

2014–2015 Influenza Activity and Antiviral Recommendations

**Clinician Outreach and
Communication Activity (COCA)**

Webinar

January 14, 2015

Objectives

At the conclusion of this session, the participant will be able to:

- ❑ Describe the current status of influenza activity in the United States.**
- ❑ Discuss the timing of antiviral treatment and implications for patient evaluation, treatment and testing.**
- ❑ State the latest antiviral recommendations for treating patients, especially older patients, with influenza.**

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Today's Presenter



Angela Campbell, MD, MPH, FAAP
Medical Officer

National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

SUMMARY OF 2014-15 INFLUENZA ACTIVITY



National Surveillance

FLUVIEW

A Weekly Influenza Surveillance Report Prepared by the Influenza Division

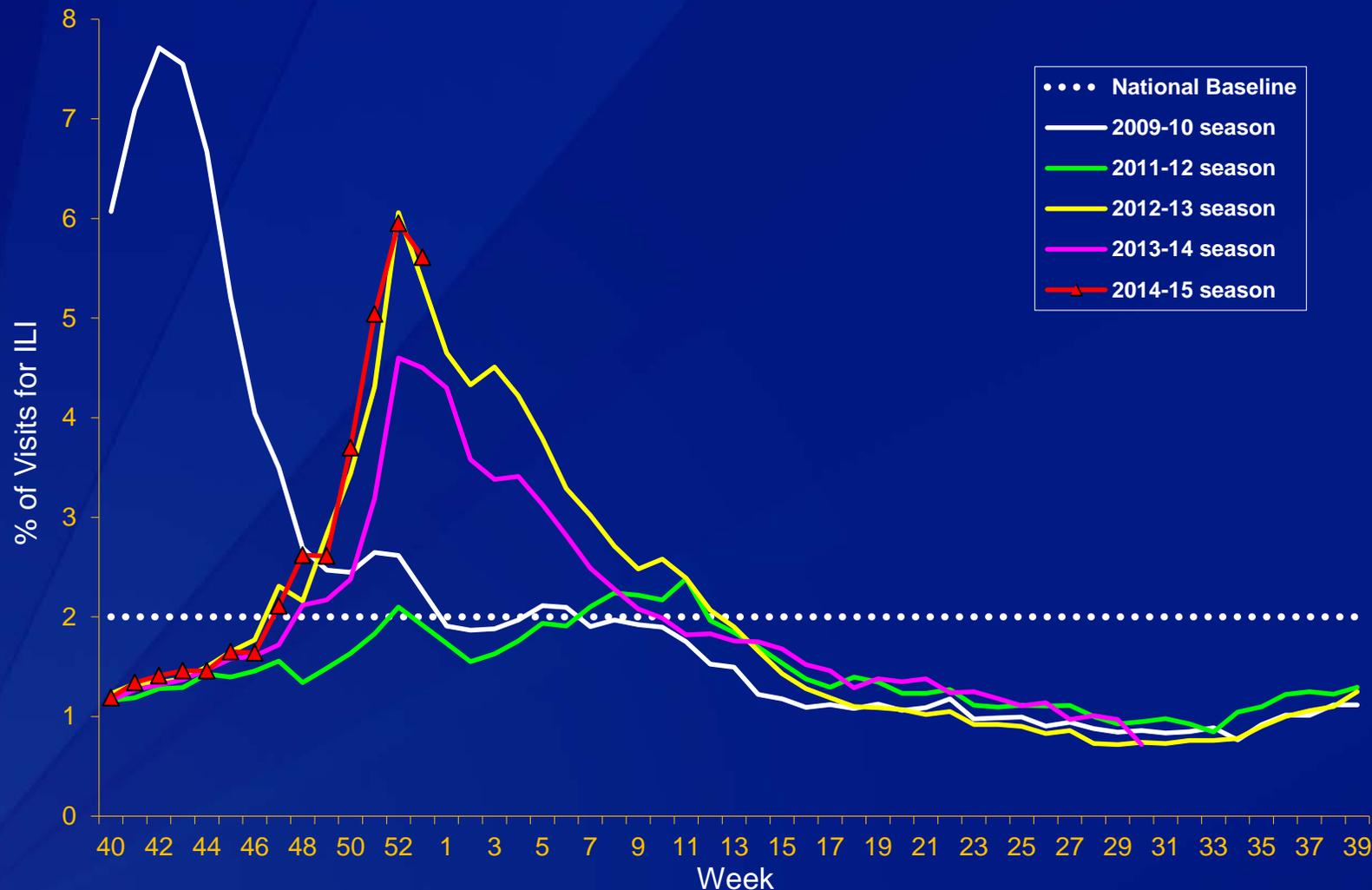


<http://www.cdc.gov/flu/weekly/fluactivitysurv.htm>

U.S. Virologic Surveillance

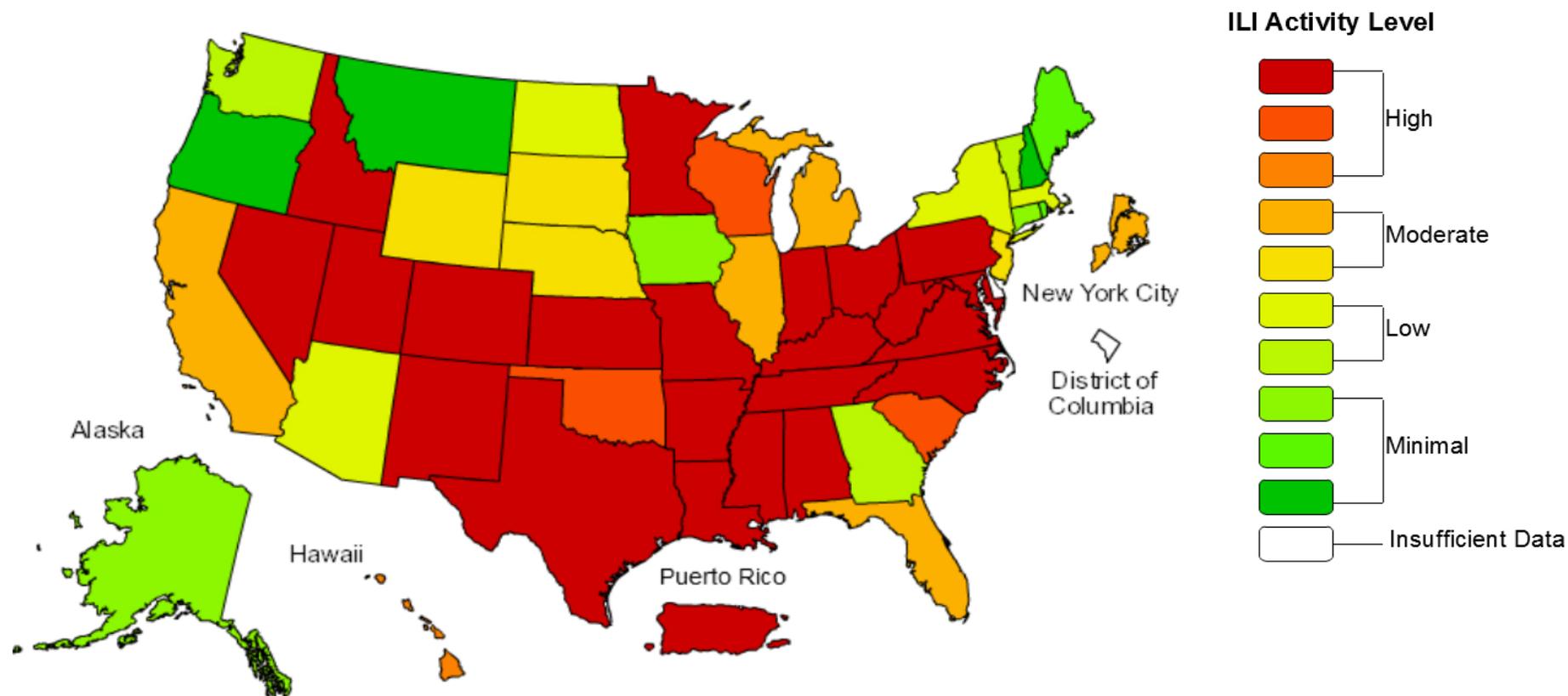
	Week 53 (ending Jan 3, 2015)
No. of specimens tested	30,469
No. of positive specimens (%)	7,515 (24.7%)
Positive specimens by type/subtype	
Influenza A	7,218 (96.0%)
2009 H1N1	8 (0.1%)
H3	2,486 (34.4%)
Subtyping not performed	4,724 (65.4%)
Influenza B	297 (4.0%)

