

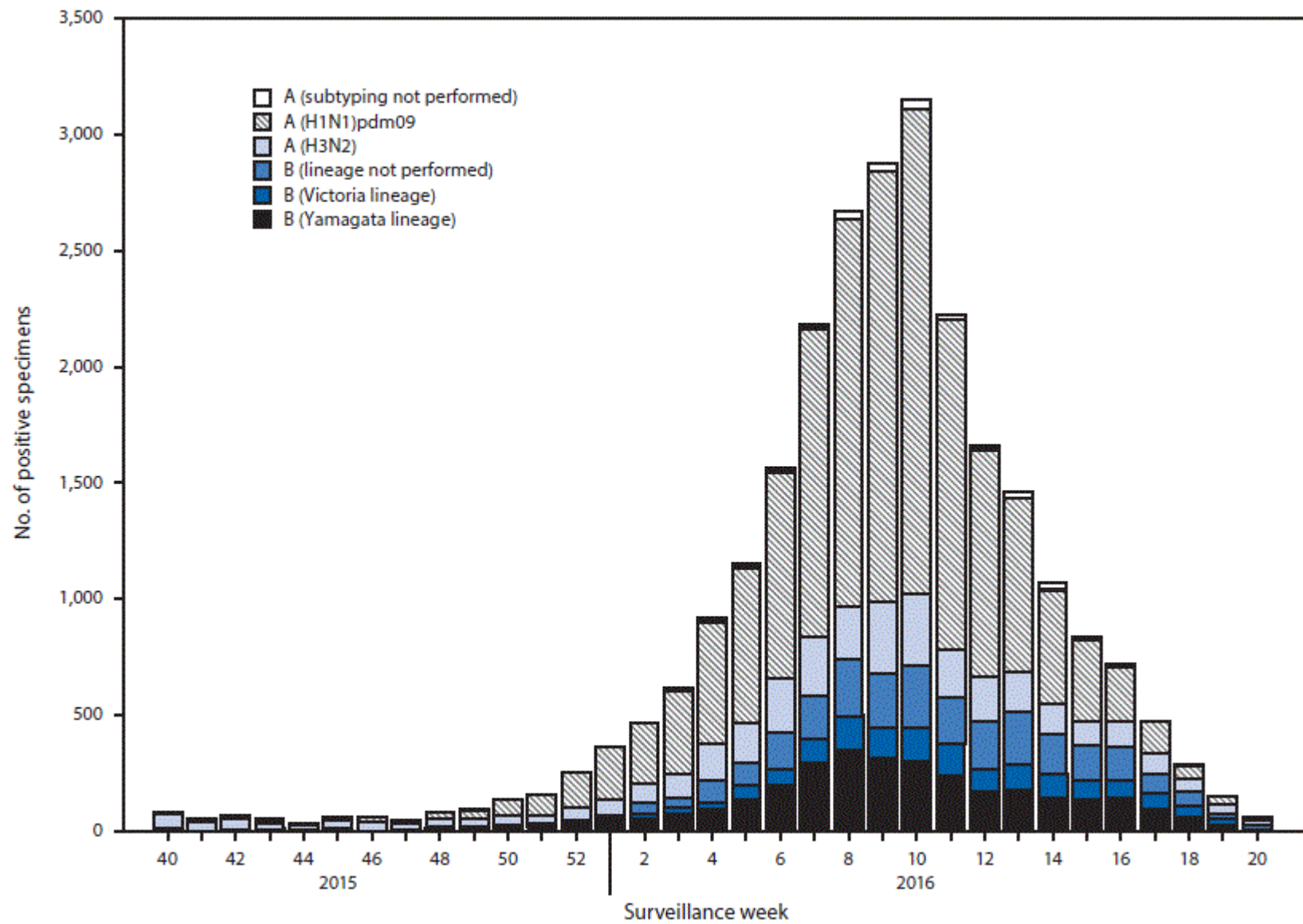
# Flu Update and the LAIV Situation

