Effectiveness of Influenza Vaccination against Medically Attended Influenza Illness during the 2013-14 Influenza Season, U.S. Flu VE Network, December 2013-January 2014

Brendan Flannery, PhD
Influenza Division, National Center for Immunization & Respiratory Diseases, CDC
Presentation to NAIIS
May 15, 2014

National Center for Immunization & Respiratory Diseases
Influenza Division

Influenza vaccination recommendations

- Routine annual influenza vaccination of all persons aged 6 months and older continues to be recommended
- Updated recommendations available at
  www.cdc.gov/flu

US Flu VE Network

Purpose

Estimate VE for prevention of healthcare visits due to influenza, by age group and type/subtype

- **Not designed to develop product-specific estimates**

Sites

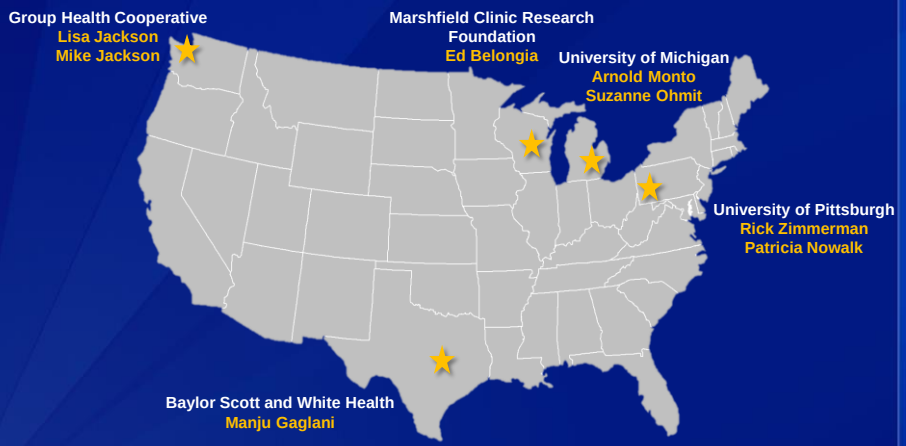
Five medical systems and geographic regions:

- Group Health Cooperative (WA)
- Marshfield Clinic (WI)
- Scott & White Healthcare (TX)
- University of Michigan (MI)
- University of Pittsburgh (PA)

Enrollees

Children and adults with medically attended acute respiratory illness

US Flu VE Network: 5 Sites and Principal Investigators



US Flu VE Network: Methods

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

Dates of enrollment: December 2, 2013–January 23, 2014

Methods: Prospective case-control study (test-negative design)

- All enrolled outpatients tested for influenza by RT-PCR
  - Cases: Outpatients with confirmed influenza (PCR-positive)
  - Controls: Outpatients without influenza (PCR-negative)
- Vaccination status: receipt of at least one dose of any 2013-14 seasonal flu vaccine confirmed by medical records and registries (2 sites) and self-report and medical records (3 sites)

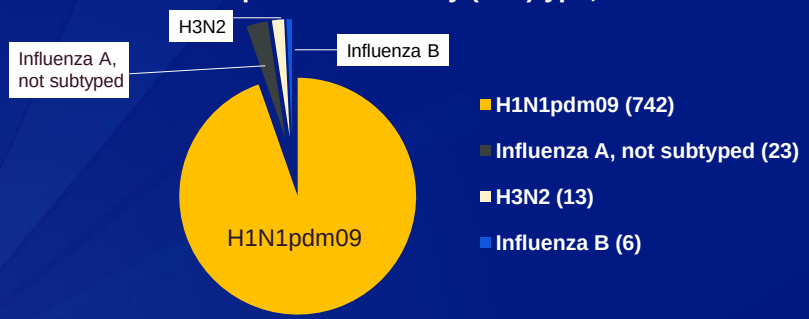
Analysis: VE = (1 – adjusted OR) x 100%

- Adjustment for study site, age, sex, race/Hispanic ethnicity, self-rated health, and days from illness onset to enrollment

