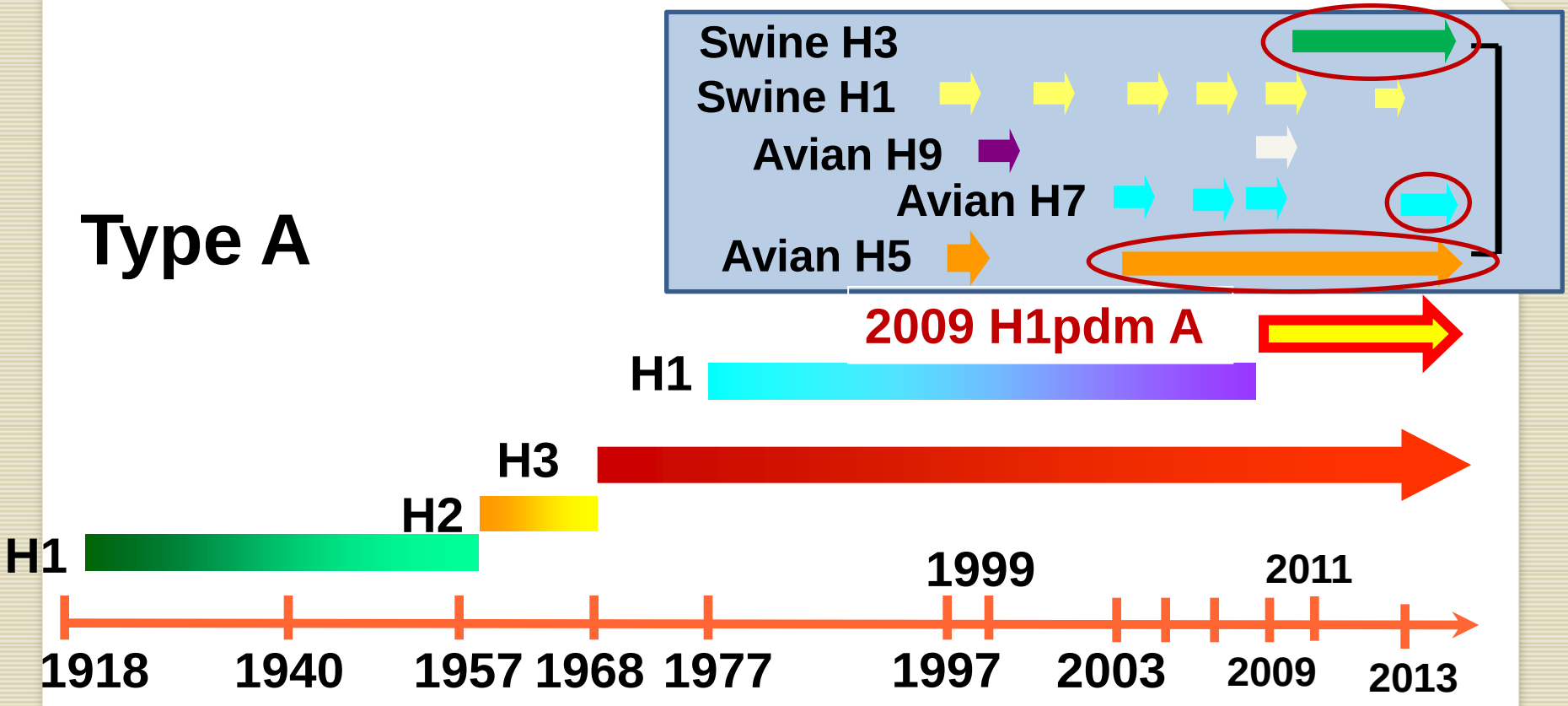
- **H1 - H18**
- **N1 – N11**

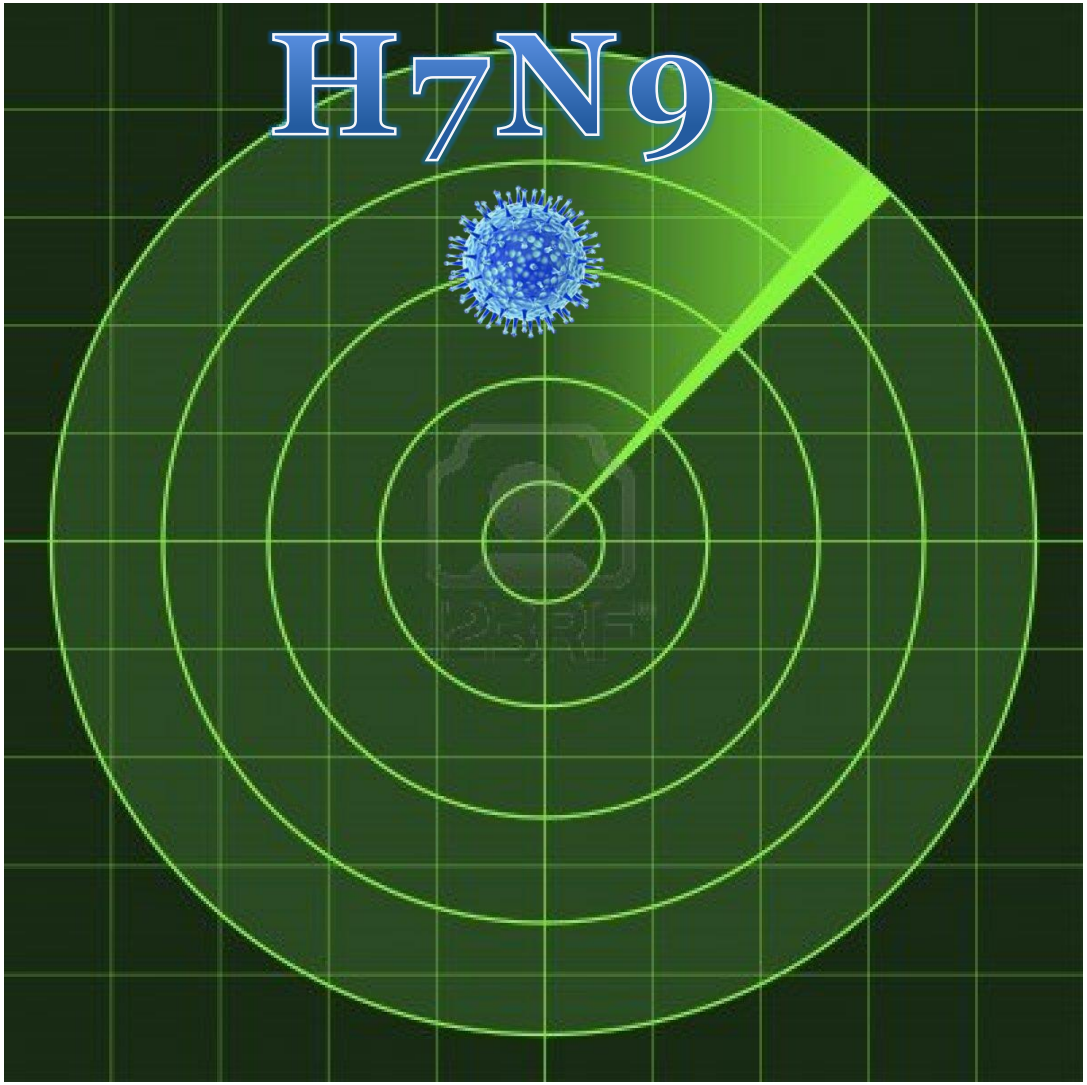


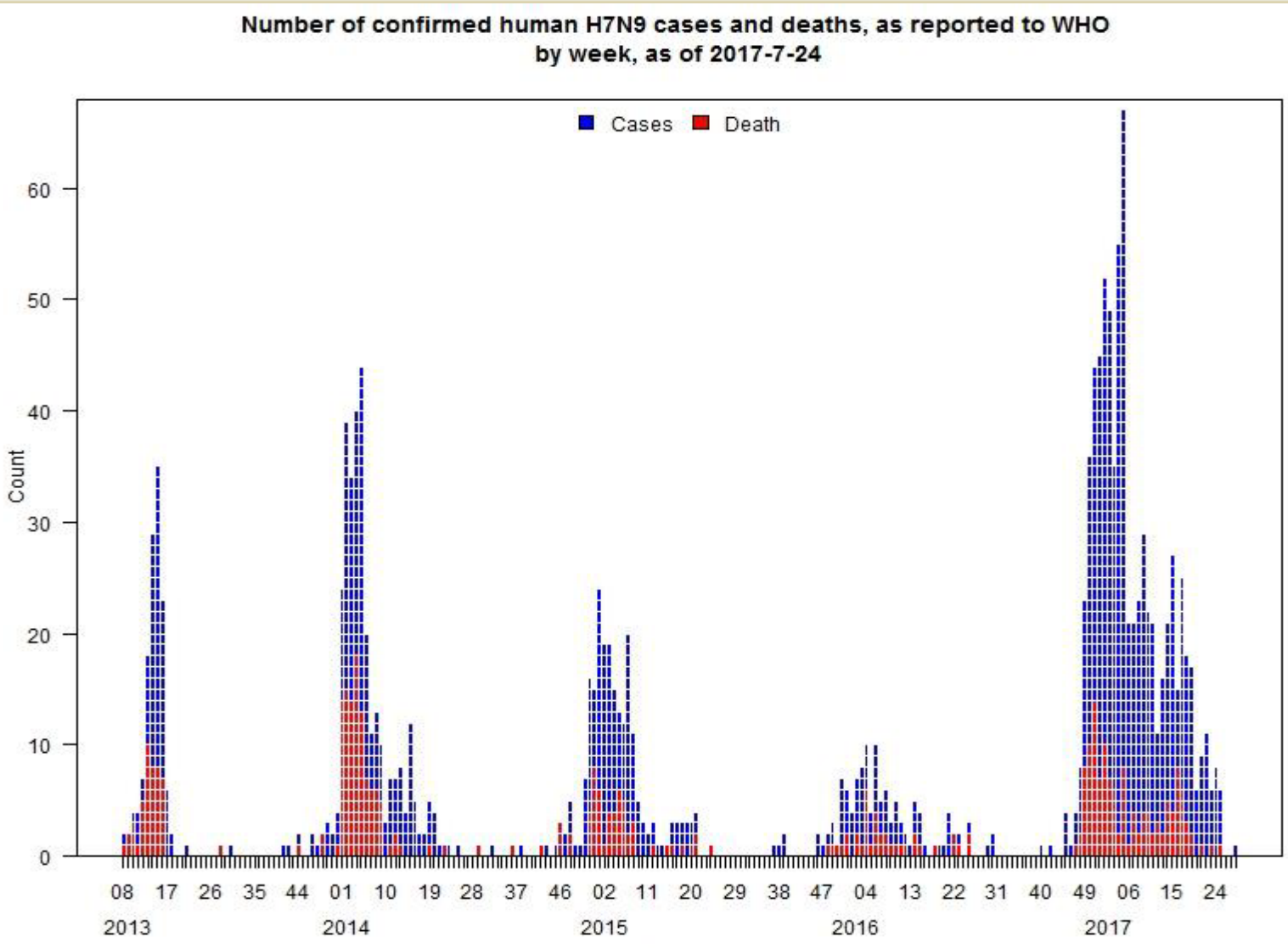
Timeline of Pandemic Influenza A Viruses in Humans



Timeline of Other Emergent Influenza A Viruses in Humans




H7N9



This suggests that the virus has spread, and emphasizes that further intensive surveillance and control measures in both the human and animal health sector remain crucial (WHO Risk Assessment, 2017)

