Influenza
Epidemiology, Treatment, and Prevention

Matt Zahn, MD
Medical Director
Epidemiology and Assessment
Orange County Health Care Agency
Orange County

- Population of 3,010,232
- 60.8% White
- 33.7% Hispanic
- 2.2% African American
- 9% Asian
Epidemiology and Assessment Staff

- Physicians-2
- Program Manager
- Public Health Nurses-5
- Epidemiologist-3
- Research Analysts-2
- Office staff
Disease Control & Epidemiology

- Surveillance for communicable diseases
- Investigation of cases (and contacts) of communicable disease
- Detection, investigation and control of outbreaks
- Post-exposure prophylaxis and other protective actions
- Preparedness planning with schools, health care, businesses, airport, other partners
- Education of medical community about local occurrence of communicable diseases
Influenza Symptoms

- Fever
- Cough
- Runny nose
- Eye drainage
- Cause illness in kids and adults
More Serious Symptoms

- Primarily Pneumonia
- Occasionally neurologic disease
  - Encephalitis
  - Guillain Barre disease
Rapid Influenza Tests

- Many clinics have this test

- Rapid diagnostic tests for influenza have:
  - High specificity (>90%)- if positive, it’s probably flu
  - Low to moderate sensitivity (20%–70%)- if the test is negative, it might have not detected virus that was there

- Sensitivities vary by test and by seasonal strain

- RIDTs appear to have higher sensitivity when used in young children

- Influenza PCR is current gold standard

- Orange County Public Health can assist with arranging testing in assessing for outbreaks
Seasonal Influenza

- During any given season, infection rates are estimated between 10% to 20% in the general population

- Thought to be higher in:
  - Schoolchildren
  - Residents of long term care facilities

- Over 90% of morbidity and mortality occurs in persons over 65 years of age

- 2,000-48,000 flu deaths occur annually
Why do we care if it’s flu?

• More likely to lead to severe disease in all ages

• Vaccine-preventable

• Antiviral preventable early in disease and for persons with underlying immune illness

• OCHCA can supply viral swabs for testing

• OCHCA labs can perform testing if circumstances warrant
Measures to Prevent Spread of Flu

• Everyone 6 months of age and older without a contraindication should receive the influenza vaccine

• Effectiveness can vary with the flu season

• Vaccine generally has been shown to best prevent severe disease

• Stay home if you are sick during flu season!

• Virus does not survive for long on surfaces
  • Wash your hands well!
2015-16 United States Influenza Season

• Overall influenza activity was moderate
• Influenza activity was lower and peaked later compared with previous three seasons
• Compared to three previous influenza seasons:
  • Lower percentage of outpatient visits for influenza-like illness
  • Lower hospitalization rates
  • Lower percentage of deaths attributed to pneumonia and influenza compared with the preceding three seasons
Current Flu Season Nationally

*This map indicates geographic spread and does not measure the severity of influenza activity.*
Figure 1. Number of Influenza Case Reports by Type and Percent of Visits for Influenza-Like-Illness by Disease Week

Table 1. Types of Influenza for Reported OC Cases

<table>
<thead>
<tr>
<th>Type of Influenza</th>
<th>#</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza A</td>
<td>1,335</td>
<td>52.0</td>
</tr>
<tr>
<td>Influenza B</td>
<td>1,225</td>
<td>47.7</td>
</tr>
<tr>
<td>Influenza A &amp; B</td>
<td>8</td>
<td>0.3</td>
</tr>
<tr>
<td>Influenza A/B-unspecified</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Total Influenza Reports</td>
<td>2,568</td>
<td>100</td>
</tr>
</tbody>
</table>

- Influenza B (All lineages)
- Influenza A (All subtypes)
- % ILI
<table>
<thead>
<tr>
<th></th>
<th>#</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Specimens Positive at OCPHL</strong></td>
<td>964</td>
<td>1,143</td>
<td>84.3%</td>
</tr>
<tr>
<td>Ili Sentinel Providers</td>
<td>40</td>
<td>98</td>
<td>40.8%</td>
</tr>
<tr>
<td><strong>Influenza A</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtype</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A/(H1N1)pdm2009</td>
<td>346</td>
<td>510</td>
<td>67.8%</td>
</tr>
<tr>
<td>A/H3</td>
<td>163</td>
<td>510</td>
<td>32.0%</td>
</tr>
<tr>
<td>Subtype Unknown</td>
<td>1</td>
<td>510</td>
<td>0.2%</td>
</tr>
<tr>
<td><strong>Influenza B</strong></td>
<td>443</td>
<td>964</td>
<td>46.0%</td>
</tr>
<tr>
<td>Lineage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yamagata</td>
<td>348</td>
<td>443</td>
<td>78.6%</td>
</tr>
<tr>
<td>Victoria</td>
<td>83</td>
<td>443</td>
<td>18.7%</td>
</tr>
<tr>
<td>Lineage Unknown</td>
<td>12</td>
<td>443</td>
<td>2.7%</td>
</tr>
<tr>
<td><strong>Other Viruses Identified</strong></td>
<td>11</td>
<td>964</td>
<td>1.1%</td>
</tr>
</tbody>
</table>

