# Preliminary Estimates of 2017–18 Seasonal Influenza Vaccine Effectiveness against Laboratory-Confirmed Influenza from the US Flu VE and HAIVEN Networks

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Advisory Committee on Immunization Practices
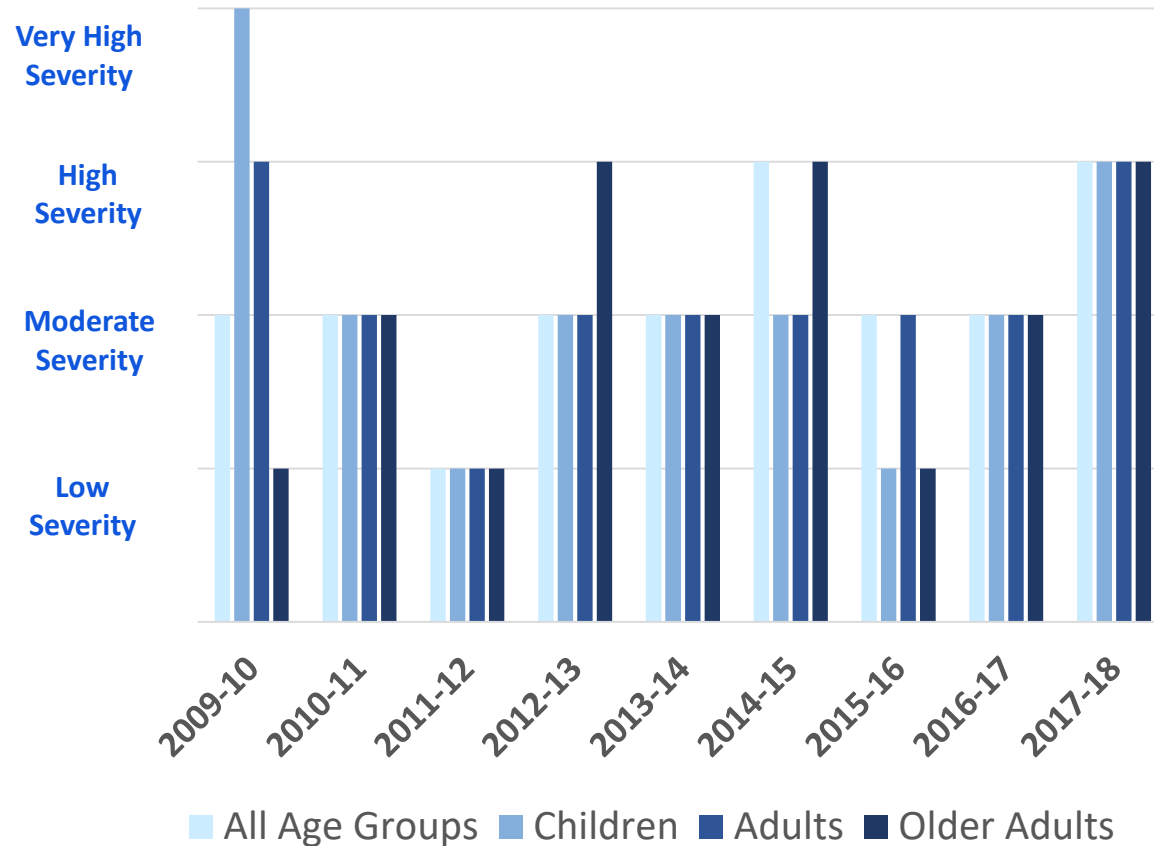June 20, 2018

# The New York Times

## *This Flu Season Is the Worst in Nearly a Decade*



An emergency room nurse treating a flu patient in Vista, Calif., this month.  Mike Blake/Reuters

Jan. 26, 2018

# 2017-18 was a High Severity season for all age groups



2017-18 was High Severity based on outpatient visits, hospitalizations, and deaths

Legend: All Age Groups, Children, Adults, Older Adults

Biggerstaff, et al Am J Epi 2018

# US Influenza Vaccine Effectiveness (Flu VE) Network preliminary results

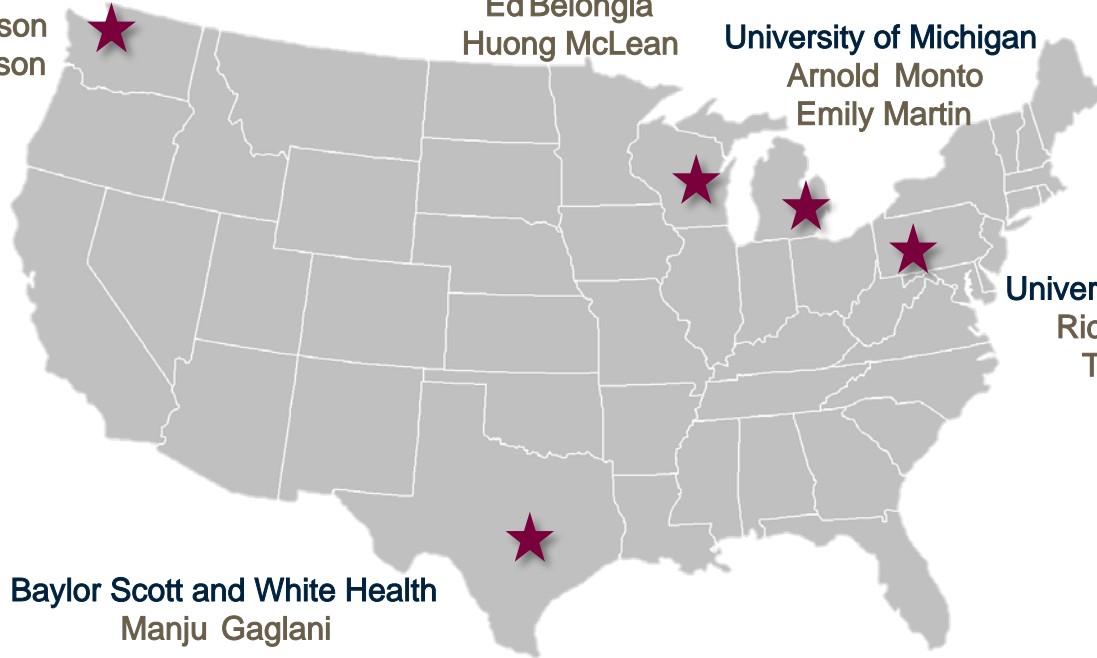# US Flu VE Network sites and principal investigators



