U.S. Influenza Surveillance and Vaccine Effectiveness Update

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FDA Vaccines and Related Biologic Products Advisory Committee Meeting

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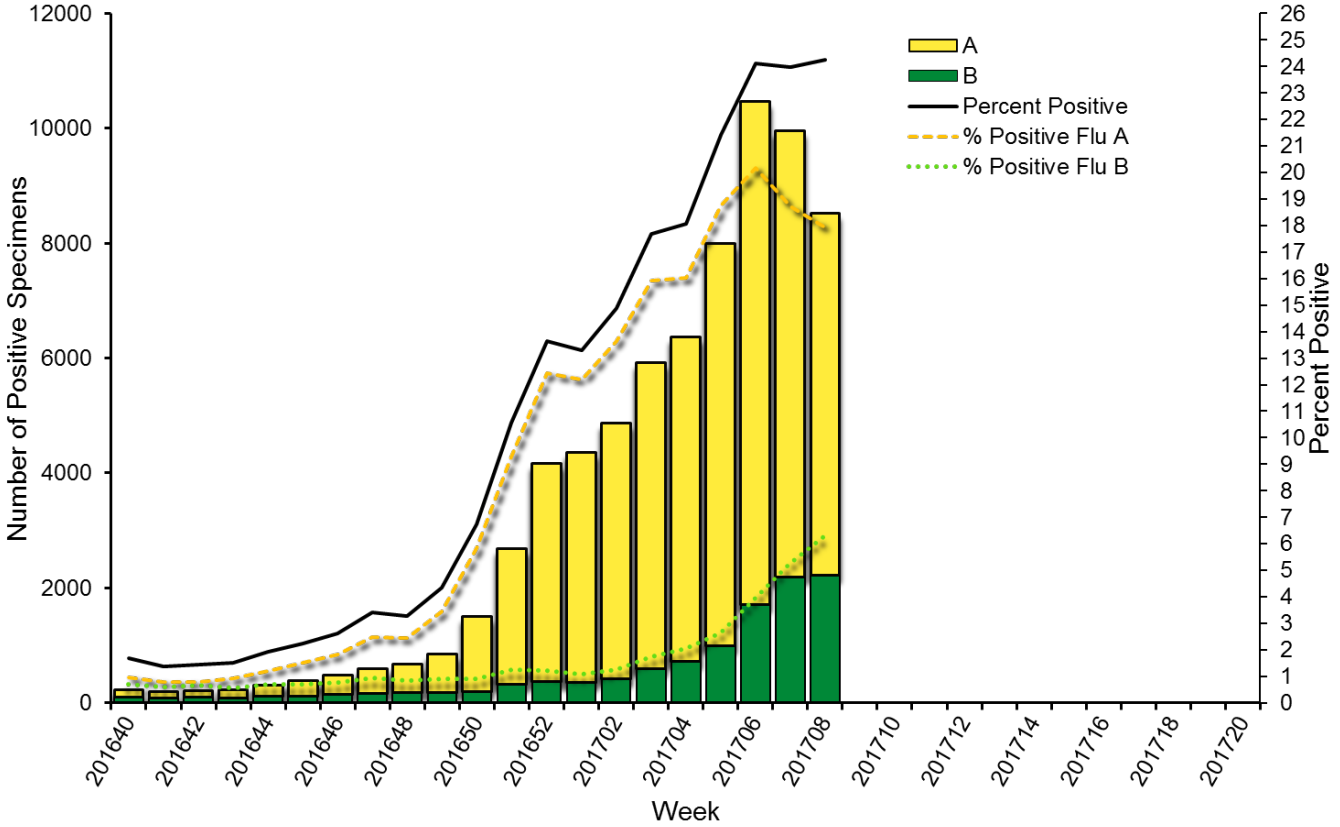
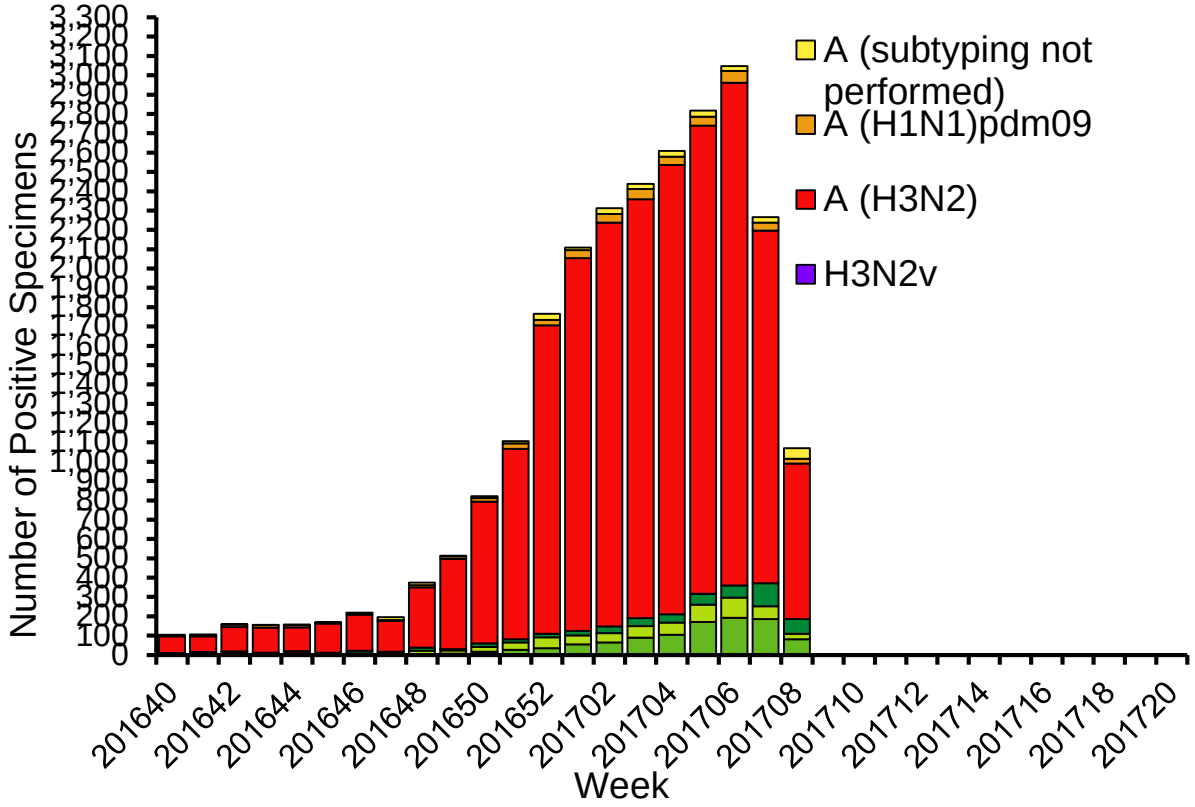
U.S. INFLUENZA SURVEILLANCE