Other viruses identified at the OCPHL include adenovirus (3), parainfluenza virus (PIV) Type 1 (5), PIV Type 3 (1), and respiratory syncytial virus (5).
Influenza Vaccine Options

- Inactivated trivalent
- High dose trivalent
- Inactivated quadrivalent
- LAIV quadrivalent
- Intradermal trivalent
- Cell culture based trivalent
- Recombinant trivalent
2016-17 Influenza Vaccine Composition

• An A/California/7/2009 (H1N1)pdm09-like virus
• A/Hong Kong/4801/2014 (H3N2)-like virus
• B/Brisbane/60/2008-like virus (B/Victoria lineage)

Recommended for everyone 6 months of age and older
Influenza Vaccine Efficacy

- RCTs of inactivated influenza vaccine among adults under 65 years of age have estimated 50-70% vaccine efficacy when vaccine well-matched to circulating viruses

- 50%–60% effective in preventing hospitalization or pneumonia

- 80% effective in preventing death among residents of LTCFs

- 30%–40% effective in preventing influenza in elderly persons residing in LTCFs

Beran et al., 2009, 2006-2007 season; Jackson et al., 2010, 2005-2006 season; Monto et al., 2009, 2007-2008 season.)
US Flu VE Network: 5 Sites and Principal Investigators

- **Group Health Cooperative**
  - Lisa Jackson
  - Mike Jackson

- **Marshfield Clinic Research Foundation**
  - Ed Belongia
  - Huong McLean

- **University of Michigan**
  - Arnold Monto
  - Suzanne Ohmit

- **University of Pittsburgh**
  - Rick Zimmerman
  - Patricia Nowalk

- **CDC**
  - Alicia Fry
  - Brendan Flannery

- **Baylor Scott and White Health**
  - Manju Gaglani
US Flu VE Network: Methods

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

Dates of enrollment: November 2, 2015–April 15, 2016

Design: Test-negative design

- Comparing vaccination odds among influenza RT-PCR positive cases and RT-PCR negative controls
- Vaccination status: receipt of at least one dose of any 2015–16 seasonal flu vaccine according to medical records, immunization registries, and/or self-report (with reported date)
- Analysis: VE = (1 – adjusted OR) x 100%
  - Adjustment for study site, age, self-rated general health status, race/Hispanic ethnicity, interval (days) from onset to enrollment, and calendar time
LAIV and IIV vaccine effectiveness among 2-8 yrs, by influenza type/subtype, 2015-16

<table>
<thead>
<tr>
<th></th>
<th>Any influenza</th>
<th>H1N1pdm09</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LAIV</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total, Flu +</td>
<td>165</td>
<td>99</td>
<td>59</td>
</tr>
<tr>
<td>Vaccinated, Flu +</td>
<td>29</td>
<td>19</td>
<td>10</td>
</tr>
<tr>
<td><strong>IIV</strong></td>
<td>198</td>
<td>119</td>
<td>72</td>
</tr>
<tr>
<td>Total, Flu +</td>
<td>62</td>
<td>39</td>
<td>23</td>
</tr>
<tr>
<td>Vaccinated, Flu +</td>
<td>62</td>
<td>39</td>
<td>23</td>
</tr>
</tbody>
</table>
# Influenza Pandemics

<table>
<thead>
<tr>
<th>Pandemic Year</th>
<th>Worldwide Excess Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1918 --H1N1</td>
<td>30 million</td>
</tr>
<tr>
<td>1957 --H2N2</td>
<td>1 million</td>
</tr>
<tr>
<td>1968 --H3N2</td>
<td>500,000</td>
</tr>
<tr>
<td>2009 –H1N1</td>
<td>18,000</td>
</tr>
</tbody>
</table>
Antigenic Drift

- Point mutations in HA or NA
- Results in relatively small changes in virus
- Apparently led to 1918 influenza virus
Hemagglutinin

- Important determinant of virulence
- Must be cleaved by proteases to be active
Antigenic Shift

- Reassortment of gene segments between two viruses
- Occurred in 1957 and 1968 pandemics
Influenza and Avian Populations