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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, 2017–April 20, 2018

**Design:** Test-negative design

- Comparing vaccination odds among influenza RT-PCR positive cases and RT-PCR negative controls

- Vaccination status: receipt of <u>at least one dose</u> of any 2017–18 seasonal flu vaccine according to medical records, immunization registries, and/or self-report
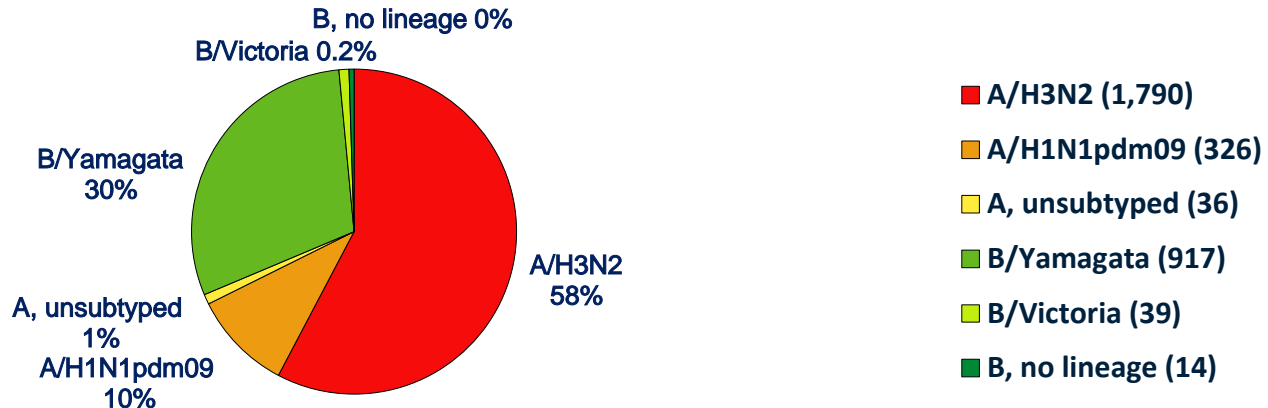
**Analysis:**  VE = (1 – adjusted OR) x 100%

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

# Preliminary End-of-Season Results

- **8635 enrolled from Nov 2, 2017–April 20, 2018 at 5 sites**

- **3097 (36%) influenza RT-PCR positive**

- **5538 (64%) influenza RT-PCR negative**

## Cases enrolled by (sub)type, N=3,097



- A/H3N2 (1,790)
- A/H1N1pdm09 (326)
- A, unsubtyped (36)
- B/Yamagata (917)
- B/Victoria (39)
- B, no lineage (14)

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

# Preliminary adjusted vaccine effectiveness against medically attended influenza by age group, 2017–18

| | 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 | 1296/3097 | (42) | 2969/5538 | (54) | 38% | (32 to 43) | 40% | (34 to 46) |
| Age group (yrs) | | | | | | | | |
| 6 mos–8 | 201/616 | (33) | 760/1380 | (55) | 60% | (52 to 68) | 53% | (42 to 62)** |
| 9–17 | 166/529 | (31) | 221/584 | (38) | 25% | (4 to 41) | 29% | (8 to 46) |
| 18–49 | 315/966 | (33) | 813/1893 | (43) | 36% | (24 to 45) | 35% | (23 to 46) |
| 50–64 | 301/571 | (53) | 583/938 | (62) | 32% | (16 to 45) | 33% | (17 to 47) |
| ≥65 | 313/415 | (75) | 592/743 | (80) | 22% | (-4 to 41) | 20% | (-9 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. ** P-value <0.001 for age group-VE interaction term compared to all other ages combined.

