Influenza and other Respiratory Viruses Update--2018

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and

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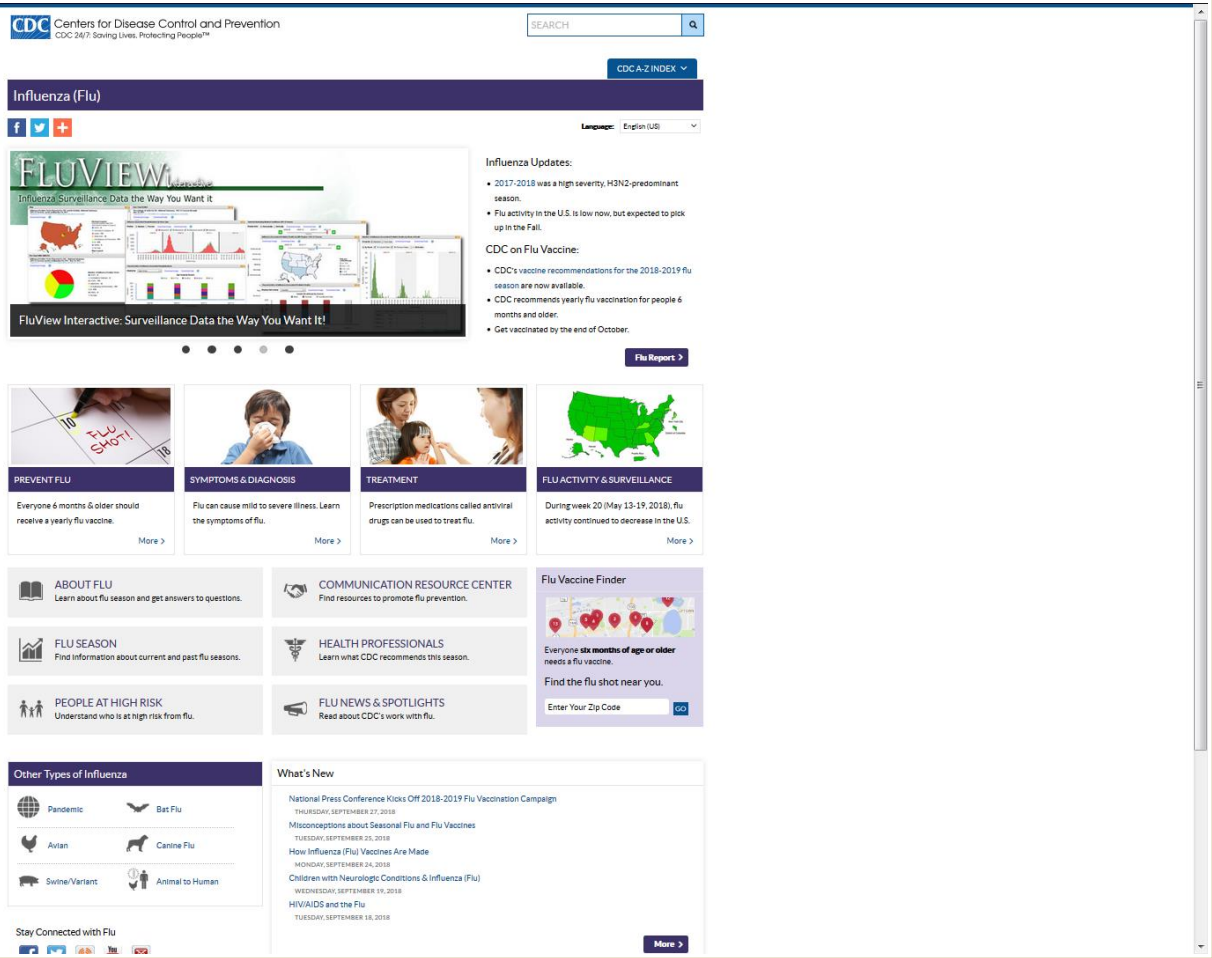
Learning Objectives

- Review of influenza basics.
- Review of the 2017-2018 influenza season.
- Influenza vaccine updates.
- Emerging viral diseases.
- Seasonal respiratory virus activity review.
- Discuss surveillance strategy for 2018-2019.

Influenza

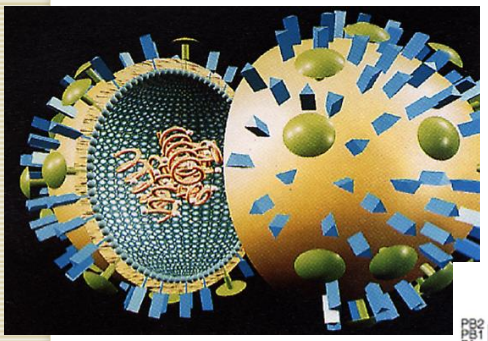
The latest information

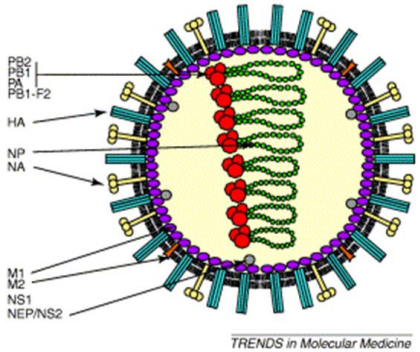
www.cdc.gov/flu/



The Changeability of Influenza

Antigenic Drift →Seasonal Influenza

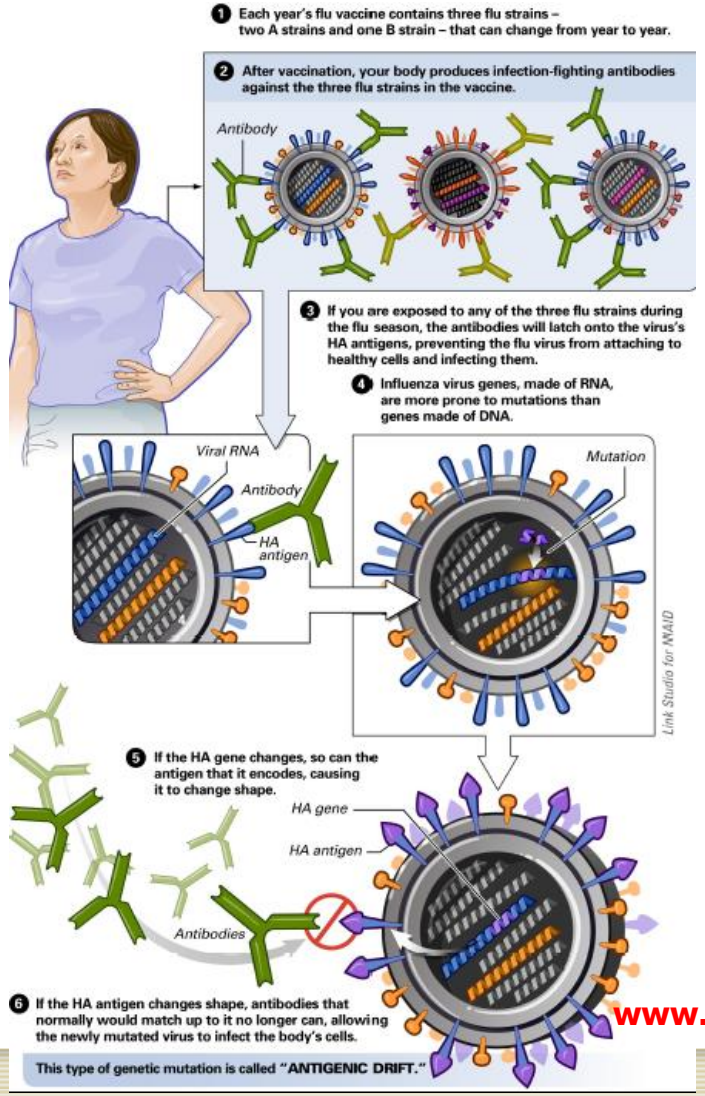




TRENDS in Molecular Medicine

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.cdc.gov/flu

Significant Annual Burden of Influenza in Humans

Influenza

United States

Global

	United States	Global
Deaths	12,000 – 56,000	291,000 – 646,000
Severe Cases Hospitalizations	140,000 – 710,000	3M to 5M
Cases	9.2M – 35.6M	1.0 B

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

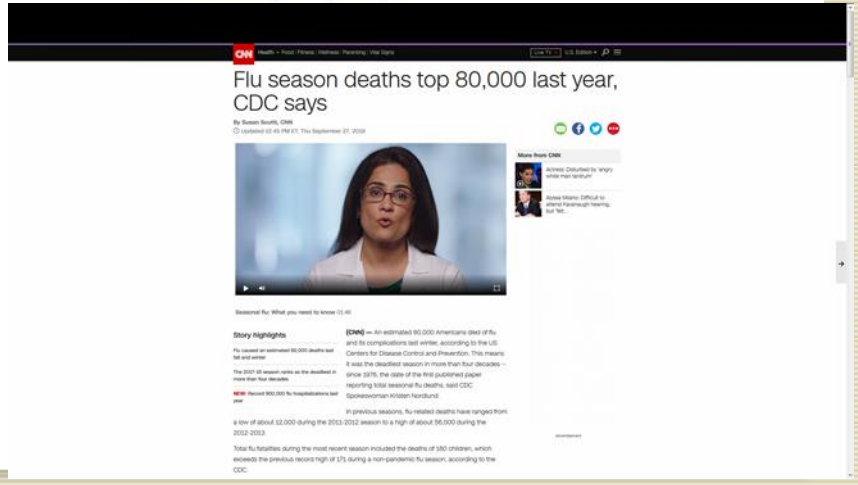
https://www.cdc.gov/flu/about/disease/2015-16.htm; http://www.who.int/immunization/topics/influenza/en/; Iuliano et al Lancet 2017

Influenza 2017-18

*An **historically** severe year*

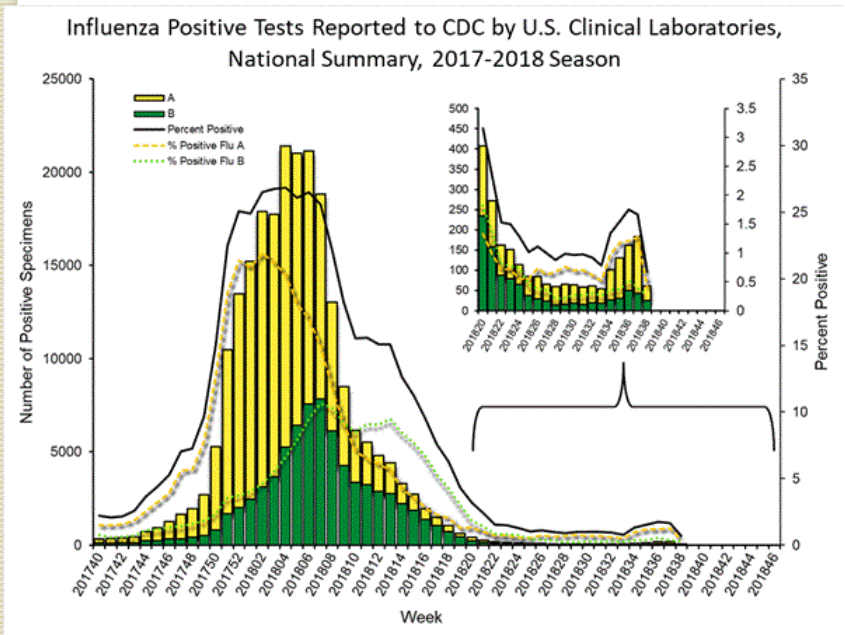
Flu outbreak in Wisconsin severe and expected to be widespread at least another month