FIGURE A **:2016-2017**

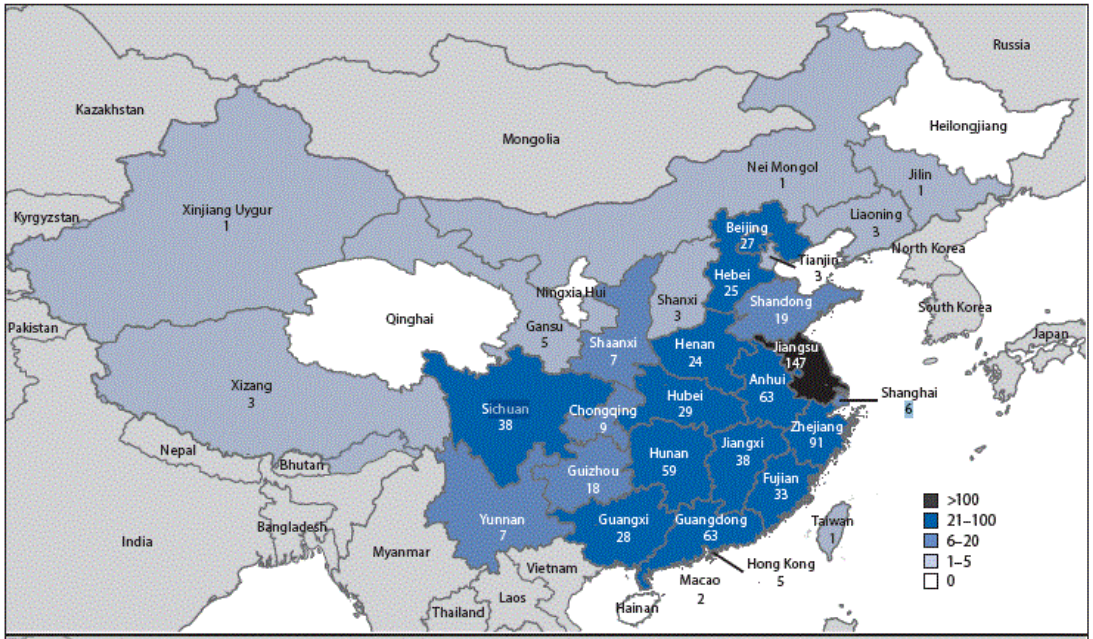
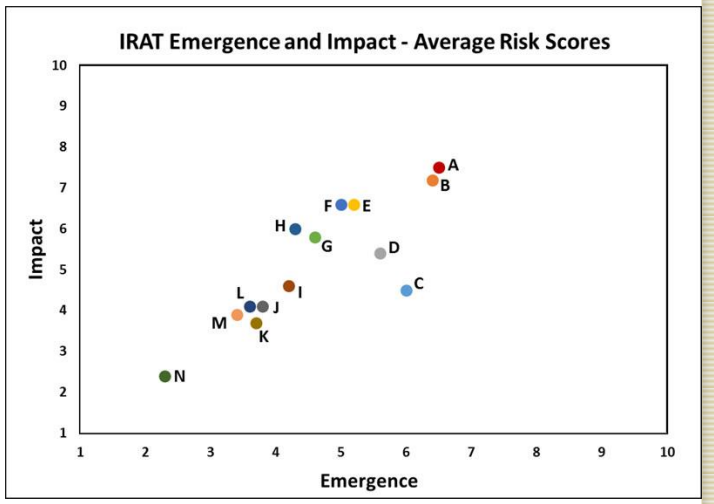


FIGURE B: **2013-2016**

MMWR
Weekly / September 8, 2017 / 66(35);928–932

Why Avian Influenza A (H7N9)?

- 5th epidemic mutations detected
  - **H**ighly **P**athogenic **A**vian **I**nfluenza (HPAI); Refers to avian species pathogenicity.
  - Reduced susceptibility to antivirals
- Antigenic drift ---new CVV required
- CDC IRAT Evaluation Tool
  - Highest pandemic risk amongst novel influenza viruses detected.



Domestic *Novel* Influenza A

States Reporting H3N2v Cases	Cases in 2011	Cases in 2012	Cases in 2013	Cases in 2014	Cases in 2015	Cases in 2016	Cases in 2017
Delaware							1
Hawaii		1					
Illinois		4	1				
Indiana	2	138	14				
Iowa	3	1	1				
Maine	2						
Maryland		12					31
Michigan		6	2		1	12	
Minnesota		5			1		
New Jersey					1		
North Dakota							1
Ohio		107	1	2		6	15
Pennsylvania	3	11					1
Texas							1
Utah		1*					
West Virginia	2	3					
Wisconsin		20		1			
Total	**12**	**309**	**19**	**3**	**3**	**18**	**50**

Source: https://www.cdc.gov/flu/swineflu/h3n2v-case-count.htm

The Recipe for a Human Influenza Pandemic

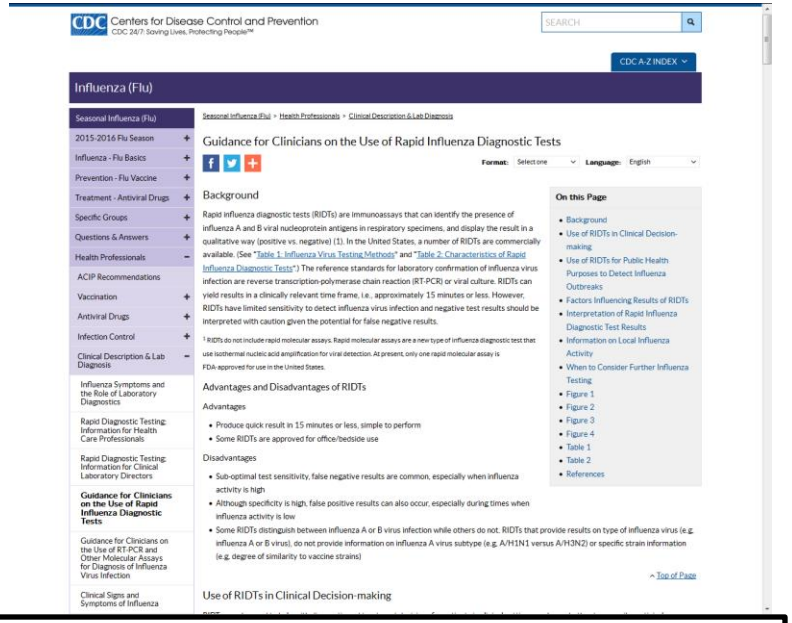
- ✓ Emergence of a novel subtype of influenza
  - ✓An immunologically naïve population
- ✓ Replication in humans → disease
- ○ **Efficient** human-to-human transmission

Influenza surveillance are strengthening (US and globally)

- Enhances our ability to monitor for novel viruses with pandemic potential.
- In Wisconsin, the number of PCR tests performed surpasses RIDT.
- In the US, the number of PCR tests reported (CDC) exceeded 40,000 per week.
- The number of global NIC's increased.

