Influenza Vaccine Effectiveness, Including LAIV vs IIV in Children and Adolescents, US Flu VE Network, 2015-16

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For the US Flu VE Network

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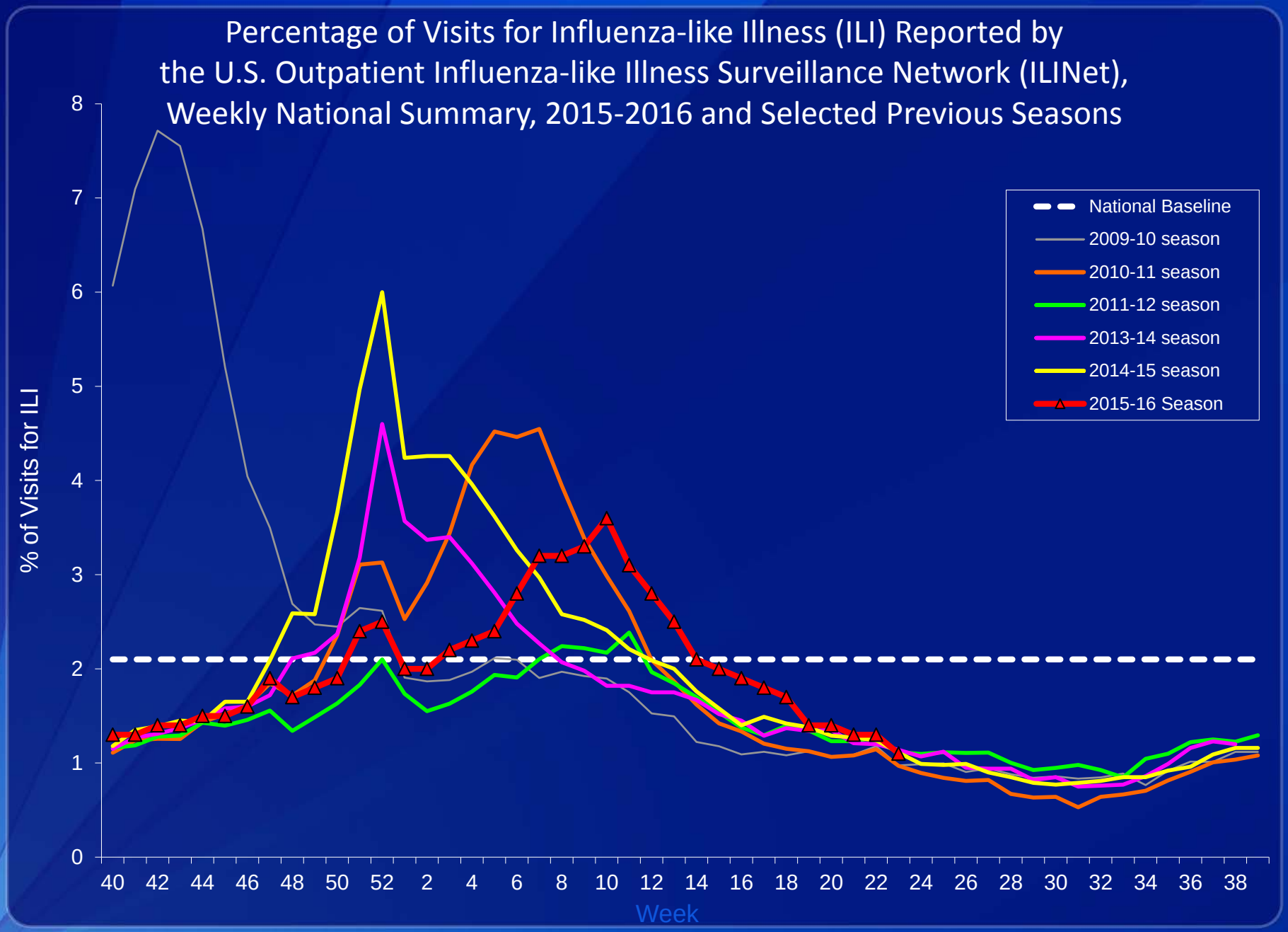
Objectives