- Reservoirs of avian influenza often apparently fowl-ducks and geese
- Migratory birds and poultry trafficking spread virus to local flocks
Spring of 2013: the World Health Organization (WHO) reported 132 human H7N9 infections, with 44 deaths. Most cases had illness onset during the month of April.
H7N9 Influenza A and Avian Populations

- H7N9 has been identified in ducks, chickens, pigeons
- The virus does not seem to make birds sick
- Will likely make controlling spread of the virus in the future difficult
- Human cases in Asia are likely to continue for the foreseeable future
H5N1 Virus in Poultry

- Large amounts of virus are secreted in bird droppings
- Airborne virus can spread the disease from bird to bird, causing infection when the virus is inhaled
- Spreads easily from one poultry farm to another via multiple mechanisms
H5 N1 Avian Influenza

- December 2003–December 2007:
- 335 human cases of avian influenza A (H5N1)
- 206 deaths
- 12 countries involved
- Vietnam with 93 cases in 2003-5
- Indonesia with 93 cases in 2006-7
Human-to-Human Transmission of H5N1

- Multiple events have apparently occurred
- Always associated with very close contact
- Remains uncommon
- No sustained human-to-human transmission
Avian Influenza Clinical Characteristics

- High mortality rate, primarily due to advanced pulmonary disease

Hien. NEJM 2004;350:1179
H7N9 and Human to Human Transmission

- No sustained human to human transmission of H7N9 has been seen
- At least one instance of outbreak in a family is suspected to be due to human to human passage
- Limited human to human transmission has been seen in the past-H5N1
HCA Laboratory

• Can currently:
  • Identify influenza by PCR
  • Identify H3N2 and H1N1 seasonal influenza
  • Samples positive for influenza by PCR and negative for seasonal flu strains would be considered suspect
  • CDPH, CDC will likely participate in testing at that point
Infection control precautions for Influenza

- Influenza is passed by droplet.
- Usually exposure within 3 feet
- Standard precautions healthcare staff use include:
  - Gown
  - Glove
  - Mask
H5N1 Virulence Factors

- Multiple genetic changes are responsible
- Non-structural protein NS1 inhibits immune response
- H5N1 isolates induce pro-inflammatory cytokines
- ‘Cytokine storm’ seems to be cause of severe disease
Antivirals

- Oseltamivir
- Zanamivir
Personal Belief Exemption Rates in Orange County
Kindergarten Up to Date Immunization Rates
2004-5 H5N1 Clades

Clade 1

Clade 2

WHO, EID, 2005
• 2006 H5N1 Fujian Strain

• Found in southern China

• Accounted for 95% of all avian samples collected from April to June 2006

• May be resistant to current avian vaccines

Fujian H5N1 Strain

From July 2005 through June 2006 in China:

- Percentage of ducks, geese, and chickens infected with H5N1 rose from 0.9% to 2.4%
- Subsequently led to human disease in China

What Will the Next Pandemic Look Like?
Annual Influenza Season

• 500,000 deaths worldwide each year

• In the United States:

  • 25-50 million infections
  
  • 290,000 (85,000–550,000) hospitalizations
  
  • 30-50,000 deaths
Pandemic Response
Rapid H5N1 Studies

- H5N1 Virus Real-Time RT-PCR
- Pharyngeal swabs more effective than nasal swabs in diagnosing H5N1 infection
- For highly pathogenic influenza A/H5 virus
- Testing limited to Laboratory Response Network
  - 140 U.S. laboratories
- FDA approved, February, 2006
Superior relative efficacy of live attenuated influenza vaccine compared with inactivated influenza vaccine in young children with recurrent respiratory tract infections

Ashkenazi, S

- Children 6 to 71 months of age were randomized to receive 2 doses of CAIV-T (n = 1101) or TIV (n = 1086) before the start of the 2002–2003 influenza season.
- 52.7% (95% CI = 21.6%–72.2%) fewer cases of influenza were observed in CAIV-T than in TIV recipients.
- Greater relative efficacy for CAIV-T observed for:
  - Influenza A/H1N1
  - Influenza B
- Relative to TIV, CAIV-T reduced the number of RTI-related healthcare provider visits by 8.9% (90% CI = 1.5%–15.8%) and missed days of school, kindergarten, or day care by 16.2% (90% CI = 10.4%–21.6%)
Live attenuated versus inactivated influenza vaccine in infants and young children

Belshe, et al.

- 7852 children 6 to 59 months of age
- Randomly assigned in a 1:1 ratio to receive either trivalent LAIV or trivalent IIV
- Influenza-like illness was monitored with cultures throughout the 2004–2005 influenza season.

Belshe, et al.