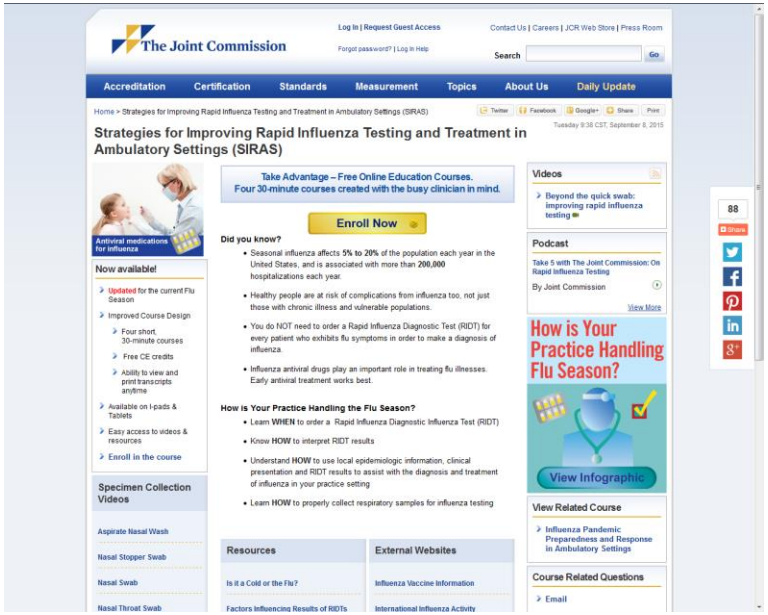
Rapid Influenza Diagnostic Tests (RIDTs)

A perennial discussion



www.cdc.gov/flu/professionals/diagnosis/clinician_guidance_ridt.htm

www.jointcommission.org/siras.aspx



Improving RIDT Performance

https://www.gpo.gov/fdsys/pkg/FR-2017-01-12/pdf/2017-00199.pdf

transport of the Samsung Galaxy Note 7 device, in particular, immediately prior to boarding is no longer warranted, due to the extensive efforts by Samsung and U.S. wireless providers to recall all Samsung Galaxy Note 7 devices and to make users aware the Samsung Galaxy Note 7 device is forbidden from transportation by air. Moreover, on December 9, 2016, Samsung reported on its Web site that more than 93 percent of all recalled Samsung Galaxy Note 7 devices had been returned to Samsung and that it would release a software update starting on December 19, 2016 that would prevent U.S. Samsung Galaxy Note 7 devices from charging and eliminate their ability to work as mobile devices.[1] We understand that major U.S. wireless providers will push out this update on or before January 8, 2017. T Mobile reported that it would push the software update on December 27, 2016.[2] Verizon Wireless and AT&T both reported that they would push the software update on January 5, 2017,[3] and Sprint reported that it would push the update on January 8, 2017.[4] We think that these efforts to render U.S. Samsung Galaxy Note 7 devices inoperable, in addition to the ongoing recall and notification efforts, will decrease the likelihood that Samsung Galaxy Note 7 devices will be brought on board aircraft. In addition, the hazardous materials regulations (HMR; 49 CFR parts 171–180) provide a systematic framework to protect the safe transportation of hazardous materials that includes procedures for notification, handling, and reporting of discrepancies and incidents at air passenger facilities and cargo facilities.

Remedial Action

To eliminate or abate the imminent hazard:

(1) Persons covered by this Amended Order shall not transport, nor offer for transportation, via air any Samsung Galaxy Note 7 device.

(2) Air carriers are required to handle Samsung Galaxy Note 7 devices consistently with other forbidden hazardous materials under 49 CFR parts 173 and 175, and to deny boarding to a passenger in possession of a Samsung Galaxy Note 7 device unless and until the passenger divests themselves and carry-on or checked baggage of the Samsung Galaxy Note 7 device.

(3) Persons covered by this Amended Order who inadvertently bring a prohibited Samsung Galaxy Note 7 device aboard an aircraft must immediately power off the device, leave it powered off until no longer aboard the aircraft, not use or charge the device while aboard the aircraft, protect the device from accidental activation, including disabling any features that may turn on the device, such as alarm clocks, and keep the device on their person and not in the overhead compartment, seat back pocket, nor in any carry-on baggage, for the duration of the flight.

(4) When a flight crew member identifies that a passenger is in possession of a Samsung Galaxy Note 7 device while the aircraft is in flight, the crew member must instruct the passenger to power off the device, not use or charge the device while aboard the aircraft, protect the device from accidental activation, including disabling any features that may turn on the device, such as alarm clocks, and keep the device on their person and not in the overhead compartment, seat back pocket, nor in any carry-on baggage, for the duration of the flight.

Rescission of This Amended Order

This Amended Order remains in effect until the Secretary determines that an imminent hazard no longer exists or a change in applicable statute or federal regulation occurs that supersedes the requirements of this Amended Order, in which case the Secretary will issue a Rescission Order.

Failure To Comply

Any person failing to comply with this Amended Order is subject to civil penalties of up to $179,933 for each violation for each day they are found to be in violation (49 U.S.C. 5123). A person violating this Order may also be subject to criminal prosecution, which may result in fines under title 18, imprisonment of up to ten years, or both (49 U.S.C. 5124).

Right To Review

Pursuant to 49 U.S.C. 5121(d)(3) and in accordance with section 554 of the Administrative Procedure Act (APA), 5 U.S.C. 500 *et seq.*, a review of this action may be filed. Any petition seeking relief must be filed within 20 calendar days of the date of this order (49 U.S.C. 5121(d)(3)), and addressed to U.S. DOT Dockets, U.S. Department of Transportation, 1200 New Jersey Avenue SE., Room W12–140, Washington, DC 20590 (*http://Regulations.gov*). Furthermore, a petition for review must state the material facts at issue which the petitioner believes dispute the existence of an imminent hazard and must include all evidence and exhibits to be considered. The petition must also state the relief sought. Within 30 days from the date the petition for review is filed, the Secretary must approve or deny the relief in writing; or find that the imminent hazard continues to exist, and extend the original Emergency Order. In response to a petition for review, the Secretary may grant the requested relief in whole or in part; or may order other relief as justice may require (including the immediate assignment the case to the Office of Hearings for a formal hearing on the record).

