



Updates on Influenza Vaccine Effects

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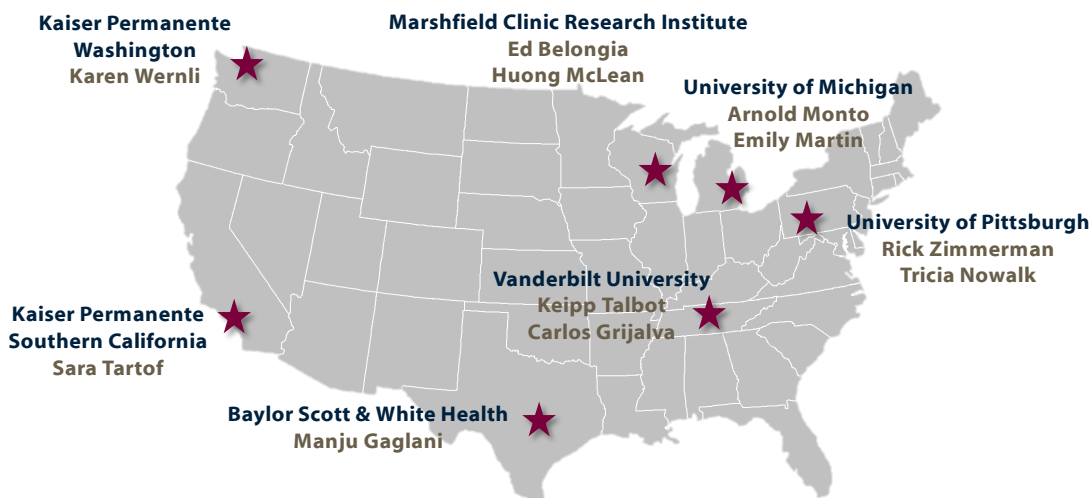
NAIIS
May 20, 2022

1

2021-22 Interim Influenza VE Estimates

2

US Flu VE Network for annual estimates of influenza vaccine effectiveness against outpatient illness, 7 sites

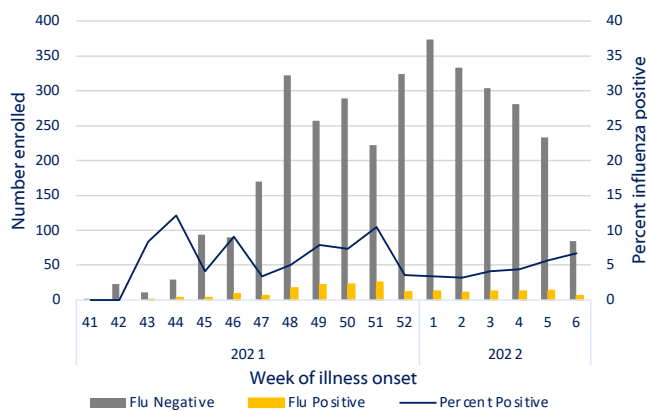


3

Interim Results: Enrollment Oct 4, 2021–Feb 12, 2022

- 3,636 enrolled at 7 sites
- 3,442 (95%) flu negative
- 194 (5%) flu positive
 - Influenza A--all subtyped viruses A(H3N2)
 - All sequenced viruses A(H3N2) belong to single genetic group (3C.2a1b subclade 2a.2)

Number enrolled by RT-PCR result and % flu positive



Note: Week 6 only includes patients with completed laboratory tests and thus does not reflect all enrolled patients during that week across study sites.