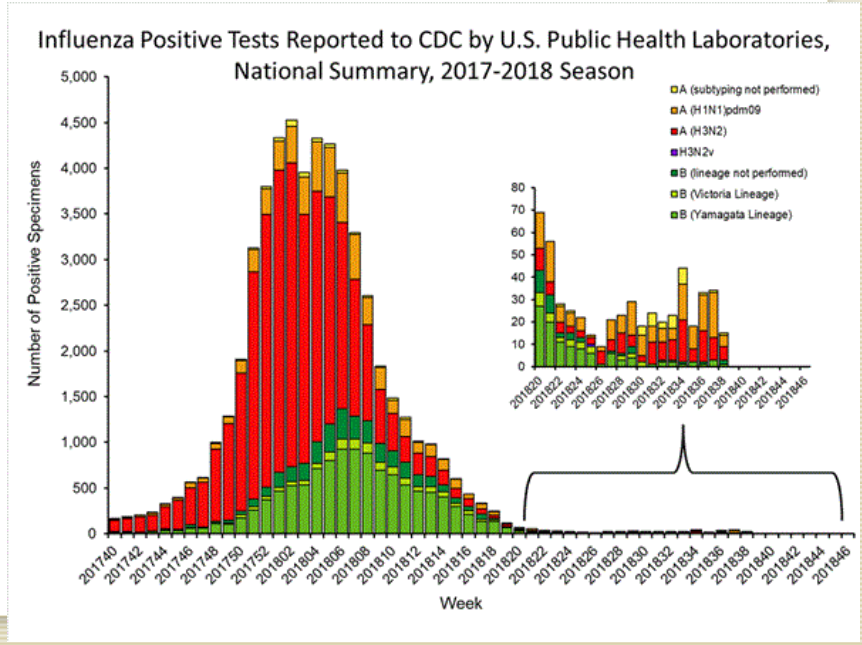
"Some hospitals have had to temporarily divert patients from emergency departments because they ran out of hospital beds… Meriter and UW hospitals in Madison were at or approaching capacity at one point last week."
---M J-S, Jan 19, 2018---



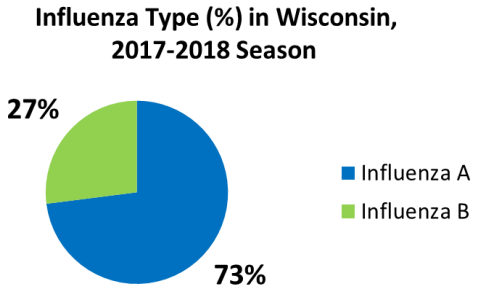
Influenza in the US: 2017-18

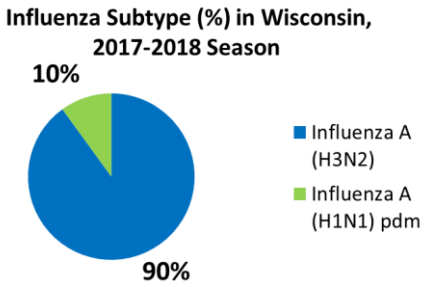
FLUVIEW
A Weekly Influenza Surveillance Report Prepared by the Influenza Division
CDC