Emergency Contact Official

If you have any questions concerning this Amended Emergency Restriction/Prohibition Order, you should call PHMSA Hazardous Materials Information Center at 1–800–467–4922 or email at *phmsa.hm-infocenter@dot.gov*.

Issued in Washington, DC, on January 9, 2017.

Reginald C. Govan,

Chief Counsel, Federal Aviation Administration.

[FR Doc. 2017–00555 Filed 1–9–17; 4:15 pm]

BILLING CODE 4910–13–P

[1] *https://news.samsung.com/us/2016/12/09/samsung-taking-bold-steps-to-increase-galaxy-note7-device-returns/; see also http://www.samsung.com/us/note7recall/.*

[2] *https://explore.t-mobile.com/samsung-galaxy-note7-recall.*

[3] *https://www.verizonwireless.com/support/samsung-galaxy-note7-recall-faqs/; https://www.att.com/esupport/article.html#!/wireless/KM1122948.*

[4] *https://support.sprint.com/support/article/FAQs-about-the-Samsung-Galaxy-Note7-recall/817d4190-b2e2-43e8-b549-97b3553d5c24.*

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 866

[Docket No. FDA–2014–N–0440]

Microbiology Devices; Reclassification of Influenza Virus Antigen Detection Test Systems Intended for Use Directly With Clinical Specimens

AGENCY: Food and Drug Administration, HHS.

ACTION: Final order.

SUMMARY: The Food and Drug Administration (FDA) is reclassifying antigen based rapid influenza virus antigen detection test systems intended to detect influenza virus directly from clinical specimens that are currently regulated as influenza virus serological reagents from class I into class II with special controls and into a new device classification regulation.

At last, the Final Rule has arrived!

If you are an RIDT user…

What do the new regulations entail?

- Reclassifying RIDTs from **Class I to Class II**
- Premarket notification to assure safety and effectiveness – 510(k) clearance
- Add **"special controls"**
  - Set minimum clinical performance criteria for sensitivity and specificity
    - Appropriate comparator tests for new assays
  - Accuracy assessed by manufacturers **each year** and when **novel strain emerges (within 30 days)**
  - By July 31, results of past 3 years analytical reactivity testing must be included in labeling

If you are an RIDT user…

When will this happen?

- For existing tests enforcement as of **1/12/2018**

What about your particular test?

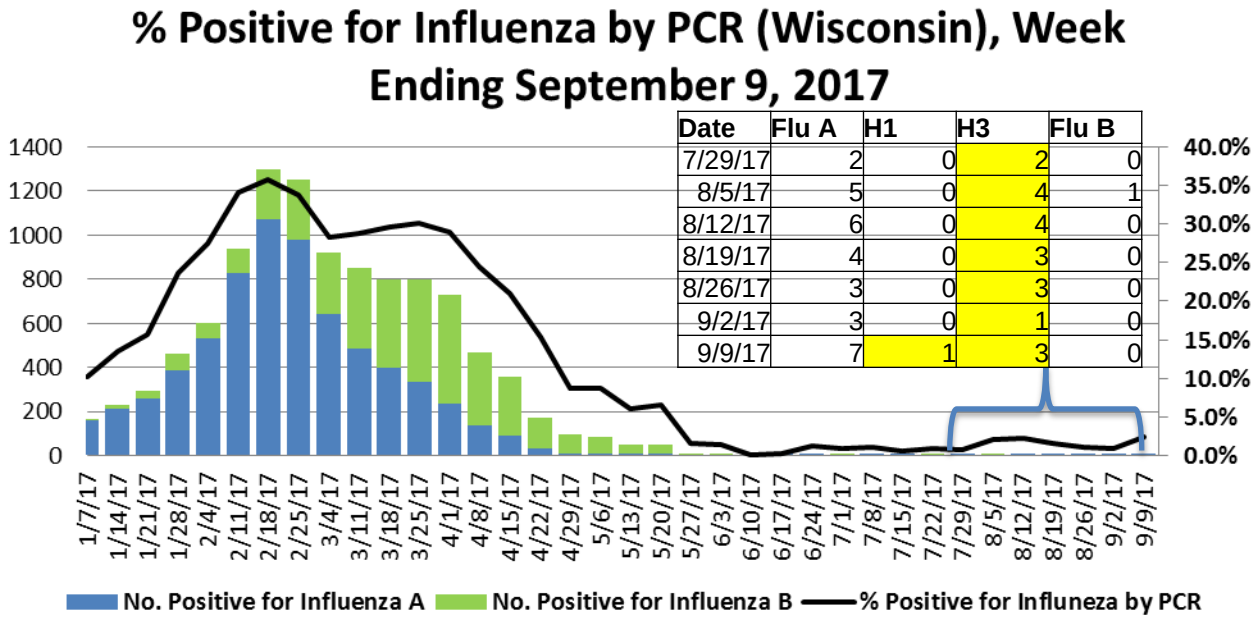
- **Contact the manufacturer**; there will not be a central resource of information at this point
- If special controls not met, manufacturers expected to stop sales/distribution. However…
  - **You may be able to get test yet – Don't!**
  - **Do not use up existing inventory**
- Keep an eye on kit labeling and company website

Likely Impact: Better tests? Fewer tests?