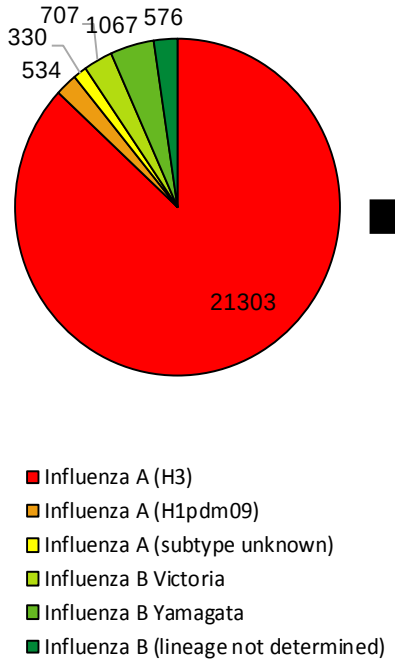
Influenza Positive Tests Reported to CDC by U.S. Clinical Laboratories, 2016-2017 Season



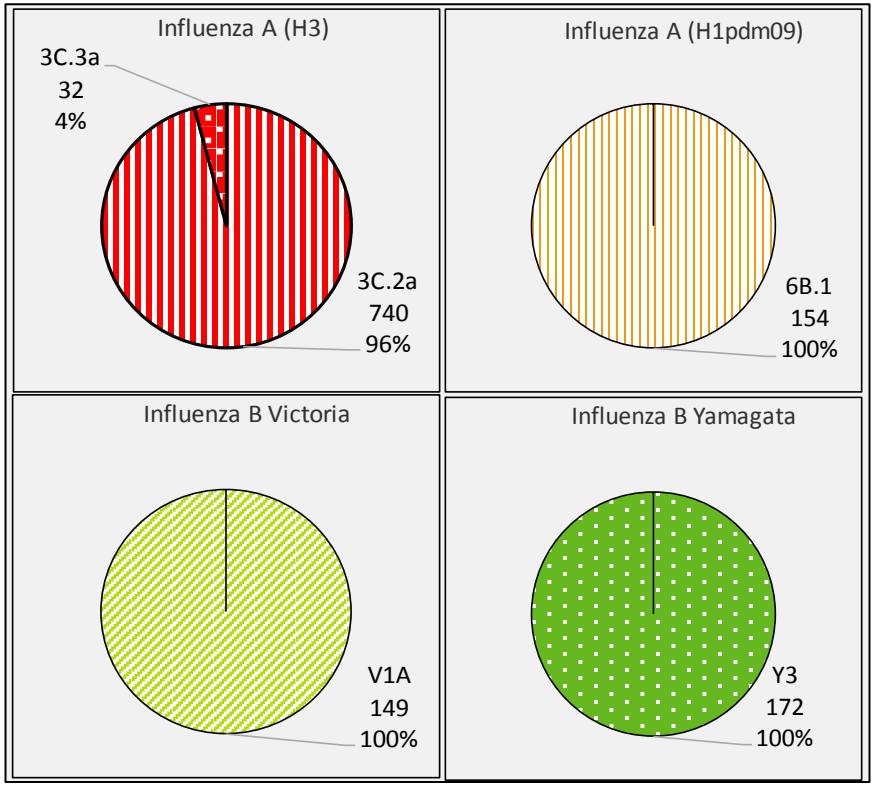
Influenza Positive Tests Reported to CDC by U.S. Public Health Laboratories, 2016-2017 Season



Influenza Positive Specimens Reported by U.S. Public Health Laboratories, Cumulative, 2016-2017 season



