


# **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

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## Influenza

### *The latest information*

[www.cdc.gov/flu/index.htm](http://www.cdc.gov/flu/index.htm)

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## The Changeability of Influenza

### *Antigenic Drift → Seasonal Influenza*

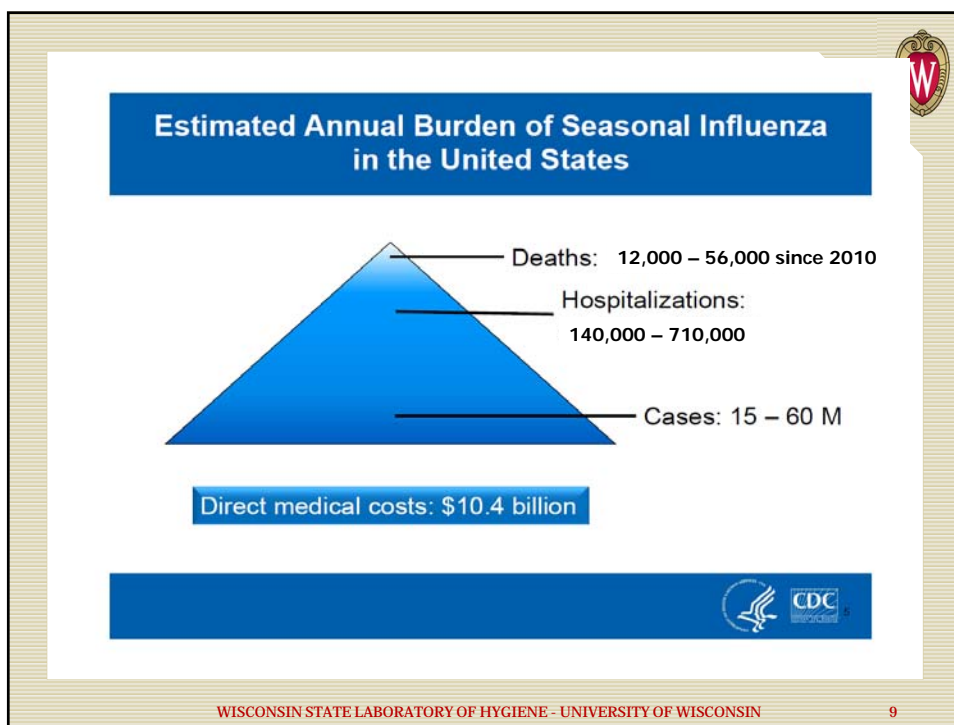
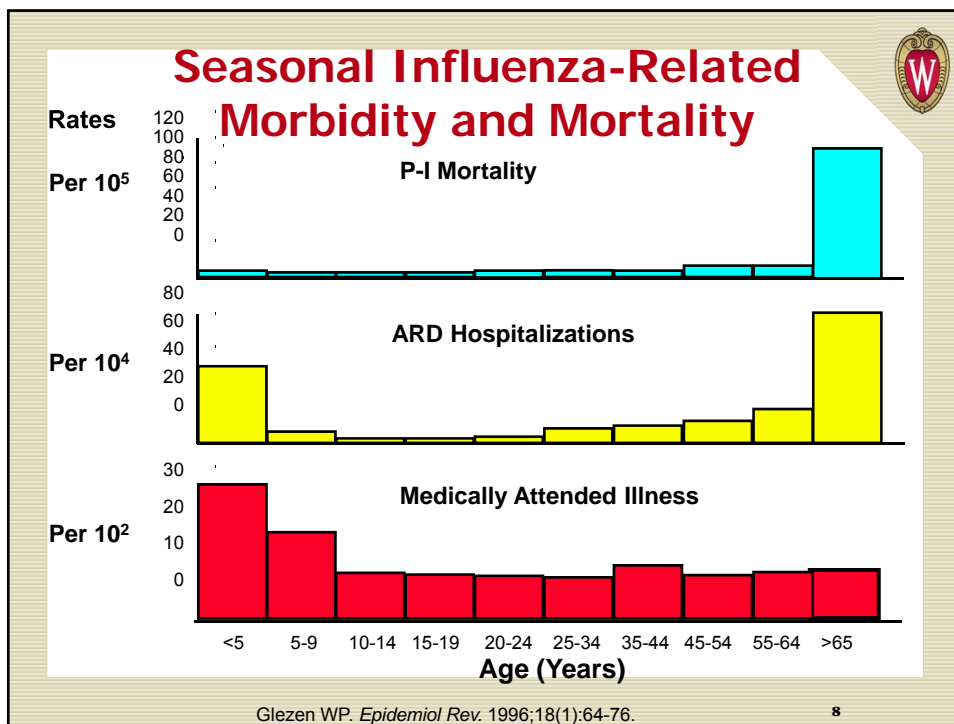
**Antigenic Drift**  
Manifests in HA and NA as a result of continuous and gradual accumulation of point mutations in the HA and NA genes

