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www.health.mo.gov/immunizations

webinar series

William Atkinson, MD, MPH

Influenza Update

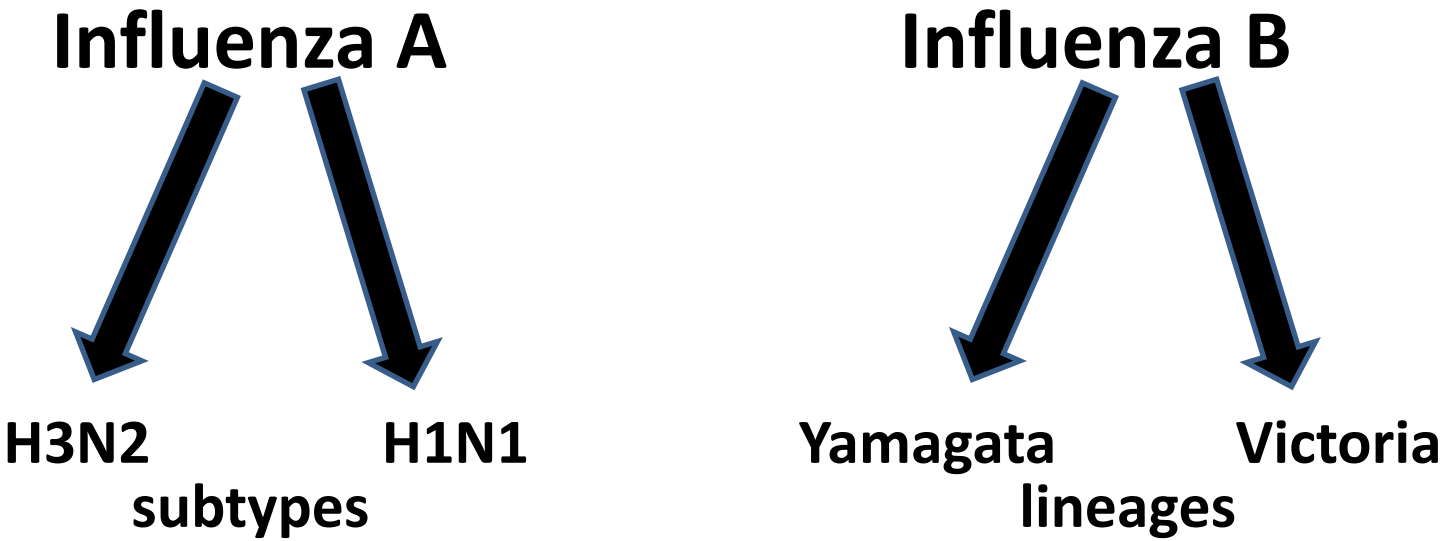
August 20, 2015

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



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**

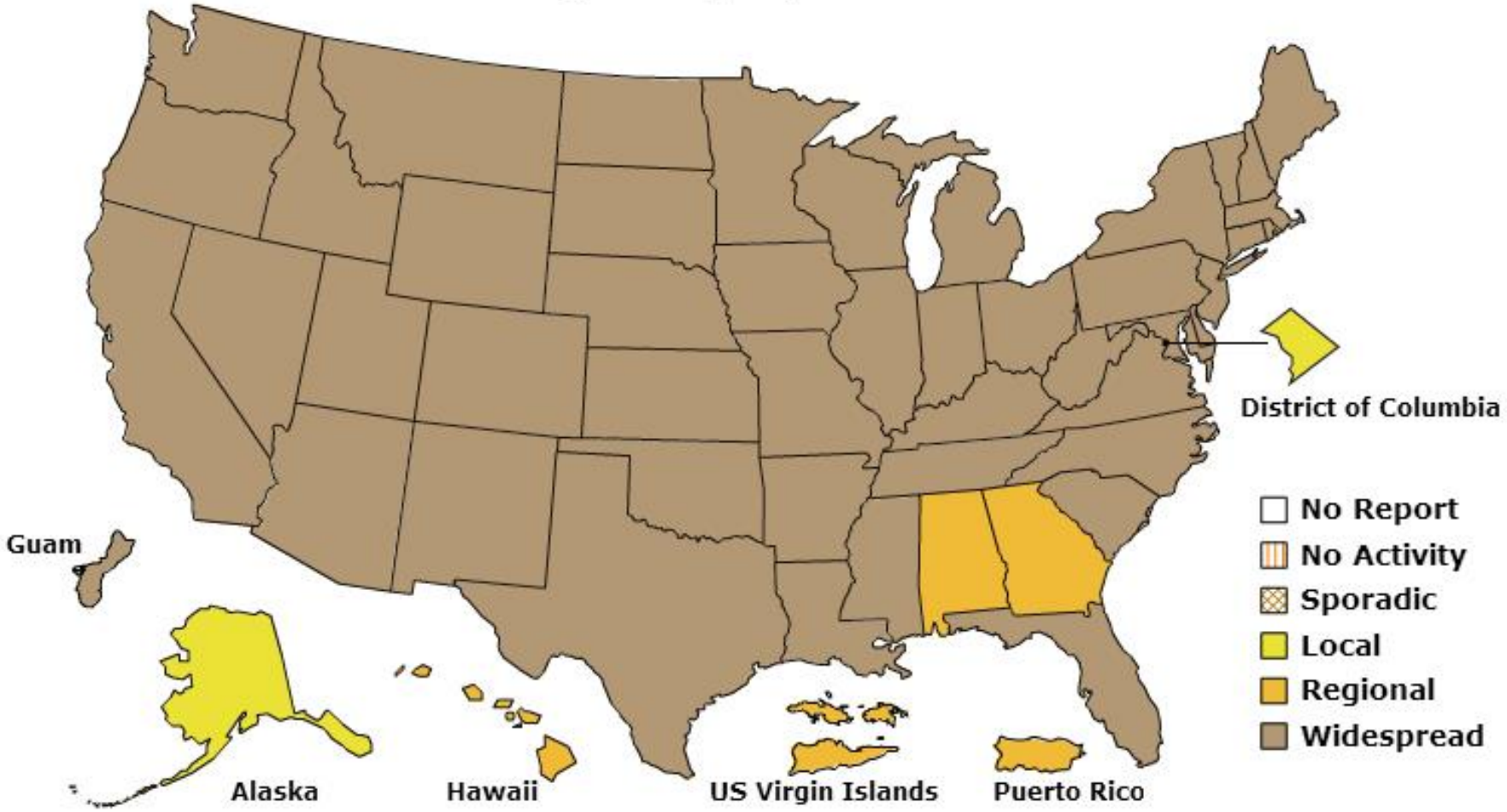