Percentage of Visits for Influenza-like Illness (ILI) Reported by the U.S. Outpatient Influenza-like Illness Surveillance Network (ILINet), 2014-15 and Selected Previous Seasons



Influenza-Like Illness (ILI) Activity Level Indicator Determined by Data Reported to ILINet

2014-15 Influenza Season Week 53 ending Jan 03, 2015

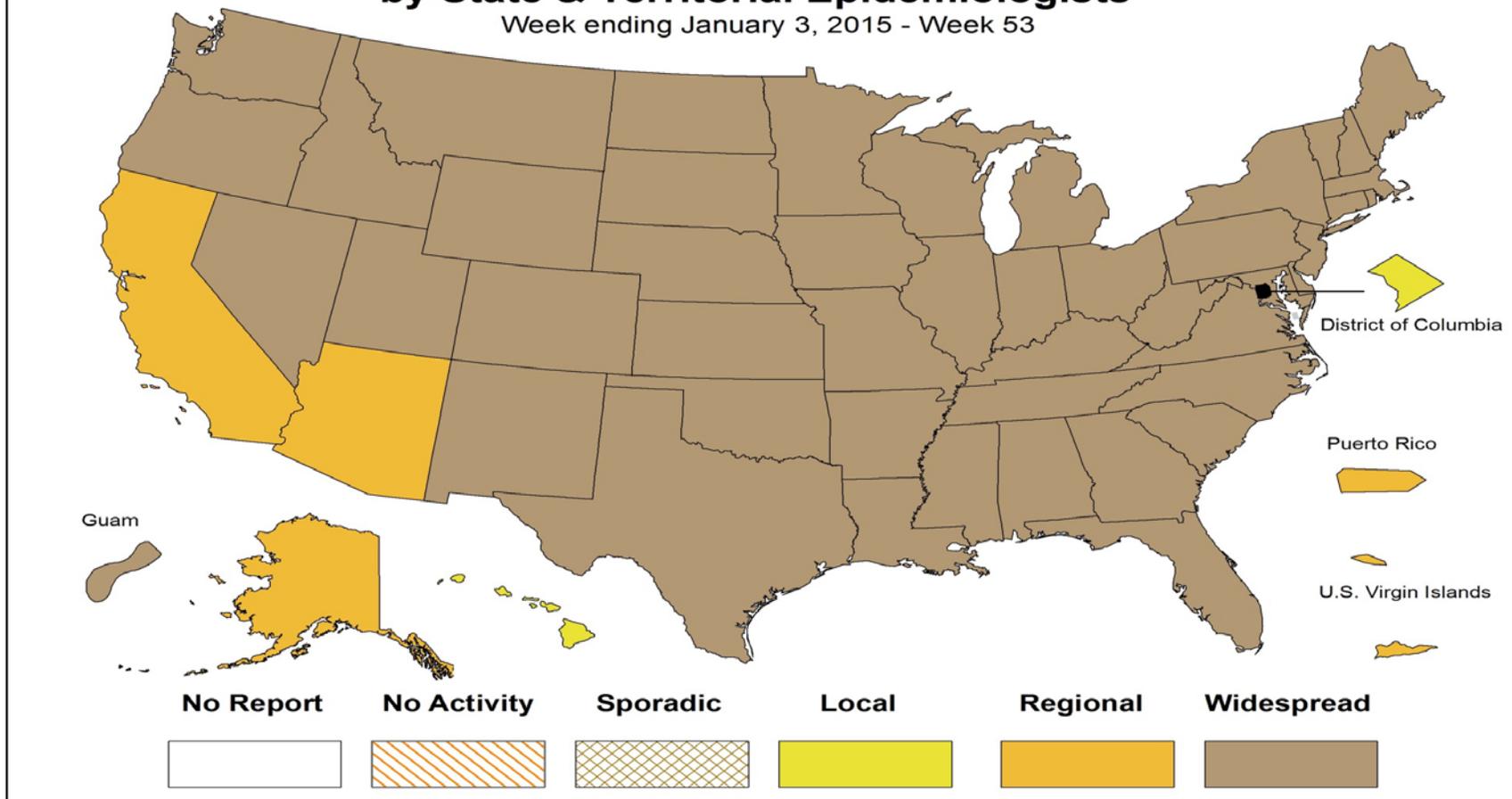


- **High / moderate ILI activity** – 34 states, PR, and NYC
- **Low / minimal activity** – 15 states



Weekly Influenza Activity Estimates Reported by State & Territorial Epidemiologists*

Week ending January 3, 2015 - Week 53



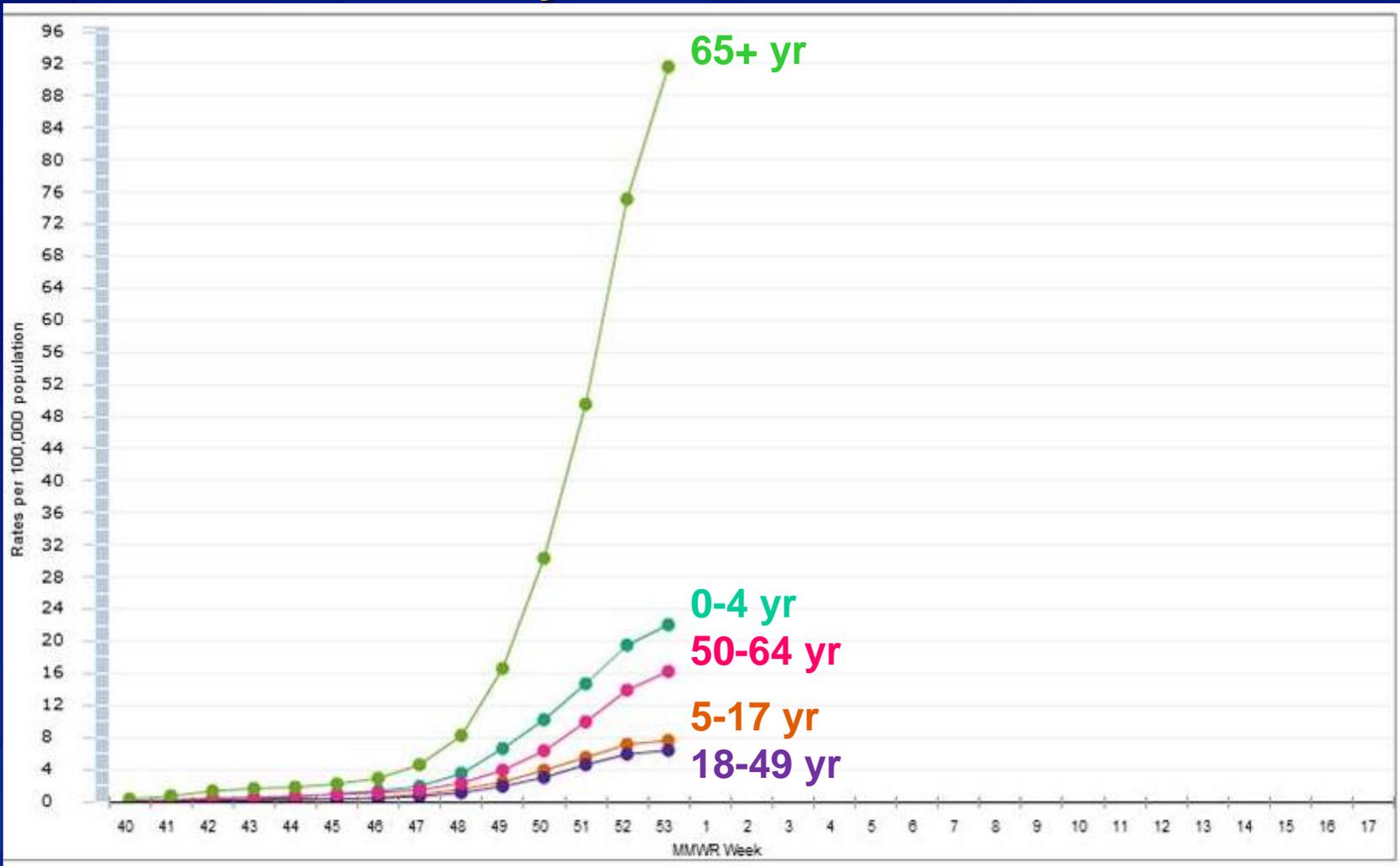
* This map indicates geographic spread & does not measure the severity of influenza activity