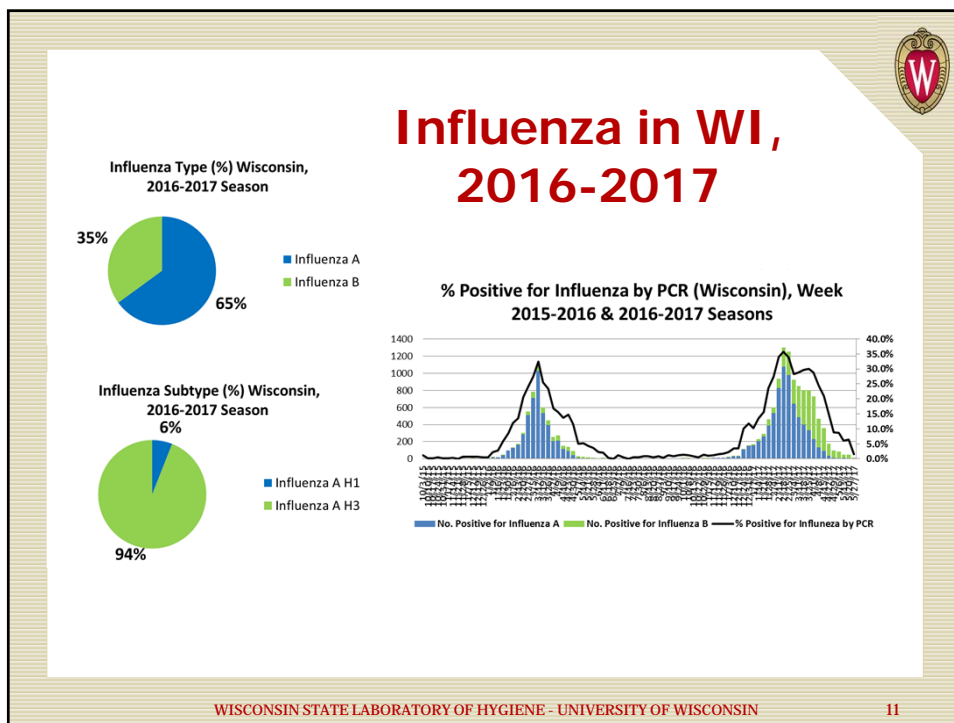
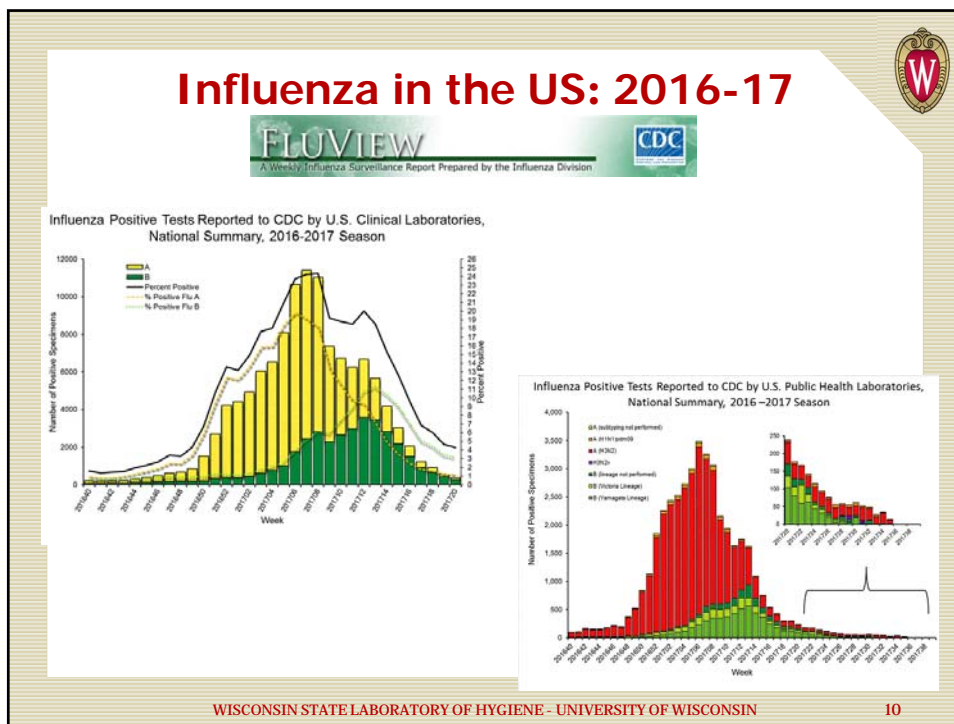
- 1 Each year's flu vaccine contains three flu strains - two A strains and one B strain - that can change from year to year.
- 2 After vaccination, your body produces infection-fighting antibodies against the three flu strains in the vaccine.
- 3 If you are exposed to any of the three flu strains during the flu season, the antibodies will latch onto the virus's HA antigens, preventing the flu virus from attaching to healthy cells and infecting them.
- 4 Influenza virus genes, made of RNA, are more prone to mutations than genes made of DNA.
- 5 If the HA gene changes, so can the antigen that it encodes, causing it to change shape.