Influenza Antigenic Changes

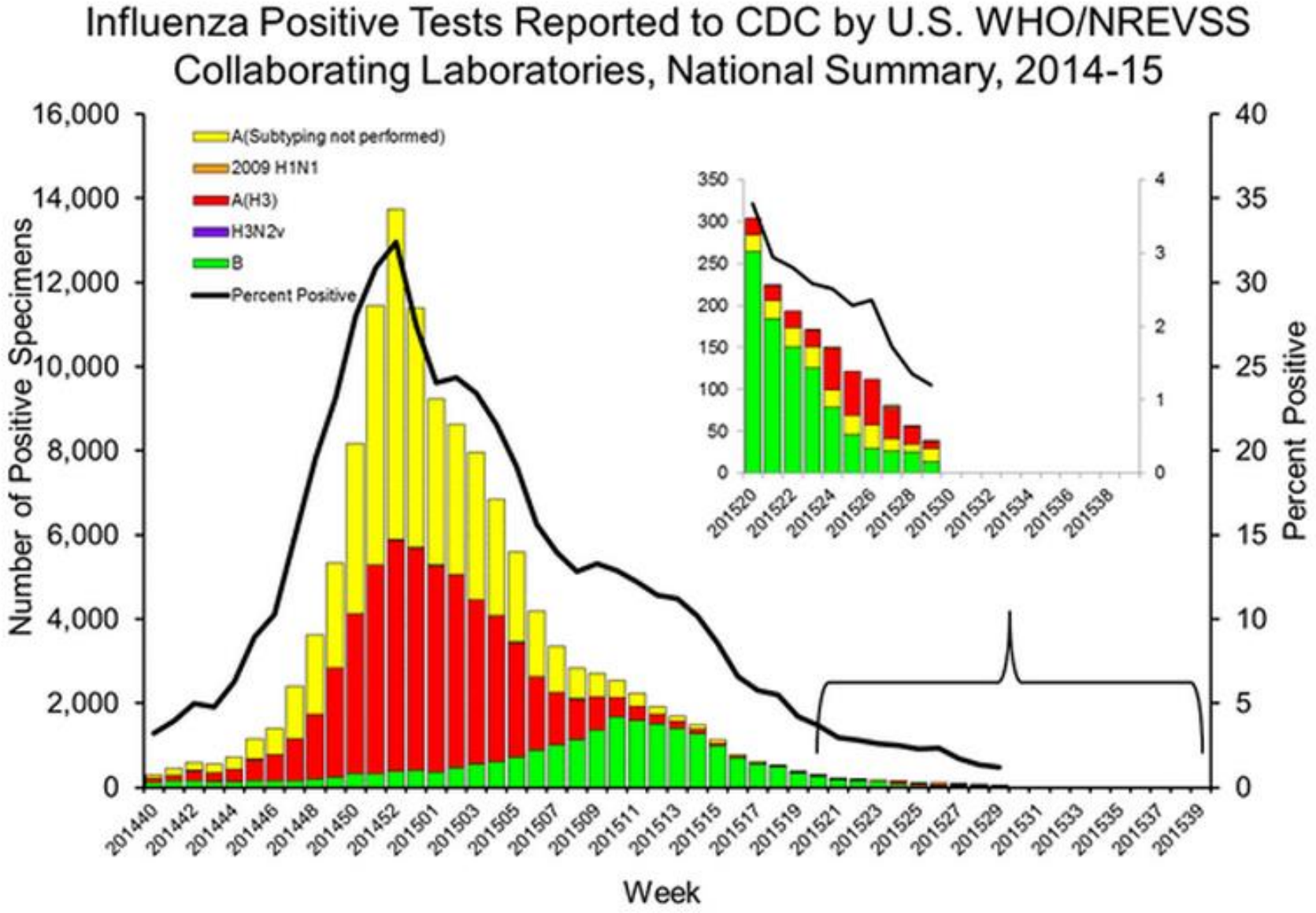
- **Antigenic Drift**
  - **Continuous, minor change, same subtype**
  - **caused by point mutations in gene**
  - **may result in epidemic**
- **Example of antigenic drift**
  - **in 2013-2014, A/Texas (H3N2) was dominant**
  - **In 2014-2015, A/Switzerland (H3N2) was dominant**