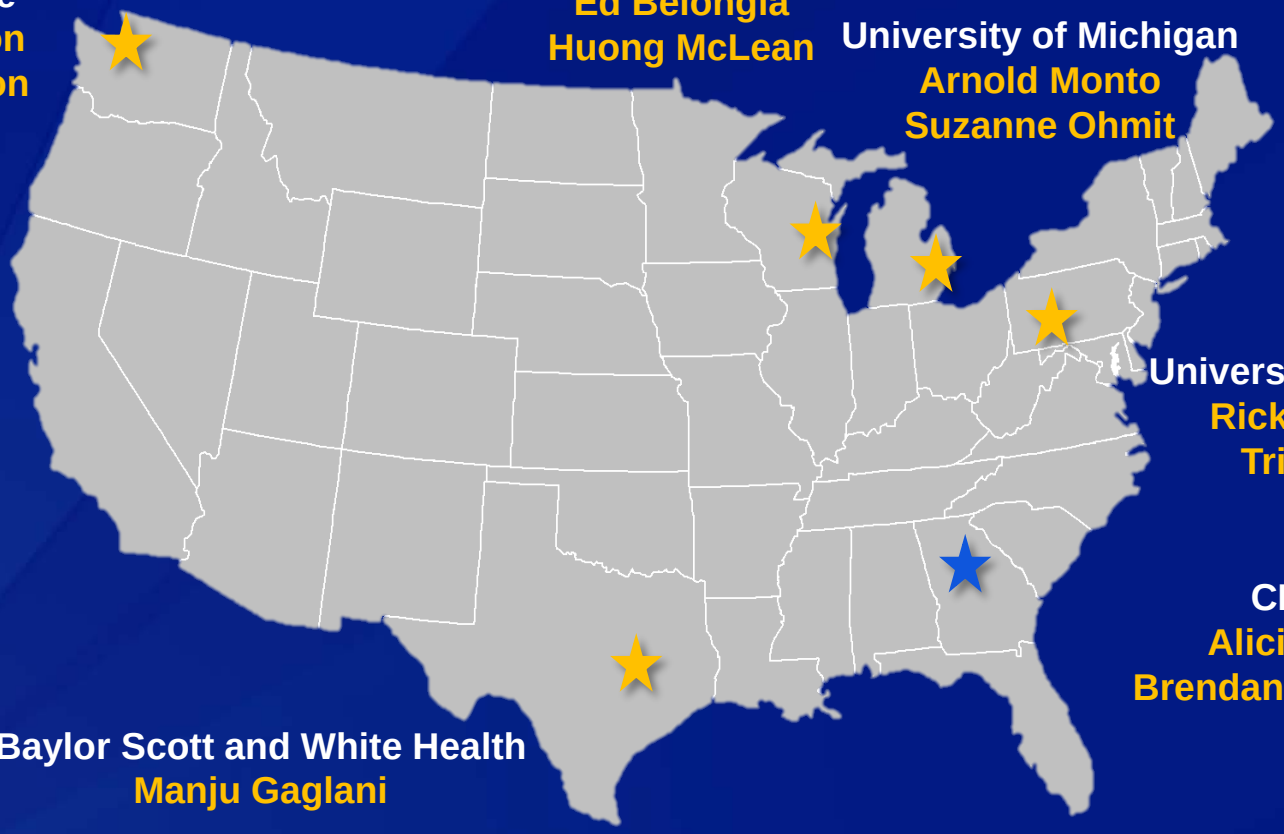
- Review end-of-season estimates of 2015-16 influenza vaccine effectiveness (VE) from US Flu VE Network
- Compare LAIV and IIV effectiveness among children and adolescents aged 2–17 years during 2015-16

2015-16 SEASON UPDATE

Percentage of Visits for Influenza-like Illness (ILI) Reported by the U.S. Outpatient Influenza-like Illness Surveillance Network (ILINet), Weekly National Summary, 2015-2016 and Selected Previous Seasons



US Flu VE Network: 5 Sites and Principal Investigators



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US Flu VE Network: Methods

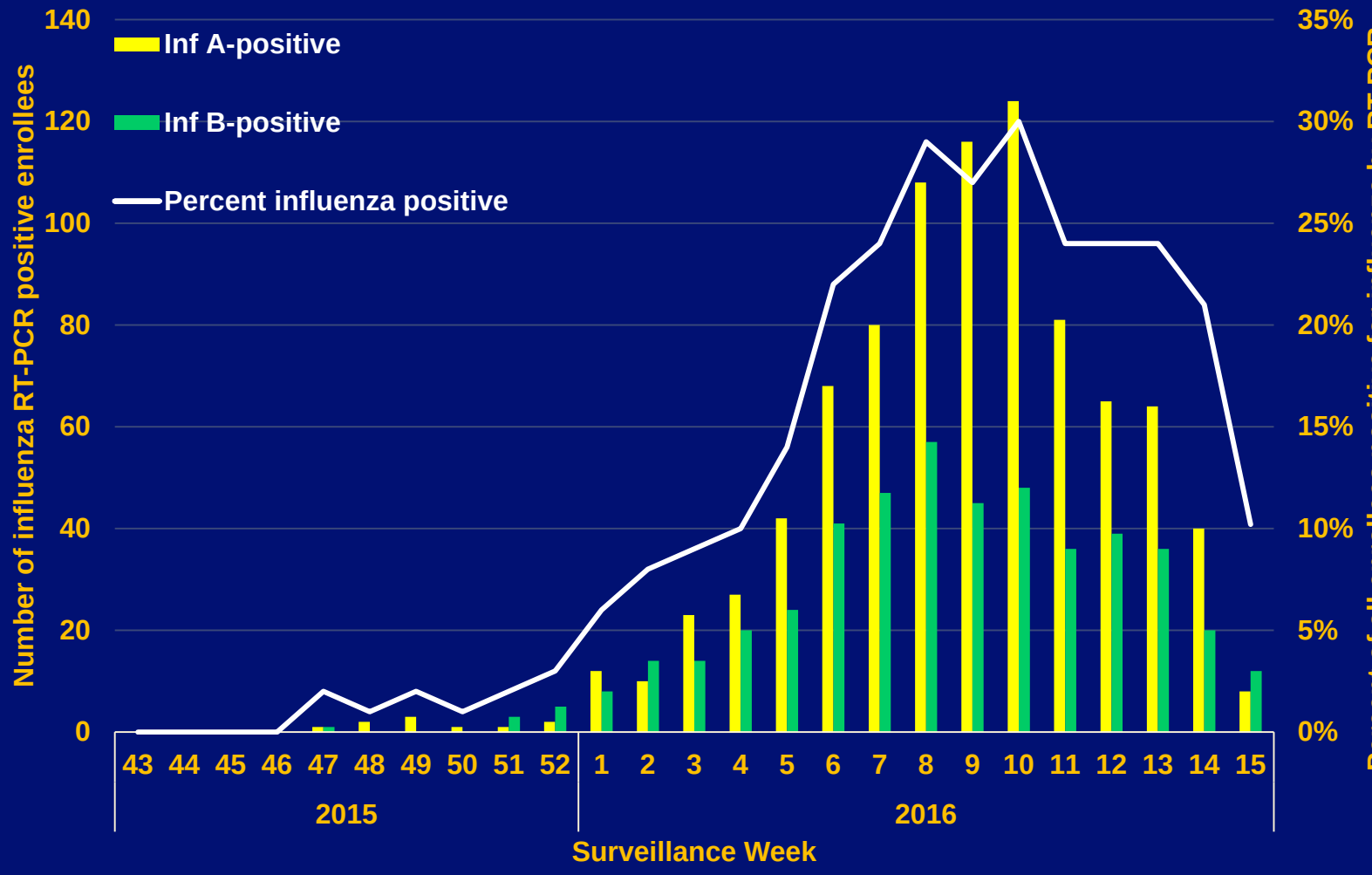
Enrollees: Outpatients aged ≥6 months with acute respiratory illness with cough ≤7 days duration