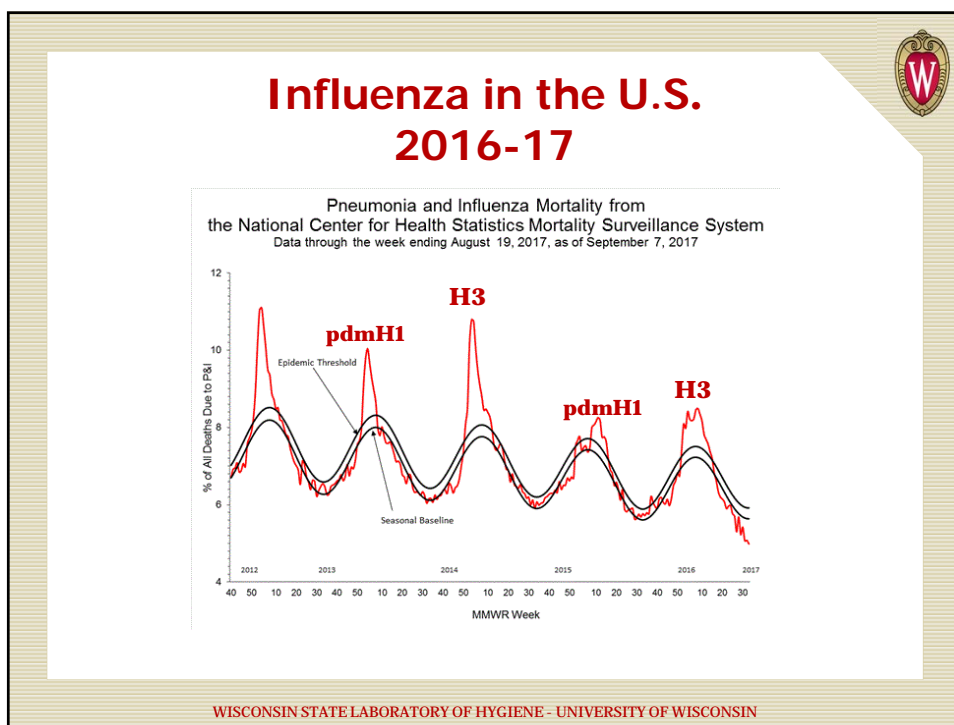
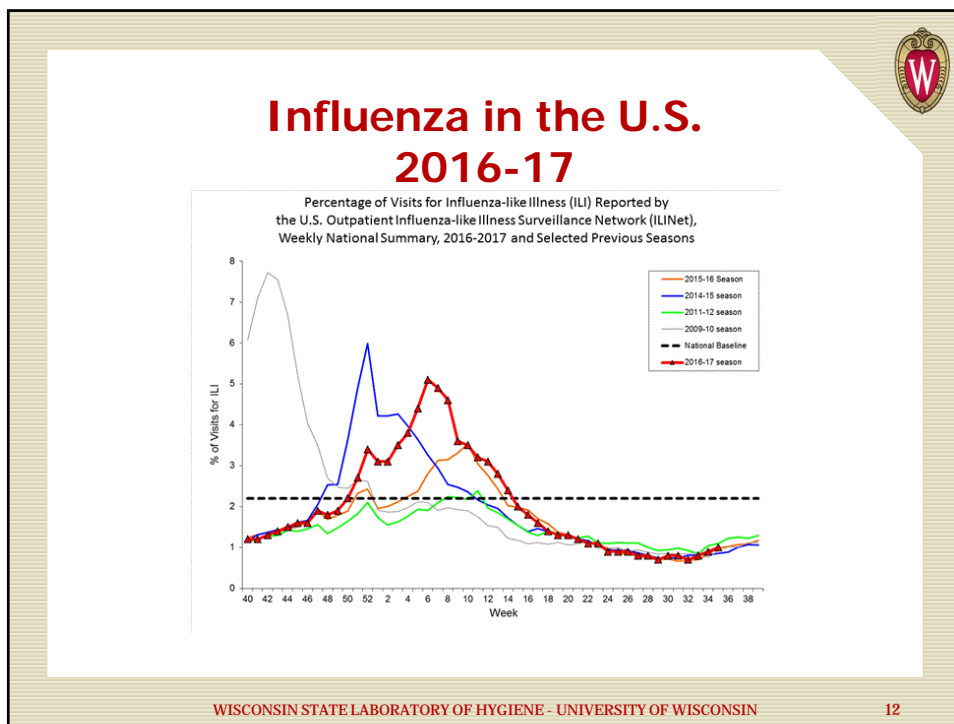
This type of genetic mutation is called "ANTIGENIC DRIFT."