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





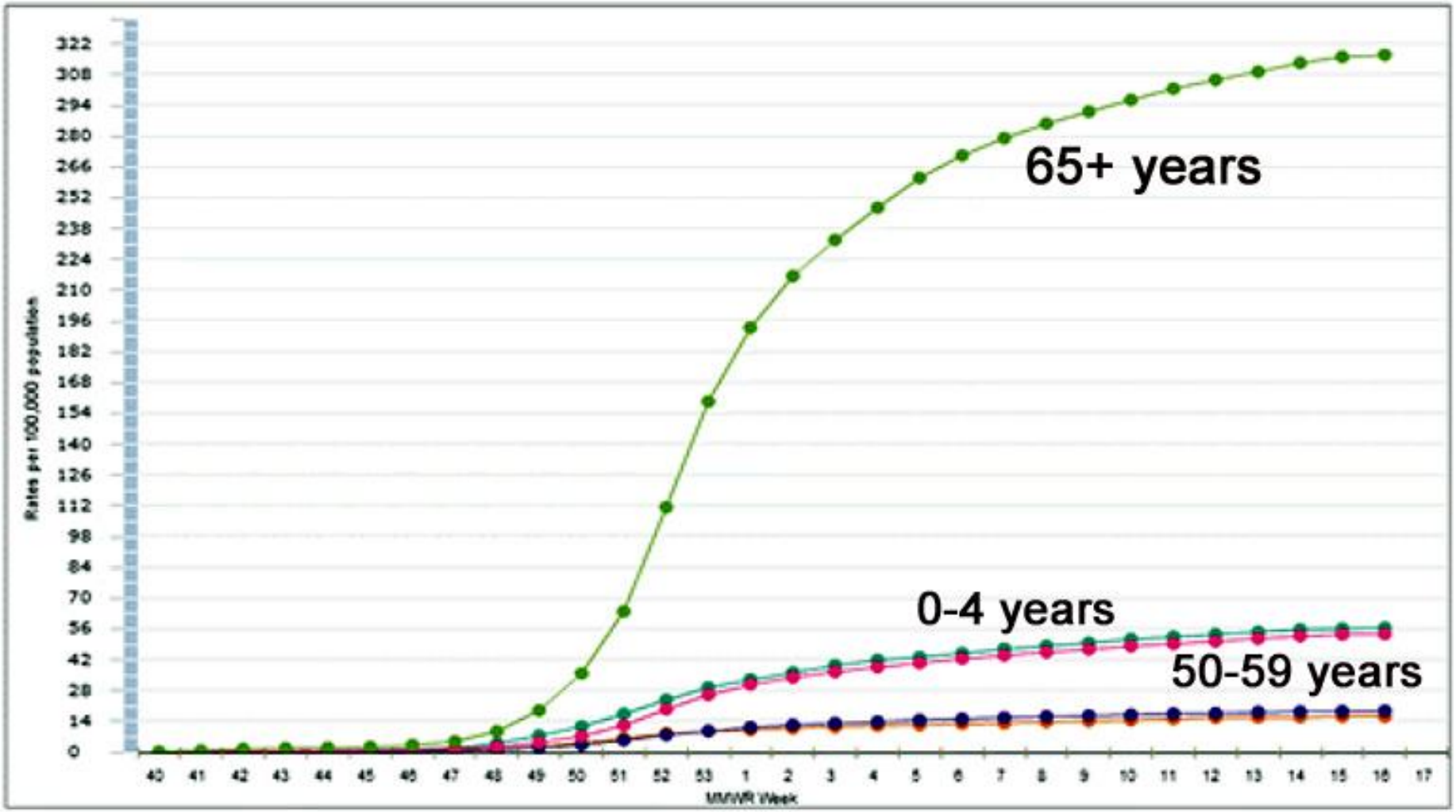
Predominant Influenza Virus by Season

Season	Early (Oct-Jan)	Late (Jan-May)
2009-2010	A/H1N1	A/H1N1
2010-2011	A/H3N2	A/H1N1, B
2011-2012	A/H3N2	B
2012-2013	A/H3N2	B
2013-2014	A/H1N1	B
2014-2015	A/H3N2	B

