





**Wisconsin State
Laboratory of Hygiene**
UNIVERSITY OF WISCONSIN-MADISON

WE'RE MOVING!



Important Update!



The WSLH Communicable Disease Division will be moving to the State Agriculture Drive, Madison, effective Monday, **October 10, 2016**.

On and after October 10, 2016, please send clinical specimens as follows:

WSLH Unit	Address
<ul style="list-style-type: none"> • Communicable Diseases (surveillance, emergency response, outbreak, etc.) • Rabies • Cytology 	<p>2601 Agriculture Drive, P.O. Box 7904 Madison, WI 53718</p> <p>(For directions, see map below. Please deliver to loading dock off Vondron Road.)</p>

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WSLH Contact Information

- Email addresses will remain the same.
- CDD Customer Service #
 - ☐ 800-862-1013
- Phone & FAX numbers are changing

WSLH will communicate new key contact phone #'s when they become available

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Influenza and other Respiratory Viruses Update-- 2016

Pete Shult, PhD
CDD Director & Emergency Laboratory Response

and

Erik Reisdorf, MPH, M(ASCP)^{CM}
Surveillance and Virology Lab-Team Lead


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Learning Objectives

- Moving Day!
- Review of the 2015-2016 influenza season.
- Vaccine strain selection and efficacy.
- Influenza “variant” virus update.
- Non-influenza respiratory pathogens.
- Technology update.
- Discuss surveillance strategy for 2016-2017


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Influenza

The latest information

www.cdc.gov/flu/index.htm



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What We've Been Dealing With: 2016

- Zika virus
- Dengue fever
- Chikungunya
- Elizabethkingia spp.
- Measles, mumps, pertussis
- Food-borne illnesses

... So what's the big deal with influenza?



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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

www.flu.gov

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Estimated Annual Burden of Seasonal Influenza in the United States

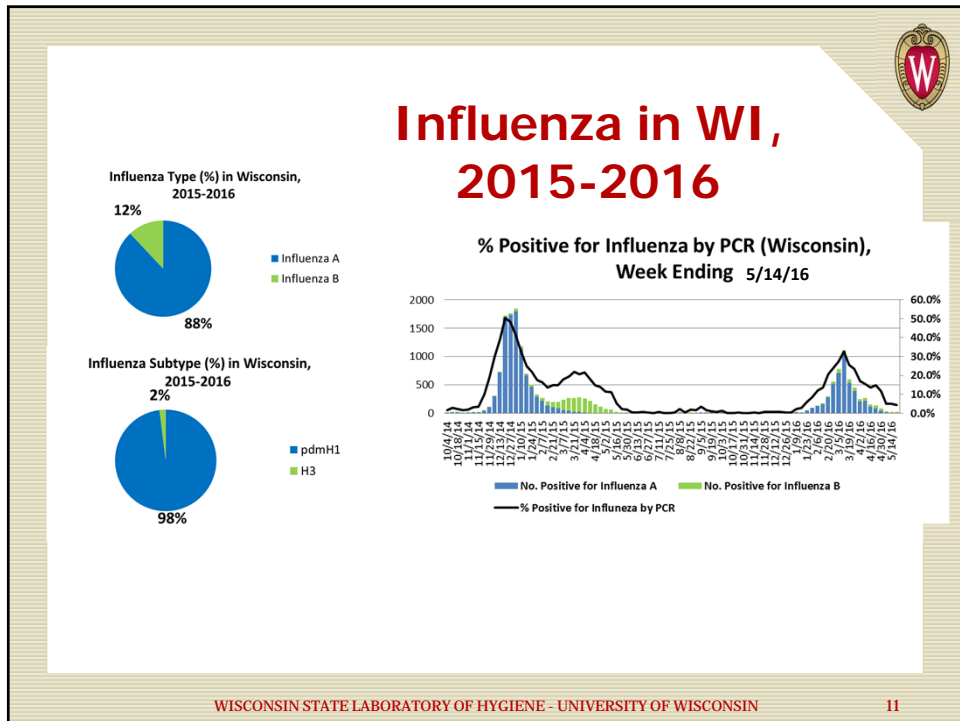
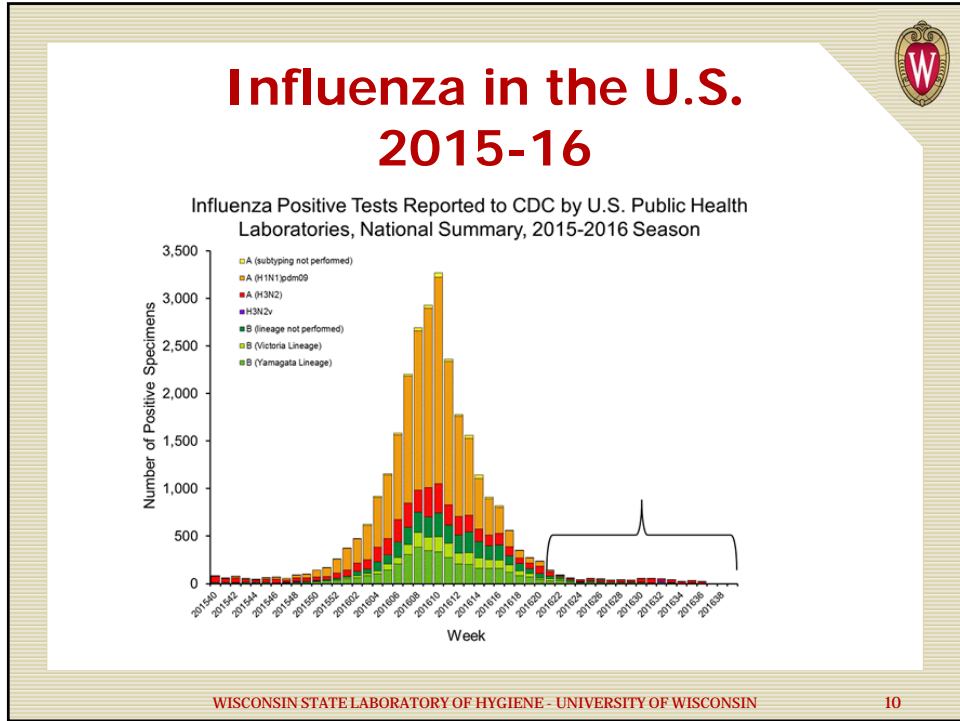
Deaths: 3,000 – 49,000