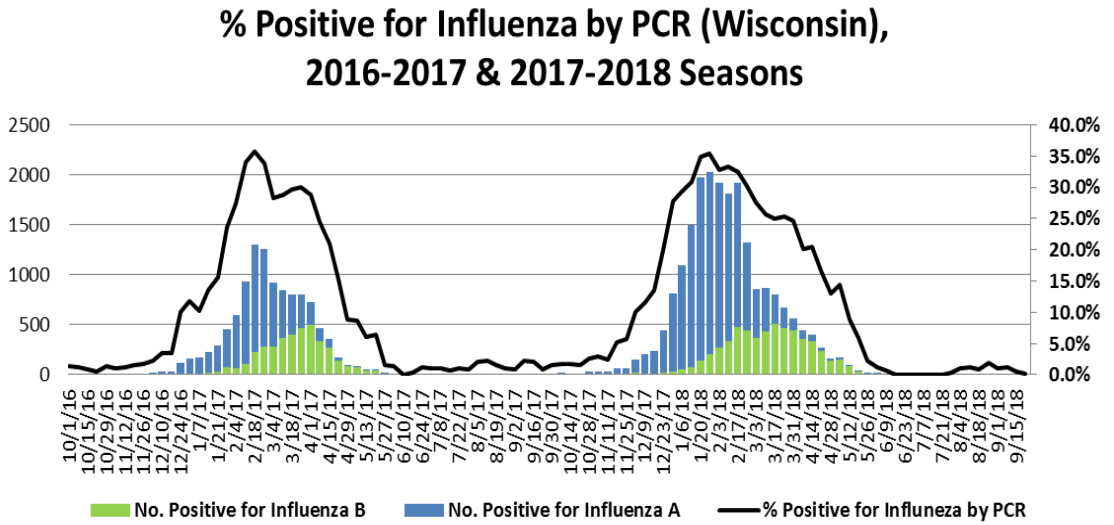




Influenza in WI, 2017-2018

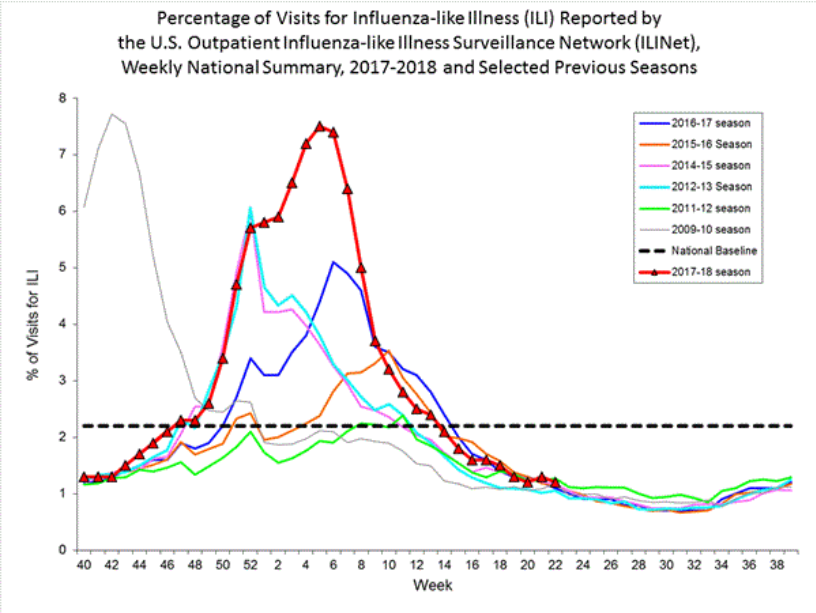


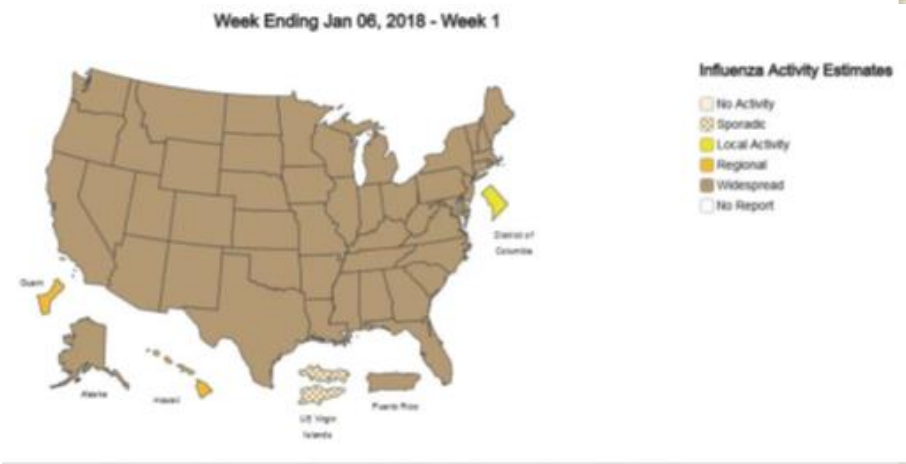




Influenza in the U.S. :2017-18

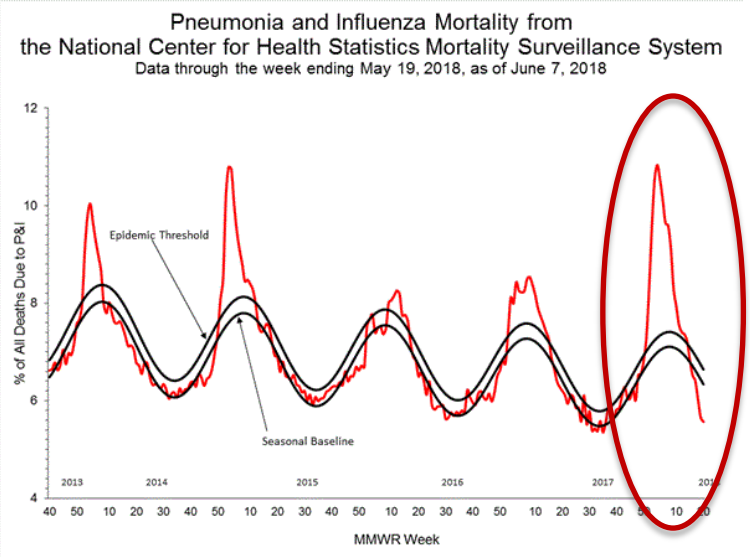
ILI Activity

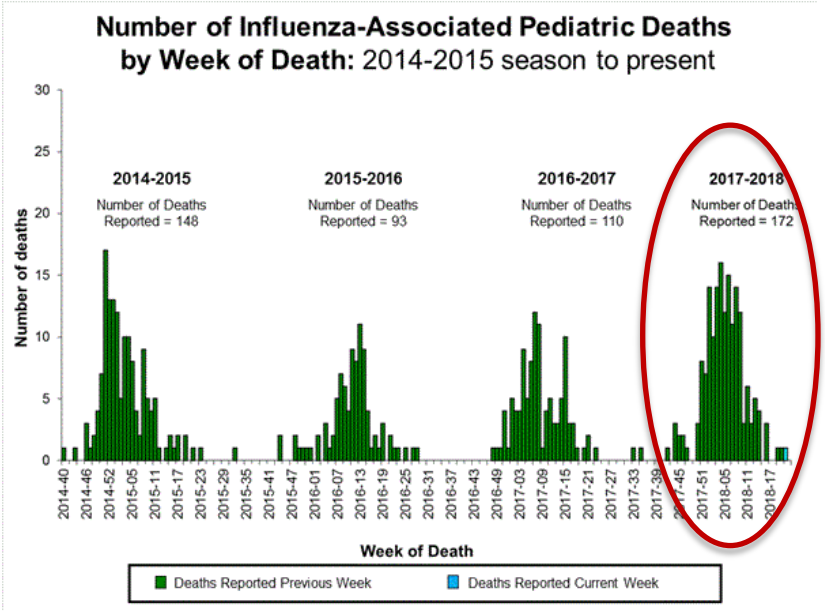




Influenza in the U.S. :2017-18

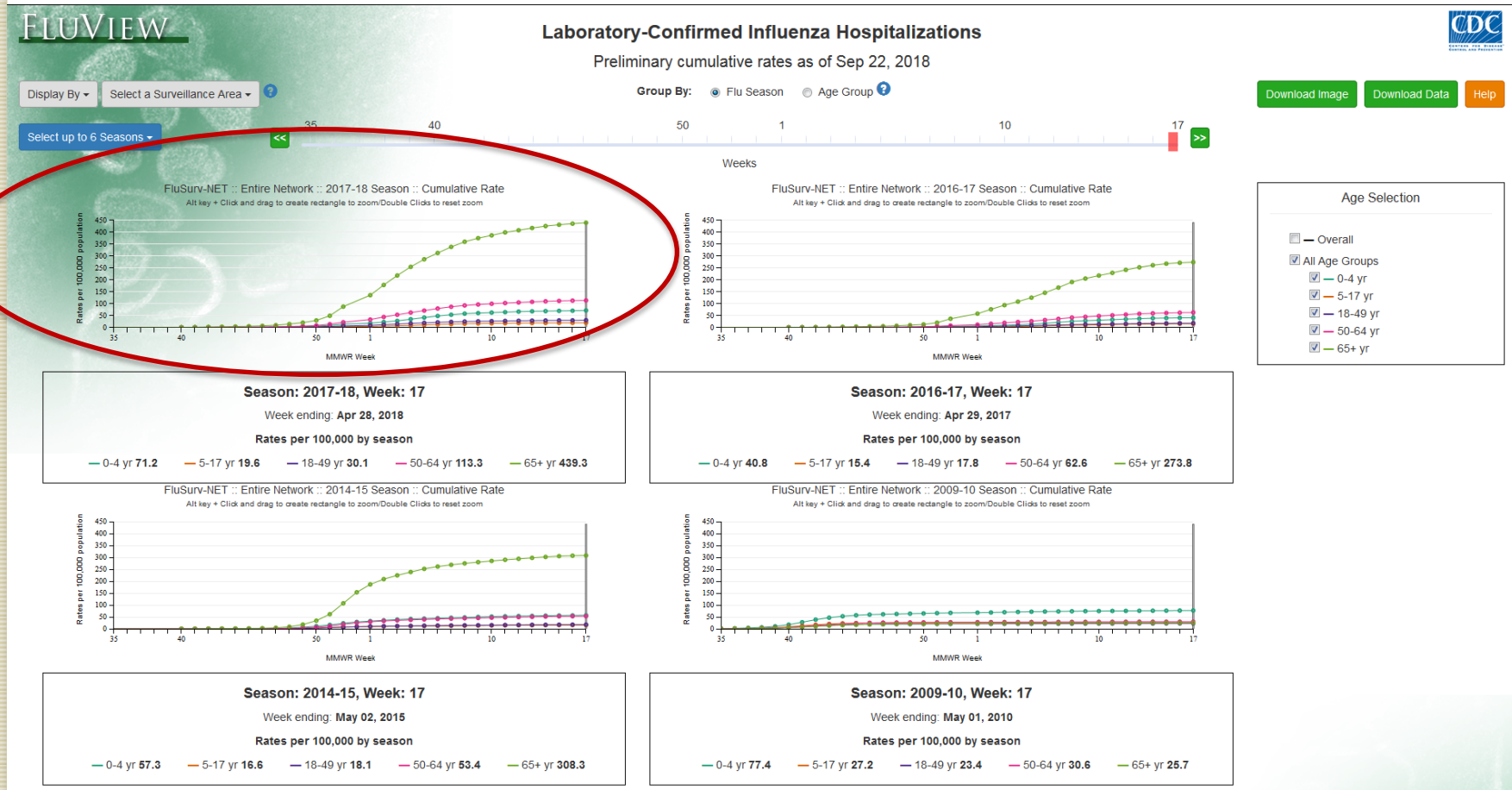
Flu Mortality





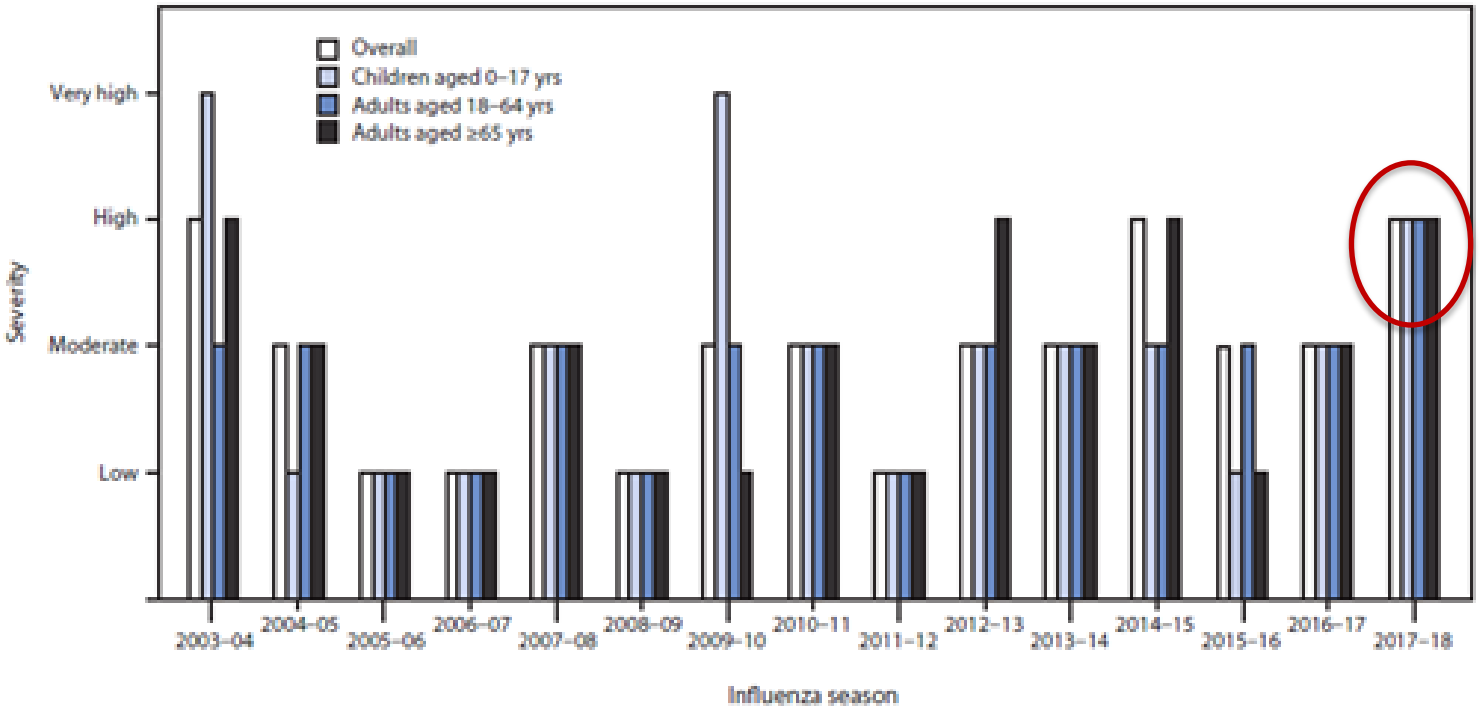
Influenza in the U.S. :2017-18

Flu Hospitalization



Influenza in the U.S. :2017-18
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.

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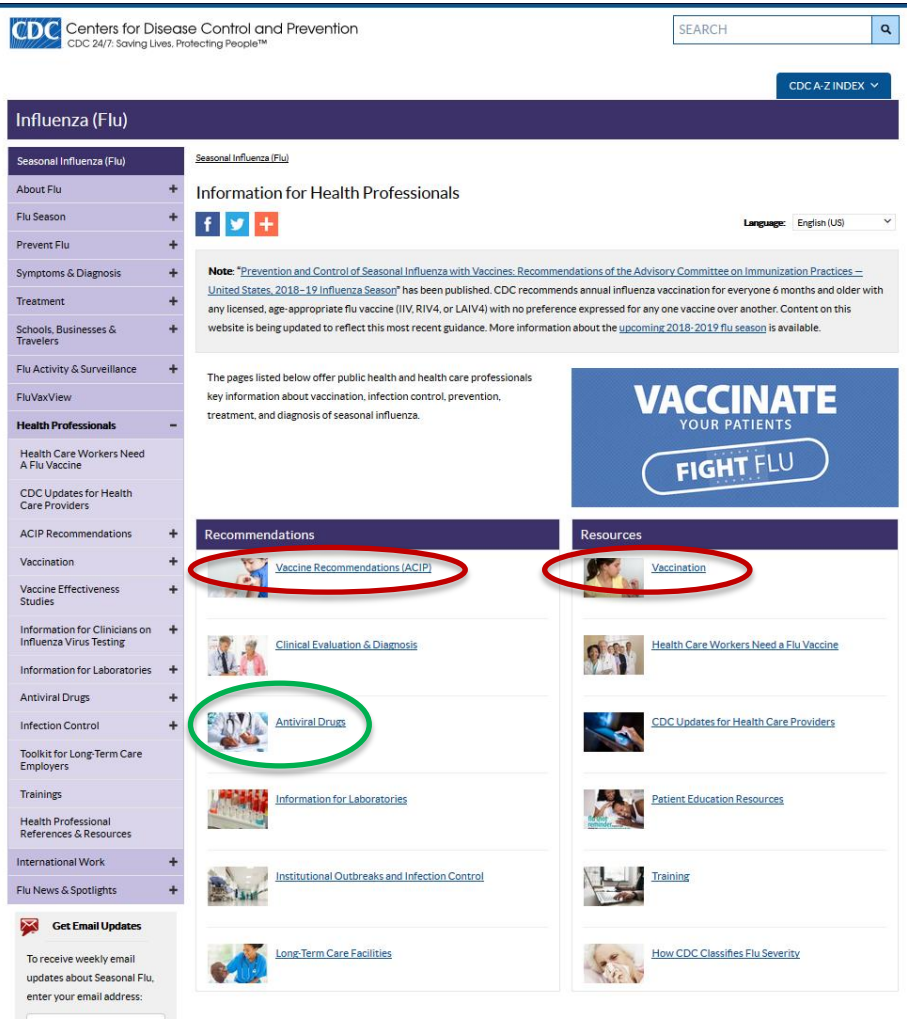
Influenza in the U.S. :2017-18

Why was the past season so severe?