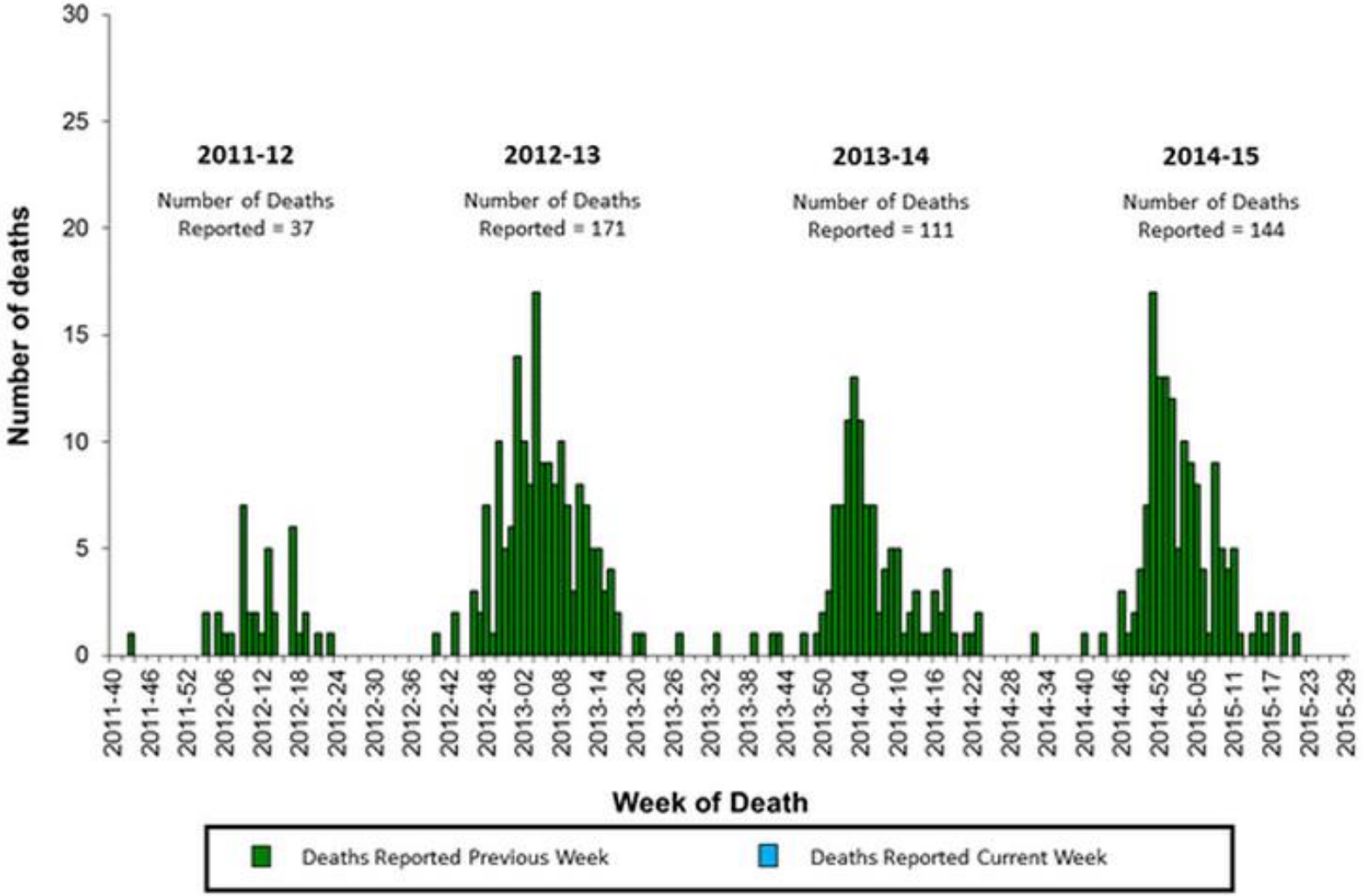
www.cdc.gov/flu/weekly/fluactivitysurv.htm