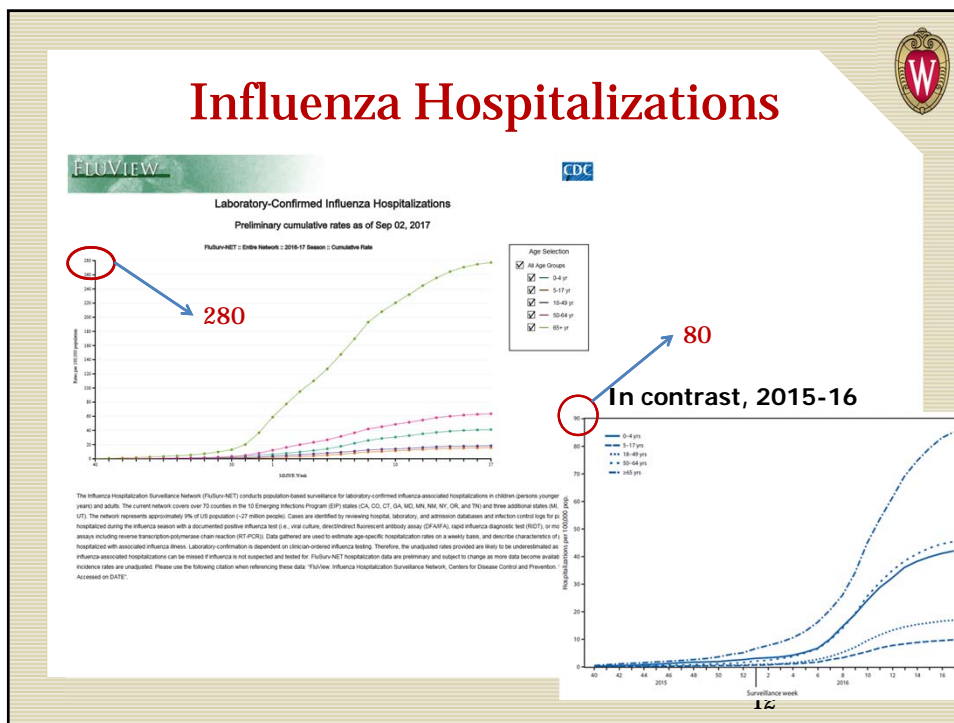
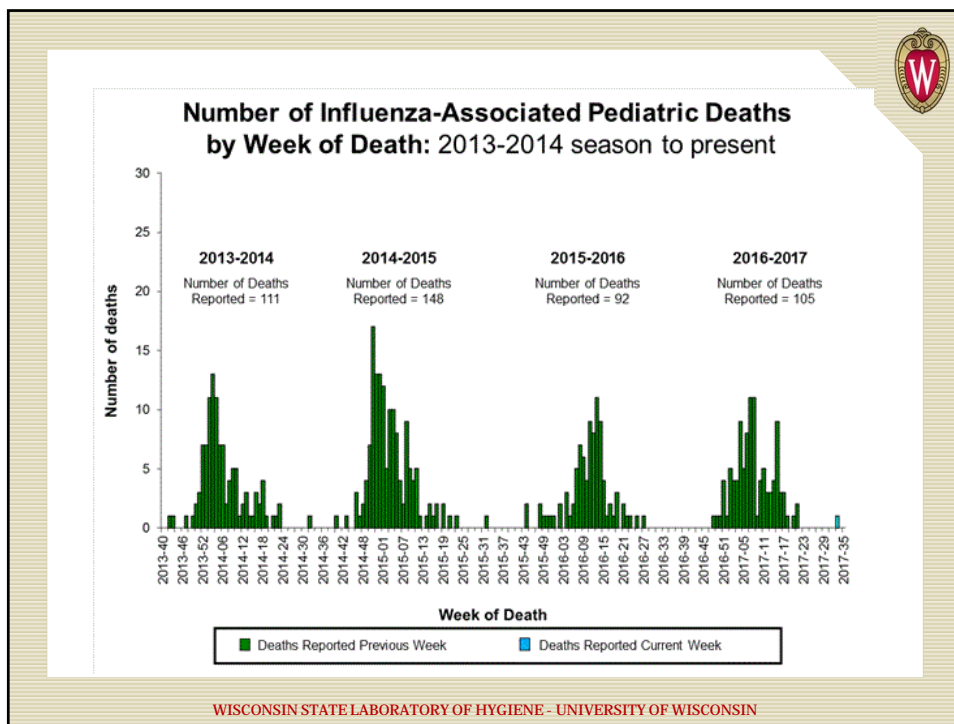
[www.flu.gov](http://www.flu.gov)


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## 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)

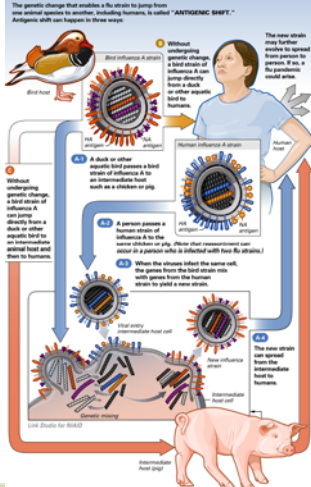
**... and that's what we got 😊**

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## The Changeability of Influenza *Antigenic Shift*

[www.flu.gov](http://www.flu.gov)



The genetic change that enables a flu strain to jump from one animal species to another, including humans, is called "ANTIGENIC SHIFT." Antigenic shift can happen in three ways:

1. Without undergoing genetic change, a bird strain of influenza A can jump directly from a duck or other aquatic bird to a human.
2. A duck or other aquatic bird passes a bird strain of influenza A to an intermediate host, such as a chicken or pig.
3. A person passes a human strain of influenza A to the intermediate host. (This dual transmission can occur in a particular host, or between hosts.)
4. When the viruses infect the same cell, the genes from the bird strain mix with genes from the human strain to yield a new strain.
5. The new strain can spread from person to person. If so, it is the pandemic model strain.

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

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### Infectious Diseases at the Human-Animal Interface

#### *Influenza as an Example*

The diagram illustrates the human-animal interface for influenza. On the left, a circular frame contains various animals (birds, pigs, horses, chickens, etc.) with the text "Circulation of animal influenza viruses within and among animal species". A red arrow points from this circle to a globe on the right, which is surrounded by a yellow ring and has the text "Circulation of seasonal and pandemic influenza viruses in humans".

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### Influenza at the Human-Animal Interface

