



Preliminary Estimates of 2018–19 Seasonal Influenza Vaccine Effectiveness against Medically Attended Influenza from three U.S. Networks

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Advisory Committee on Immunization Practices

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Preliminary results

Three networks to evaluate vaccine effectiveness against laboratory-confirmed influenza in ambulatory and inpatient settings

Ambulatory patients—all ages: US Flu VE* Network sites and principal investigators

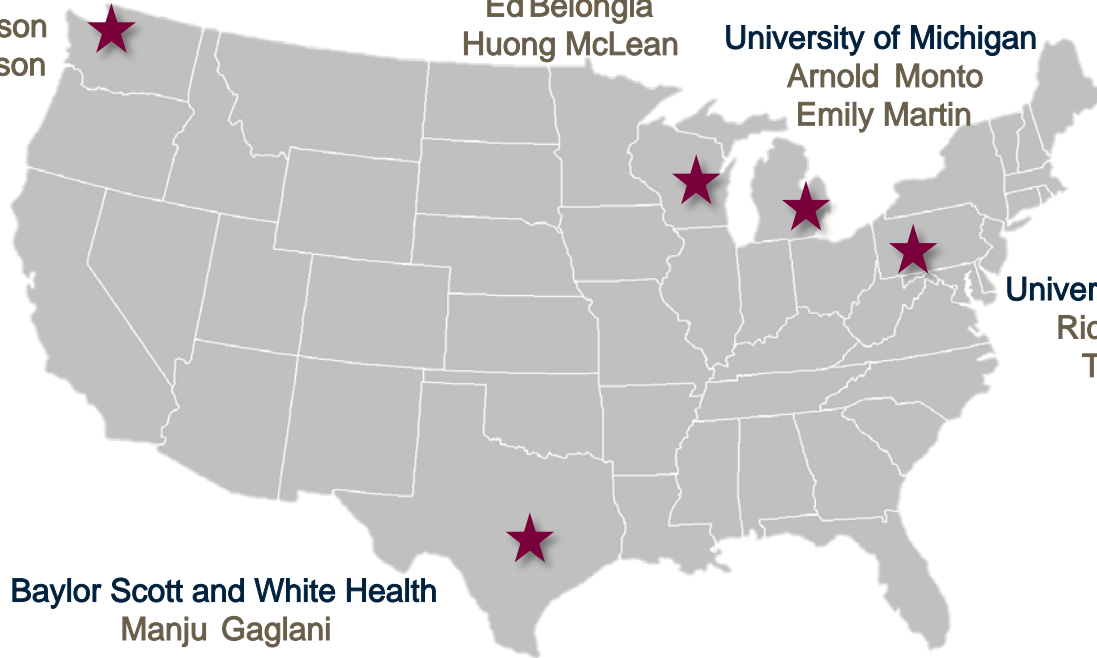
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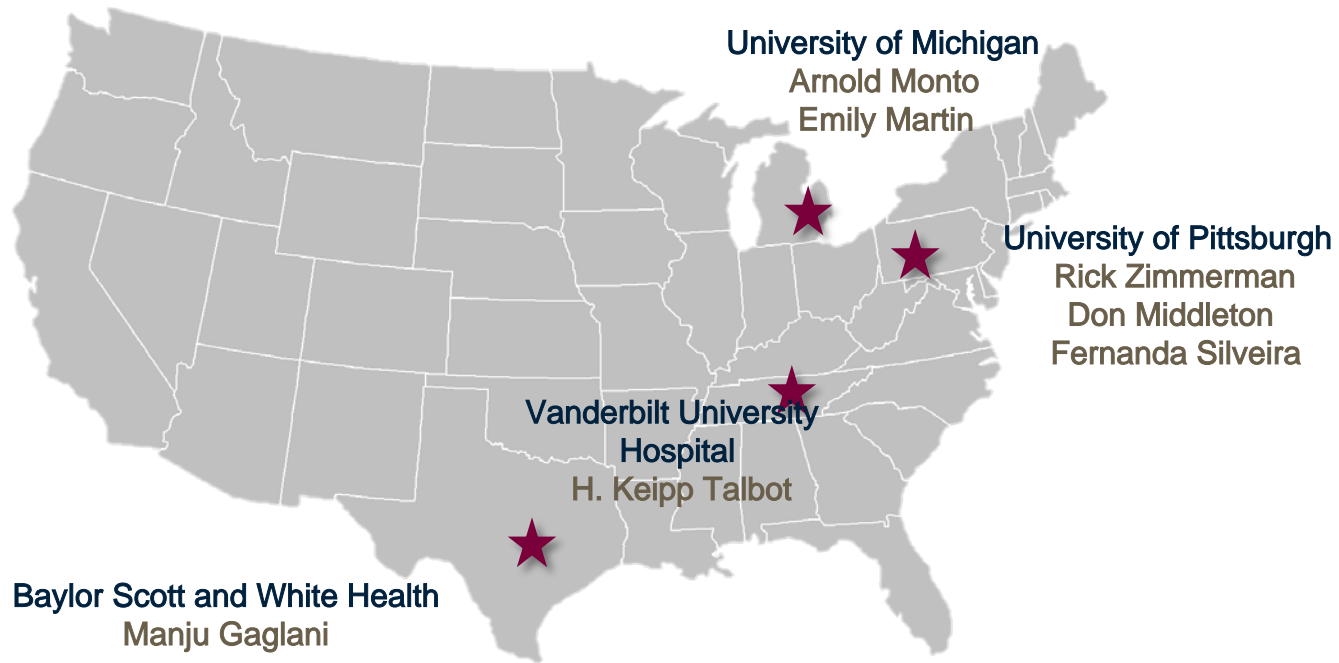
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*US Flu VE US Influenza Vaccine Effectiveness Network