Dates of enrollment: November 2, 2015–April 15, 2016

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 2015-16 seasonal flu vaccine according to medical records, immunization registries, and plausible 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

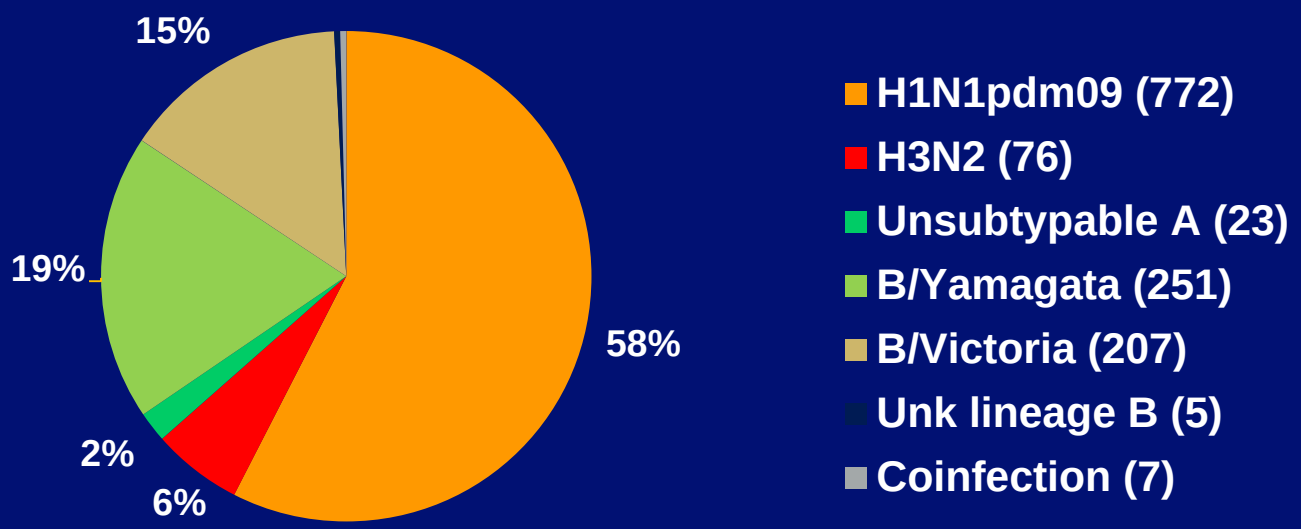
Number of enrolled participants with RT-PCR confirmed influenza and percent positivity by week of onset



US Flu VE Network: Interim Results

- 7563 enrolled from Nov 2, 2015–Apr 15, 2016 at 5 sites
- 6213 (82%) influenza RT-PCR negative
- 1341 (18%) influenza RT-PCR positive
- 9 (<1%) influenza RT-PCR inconclusive/unrepeatable

Cases enrolled by (sub)type



Laboratory characterization of influenza viruses from US Flu VE Network, 2015-16

- **A/H1N1pdm09**
  - 100% A/CALIFORNIA/07/2009-LIKE (n=67)
  - 99% clade 6B.1 (n=72), 1 clade 6B (A/CALIFORNIA/07/2009-LIKE)
- **A/H3N2**
  - 100% A/SWITZERLAND/9715293/2013-LIKE (H3N2) (n=16)
  - 62% (n=11) A/Hong Kong/14 (clade 3C.2a) and
    38% (n=18) A/Switzerland/13 (clade 3C.3a)
- **B/Yamagata**
  - 100% B/PHUKET/3073/2013-LIKE (n=43)
  - 97% clade Y3 (n=33) and 1 clade Y3V1A (B/PHUKET/3073/2013-LIKE)
- **B/Victoria**
  - 100% B/BRISBANE/60/2008-LIKE (n=43)
  - 100% clade V1A (n=34)