5

Interim vaccine effectiveness against influenza A and A/H3N2 among patients aged 6 months and older, US Flu VE, 2021–22

| | Influenza positive | | Influenza negative | | Vaccine Effectiveness | | | |
|-------------------------------------|---------------------|-----|---------------------|-----|-----------------------|------------|-----------------------|-------------|
| | N vaccinated /Total | (%) | N vaccinated /Total | (%) | Unadjusted | | Adjusted ¹ | |
| Influenza A | | | | | VE % | 95% CI | VE % | 95% CI |
| Ages ≥6 mos | 79/194 | 41 | 1738/3442 | 50 | 32 | (10 to 50) | 14 | (-17 to 37) |
| Influenza A/H3N2² | | | | | | | | |
| Ages ≥6 mos | 69/177 | 39 | 1564/3174 | 49 | 34 | (11 to 52) | 16 | (-16 to 39) |

Chung, et al, MMWR 2022

¹ Multivariable logistic regression models adjusted for site, age group, and month of onset.

² Excludes influenza test-negatives enrolled at one site from which subtype results were not available.

6

Summary

- Interim estimates suggested null vaccine effectiveness against A(H3N2)
- More limitations this year than usual:
 - Lowest influenza positivity (5%) observed over past 10 seasons among US Flu VE Network participants with respiratory illness
 - Numbers of influenza-positive participants were insufficient to estimate age group-specific VE or compare effectiveness of different influenza vaccine products against predominant A(H3N2) virus
 - COVID-19 vaccination may be correlated with influenza vaccination and bias results
 - Health care seeking behavior has changed during COVID-19 pandemic in ways that may affect influenza vaccine effectiveness estimates
- Updated estimates including outpatient and hospital outcomes will be presented at ACIP in June