# Preliminary adjusted vaccine effectiveness against medically attended influenza A(H3N2) by age group, 2017–18

| | Influenza positive | | Influenza negative | | Vaccine Effectiveness | | | |
| | | | | | Unadjusted | | Adjusted* | |
| | N vaccinated /Total | (%) | N vaccinated /Total | (%) | VE % | 95% CI | VE % | 95% CI |
|---|---|---|---|---|---|---|---|---|
| **Influenza A/H3N2** | | | | | | | | |
| **Overall** | 813/1790 | (45) | 2969/5538 | (54) | 28% | (20 to 35) | **24%** | **(15 to 33)** |
| **Age group (yrs)** | | | | | | | | |
| **6 mos–8** | 131/337 | (39) | 760/1380 | (55) | 48% | (34 to 59) | **37%** | **(17 to 52)**\*\* |
| **9–17** | 118/335 | (35) | 221/584 | (38) | 11% | (-18 to 32) | **10%** | **(-23 to 35)** |
| **18–49** | 218/581 | (38) | 813/1893 | (43) | 20% | (3 to 34) | **14%** | **(-6 to 30)** |
| **50–64** | 166/298 | (56) | 583/938 | (62) | 23% | (0 to 41) | **25%** | **(0 to 44)** |
| **≥65** | 180/239 | (75) | 592/743 | (80) | 22% | (-10 to 45) | **17%** | **(-22 to 44)** |

\* Multivariable logistic regression modelsadjusted for site, age, sex, race/ethnicity, self-rated general health status, interval from onset to enrollment, and calendar time. \*\* P-value = 0.05 for age group-VE interaction term compared to all other ages combined.

# Preliminary adjusted vaccine effectiveness against medically attended influenza A(H1N1)pdm09 by age group, 2017–18

| | Influenza positive | | Influenza negative | | Vaccine Effectiveness | | | |
| | | | | | Unadjusted | | Adjusted* | |
| | N vaccinated /Total | (%) | N vaccinated /Total | (%) | VE % | 95% CI | VE % | 95% CI |
|---|---|---|---|---|---|---|---|---|
| **Influenza A/H1N1pdm09** | | | | | | | | |
| **Overall** | 96/326 | (29) | 2969/5538 | (54) | 64% | (54 to 72) | **65%** | **(55 to 73)** |
| **Age group (yrs)** | | | | | | | | |
| **6 mos–17** | 26/154 | (17) | 981/1964 | (50) | 80% | (69 to 87) | **82%** | **(71 to 88)** |
| **18–49** | 27/99 | (27) | 813/1893 | (43) | 50% | (22 to 68) | **48%** | **(17 to 67)** |
| **50–64** | 18/40 | (45) | 583/938 | (62) | 50% | (6 to 74) | **45%** | **(-6 to 72)** |
| **≥65** | 25/33 | (76) | 592/743 | (80) | 20% | (-80 to 65) | **10%** | **(-116 to 63)** |

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

# Preliminary adjusted vaccine effectiveness against medically attended influenza B by age group, 2017–18

| | | | | | Vaccine Effectiveness | | | |
| | Influenza positive | | Influenza negative | | Unadjusted | | Adjusted* | |
| | N vaccinated /Total | (%) | N vaccinated /Total | (%) | VE % | 95% CI | VE % | 95% CI |
|---|---|---|---|---|---|---|---|---|
| **Influenza B/Yamagata** | | | | | | | | |
| **Overall** | 372/917 | (41) | 2969/5538 | (54) | 41% | (32 to 49) | **49%** | **(40 to 56)** |
| **Age group (yrs)** | | | | | | | | |
| **6 mos–8** | 44/130 | (34) | 760/1380 | (55) | 58% | (39 to 71) | **46%** | **(19 to 64)** |
| **9–17** | 45/161 | (28) | 221/584 | (38) | 36% | (7 to 57) | **39%** | **(9 to 59)** |
| **18–49** | 68/268 | (25) | 813/1893 | (43) | 55% | (40 to 66) | **57%** | **(42 to 68)** |
| **50–64** | 108/216 | (50) | 583/938 | (62) | 39% | (18 to 55) | **45%** | **(24 to 60)** |
| **≥65** | 107/142 | (75) | 592/743 | (80) | 22% | (-19 to 49) | **29%** | **(-12 to 55)** |
| **Influenza B/Victoria** | | | | | | | | |
| **Overall** | 8/39 | (21) | 2969/5538 | (54) | 78% | (51 to 90) | | |