Figure 1. Kaplan–Meier Curves for the Time to the First Culture-Confirmed Report of Influenza in the Two Vaccine Groups.
### 2013-2014 LAIV Effectiveness

**TABLE.** Mid-season influenza vaccine effectiveness (VE) among different populations for the 2013–2014 influenza season

<table>
<thead>
<tr>
<th>Population</th>
<th>Viral subtype</th>
<th>Vaccine type</th>
<th>No. of cases (% vaccinated)</th>
<th>No. of controls (% vaccinated)</th>
<th>Crude VE (95% CI)</th>
<th>Adjusted VE (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active component service members (AFHSC)</td>
<td>Overall</td>
<td>Any type</td>
<td>518 (90)</td>
<td>2060 (91)</td>
<td>11 (-27–37)</td>
<td>7 (-32–35)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IIV</td>
<td>183 (32)</td>
<td>1086 (48)</td>
<td>31 (0–53)</td>
<td>28 (-5–51)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LAIV</td>
<td>324 (56)</td>
<td>910 (40)</td>
<td>-13 (-63–22)</td>
<td>-17 (-70–19)</td>
</tr>
<tr>
<td>Civilians and dependents (NHRC)</td>
<td>Overall</td>
<td>Any type</td>
<td>106 (19)</td>
<td>278 (33)</td>
<td>52 (17–72)</td>
<td>53c (17–74)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Influenza A (H1)</td>
<td>Any type</td>
<td>84 (17)</td>
<td>278 (33)</td>
<td>59 (23–78)</td>
</tr>
<tr>
<td>Dependents (USAFSAM)</td>
<td>Overall</td>
<td>Any type</td>
<td>339 (25)</td>
<td>469 (39)</td>
<td>44 (24–59)</td>
<td>66c (51–76)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IIV</td>
<td>302 (17)</td>
<td>425 (33)</td>
<td>57 (38–70)</td>
<td>74c (60–83)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LAIV</td>
<td>234 (15)</td>
<td>248 (16)</td>
<td>6 (-54–42)</td>
<td>40 (-5–66)</td>
</tr>
</tbody>
</table>

Cost et al 2014
### Adjusted VE against any influenza for fully vaccinated children and adolescents, by vaccine type, 2014-15

**Influenza-positive and influenza-negative vaccinated**

**Adjusted VE**

*Adjustment for age (groups or years), site, race/ethnicity, sex, general health status, calendar time, interval from onset to enrollment*

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Live Attenuated (LAIV4)</th>
<th>Influenza-positive %</th>
<th>Influenza-negative %</th>
<th>Adjusted VE (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2–17 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2–17 years</td>
<td>623</td>
<td>19%</td>
<td>1677</td>
<td>22%</td>
</tr>
<tr>
<td>2–8 yrs</td>
<td>316</td>
<td>22%</td>
<td>985</td>
<td>25%</td>
</tr>
<tr>
<td>9–17 yrs</td>
<td>307</td>
<td>16%</td>
<td>692</td>
<td>18%</td>
</tr>
<tr>
<td>2–17 years</td>
<td>693</td>
<td>27%</td>
<td>2068</td>
<td>37%</td>
</tr>
<tr>
<td>2–8 yrs</td>
<td>348</td>
<td>29%</td>
<td>1235</td>
<td>40%</td>
</tr>
<tr>
<td>9–17 yrs</td>
<td>345</td>
<td>25%</td>
<td>833</td>
<td>32%</td>
</tr>
</tbody>
</table>
Live Attenuated Vaccine Effectiveness in 2014-15

• Live attenuated influenza vaccine (LAIV) had no significant vaccine effectiveness based on CDC data from 2014-15

• No evidence of improved effectiveness in preventing disease caused by influenza A H3N2 drifted strain

• Preferential recommendation to provide LAIV to children 2-8 years of age was rescinded by ACIP
LAIV and Temperature Instability

- Hypothesized that reduced effectiveness of LAIV against the influenza A (H1N1)pdm09 virus was due to the reduced vaccine stability of the LAIV vaccine virus, A/California/2009/(H1N1) caused by a single amino acid mutation.

- New H1N1 vaccine virus - (A/Bolivia/559/2013) was used for LAIV in 2015-16 season.
LAIV and IIV vaccine effectiveness ages 2-17 years by influenza type/subtype, 2015-16

Adjusted Vaccine Effectiveness (%)

Any influenza
H1N1pdm09
B/Yamagata
B/Victoria

LAIV4
IIV3/4
LAIV4
IIV3/4
LAIV4
IIV3/4
LAIV4
IIV3/4

Total, flu+
Vaccinated, flu+

ACIP, June, 2016
In a 2004-2005 Randomized Trial, LAIV Had Higher Efficacy Against All Influenza Strains Compared to IIV Regardless of Prior Vaccination

(Belshe et al, Children 6-59 Months)*

*22% of LAIV recipients and TIV recipients who had previously been vaccinated with TIV received a single dose of LAIV in Study CP111. Data for all strains, regardless of antigenic match. Data on file at MedImmune. LAIV is not approved for children under 24 months of age.
LAIV Efficacy in 1st and 2nd Seasons of Vaccination

4 Randomized Placebo-controlled Studies, All Matched Strains
Children 6-71 months in Year 1; Two doses in Year 1, One dose in Year 2

- LAIV is not approved for children under 24 months of age.