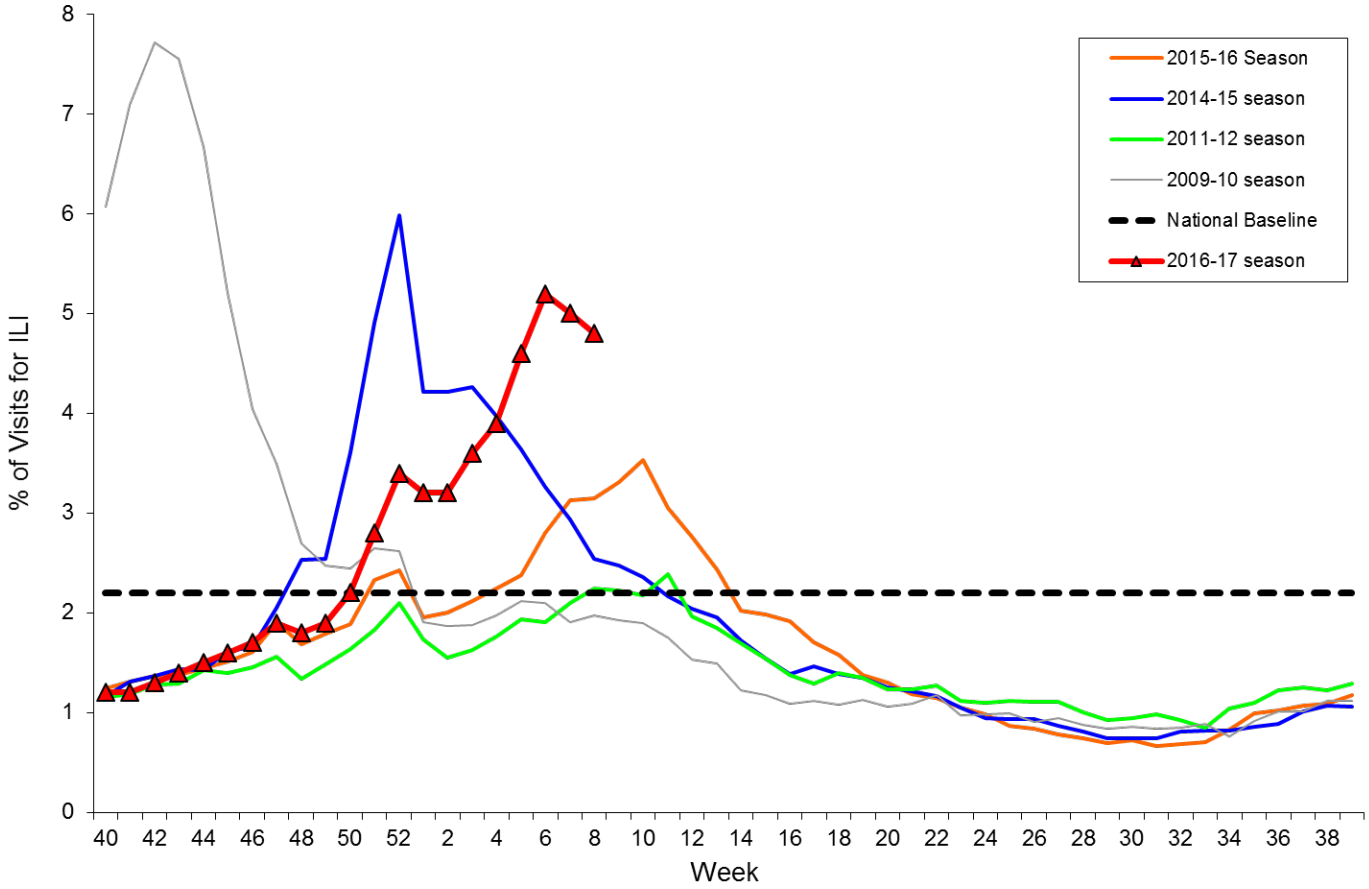
Sequence Results, by Genetic Group, of Specimens Submitted to CDC by U.S. Public Health Laboratories, Cumulative, 2016-2017 season



Antigenic Characterization of U.S. Influenza Viruses Collected October 1, 2016 to Present