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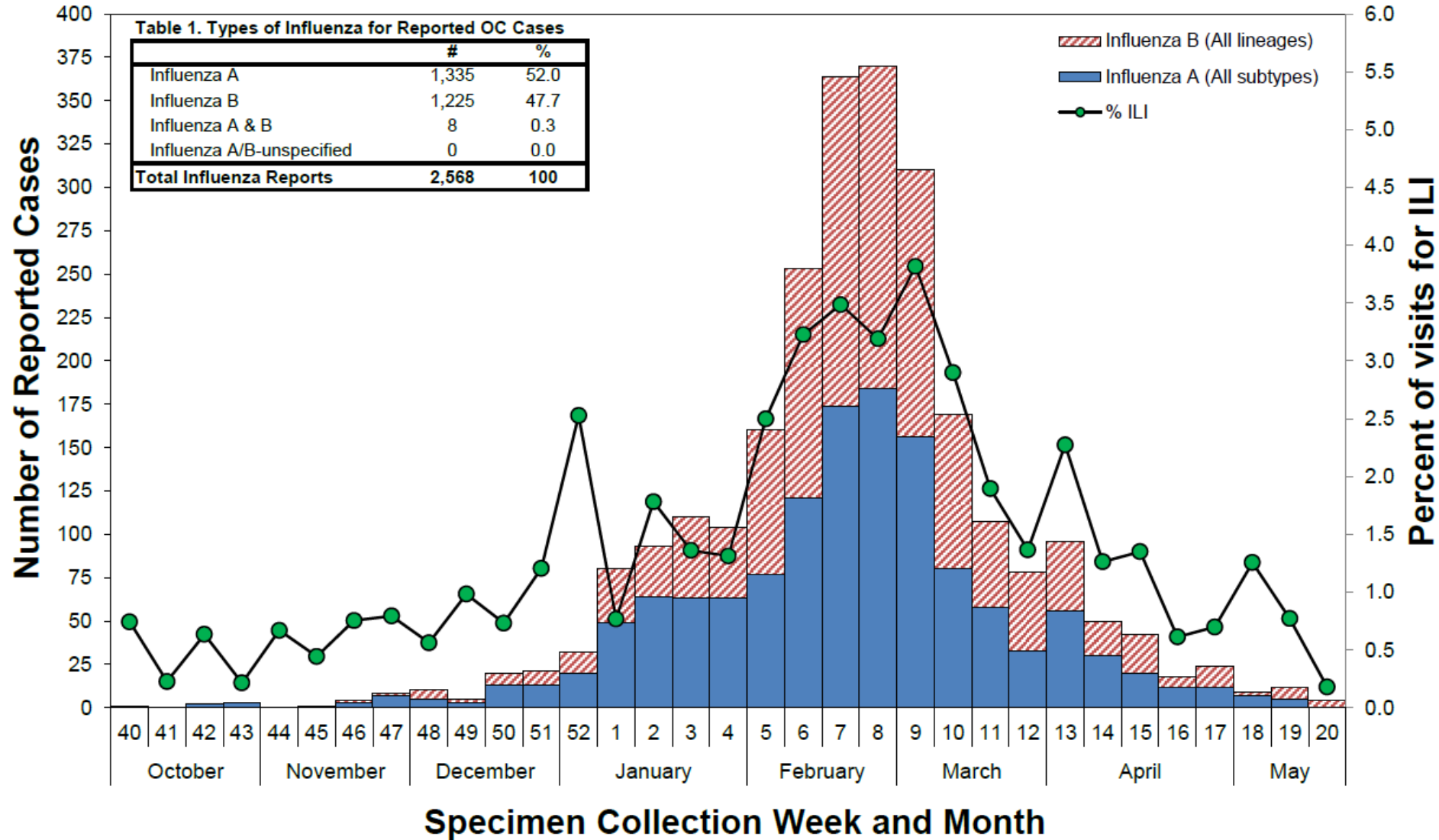