Adjusted VE against medically attended influenza, US Flu VE Network, 2015-16

	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	514/1332	39	3037/5708	53	45	(38 to 51)	**47**	**(39 to 53)**
6m – 8 y	108/277	39	765/1410	54	46	(30 to 59)	**48**	**(31 to 61)**
9–17 y	33/164	20	277/694	40	62	(43 to 75)	**64**	**(44 to 77)**
18–49 y	146/499	29	841/1957	43	45	(32 to 56)	**48**	**(35 to 59)**
50–64 y	149/283	53	562/918	61	30	(8 to 46)	**23**	**(-3 to 43)**
≥65 y	78/109	72	592/729	81	42	(8 to 63)	**45**	**(10 to 66)**
IIV3/4, all ages	472/1290	37	2893/5564	52	47	(40 to 53)	**49**	**(41 to 56)**

* Multivariate logistic regression models adjusted for site, age categories (6m-8y, 9-17y 18-49y, 50-64y, ≥65y), sex, race/Hispanic ethnicity, self-rated general health status, interval from onset to enrollment, and calendar time (biweekly intervals)

Adjusted VE against A/H1N1pdm09
US Flu VE Network, 2015–2016

	Influenza positive		Influenza negative		Vaccine Effectiveness			
					Unadjusted		Adjusted*	
Influenza A (H1N1)pdm09	N vaccinated /Total	(%)	N vaccinated /Total	(%)	VE %	95% CI	VE %	95% CI
Overall	320/781	41	3037/5708	53	39	(29 to 47)	**41**	**(31 to 51)**
6m–8 y	70/173	40	765/1410	54	43	(21 to 58)	**47**	**(25 to 63)**
9–17 y	11/51	22	277/694	40	59	(18 to 79)	**62**	**(21 to 82)**
18–49 y	98/311	32	841/1957	43	39	(21 to 53)	**42**	**(23 to 56)**
50–64 y	110/194	57	562/918	61	17	(-14 to 39)	**9**	**(-30 to 36)**
≥65 y	31/52	60	592/729	81	66	(39 to 81)	**68**	**(39 to 83)**
IIV3/4, all ages	295/756	39	2893/5564	52	41	(31 to 49)	**44**	**(33 to 53)**

* Multivariate logistic models adjusted for site, age categories (6m-8y, 9-17y 18-49y, 50-64y, ≥65y), sex, race/Hispanic ethnicity, self-rated general health status, interval from onset to enrollment, and calendar time (biweekly intervals).

Adjusted VE against A/H3N2 and B lineage US Flu VE Network, 2015–2016

	Influenza positive		Influenza negative		Vaccine Effectiveness			
					Unadjusted		Adjusted*	
Influenza A(H3N2)	**N vaccinated /Total**	**(%)**	**N vaccinated /Total**	**(%)**	**VE %**	**95% CI**	**VE %**	**95% CI**
All ages	32/75	43	3037/5708	53	34	(-4 to 59)	**45**	**(9 to 66)**
IIV, all ages	32/75	43	2893/5564	52	31	(-9 to 57)	**43**	**(6 to 65)**
Influenza B/Yamagata								
All ages	92/256	36	3037/5708	53	51	(36 to 62)	**55**	**(41 to 66)**
IIV, all ages	82/246	33	2893/5564	52	54	(39 to 65)	**59**	**(45 to 69)**
Influenza B/Victoria								
All ages	64/207	31	3037/5708	53	61	(47 to 71)	**55**	**(38 to 68)**
IIV, all ages	57/200	29	2893/5564	52	63	(50 to 73)	**58**	**(40 to 70)**

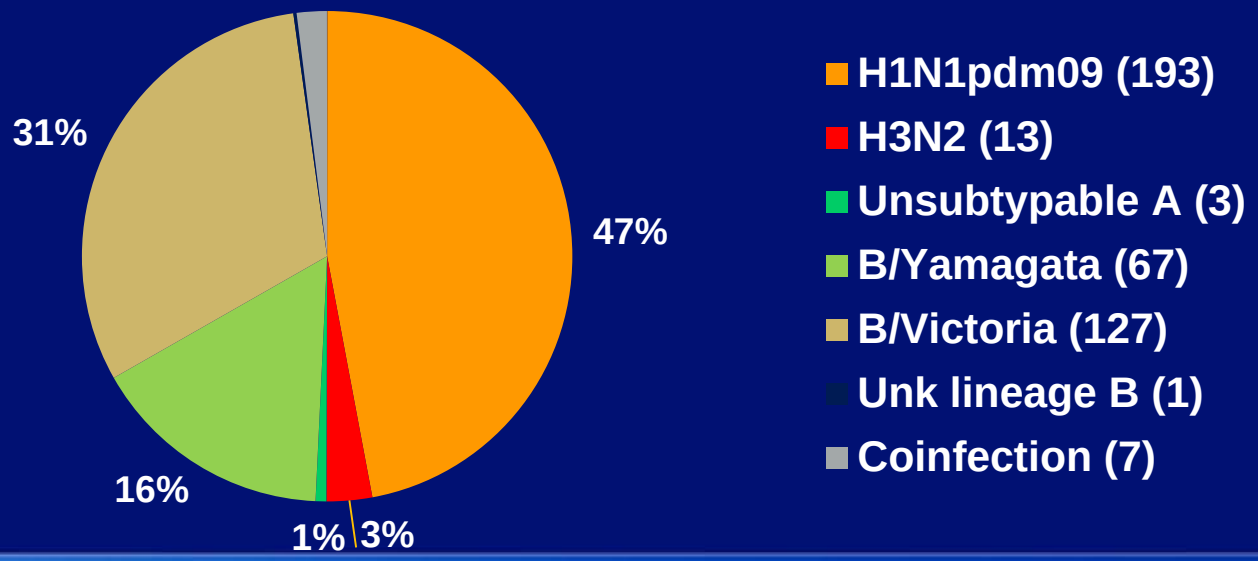
* Multivariate logistic models adjusted for site, age categories (6m-8y, 9-17y 18-49y, 50-64y, ≥65y), sex, race/Hispanic ethnicity, self-rated general health status, interval from onset to enrollment, and calendar time (biweekly intervals).