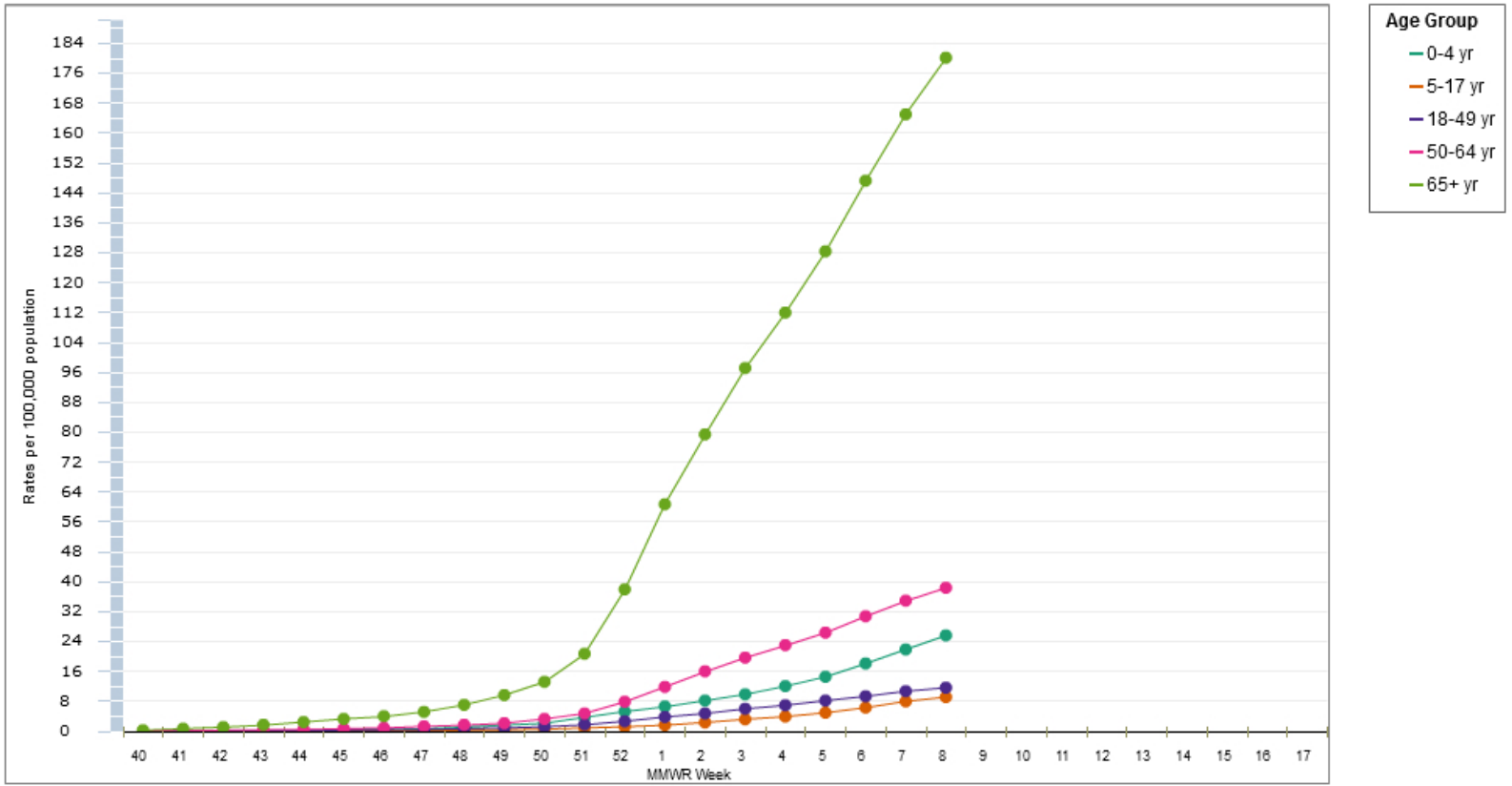
- A (H1N1)pdm09: all 112 viruses antigenically characterized using ferret post-infection antisera are A/California/07/2009-like, the H1N1 component of the 2016-17 vaccine
- A(H3N2): 387 of 399 (97%) were antigenically characterized as A/Hong Kong/4801/2014-like, the H3N2 component of the 2016-17 vaccine
- B/Victoria linage: 123 of 134 (92%) were antigenically characterized as B/Brisbane/60/2008-like, which is included in both quadrivalent and trivalent influenza vaccines for the 2016-17 season
- B/Yamagata lineage: All 121 were antigenically characterized as B/Phuket/3073/2013-like, an influenza B virus included in the quadrivalent influenza vaccines for the 2016-17 season

Percentage of Visits for Influenza-like Illness (ILI) Reported by the U.S. Outpatient Influenza-like Illness Surveillance Network (ILINet), Weekly National Summary, 2016-2017 and Selected Previous Seasons



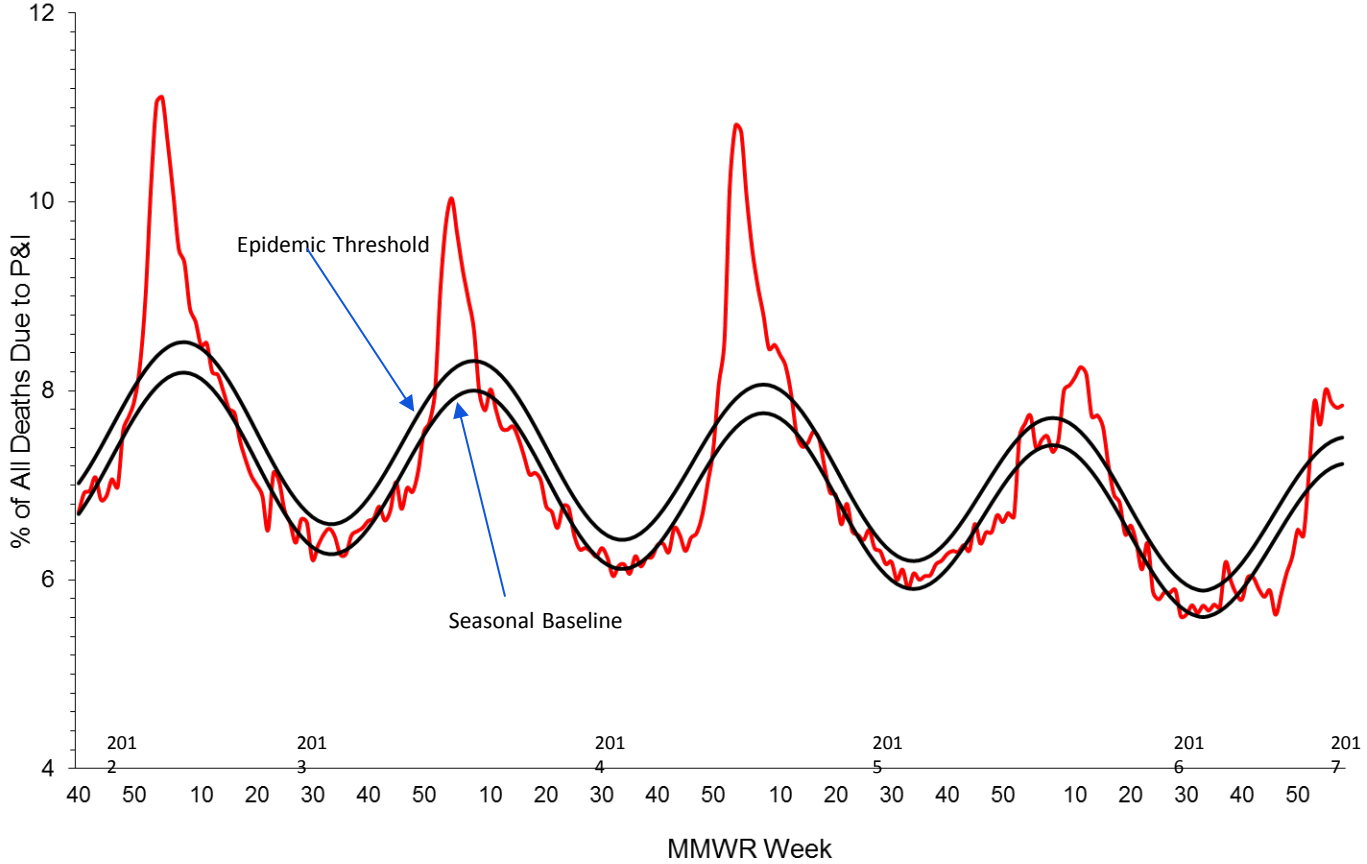
Laboratory-Confirmed Influenza Hospitalizations