- **Widespread** – 46 states, Guam
- **Regional / local activity** – 4 states, DC, PR, USVI

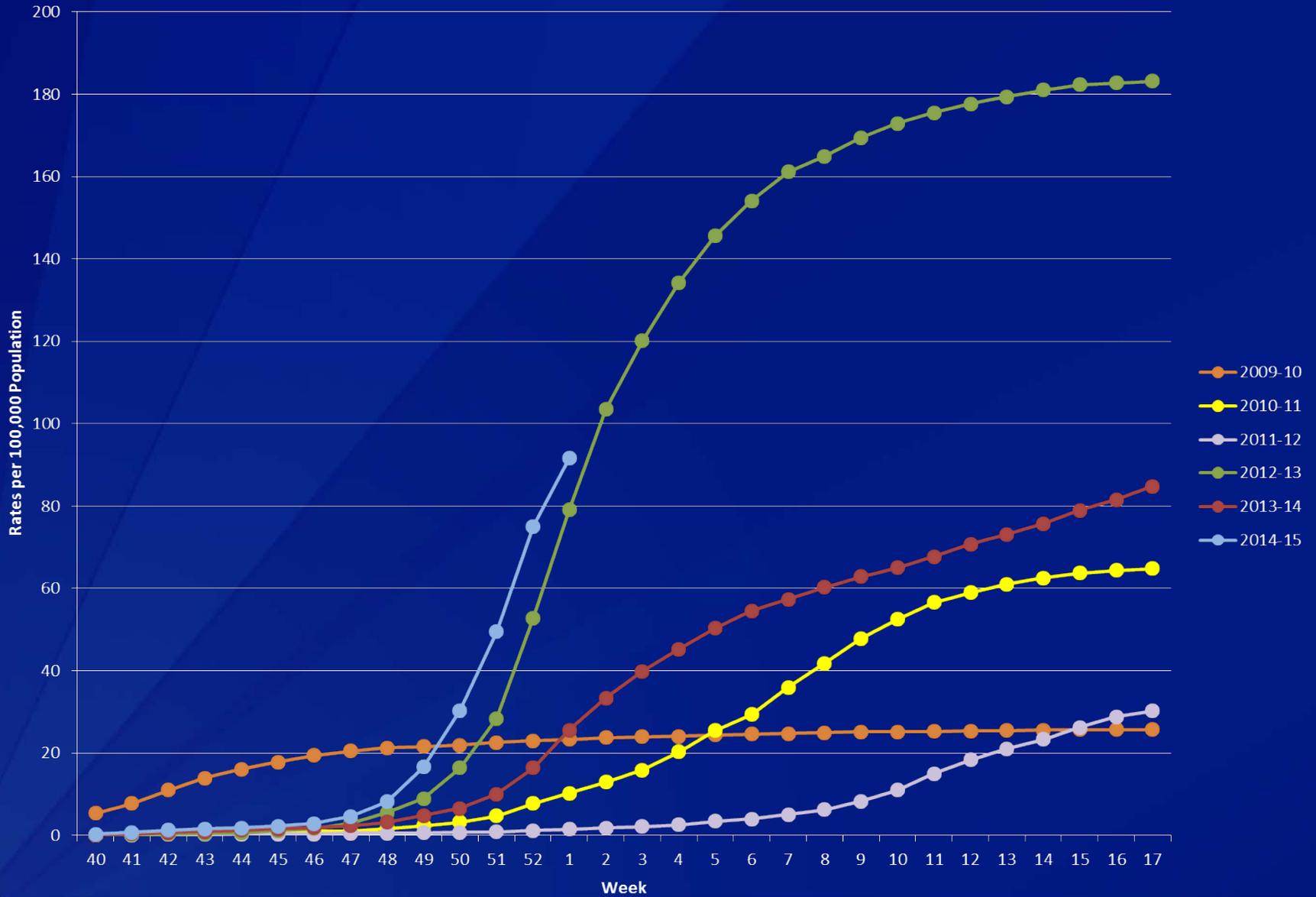


Laboratory-Confirmed Influenza Hospitalizations

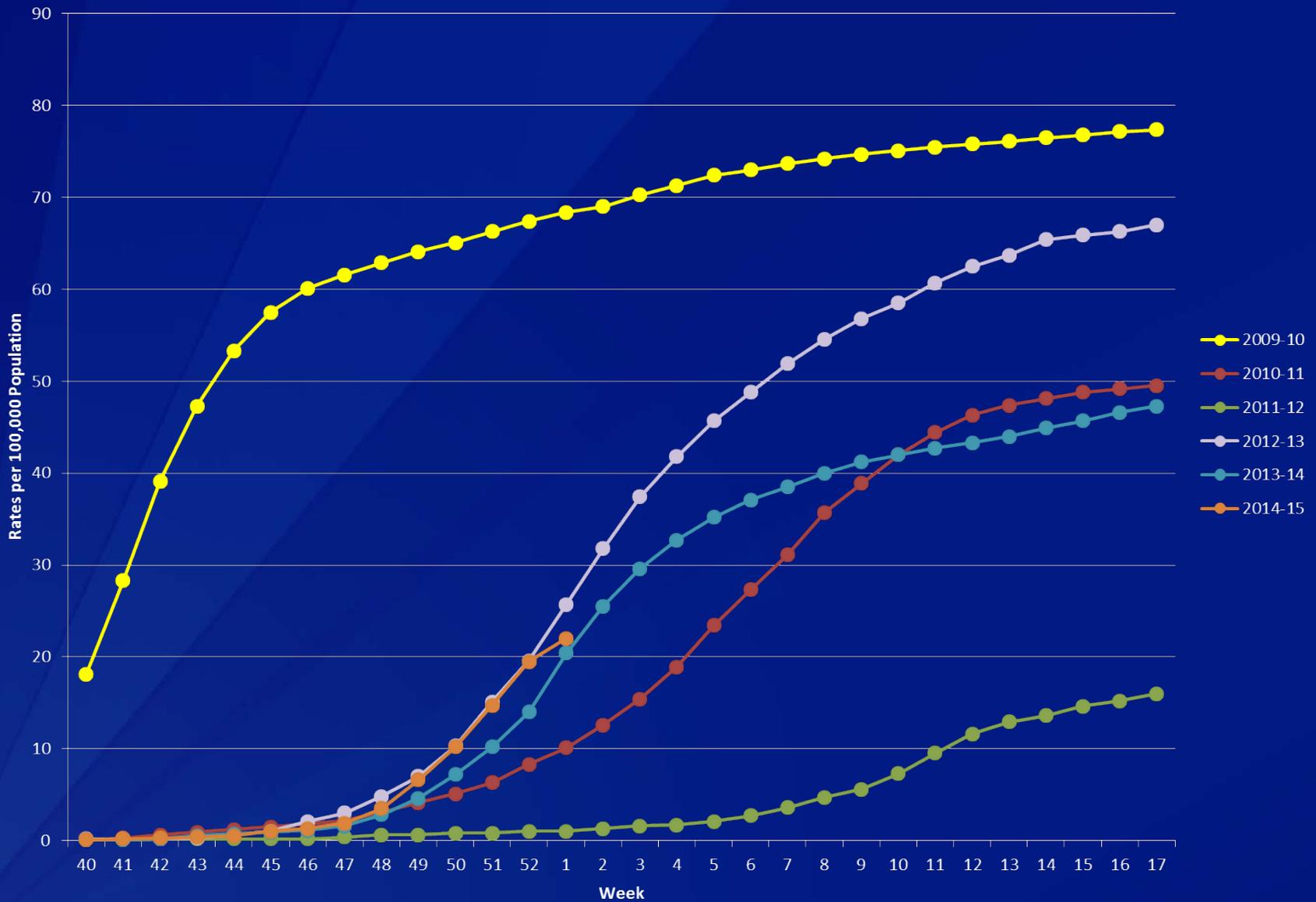
Preliminary rates as of Jan 3, 2015