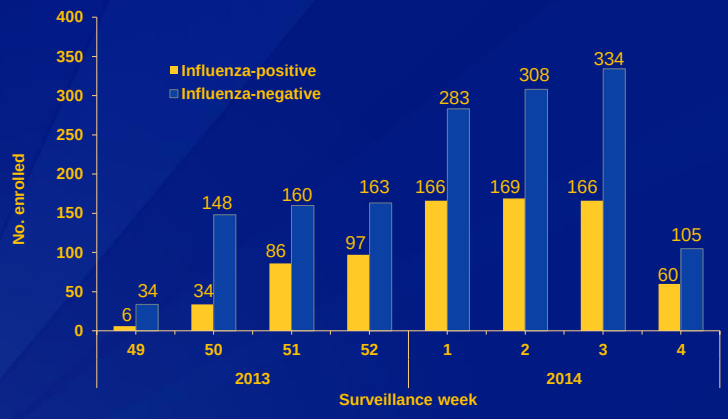
US Flu VE Network: Interim results

- 2,319 enrolled from Dec 2, 2013–Jan 23, 2014
- 1,535 (66%) influenza RT-PCR negative
- 784 (34%) influenza RT-PCR positive

Influenza-positive cases by (sub)type, N=784



Number of participants with ARI enrolled at 5 US Flu VE Network sites according to influenza RT-PCR result, by week of onset, December 2013-January 2014



Note: Week 4 only includes patients with completed laboratory tests and thus does not reflect all enrolled patients during that week across study sites.

Interim adjusted VE estimates for ≥1 dose of 2013-14 seasonal influenza vaccine

	Flu pos	% vaccinated	Flu neg	% vaccinated	Adjusted VE	(95% CI)
Influenza A and B						
All ages	784	29%	1535	50%	61%	(52 to 68)
Age group (yrs)						
6 mos–17	172	24%	528	48%	67%	(51 to 78)
18–49	360	21%	536	38%	60%	(44 to 71)
50–64	195	37%	286	59%	60%	(39 to 73)
≥65	57	61%	185	79%	52%	(2 to 77)
Influenza A (H1N1pdm09)						
All ages	742	28%	1535	50%	62%	(53 to 69)
Age group (yrs)						
6 mos–17	168	24%	528	48%	67%	(51 to 78)
18–49	339	21%	536	38%	61%	(45 to 72)
50–64	184	36%	286	59%	62%	(42 to 75)
≥65	51	59%	185	79%	56%	(7 to 79)

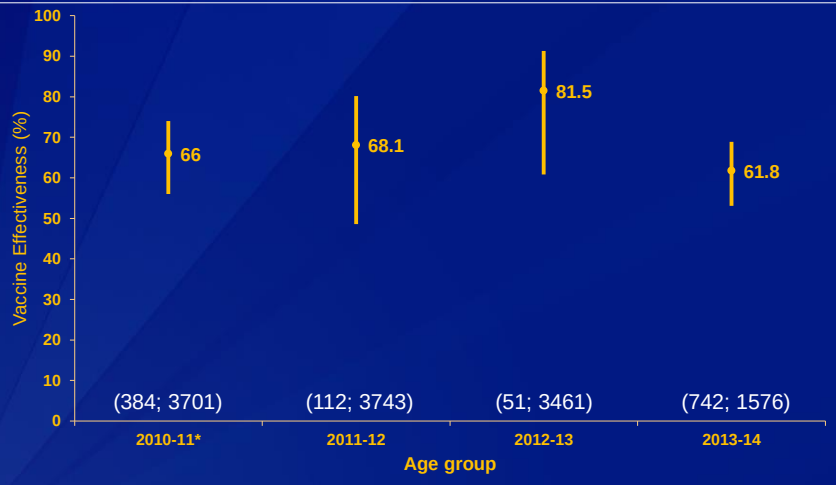
* Vaccine effectiveness was estimated as 100% X (1 – odds ratio [ratio of odds of vaccination among flu-positive cases to odds of vaccination among flu-negative controls]) using logistic regression. Multivariate models adjusted for study site, age, sex, race/Hispanic ethnicity, self-rated health status, and days from illness onset to enrollment. Models for "all ages" include age as a categorical variable; age-specific models include age in years as a continuous variable.