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

# US Hospitalized Influenza Vaccine Effectiveness Network (HAIVEN) preliminary results

# US Hospitalized Influenza Vaccine Effectiveness Network (HAIVEN) sites and principal investigators
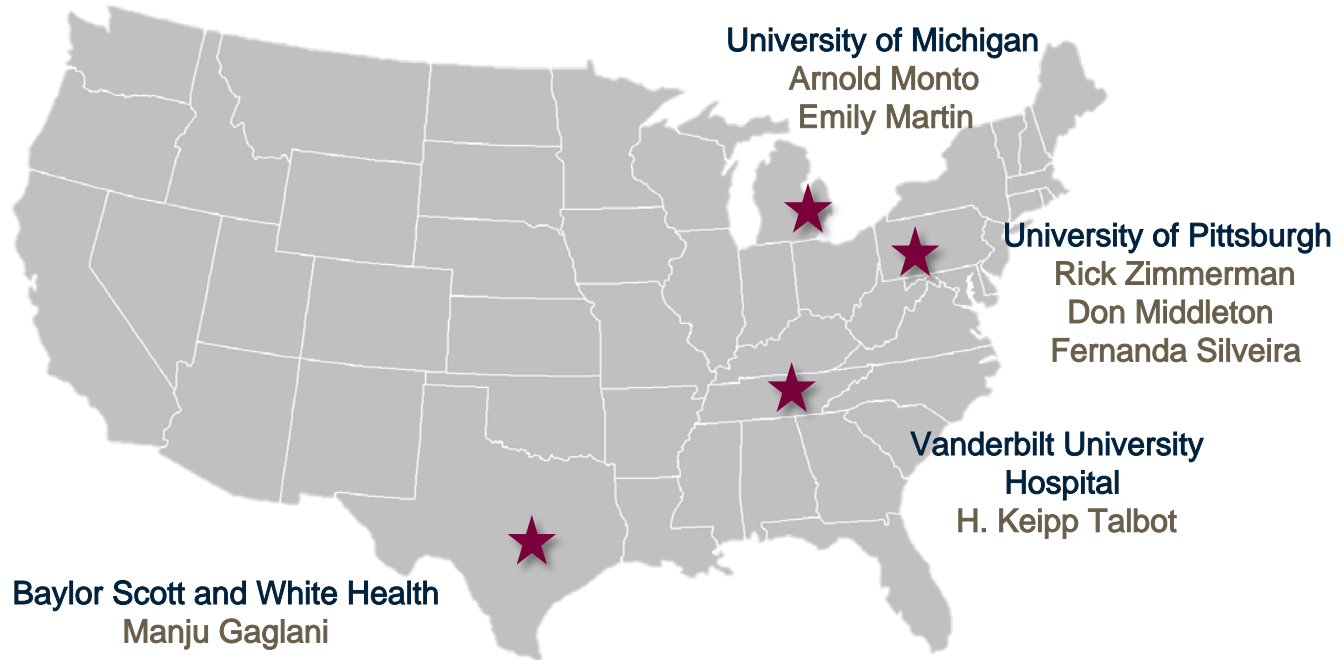
# HAIVEN Methods

**Enrollees:** Inpatients aged >18 years with acute respiratory illness with new or worsening cough or sputum production ≤10 days duration

**Dates of enrollment:** October 6, 2017 - April 28, 2018

**Design:** Test-negative design

- Comparing odds of influenza among vaccinated and unvaccinated enrollees

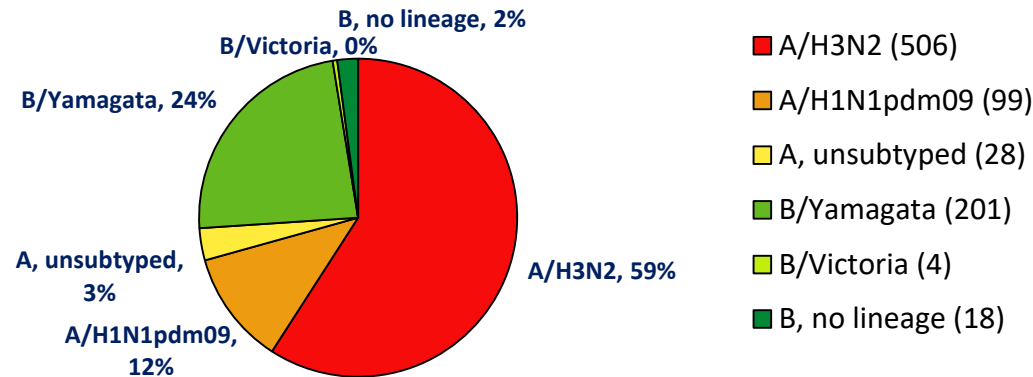- Vaccination status: receipt of 2017–18 flu vaccine by self-report

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

- Adjustment for age, site, days from illness onset to specimen collection, timing of illness onset, home oxygen use, and number of self-reported hospitalizations in the prior year

# Preliminary HAIVEN end-of-season results

- **3597 enrolled from Oct. 6, 2017 - April 28, 2018 at 4 sites (10 hospitals)**
- **856 (24%) influenza RT-PCR positive**
- **2741 (76%) influenza RT-PCR negative**

**Cases enrolled by (sub)type, N = 856**

B, no lineage, 2%
B/Victoria, 0%
B/Yamagata, 24%
A, unsubtyped, 3%
A/H1N1pdm09, 12%
A/H3N2, 59%

- A/H3N2 (506)
- A/H1N1pdm09 (99)
- A, unsubtyped (28)
- B/Yamagata (201)
- B/Victoria (4)
- B, no lineage (18)