Hospitalization Rates in People 65 and older, by Season

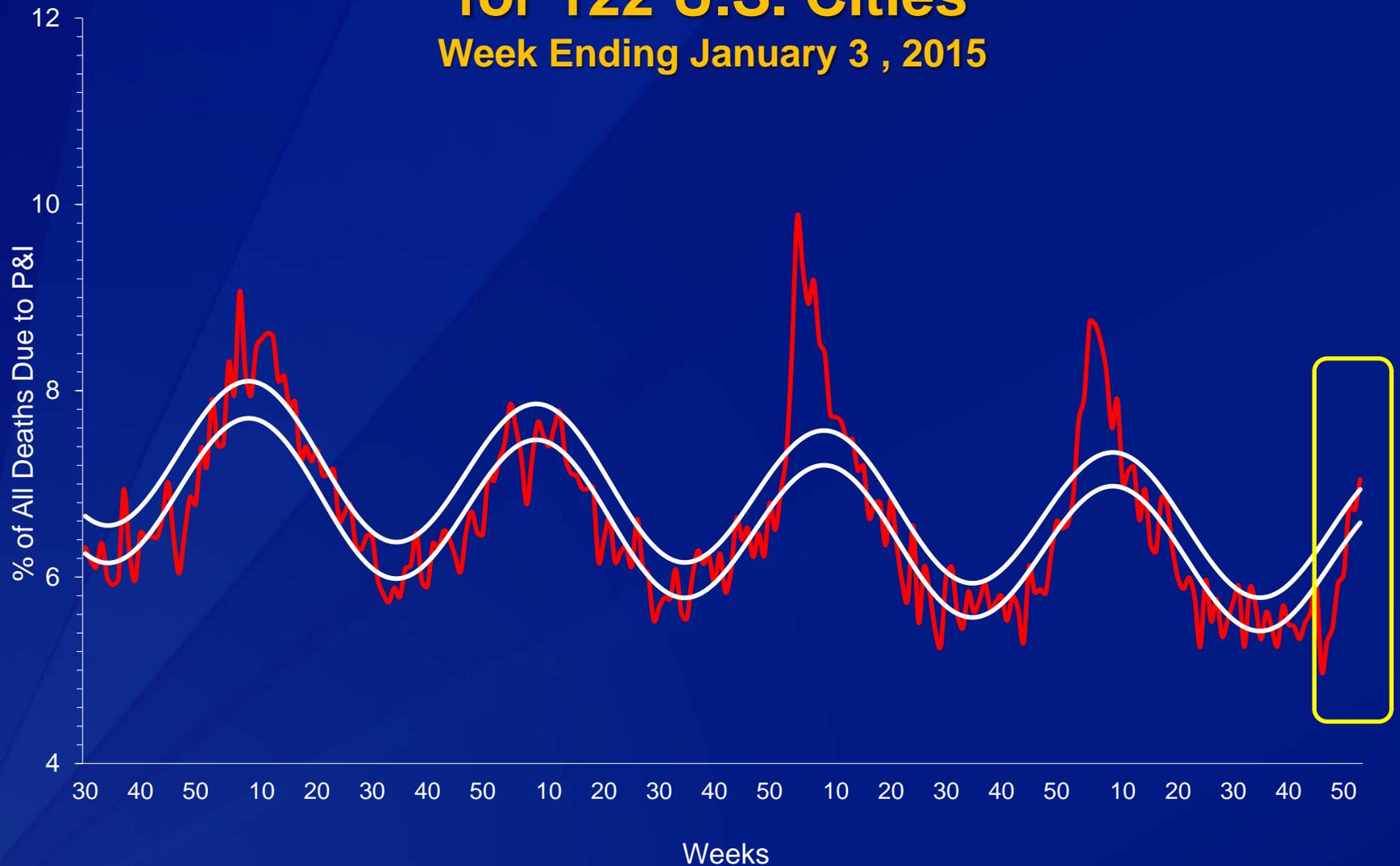


Hospitalization Rates in Children <5 Years, by Season



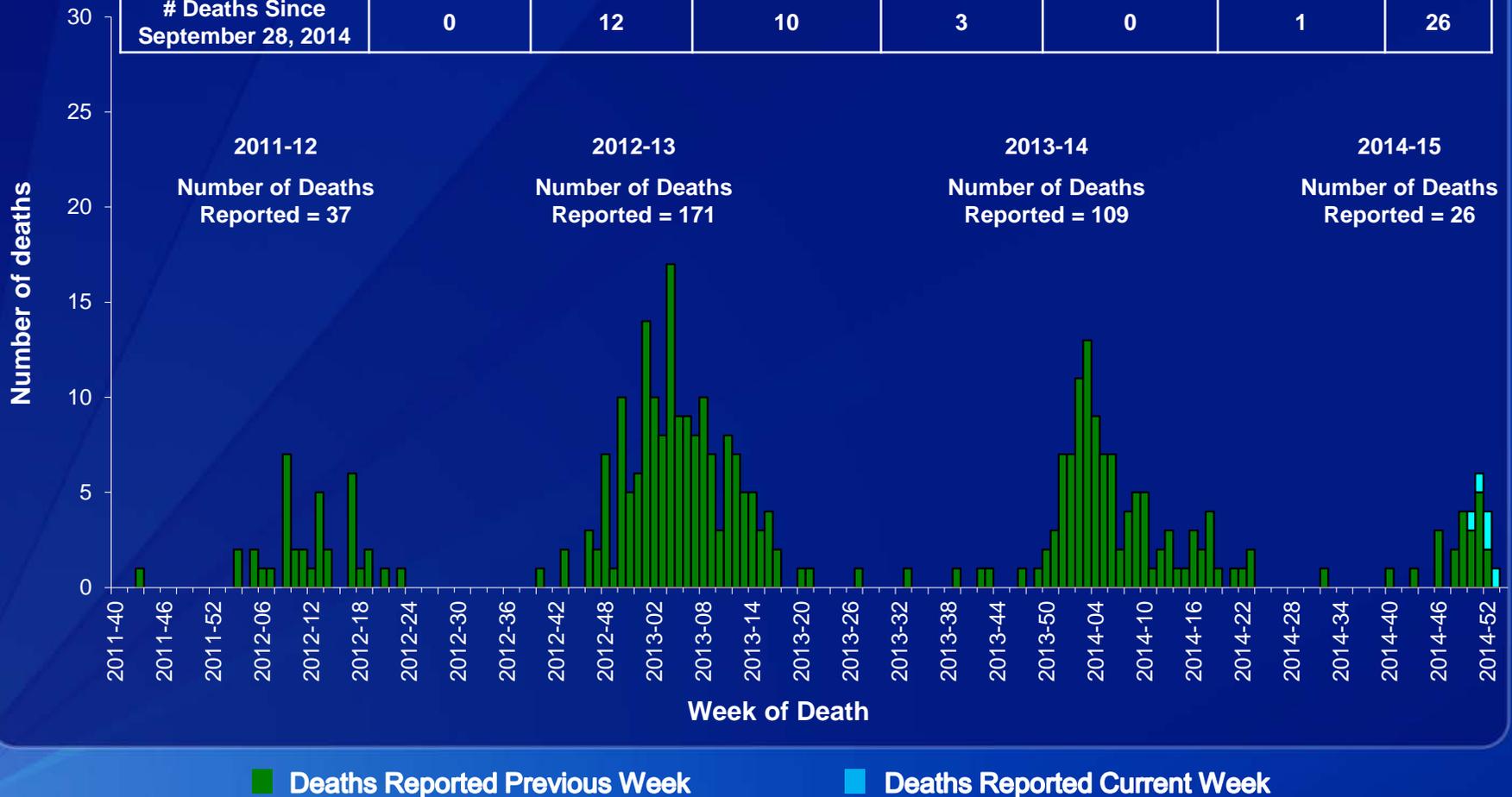
Pneumonia and Influenza Mortality for 122 U.S. Cities