Preliminary cumulative rates as of Feb 25, 2017

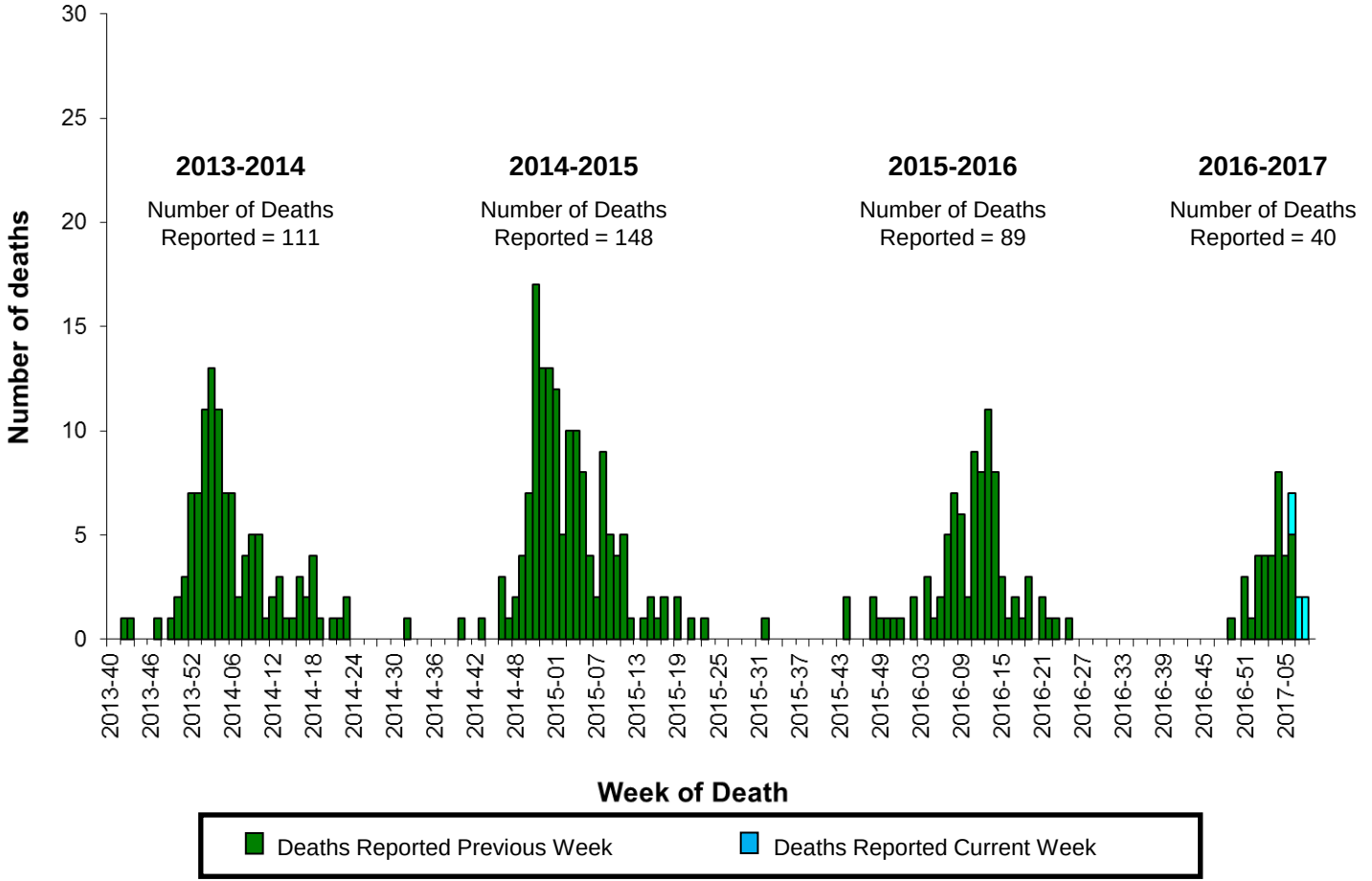


Pneumonia and Influenza Mortality from the National Center for Health Statistics Mortality Surveillance System