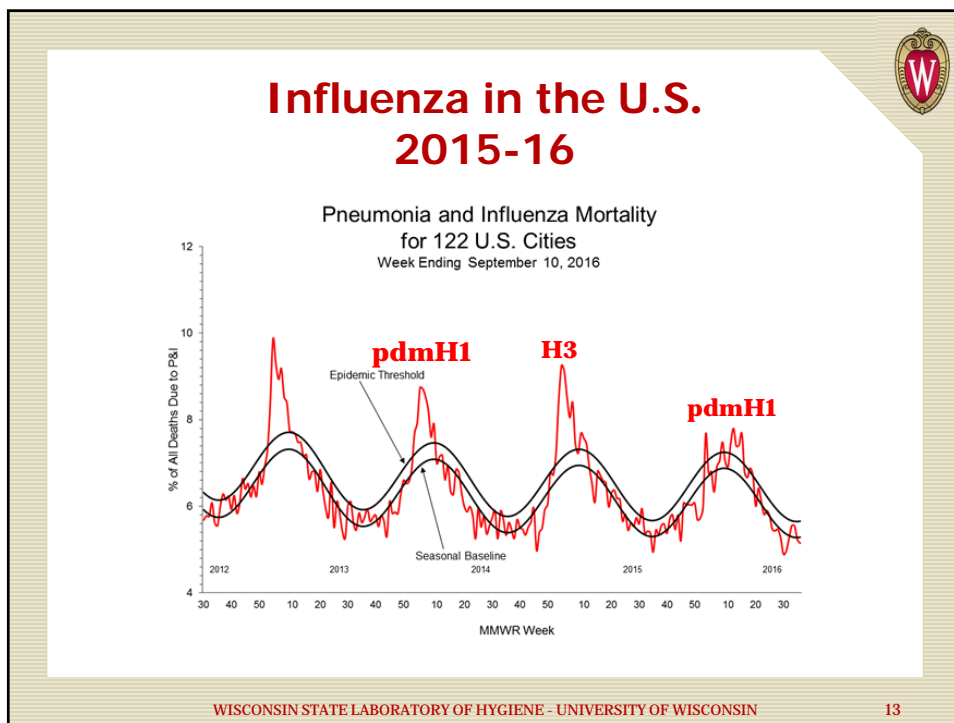
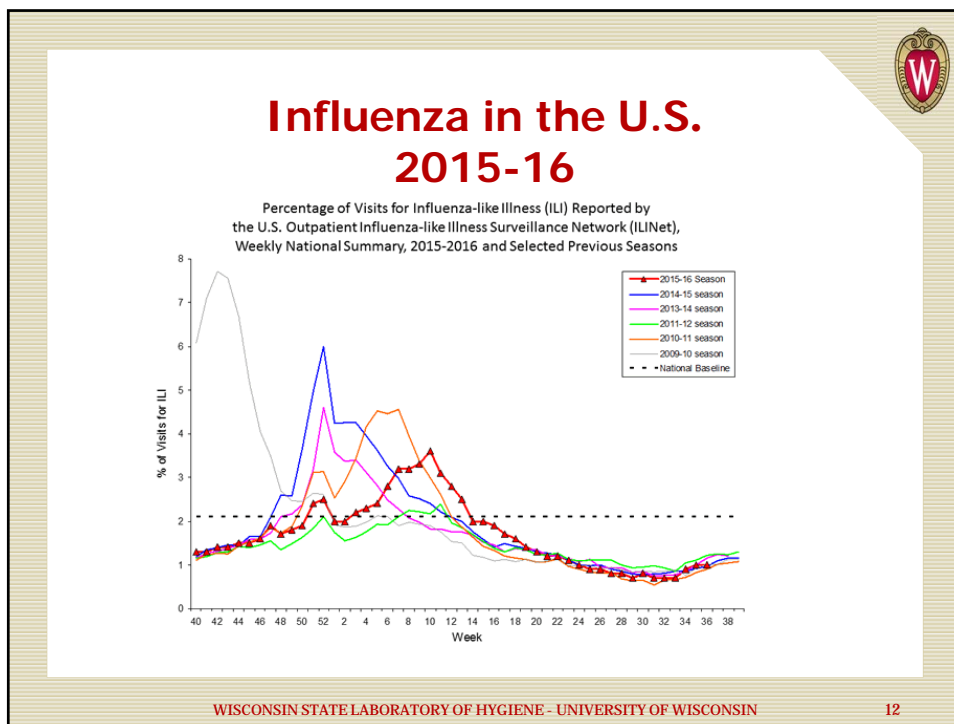
Hospitalizations:
54,000 – 430,000