Week Ending January 3, 2015



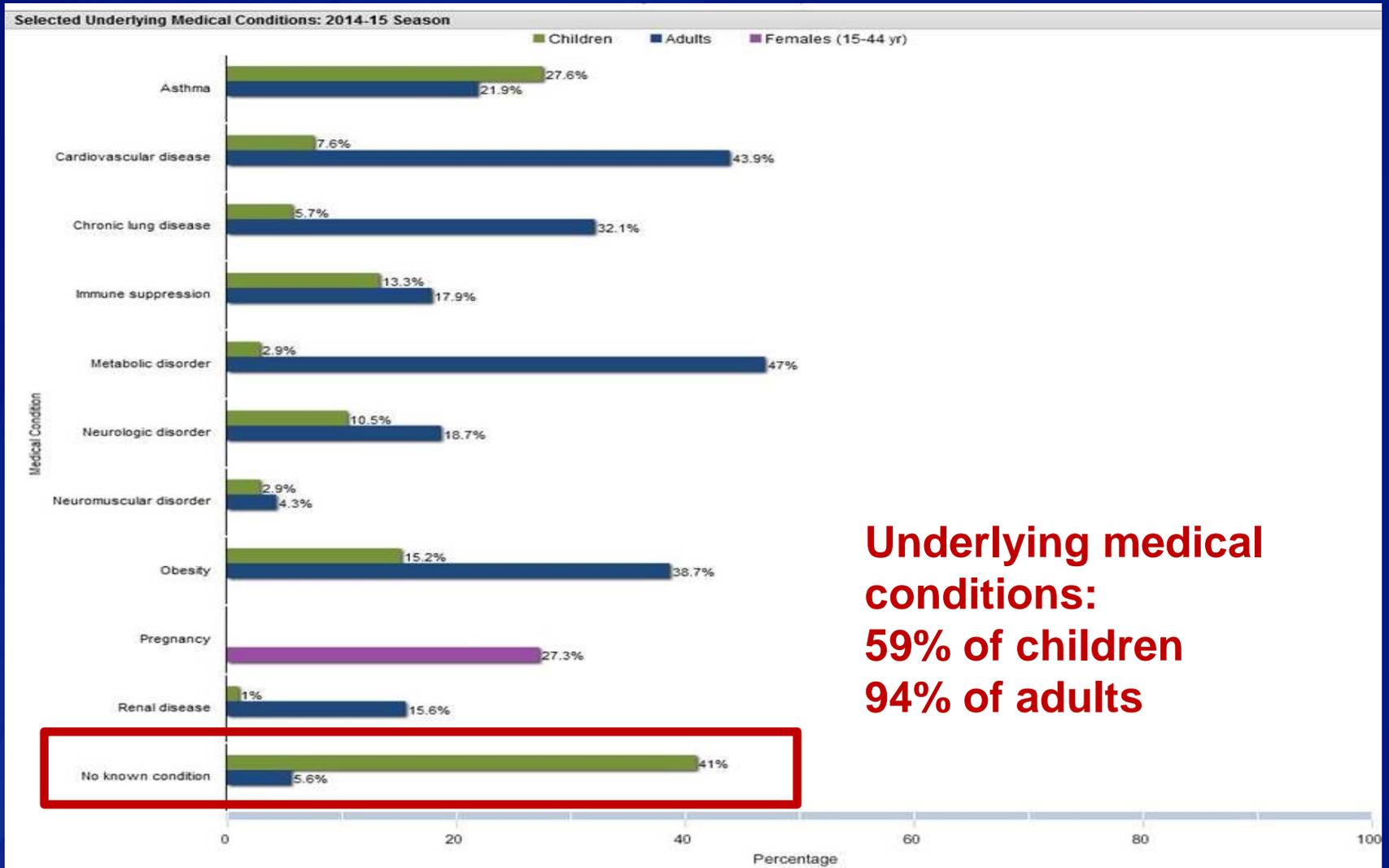
Number of Influenza-Associated Pediatric Deaths by Week of Death: 2011-12 Season to Present

	Influenza A (2009 H1N1)	Influenza A (H3N2)	Influenza A (Subtype not Determined)	Influenza B	Influenza A and B Co-infection	Type not Determined	Total
# Deaths Reported Current Week – 53	0	0	5	0	0	0	5
# Deaths Since September 28, 2014	0	12	10	3	0	1	26



Laboratory-Confirmed Influenza Hospitalizations

Preliminary rates as of Jan 3, 2015



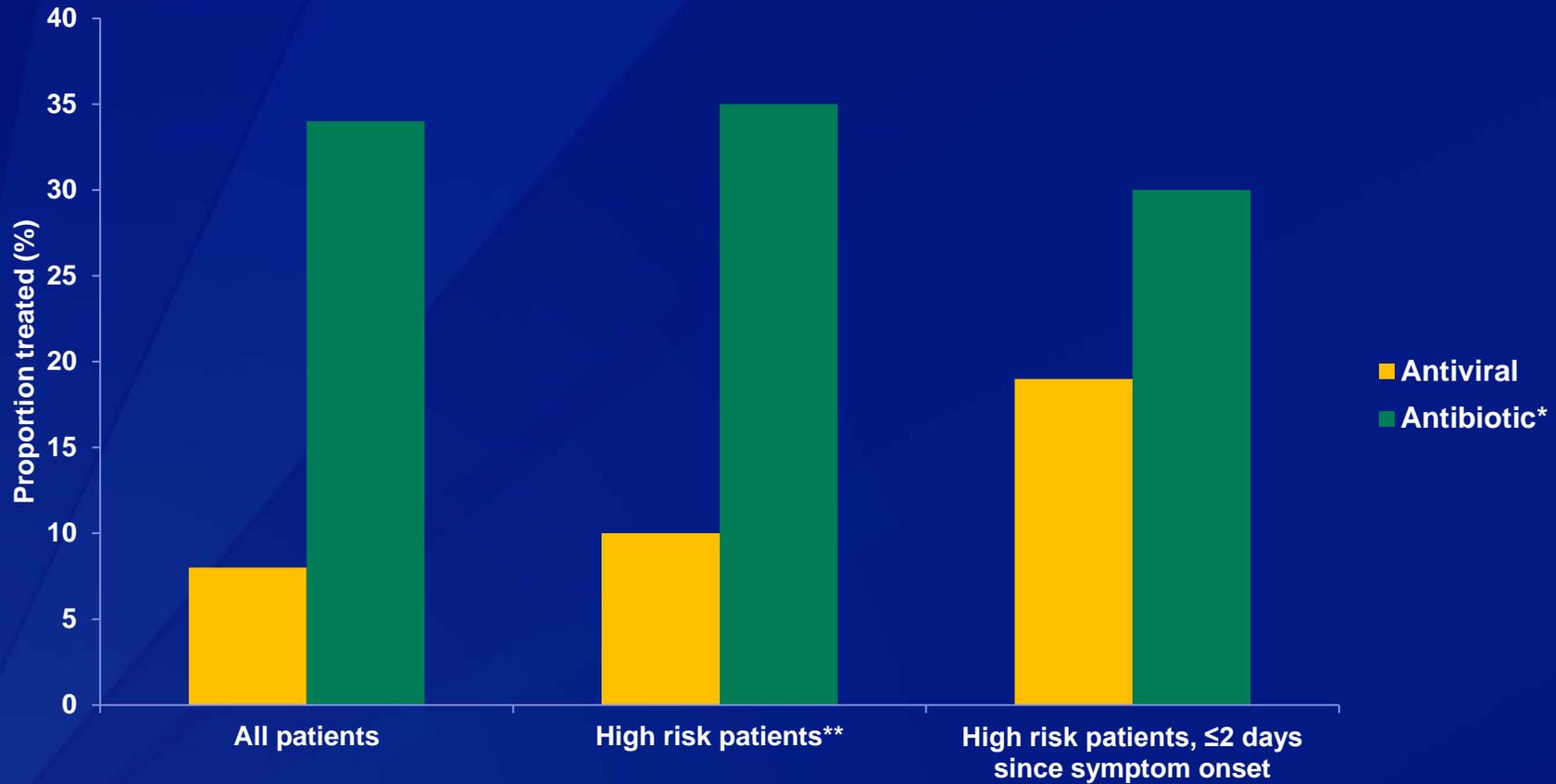
Season Overview

- ❑ **Influenza A(H3N2) viruses continue to be the most common so far in the United States**
 - H3N2 predominant years are often associated with higher mortality and hospitalization rates among older adults and young children
- ❑ **Activity so far this season is similar to the 2012-2013 season, the last season when H3N2 viruses predominated**
- ❑ **So far ~2/3 of H3 viruses analyzed are antigenically or genetically different from the H3N2 component in the 2014-15 vaccine**

Antiviral Use

- ❑ Evidence from current and previous influenza seasons suggests that antiviral drugs are underutilized
 - Low awareness of antiviral recommendations
 - Wide range in perception about antiviral effectiveness
 - Many clinicians may require a positive diagnostic test before prescribing; results of rapid influenza diagnostic tests (not molecular) may not be accurate
 - Some clinicians may not prescribe after the 48-hour window that is optimal for treatment