Influenza – Prevention and Treatment

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



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

Seasonal Influenza

Vaccine

- **Primary strategy to reduce influenza infections and their complications**
  - Safe and **effective(?)**
- 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 2017-18

What was expected…

- **A/Hong Kong/4801/2014(H3N2)**
- A/Michigan/45/2015 (H1N1pdm09)
- B/Phuket/3073/2013 (B/Yamagata-lineage)
- B/Brisbane/60/2008 (B/Victoria-lineage)

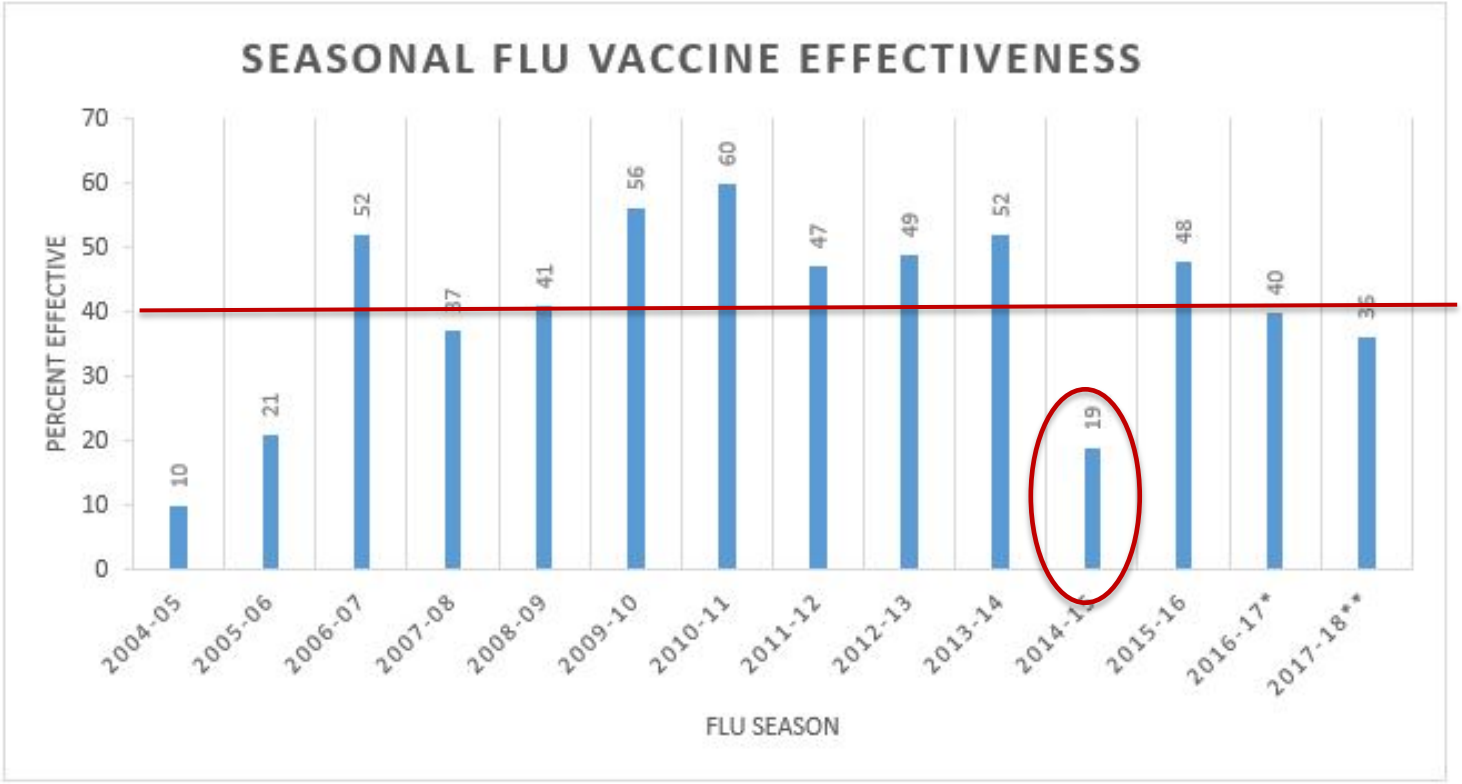
… and that's **largely** what we got,

however …

Seasonal Influenza Vaccines

How effective ?

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

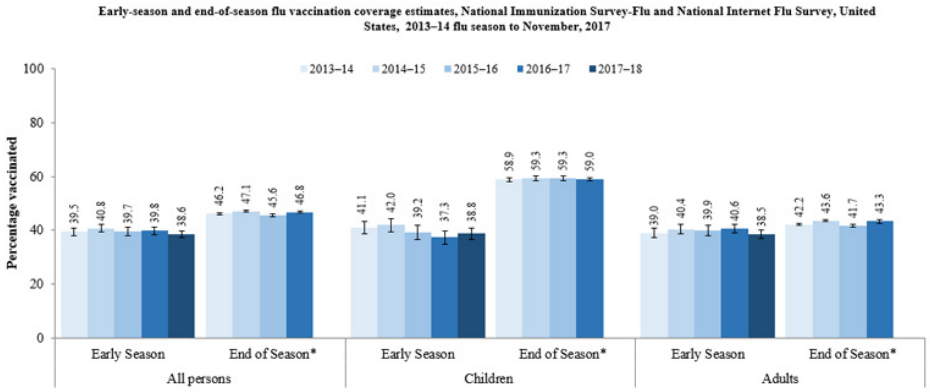


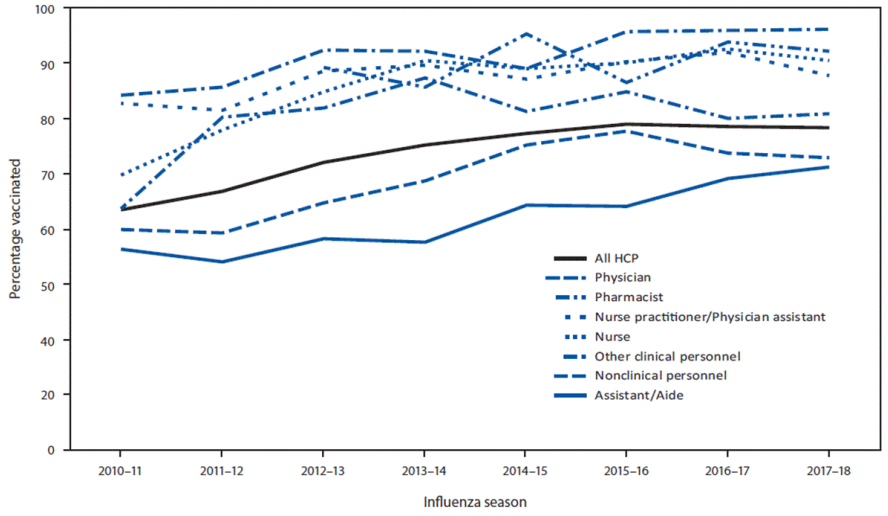
VE= percent reduction of frequency of flu among vaccinated people compared to unvaccinated people

Vaccination Rates---2013-2018

General Population and Healthcare Personnel

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





Seasonal Influenza Vaccines

Why isn't everyone getting vaccinated?

"Influenza is a trivial disease…why bother?"
"Influenza is not safe during pregnancy"
"Flu vaccine gives me the flu"
"Not another vaccine for my children!"
"I got the flu shot and still got the flu"
"Bad things, e.g. GBS, happen after vaccination"
"The flu vaccine still has thimerosol in it"
"It costs too much"
"It's not as effective as the Govt. says"

Seasonal Influenza Vaccines

Could there be other problems with the vaccines?

Vaccine Effectiveness : 2014-15

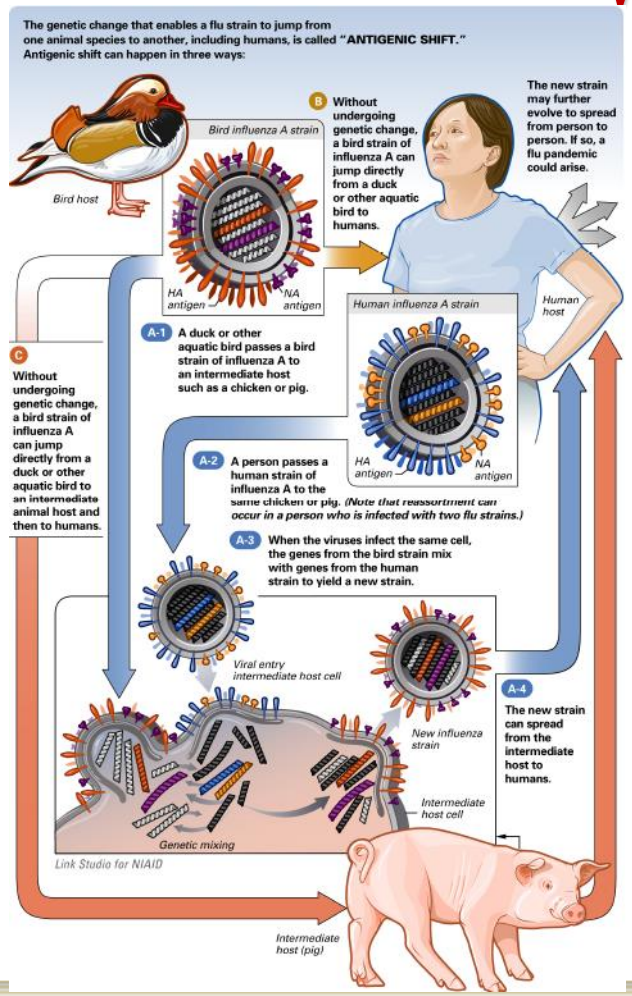
http://www.cdc.gov/flu/professionals/vaccination/effectivenessqa.htm

"It may not be perfect, but it protects a substantial number of people and it's the best we have"