Data through the week ending February 11, 2017, as of March 2, 2017



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



Summary of the U.S. Season

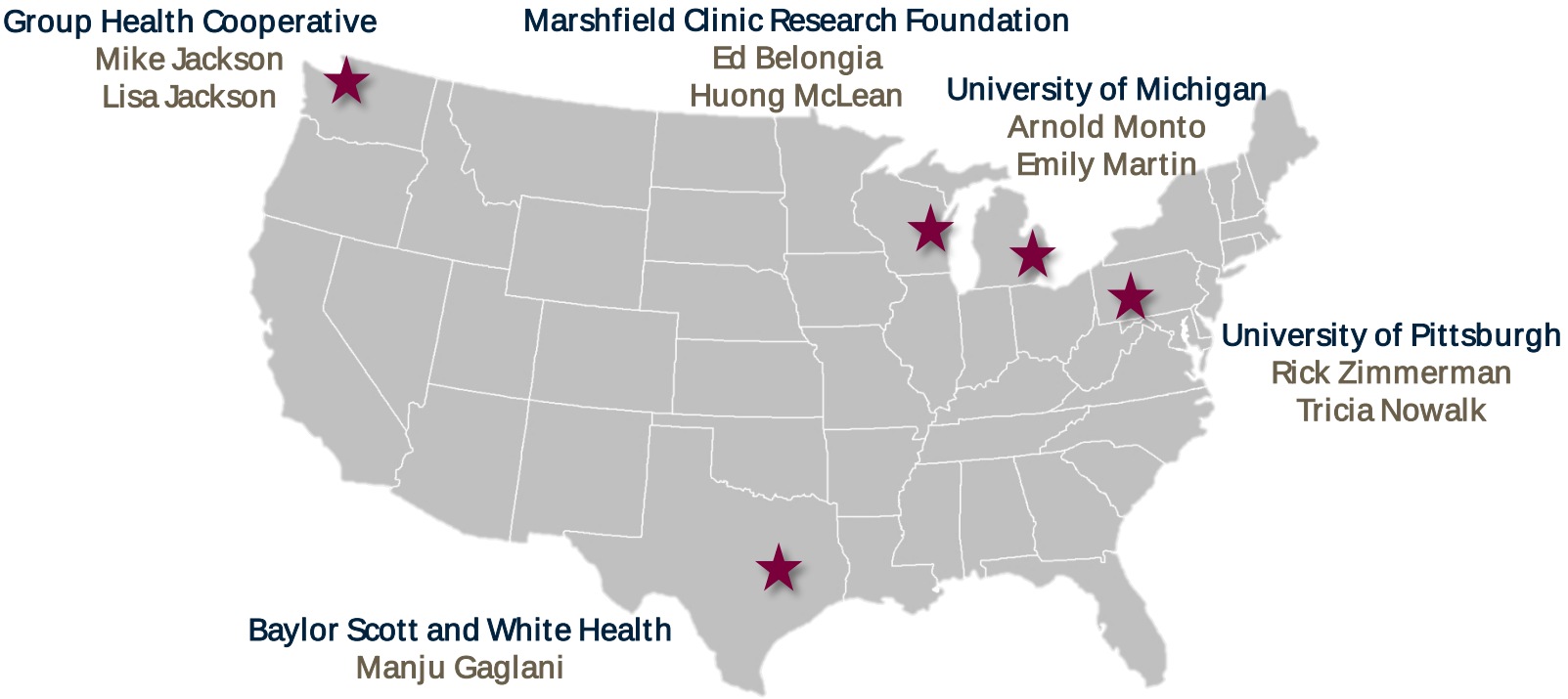
- Influenza A(H3N2) viruses have predominated during the 2016-17 season
  - Influenza B activity has increased in recent weeks
- So far, influenza activity has been moderate, and may have peaked nationally
- The circulating stains are similar to those contained in the 2016-17 vaccine

From the U.S. Influenza Vaccine Effectiveness (U.S. Flu VE) Network

Presented to the Advisory Committee on Immunization Practices (ACIP), February 22, 2017

U.S. VACCINE EFFECTIVENESS--INTERIM ESTIMATES

US Flu VE Network sites and principal investigators



US Flu VE Network Methods

Enrollees: Outpatients aged ≥6 months with acute respiratory illness with cough ≤7 days duration