2009-2014 US VE Against H1N1pdm09 in Children <9 Years

Adjusted VE (%)

- 2009-10 CDC
  - IIV ≥14 Days: 32%
  - LAIV ≥7 Days: 55%
- 2010-11 CDC
  - IIV ≥14 Days: 82%
- 2013-14 CDC
  - IIV ≥14 Days: 60%
  - LAIV ≥14 Days: 69%
- 2013-14 ICICLE
  - IIV: -31%
  - LAIV: -8%

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* LAIV data for children 2-8 years of age and IIV data for children 6mo-9 years of age from Griffin, 2011. LAIV is not indicated for children under 24 months; * Data for children 2-8 years of age from CDC personal communication; ** Data for children 2-8 years of age from CDC personal communication and MedImmune data on file. No data is available regarding effectiveness against H1N1pdm09 strains in 2011-12 or 2012-13 as H1N1 strains did not circulate to a meaningful degree during those seasons. CI's truncated at 0 to enable graphical display.
## Adjusted vaccine effectiveness against medically attended influenza, 2015–2016

<table>
<thead>
<tr>
<th>Any influenza A or B virus</th>
<th>N vaccinated/Total (%)</th>
<th>N vaccinated/Total (%)</th>
<th>Influenza positive</th>
<th>Influenza negative</th>
<th>Unadjusted VE % (95% CI)</th>
<th>Adjusted* VE % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>541/1310</td>
<td>3222/5652</td>
<td>41</td>
<td>57</td>
<td>47 (40 to 53)</td>
<td>48 (41 to 55)</td>
</tr>
<tr>
<td>6m – 8 y</td>
<td>114/264</td>
<td>804/1382</td>
<td>43</td>
<td>58</td>
<td>45 (29 to 58)</td>
<td>47 (30 to 60)</td>
</tr>
<tr>
<td>9–17 y</td>
<td>41/162</td>
<td>303/681</td>
<td>25</td>
<td>44</td>
<td>58 (38 to 71)</td>
<td>62 (43 to 75)</td>
</tr>
<tr>
<td>18–49 y</td>
<td>155/494</td>
<td>917/1946</td>
<td>31</td>
<td>47</td>
<td>49 (37 to 58)</td>
<td>50 (38 to 61)</td>
</tr>
<tr>
<td>50–64 y</td>
<td>152/282</td>
<td>592/916</td>
<td>54</td>
<td>65</td>
<td>36 (16 to 51)</td>
<td>32 (9 to 49)</td>
</tr>
<tr>
<td>≥65 y</td>
<td>79/108</td>
<td>606/727</td>
<td>73</td>
<td>83</td>
<td>46 (13 to 66)</td>
<td>46 (11 to 67)</td>
</tr>
<tr>
<td>Overall, any IIIV</td>
<td>499/1268</td>
<td>3087/5510</td>
<td>39</td>
<td>56</td>
<td>49 (42 to 55)</td>
<td>51 (43 to 57)</td>
</tr>
</tbody>
</table>

* Multivariate logistic regression models adjusted for site, age categories (6m-8y, 9-17y, 18-49y, 50-64y, ≥65y), sex, race/Hispanic ethnicity, self-rated general health status, interval from onset to enrollment, and month of onset.
Effectiveness of LAIV and IIV against influenza A/H1N1pdm09, 2009-11

<table>
<thead>
<tr>
<th></th>
<th>LAIV %</th>
<th>IIV %</th>
<th>Total # of flu +'s</th>
<th>Vacc flu+'s</th>
</tr>
</thead>
<tbody>
<tr>
<td>School Children</td>
<td>81</td>
<td>58</td>
<td>92</td>
<td>4, 19</td>
</tr>
<tr>
<td>Hospitalized</td>
<td>100</td>
<td>66</td>
<td>78</td>
<td>0, 1</td>
</tr>
<tr>
<td>School-based vaccination</td>
<td>60</td>
<td>48</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>

Adapted from ACIP presentation, Uzicanin, JID 2012, Hadler JID 2012, Pannaraj, 2014
Background