Outpatients with Acute Respiratory Illness Treated with an Influenza Antiviral Medication or Antibiotics During Influenza Season, US Flu VE Network, 2012-13



* Antibiotics limited to amoxicillin, amoxicillin-clavulanate, and azithromycin

- ❑ **RESPONSE TO THE 2014-15 influenza season**

This is an official
CDC HEALTH ADVISORY

Distributed via the CDC Health Alert Network
December 03, 2014, 16:00 ET (4:00 PM ET)
CDCHAN-00374

**CDC Health Advisory Regarding the Potential for Circulation of Drifted
Influenza A (H3N2) Viruses**

- ❑ **Vaccination should still be the most important first step in protecting against flu**
 - Even a vaccine with low vaccine effectiveness can prevent some infection
 - Protection against other viruses (e.g., H1N1 & B) that may circulate this season
- ❑ **This season, the use of neuraminidase inhibitor (NAI) antiviral medications is especially important when indicated for treatment and prevention of influenza**

CDC Health Update – Take Two

This is an official
CDC HEALTH UPDATE

Distributed via the CDC Health Alert Network
January 9, 2015, 11:00 ET
CDCHAN-00375

CDC Health Update Regarding Treatment of Patients with Influenza with Antiviral Medications

As a follow-up to HAN 00374 (<http://emergency.cdc.gov/han/han00374.asp>, Dec. 3, 2014), CDC is providing 1) a summary of influenza antiviral drug treatment recommendations, 2) an update about approved treatment drugs and supply this season, and 3) background information for patients regarding anti-influenza treatment.

CDC Health Update: Jan 9, 2015

Reminders to Clinicians

- 1) Influenza should be high on the list of possible diagnoses for ill patients**
- 2) All hospitalized and all high-risk patients with suspected or confirmed influenza should be treated as soon as possible without waiting for confirmatory testing**

CDC Antiviral Recommendations

- ❑ All patients in the following categories with suspected or confirmed influenza **should** be treated as soon as possible, without waiting for confirmatory influenza testing
 - Hospitalized patients
 - Patients with severe, complicated, or progressive illness
 - Patients at high risk for complications from influenza (either outpatient or hospitalized)

CDC Antiviral Recommendations

- Antiviral treatment may be prescribed on the basis of clinical judgment for any previously healthy (non-high risk) outpatient with suspected or confirmed influenza

Influenza Antiviral Medications: The Data Behind the Recommendations

Clinical trials and observational data show that early antiviral treatment can:

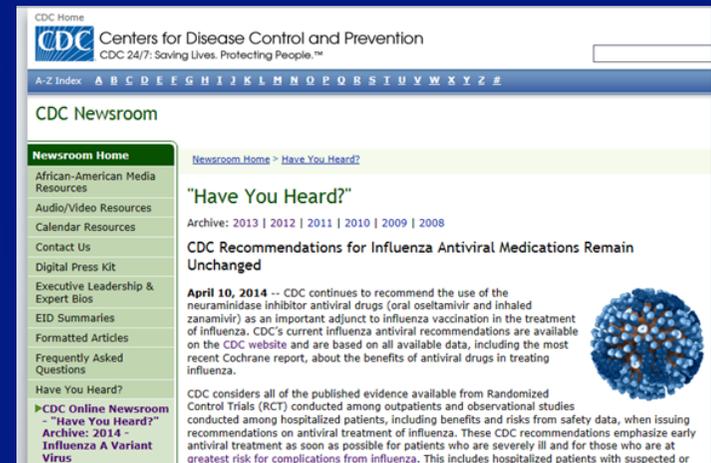
- ❑ Shorten the duration of fever and illness symptoms**
- ❑ Reduce the risk of complications (such as otitis media in children and pneumonia requiring antibiotics in adults)**
- ❑ Reduce the risk of death among hospitalized patients**

Data Regarding Effectiveness for Uncomplicated Influenza: Cochrane Review 2014

- ❑ **Analyzed treatment RCTs evaluating outcomes in the intention-to-treat (ITT) population (with and without flu): 15 oral oseltamivir and 16 inhaled zanamivir trials**
 - Most among otherwise healthy persons with influenza-like illness (ILI) during seasonal epidemics
- ❑ **NAIs reduced time to symptom alleviation**
 - Oseltamivir vs placebo in adults by ~17 hr, in children by ~29 hr
 - Zanamivir vs placebo in adults by ~14 hr
- ❑ **Reduced investigator-mediated unverified pneumonia by 45%; no benefits in studies that recorded pneumonia in more detail**
- ❑ **No evidence to support reduction in other flu-related complications (sinusitis, bronchitis, OM) or hospitalizations**
- ❑ **4-5% increased N/V in adults; 5% increased vomiting in children**

Assessment and Limitations of Cochrane Review

- ❑ Findings similar to previously published RCTs
 - All showed 1-2 day reduction in illness duration for early NAI treatment
- ❑ Analyzed only ITT results – because neuraminidase inhibitors are active against influenza, one analysis should have evaluated outcomes in the Intention-to-Treat-Infected (ITTI) patients
- ❑ Placebo controlled RCTs evaluated effect of treatment in healthy, non high-risk outpatients
 - None designed or powered to assess severe outcomes (hospitalization, ICU, death) or outcomes in high-risk persons
 - Persons at high-risk of influenza complications generally not in RCTs
- ❑ No published RCTs evaluating hospitalized patients



The screenshot shows the CDC Newsroom website. The header includes the CDC logo and the text 'Centers for Disease Control and Prevention' and 'CDC 24/7: Saving Lives. Protecting People.' Below the header is a navigation bar with an 'A-Z Index' and a list of letters. The main content area is titled 'CDC Newsroom' and features a sidebar on the left with links to 'Newsroom Home', 'African-American Media Resources', 'Audio/Video Resources', 'Calendar Resources', 'Contact Us', 'Digital Press Kit', 'Executive Leadership & Expert Bios', 'EID Summaries', 'Formatted Articles', 'Frequently Asked Questions', 'Have You Heard?', and 'CDC Online Newsroom - "Have You Heard?" Archives: 2014 - Influenza A Variant Virus'. The main article is titled '"Have You Heard?"' and is dated 'April 10, 2014'. The article text states: 'CDC continues to recommend the use of the neuraminidase inhibitor antiviral drugs (oral oseltamivir and inhaled zanamivir) as an important adjunct to influenza vaccination in the treatment of influenza. CDC's current influenza antiviral recommendations are available on the CDC website and are based on all available data, including the most recent Cochrane report, about the benefits of antiviral drugs in treating influenza. CDC considers all of the published evidence available from Randomized Control Trials (RCT) conducted among outpatients and observational studies conducted among hospitalized patients, including benefits and risks from safety data, when issuing recommendations on antiviral treatment of influenza. These CDC recommendations emphasize early antiviral treatment as soon as possible for patients who are severely ill and for those who are at greatest risk for complications from influenza. This includes hospitalized patients with suspected or'.

CDC Influenza Treatment Guidelines

- ❑ **Focus is on prevention of severe outcomes**
 - Treatment of those with severe disease and persons at highest risk of severe influenza complications
 - No RCTs available
- ❑ **Include observational studies and meta-analyses of antiviral effectiveness**
 - Cochrane review did not consider data from observational studies
- ❑ **Antiviral recommendations are common to ACIP, IDSA, AAP**