-CDC Source-

The Changeability of Influenza
Antigenic Shift

www.flu.gov



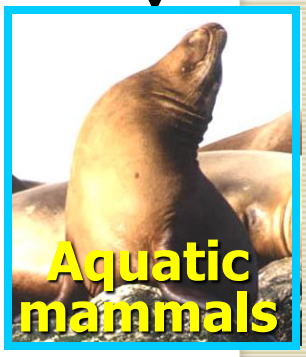
<u>Antigenic Shift</u>

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

Influenza at the Human-Animal Interface

Influenza A

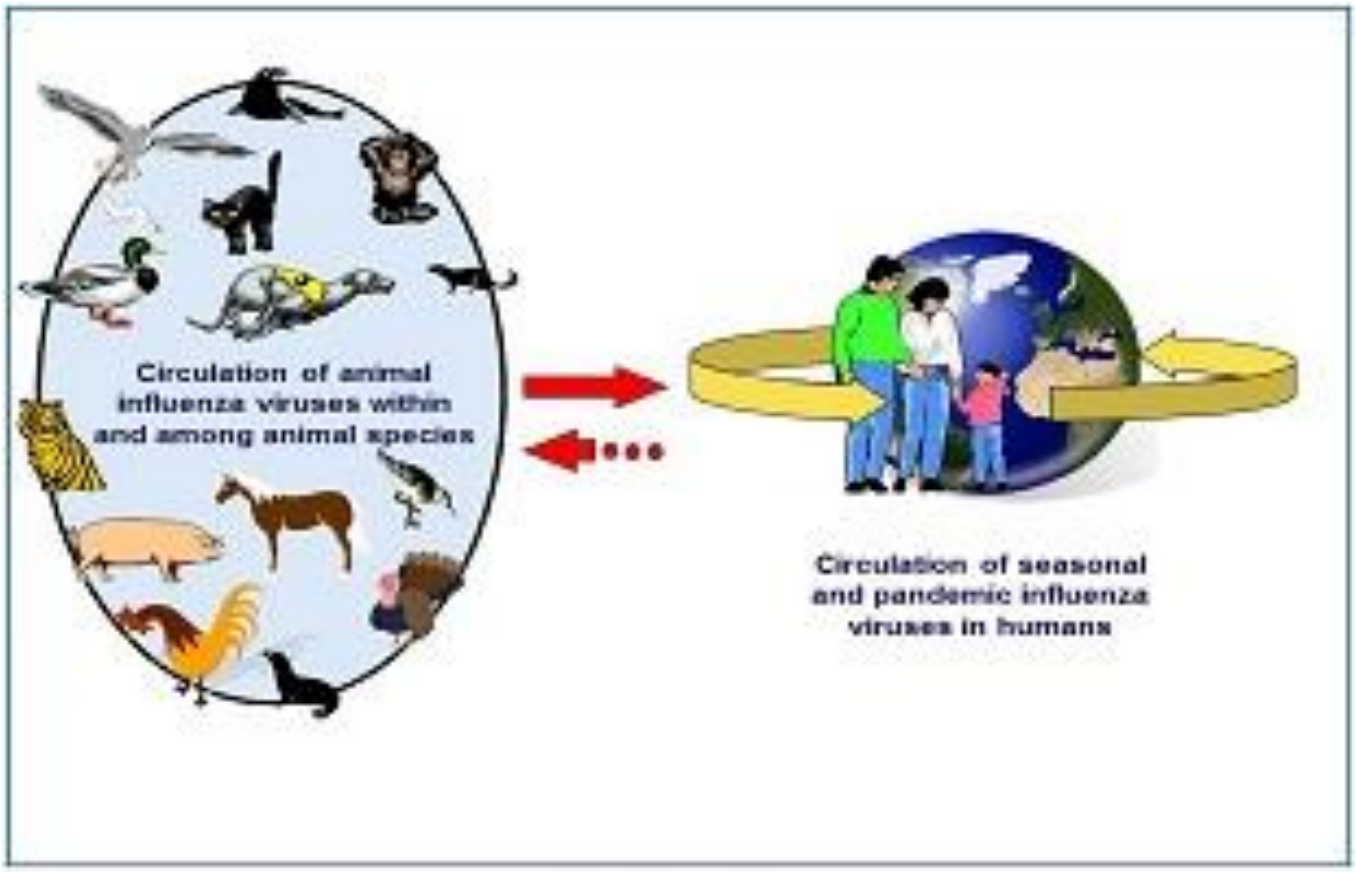
- **H1 - H16***
- **N1 – N9***



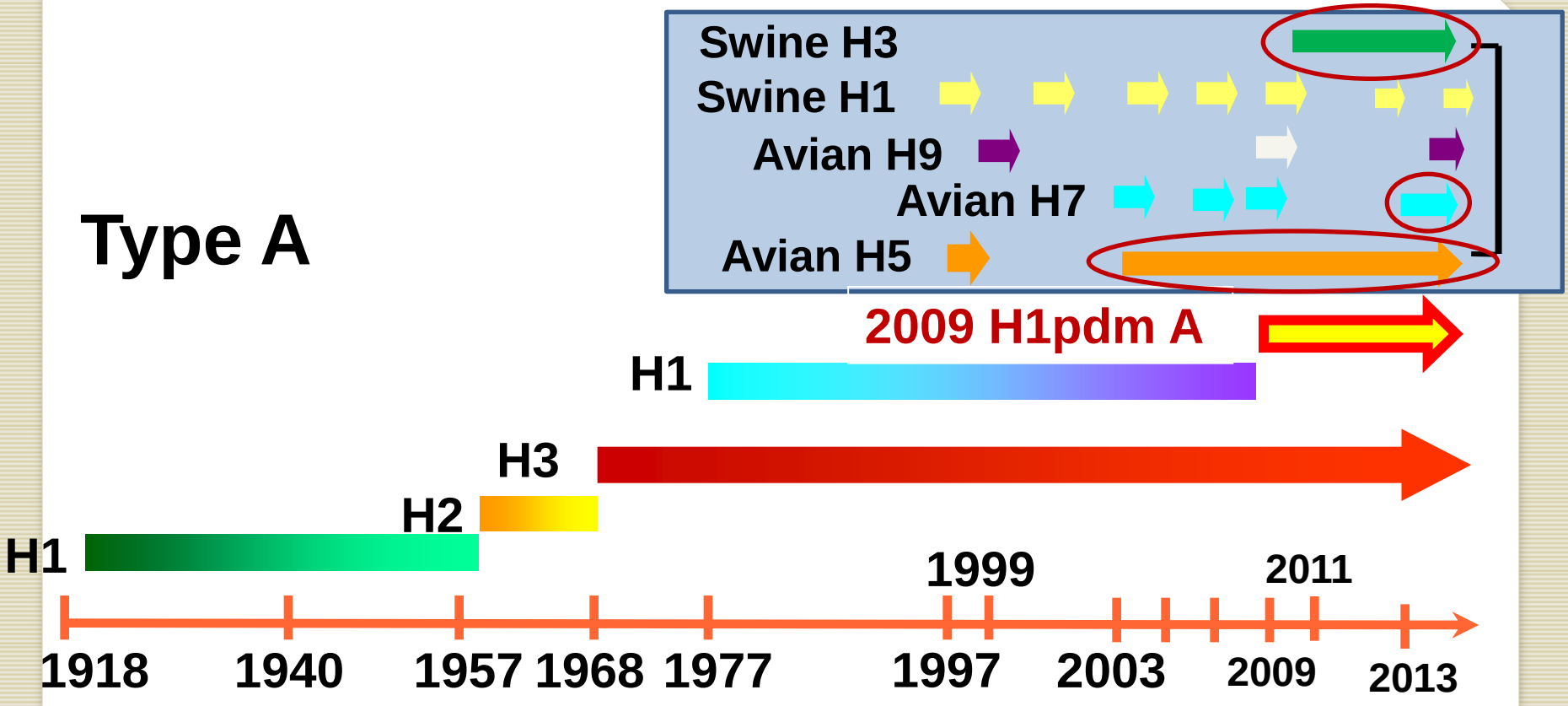
*Bats – H17/18, N10/11

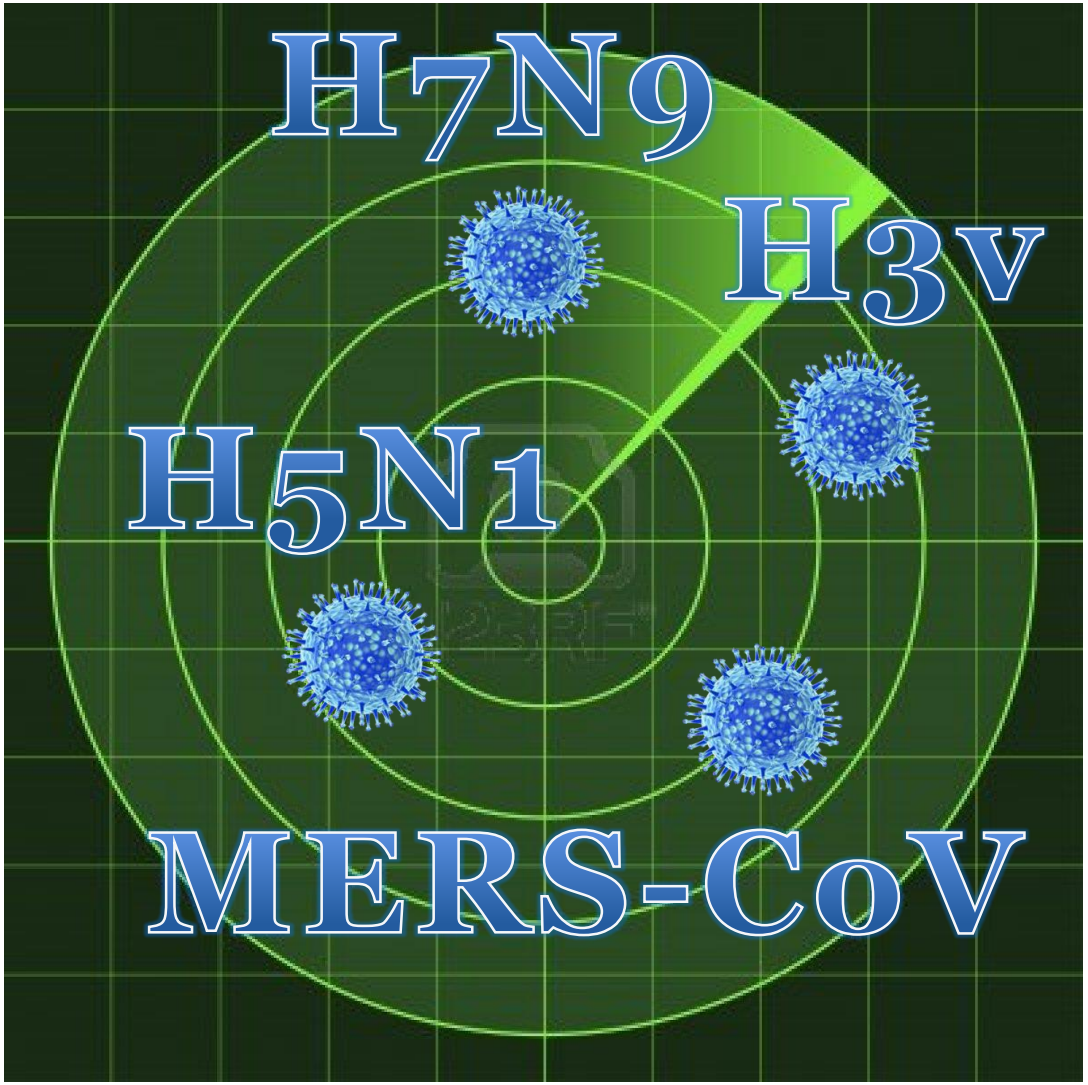
Infectious Diseases at the Human-Animal Interface