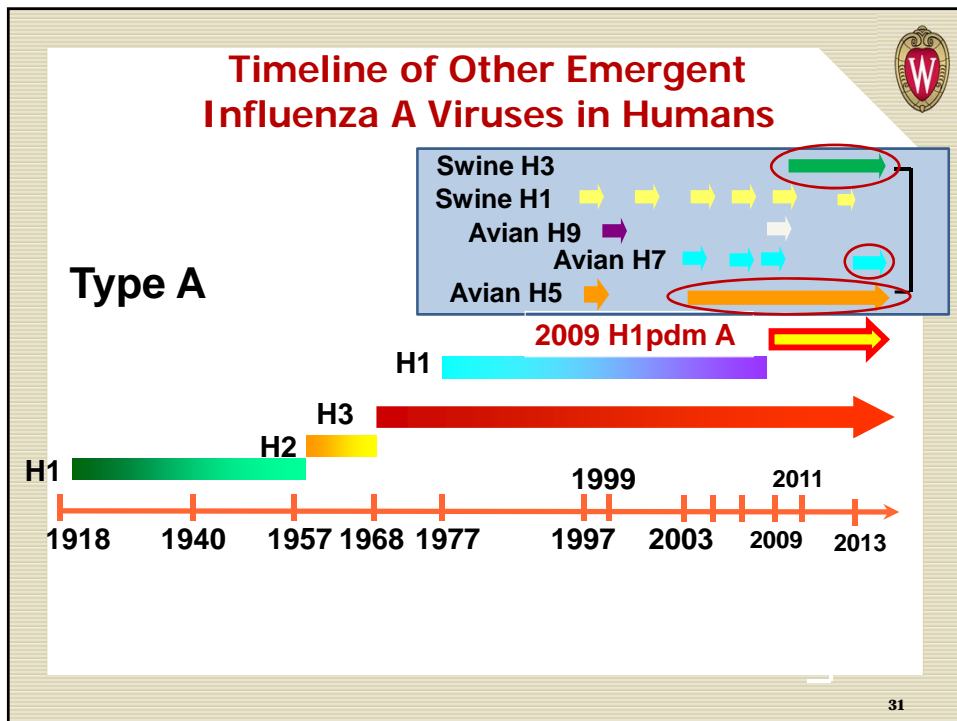
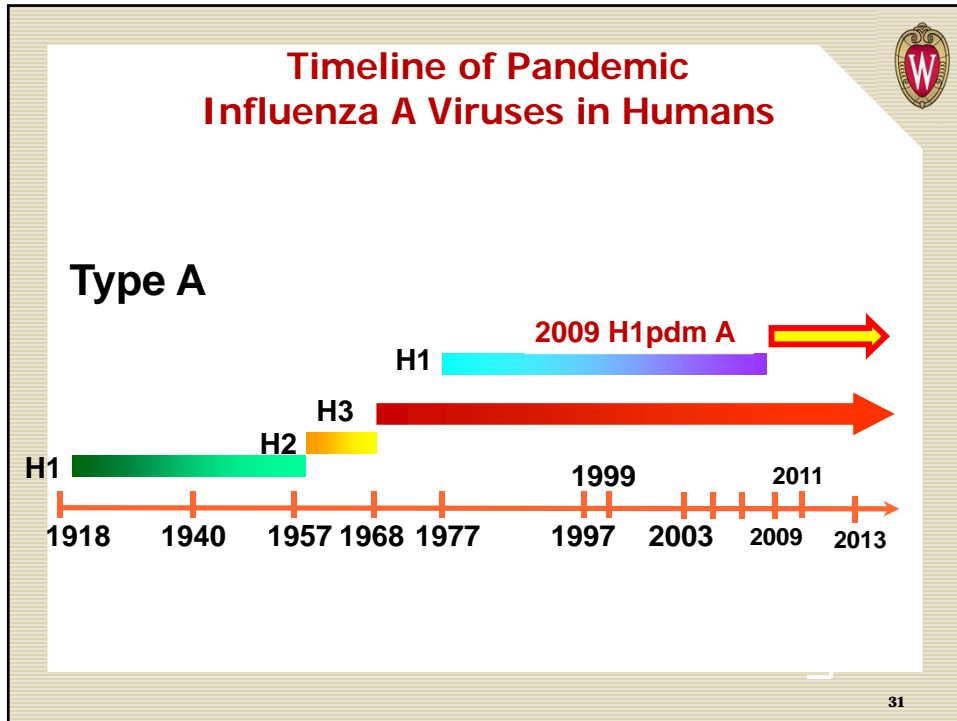
#### Influenza A

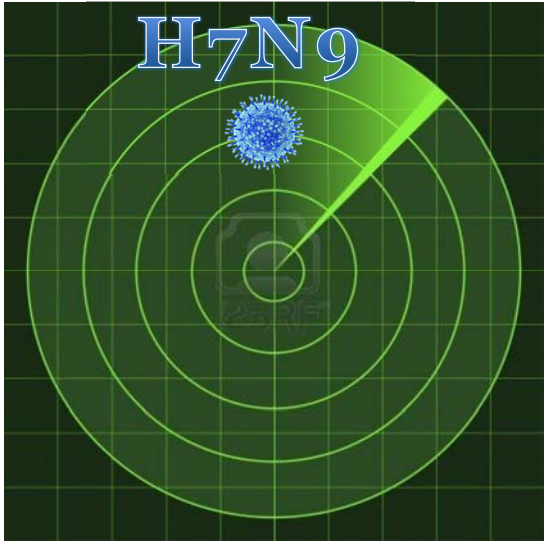
- H1 - H18
- N1 - N11

The flowchart shows the transmission of Influenza A. It starts with "Aquatic birds" (represented by a photo of birds in flight). Arrows point from this box to five other boxes: "Poultry", "Humans", "Pigs", "Horses", and "Aquatic mammals". Below "Poultry" is a box for "Cats", and below "Horses" is a box for "Dogs". The "Humans" box is highlighted with a red border, and the "Pigs" box is also highlighted with a red border. Arrows indicate bidirectional transmission between "Poultry" and "Humans", and between "Humans" and "Pigs".