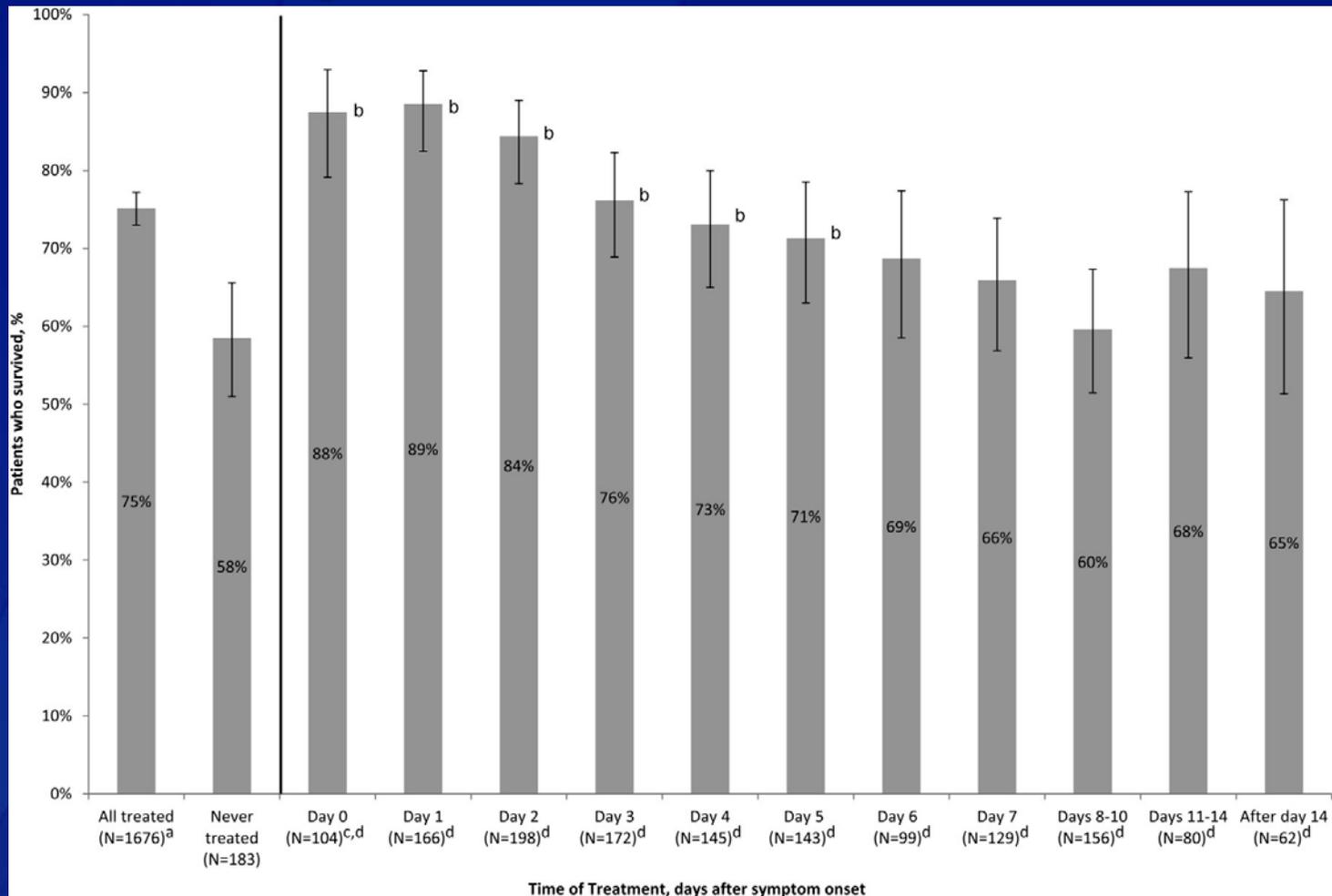
Data Regarding Oseltamivir Effectiveness: Hospitalized Patients

Study	Med. age (yr)	Setting; % Treated	Antiviral Effect (against death unless specified)
McGeer* 2007	77	Hosp; 32%	Treated vs untreated: aOR 0.21 (0.06-0.80)
Lee* 2010	70	Hosp; 52%	Treated vs untreated: aHR 0.27 (0.13-0.55); Treated vs untreated <2 d: aHR 0.29 (0.14-0.61); Treated vs untreated <4 d aHR 0.34 (0.17-0.70)
Hiba 2011	39-48	Hosp; 100%	Late vs early treatment: aOR 3.28 (1.56-6.89), for severe complications (death, ICU, MV)
Louie* 2012	37	ICU; 90%	No treatment: 58% survival; Early treatment (day 0): 88% survival; Treatment \leq 4 d: 73% survival
Louie 2013	6	ICU; 83%	Treated vs untreated: aOR 0.36 (0.16-0.83)

} p for trend <0.0001

***Studies suggesting that treatment initiation >48 hours may be beneficial**

Survival by Timing of Treatment in Critically Ill Patients with 2009 H1N1



Data Regarding NAIs Effectiveness: Hospitalized Patients

- Recent large meta-analysis compiled individual patient-level data from 78 observational studies on >29,000 patients hospitalized during 2009-10 H1N1 pandemic
 - Adults: treatment with a NAI was associated with a 25% reduction in likelihood of death compared to no antiviral treatment; aOR **0.75** (0.64-0.87)
 - Pregnant women: aOR **0.46** (0.23-0.89)
 - Children: aOR 0.82 (0.58-1.17)
 - Treatment within 48 hr of symptom onset halved the risk of death compared to no antiviral treatment; aOR **0.51** (0.45-0.58)

Effectiveness of Oseltamivir to Prevent Complications: Outpatients – Children

Study	Method	Outcome	Antiviral Effect among Influenza + (Intent to Treat Infected; ITTI)
Whitley 2001	RCT secondary outcome; Children 1-12 yrs	Otitis media	44% reduction
Heinonen 2010	RCT; Children 1-3 yrs	Otitis media	Initiate ≤ 12 hr: 85% reduction; Initiate > 24 hr: no reduction

Effectiveness of NAI Treatment to Prevent Complications: Outpatients

Study	Method	Outcome	Antiviral Effect among Influenza + (ITTI)
Hernan 2011	Meta-analysis, 11 pub & unpub RCTs	LRTC requiring antibiotics	37% (18-52%) reduction
Lipsitch 2013	Re-analysis 2011 data: excl. serology +	LRTC requiring antibiotics	33% (3-54%) reduction
Hsu 2012	Meta-analysis, 74 pub & unpub obs. studies	Hospitalization	OR 0.75 (0.66-0.89); <48 hr: OR 0.52 (0.33-0.81)
Ebell 2013	Meta-analysis, 11 pub & unpub RCTs	Pneumonia All complications* Hospitalization	Pneumonia ITTI: -0.9% ; All comps ITTI: -2.8% ; Hosp ITT: no diff
Cochrane Review 2014	Meta-analysis, 31 pub & unpub RCTs	Pneumonia (Investigator-mediated unverified)	ITT: RR 0.55 (0.33-0.90)

LRTC = lower respiratory tract complications;

*** All complications = otitis media, sinusitis, pneumonia, bronchitis**

Summary of Data Evaluating Reduction in Complications after Outpatient Treatment

- ❑ Not enough hospitalizations to evaluate
- ❑ Persons at highest risk of developing severe complications generally not studied in RCTs
- ❑ Pooled data from RCTs consistently show a reduction in pneumonia requiring antibiotics among adults; reduction in otitis media shown for children
- ❑ *Pending* – Individual patient data meta-analysis of RCTs comparing oseltamivir with placebo for treatment of outpatients with influenza (Multiparty Group for Advice on Science)

Adverse Events

- ❑ **Oral oseltamivir: Slightly increased risk of nausea, vomiting over placebo**
 - Mild, transient
 - Improved when taken with food
- ❑ **Inhaled zanamivir: Cases of bronchospasm reported during postmarketing – not recommended for persons with underlying airways disease such as asthma, COPD**
- ❑ **Intravenous peramivir: Slightly increased risk of diarrhea, neutropenia over placebo**

CDC Antiviral Recommendations

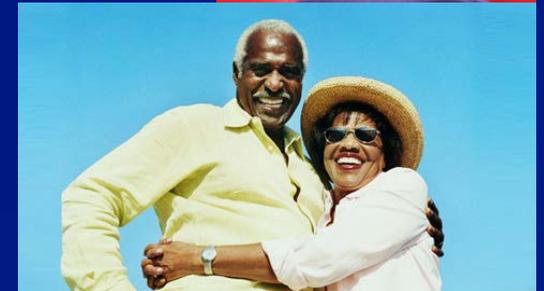
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 - Patients with severe, complicated, or progressive illness
 - Patients at high risk for complications from influenza (either outpatient or hospitalized)

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Persons at High Risk for Influenza Complications

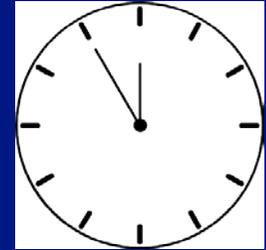
- ❑ Children <2 years
- ❑ Adults ≥ 65 years
- ❑ Pregnant and postpartum women (within 2 weeks after delivery)
- ❑ American Indians and Alaska Natives
- ❑ Persons who are morbidly obese (BMI ≥ 40)
- ❑ Residents of long-term care facilities



Persons at High Risk for Influenza Complications (continued)