Influenza as an Example

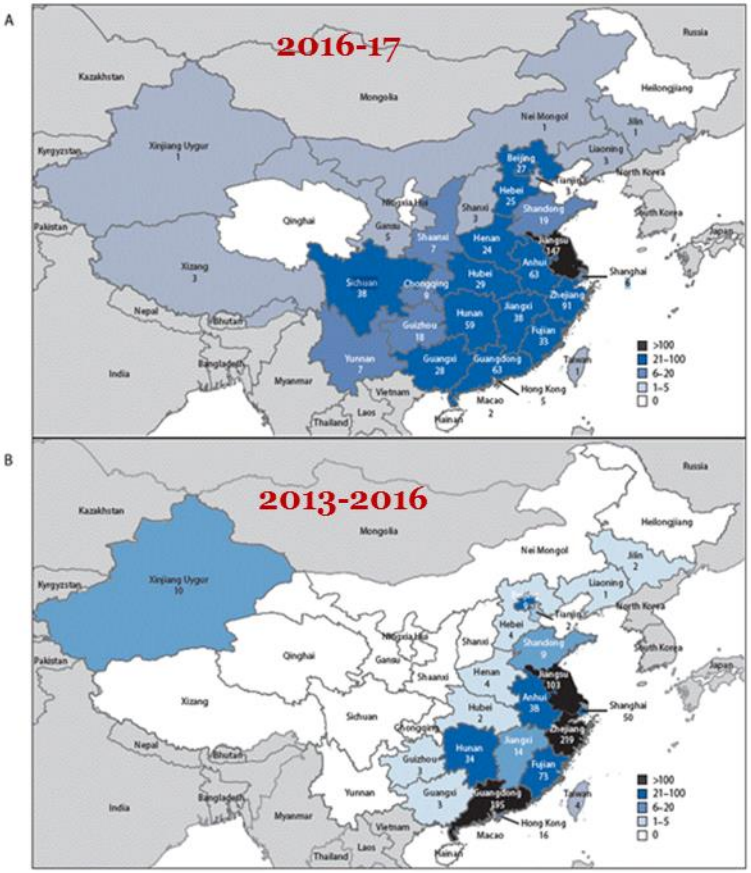


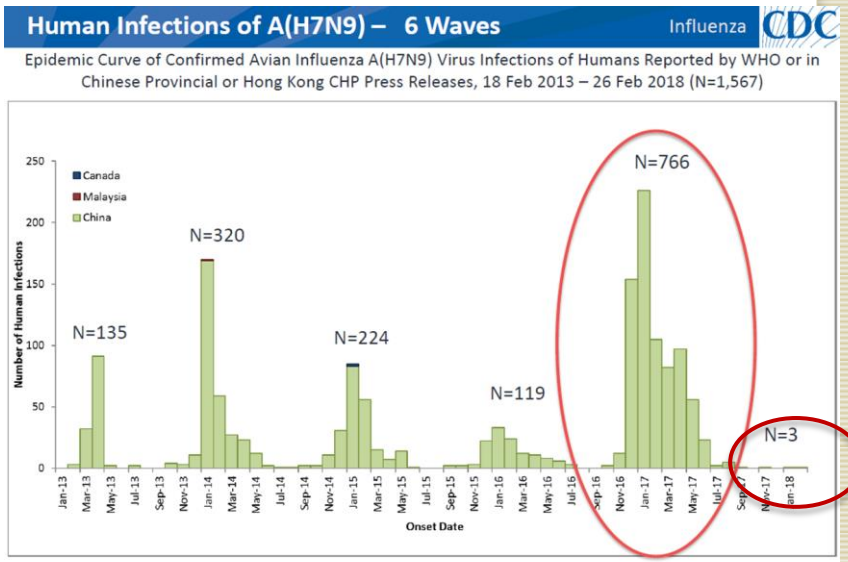
Timeline of Other Emergent Influenza A Viruses in Humans




H7N9
H3v
H5N1
MERS-CoV

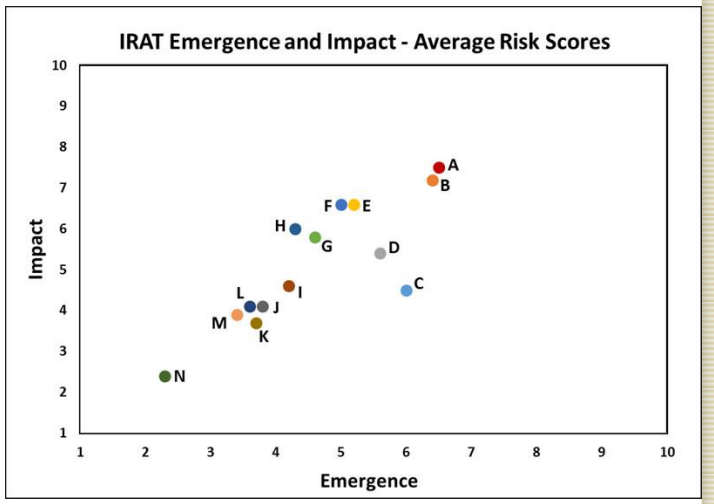
Influenza A (H7N9)
The latest global concern





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.



Avian Influenza A (H5N1)

Cumulative number of confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2018

Country	2003-2009*		2010-2014**		2015		2016		2017		2018		Total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths
Azerbaijan	8	5	0	0	0	0	0	0	0	0	0	0	8	5
Bangladesh	1	0	6	1	1	0	0	0	0	0	0	0	8	1
Cambodia	9	7	47	30	0	0	0	0	0	0	0	0	56	37
Canada	0	0	1	1	0	0	0	0	0	0	0	0	1	1
China	38	25	9	5	6	1	0	0	0	0	0	0	53	31
Djibouti	1	0	0	0	0	0	0	0	0	0	0	0	1	0
Egypt	90	27	120	50	136	39	10	3	3	1	0	0	359	120
Indonesia	162	134	35	31	2	2	0	0	1	1	0	0	200	168
Iraq	3	2	0	0	0	0	0	0	0	0	0	0	3	2
Lao People's Democratic Republic	2	2	0	0	0	0	0	0	0	0	0	0	2	2
Myanmar	1	0	0	0	0	0	0	0	0	0	0	0	1	0
Nigeria	1	1	0	0	0	0	0	0	0	0	0	0	1	1
Pakistan	3	1	0	0	0	0	0	0	0	0	0	0	3	1
Thailand	25	17	0	0	0	0	0	0	0	0	0	0	25	17
Turkey	12	4	0	0	0	0	0	0	0	0	0	0	12	4
Viet Nam	112	57	15	7	0	0	0	0	0	0	0	0	127	64
Total	**468**	**282**	**233**	**125**	**145**	**42**	**10**	**3**	**4**	**2**	**0**	**0**	**860**	**454**

* 2003-2009 total figures. Breakdowns by year available on subsequent tables.
** 2010-2014 total figures. Breakdowns by year available on subsequent tables.

Total number of cases includes number of deaths.
WHO reports only laboratory cases.
All dates refer to onset of illness.

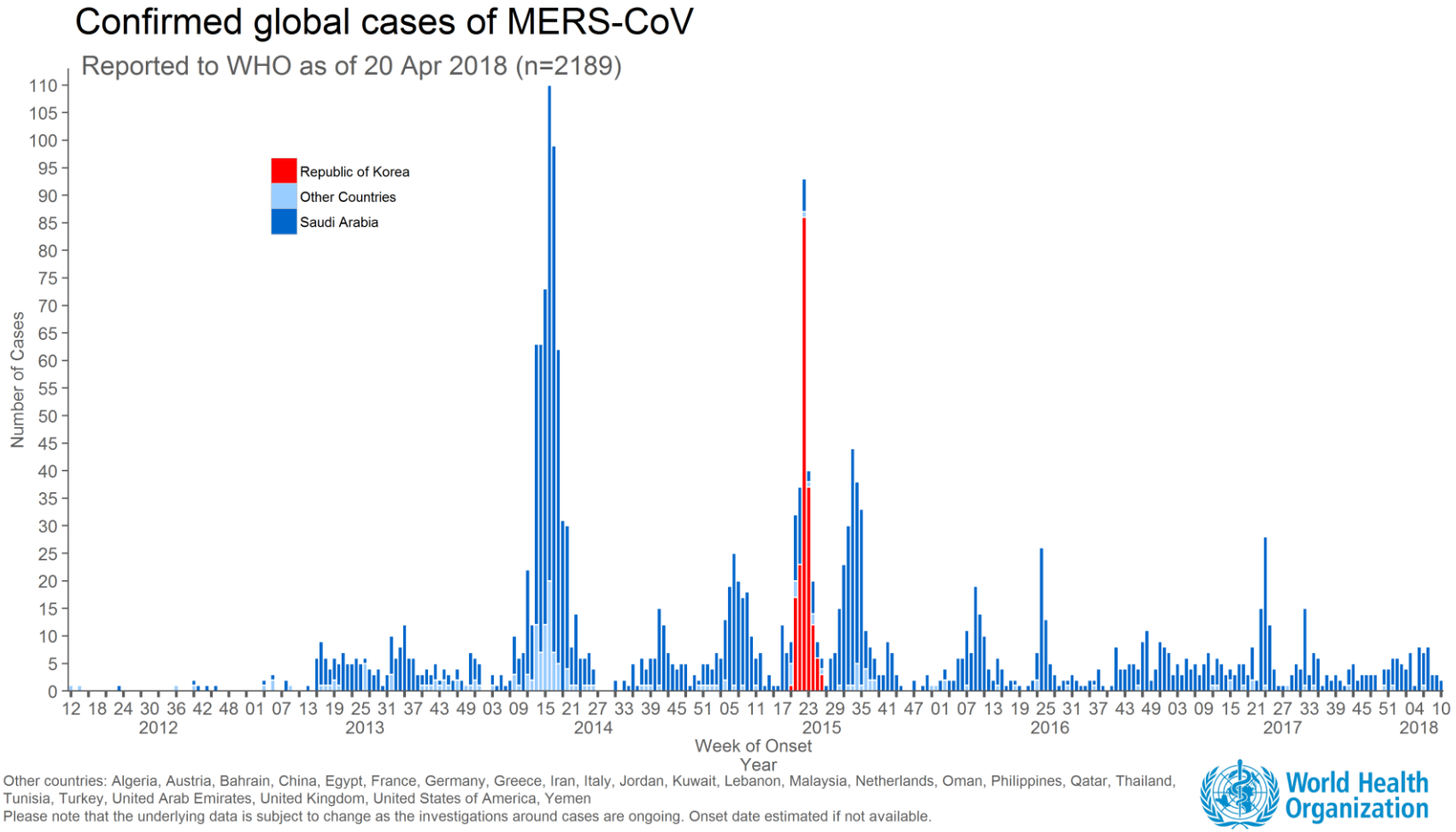
Source: WHO/GIP, data in HQ as of 20 July 2018

World Health Organization

MERS-CoV What we know!

