William Atkinson, MD, MPH
Influenza Update
August 20, 2015
Advisory Committee on Immunization Practices (ACIP)

- The recommendations to be discussed are primarily those of the ACIP
  - composed of 15 experts in clinical medicine and public health who are not government employees
  - provides guidance on the use of vaccines and other biologic products to the Department of Health and Human Resources, CDC, and the U.S. Public Health Service

www.cdc.gov/vaccines/acip/
Human Influenza Viruses

Influenza A
- H3N2 subtypes
- H1N1

Influenza B
- Yamagata lineages
- Victoria

Example nomenclature
- A/Texas/50/2012 (H3N2)
- B/Brisbane/60/2008
Influenza Antigenic Changes

• Antigenic Shift
  – major change, new subtype
  – caused by exchange of gene segments
  – may result in pandemic

• Example of antigenic shift
  – H2N2 virus circulated in 1957-1967
  – H3N2 virus appeared in 1968 and completely replaced H2N2 virus
  – 2009 H1N1 pandemic was atypical
Influenza Antigenic Changes

• Antigenic Drift
  – Continuous, minor change, same subtype
  – caused by point mutations in gene
  – may result in epidemic

• Example of antigenic drift
  – in 2013-2014, A/Texas (H3N2) was dominant
  – In 2014-2015, A/Switzerland (H3N2) was dominant
A Weekly Influenza Surveillance Report Prepared by the Influenza Division
Weekly Influenza Activity Estimates Reported by State and Territorial Epidemiologists*

Week Ending January 10, 2015- Week 1

District of Columbia

No Report
No Activity
Sporadic
Local
Regional
Widespread

Alaska
Hawaii
US Virgin Islands
Puerto Rico

immunizations
LINK LOGIN LEARN
webinar series
# Predominant Influenza Virus by Season

<table>
<thead>
<tr>
<th>Season</th>
<th>Early (Oct-Jan)</th>
<th>Late (Jan-May)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009-2010</td>
<td>A/H1N1</td>
<td>A/H1N1</td>
</tr>
<tr>
<td>2010-2011</td>
<td>A/H3N2</td>
<td>A/H1N1, B</td>
</tr>
<tr>
<td>2011-2012</td>
<td>A/H3N2</td>
<td>B</td>
</tr>
<tr>
<td>2012-2013</td>
<td>A/H3N2</td>
<td>B</td>
</tr>
<tr>
<td>2013-2014</td>
<td>A/H1N1</td>
<td>B</td>
</tr>
<tr>
<td>2014-2015</td>
<td>A/H3N2</td>
<td>B</td>
</tr>
</tbody>
</table>

[www.cdc.gov/flu/weekly/fluactivitysurv.htm](http://www.cdc.gov/flu/weekly/fluactivitysurv.htm)
Laboratory-Confirmed Influenza Hospitalizations
Preliminary rates as of Apr 25, 2015

- 65+ years
- 0-4 years
- 50-59 years
Number of Influenza-Associated Pediatric Deaths by Week of Death: 2011-12 season to present

- **2011-12**: Number of Deaths Reported = 37
- **2012-13**: Number of Deaths Reported = 171
- **2013-14**: Number of Deaths Reported = 111
- **2014-15**: Number of Deaths Reported = 144

Week of Death

- **Deaths Reported Previous Week**
- **Deaths Reported Current Week**
Influenza-Associated Pediatric Deaths by Age Group

Of 121 with known vaccination status, only 16 were fully vaccinated!

*Data from week 40, 2014 – week 21, 2015
Influenza Vaccine Virus Strains 2015-2016

• Trivalent vaccines contain:
  – an A/California/7/2009 (H1N1)-like virus
  – an A/Switzerland/9715293/2013 (H3N2)-like* virus
  – a B/Phuket/3073/2013-like* virus (Yamagata lineage)

• Quadrivalent vaccines also contain:
  – a B/Brisbane/60/2008-like virus (Victoria lineage)

*new for the 2015-2016 season.