LAIV and IIV vaccine effectiveness among patients aged 2–17 years by influenza type/subtype

US Flu VE Network: Children 2–17 years

- 2286 enrolled from Nov 2, 2015–Apr 15, 2016 at 5 sites
- 1871 (82%) influenza RT-PCR negative
- 411 (18%) influenza RT-PCR positive
- 4 (<1%) influenza RT-PCR inconclusive/unrepeatable

Cases enrolled by (sub)type



US Flu VE Network Methods

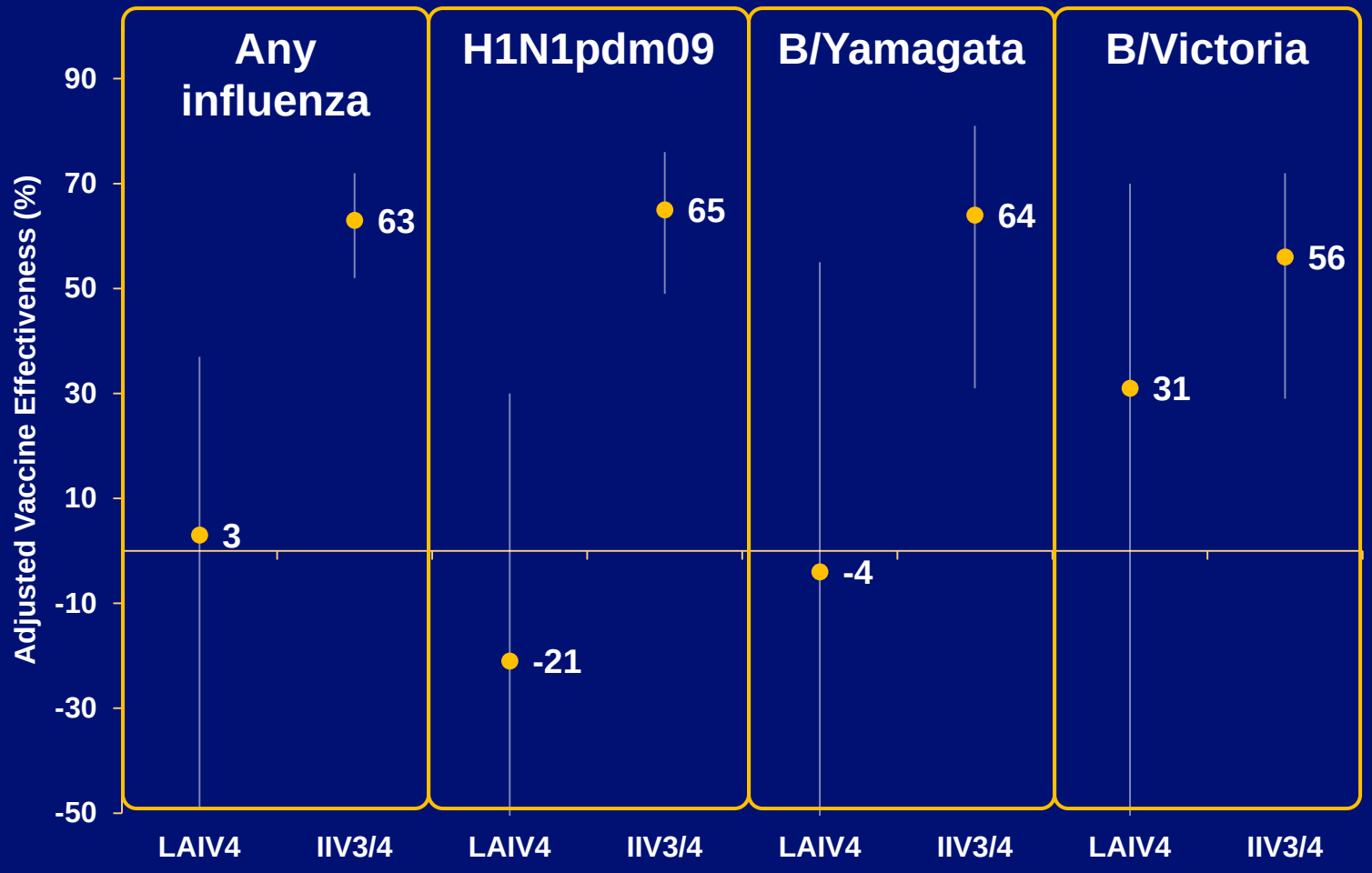
- **Vaccination status:** **receipt of at least one dose of any 2015-16 seasonal flu vaccine**
  - Documented vaccination only for those aged 2–8 years
  - Documented + plausible report for those aged 9–17 years
- **Vaccine type:** **From medical record/immunization system or parent report if electronic record has no information**
- **Analysis:** **VE = (1 – adjusted OR) x 100%**
  - **Adjustment for study site, age (2–4, 5–8, 9–17 years), self-rated general health status (excellent/very good, good/fair/poor), race/Hispanic ethnicity, interval from onset to enrollment, and calendar time (biweekly intervals)**
  - **Independent analysis by Jessica Pruszynski, Baylor Scott&White Health**