- Virus is ***different*** than SARS-Coronavirus and seasonal coronavirues.
- First cases in 2012.
- All cases linked to the Arabian Peninsula (80% Saudi Arabia).
- Virus does *not easily* transmit from person-to-person.
- Requires close personal contact.
- Genetically stable.
- Bats and camels play a role in host transmission; dynamics not well understood.
- WSLH performs RT-PCR on PUI's.

MERS - Coronavirus



Other countries: Algeria, Austria, Bahrain, China, Egypt, France, Germany, Greece, Iran, Italy, Jordan, Kuwait, Lebanon, Malaysia, Netherlands, Oman, Philippines, Qatar, Thailand, Tunisia, Turkey, United Arab Emirates, United Kingdom, United States of America, Yemen

Please note that the underlying data is subject to change as the investigations around cases are ongoing. Onset date estimated if not available.

World Health Organization

Global Flight Map

(Image courtesy of The Guardian's interactive flight map

Domestic *Novel* Influenza A

Table. Case Count: Detected U.S. Infections with Variant Influenza Viruses by State since December 2005-2018

Reporting State	H3N2v	H1N1v	H1N2v	Total Detected Influenza Variant Virus infections
Arkansas		2		
Colorado			1	
Delaware	1			
Hawaii	1			
Illinois	5	1		
Indiana	154			
Iowa	7	5	1	
Kansas	1			
Maine	2			
Maryland	51			
Michigan	23		1	
Minnesota	9	4	6	
Missouri		2		
Nebraska	1			
New Jersey	1			
North Dakota	1			
Ohio	131	3	3	
Pennsylvania	17			
South Dakota		1		
Texas	1	1		
Utah	1			
West Virginia	5			
Wisconsin	22	2	1	
Total	434	21	13	468

For more detailed information about previously detected human cases of variant influenza infection, see Reports of Human Infections with Variant Viruses
Source:https://www.cdc.gov/flu/swineflu/variant-cases-us.htm

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

The Recipe for a Human Pandemic

- ✓ Emergence of a <u>novel virus</u>
  - ✓An immunologically naïve population
- ✓ Replication in humans → disease
- ✗ **Efficient** human-to-human transmission

Virus Activity Resources

Wisconsin

- Bi-weekly Laboratory Surveillance Report

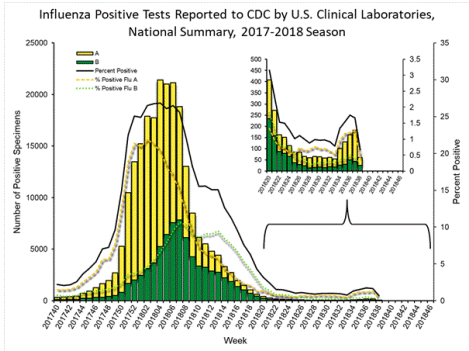
  Subscribe at: wcln@slh.wisc.edu

- Virus Activity Graphs

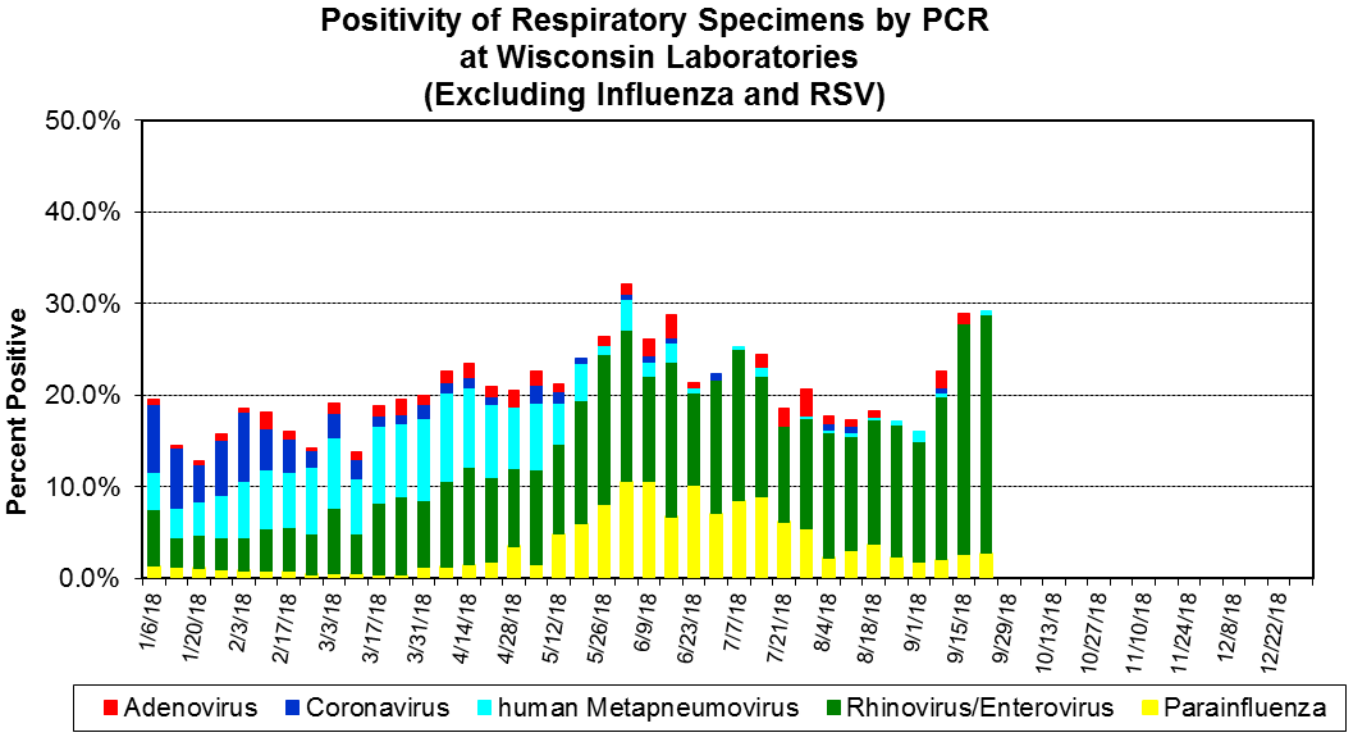
  http://www.slh.wisc.edu/wcln-surveillance/surveillance/virology-surveillance/

National

- FluView (CDC)
- NREVSS (CDC)

