Interim Within-Season Estimate of the Effectiveness of Trivalent Inactivated Influenza Vaccine – Marshfield, Wisconsin, 2007-08 Influenza Season

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Objectives

- Estimate VE for preventing medically attended acute respiratory illness (MAARI) that is confirmed as influenza
- Provide interim and final estimates of VE for the 2007-08 influenza season
- Include all groups for which ACIP recommends annual vaccination in VE estimates

Methods - 1

- Patients living in a 14 postal-code area surrounding the Marshfield Clinic eligible for the study (N=49,712 residents)
- Enrollment began on 21 Jan 2008; interim data through 8 Feb reported
- Patients with MAARI (must include feverishness, chills, or cough) were recruited during or after a clinical encounter
- Patients with illness duration $\leq$ 8 days were excluded

Methods - 2

- Consenting persons tested for influenza by real-time RT-PCR with nasal (children) or nasopharyngeal swab specimens
- RT-PCR positive specimens also cultured
- CDC antigenically characterized isolates
- Immunization status determined using a regional electronic vaccine registry
- Individuals classified as immunized beginning 14 days after receipt of vaccine

Study Design

- Case-control study
- Cases: enrolled MAARI patients with influenza infection diagnosed by RT-PCR
- Controls: enrolled MAARI patients negative by RT-PCR
- Likelihood of vaccination associated with propensity to seek health care, particularly among older Marshfield Clinic patients

Study Design

- Vaccinated persons aged 65+ twice as likely to have MAARI visit as unvaccinated persons during Jan-Feb ($p < 0.001$)
- Use of test-negative controls helped to adjust for this source of bias in VE, as all study subjects sought care for MAARI
- Logistic regression models adjusted for age, week of enrollment, and the presence of a chronic medical condition
- VE = 100 x (1 – adjusted odds ratio)

Results

- During 21 Jan – 8 Feb, 1779 MAARI patients were assessed for eligibility
- 48% not eligible; 91% of exclusions due to absence of feverishness, chills, or cough or illness duration 8 days or longer
- 639 (69%) of eligible patients enrolled
- After exclusion of 23 partially immunized children, enrollment was 616
- 191 (31%) of 616 enrolled tested positive for influenza by RT-PCR; 75% had influenza A

Data from 8 Jan – 21 Feb 2008	Influenza positive cases (n=191) % Vaccinated	Influenza negative controls (n=425) % Vaccinated	Adjusted VE % (95% CI)
All influenza			
All case	19	39	44 (11-65)
ACIP	35	51	34 (-31-67)
Healthy	11	24	54 (12-76)
Influenza A			
All cases	15	38	58 (28-76)
ACIP	35	50	49 (-14-77)
Healthy	8	24	68 (29-86)
Influenza B			
All cases	30	33	-35 (-172-33)
ACIP	39	49	-32 (-287-55)
Healthy	7	18	-33 (-241-48)

Preliminary Laboratory Data

- Subtyping by RT-PCR found all submitted influenza A specimens were H3N2
- Most H3N2 viruses characterized were were A/Brisbane/10/2007-like, a drift variant of the vaccine strain
- All B viruses characterized were B/Florida/04/2006-like, in the B/Yamagata lineage, distinct from B/Victoria lineage in the 2007-08 vaccine

Limitations

- VE estimates only for medically attended influenza, not all symptomatic influenza infections
- Possibility for false-negative results despite using RT-PCR
- Not necessarily powered to examine VE by age or severity
- Results apply to patients enrolled in one specific area

Conclusions

- Despite a suboptimal match between 2 of 3 vaccine strains and viruses isolated from study participants, interim VE was 44%
- VE for H3N2 medically attended infections was 58%; VE not demonstrated for B
- Need to interpret antigenic characterization data with clinical effectiveness data
- Feasible to produce within-season estimates of VE in the United States

Next Steps

- Final estimates available soon, pending the integration of laboratory results
- Plan to examine effectiveness by age
- Through new cooperative agreement, use rapid VE methods developed with Marshfield Clinic at 4 sites beginning in the 2008-09 season
  - Plan to make interim estimates by age group
  - May have power for effectiveness against hospitalized outcomes

Investigators

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