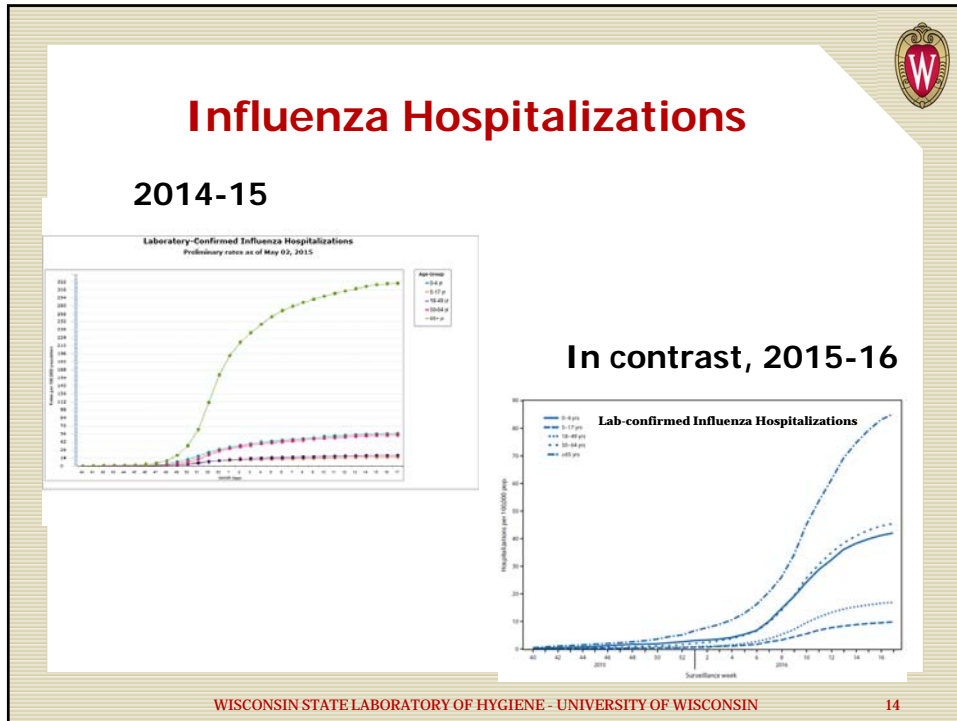
Cases: 15 – 60 M

Direct medical costs: \$10.4 billion

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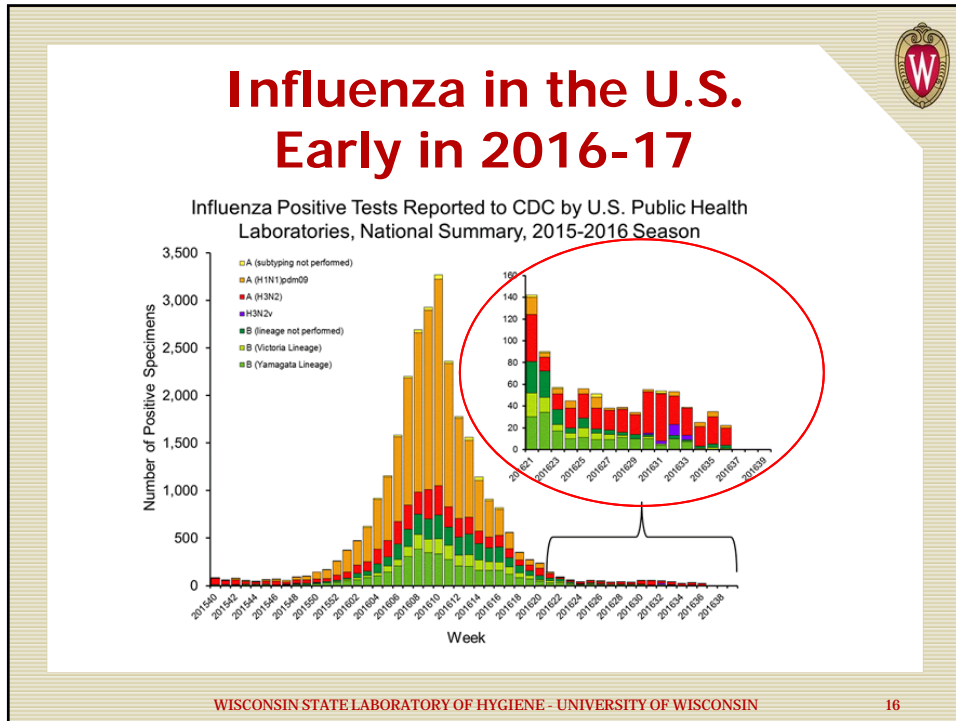
Influenza 2015-16

What was expected...

- A/Switzerland/9715293/2013(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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Early 2016-2017 Season....

PH Region	Date Received	Influenza type
?	7/14/2016	Flu A (H3)
?	7/28/2016	Flu A (H3)
Travel (AK)	8/10/2016	Flu A (H3)
Travel (India)	8/30/2016	Flu A (H3), FluB
?	9/15/2016	Flu A (H3)
?	9/21/2016	Flu A (H3)
Monroe Co.	June 2016	Flu A H1N2v

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The Changeability of Influenza

Antigenic Shift

www.flu.gov

The genetic change that enables a flu virus 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 humans.
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 same chicken or pig. (These two reassortment events occur in a person who is infected with two flu strains.)
4. When the viruses share 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 the intermediate host to humans.