# Number of HAIVEN participants by influenza RT-PCR result and percent positivity by week of onset
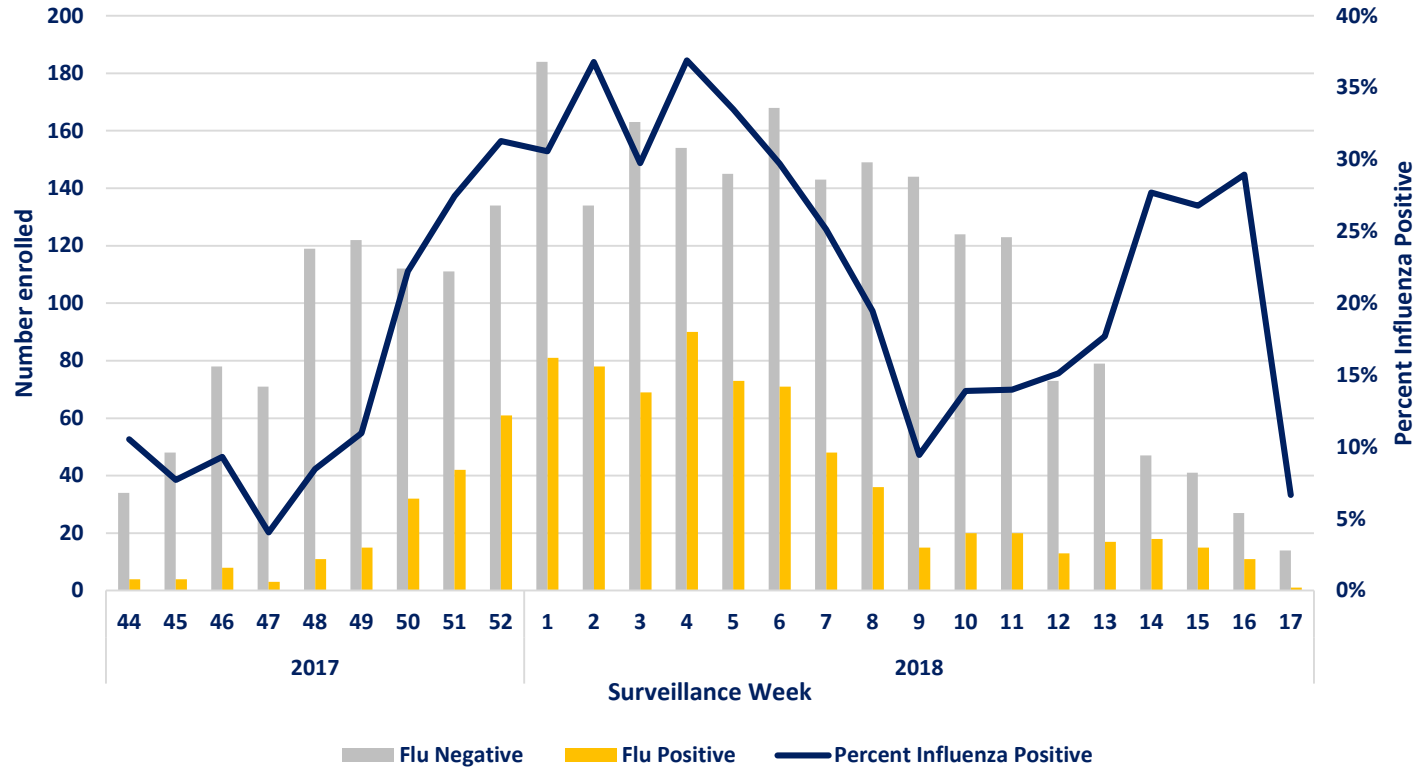
# Preliminary HAIVEN adjusted vaccine effectiveness against influenza hospitalization by age group, 2017–18

| Any influenza A or B virus | Influenza positive | | Influenza negative | | Vaccine Effectiveness | | | |
| | N vaccinated /Total | (%) | N vaccinated /Total | (%) | Unadjusted | | Adjusted* | |
| | | | | | VE % | 95% CI | VE % | 95% CI |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Overall** | 509/856 | (59) | 1762/2741 | (64) | 19% | (5 to 30) | **22%** | **(8 to 35)** |
| **Age group (yrs)** | | | | | | | | |
| **18–49** | 69/160 | (43) | 325/639 | (51) | 27% | (-4 to 48) | **18%** | **(-20 to 44)** |
| **50–64** | 121/258 | (47) | 551/959 | (57) | 35% | (14 to 50) | **32%** | **(9 to 49)** |
| **≥65** | 319/438 | (73) | 886/1143 | (78) | 22% | (0 to 40) | **24%** | **(0 to 41)** |

*Multivariate logistic regression models adjusted forage, site, days from illness onset to specimen collection, timing of illness onset, home oxygen use and number of self-reported hospitalizations in the prior year

# Preliminary HAIVEN adjusted vaccine effectiveness against influenza A(H3N2) hospitalization by age group, 2017–18

| | Influenza positive | | Influenza negative | | Vaccine Effectiveness | | | |
| | | | | | Unadjusted | | Adjusted* | |
| | N vaccinated /Total | (%) | N vaccinated /Total | (%) | VE % | 95% CI | VE % | 95% CI |
|---|---|---|---|---|---|---|---|---|
| **Influenza A/H3N2** | | | | | | | | |
| Overall | 314/506 | (62) | 1762/2741 | (64) | 9% | (-11 to 25) | **16%** | **(-5 to 32)** |
| Age group (yrs) | | | | | | | | |
| **18–49** | 41/89 | (46) | 325/639 | (51) | 17% | (-29 to 47) | **7%** | **(-53 to 44)** |
| **50–64** | 68/145 | (47) | 551/959 | (57) | 35% | (7 to 54) | **33%** | **(2 to 54)** |
| **≥65** | 205/272 | (75) | 886/1143 | (78) | 11% | (-21 to 35) | **14%** | **(-19 to 38)** |

*Multivariate logistic regression models adjusted forage, site, days from illness onset to specimen collection, timing of illness onset, home oxygen use and number of self-reported hospitalizations in the prior year