Antigenic characterization data US influenza surveillance, 2013-14

- A/California/7/2009 (pH1N1) has been included as the H1N1 component of seasonal influenza vaccines since 2010
- Vaccine effectiveness in 2013-14 consistent with protection against pH1N1 influenza seen in each season since 2009
- 99% H1N1 viruses submitted to CDC during 2013-14 season were antigenically similar to A/California/7/2009 (vaccine strain)
- A/California/7/2009 (pH1N1) remains H1N1 component of 2014-15 flu vaccine

Source: U.S. WHO and National Respiratory and Enteric Virus Surveillance System collaborating laboratories

Effectiveness of seasonal influenza vaccines against pH1N1 influenza over four seasons, US Flu VE Network



- No. of pH1N1 cases and influenza-negative (control) participants shown in parentheses

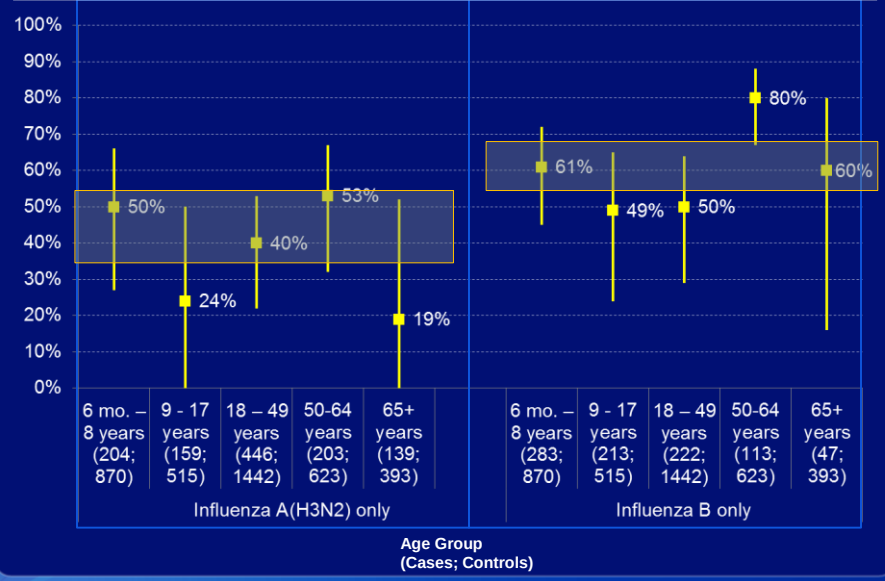
* US Flu VE Network sites in 2010-11 included New York, Wisconsin, Tennessee and Michigan.

A(H3N2) and B influenza vaccine components for 2014-15 season

- Circulating influenza A (H3N2) viruses in U.S. were characterized as A/Texas/50/2012-like (vaccine strain)
- A/Texas/50/2012 retained as H3N2 component of 2014-15 flu vaccine
- Influenza vaccine effectiveness against A(H3N2) has been lower than VE against A(H1N1), especially in some age groups
- Both lineages of influenza B viruses circulated during 2013-14 flu season
- Live-attenuated and quadrivalent inactivated flu vaccines include viruses from both B lineages, trivalent inactivated vaccines include B/Massachusetts/02/2012 (Yamagata)

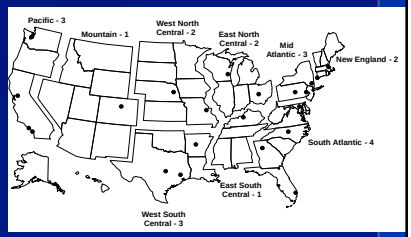
Source: U.S. WHO and National Respiratory and Enteric Virus Surveillance System collaborating laboratories

VE against Influenza A(H3N2) and B, 2012-13



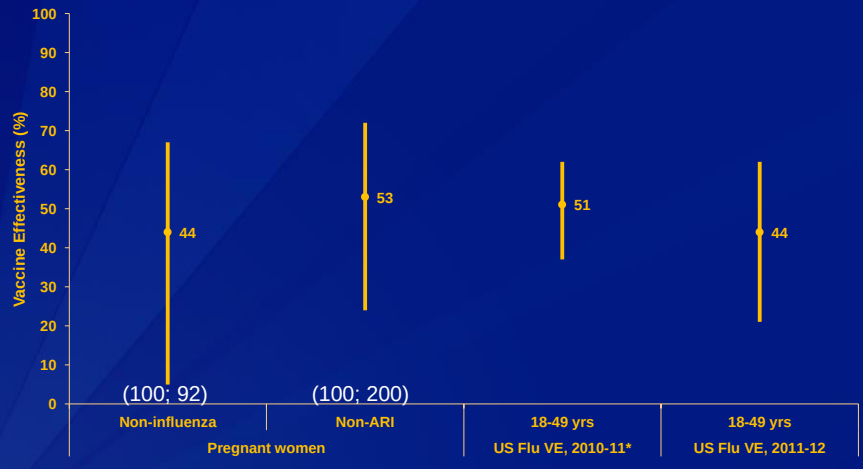
Effectiveness of influenza vaccine among pregnant women, 2010-11 and 2011-12