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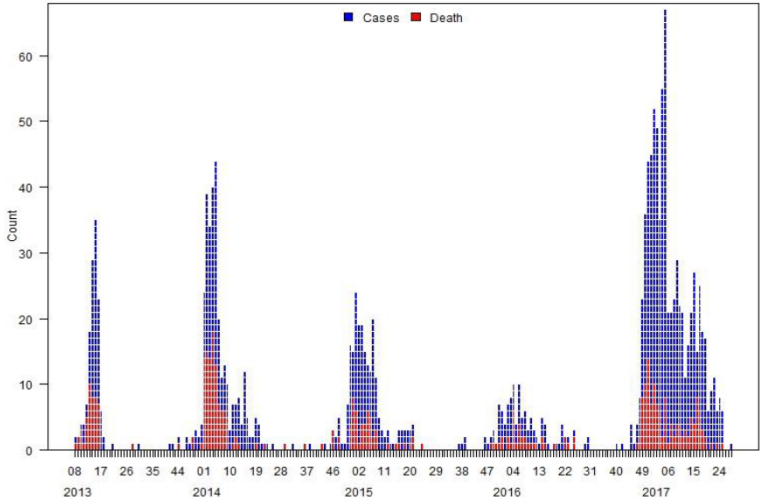




A graphic featuring the text "H7N9" in a blue, stylized font at the top. Below the text is a blue, spiky virus particle. The background consists of concentric green circles on a dark green grid, resembling a target. A green wedge-shaped highlight is positioned on the right side of the target.

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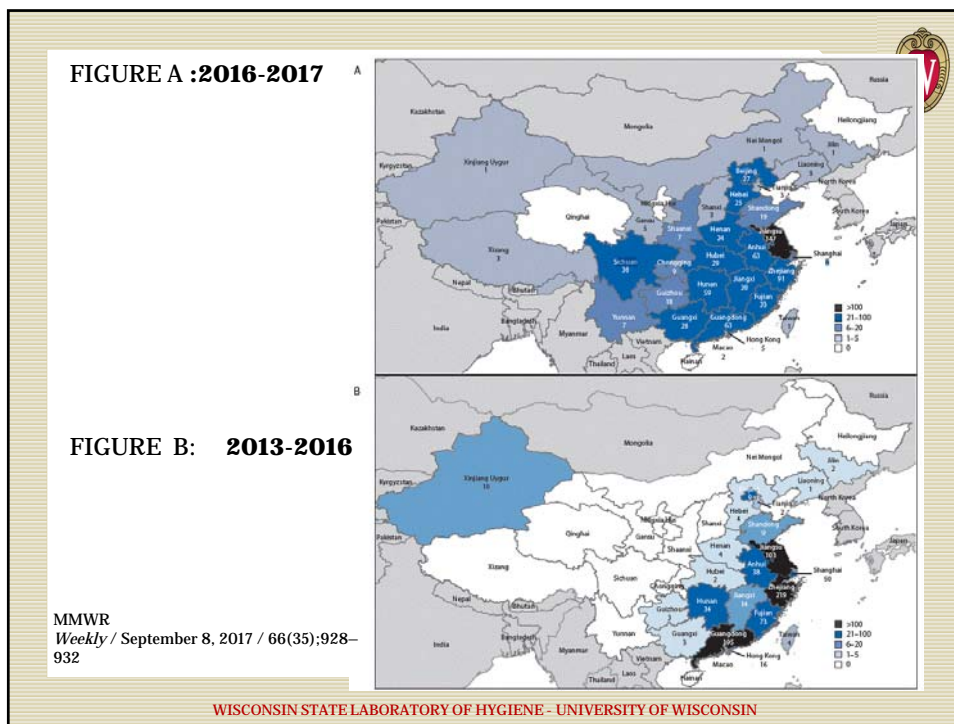
Number of confirmed human H7N9 cases and deaths, as reported to WHO by week, as of 2017-7-24



A bar chart showing the number of confirmed human H7N9 cases (blue bars) and deaths (red bars) reported to WHO by week from 2013 to 2017. The y-axis is labeled "Count" and ranges from 0 to 60. The x-axis shows weeks from 08 to 24 for each year. There are four distinct waves of cases: a small wave in late 2013, a larger wave in early 2014, a moderate wave in early 2015, and a very large wave in early 2017. The 2017 wave shows a peak of over 60 cases and several deaths.

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)

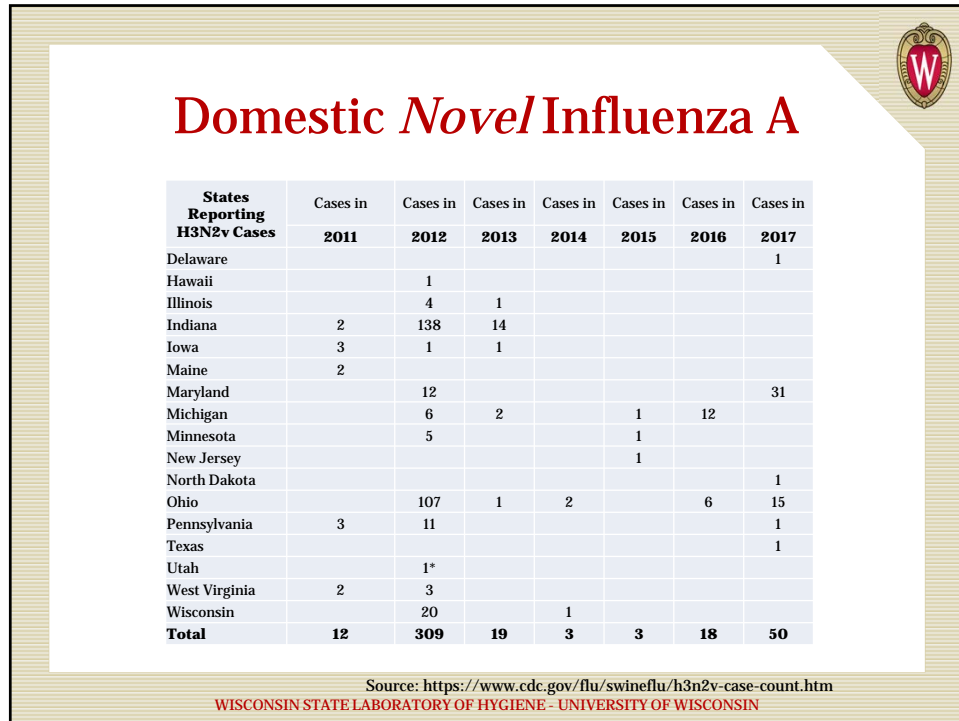
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## Why Avian Influenza A (H7N9)?