# Preliminary HAIVEN adjusted vaccine effectiveness against influenza A(H1N1)pdm09 hospitalization by age group, 2017–18

| | Influenza positive | | Influenza negative | | Vaccine Effectiveness | | | |
| | | | | | Unadjusted | | Adjusted* | |
| | N vaccinated /Total | (%) | N vaccinated /Total | (%) | VE % | 95% CI | VE % | 95% CI |
|---|---|---|---|---|---|---|---|---|
| **Influenza A/H1N1pdm09** | | | | | | | | |
| **Overall** | 39/99 | (39) | 1762/2741 | (64) | 64% | (46 to 76) | **58%** | **(36 to 73)** |
| **Age group (yrs)** | | | | | | | | |
| **18–49** | 9/29 | (31) | 325/639 | (51) | 57% | (3 to 81) | **33%** | **(-59 to 71)** |
| **50–64** | 15/37 | (41) | 551/959 | (57) | 50% | (1 to 74) | **48%** | **(-3 to 74)** |
| **≥65** | 15/33 | (45) | 886/1143 | (78) | 76% | (51 to 88) | **69%** | **(34 to 85)** |

*Multivariate logistic regression models adjusted forage, site, days from illness onset to specimen collection, timing of illness onset, home oxygen use and number of self-reported hospitalizations in the prior year
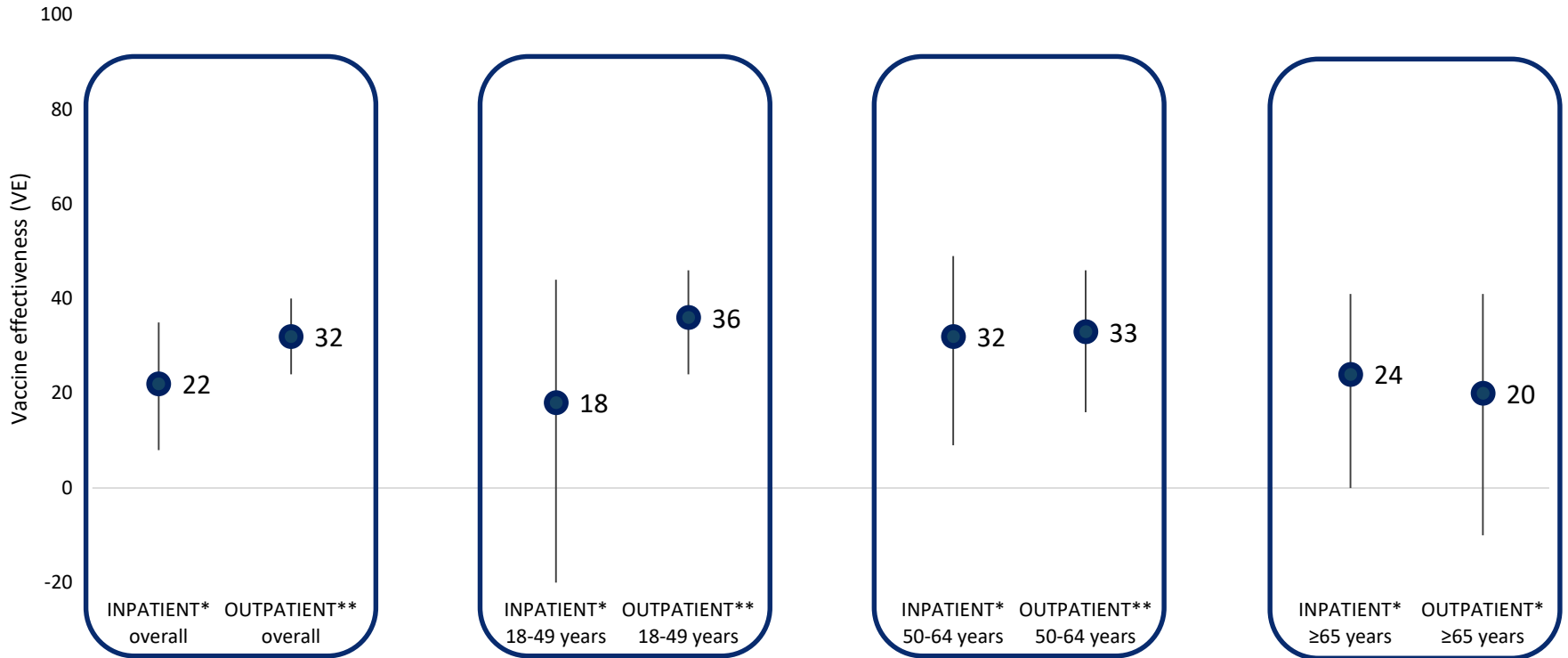
# Preliminary HAIVEN adjusted vaccine effectiveness against influenza B/Yamagata hospitalization by age group, 2017–18

| | Influenza positive | | Influenza negative | | Vaccine Effectiveness | | | |
| | | | | | Unadjusted | | Adjusted* | |
| | N vaccinated /Total | (%) | N vaccinated /Total | (%) | VE % | 95% CI | VE % | 95% CI |
|---|---|---|---|---|---|---|---|---|
| **Influenza B/Yamagata** | | | | | | | | |
| **Overall** | 117/201 | (58) | 1762/2741 | (64) | 23% | (-4 to 42) | **35%** | **(11 to 52)** |
| **Age group (yrs)** | | | | | | | | |
| **18–49** | 11/29 | (38) | 235/639 | (51) | 41% | (-27 to 73) | **46%** | **(-21 to 76)** |
| **50–64** | 27/61 | (44) | 551/959 | (57) | 41% | (1 to 65) | **34%** | **(-13 to 62)** |
| **≥65** | 79/111 | (71) | 886/1143 | (78) | 28% | (-10 to 54) | **33%** | **(-6 to 57)** |