- Kaiser Permanente health plan members, 2 metro areas in California and Oregon
- 2010-11 and 2011-12 seasons
- Case-control design
  - Cases: Flu + acute resp. illness, pregnant
  - Controls: Flu-neg acute resp. illness, pregnant
  - Non-ARI controls: No resp. illness, matched by trimester of pregnancy, influenza season and site



Source: M Thompson et al, J Infect Dis 2014

VE against influenza A and B among pregnant women vs. all adults 18-49 years, 2010-11 and 2011-12



- No. of pH1N1 cases and influenza-negative (control) participants shown in parentheses

* US Flu VE Network sites in 2010-11 included New York, Wisconsin, Tennessee and Michigan.

Source: M Thompson et al, J Infect Dis 2014

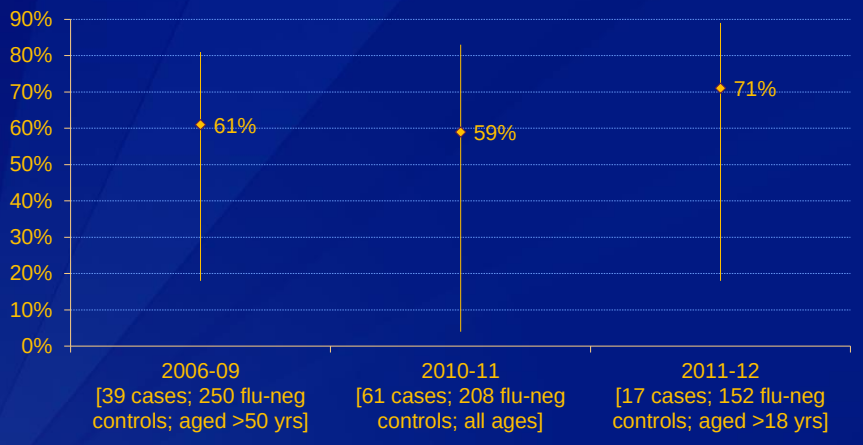
Conclusions

- **2009 H1N1pdm virus predominated during 2013-14 season in U.S.**
- **Estimated vaccine effectiveness against medically attended pH1N1 illness was 62% (95% CI: 53-69)**
  - Similar for all age groups
  - Similar to VE estimates for H1N1pdm09 from previous seasons
  - Consistent with laboratory data for current season
- **Final analyses for 2013-14 season will investigate effects of prior vaccination**
- **Ability to estimate VE for influenza A(H3N2) or B infections for 2013-14 season will depend upon final sample size**

Other VE Outcomes

VE AGAINST INPATIENT OUTCOMES

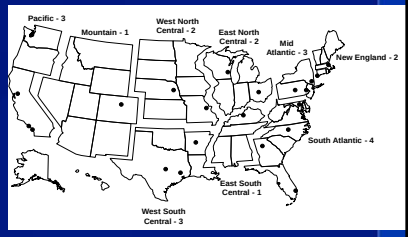
Adjusted VE (95% CI) against hospitalization using influenza-negative control design



Talbot et al. (2011) JID 203: 500-8
Costilla (2013) BMC Public Health 13:191
Talbot et al. (2013) CID 56:1774-7