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

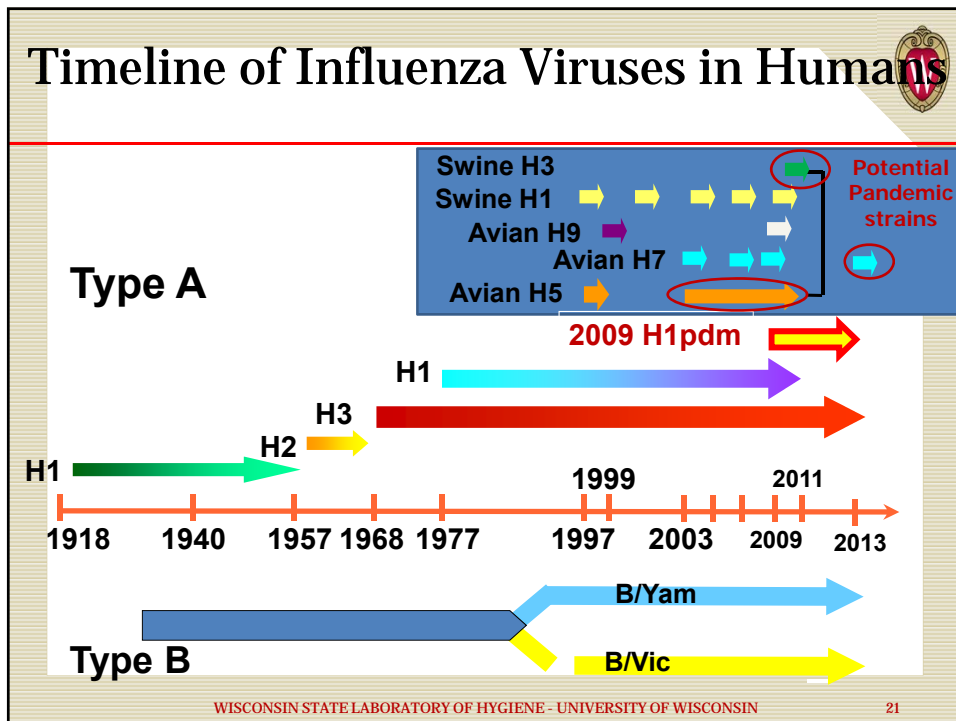
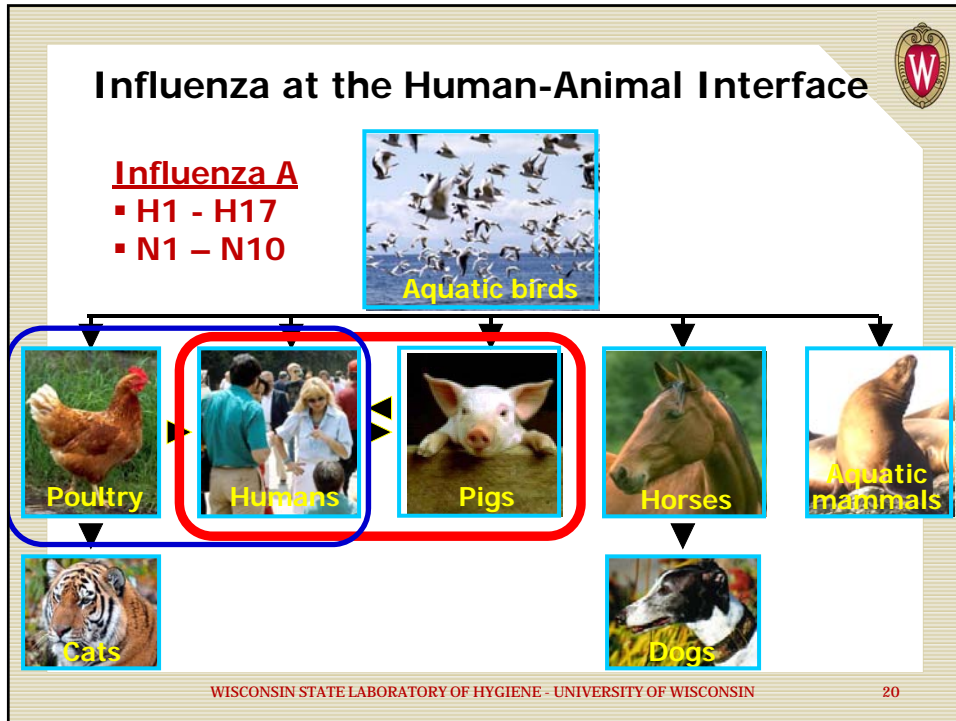
Circulation of animal influenza viruses within and among animal species

→

←

Circulation of seasonal and pandemic influenza viruses in humans

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Global Influenza Concerns: A(H5N1) and A(H7N9)

http://www.who.int/csr/disease/avian_influenza/en/

Areas with confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2013*

Number of Confirmed Human A(H5N1) Cases by Year (2003-2013)

Number of Confirmed Human A(H5N1) Cases and Deaths by Week (2003-2013)

Areas reporting confirmed human cases for influenza A(H7N9) to WHO from 2013-06-01*

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Influenza: Emergence of Novel Flu A Subtypes

Chickens and turkeys take center stage in 2015

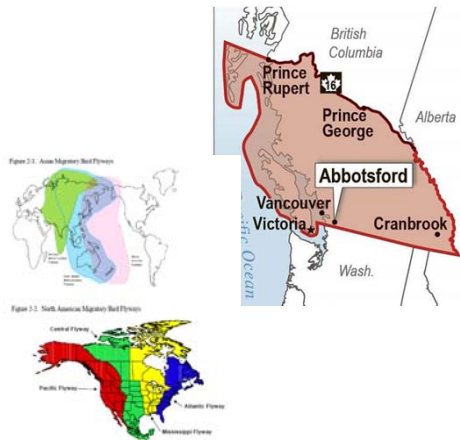
Influenza A

- H1 - H17
- N1 - N10

Aquatic birds

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Emergence of Avian Flu (H5Nx) in U.S.



- Avian Influenza (H5Nx) emerged in North America (November 2014).
- Many flocks in the area were infected by December including those in the US.

Avian Influenza Terminology



- Highly Pathogenic Avian Influenza
- Bird flu
- Pathogenicity refers to avian NOT human
- **H5N1, H5N2** and **H5N8** are collectively referred to as **H5Nx**
- **H5N2** and **H5N8** have both been detected in the US in 2015.



dcfeliciano.blogspot.com

Current Situation

ALL Findings

Update on Avian Influenza Findings
Poultry Findings Confirmed by USDA's National Veterinary Services Laboratories

Confirmed in the past

- 15 days: Red
- 15 to 30 days: Orange
- 30 to 60 days: Yellow
- 60 to 90 days: Green
- 90 plus days: Dark Green

223
Detections Reported

48,091,293
Birds Affected

12/19/14
First Detection Reported

6/17/15
Last Detection Reported

[View detailed list of detections](#) [Download list of detections](#)

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The question going into the 2015-16 influenza season?

What impact will this have on the U.S. in the 2015-16 influenza season?


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Influenza: Emergence of Novel Flu A Subtypes

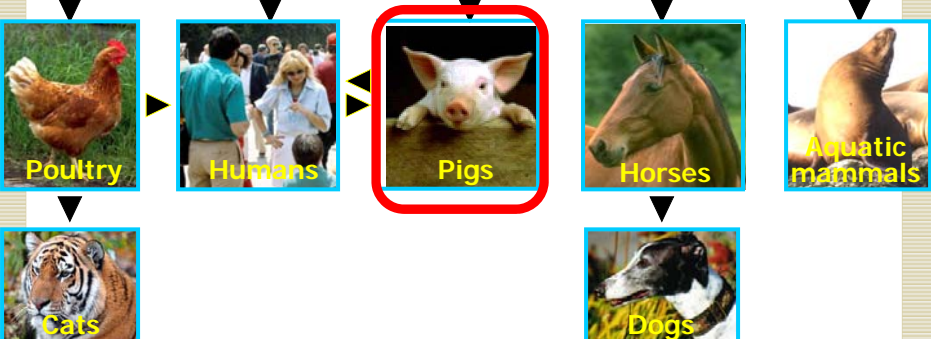
Don't forget about the little piggies

Influenza A

- H1 - H17
- N1 - N10




Aquatic birds

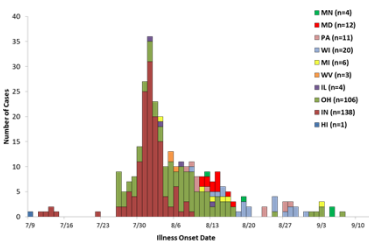


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Influenza A H3N2v: July-Sept, 2012


Novel Flu A events happen in the U.S. too!