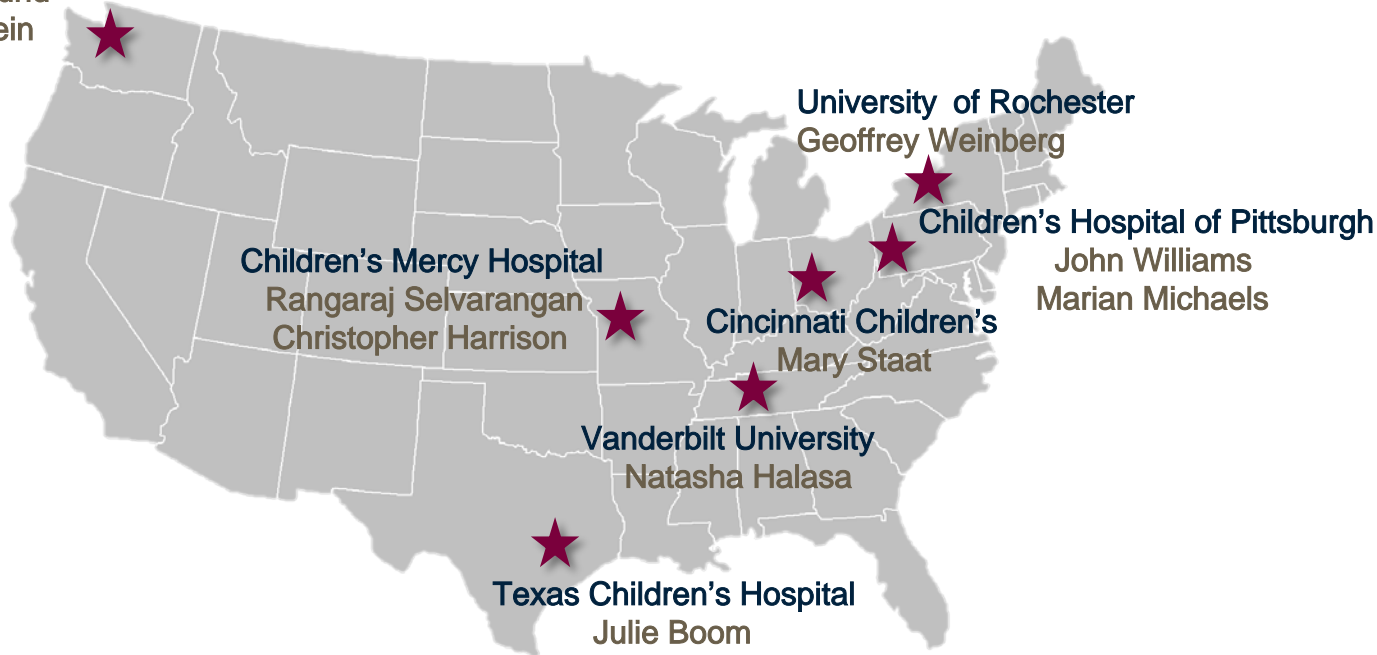
Inpatients—adults aged 18 years and older: HAIVEN* sites and principal investigators