- Preliminary data indicate poor LAIV VE for past three influenza seasons in the U.S. (2013-14 through 2015-16) among 2 through 17 year olds
  - 2013-14: H1N1-predominant—poor HA stability? IIV effective
  - 2014-15: H3N2-predominant—drift; poor VE for LAIV and IIV
  - 2015-16: H1N1-predominant—poor performance of LAIV with new H1N1; IIV effective

- Comparison among datasets for LAIV VE against H1N1pdm09 (again, all preliminary):
  - US Flu VE -21% (-108% to 30%)
  - MedImmune 47% (-6% to 74%)
  - DoD 15% (-8% to 31%)

- Cause of low VE of LAIV for H1N1pdm09 not yet known
Current Influenza Season

- Influenza A and B infections are being seen locally and nationally

- Influenza A H1N109 is predominant influenza A strain this year-covered by the vaccine

- Both H3N2 and H1N1 influenza A strains are being seen in Orange County
CDC Recommendations for Response to Influenza in Long Term Care Facilities

- Vaccination
- Influenza testing
- Infection control measures
- Antiviral treatment
- Antiviral prophylaxis
Influenza vaccine
Infection Control
Antiviral Treatment and Prophylaxis
Antiviral Chemoprophylaxis and Staff

- Antiviral chemoprophylaxis can be considered or offered to unvaccinated personnel who provide care to persons at high risk of complications.

- Chemoprophylaxis may be considered for all employees, regardless of their vaccination status, if the outbreak is caused by a strain of influenza virus that is not well matched by the vaccine.

- Antiviral chemoprophylaxis should also be considered in personnel for whom influenza vaccine is contraindicated.

- An emphasis on early treatment is an alternative to chemoprophylaxis in managing certain persons who have had a suspected exposure to influenza virus.
Multicenter Study of Nursing Home Residents Receiving Oseltamivir During Influenza Season

- Randomized controlled trial
- 1998-1999 influenza season
- Thirty-one residential homes for seniors across United States and Europe
- Five hundred forty-eight frail seniors living in long term care facilities enrolled
- Mean age 81 years
- >80% vaccinated
- Received either oseltamivir or placebo for 6 weeks during peak flu season
Multicenter Study of Nursing Home Residents Receiving Oseltamivir During Influenza Season

- Oseltamivir administration resulted in a 92% reduction in the incidence of laboratory-confirmed clinical influenza compared with placebo.

- Influenza illness occurred in:
  - Placebo group in 12/272 (4.4%)
  - Prophylaxis group in 1/276 (0.4%)

- Of subjects vaccinated against influenza, oseltamivir was 91% effective in preventing laboratory-confirmed clinical influenza (placebo 11/218 (5.0%), oseltamivir 1/222 (0.5%); P = .003).

- Oseltamivir associated with reduction in the incidence of secondary complications:
  - Placebo 7/272 (2.6%)
  - Oseltamivir 1/276 (0.4%); P = .037

- Similar incidence of adverse events, including gastrointestinal effects, occurred in both groups.

JAGS 49:1025–1031, 2001
Multicenter Study of Nursing Home Residents Receiving Oseltamivir During Influenza Season

Figure 1. The incidence of laboratory-confirmed clinical influenza in subjects receiving oral oseltamivir 75 mg or placebo once daily for 6 weeks.
Wisconsin Veterans LTCF Study

- Skilled nursing facility with four buildings
- Review of influenza outbreaks from 1993–2000
- Daily census was 721
- Residents 78.5% male
- Average age 76 years, and the annual mortality rate was 17.4%