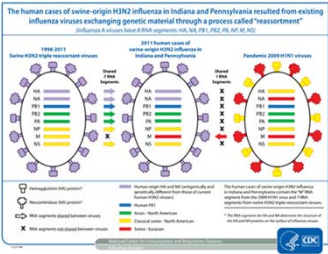




These slides contain unpublished data, please DO NOT distribute or reproduce.

H3N2v Cases –September 14, 2012
(n=20*)





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U.S. Influenza Surveillance

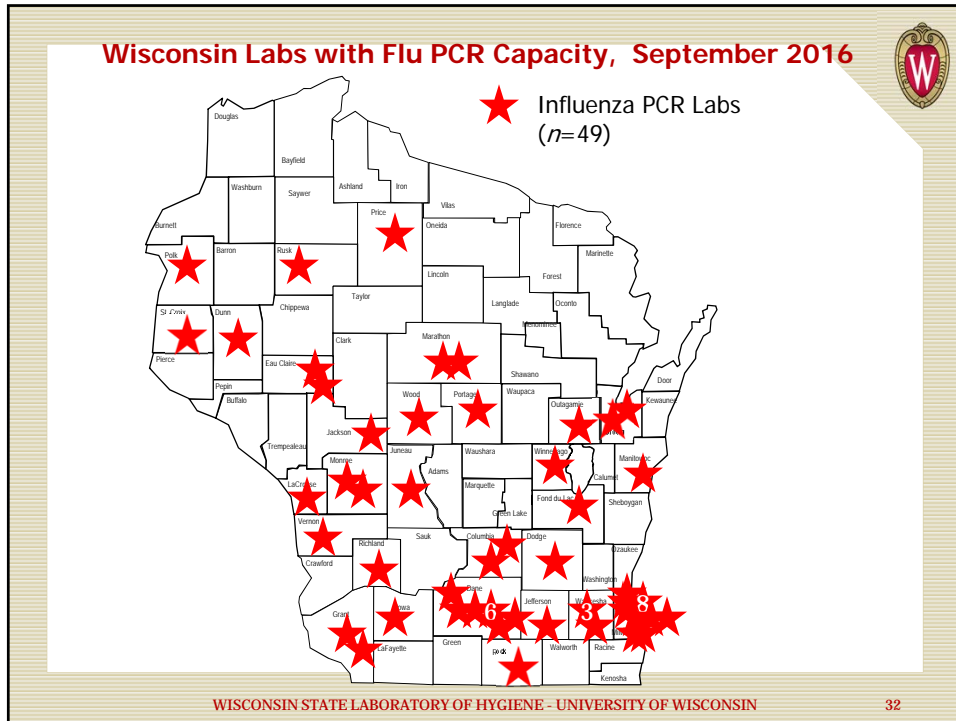
www.cdc.gov/flu/weekly

The diagram illustrates the U.S. Influenza Surveillance system. At the top, three ovals represent 'Morbidity Surveillance', 'Mortality Surveillance', and 'Virologic Surveillance'. Arrows from these ovals point to a central green oval labeled 'Health Departments'. Below 'Health Departments' is a white oval containing 'CDC'. Arrows point from 'Health Departments' and 'CDC' to a green box labeled 'FLUVIEW'. Below 'FLUVIEW' is the text 'A Weekly Influenza Surveillance Report Prepared by the Influenza Division'. To the right, another green box is labeled 'State-level data to state surveillance coordinators'. The CDC logo is in the top right corner. At the bottom, it says 'WISCONSIN STATE LABORATORY OF HYGIENE - UNIVERSITY OF WISCONSIN' and the number '30'.

"Right-Sizing" Influenza Virologic Surveillance

The Importance of "Alternative Data"

The diagram shows three data sources on the left: 'IVAD Alternative Data' (blue), 'PHL Lab Testing Data' (teal), and 'Molecular Alternative Data' (green). Arrows from these three sources point to a single arrow on the right labeled 'Situational Awareness Sample Size'. Below the diagram is the text: 'Alternative data is existing virologic data from non-PHL sources that can be used to supplement PHL data for improved situational awareness'. On the left, there is a cover image for 'Influenza Virologic Surveillance Right Size Roadmap 1st Edition' with logos for APHL and CDC. At the bottom, it says 'Right Size Roadmap' and provides the URL: <http://www.aphl.org/aphlprograms/infectious/influenza/Pages/Influenza-Virologic-Surveillance-Right-Size-Roadmap.aspx>. At the bottom of the slide, it says 'WISCONSIN STATE LABORATORY OF HYGIENE - UNIVERSITY OF WISCONSIN' and the number '31'.



Influenza Virologic Surveillance

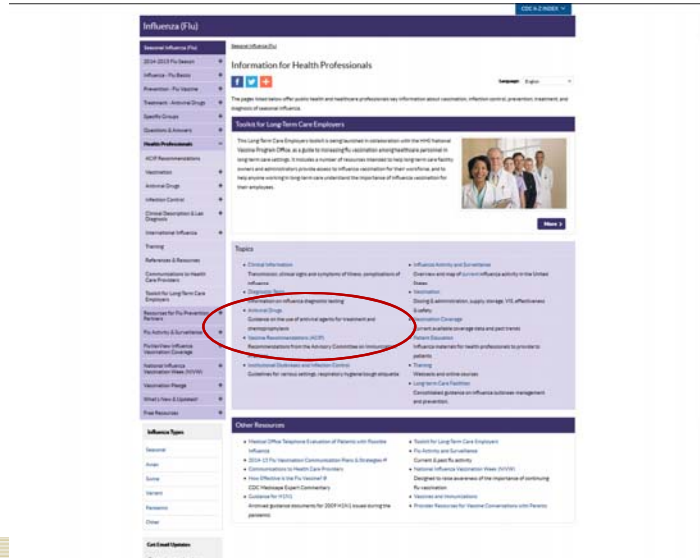
Increasing Role for the Clinical Lab

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

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Influenza – Prevention and Treatment

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



Seasonal Influenza Vaccines

How effective in 2015-16?