- 5<sup>th</sup> epidemic mutations detected
  - **Highly Pathogenic Avian Influenza (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.

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## 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




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## 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.

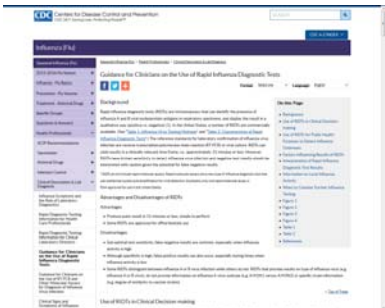


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## Rapid Influenza Diagnostic Tests (RIDTs)

### *A perennial discussion*




[www.cdc.gov/flu/professionals/diagnosis/clinician\\_guidance\\_ridt.htm](http://www.cdc.gov/flu/professionals/diagnosis/clinician_guidance_ridt.htm)

[www.jointcommission.org/siras.aspx](http://www.jointcommission.org/siras.aspx)



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## Improving RIDT Performance

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

At last, the Final Rule has arrived!

21 CFR Part 808

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## 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

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## 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?**

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## Influenza and non-influenza virus respiratory surveillance

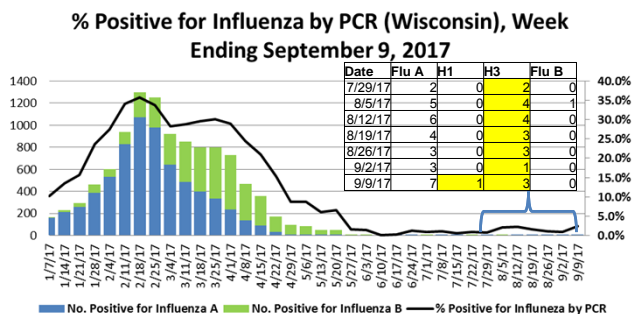


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# Influenza season, 2017-2018



## Early season

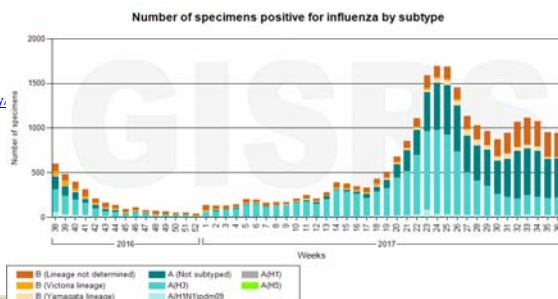


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Tasmania (Australia) is in the "peak phase" of the most devastating flu season in recent memory, Health Minister Michael Ferguson warned.

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>



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## 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

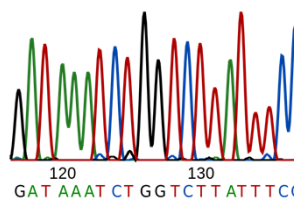
B/Phuket/3073/2013-like virus.

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## 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



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## Antiviral Resistance Monitoring- Wisconsin, 2017



WI neuraminidase inhibition testing 2017

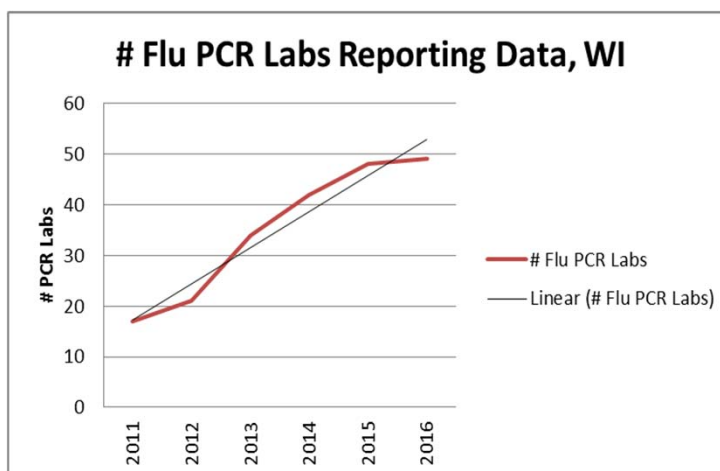
YR	Month	# Reduced inhibition	# Tested
2017	January	0	11
	February	0	13
	March	0	10
	April	0	13
	May	0	8
	June	0	5
	July	0	3
	August	0	3
	September	0	5
<b>Total</b>		<b>0</b>	<b>71</b>