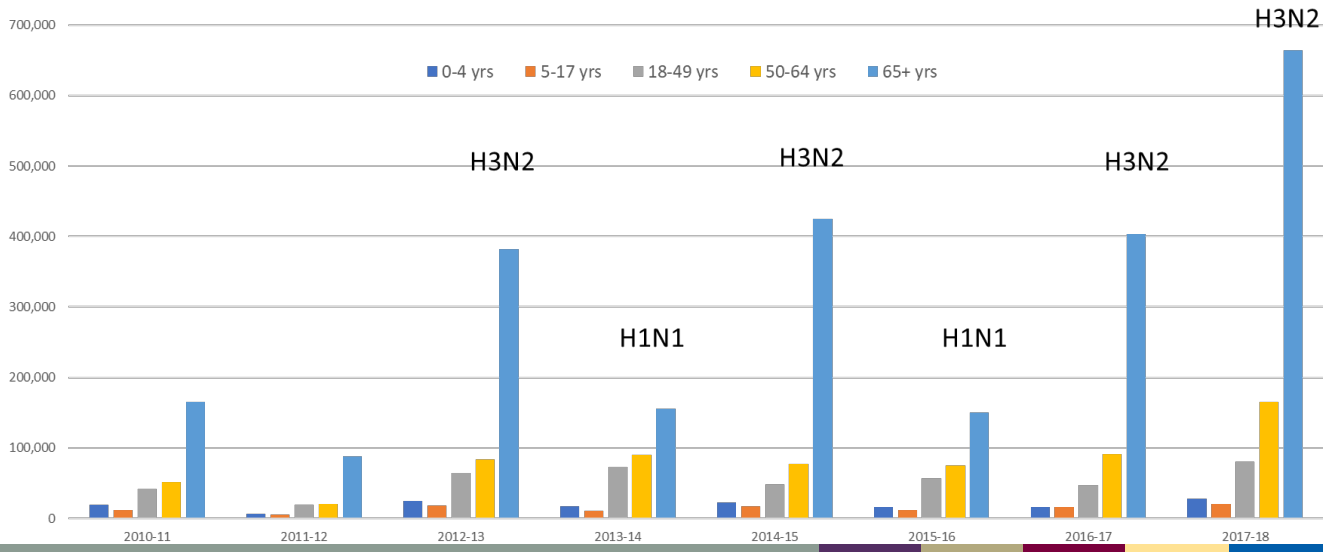
7

Vaccines for older adults

8

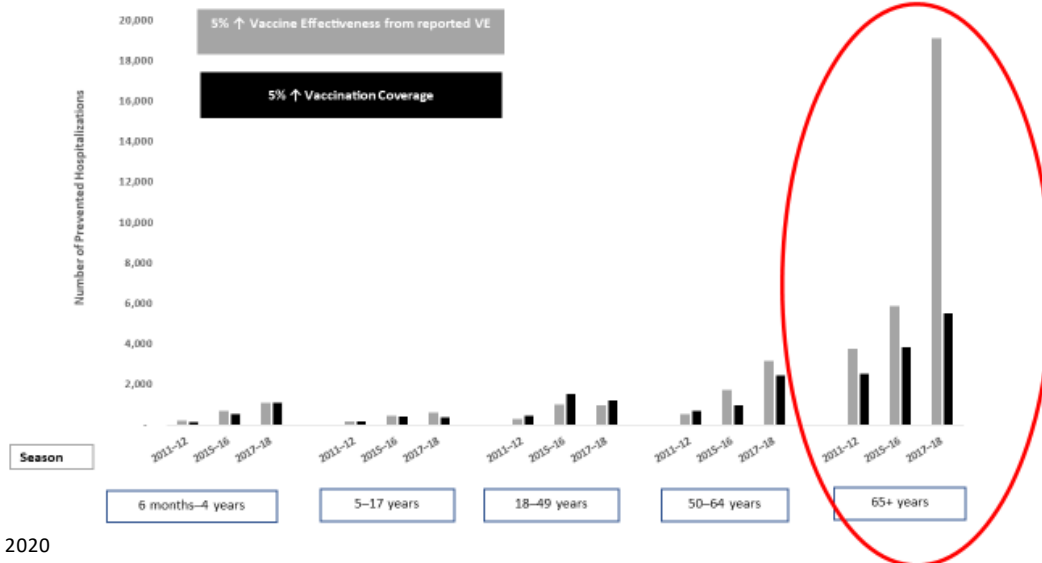
Older adults account for a large fraction of burden

Estimated number of influenza-associated hospitalizations by age group and season



9

A small increase in VE can reduce a substantial burden in high burden seasons



10

There are many vaccine options for older adults



US-licensed 2021-22 vaccines, based *solely* on FDA age indications:

| Vaccine type | 6 through 23 mos | 2 through 3 yrs | 4 through 17 yrs | 18 through 49 yrs | 50 through 64 yrs | ≥65 yrs |
|----------------|------------------|-----------------|------------------|-------------------|-------------------|------------|
| Egg IIV3/4 | 5 products | 5 products | 5 products | 5 products | 5 products | 5 products |
| Cell IIV4 | 1 product | 1 product | 1 product | 1 product | 1 product | 1 product |
| RIV4 | | | | 1 product | 1 product | 1 product |
| Adjuvant IIV3 | | | | | | 1 product |
| High-dose IIV3 | | | | | | 1 product |
| LAIV4 | | 1 product | 1 product | 1 product | | |

11

Enhanced influenza vaccines



- Definition: influenza vaccine with higher antigen dose or adjuvant
 - HD-IIV3, RIV4, and MF-59 adjuvanted IIV3
- ~75% of older adults received an enhanced vaccine in 2019-20 (Medicare)
- There are disparities related to vaccine type receipt
 - In 2015-16 study with Medicare data, minority groups (Black, Hispanic, and Asian) were 26%-32% less likely to receive HD-IIV3 compared to white people (Mahmud, et al, *Lancet* 2021)

12

Clinical trials comparing an enhanced vaccine to standard dose vaccine

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efficacy of High-Dose versus Standard-Dose Influenza Vaccine in Older Adults