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

Table. Adjusted vaccine effectiveness estimates for influenza seasons from 2005-2016

Influenza Season	Reference	Study Size ⁽¹⁾	No. of Patients	Adjusted Overall VE (%)	95% CI
2005-06	Balmeron 2009	381	782	33	-16-40
2006-07	Balmeron 2009	381	346	21	-62-39
2009-10	Balmeron 2009	381	871	32	22-70
2010-11	Balmeron 2011	381	894	47	22-68
2011-12	Giffin 2011	381, 161, 79	8737	38	23-75
2012-13	Traynor 2011	381, 161, 79	4757	80	53-88
2013-14	Doshi 2014	381, 161, 79, 74	4775	47	38-56
2014-15	McLean 2014	381, 161, 79, 74	6432	48	43-55
2015-16*	Unpublished	381, 161, 79, 74, 74	8990	51	42-58
2015-16*	ACIP presentation, February	381, 161, 79, 74, 74	8529	23	15-31
2015-16*	ACIP presentation, February	381, 161, 79, 74, 74	8629	47 ⁽²⁾	38-57 ⁽²⁾

*Estimate from Nov 2, 2015–April 23, 2016.

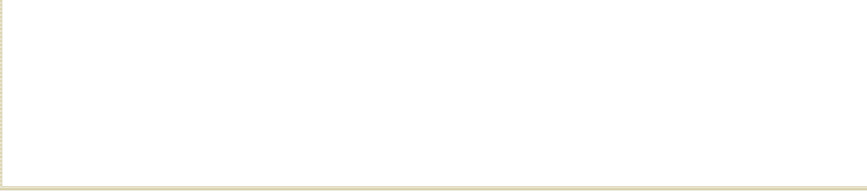


Vaccine usage and effectiveness 2015-16


All is not sunshine and roses

ACIP: Don't Use LAIV During 2016-17 Flu Season

-AAFP News, June 23, 2016-



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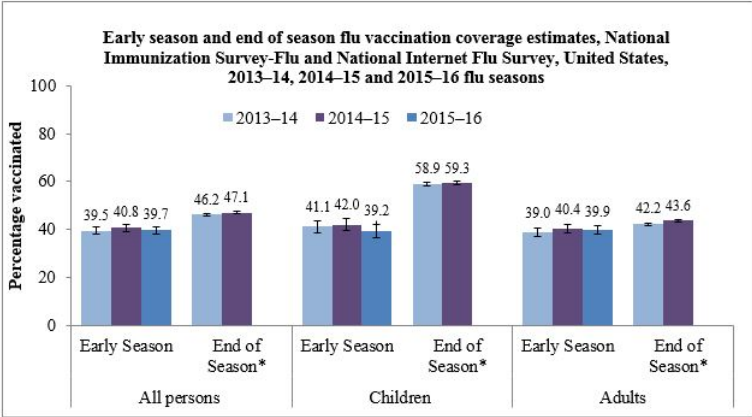


Vaccination Rates---2013-14, 2014-15, 2015-16

General Population

<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, 2014-15 and 2015-16 flu seasons



Group	Season	2013-14	2014-15	2015-16
All persons	Early Season	39.5	40.8	39.7
	End of Season*	46.2	47.1	
Children	Early Season	41.1	42.0	39.2
	End of Season*	58.9	59.3	
Adults	Early Season	39.0	40.4	39.9
	End of Season*	42.2	43.6	

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Influenza Surveillance in Wisconsin

Multi-element approach

- Rapid Influenza Diagnostic Testing (RIDT) Sites**
 - >50% of Influenza testing in WI.
 - Confirmatory testing during periods of low prevalence!


WSLH can provide confirmatory testing for out-of-season positives and the first two positive influenza A and influenza B specimens.

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Influenza Surveillance in Wisconsin

Multi-element approach

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



Request to continue to submit the first 3 specimens per week with influenza test requests to WSLH.

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Influenza Surveillance in Wisconsin

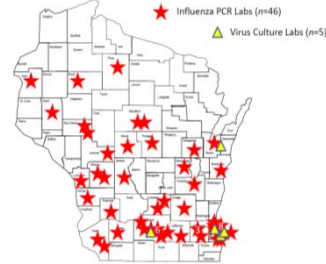


Multi-element approach

3. PCR Labs

- “Gold Standard” testing.
- Provide weekly testing data summary reports.
- 48 WI PCR labs! ↑

Wisconsin Labs with Flu PCR & Virus Culture Capacity, September 2014



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
- *Sampling* of influenza-related hospitalizations
- Unusual presentations/results
- Contact with swine/ sick or dead poultry
- Antiviral treatment failure

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Other Pathogens of Public Health Importance to Report



- *B. pertussis/ parapertussis*
- RSV
- Non-influenza respiratory viruses
- Grp A Strep
- VZV
- Rotavirus

NEW! Gastropathogen PCR


Gastrointestinal Pathogens PCR Testing

Please report the number of specimens tested and the number positive.