# 2015-16 United States Influenza Season

- Overall influenza activity was moderate
- Influenza activity was lower and peaked later compared with previous three seasons
- Compared to three previous influenza seasons:
  - Lower percentage of outpatient visits for influenza-like illness (ILI)
  - Lower hospitalization rates
  - Lower percentage of deaths attributed to pneumonia and influenza (P&I) compared with the preceding three seasons



**Figure 1. Number of Influenza Case Reports by Type and Percent of Visits for Influenza-Like-Illness by Disease Week**



	#	N	%
<b>Specimens Positive at OCPHL</b>	<b>964</b>	<b>1,143</b>	<b>84.3%</b>
ILI Sentinel Providers	40	98	40.8%
<b>Influenza A</b>	<b>510</b>	<b>964</b>	<b>52.9%</b>
<u>Subtype</u>			
A/(H1N1)pdm2009	346	510	67.8%
A/H3	163	510	32.0%
Subtype Unknown	1	510	0.2%
<b>Influenza B</b>	<b>443</b>	<b>964</b>	<b>46.0%</b>
<u>Lineage</u>			
Yamagata	348	443	78.6%
Victoria	83	443	18.7%
Lineage Unknown	12	443	2.7%
<b>Other Viruses Identified</b>	<b>11</b>	<b>964</b>	<b>1.1%</b>
<i>Other viruses identified at the OCPHL include adenovirus (3), parainfluenza virus (PIV) Type 1 (5), PIV Type 3 (1), and respiratory syncytial virus (5).</i>			

# Influenza Vaccine Options

- Inactivated trivalent
- High dose trivalent
- Inactivated quadrivalent
- LAIV quadrivalent
- Intradermal trivalent
- Cell culture based trivalent
- Recombinant trivalent

# Live Attenuated Influenza Vaccine

- Administered intranasally
- Flumist is only LAIV licensed in the United States
  - In use since 2003
- Has been recommended for ages 2-49
- Not recommended for immune compromised patients

# 2014 ACIP Preferential LAIV Recommendation

June 25, 2014:

- When LAIV is available, it should be used for children aged 2 through 8 years
- First preferential recommendation made for an influenza vaccine
- Used grade analysis, Category A recommendation made



Superior relative efficacy of live attenuated influenza vaccine compared with inactivated influenza vaccine in young children with recurrent respiratory tract infections