Influenza and non-influenza virus respiratory surveillance

Influenza season, 2017-2018

Early season

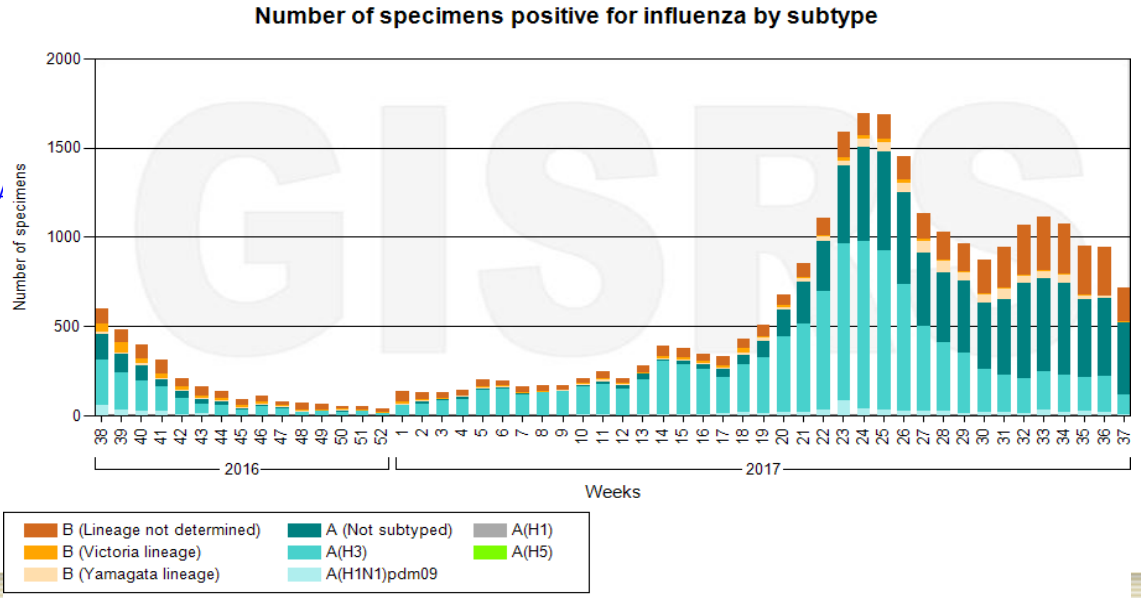


Date	Flu A	H1	H3	Flu B
7/29/17	2	0	2	0
8/5/17	5	0	4	1
8/12/17	6	0	4	0
8/19/17	4	0	3	0
8/26/17	3	0	3	0
9/2/17	3	0	1	0
9/9/17	7	1	3	0

Tasmania (Australia) is in the "peak phase" of the most devastating flu season in recent memory, Health Minister Michael Ferguson warned.

As of [12 Sep 2017], there were 2337 confirmed cases of influenza and 21 deaths since [1 Jan 2017]. Last year [2016], 14 people died, and only 969 influenza cases were reported.

Date: Sun 17 Sep 2017 3:00 pm AEST
Source: The Advocate [edited]
http://www.theadvocate.com.au/story/



Influenza Vaccine composition

2017-2018 **Northern** Hemisphere

A/Michigan/45/2015 (H1N1)pdm09-like virus;

A/Hong Kong/4801/2014 (H3N2)-like virus;

B/Brisbane/60/2008-like virus;

B/Phuket/3073/2013-like virus

2018 **Southern** Hemisphere

A/Michigan/45/2015 (H1N1)pdm09-like virus;

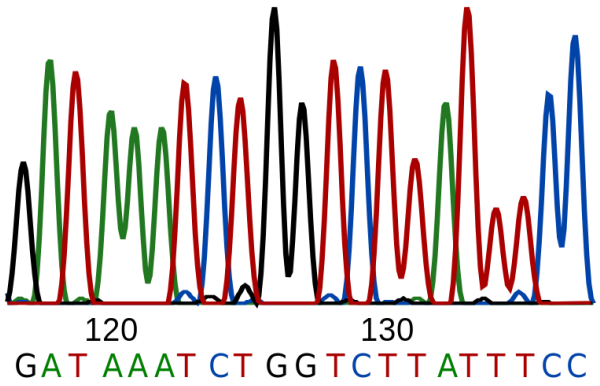
A/Singapore/INFIMH-16-0019/2016 (H3N2)-like virus;

B/Brisbane/60/2008-like virus

B/Phuket/3073/2013-like virus.

What do we do with the specimens submitted?

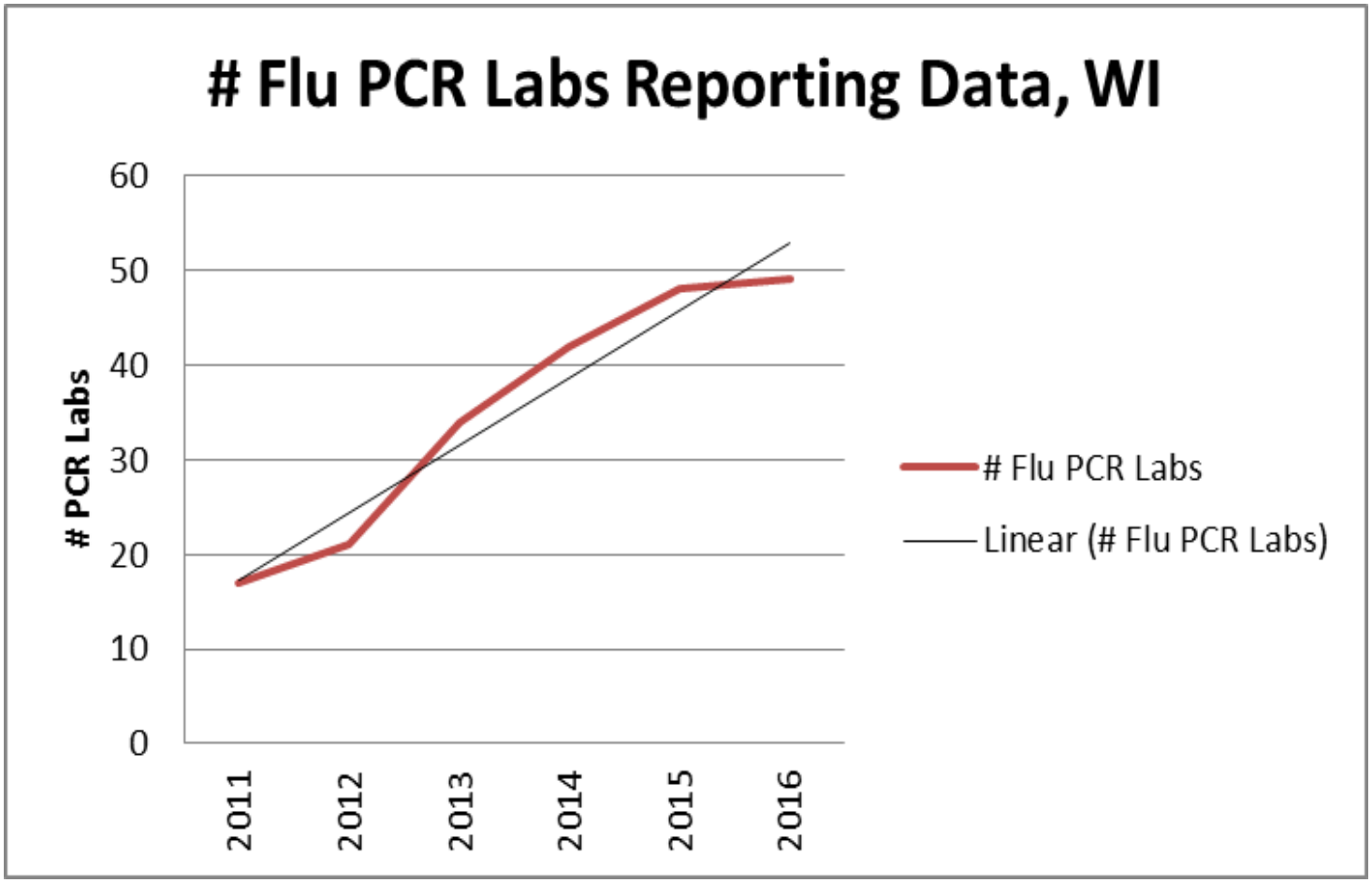
- Subtype characterization
- Antiviral resistance monitoring
- Whole genome sequencing
  - 3c.2a and 3c.2a1
- Provide specimen/ isolates to CDC
- Provide weekly summary of testing data