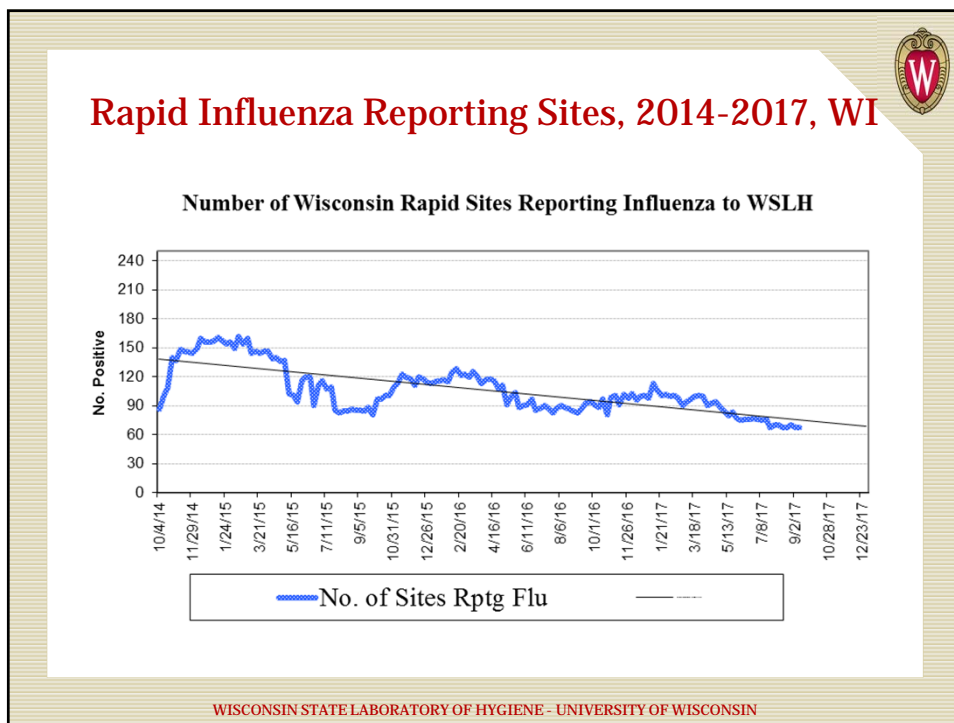
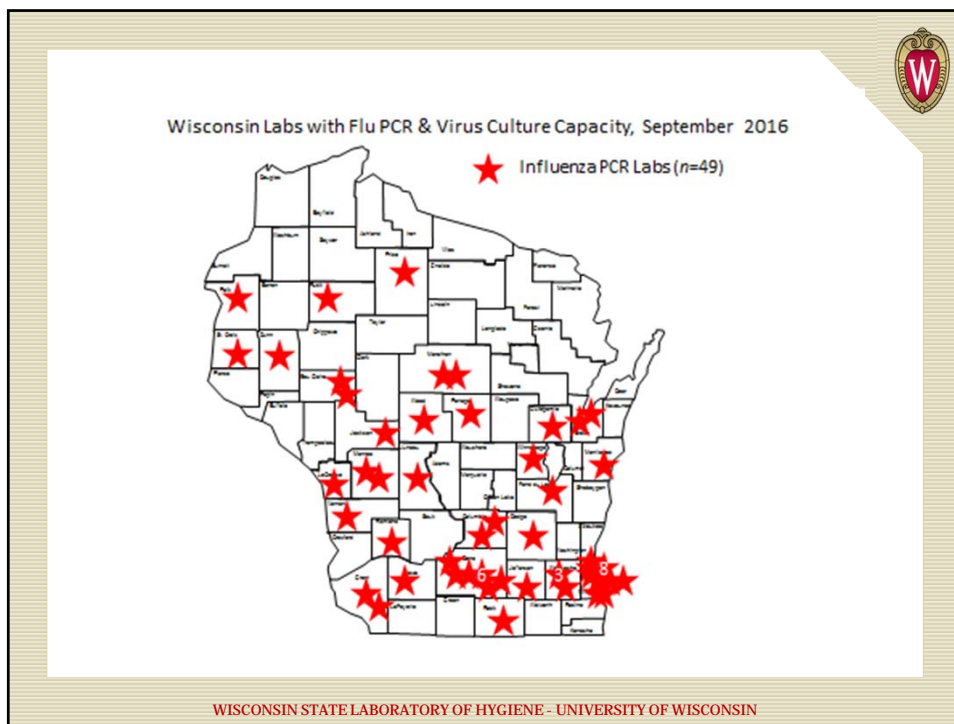
- Oseltamivir
- Zanamivir
- Peramivir

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### # Flu PCR Labs Reporting Data, WI



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## Influenza Surveillance in Wisconsin



### Multi-element approach

#### 1. Rapid Influenza Diagnostic Testing (RIDT) Sites

**BREAKING NEWS**

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.**

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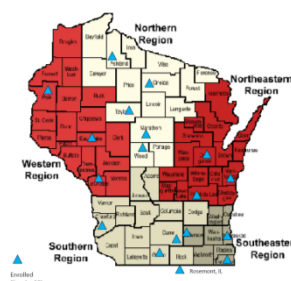
## Influenza Surveillance in Wisconsin



### 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.**

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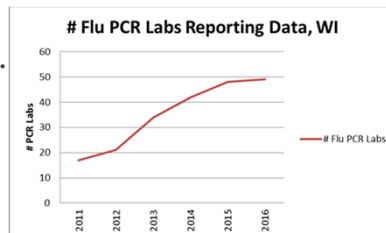
## Influenza Surveillance in Wisconsin



### 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 unsubtypeable specimens when subtyping for both 2009 H1N1 and seasonal H3 were attempted (Ct<35).

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## 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


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## BREAKING NEWS

- 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.

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## 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).**

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## Laboratory-based Surveillance



### All Clinical Laboratories performing influenza diagnostic testing

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