Laboratory-Confirmed Influenza Hospitalizations

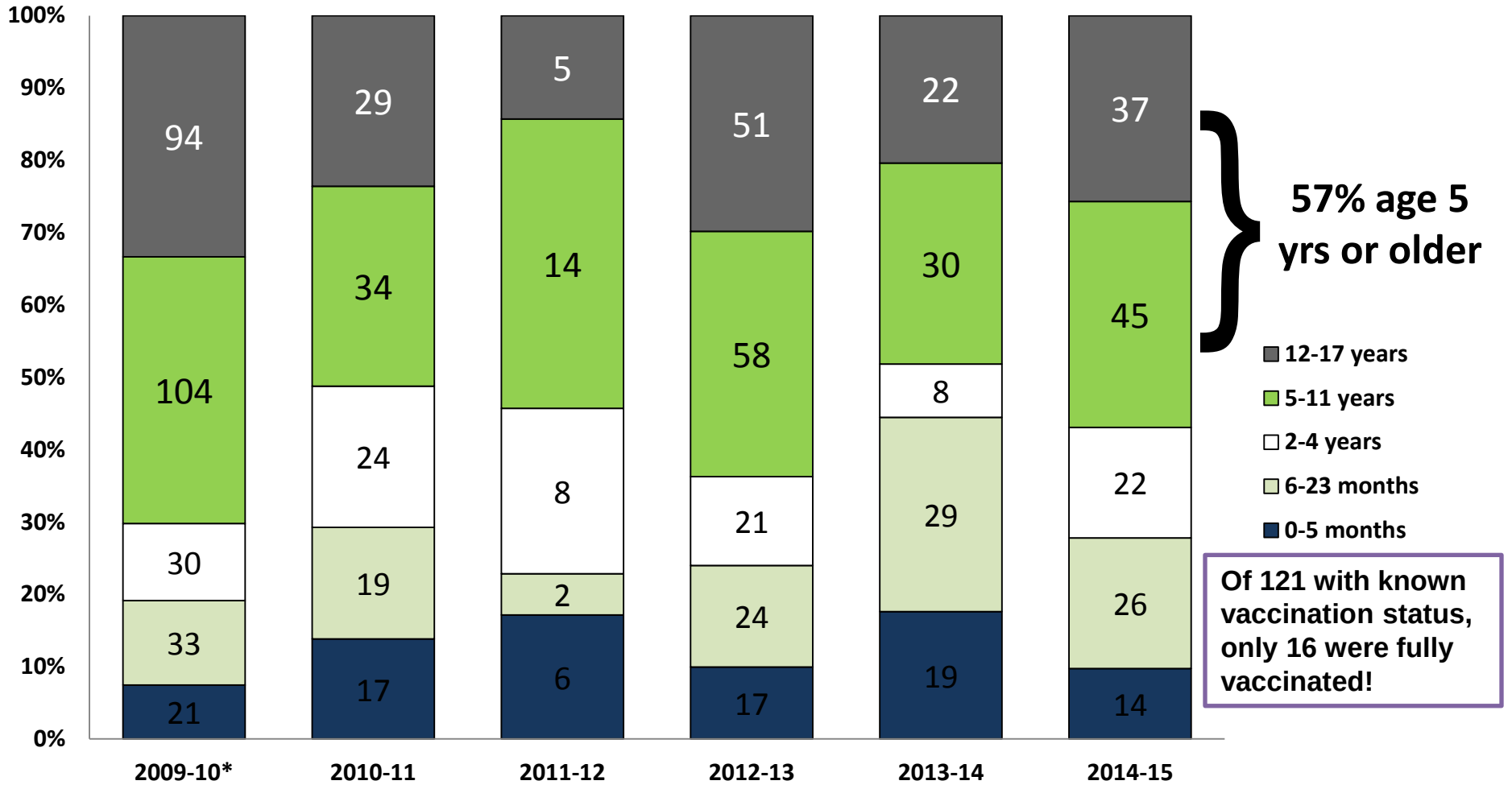
Preliminary rates as of Apr 25, 2015



Number of Influenza-Associated Pediatric Deaths by Week of Death: 2011-12 season to present



Influenza-Associated Pediatric Deaths by Age Group



*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

Manufacturer	Trade Name (vaccine abbreviation)[1]	How Supplied	Mercury Content (µg Hg/0.5mL)	Age Group	Vaccine Product Billing Code[2]	
					CPT	Medicare[3]
bioCSL, Inc.	Afluria (IIV3)	0.5 mL (single-dose syringe)	0	9 years & older[4,5]	90656	90656
		5.0 mL (multi-dose vial)	24.5		90658	Q2035
GlaxoSmithKline	Fluarix (IIV3)	0.5 mL (single-dose syringe)	0	3 years & older	90656	90656
	Fluarix (IIV4)	0.5 mL (single-dose syringe)	0	3 years & older	90686	90686
ID Biomedical Corp. of Quebec, a subsidiary of GlaxoSmithKline	FluLaval (IIV3)	0.5 mL (single-dose syringe)	0	3 years & older	90656	90656
		5.0 mL (multi-dose vial)	<25	3 years & older	90658	Q2036
	FluLaval (IIV4)	0.5 mL (single-dose syringe)	0	3 years & older	90686	90686
		5.0 mL (multi-dose vial)	<25	3 years & older	90688	90688
MedImmune	FluMist (LAIV4)	0.2 mL (single-use nasal spray)	0	2 through 49 years	90672	90672
Novartis Vaccines and	Fluvirin (IIV3)	0.5 mL (single-dose syringe)	≤1	4 years & older	90656	90656
		5.0 mL (multi-dose vial)	25		90658	Q2037

www.immunize.org/catg.d/p4072.pdf

Influenza Vaccines by Approved Age Group, 2015-2016

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

*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)
  - 0.5mL 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