*HAIVEN-Hospitalized Adult Influenza Vaccine Effectiveness Network

Inpatients—children aged <18 years: NVSN* sites and principal investigators

Seattle Children's
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*NVSN-New Vaccine Surveillance Network

VE Networks: Methods

	US Flu VE	HAIVEN	NVSN
Setting	Ambulatory	Inpatient	Inpatient
Ages	≥ 6 months	≥ 18 years	6m-17 years
Symptoms	ARI	ARI	ARI
Symptom duration	≤ 7	≤ 10	≤ 10

Methods

Design: Test-negative design

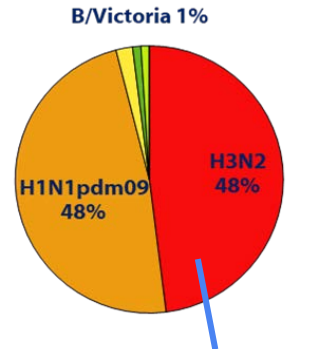
- Comparing odds of laboratory-confirmed influenza among vaccinated vs. unvaccinated patients
- Vaccination status: receipt of one dose (≥ 1 dose for children 6m-8 years) of any 2018–19 seasonal flu vaccine at least 14 days prior to illness onset
- Sources: Medical records, immunization registries, and/or self-report (self-report only for inpatient networks)

Analysis: $VE = (1 - \text{adjusted OR}) \times 100\%$

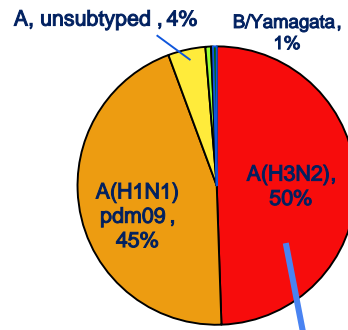
- Adjustment for potential confounding variables (i.e. study site, age, calendar time)

Equal distribution of H1N1 and H3N2 in all networks

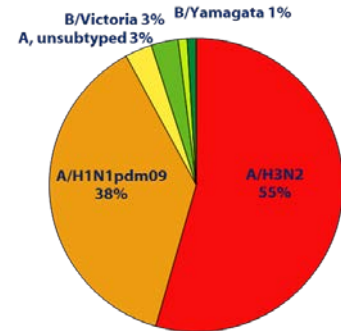
	US Flu VE	HAIVEN	NVSN
Enrollment period	Nov 23-May 3	Nov 2-May 3	Nov 7-May 13
Enrolled	10,041	2,873	1,481
Influenza pos (%)	2,795 (28%)	461 (16%)	190 (13%)