Drinka, et al. ICHE, October, 2002
<table>
<thead>
<tr>
<th>Season</th>
<th>Residents Vaccinated</th>
<th>Staff Vaccinated</th>
<th>No. of Cultures Performed</th>
<th>Positive Cultures</th>
<th>Culture Refusals</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993–1994</td>
<td>86%</td>
<td>41%</td>
<td>351</td>
<td>19.4%</td>
<td>–</td>
</tr>
<tr>
<td>1994–1995</td>
<td>88%</td>
<td>41%</td>
<td>410</td>
<td>2.9%</td>
<td>–</td>
</tr>
<tr>
<td>1996–1997</td>
<td>92%</td>
<td>48%</td>
<td>392</td>
<td>1.0%</td>
<td>–</td>
</tr>
<tr>
<td>1997–1998</td>
<td>91%</td>
<td>55%</td>
<td>750</td>
<td>20.5%</td>
<td>16</td>
</tr>
<tr>
<td>1998–1999</td>
<td>90%</td>
<td>50%</td>
<td>394</td>
<td>4.8%</td>
<td>6</td>
</tr>
<tr>
<td>1999–2000</td>
<td>90%</td>
<td>55%</td>
<td>243</td>
<td>9.5%</td>
<td>3</td>
</tr>
<tr>
<td>Season</td>
<td>Days From Initial Isolate</td>
<td>Building Attack Rate</td>
<td>Examples of Delayed Prophylaxis*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------------------</td>
<td>---------------------------</td>
<td>----------------------</td>
<td>----------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(No. of Positive Cultures)</td>
<td>In the Entire Facility</td>
<td>in the Building</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1993–1994 (68)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building S</td>
<td>Initial</td>
<td>9.0%</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building A</td>
<td>8</td>
<td>1.5%</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building O</td>
<td>26</td>
<td>15.5%</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building M</td>
<td>27</td>
<td>13.8%</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1994–1995 (12)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building S</td>
<td>Initial</td>
<td>4.0%</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building A</td>
<td>6</td>
<td>1.5%</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building O</td>
<td>29</td>
<td>0.5%</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building M</td>
<td>–</td>
<td>0%</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1996–1997 (4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building M</td>
<td>Initial</td>
<td>0.9%</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building O</td>
<td>11</td>
<td>1.0%</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building S</td>
<td>64</td>
<td>0.5%</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building A</td>
<td>–</td>
<td>0%</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1997–1998 (154)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building O</td>
<td>Initial</td>
<td>14.5%</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building M</td>
<td>5</td>
<td>25.0%</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building A</td>
<td>33</td>
<td>19.5%</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building S</td>
<td>42</td>
<td>28.0%</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1998–1999 (19)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building A</td>
<td>Initial</td>
<td>6.8%</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building O</td>
<td>32</td>
<td>2.5%</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building S</td>
<td>–</td>
<td>0%</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building M</td>
<td>–</td>
<td>0%</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1999–2000 (23)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building O</td>
<td>Initial</td>
<td>2.5%</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building S</td>
<td>8</td>
<td>1.0%</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building M</td>
<td>28</td>
<td>9.5%</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building A</td>
<td>29</td>
<td>2.4%</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Four or more residents on a floor with positive cultures whose specimens had been collected within 5 days before the application of prophylaxis.
Influenza in LTCF

Roommates

- Influenza A was cultured in 62 double rooms
- The roommate was infected in 12 (19.4%)
- During 3,294 resident-seasons, influenza was cultured in 208 single rooms (6.3%).
- Roommates had a 3.07 relative risk (CI 95%, 1.61–5.78) of acquiring influenza

Drinka ICHE Nov 2003
Use of Oseltamivir During Influenza Outbreaks in Ontario Nursing Homes

- 11 facilities were had outbreaks in Ontario, Canada, in 1999-2000
- One facility used oseltamivir for treatment and amantadine for prophylaxis
- Nine (10 outbreaks) recommended oseltamivir for treatment and prophylaxis (after amantadine failure in five and as primary prophylaxis in five).
- Use of oseltamivir was associated with termination of the outbreak in all eight evaluable outbreaks
- 185 cases in 993 residents
- 63 (35%) were treated with antibiotics
- 37 (21%) were diagnosed with pneumonia
- 19 (11%) were hospitalized, and 16 (9%) died

JAGS 50:508, 2002
Table 4. Resident Characteristics and Outcomes Associated with Influenza Cases in Residents in Long-Term Care Facilities: Ontario Oseltamivir Compassionate Use Program, 1999–2000