Pathogen	Number Tested	Number Positive
Aeromonas	<input type="text"/>	<input type="text"/>
Campylobacter	<input type="text"/>	<input type="text"/>
Clostridium difficile (Toxin A/B)	<input type="text"/>	<input type="text"/>
E. coli O157	<input type="text"/>	<input type="text"/>
Enterohemorrhagic E. coli (EHEC)	<input type="text"/>	<input type="text"/>
Enteropathogenic E. coli (EPEC)	<input type="text"/>	<input type="text"/>
Enterotoxigenic E. coli (ETEC)	<input type="text"/>	<input type="text"/>
Flexomonas shigeloides	<input type="text"/>	<input type="text"/>
Salmonella	<input type="text"/>	<input type="text"/>
Shiga-like toxin-producing E. coli (STEC)	<input type="text"/>	<input type="text"/>
Shigella	<input type="text"/>	<input type="text"/>
Shigella/Enteroinvasive E. coli (EIEC)	<input type="text"/>	<input type="text"/>
Vibrio	<input type="text"/>	<input type="text"/>
Vibrio cholerae	<input type="text"/>	<input type="text"/>
Yersinia enterocolitica	<input type="text"/>	<input type="text"/>
Adenovirus 40/41	<input type="text"/>	<input type="text"/>
Astrovirus	<input type="text"/>	<input type="text"/>
Norovirus GI/GII	<input type="text"/>	<input type="text"/>
Rotavirus A	<input type="text"/>	<input type="text"/>
Sapovirus	<input type="text"/>	<input type="text"/>
Cryptosporidium	<input type="text"/>	<input type="text"/>
Cyclospora cayentensis	<input type="text"/>	<input type="text"/>
Entamoeba histolytica	<input type="text"/>	<input type="text"/>
Giardia lamblia	<input type="text"/>	<input type="text"/>

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Reporting Lab Results



There are two options.....

1. Web-based reporting

Select the method below to enter data; you must also select "Next".

Antigen Detection
 PCR
 Culture


Back
Next
2. FAX reporting

Please Fax to <http://www.wisconsin.gov> of each week for Erik Rensdorf or Mary Weig, Wisconsin State Laboratory of Hygiene at 608-265-5921. Contact Mary Weigly (608-265-0332) or Erik Rensdorf (608-262-1021) with questions. Please report the number of specimens tested and the number of specimens positive for each [pathogen](http://www.wisconsin.gov) through [this link](http://www.wisconsin.gov) <http://www.wisconsin.gov> <http://www.wisconsin.gov>

WISCONSIN TESTING FAX REPORT

Identification Number: Your Institution's Name, Address & Telephone Number:
 Change of Institution Address:

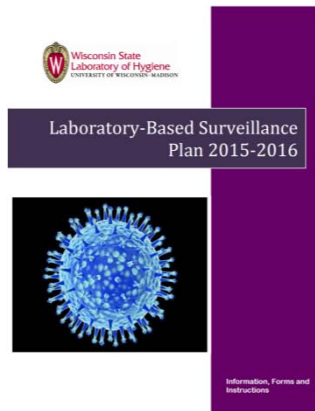
Report For Week (Sunday through Saturday) Ending:	Number Tested	Number Positive				
		Influenza A	Influenza B	RSV	RSV	Other
Influenza A and B (Differentiated)						
Influenza A and B (Combined)						
RSV						
Other						
Rapid Strep (Streptococcus Group A)						



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What is the WSLH able to provide to support participating labs?

- Specimen collection supplies.
- Specimen shippers & packaging supplies.
- NO cost specimen transport.
- Influenza confirmatory testing.
- Influenza PCR validation specimen panel.
- Weekly updated surveillance data (*B. pertussis*, *Influenza*, *RSV* & others).
- Laboratory Surveillance Reports




Influenza Surveillance Strategy

WSLH Surveillance Coordinators

1. Erik Reisdorf
Virology Lab-Team Lead
erik.reisdorf@slh.wisc.edu

2. Mary Wedig
Electronic Reporting Coordinator
mary.wedig@slh.wisc.edu

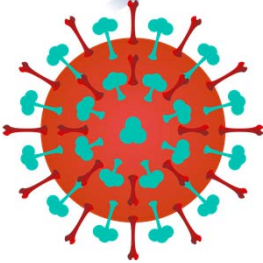


Other Respiratory Pathogens of Public Health Importance.....


RSV **Metapneumovirus**

**Rhinovirus/
Enterovirus**

ADENOVIRUS



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New viral pathogens discovered since 2001





- Human metapneumovirus (2001)
- SARS-coronavirus (2003)
- Coronavirus NL63 (2004)
- Coronavirus HKU1 (2005)
- Human bocavirus (2005)
- MERS- coronavirus (2012)

Other “not so new” ones impacting public health.....

- Enterovirus D68 (2014)

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Rapid Molecular Platforms

Coming Soon!

Flu A/B
GAS

GAS

GAS
Flu A/B
Flu A/B & RSV

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Benefits of NIRV Testing

- Establishes situational awareness
- Establishes etiology when influenza is not detected
- NIRV have similar clinical presentations
- Antibiotic stewardship
- Broaden capacity for outbreak investigations
- Define etiologies with severe acute respiratory illness (SARI)
- Understand burden of co-infections, emerging pathogens

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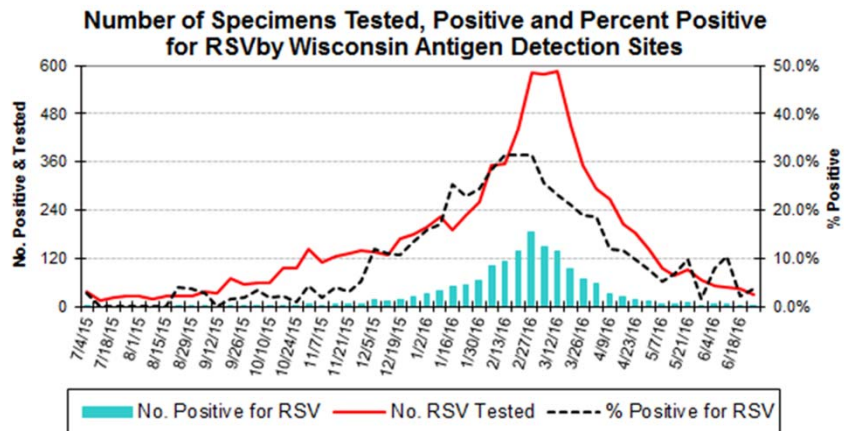


The Major Players- RSV

- Types A and B
- Leading cause of severe disease in infants and young children
- Bronchiolitis, hospitalizations (1-2% infants)
- Burden on elderly
- Seasonality varies with geography
- Infections occur throughout life
- Prophylaxis for vulnerable population--\$\$
- Vaccines in development