*Multivariate logistic regression models adjusted forage, site, days from illness onset to specimen collection, timing of illness onset, home oxygen use and number of self-reported hospitalizations in the prior year

# Comparing Outpatient vs Inpatient Adult Vaccine Effectiveness results, 2017-18

# Comparison of VE estimates by age group among inpatient (HAIVEN) and outpatient (Flu VE) adults aged ≥18 yrs, 2017-18

Vaccine effectiveness (VE)

| | | | |
|---|---|---|---|
| INPATIENT* overall — 22 | OUTPATIENT** overall — 32 | | |
| INPATIENT* 18-49 years — 18 | OUTPATIENT** 18-49 years — 36 | | |
| INPATIENT* 50-64 years — 32 | OUTPATIENT** 50-64 years — 33 | | |
| INPATIENT* ≥65 years — 24 | OUTPATIENT* ≥65 years — 20 | | |

*Multivariate logistic regression models adjusted for age, site, days from illness onset to specimen collection, timing of illness onset, home oxygen use, and number of self-reported hospitalizations in the prior year

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

# Comparison of VE estimates by virus type among inpatient (HAIVEN) and outpatient (Flu VE) adults aged ≥18 yrs, 2017-18
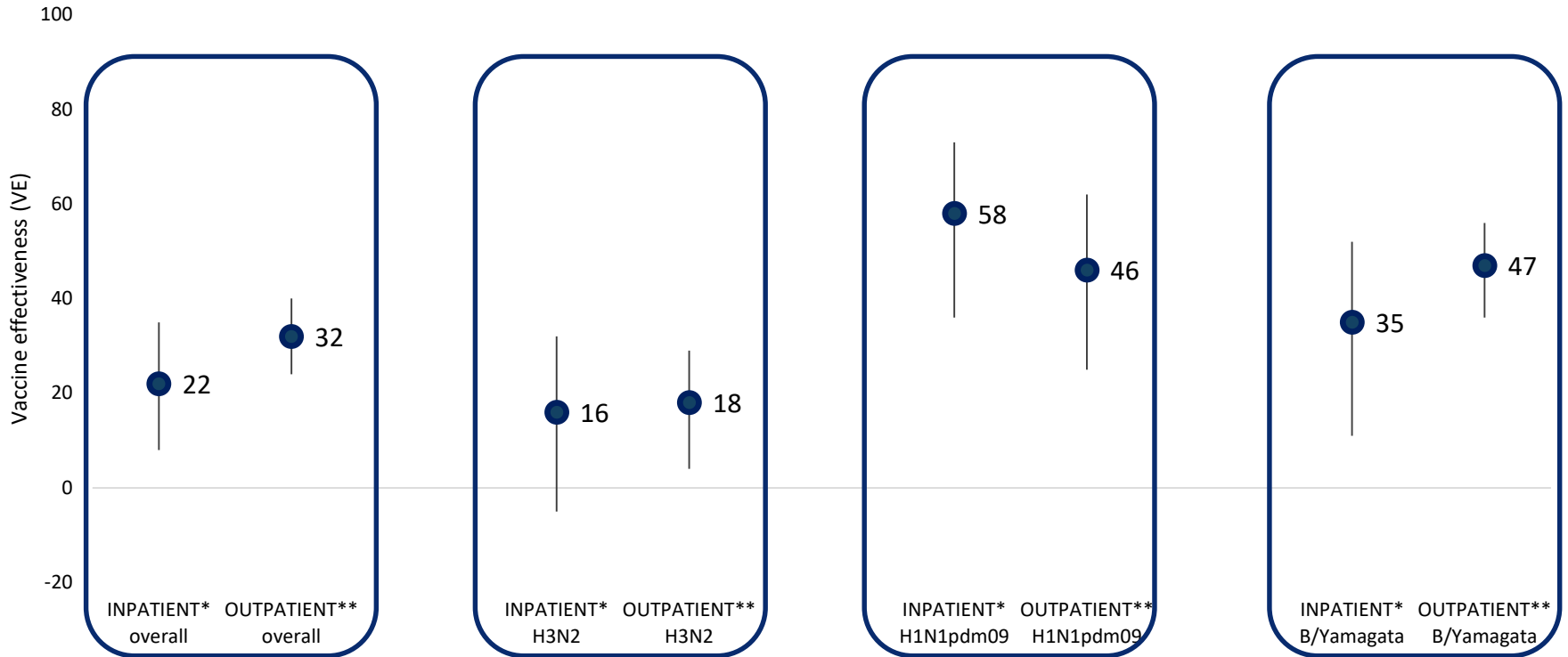


*Multivariate logistic regression models adjusted for age, site, days from illness onset to specimen collection, timing of illness onset, home oxygen use, and number of self-reported hospitalizations in the prior year

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

# Summary and Future Directions

# Summary

- 2017-18 was an influenza season with high severity.  A(H3N2) viruses were the predominant circulating virus.