Dates of enrollment: November 28, 2016–February 4, 2017

Design: Test-negative design

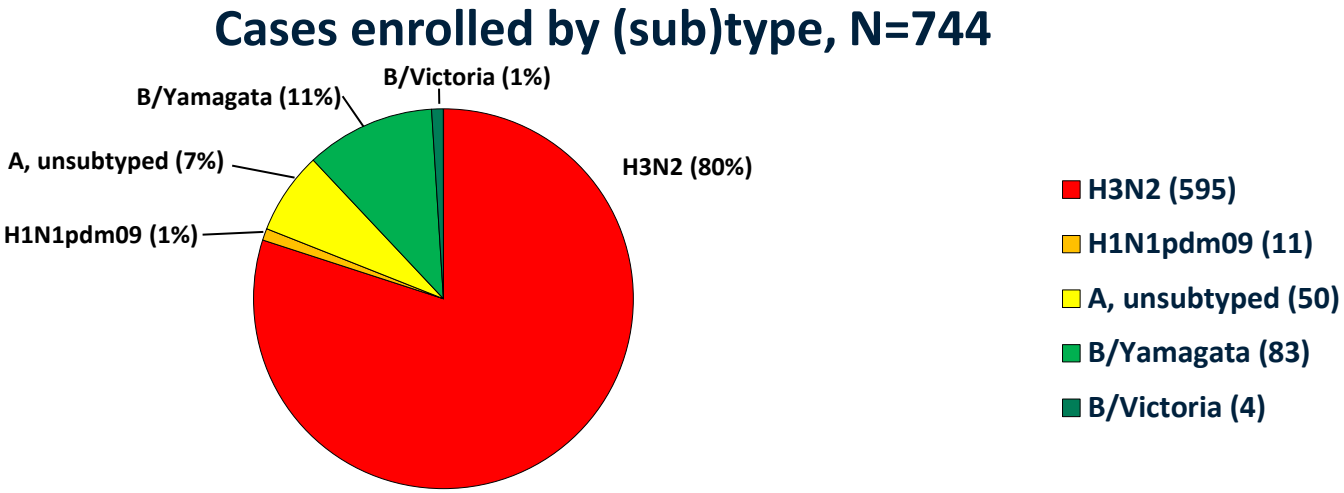
- Comparing vaccination odds among influenza RT-PCR positive cases and RT-PCR negative controls
- Vaccination status: receipt of at least one dose of any 2016–17 seasonal flu vaccine according to medical records, immunization registries, and/or self-report

Analysis: VE = (1 – adjusted OR) x 100%

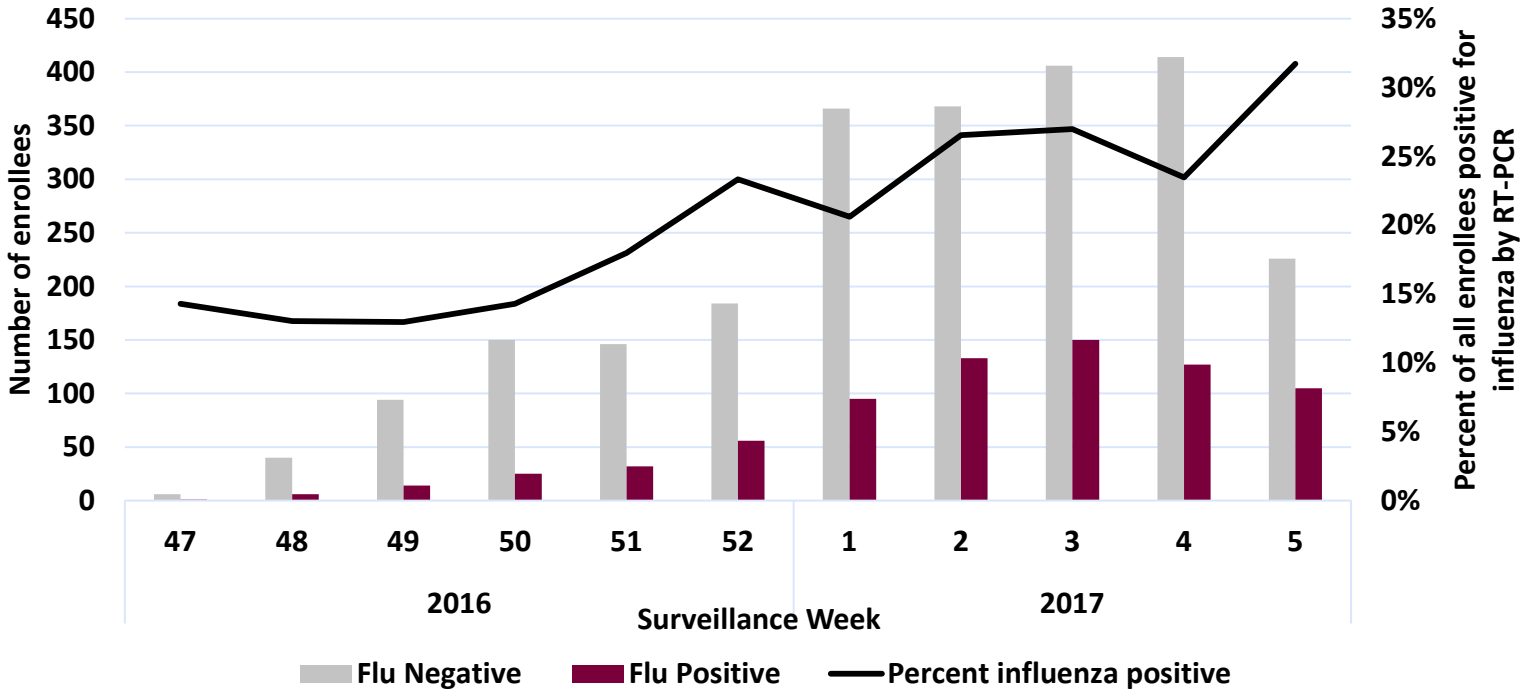
- Adjustment for study site, age, self-rated general health status, race/Hispanic ethnicity, interval (days) from onset to enrollment, and calendar time

Interim Results

- 3,144 enrolled from Nov 28, 2016–Feb 4, 2017 at 5 sites
- 744 (24%) influenza RT-PCR positive
- 2,400 (76%) influenza RT-PCR negative



Number of enrolled participants by influenza RT-PCR result and percent positivity by week of onset



Note: Week 5 only includes patients with completed laboratory tests and thus does not reflect all enrolled patients during that week across study sites.