N Engl J Med 2014;371:635-45

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

PharmaJet®

HOME ABOUT NEEDLE-FREE PRODUCT FAQs NEWS RESOURCES CONTA

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)**

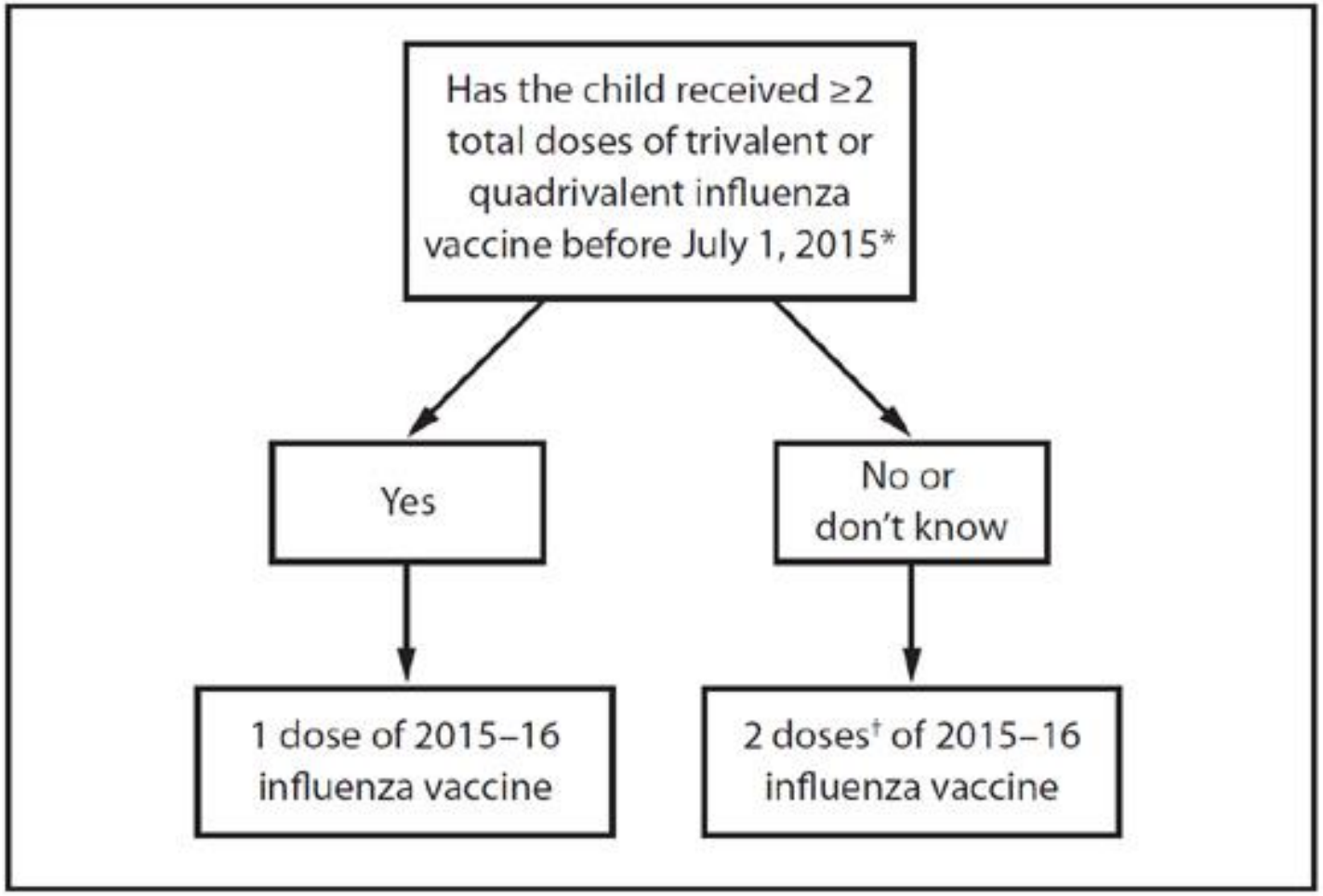
***MMWR* 2015;64:818-25**

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



* The two doses need not have been received during the same season or consecutive seasons.

† Doses should be administered ≥4 weeks apart.

***MMWR* 2015;64:818-25**

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**

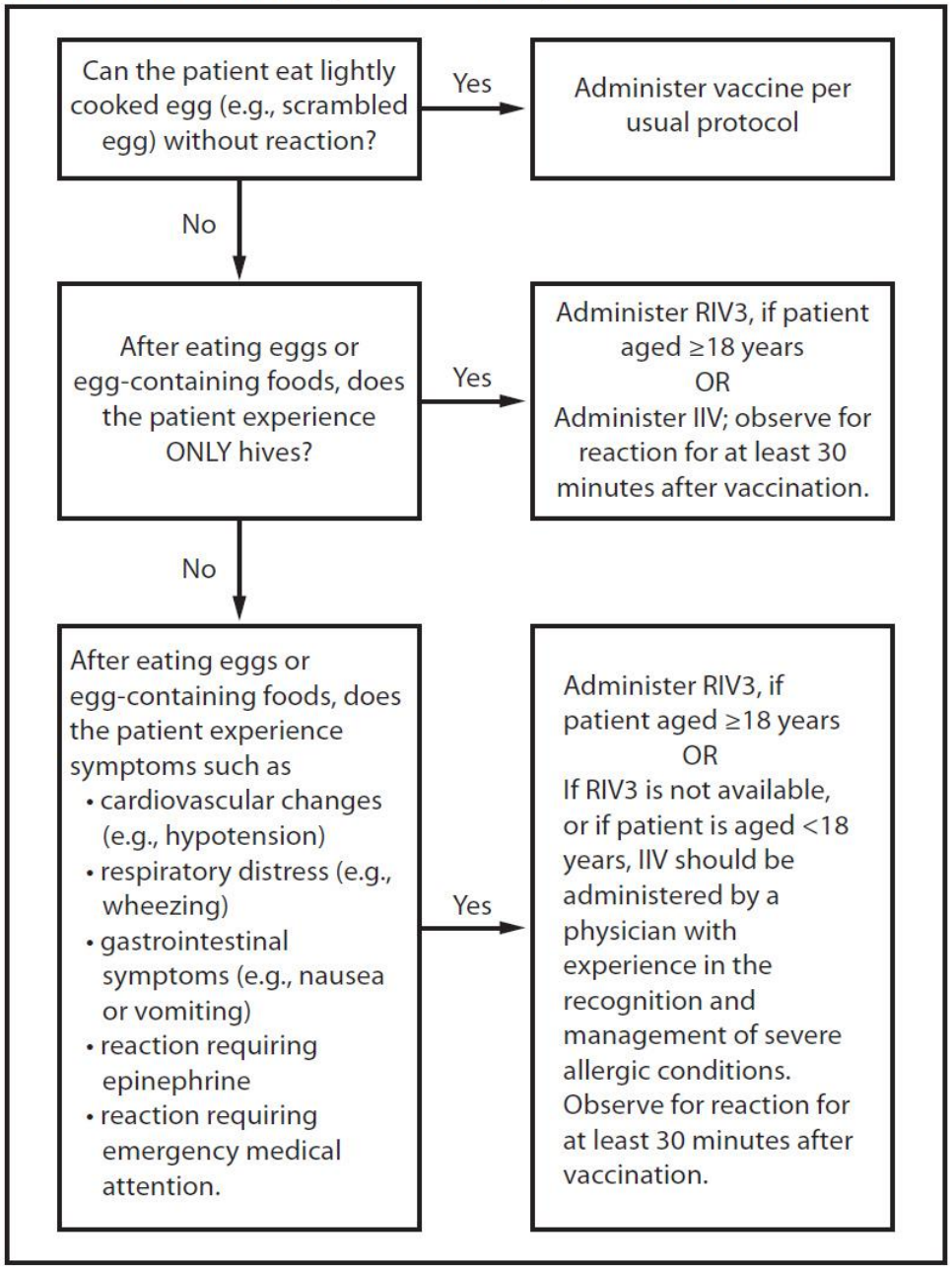
Influenza Vaccination for Persons with Egg Allergy