- Influenza vaccination reduced outpatient visits for influenza-associated ARI by 40% (CI, 34% to 46%) among persons aged 6 months and older.

- Among adults, VE estimates were similar for outpatients and inpatients. Vaccination reduced influenza-associated hospitalization among adults by 22% (CI, 8% to 35%).

- VE estimates against A(H1N1)pdm09 (65%) and B/Yamagata (49%) viruses were higher than VE against A(H3N2) viruses (24%), similar to previous seasons.

- Final VE results will include VE by vaccine type (standard dose vs high dose IIVs for patients aged ≥65 yrs) and effects of prior season vaccination

# Averted Burden 2016-17

Hospitalizations — 84,700

Medical visits — 2.64 million

Influenza illnesses — 5.29 million
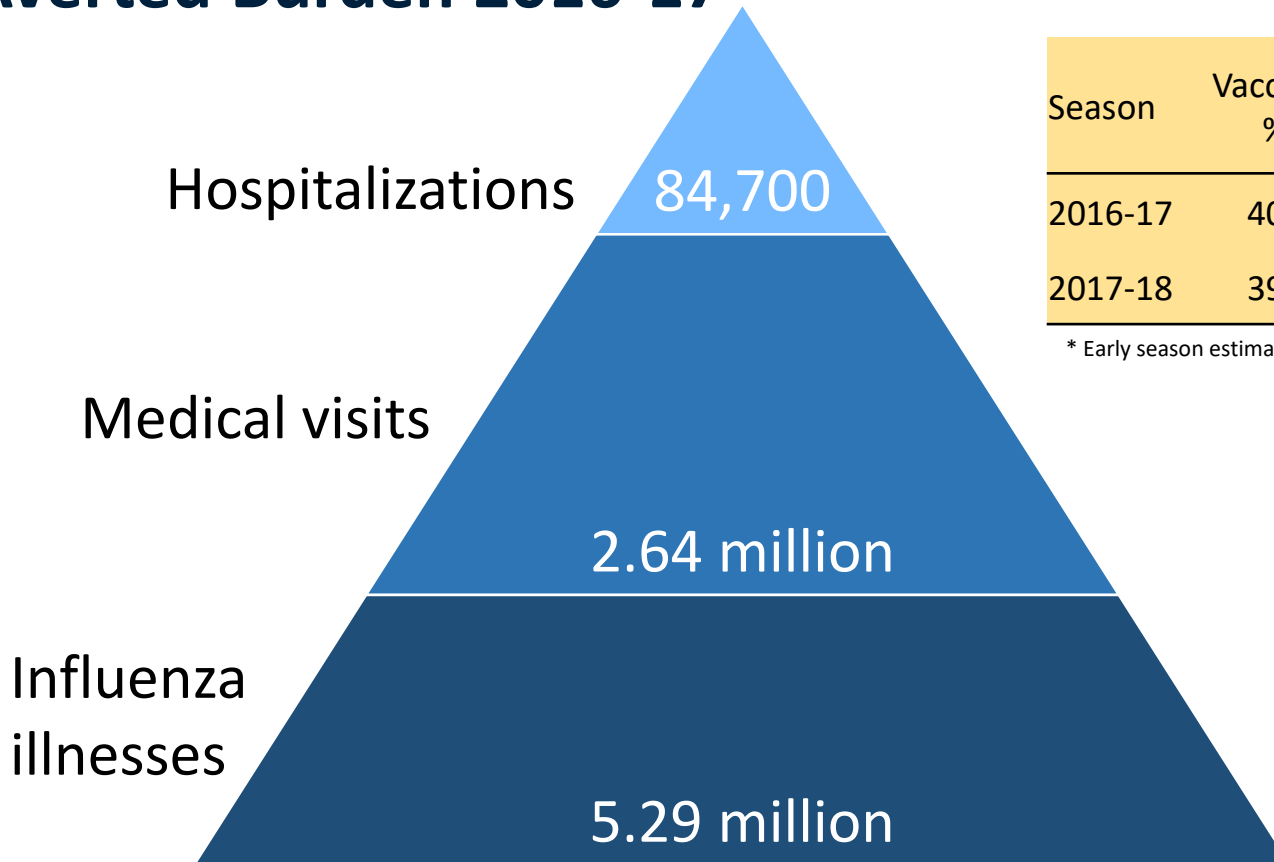
| Season | Vaccine coverage % (95% CI) | Vaccine effectiveness % (95% CI) |
|---|---|---|
| 2016-17 | 40 (38–43) * | 40 (32–46) |
| 2017-18 | 39 (37–40) * | 40 (34–46) |

* Early season estimate, Nov 2016 and Nov 2017

Estimates of 2017-18 averted burden expected in fall 2018

www.cdc.gov/flu/about/disease/2016-17.htm

# Enhancements to work towards better vaccines and expand our evidence base

- Investigation into immunologic basis of influenza vaccine failures
  - Initiating collection of acute/convalescent sera from subset of influenza cases in US VE Network and HAIVEN
- Expanded enrollment for US Flu VE and HAIVEN Networks
- Expand evidence base for contribution of antigen dose and adjuvants on VE
- Understand effects of egg-adaptive changes on VE
  - Determining differences between egg-based and non-egg vaccines
- Engineer optimal vaccine viruses that have fewer disruptive egg-adaptive changes

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