Interim adjusted vaccine effectiveness against medically attended influenza, 2016–17

	Influenza positive		Influenza negative		Vaccine Effectiveness			
					Unadjusted		Adjusted*	
Any influenza A or B virus	**N vaccinated /Total**	**(%)**	**N vaccinated /Total**	**(%)**	**VE %**	**95% CI**	**VE %**	**95% CI**
Overall	333/744	(45)	1317/2400	(55)	33	(21 to 44)	**48**	**(37 to 57)**
Age group (yrs)								
6 mos–8	32/97	(33)	330/614	(54)	58	(33 to 73)	**53**	**(22 to 72)**
9–17	36/122	(30)	92/247	(37)	29	(-12 to 56)	**32**	**(-20 to 61)**
18–49	89/208	(43)	363/783	(46)	13	(-18 to 36)	**19**	**(-17 to 43)**
50–64	76/189	(40)	261/425	(61)	58	(40 to 70)	**58**	**(38 to 72)**
≥65	100/128	(78)	271/331	(82)	21%	(-31 to 52)	**46**	**(4 to 70)**

* Multivariate logistic regression models adjusted for site, age, sex, race/ethnicity, self-rated general health status, interval from onset to enrollment, and calendar time.

Interim adjusted vaccine effectiveness against medically attended influenza by virus type, 2016–17

	Influenza positive		Influenza negative		Vaccine Effectiveness			
					Unadjusted		Adjusted*	
	N vaccinated /Total	(%)	N vaccinated /Total	(%)	VE %	95% CI	VE %	95% CI
Influenza A/H3N2								
Overall	282/595	(47)	1317/2400	(55)	26	(11 to 38)	**43**	**(29 to 54)**
Age group (yrs)								
6 mos–8	24/68	(35)	330/614	(54)	53	(21 to 72)	**53**	**(16 to 74)**
9–17	28/94	(30)	92/247	(37)	29	(-19 to 57)	**23**	**(-43 to 59)**
18–49	73/168	(43)	363/783	(46)	11	(-24 to 36)	**13**	**(-30 to 41)**
50–64	70/154	(45)	261/425	(61)	48	(24 to 64)	**50**	**(23 to 67)**
≥65	87/111	(78)	271/331	(82)	20	(-37 to 53)	**44**	**(-3 to 69)**
Influenza B								
Overall	23/90	(26)	1317/2400	(55)	72	(54 to 83)	**73**	**(54 to 84)**

* Multivariate logistic regression models adjusted for site, sex, race/ethnicity, self-rated general health status, interval from onset to enrollment, and calendar time.

Summary

- Interim results for 2016–17 season (through February 4, 2017) indicate vaccine effectiveness of 48% against medically attended influenza
  - Interim estimate similar to previous seasons when vaccine was well matched to circulating influenza viruses
- Significant protection against circulating influenza A(H3N2) and B viruses (predominantly B/Yamagata)
  - VE not estimated against H1N1pdm09 or B/Victoria due to small number of cases
- Enrollment continues – end-of-season VE estimates may differ from interim estimates

VE against influenza A (H3N2) viruses

- VE of 43% against A (H3N2) similar to antigenically matched H3N2 viruses
  - 2011-12 (39%) and 2012-13 (39%)
  - Meta-analysis[1] of test-negative VE studies: 33% (26% - 39%)
- VE against A (H1N1)pdm09 (61%) and B viruses (54%) tend to be higher[1]
- A (H3N2) viruses have required more frequent vaccine updates
- Candidate A (H3N2) vaccine viruses more often have antigenic changes after adaptation to growth in eggs
- Efforts ongoing to improve VE against A (H3N2) viruses

[1] Belongia et al. Lancet Infect Dis, 2016

Repeat Vaccination

- Prior season vaccination is a significant effect modifier for most seasons
- The point estimate for current season only vaccination is consistently higher than current plus prior season vaccination, overlapping CIs
- There is evidence for residual protection from the prior season vaccination, consistently for B and H1N1pdm and sometimes for H3N2
- Complex issue that is an actively evolving area of research

US Flu VE Network

- **University of Michigan and Henry Ford Health System:** Arnold S. Monto, Emily Martin, Joshua G. Petrie, Lois E. Lamerato, Ryan E. Malosh, E.J. McSpadden, Hannah Segaloff, Caroline K. Cheng, Rachel Truscon, Emileigh Johnson, Anne Kaniclides, Heather R. Lipkovich, Nishat Islam, Michelle Groesbeck, Andrea Lee, Joey Lundgren, Erika Chick, Lindsey Benisatto, Tosca Le, Dexter Hobdy, Kristyn Brundidge, Christina Rincon, Stephanie Haralson, Jennifer Hessen, Ahn Trinh
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