Carlos A. DiazGranados, M.D., Andrew J. Dunning, Ph.D., Murray Kimmel, D.O., Daniel Kirby, B.Sc., John Treanor, M.D., Avi Collins, B.Sc.N., Richard Pollak, D.P.M., Janet Christoff, R.N., John Earl, M.D., Victoria Landolfi, M.Sc., M.B.A., Earl Martin, D.O., Sanjay Gurunathan, M.D., Richard Nathan, D.O., David P. Greenberg, M.D., Nadia G. Tornieporth, M.D., Michael D. Decker, M.D., M.P.H., and H. Keipp Talbot, M.D., M.P.H.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efficacy of Recombinant Influenza Vaccine in Adults 50 Years of Age or Older

Lisa M. Dunkle, M.D., Ruvim Izikson, M.D., M.P.H., Peter Patriarca, M.D., Karen L. Goldenthal, M.D., Derek Muse, M.D., Janice Callahan, Ph.D., and Manon M.J. Cox, Ph.D., for the PSC12 Study Team*

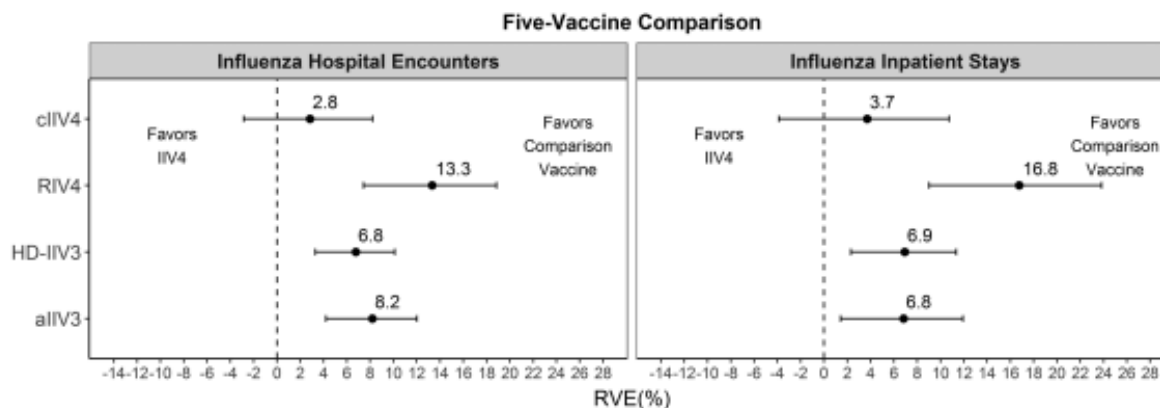
Post hoc analysis of 65+ years:
PCR+ ILI: RVE 17% (-20 to 43)
Cx+ ILI: 42% (9 to 65)