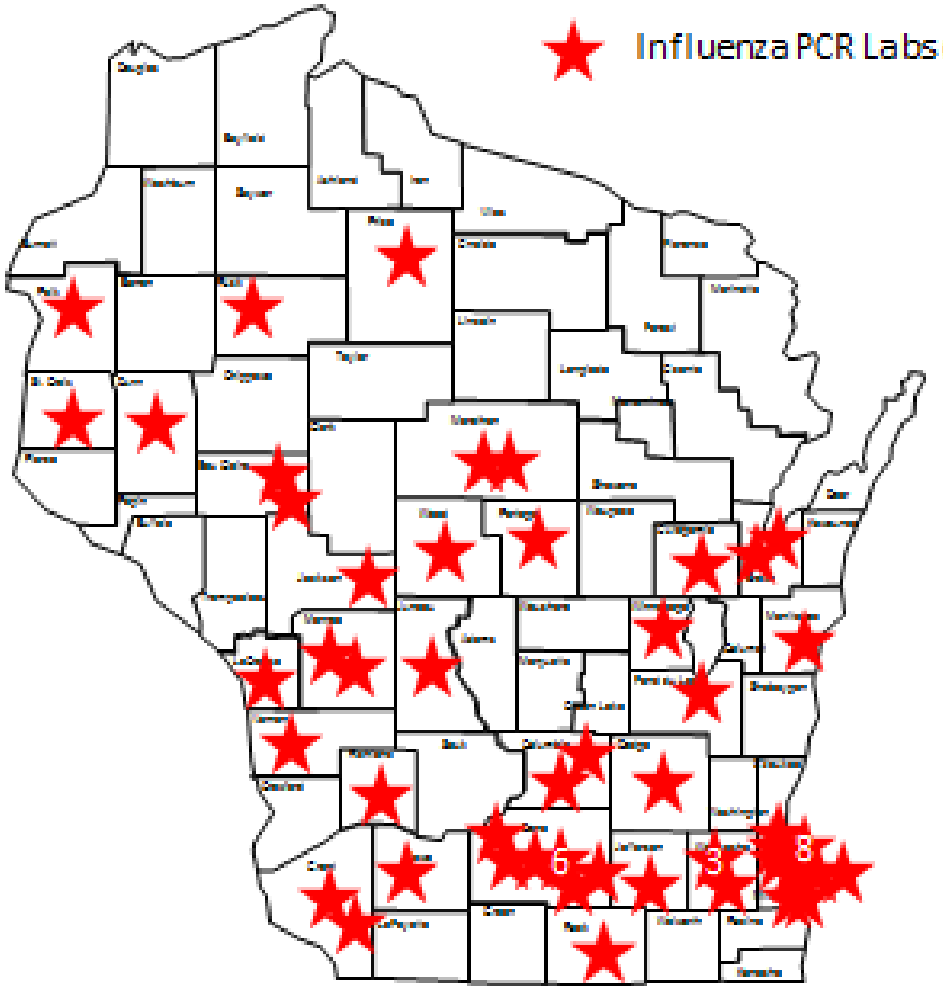
Antiviral Resistance Monitoring- Wisconsin, 2017

WI neuraminidase inhibition testing 2017			
YR	Month	# Reduced inhibition	# Tested
2017	January	0	11
	February	0	13
	March	0	10
	April	0	13
	May	0	8
	June	0	5
	July	0	3
	August	0	3
	September	0	5
	Total	**0**	**71**