Exclusions from vaccine type analyses for children and adolescents ages 2–17 years

154/2286 (7%) of enrollees aged 2–17 years excluded from analysis

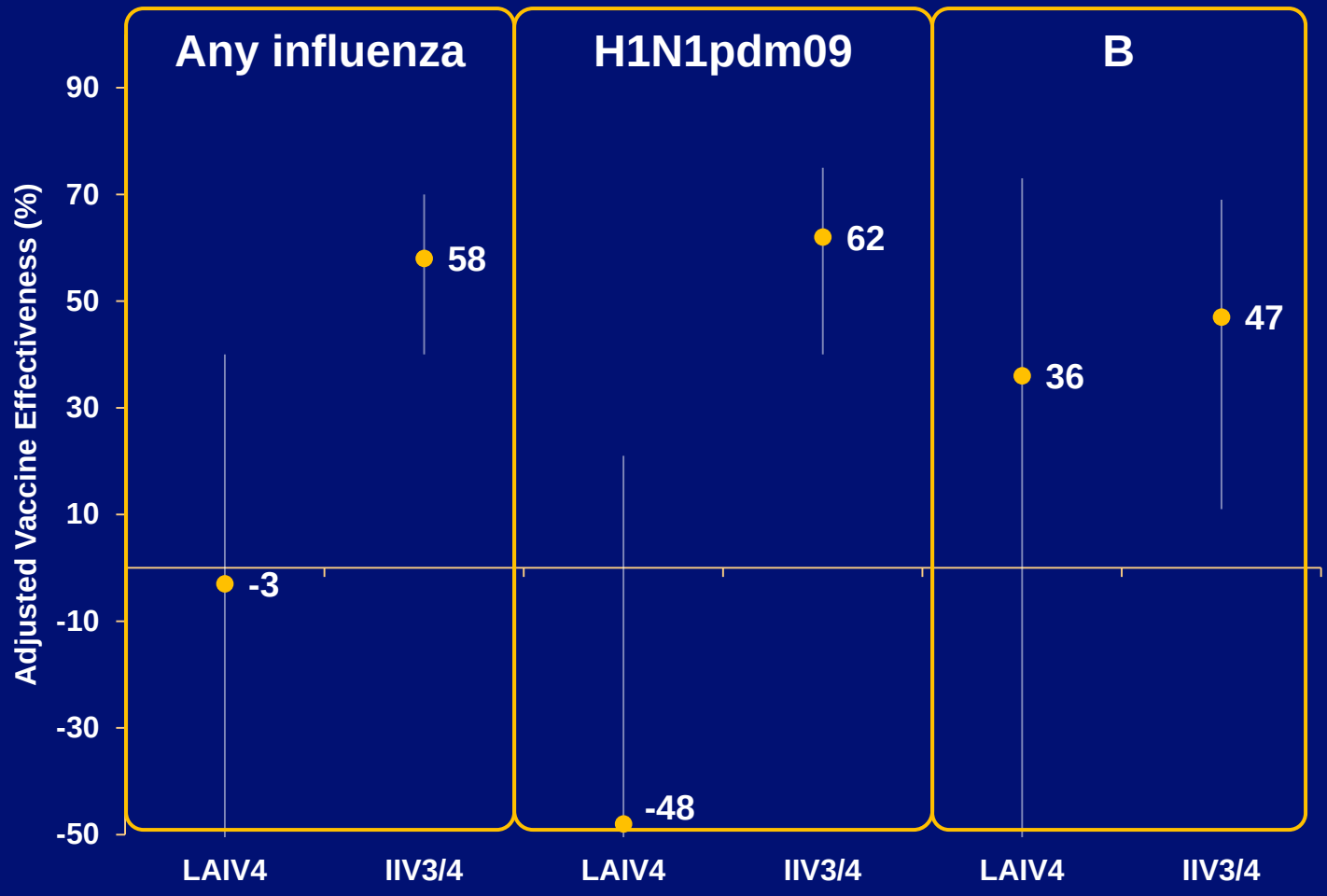
- 127 illness onset prior to confirmed influenza circulation
- 18 vaccinated 0–14 days prior to onset
- 4 inconclusive/unrepeatable lab results
- 3 illness onset after last confirmed influenza case
- 2 mixed vaccine types

LAIV and IIV vaccine effectiveness ages 2–17 years, by influenza type/subtype, 2015-16