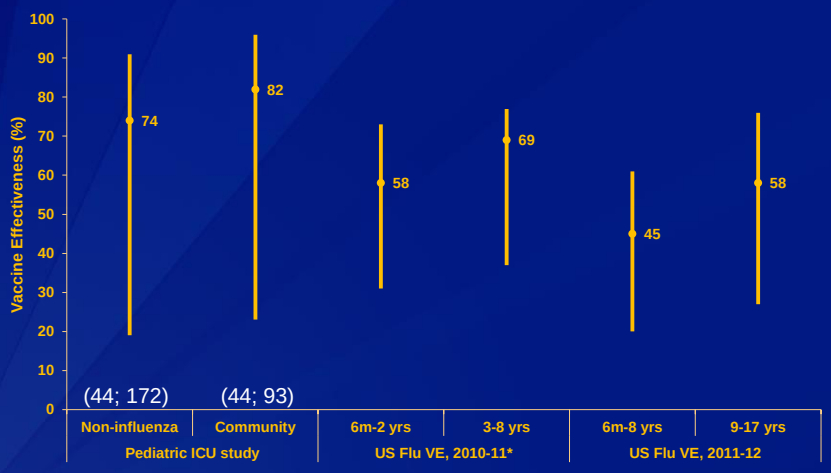
Effectiveness of influenza vaccine against life-threatening RT-PCR-confirmed influenza illness in US children, 2010-12

- Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network: 21 Pediatric ICUs
- 2010-11 and 2011-12 seasons
- Case-control design
  - Cases: Flu +, Ped ICU admission, aged <18 yrs
  - Controls: Flu-neg, Ped ICU admission, aged <18 yrs
  - Community controls: Matched by age, region, comorbidities



Source: J Ferdinands et al, J Infect Dis 2014

Comparison of VE estimates against severe influenza vs. medically attended illness <18 yrs, 2010-11 and 2011-12



- No. of pH1N1 cases and influenza-negative (control) participants shown in parentheses

* US Flu VE Network sites in 2010-11 included New York, Wisconsin, Tennessee and Michigan.

Source: J Ferdinands et al, J Infect Dis 2014

US Flu VE Network

- *University of Michigan and Henry Ford Health System:* Arnold S. Monto, MD, Suzanne E. Ohmit, DrPH, Joshua G. Petrie, MPH, Emileigh Johnson, Rachel T. Cross, MPH, Casey Martens, Marcus Zervos, MD, Lois Lamerato, PhD, Mary Ann Aubuchon, William Fredrick;
- *University of Pittsburgh Schools of the Health Sciences and UPMC:* Richard K. Zimmerman, MD, Mary Patricia Nowalk, PhD, Jonathan M. Raviotta, MPH, Heather Eng, Stephen R. Wisniewski, PhD, Charles R. Rinaldo, Jr, MD, Arlene Bullotta, Joe Suyama, MD, Evelyn Reis, MD, Donald B. Middleton, MD, Rhett H. Lieberman, MD, Michael Susick, MPH, Krissy K. Moehling, MPH, Mallory Schaffer, BS;
- *Baylor Scott and White Health, Texas A&M University Health Science Center College of Medicine:* Manjusha Gaglani, MBBS, Lydia Clipper, RN, Anne Robertson, AA, Kempapura Murthy, MPH, Monica Weir, Hope Gonzales, Martha Zayed, Teresa Ponder, Virginia Gandy, RN, Patricia Sleeth, RN, Sophia V James, MS, , Michael Reis, MD, Cathleen Rivera, MD, David Morgan, MD, and Baylor College of Medicine : Pedro Piedra, MD, Vasanthi Avadhanula, PhD;
- *Group Health Research Institute* : Michael L. Jackson, PhD, Lisa A. Jackson, MD, C. Hallie Phillips, MEd, Joyce Benoit, RN, Lawrence T. Madziwa, MS, Matt B. Nguyen, MPH, Julia P. Anderson, MA;
- *Marshfield Clinic Research Foundation:* Edward A. Belongia, MD, Huong Q. McLean, PhD, Deanna Cole, Donna David, Sarah Kopitzke, MS, Tamara A. Kronenwetter Koepel, Jennifer K. Meece, PhD, Carla Rottscheit, Sandra K. Strey, Maria E. Sundaram, MSPH, Laurel A. Verhagen;
- *CDC*: Alicia M. Fry, MD, Swathi N. Thaker, PhD, Jessie Clippard, MPH, Ivo Foppa, PhD, Jill Ferdinands, PhD, LaShondra Berman, MS, Angie Foust, MS, Wendy Sessions, MPH, Sarah Spencer, PhD, Erin Burns, MA, Mark Thompson, PhD, Joseph Bresee, MD, Nancy Cox, PhD.