Ashkenazi, S

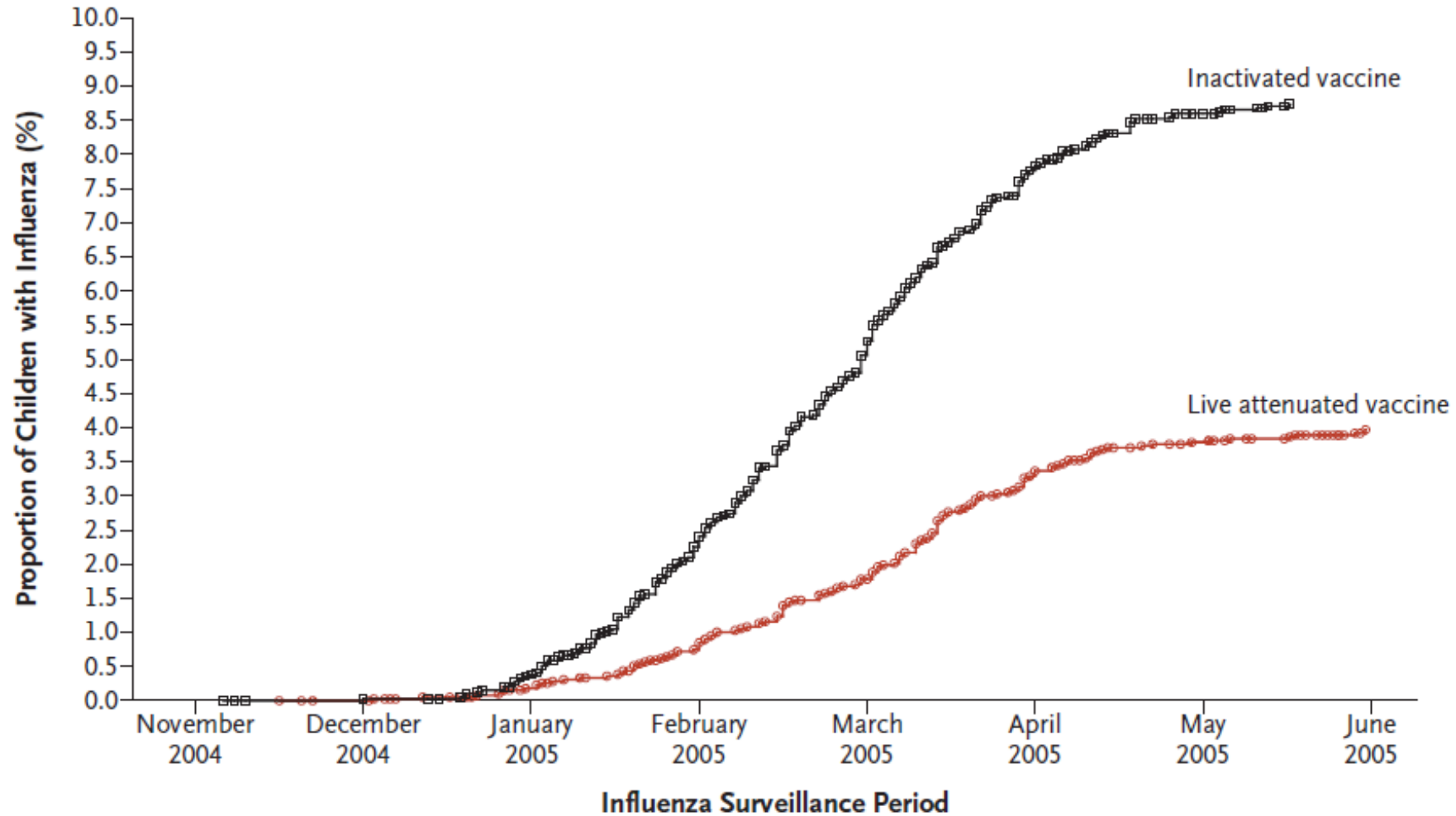
- Children 6 to 71 months of age were randomized to receive 2 doses of CAIV-T (n = 1101) or TIV (n = 1086) before the start of the 2002–2003 influenza season
- 52.7% (95% CI = 21.6%–72.2%) fewer cases of influenza were observed in CAIV-T than in TIV recipients.
- Greater relative efficacy for CAIV-T observed for:
  - Influenza A/H1N1
  - Influenza B
- Relative to TIV, CAIV-T reduced the number of RTI-related healthcare provider visits by 8.9% (90% CI = 1.5%–15.8%) and missed days of school, kindergarten, or day care by 16.2% (90% CI = 10.4%–21.6%)

# Live attenuated versus inactivated influenza vaccine in infants and young children

Belshe, et al.

- 7852 children 6 to 59 months of age
- Randomly assigned in a 1:1 ratio to receive either trivalent LAIV or trivalent IIV
- Influenza-like illness was monitored with cultures throughout the 2004–2005 influenza season.

# Belshe, et al.



**Figure 1.** Kaplan–Meier Curves for the Time to the First Culture-Confirmed Report of Influenza in the Two Vaccine Groups.