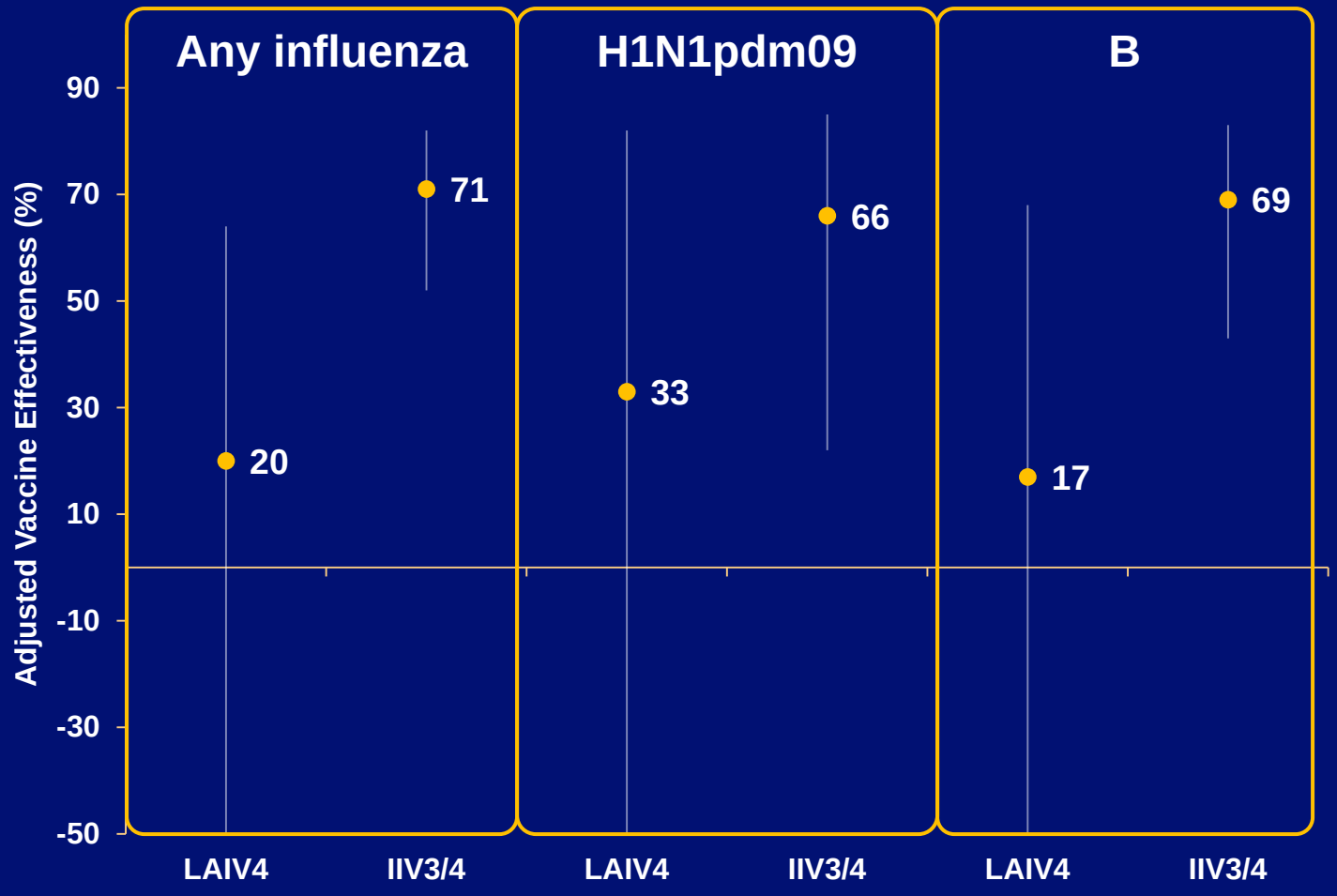
Total, Flu +	324	367	156	174	59	63	100	121
Vaccinated, Flu +	38	81	23	41	8	12	7	28

LAIV and IIV vaccine effectiveness ages 2–8 years, by influenza type/subtype, 2015-16



Total, Flu +	183	213	113	126	66	83
Vaccinated, Flu +	28	58	20	33	8	25

LAIV and IIV vaccine effectiveness ages 9–17 years, by influenza type/subtype, 2015-16



Total, Flu +	141	154	43	48	92	100
Vaccinated, Flu +	10	23	3	8	7	15

Adjusted odds of influenza for LAIV vs IIV (relative effectiveness) ages 2–17 years