- **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

FIGURE 2. Recommendations regarding influenza vaccination of persons who report allergy to eggs*† — Advisory Committee on Immunization Practices, United States, 2015–16 influenza season



***MMWR* 2015;64:818-25**

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 (ccIIV3) (Novartis)

- **Estimated to contain 50 femtograms of egg protein per 0.5 mL dose**
- **$5x10^{-14}$ grams per dose**
- **A femtogram is a unit of mass equal to**

0.000 000 000 000 001 grams

***MMWR* 2013;62(RR-7) and http://en.wiktionary.org/wiki/femtogram**

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"**

VACCINE INFORMATION STATEMENT

Influenza (Flu) Vaccine (Inactivated or Recombinant): *What you need to know*

1 Why get vaccinated?

Influenza ("flu") is a contagious disease that spreads around the United States every year, usually between October and May.

Flu is caused by influenza viruses, and is spread mainly by coughing, sneezing, and close contact.

Anyone can get flu. Flu strikes suddenly and can last several days. Symptoms vary by age, but can include:

- fever/chills
- sore throat
- muscle aches
- fatigue
- cough
- headache
- runny or stuffy nose

Flu can also lead to pneumonia and blood infections, and cause diarrhea and seizures in children. If you have a medical condition, such as heart or lung disease, flu can make it worse.

Flu is more dangerous for some people. Infants and young children, people 65 years of age and older, pregnant women, and people with certain health conditions or a weakened immune system are at greatest risk.

Each year **thousands of people in the United States die from flu**, and many more are hospitalized.

Flu vaccine can:

- keep you from getting flu,
- make flu less severe if you do get it, and
- keep you from spreading flu to your family and other people.

2 Inactivated and recombinant flu vaccines

A dose of flu vaccine is recom
Children 6 months through 8 y
doses during the same flu seas
only one dose each flu season.

Some inactivated flu vaccines
amount of a mercury-based pr
thimerosal. Studies have not s
vaccines to be harmful, but flu
contain thimerosal are availabl

There is no live flu virus in flu s
the flu.

There are many flu viruses, and
changing. Each year a new flu v
against three or four viruses tha
disease in the upcoming flu seas
vaccine doesn't exactly match t
provide some protection.

Flu vaccine cannot prevent:

- flu that is caused by a virus no
  or
- illnesses that look like flu but

It takes about 2 weeks for prote
vaccination, and protection lasts

3 Some people s this vaccine

Tell the person who is giving yo

- **If you have any severe, life-t**
  If you ever had a life-threaten
  after a dose of flu vaccine, or
  any part of this vaccine, you m
  get vaccinated. Most, but not
  contain a small amount of egg
- **If you ever had Guillain-Ba**
  called GBS).
  Some people with a history o
  vaccine. This should be discu
- **If you are not feeling well.**
  It is usually okay to get flu va
  a mild illness, but you might h
  when you feel better.

VACCINE INFORMATION STATEMENT

Influenza (Flu) Vaccine (Live, Intranasal): *What You Need to Know*

Many Vaccine Information Statements are available in Spanish and other languages. See www.immunize.org/vis

Hojas de información sobre vacunas están disponibles en español y en muchos otros idiomas. Visite www.immunize.org/vis

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Flu vaccine can:

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- make flu less severe if you do get it, and

LAIV is sprayed into the nose. LAIV does not contain thimerosal or other preservatives. It is made from weakened flu virus and **does not cause flu**.

There are many flu viruses, and they are always changing. Each year LAIV is made to protect against four viruses that are likely to cause disease in the upcoming flu season. But even when the vaccine doesn't exactly match these viruses, it may still provide some protection.

Flu vaccine cannot prevent:

- flu that is caused by a virus not covered by the vaccine, or
- illnesses that look like flu but are not.

It takes about 2 weeks for protection to develop after vaccination, and protection lasts through the flu season.

3 Some people should not get this vaccine

Some people should not get LAIV because of age, health conditions, or other reasons. Most of these people should get an injected flu vaccine instead. Your healthcare provider can help you decide.