721/786 (92%) of H3 viruses were 3C.3a



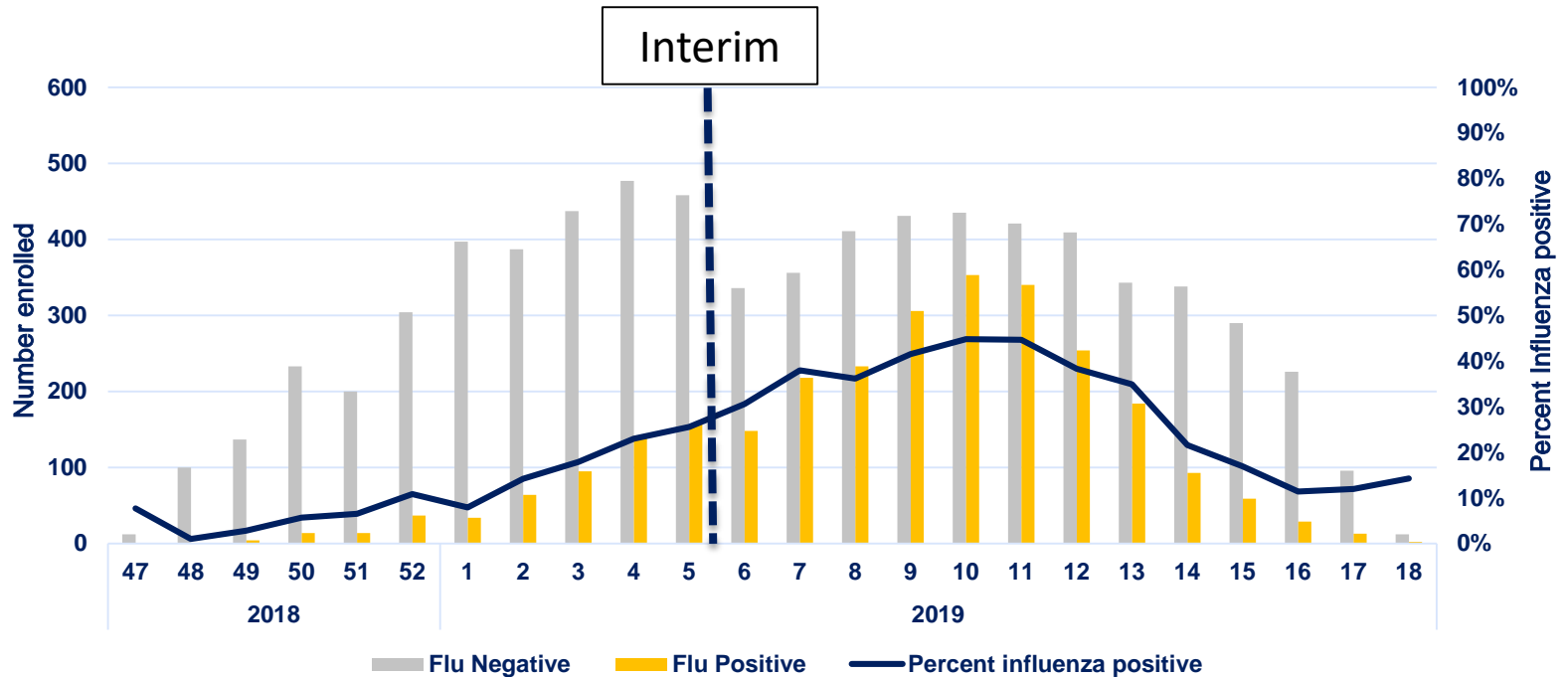
85/93 (91%) of H3 viruses were 3C.3a



Ambulatory settings – all ages

US Flu VE Network

US Flu VE Network: Number of enrolled participants by influenza RT-PCR result and percent positivity by week of onset