MMWR 2015;64:583-90
Quadrivalent Influenza Vaccines
Rationale

• Two lineages of influenza B viruses: Victoria and Yamagata
  – immunization against virus from one lineage provides only limited cross-protection against viruses in the other
• Trivalent vaccines contain only one lineage of B vaccine virus
• Predominant lineage is difficult to predict in advance of the season
• Quadrivalent vaccines contain one virus from each B lineage in addition to 2 influenza A subtypes (H1N1, H3N2)

MMWR 2013;62(RR-7)
What’s New for Influenza

• 2015-2016 ACIP recommendations published in MMWR on August 7
  – H3N2 and B virus strains changed
  – new vaccines
  – removal of preference for LAIV for children 2 through 8 years of age
  – revised (simplified!) algorithm for determining the number of doses for children 6 months through 8 years of age
Influenza Vaccine Recommendations, 2015-2016

• Routine annual influenza vaccination is recommended for all persons age 6 months and older who do not have a contraindication

• Special effort should be made to vaccinate
  – infants and young children and their contacts
  – persons age 65 years and older and their contacts
  – persons with underlying medical conditions (including pregnancy) and their contacts
  – healthcare providers

*MMWR 2015;64:818-25*
Influenza Vaccine Timing, 2015-2016

• To avoid missed opportunities for vaccination, providers should offer influenza vaccine during routine health care visits and hospitalizations when vaccine is available

• Children age 6 months through 8 years who require 2 doses should receive their first dose as soon as possible after vaccine becomes available, and the second dose at least 4 weeks later

• Healthcare providers should offer vaccine by October, if possible

MMWR 2015;64:818-25
New Influenza Vaccines for the 2015-2016 Season

- Afluria (trivalent, bioCSL) approved by FDA for intramuscular administration via the Stratis needle-free jet injector (PharmaJet, Inc)
- FluBlok (trivalent, Protein Sciences) expanded age range
- Fluzone Intradermal quadrivalent replaces Fluzone Intradermal trivalent
- Fluzone trivalent SDS 0.5 mL no longer available (only quadrivalent)

MMWR 2015;64:818-25
Listing of Influenza Vaccines Available in the United States for the 2015-2016 Season

Influenza Vaccine Products for the 2015–2016 Influenza Season

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Trade Name</th>
<th>How Supplied</th>
<th>Mercury Content [µg Hg/0.5 mL]</th>
<th>Age Group</th>
<th>Vaccine Product Billing Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>bioCSL, Inc.</td>
<td>Affuria (IIV3)</td>
<td>0.5 mL (single-dose syringe); 5.0 mL (multi-dose vial)</td>
<td>0</td>
<td>9 years &amp; older</td>
<td>90656; 90658</td>
</tr>
<tr>
<td>GlaxoSmithKline</td>
<td>Fluarix (IIV3)</td>
<td>0.5 mL (single-dose syringe)</td>
<td>0</td>
<td>3 years &amp; older</td>
<td>90656</td>
</tr>
<tr>
<td></td>
<td>Fluarix (IIV4)</td>
<td>0.5 mL (single-dose syringe)</td>
<td>0</td>
<td>3 years &amp; older</td>
<td>90658</td>
</tr>
<tr>
<td>ID Biomedical Corp. of Quebec, a subsidiary</td>
<td>FluLaval (IIV3)</td>
<td>0.5 mL (single-dose syringe); 5.0 mL (multi-dose vial)</td>
<td>&lt;25</td>
<td>3 years &amp; older</td>
<td>90656</td>
</tr>
<tr>
<td>of GlaxoSmithKline</td>
<td>FluLaval (IIV4)</td>
<td>0.5 mL (single-dose syringe); 5.0 mL (multi-dose vial)</td>
<td>&lt;25</td>
<td>3 years &amp; older</td>
<td>90658</td>
</tr>
<tr>
<td>Medimmune</td>
<td>FluMist (LAIV4)</td>
<td>0.2 mL (single-use nasal spray)</td>
<td>≤1</td>
<td>2 through 49 years</td>
<td>90672</td>
</tr>
<tr>
<td>Novartis Vaccines and Biotech</td>
<td>Fluvirin (IIV3)</td>
<td>0.5 mL (single-dose syringe); 5.0 mL (multi-dose vial)</td>
<td>≤1</td>
<td>4 years &amp; older</td>
<td>90656</td>
</tr>
</tbody>
</table>

www.immunize.org/catg.d/p4072.pdf
### Influenza Vaccines by Approved Age Group, 2015-2016