13

Difficult to compare enhanced vaccines to each other

- Few studies have sample size to compare multiple vaccines

Comparison of Vaccines to IIV4 in Medicare Beneficiaries 65+ yrs of age, 2019-20

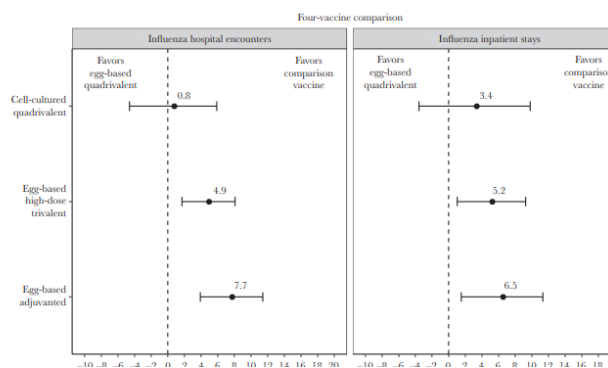


14

Influenza Vaccine Comparisons Vary by Season

Comparison of Vaccines to IIV4 in Medicare Beneficiaries 65+ yrs of age, 2018-19

Izurieta, et al, JID 2020



Comparison of Vaccines in Medicare Beneficiaries 65+ yrs, 2017-18

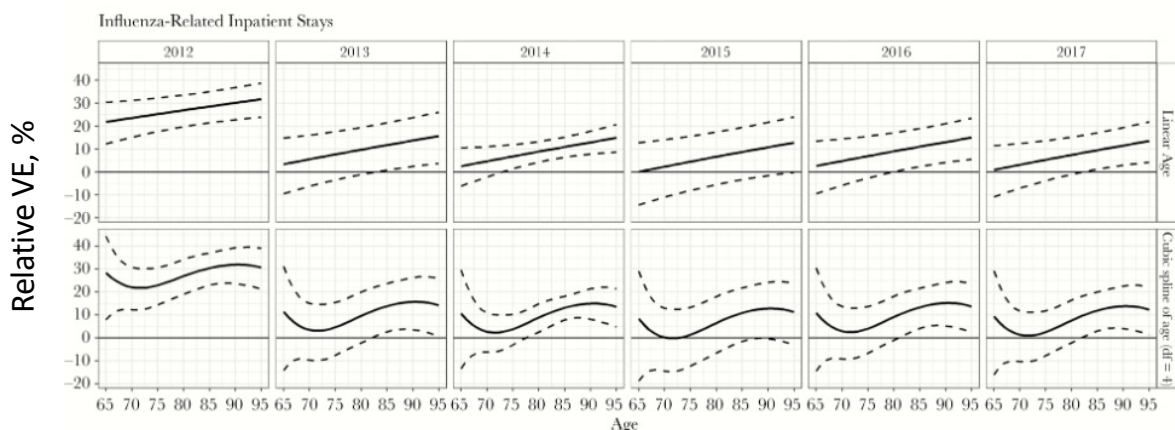
Izurieta, et al, JID 2018

| Cohort | RVE by Reference Group (95% CI), % | | | |
|--------------------------------|------------------------------------|------------------------------|--------------------------------|------------------------|
| | Egg-Based Quadrivalent | Egg-Based SD Trivalent | Egg-Based Adjuvanted Trivalent | Egg-Based HD Trivalent |
| Cell-cultured quadrivalent | 11.0 (7.9–14.0) ^a | 10.8 (7.4–14.1) ^a | 7.5 (4.1–10.7) ^a | 2.3 (–.8, to 5.3) |
| Egg-based HD trivalent | 9.0 (7.2–10.6) ^a | 8.7 (6.5–10.9) ^a | 5.3 (3.3–7.3) ^a | ... |
| Egg-based adjuvanted trivalent | 3.9 (1.4–6.3) ^a | 3.6 (1.7–6.4) ^a | ... | ... |
| Egg-based SD trivalent | 0.3 (–2.6 to 3.1) | ... | ... | ... |

15

Vaccine effects vary by season and age

Relative VE of HD-IIV vs SD among Medicare Beneficiaries, 2012-13 to 2017-18



Lu, et al, JID 2019

16

Summary

- Although, use of enhanced vaccines is high among older adults, there is disparity in use
- For most seasons, enhanced vaccines have a higher relative VE compared to standard dose vaccines
- Vaccine effects vary by season and may be greatest in the oldest age groups
- June ACIP meeting will discuss use of enhanced vaccines in older adults

17

Attenuation of illness among vaccinated individuals who are infected with influenza

18

Lower odds of ICU admission among hospitalized vaccinated adults compared to unvaccinated adults