Tell the provider if you or the person being vaccinated:

- have any allergies, including an allergy to eggs, or have ever had an allergic reaction to an influenza vaccine.
- have ever had Guillain-Barré Syndrome (also called GBS).
- have any long-term heart, breathing, kidney, liver, or nervous system problems.
- hma or breathing problems, or are a child who wheezing episodes.
- gnant.
- ild or adolescent who is receiving aspirin or containing products.
- weakened immune system.
- visiting or taking care of someone, within the days, who requires a protected environment (for e, following a bone marrow transplant)

The live, attenuated influenza vaccine (called LAIV) may be given to healthy, non-pregnant people **2 through 49 years of age**. It may safely be given at the same time as other vaccines.

CDC U.S. Department of Health and Human Services Centers for Disease Control and Prevention

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/fluvaxview/1415season.htm

Preliminary Influenza Vaccination Coverage for the 2014-15 Season *

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

- **Significant racial and ethnic disparities still exist**

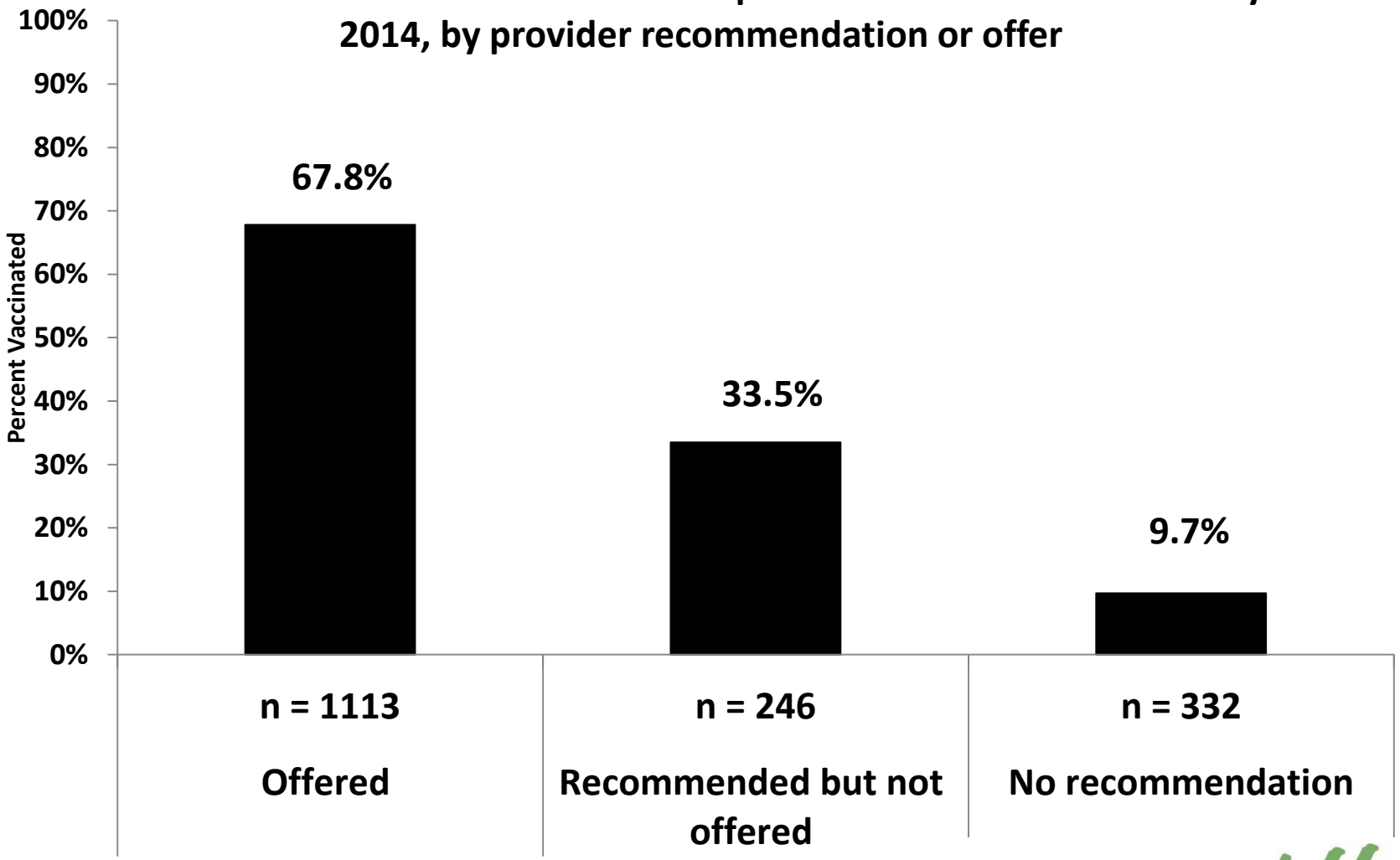
***Preliminary adult results from BRFSS interviews conducted July through December 2014**

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



Health Care Personnel and Influenza Vaccination, U.S., 2014

Influenza Vaccination Rates (internet panel, Nov 2014)	
Occupation	**Rate**
Pharmacists	87%
NP/PA	86%
Physicians	82%
Nurses	81%

2020 Healthy People Goal is 90%

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

www.cdc.gov/flu/pdf/fluvaxview/hcp-ips-nov2014.pdf

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?