# US Flu VE Network: 5 Sites and Principal Investigators

Group Health  
Cooperative  
Lisa Jackson  
Mike Jackson

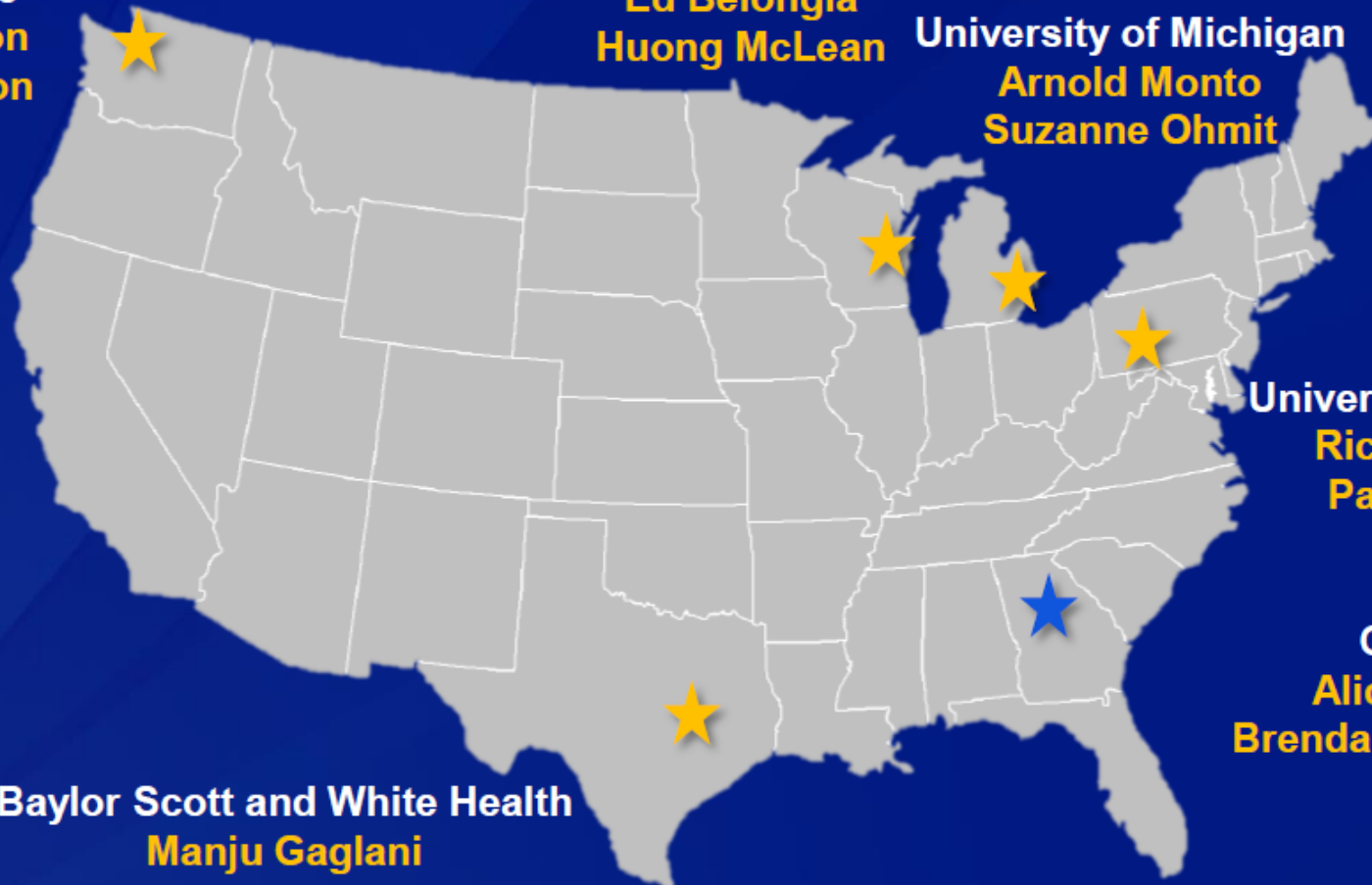
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## US Flu VE Network: Methods