| Source | Age (yr) | Season | OR (95% CI) |
|---|----------|------------------|-------------------|
| Arriola (2017) | 18-49 | 2013-14: H1 | 0.63 (0.42, 0.93) |
| Arriola (2017) | 50-64 | 2013-14: H1 | 1.05 (0.80, 1.37) |
| Arriola (2017) | 65+ | 2013-14: H1 | 0.63 (0.48, 0.81) |
| Casado (2018) | 65+ | 2013-15: H1/H3 | 0.34 (0.20, 0.58) |
| Joshi (2015) | 18+ | 2013-14: H1/H3 | 2.89 (0.97, 8.60) |
| Loubet (2016) | 18+ | 2012-15: H1/H3/B | 0.50 (0.28, 0.90) |
| Martinez (2019) | 18+ | 2010-16: H1 | 0.68 (0.42, 1.10) |
| Martinez (2019) | 18+ | 2010-16: H3 | 0.67 (0.41, 1.10) |
| Martinez (2019) | 18+ | 2010-16: B | 0.57 (0.30, 1.08) |
| Segaloff (2018) | 18+ | 2014-15: H1/H3 | 1.00 (0.30, 3.10) |
| Taylor (2016) | 16+ | 2006-09: A/B | 1.49 (0.68, 3.33) |
| Taylor (2016) | 16+ | 2009-10: H1 | 0.74 (0.50, 1.09) |
| Taylor (2016) | 16+ | 2010-12: A/B | 1.59 (0.82, 3.03) |
| Thompson (2018) | 18+ | 2012-15: H1/H3/B | 0.41 (0.18, 0.96) |
| Total | | | |
| Heterogeneity: $\chi^2_{13} = 35.82$ ($P < .001$), $I^2 = 64\%$ | | | |
| Overall OR = 0.74 (0.58, 0.93) | | | |

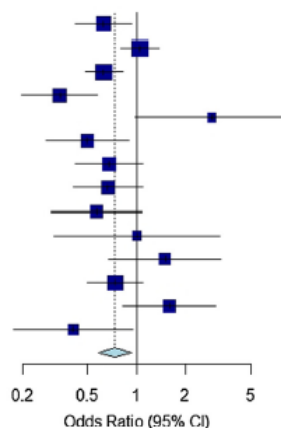
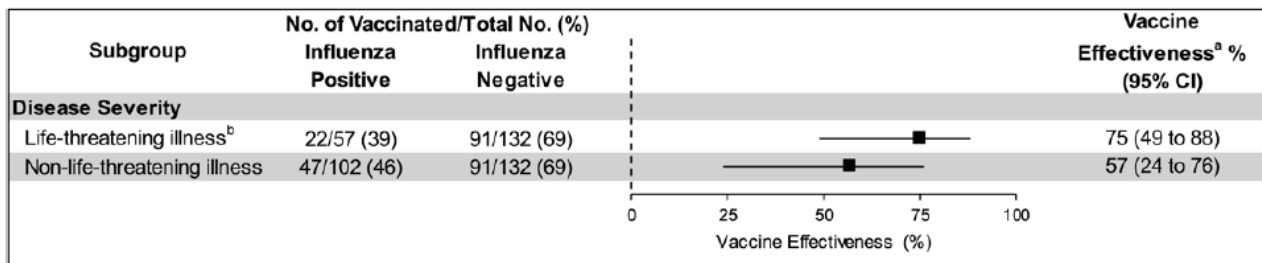


Fig. 1. Odds ratios for intensive care unit admission among hospitalized adults with laboratory-confirmed influenza illness, comparing vaccinated to unvaccinated individuals. Summary odds ratio (95% CI) is 0.74 (0.58, 0.93).

Ferdinands, et al Vaccine 2021

19

Higher VE estimates against life threatening illness in children admitted to PICU, 2019-2020



- Higher VE estimates against PICU admission compared to outpatient

| Subgroup | VE (95% CI) | |
|----------------------------|----------------|------------------|
| | ICU | Outpatient* |
| Overall - Full vaccination | 65 (41 to 79) | 37 (26-46) |
| H1: 5A+156K viruses | 51 (-14 to 79) | -22% (-75 to 16) |
| H1: 5A+187A,189E | 80 (45 to 93) | 48% (20 to 66) |
| B-Vic: V1A.3 viruses | 77 (40 to 91) | 41% (28 to 51) |

Olsen, et al CID 2022

20

Summary

- Evidence that influenza vaccine attenuates illness severity is growing for adults and children
- Even in seasons with circulating viruses that are antigenically drifted from vaccine viruses, the vaccine may attenuate illness

21

Thank you

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For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