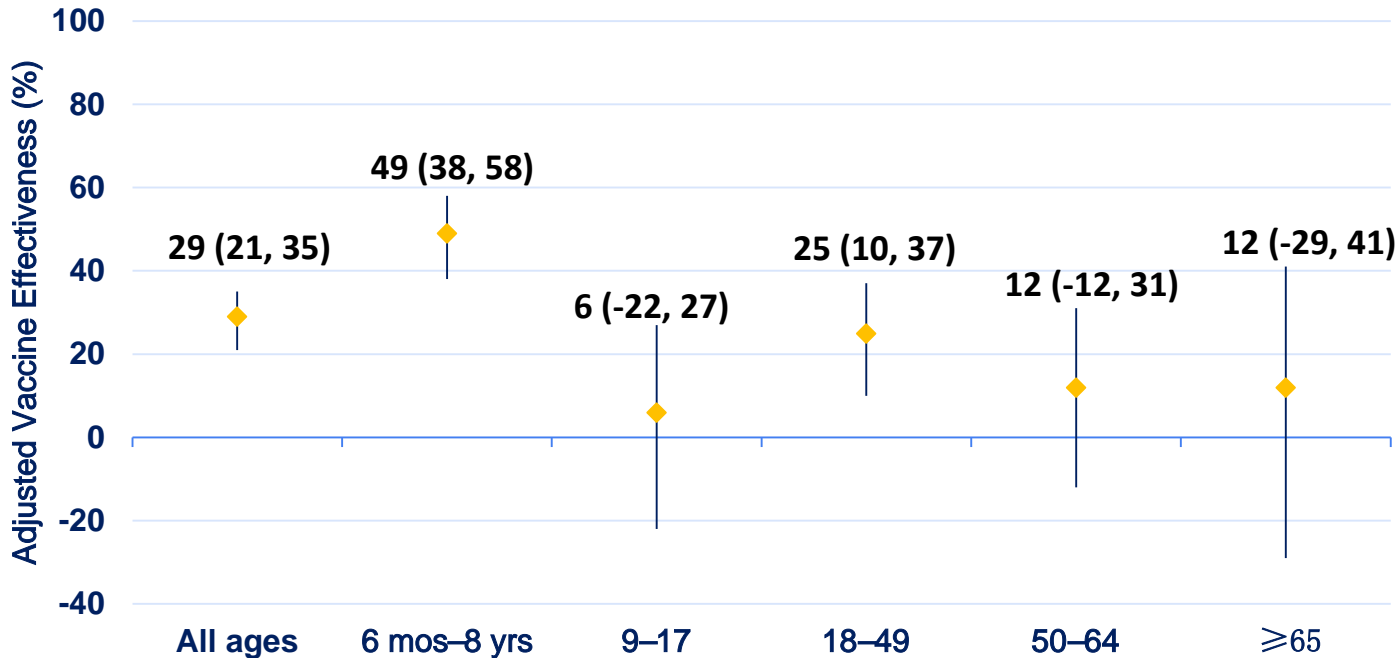


Adjusted vaccine effectiveness against medically attended influenza by age group, US Flu VE Network, 2018–19

	Influenza positive		Influenza negative		Vaccine Effectiveness			
	N vaccinated /Total	(%)	N vaccinated /Total	(%)	VE %	95% CI	VE %	95% CI
Any influenza A or B virus								
Overall	1333/2795	48	4059/7246	56	28	(21 to 34)	29	(21 to 35)
Age group (yrs)								
6 mos–8	303/759	40	977/1675	58	53	(43 to 60)	49	(38 to 58)
9–17	221/493	45	319/772	41	-15	(-45 to 8)	6	(-22 to 27)
18–49	323/831	39	1074/2435	44	19	(5 to 31)	25	(10 to 37)
50–64	271/448	60	827/1324	62	8	(-15 to 26)	12	(-12 to 31)
≥65	215/264	81	862/1040	83	9	(-29 to 36)	12	(-29 to 41)