<table>
<thead>
<tr>
<th>Age group</th>
<th>Vaccines Approved for This Age Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 through 5 months</td>
<td>None</td>
</tr>
<tr>
<td>6 months and older</td>
<td>Fluzone IIV3 (MDV) and IIV4 (not ID or HD)</td>
</tr>
<tr>
<td>2 through 49 years</td>
<td>Flumist LAIV4</td>
</tr>
<tr>
<td>3 years and older</td>
<td>Fluarix IIV4, FluLaval IIV4</td>
</tr>
<tr>
<td>4 years and older</td>
<td>Fluvirin IIV3</td>
</tr>
<tr>
<td>9 years and older</td>
<td>Afluria IIV3*</td>
</tr>
<tr>
<td>18 years and older</td>
<td>Flucelvax IIV3, Flublok RIV3</td>
</tr>
<tr>
<td>18 through 64 years</td>
<td>Fluzone IIV4 intradermal</td>
</tr>
<tr>
<td>65 years and older</td>
<td>Fluzone IIV3 high dose</td>
</tr>
</tbody>
</table>

*Afluria IIV3 is approved by FDA for persons 5 years and older but recommended by ACIP for persons 9 years and older. Afluria is approved for persons 18 through 64 years when given by Stratis jet injector.*

*MMWR* 2015;64:818-25
Influenza Vaccine Administration Errors

• Clinicians should not administer Influenza vaccine (IIV and LAIV) to persons outside the licensed age range for the vaccine they are using.

• If LAIV or IIV* is given outside the licensed age ranges it is not necessary to repeat the dose unless a 0.25 mL dose was administered to a person 3 years or older.

*except Fluzone Intradermal in some circumstances
Fluzone (sanofi)

• Approved for persons age 6 months and older

• The only IIV approved for children younger than 3 years of age

• Multiple presentations
  – 0.25 mL prefilled syringe for 6 through 35 months (IIV4 only)
  – 0.5 mL syringe and 0.5 mL vial (IIV4 only)
  – 5.0 mL multi-dose vial (IIV3 and IIV4)
  – intradermal (IIV4 only)
  – high dose (IIV3 only)

MMWR 2015;64:818-25
Fluzone Intradermal microneedle and injection system
Fluzone Intradermal

- Quadrivalent formulation approved FDA in December 2014
- Approved only for persons 18 through 64 years of age
- Dose is 0.1 mL administered in the deltoid area by a specially designed microneedle and injector system
- Formulated to contain more HA (27 mcg) than a 0.1 mL dose of regular Fluzone formulation (9 mcg)
- Local reactions more frequent than IM vaccine

MMWR 2015;64(30):818-25
TIV Intradermal Administration Error

• Persons older than 65 years or much younger than 18 years are more likely to have skin that is too thin for proper intradermal administration

• Persons younger than 9 years and 65 and older: Fluzone ID is invalid. Re-immunize appropriately

• Persons 9 through 17 years: if the HCP is certain that the dose was given intradermally, the dose may be counted and does not need to be repeated
Fluzone High-Dose

• Available since December 2009
• Trivalent formulation only
• Contains 4 X amount of influenza antigen than regular Fluzone
• Approved only for persons 65 years and older
• Produces higher antibody levels
• Local reactions more frequent than with standard dose vaccine

MMWR 2011;60:1128-32
Fluzone High Dose Clinical Trial

- Multi-center randomized clinical trial
- 32,000 persons 65 years or older
- Compared to standard Fluzone
  - 24.2% reduction in laboratory-confirmed influenza
  - Effective against both influenza A and B
  - Reduction in risk of pneumonia and hospitalization

Afluria Administered by Stratis Jet Injector (PharmaJet)

• Approved by FDA in August 2014
• Persons age 18 through 64 years
• Antibody in titer and seroprotection rates similar to IM
• Local reactions more common than with IM
  – no difference in systemic AEs

MMWR 2015;64:818-25
Components

Reusable hardware:
- Injector
- Reset Station

Disposables:
- Syringe
- Filling/Vial Adapter

Simple, Robust Design Injector Unique features:
- Durable
- Double safety feature
- Tested for 20,000 cycles
Live Attenuated Influenza Vaccine (LAIV)