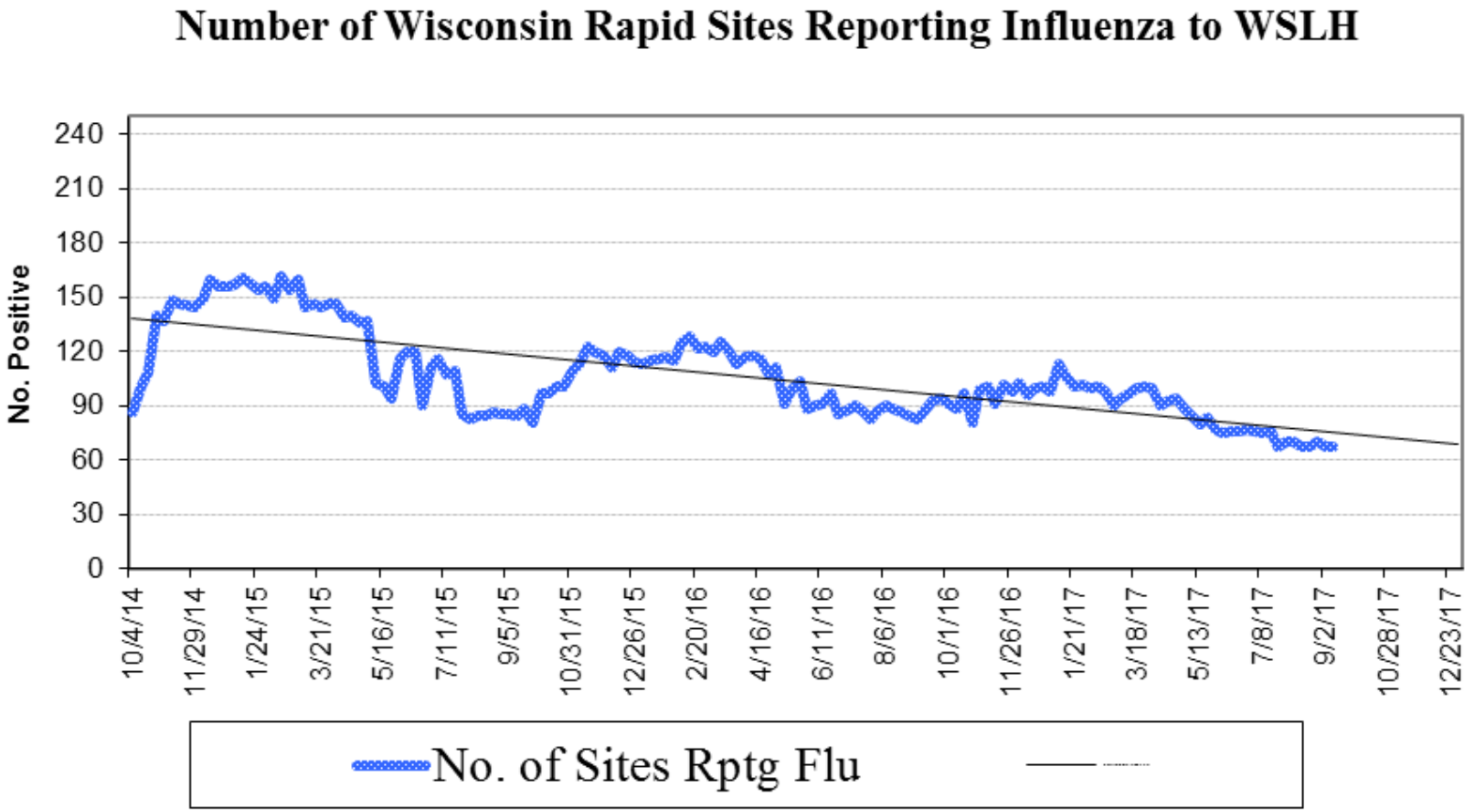
- Oseltamivir
- Zanamivir
- Peramivir


Flu PCR Labs Reporting Data, WI
PCR Labs
60
50
40
30
20
10
0
2011
2012
2013
2014
2015
2016
Flu PCR Labs
Linear (# Flu PCR Labs)

Wisconsin Labs with Flu PCR & Virus Culture Capacity, September 2016



Rapid Influenza Reporting Sites, 2014-2017, WI



Influenza Surveillance in Wisconsin

Multi-element approach

1. Rapid Influenza Diagnostic Testing (RIDT) Sites

Now <50% of influenza testing in WI!

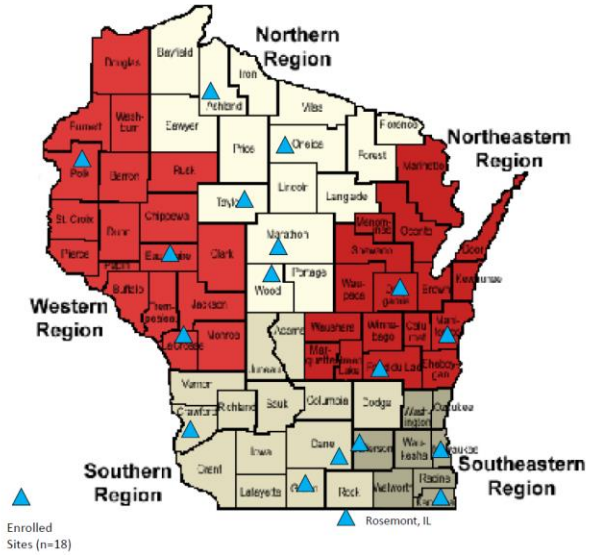
- Confirmatory testing during periods of low prevalence (June to October).
- Please notify WSLH of suspected performance issues (e.g. False positives/negatives)

WSLH can provide confirmatory testing for the first positive influenza specimens.

Influenza Surveillance in Wisconsin

Multi-element approach

2. Enrolled Surveillance Sites
   - 17 labs in 5 public health regions.
   - Provide randomized specimens weekly.

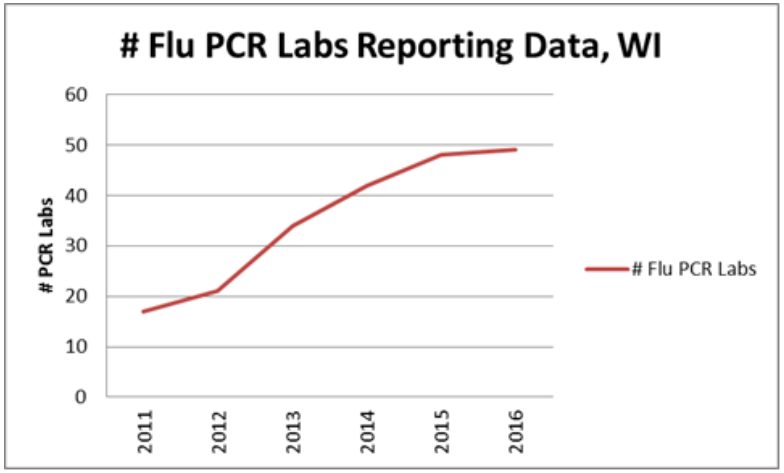


Request to continue to submit the first 1-2 specimens per week with influenza test requests to WSLH.

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).

Laboratory-based Surveillance

All Clinical Laboratories performing influenza diagnostic testing

All Labs:

- Send those with international travel histories
- *One* influenza-related hospitalization per week
- Unusual presentations/results
- Contact with swine/ sick or dead poultry
- Antiviral treatment failure

- 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 Changes

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

- Limit to one specimen/week

All labs: Please continue to send all out-of-season positive influenza A specimens (e.g. June-October 1).

Laboratory-based Surveillance

All Clinical Laboratories performing influenza diagnostic testing

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- *One* influenza-related hospitalization per week
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- Contact with swine/ sick or dead poultry
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THANK
YOU