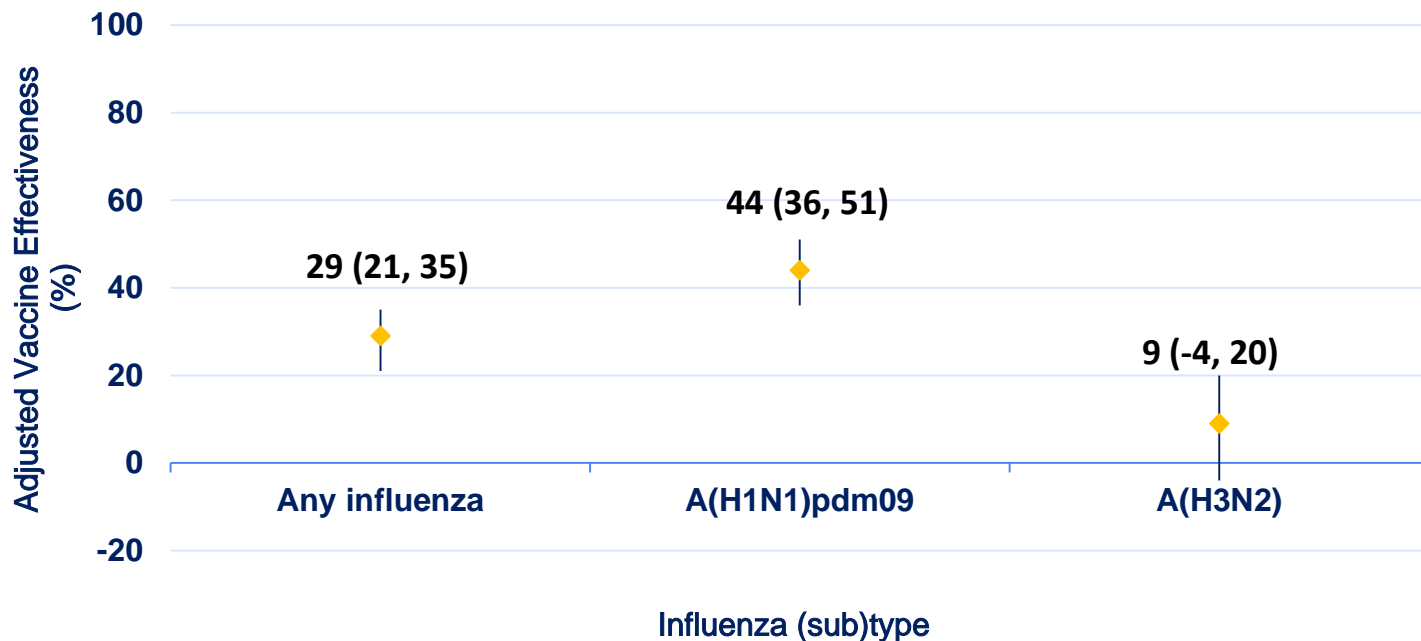
* Multivariable logistic regression models adjusted for site, age, sex, race/ethnicity, self-rated general health status, interval from onset to enrollment, and calendar time.

Adjusted vaccine effectiveness* against medically attended influenza by age group, US Flu VE Network, 2018–19



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

Adjusted vaccine effectiveness* against medically attended influenza by virus subtype, US Flu VE Network, 2018–19



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

Adjusted vaccine effectiveness against influenza A/H3N2 by clade, US Flu VE Network, 2018–19 (seq. data as of 6/21/19)

	Influenza positive		Influenza negative		Vaccine Effectiveness			
	N vaccinated /Total	(%)	N vaccinated /Total	(%)	Unadjusted		Adjusted*	
					VE %	95% CI	VE %	95% CI
<u>All Influenza A/H3N2</u>								
All H3N2	710/1352	53	4065/7249	56	13	(3 to 23)	9	(-4 to 20)
Sequenced H3N2	404/773	52	4065/7249	56	14	(1 to 26)	15	(-1 to 28)
A(H3N2) clade 3C.3a	372/709	52	4065/7249	56	14	(-1 to 26)	11	(-6 to 26)
A(H3N2) clade 3C.2a1	30/61	49	4065/7249	56	24	(-25 to 54)	45	(5 to 68)

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

**Hospitalized Adult Influenza Vaccine
Effectiveness Network (HAIVEN)
preliminary results**

Adjusted vaccine effectiveness against influenza, by age group and virus subtype, HAIVEN, 2018–19 (n=2810)