• Approved only for healthy persons 2 through 49 years of age
• Should not be administered to
  – pregnant women
  – immunosuppressed persons or person caring for severely immunosuppressed person
  – persons with severe egg allergy or allergic reaction after prior dose
  – children 2-17 taking aspirin
  – children 2-4 with asthma or wheezing
  – persons taking influenza antivirals in the prior 48 hours
• May be administered to close contacts of these persons

MMWR 2015;64:818-25
LAIV for Children

• Two randomized studies have been conducted in young children that compare the benefits provided by the LAIV and IIV
  – one study was conducted in children 6 to 59 months of age and the other was conducted in children 6 to 71 months of age

• Both studies indicated that LAIV provided about 50% better protection than IIV in young children

• Based on these studies ACIP stated a preference for LAIV for children 2-8 years of age in 2014

*MMWR* 2014;63:691-7
Influenza Vaccine Effectiveness for 2014-15

• During November 10, 2014–January 2, 2015 overall vaccine effectiveness (VE) against laboratory-confirmed influenza associated with medically attended ARI was 23% (95% CI = 8%–36%)

• VE for 24% for persons 6 months-17 years, 14% for 50 years and older

• No apparent benefit of LAIV vs. IIV

• Low VE consistent with circulation of drifted influenza A H3N2 strain

*MMWR 2014;63:691-7*
LAIV – No Preference, 2015-2016

• In the absence of data demonstrating consistent greater relative effectiveness of the current quadrivalent formulation of LAIV, preference for LAIV over IIV is no longer recommended

• For healthy children aged 2 through 8 years who have no contraindications or precautions either LAIV or IIV can be used

*MMWR 2015;64:818-25*
Choice of Influenza Vaccine

• Where more than one type of vaccine is appropriate and available, ACIP has no preferential recommendation for use of any influenza vaccine product over another
  – quadrivalent vs trivalent
  – high-dose vs standard dose (65+ years)
  – IIV vs LAIV (2 through 49 years)
Influenza Vaccine for Children 6 Months Through 8 Years

• Two doses this season if
  – first season they are vaccinated, or
  – did not receive a total of at least two doses of trivalent or quadrivalent influenza vaccine before July 1, 2015*, or
  – child’s vaccination history is unknown

• Otherwise 1 dose this season

*The two doses need not have been received during the same season or consecutive seasons *MMWR 2015;64:818-25
FIGURE 1. Influenza vaccine dosing algorithm for children aged 6 months through 8 years — Advisory Committee on Immunization Practices, United States, 2015–16 influenza season

Has the child received ≥2 total doses of trivalent or quadrivalent influenza vaccine before July 1, 2015*

- Yes
  - 1 dose of 2015–16 influenza vaccine

- No or don’t know
  - 2 doses† of 2015–16 influenza vaccine

* The two doses need not have been received during the same season or consecutive seasons.
† Doses should be administered ≥4 weeks apart.
Influenza Vaccination for Persons with Egg Allergy

• Most IIV and all LAIV contain residual egg protein

• Most people with “egg allergy” can receive influenza vaccine

• Persons age 18 years and older with severe egg allergy should receive RIV3 (Flublok, Protein Sciences) which is egg-free

MMWR 2015;64:818-25
Influenza Vaccination for Persons with Egg Allergy

• If RIV3 is not available or the person is not within the licensed age range (younger than 18 years) then
  – IIV should be administered by a physician with experience in the recognition and management of severe allergic conditions

*MMWR 2015;64:818-25*
No change from the 2014-2015 recommendations.
Flucelvax (ccIIV3) (Novartis)

- Approved for persons 18 years and older
- Available in 0.5mL single dose vials for IM injection
- Vaccine viruses for ccIIV3 are not propagated in eggs; however, initial reference strains have been passaged in eggs
  - cannot be considered egg-free, though expected to contain less egg protein than other IIVs

*MMWR* 2013;62(RR-7)
Flucelvax (cClIV3) (Novartis)

- Estimated to contain 50 femtograms of egg protein per 0.5 mL dose
- \(5 \times 10^{-14}\) grams per dose
- A femtogram is a unit of mass equal to 0.000 000 000 000 001 grams

FluBlok (RIV3) (Protein Sciences)

• Approved for persons 18 years and older
• Vaccine contains recombinant influenza virus hemagglutinin
  – protein is produced in insect cell line
  – no eggs or influenza viruses used in production
• Available in 0.5mL single-dose vials for IM injection
• Egg-free