<table>
<thead>
<tr>
<th>Characteristic/Octome</th>
<th>No Therapy (n = 23)</th>
<th>Amantadine Early* (n = 19)</th>
<th>Illness Onset While Receiving Amantadine Prophylaxis, No Further Therapy (n = 47)</th>
<th>Oseltamivir Late** (n = 23)</th>
<th>Oseltamivir Early *1(n = 50)</th>
<th>Illness Onset While Receiving Oseltamivir Prophylaxis, No Further Therapy*6 (n = 14)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, median (range)</td>
<td>84 (53–99)</td>
<td>88 (60–93)</td>
<td>85 (65–101)</td>
<td>82 (69–95)</td>
<td>84 (66–97)</td>
<td>87 (76–100)</td>
<td>.42</td>
</tr>
<tr>
<td>Gender, n (% male)</td>
<td>5 (22)</td>
<td>4 (21)</td>
<td>16 (34)</td>
<td>3 (13)</td>
<td>18 (37)</td>
<td>2 (14)</td>
<td>.17</td>
</tr>
<tr>
<td>Comorbid illnesses,</td>
<td>2 (1–4)</td>
<td>2 (0–4)</td>
<td>2 (1–5)</td>
<td>2 (1–4)</td>
<td>2 (0–5)</td>
<td>2 (1–4)</td>
<td>.21</td>
</tr>
<tr>
<td>median (range)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dependent in ADLs, n (%)</td>
<td>16 (73%)</td>
<td>12 (63%)</td>
<td>33 (70%)</td>
<td>16 (70%)</td>
<td>31 (62%)</td>
<td>9 (64%)</td>
<td>.94</td>
</tr>
<tr>
<td>Received influenza</td>
<td>17 (74%)</td>
<td>18 (95%)</td>
<td>45 (96%)</td>
<td>19 (83%)</td>
<td>46 (92%)</td>
<td>12 (86%)</td>
<td>.01</td>
</tr>
<tr>
<td>vaccine, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outcome, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotic therapy</td>
<td>15 (65%)</td>
<td>7 (37%)</td>
<td>12 (26%)</td>
<td>15 (70%)</td>
<td>10 (20%)</td>
<td>2 (14%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Serious complication†</td>
<td>11 (48%)</td>
<td>3 (16%)</td>
<td>13 (28%)</td>
<td>8 (35%)</td>
<td>3 (6%)</td>
<td>0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>5 (22%)</td>
<td>2 (11%)</td>
<td>8 (17%)</td>
<td>4 (17%)</td>
<td>0</td>
<td>0</td>
<td>.015</td>
</tr>
<tr>
<td>Death</td>
<td>5 (22%)</td>
<td>2 (11%)</td>
<td>7 (15%)</td>
<td>1 (4%)</td>
<td>1 (2%)</td>
<td>0</td>
<td>.04</td>
</tr>
</tbody>
</table>
Review of New York State LTCF Influenza Outbreaks

- Over 3 winter seasons
- 89 identified outbreaks in 59 of 180 LTCFs
- 21 facilities reported multiple outbreaks
- Influenza A virus identified in 69
Review of New York State LTCF Influenza Outbreaks

- Amantadine chemoprophylaxis was initiated in 56 of these outbreaks

- Complete data for analysis in 52 (93%)

- Amantadine chemoprophylaxis was initiated facility-wide in 40 (77%)

- In affected unit in 16

- The time between onset of influenza A outbreak and initiation of chemoprophylaxis ranged from 0 to 34 days (median duration, 5 days)

CID 2008:47 July
Table 2. Multivariate analysis of covariance in a study of outbreaks of influenza A by timing of chemoprophylaxis.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Interval between outbreak and initiation of chemoprophylaxis</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of outbreak, mean days (95% CI)</td>
<td>6.7 (2.8–10.7)</td>
<td>18.3 (14.2–22.5)</td>
</tr>
<tr>
<td>Incidence rate, mean no. of cases per 100 residents (95% CI)</td>
<td>6.2 (3.7–6.8)</td>
<td>10.5 (7.9–13.2)</td>
</tr>
<tr>
<td>Case-fatality rate, mean no. of deaths per 100 residents (95% CI)</td>
<td>0.5 (−0.86 to 1.8)</td>
<td>3.3 (1.9–4.6)</td>
</tr>
</tbody>
</table>

**NOTE.** The analysis was adjusted for the following covariates: season year, facility bed capacity, and proportion of residents who were vaccinated.
Table 1. Outbreaks of influenza A by timing of chemoprophylaxis.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Interval between outbreak and initiation of chemoprophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤5 days</td>
</tr>
<tr>
<td>Proportion (%) of outbreaks</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>27/52 (52)</td>
</tr>
<tr>
<td>By influenza season year</td>
<td></td>
</tr>
<tr>
<td>2001–2002</td>
<td>9/17 (53)</td>
</tr>
<tr>
<td>2002–2003</td>
<td>3/5 (60)</td>
</tr>
<tr>
<td>2003–2004</td>
<td>15/30 (50)</td>
</tr>
<tr>
<td>Facility bed capacity, mean no. of beds ± SD</td>
<td>360 ± 205</td>
</tr>
<tr>
<td>Percentage of residents vaccinated, mean % ± SD</td>
<td>93 ± 4.8</td>
</tr>
<tr>
<td>Duration of outbreak, mean days ± SD</td>
<td>6.6 ± 4.9</td>
</tr>
<tr>
<td>Incidence rate, mean no. of cases per 100 residents ± SD</td>
<td>6.4 ± 5.9</td>
</tr>
<tr>
<td>Case-hospitalization rate, mean no. of hospitalizations per 100 residents ± SD</td>
<td>9.2 ± 19.9</td>
</tr>
<tr>
<td>Case-fatality rate, mean no. of deaths per 100 residents ± SD</td>
<td>0.6 ± 1.9</td>
</tr>
<tr>
<td>Time between initiation of chemoprophylaxis and end of outbreak, mean days ± SD</td>
<td>4.0 ± 4.8</td>
</tr>
</tbody>
</table>