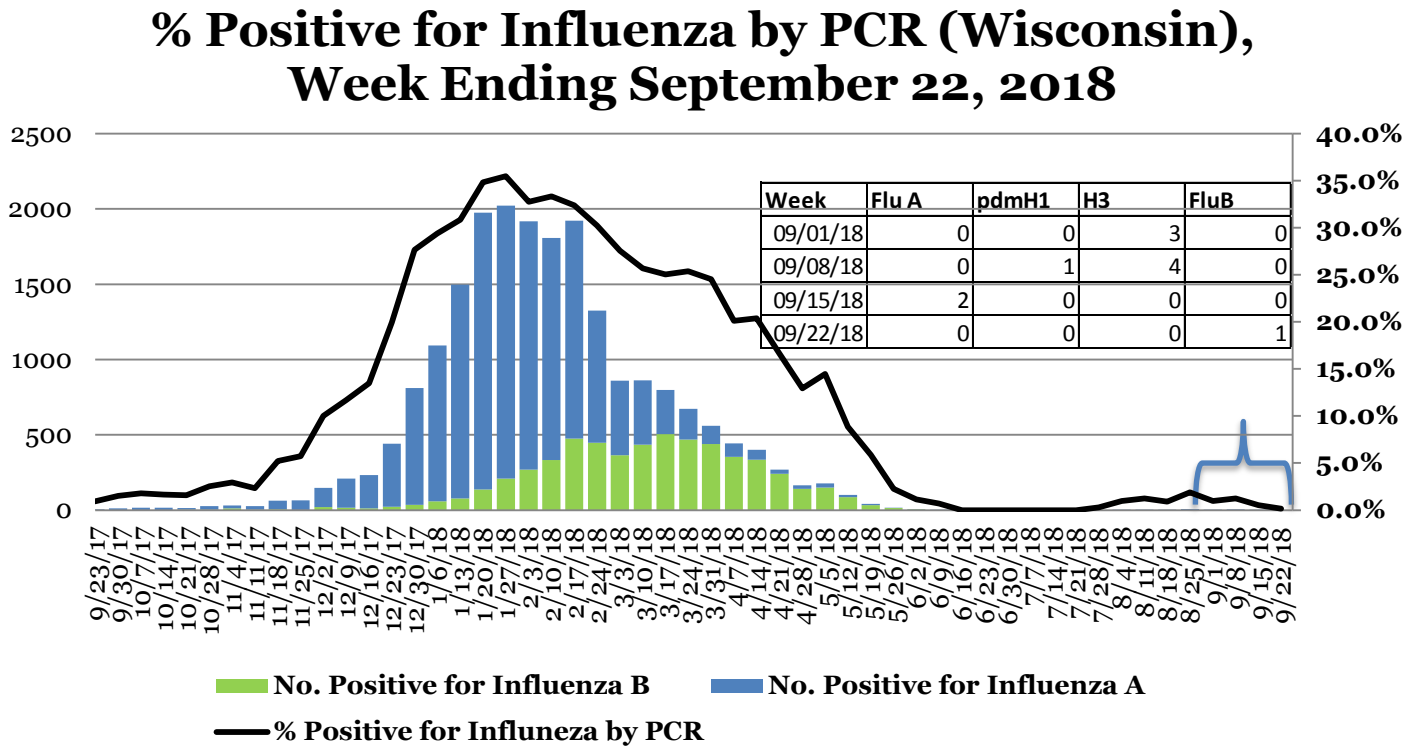


Current Seasonal Respiratory Virus Activity



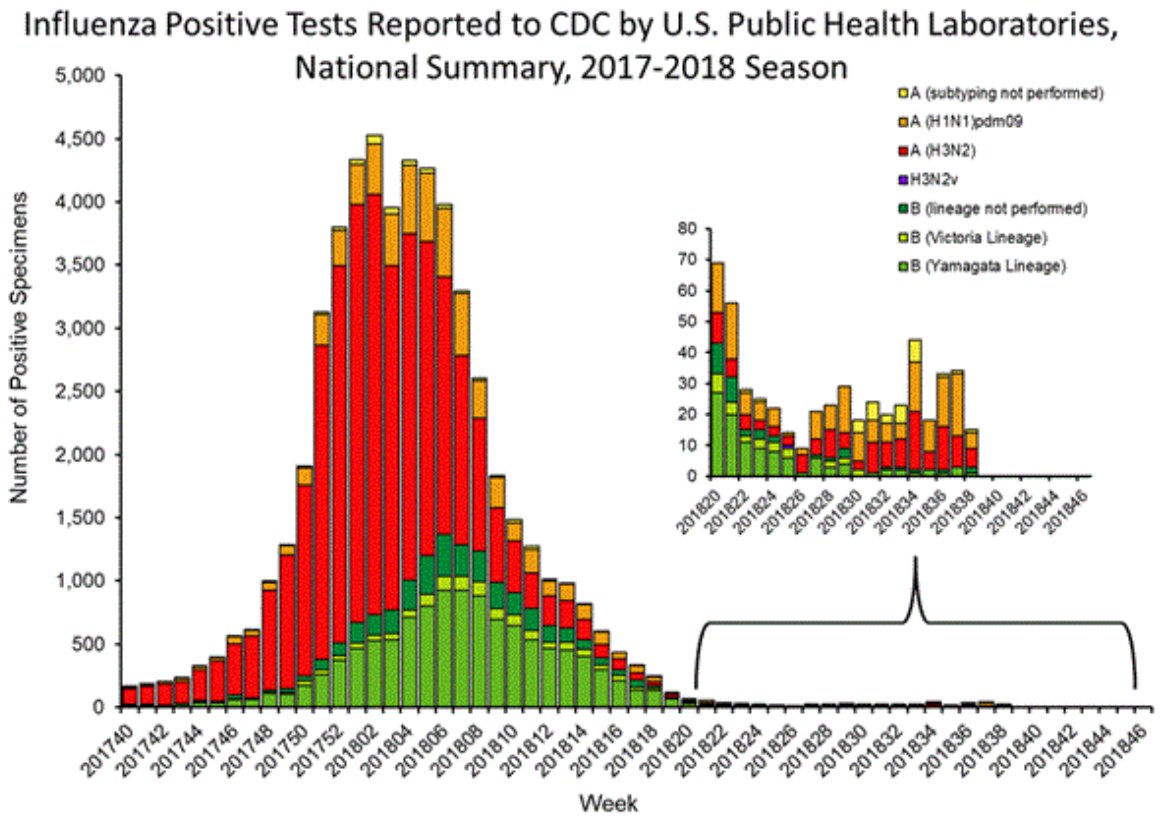
Influenza and non-influenza virus respiratory surveillance

Early……
Influenza season, 2018-2019



Week	Flu A	pdmH1	H3	FluB
09/01/18	0	0	3	0
09/08/18	0	1	4	0
09/15/18	2	0	0	0
09/22/18	0	0	0	1

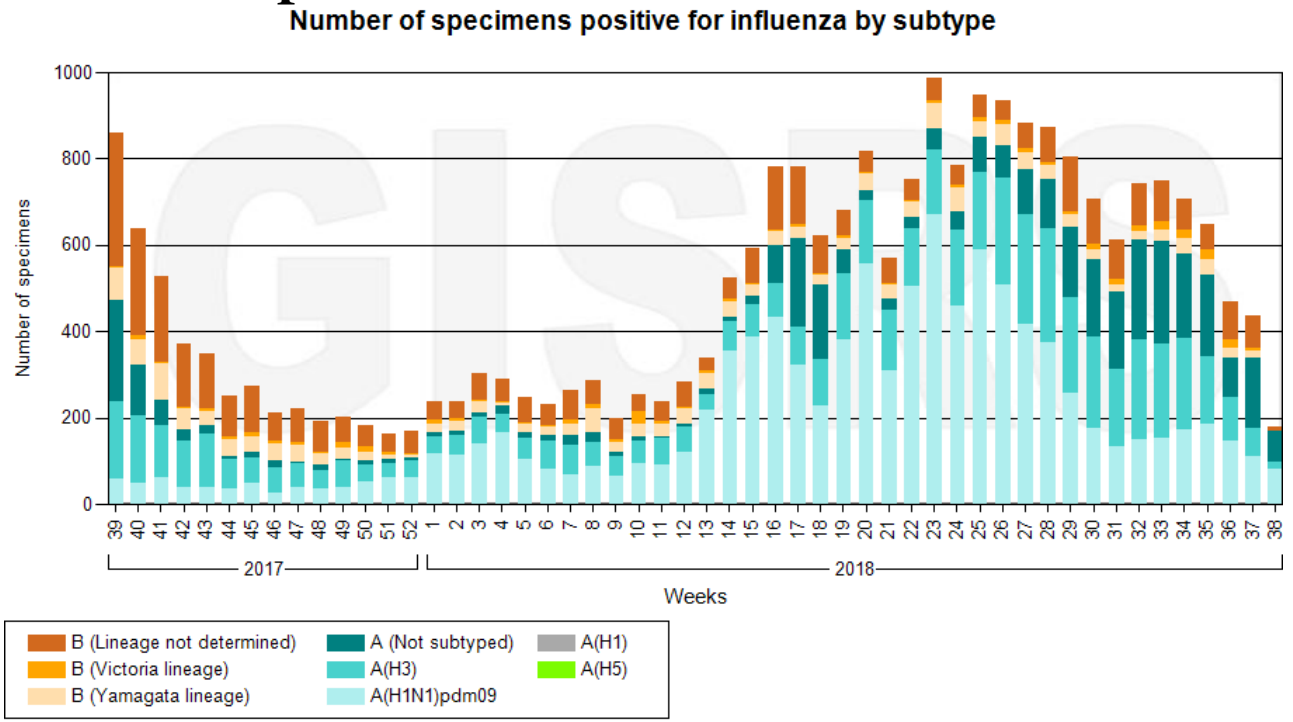
Early……
Influenza season, 2018-2019



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

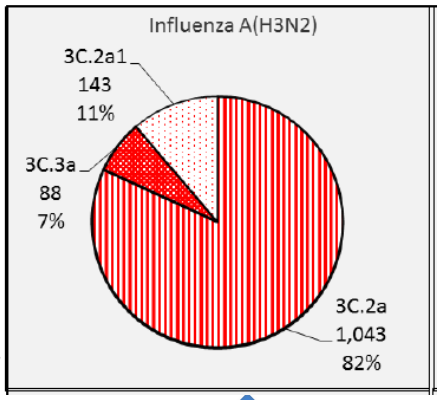
Influenza Laboratory Surveillance Information
generated on 28/09/2018 20:37:07 UTC
by the Global Influenza Surveillance and Response System (GISRS)—

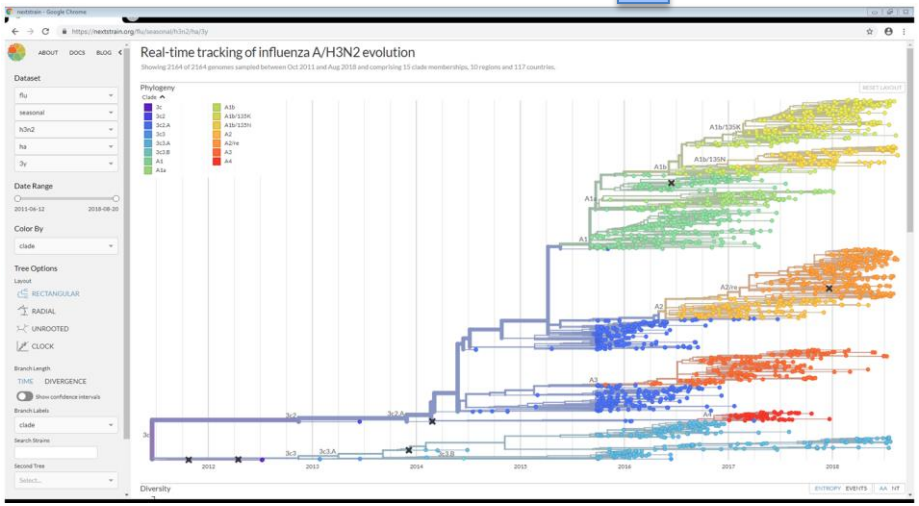
Southern hemisphere



What do we do with the specimens submitted?

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





Antiviral Resistance Monitoring- Wisconsin, 2018

WI neuraminidase inhibition testing			
YR	Month	# Reduced inhibition	# Tested
2018	January	0	18
	February	0	16
	March	0	12
	April	0	10
	May	0	6
	June	0	5
	July	0	3
	August	0	7
	September	0	11
	Total	**0**	**88**

- Oseltamivir
- Zanamivir
- Peramivir
- Laninamivir

Respiratory Pathogen Surveillance

2018-2019 Season

Influenza Surveillance in Wisconsin

Multi-element approach

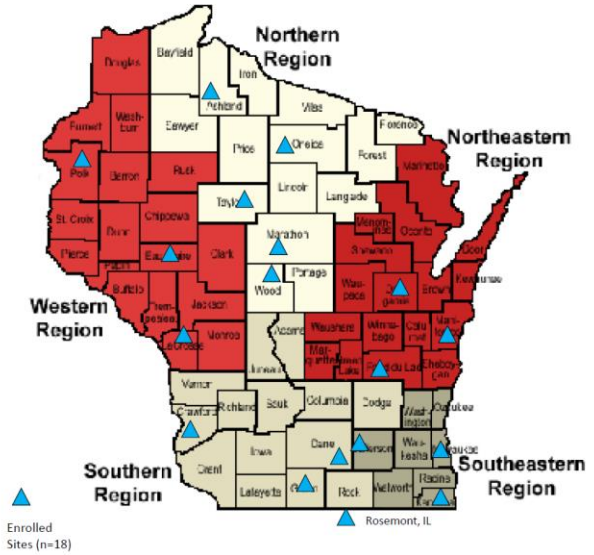
1. Rapid Influenza Diagnostic Testing (RIDT) Sites
   - Now ~50% of influenza testing in WI
   - Confirmatory testing during periods of low prevalence (June to October).
   - Please notify WSLH of suspected performance issues (e.g. False positives/negatives)

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.

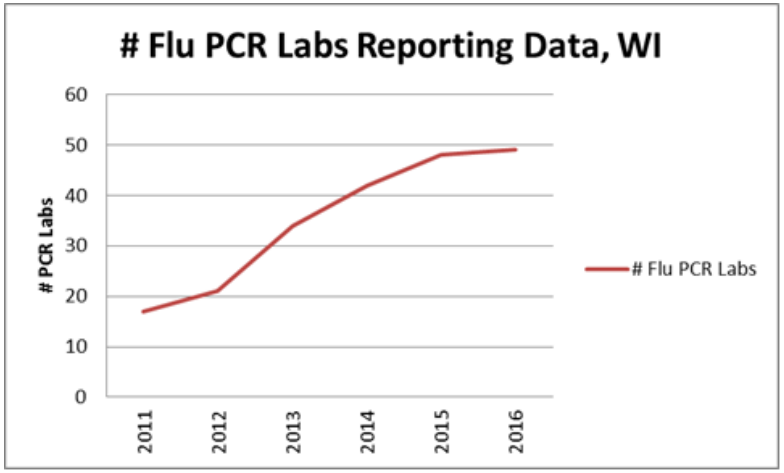


Request to continue to submit the first 1-2 specimens per week with influenza test requests to WSLH.

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
- *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

- Limit to one 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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