*MMWR 2015;64:818-25*
Influenza Vaccine Revaccination

• ACIP recommends only 1 dose of influenza vaccine per season except for certain children younger than 9 years

• IIV4 is not recommended if IIV3 has already been given

• Fluzone High Dose is not recommended if standard IIV has already been given

MMWR 2013;62(RR-7)
Influenza Vaccine Cannot Cause Influenza

• Influenza-like illness following influenza vaccination is usually due to
  – influenza infection AFTER vaccination (influenza virus incubation period is 2-3 days - immunity after vaccination takes a week to develop)
  – infection with a respiratory virus other than influenza (influenza vaccine won’t prevent this)
  – coincidental illness interpreted by the patient to be “the flu”
Influenza VISs now available and now good indefinitely!
2014-2015 Influenza Vaccination Coverage (preliminary results)*

- 40.3% of those 6 months of age and older vaccinated (39.5% in November 2013)
- 42.0% of those 6 months-17 years of age vaccinated (41.1% in November 2013)
- 39.7% of adults 18 years of age and older vaccinated (39.0 in November 2013)
  - Only 61.3% of those 65 years of age and older vaccinated (61.8% in November 2013, but 66% in 2005)
  - 43.0% of adults 18-64 years of age with at least one high-risk medical condition vaccinated (44.2% in November 2014)

*Early season, November 2014
www.cdc.gov/flu/fluvoxview/1415season.htm
Preliminary Influenza Vaccination Coverage for the 2014-15 Season *

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>2013-14 Season through November 2013 - % (95% CI)</th>
<th>2014-15 Season through November 2014 - % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hispanic, White*</td>
<td>38.7 ± 0.8</td>
<td>40.4 ± 1.0</td>
</tr>
<tr>
<td>Non-Hispanic, Black</td>
<td>27.2 ± 2.4</td>
<td>28.3 ± 2.4</td>
</tr>
<tr>
<td>Hispanic</td>
<td>25.7 ± 2.5</td>
<td>27.3 ± 2.7</td>
</tr>
<tr>
<td>Non-Hispanic, Other/Multiple</td>
<td>35.5 ± 3.9</td>
<td>33.3 ± 3.5</td>
</tr>
</tbody>
</table>

- Significant racial and ethnic disparities still exist

*Preliminary adult results from BRFSS interviews conducted July through December 2014
2014-2015 Influenza Vaccination Coverage (preliminary results)

• Pregnant Women (HP 2020 goal of 80%)
  – 50% vaccinated between October 2014 and January 2015 (includes pregnant women vaccinated from July 1 and later (52% previous year)

Influenza vaccination (inactivated vaccine only) was first recommended for women who were in the second or third trimester of pregnancy during the influenza season in 1997; recommended regardless of trimester in 2004.
Influenza vaccination coverage before and during pregnancy among women pregnant any time during October 1, 2014 – January 31, 2015 and who visited a health care provider at least once since July 2014, by provider recommendation or offer

- **Offered**: 67.8% (n = 1113)
- **Recommended but not offered**: 33.5% (n = 246)
- **No recommendation**: 9.7% (n = 332)

Percent Vaccinated
# Health Care Personnel and Influenza Vaccination, U.S., 2014

## Influenza Vaccination Rates

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacists</td>
<td>87%</td>
</tr>
<tr>
<td>NP/PA</td>
<td>86%</td>
</tr>
<tr>
<td>Physicians</td>
<td>82%</td>
</tr>
<tr>
<td>Nurses</td>
<td>81%</td>
</tr>
</tbody>
</table>

**2020 Healthy People Goal is 90%**

Lowest among administrative/non-clinical support staff (59%) and assistants/aides (47%)

How To Improve Influenza Vaccination Coverage in Your Practice

• Give a strong, unequivocal recommendation for the vaccine
• Be a role model* and be vaccinated yourself
• Make the vaccine available
• Publicize that you have vaccine available
• Consider the use of standing orders to “automate” the vaccination process
  – standing orders for influenza and all other vaccines available from IAC at www.immunize.org

*and protect yourself, your patients and your family!
Resources

• CDC Influenza Website
  – www.cdc.gov/flu/index.htm

• Immunization Action Coalition
  – www.immunize.org

• National Adult and Influenza Immunization Summit (NAIIS)
  – www.izsummitpartners.org/
Questions?