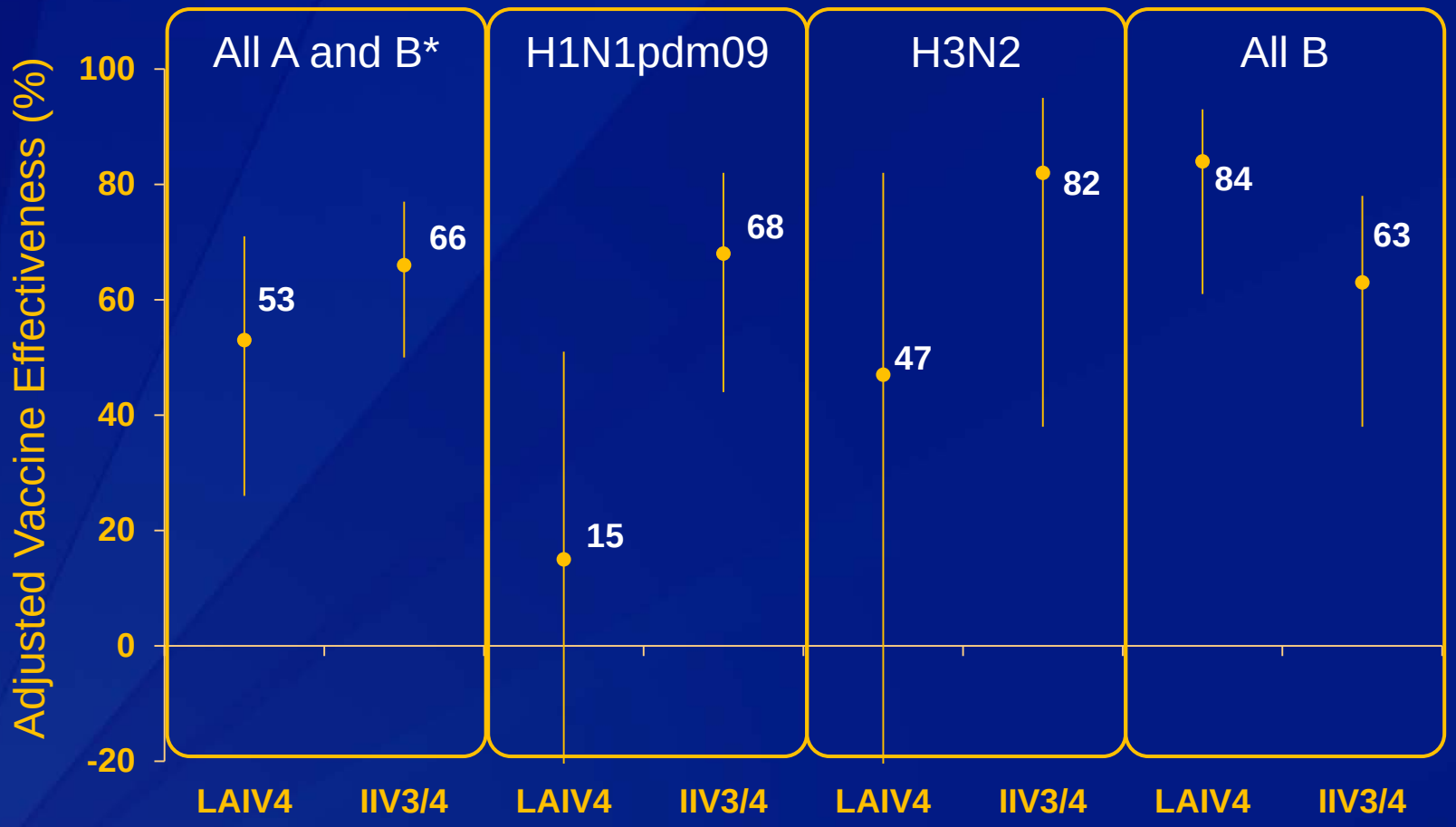
		Influenza positive	Influenza negative	Adjusted* Influenza Odds Ratio LAIV vs IIV	
Any influenza A or B virus	**Vaccine type**	**N vaccinated**	**N vaccinated**	**OR**	**95% CI**
2–17 y	IIV	81	672	**REF**	
	LAIV	38	110	**2.63**	**(1.59, 4.37)**
H1N1pdm09					
2–17 y	IIV	41	672	**REF**	
	LAIV	23	110	**3.67**	**(1.86, 7.31)**
Influenza B					
2–17 y	IIV	40	672	**REF**	
	LAIV	15	110	**1.62**	**(0.78, 3.33)**

*Odds Ratios > 1.0 favor IIV. Adjusted for site, age (2–4 y, 5–8 y, 9–17 y), race/Hispanic ethnicity, sex, interval from onset to enrollment, general self/parent-rated health status, and calendar time (biweekly intervals)

DoD Laboratory-based Influenza Surveillance

- Military dependents aged 2-17 years presenting to participating facilities with influenza-like illness
- Laboratory testing by RT-PCR or culture
- Test-negative design: influenza RT-PCR negative controls
- Vaccination status from electronic medical records
- Estimates adjusted for age group (2-8; 9-17 years) and 3 time periods

DoD Laboratory-based Influenza Surveillance: LAIV and IIV effectiveness by influenza type/subtype, children 2-17 yrs, 2015-16



	All A and B*		H1N1pdm09		H3N2		All B	
	LAIV4	IIV3/4	LAIV4	IIV3/4	LAIV4	IIV3/4	LAIV4	IIV3/4
Total, Flu +	353	353	156	156	32	32	165	165
Vaccinated, Flu +	33	42	23	18	4	3	6	21

* Data provided by Lt Col Susan Federinko, US Air Force

Limitations

- **Final end-of-season analyses pending**
  - Prior season vaccination status pending for one site
  - Chronic conditions not included in adjusted estimates
- **Limited precision for some VE estimates due to small numbers**

Summary

- **Late influenza season (peak enrollment in March) with mixed A/H1N1pdm09 and B circulation**
- **Overall 47% VE against influenza A and B**
  - 41% VE against H1N1pdm09, 55% VE against influenza B
- **VE for LAIV significantly lower than IIV among 2–17 y**
  - No significant LAIV effectiveness against A/H1N1pdm09 or B
  - Relative effectiveness favoring IIV against A/H1N1pdm09

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- **US Flu VE Network** [next page]

US Flu VE Network

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