Any influenza A or B virus	Vaccine Effectiveness							
	Influenza positive		Influenza negative		Unadjusted		Adjusted*	
	N vaccinated /Total	(%)	N vaccinated /Total	(%)	VE %	95% CI	VE %	95% CI
Overall	307/474	65	1615/2336	69	18	(-1 to 33)	25	(1 to 41)
By age group								
18-49 yr	52/95	55	281/500	56	6	(-46 to 39)	1	(-58 to 38)
50-64 yr	76/152	50	518/809	64	44	(20 to 60)	47	(22 to 63)
≥65 yr	179/227	79	816/1027	79	4	(-37 to 32)	15	(-24 to 41)
By virus subtype								
H3N2	183/234	78	1615/2336	69	-60	(-121 to -16)	-43	(-102 to -2)
H1N1pdm09	107/213	50	1615/2336	69	55	(40 to 66)	60	(46 to 71)

*Adjusted for study site, age, race/Hispanic ethnicity, days from illness onset to respiratory specimen collection, calendar time of illness onset, home oxygen use, immunosuppressive conditions/medication(s), and number of self-reported hospitalizations in the prior year

**Inpatient Pediatric VE – 6 months to 17
years**

NVSN preliminary results

Adjusted vaccine effectiveness against pediatric influenza hospitalization, by patient age/virus subtype, NVSN, 2018–19

	Influenza positive		Influenza negative		Vaccine Effectiveness			
	N vaccinated /Total	(%)	N vaccinated /Total	(%)	Unadjusted		Adjusted*	
					VE %	95% CI	VE %	95% CI
Any influenza A or B virus								
Overall	80/190	42	646/1291	50	27	(1 to 47)	31	(5 to 51)
By age group								
6 mo to 8 yr	64/142	45	553/1119	49	16	(-19 to 41)	26	(-6 to 49)
9 to 17 yr	16/48	33	93/172	54	57	(16 to 78)	53	(5 to 77)
By virus subtype								
H3N2	50/105	48	646/1291	50	9	(-35 to 39)	13	(-31 to 43)
H1N1pdm09	26/73	36	646/1291	50	44	(9 to 66)	48	(14 to 68)

*Multivariable logistic regression models adjusted for age, study site, and calendar time (month of enrollment)

Discussion

Interpreting VE estimates for influenza A(H3N2)

- Three US networks identified no vaccine protection against predominant H3N2 virus this season, consistent with laboratory data on 3C.3a clade
- Negative VE for H3N2 in adult inpatient network (HAIVEN) based on small number of cases and could be related to chance or bias
 - Findings are “unstable” in that they are subject to changes with small alterations in case or vaccine classification
 - No similar finding using an alternative control group (VE was no longer negative when using RSV-positive comparison group), suggesting bias
 - No similar findings of increased influenza vaccination rates in cases from other US platforms (US Flu VE Network or US FluSurvNet) compared to HAIVEN
- Cannot exclude possibility of alternative biological explanations

Next steps for finalizing VE estimates

- Updated data, vaccine verification and analysis
 - Review of preliminary data: no issues identified related to data miscoding or analysis
 - Data extraction (underlying conditions) ongoing
 - Verification of vaccination status, prior vaccination history, and vaccine type
- Evaluate serologic specimens and virus sequencing (US Flu VE and HAIVEN)
- Collaborating with partners to compare findings in other networks and consider possible explanations
- Update to ACIP Influenza Working Group early fall 2019

Summary

- Overall VE was ~30% against influenza illness and hospitalizations.
 - Vaccine likely prevented between ~40,000 to 90,000 hospitalizations based on previous seasons' estimates
- Vaccine reduced A(H1N1)pdm09- associated outpatient influenza illness by 44% and hospitalizations by 48%-60%
- No significant protection against H3N2 illnesses likely due to emergence of antigenically different A(H3N2) clade 3C.3a
 - WHO has updated the A(H3N2) component of 2019-2020 Northern Hemisphere influenza vaccines
- These VE estimates are preliminary and will be updated when final data are available

Acknowledgments

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