**Enrollees:** Outpatients aged  $\geq 6$  months with acute respiratory illness with cough  $\leq 7$  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/or self-report (with reported date)
- ❑ **Analysis:**  $VE = (1 - \text{adjusted OR}) \times 100\%$ 
  - Adjustment for study site, age, self-rated general health status, race/Hispanic ethnicity, interval (days) from onset to enrollment, and calendar time

# 2013-2014 LAIV Effectiveness

**TABLE.** Mid-season influenza vaccine effectiveness (VE) among different populations for the 2013–2014 influenza season

Population	Viral subtype	Vaccine type	No. of cases (% vaccinated)	No. of controls (% vaccinated) <sup>a</sup>	Crude VE (95% CI)	Adjusted VE (95% CI) <sup>b</sup>
Active component service members (AFHSC)	Overall	Any type	518 (90)	2060 (91)	11 (-27–37)	7 (-32–35)
		IIV	183 (32)	1086 (48)	31 (0–53)	28 (-5–51)
		LAIV	324 (56)	910 (40)	-13 (-63–22)	-17 (-70–19)
Civilians and dependents (NHRC)	Overall	Any type	106 (19)	278 (33)	52 (17–72)	53 <sup>c</sup> (17–74)
	Influenza A (H1)	Any type	84 (17)	278 (33)	59 (23–78)	63 <sup>c</sup> (33–81)
Dependents (USAFSAM)	Overall	Any type	339 (26)	469 (39)	44 (24–59)	66 <sup>c</sup> (51–76)
		IIV	302 (17)	425 (33)	57 (38–70)	74 <sup>c</sup> (60–83)
		LAIV	234 (15)	248 (16)	6 (-54–42)	40 (-5–66)

## Adjusted VE against any influenza for fully vaccinated children and adolescents, by vaccine type, 2014-15

	Influenza-positive	% vaccinated	Influenza-negative	% vaccinated	Adjusted VE*	(95% CI)
<b>Live attenuated (LAIV4)</b>						
2–17 years	623	19%	1677	22%	9%	(-18 to 29)
2–8 yrs	316	22%	985	25%	9%	(-28 to 35)
9–17 yrs	307	16%	692	18%	17%	(-27 to 46)
<b>Inactivated (IIV3/IIV4)</b>						
2–17 years	693	27%	2068	37%	31%	(16 to 44)
2–8 yrs	348	29%	1235	40%	26%	(2 to 44)
9–17 yrs	345	25%	833	32%	33%	(9 to 51)

\*Adjustment for age (groups or years), site, race/ethnicity, sex, general health status, calendar time, interval from onset to enrollment

## Live Attenuated Vaccine Effectiveness in 2014-15

- Live attenuated influenza vaccine (LAIV) had no significant vaccine effectiveness based on CDC data from 2014-15
- No evidence of improved effectiveness in preventing disease caused by influenza A H3N2 drifted strain
- Preferential recommendation to provide LAIV to children 2-8 years of age was rescinded by ACIP



# LAIV and Temperature Instability

- Hypothesized that reduced effectiveness of LAIV against the influenza A (H1N1)pdm09 virus was due to the reduced vaccine stability of the LAIV vaccine virus, A/California/2009/(H1N1) caused by a single amino acid mutation
- New H1N1 vaccine virus- (A/Bolivia/559/2013) was used for LAIV in 2015-16 season

# Caveats

- Small samples size of studies
- Other studies have shown LAIV effectiveness in 2015-16 season, though still trend toward less effective than IIV
- LAIV effectiveness against Influenza A H3N2 is less clear

# Possible Reasons for Poor Performance of Quadrivalent LAIV in 2015-16 Season

- Suboptimal performance of the A/Bolivia/5592013 (H1N1)pdm09 HA vaccine component
- Potential interference among viruses in the quadrivalent vaccine
- Reduced immunogenicity of LAIV as a result of more high vaccinated population in recent years, compared with populations in previous studies, in which it is likely that a higher proportion of children were vaccine-naive

# ACIP Recommendation

June 22, 2016

Live attenuated influenza vaccine is not recommended for use in the 2016-17 influenza season