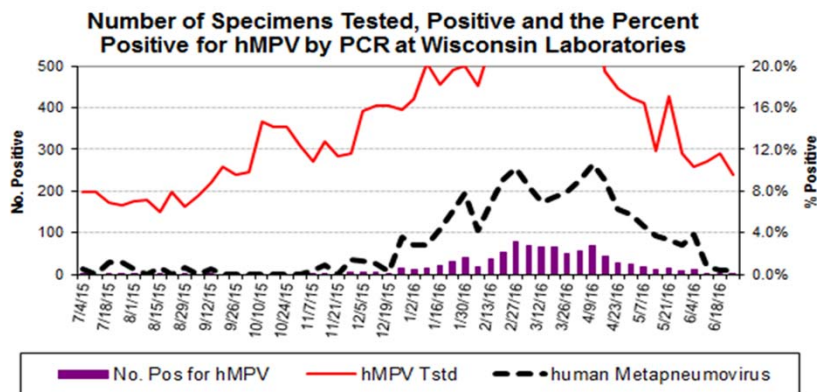
RSV Seasonality- Wisconsin




The Major Players- **Metapneumovirus**

- Burden primarily on children, elderly immunocompromised, COPD
- Occurs every year
- Symptoms indistinguishable with RSV
- No antivirals, treatments, or vaccines
- 51% hMPV patients prescribed antibiotics (Williams J et al. J Infect Dis 2006, 193: 387-95)

Human Metapneumovirus-Seasonality






The Major Players- Rhino/Enterovirus

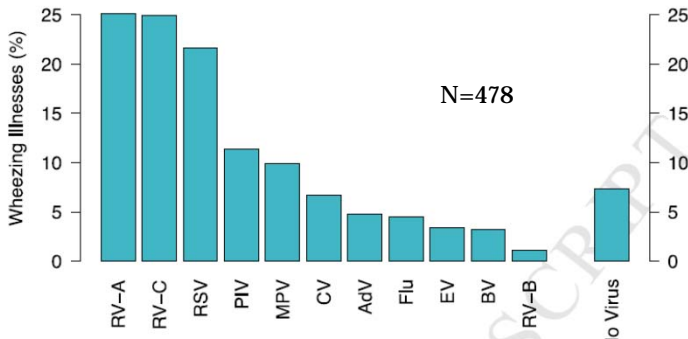
- “Common cold”, URI sinusitis but.....LRI
- Exacerbations of asthma, wheezing
- Occurs every year, year-round
- Re-infections common
- Many types co-circulate, diversity
- Some types associated with more severe disease (e.g. paralysis, myocarditis, encephalitis); Others are mild

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Rhinovirus and Wheezing

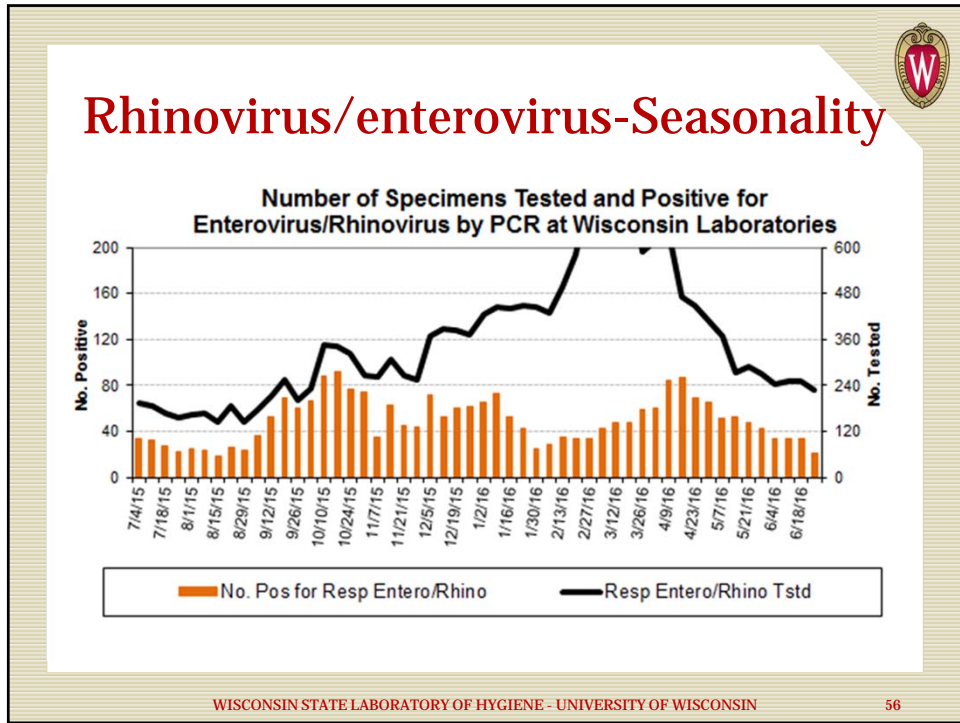
N=478



Category	Wheezing Illnesses (%)
RV-A	25
RV-C	25
RSV	22
PIV	12
MPV	10
CV	7
AdV	5
Flu	4
EV	3
BV	3
RV-B	1
No Virus	7

Anderson H, et al., (2016) Assessment of Wheezing Frequency and Viral Etiology on Child and Adolescent Asthma Risk. J Allergy and Clin Immun 26 July 2016

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WI Pediatric SARI Patients (2016)

	Infants (n=51)	Toddlers (n=47)	School-Aged Children (n=37)
Bacterial growth	4 (8%)	3 (6%)	3 (8%)
Coinfection	11 (22%)	11 (23%)	5 (14%)
Virus Detected	45 (88%)	42 (89%)	27 (73%)
RSV	25 (62%)	6 (14%)	2 (7%)
Influenza	2 (4%)	1 (2%)	5 (19%)
Coronavirus	4 (9%)	4 (10%)	5 (19%)
Adenovirus	5 (11%)	7 (17%)	3 (11%)
Bocavirus	3 (7%)	3 (7%)	1 (4%)
Metapneumovirus	1 (2%)	5 (12%)	0 (0%)
Rhinovirus	14 (31%)	19 (45%)	10 (37%)
Parinfluenza	1 (2%)	3 (7%)	2 (7%)

Preliminary data courtesy of Lina Elbadawi, MD (CDC) and the WI Div. of Public Health (unpublished)

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Thank you!



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.