- ❑ Persons with immunosuppression**
- ❑ Persons <19 years who are receiving long-term aspirin therapy**
- ❑ Persons with underlying medical conditions: chronic pulmonary, cardiovascular (except hypertension alone), renal, hepatic, hematologic, and metabolic disorders (incl. diabetes), or neurologic and neurodevelopment conditions**

Timing of Treatment



- ❑ When indicated, antiviral treatment should be started as soon as possible after illness onset
- ❑ Ideally, treatment should be initiated within 48 hours of symptom onset
- ❑ Treatment should not be delayed even for a few hours to wait for the results of testing
 - A negative rapid influenza antigen diagnostic test does **not** exclude a diagnosis of influenza

High-Risk Outpatients and Early Treatment

- ❑ During influenza season, providers should advise high-risk patients to call promptly if they have symptoms of influenza
- ❑ Phone triage lines may be useful to enable high risk patients to discuss symptoms over the phone
- ❑ To facilitate early initiation of treatment, when feasible, an antiviral prescription can be provided without testing and before an office visit

Antiviral Treatment Initiated after 48 Hours Can Still be Beneficial in Some Patients

- ❑ Observational studies of hospitalized patients suggest that treatment might still be beneficial when initiated 4 or 5 days after symptom onset**
- ❑ Observational data in pregnant women has shown antiviral treatment to provide benefit when started 3-4 days after onset**
- ❑ A randomized placebo controlled study suggested clinical benefit when oseltamivir was initiated 72 hours after illness onset among febrile children with uncomplicated influenza**

Antiviral Medications

❑ Oral oseltamivir (Tamiflu®)

- Recommended for treatment of all ages, chemoprophylaxis for age ≥ 3 months

❑ Inhaled zanamivir (Relenza®)

- Recommended for treatment for age ≥ 7 years, chemoprophylaxis for age ≥ 5 years

❑ Intravenous peramivir (Rapivab®)

- Approved on December 19, 2014, for treatment of acute uncomplicated influenza in persons ≥ 18 years
- 600 mg dose infused over 15-30 min

Outpatient Treatment

- ❑ **Any neuraminidase inhibitor may be used for treatment of outpatients**
 - 5-day course of oseltamivir or inhaled zanamivir
 - 1-day of IV peramivir
- ❑ **Oral oseltamivir is preferentially recommended for pregnant women**

Treatment for Hospitalized Patients

- ❑ **Treatment with oral or enterically administered oseltamivir is recommended**
 - Limited data suggest that oseltamivir administered by oro/naso gastric tube is well absorbed in critically ill influenza patients, including those in the intensive care unit, on continuous renal replacement therapy, and/or on extracorporeal membrane oxygenation
- ❑ **Inhaled zanamivir is not recommended because of lack of data for use in patients with severe influenza disease**
- ❑ **Insufficient data regarding efficacy of intravenous peramivir for hospitalized patients**

Treatment for Hospitalized Patients: Concern Regarding Oseltamivir Absorption

- ❑ For patients who cannot tolerate or absorb oral oseltamivir because of suspected or known gastric stasis, malabsorption, or gastrointestinal bleeding, the use of IV peramivir or investigational IV zanamivir should be considered
 - If peramivir used in severely ill patients, single dose should not be given
 - For severely ill patients, adult dose of 600 mg IV once daily for 5 days is recommended (dose for children >6 years: 10 mg/kg once daily [up to 600 mg] for 5 days)

Treatment for Hospitalized Patients: Concern Regarding Oseltamivir Resistance

- ❑ **Some influenza viruses may become resistant to oseltamivir and peramivir during antiviral treatment with one of these agents and remain susceptible to zanamivir**
 - Investigational use of intravenous zanamivir should be considered for treatment of severely ill patients with oseltamivir-resistant virus infection

Additional Information: Antibiotics and Bacterial Infections

- ❑ Antibiotics are not effective against influenza**
- ❑ Several reports suggest inappropriate use of antibiotics for patients with influenza**
- ❑ Bacterial infections can occur as a complication of influenza, so should be considered and appropriately treated if suspected**

Additional Information: Pneumococcal Vaccine Recommendations

- ❑ **Pneumococcal infections are a serious complication of influenza infection**
- ❑ **New pneumococcal vaccine recommendations for adults ≥ 65 years, and adults and children at increased risk for invasive pneumococcal disease due to chronic underlying medical conditions should be followed:**
 - <http://www.cdc.gov/vaccines/vpd-vac/pneumo/vac-PCV13-adults.htm>
 - <http://www.cdc.gov/vaccines/vpd-vac/pneumo/vacc-in-short.htm>

Institutional Outbreaks

(Long-Term Care Facilities, Nursing Homes, other Living Facilities that House High-Risk Persons)

- **Use of antiviral chemoprophylaxis to control outbreaks among high-risk persons in institutional settings is recommended**
 - For all residents (regardless of vaccination status)
 - For unvaccinated healthcare personnel
 - Consider for all, regardless of vaccination status, if outbreak is caused by a virus that is not well matched to the vaccine
 - For a minimum of 2 weeks, continuing at least 7 days after last known case identified

Antiviral Supply

- ❑ **No current national shortages**
 - Manufacturers have stated they have sufficient product on hand to meet the projected high demand
- ❑ **Local spot shortages have been reported, specifically for Tamiflu formulations**
- ❑ **It may be necessary to contact more than one pharmacy to fill a prescription for an antiviral medication**
- ❑ **Pharmacies that are having difficulties getting orders filled should contact their distributor or the manufacturer directly**

CDC Antiviral Call Center – 1

- ❑ For long-term care facilities or institutions experiencing difficulty accessing antiviral supplies in outbreak settings**
- ❑ CDC will coordinate with commercial partners to facilitate the rapid resolution of large orders of antiviral drugs**

CDC Antiviral Call Center – 2

- ❑ **As of Jan. 12, the Division of Strategic National Stockpile (DSNS) is available from 7:00 AM to 7:00 PM EST, Mon – Fri, to assist public health officials and health care facilities by coordinating with supply chain partners to rapidly redirect supply to the identified location**
- ❑ **Contact DSNS at dsns-Request@cdc.gov for assistance with facility specific unmet antiviral drug supply needs**

Summary of Antiviral Recommendations

- ❑ Early empiric antiviral treatment **is recommended** for suspected or confirmed influenza among the following:
 - Hospitalized patients
 - Patients with severe or progressive illness
 - Patients at high risk for complications
- ❑ Decisions about antiviral treatment should not wait for laboratory confirmation of influenza
- ❑ Clinical benefit is greatest when antiviral treatment is initiated early, but treatment initiated later than 48 hours after onset can still be beneficial for some patients

For Additional Information

- ❑ **Summary of Influenza Antiviral Treatment Recs for Clinicians:**
<http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm>
- ❑ **Guidance for Clinicians on the Use of RT-PCR and Other Molecular Assays for Diagnosis of Influenza Virus Infection:**
<http://www.cdc.gov/flu/professionals/diagnosis/molecular-assays.htm>
- ❑ **Interim Guidance for Influenza Outbreak Management in Long-Term Care Facilities:**
<http://www.cdc.gov/flu/professionals/infectioncontrol/ltc-facility-guidance.htm>
- ❑ **FDA Influenza (Flu) Antiviral Drugs and Related Information (including package inserts):**
<http://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm100228.htm>

To Ask a Question

❑ Using the Webinar System

- “Click” the Q&A tab at the top left of the webinar tool bar
- “Click” in the white space
- “Type” your question
- “Click” ask

❑ On the Phone

- Press Star (*) 1 to enter in the queue to ask a question
- State your name
- Listen for the operator to call your name

Thank you for joining!
Please email us questions at coca@cdc.gov



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CECH: Sponsored by the Centers for Disease Control and Prevention, a designated provider of continuing education contact hours (CECH) in health education by the National Commission for Health Education Credentialing, Inc. This program is designated for Certified Health Education Specialists (CHES) and/or Master Certified Health Education Specialists (MCHES) to receive up to 1.0 total Category I continuing education contact hours. Maximum advanced level continuing education contact hours available are 0. CDC provider number GA0082.



CPE: The Centers for Disease Control and Prevention is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This program is a designated event for pharmacists to receive 0.1 CEUs in pharmacy education. The Universal Activity Number is 0387-0000-15-072-L04-P and enduring 0387-0000-15-072-H04-P. This program is knowledge based.

AAVSB/RACE: This program was reviewed and approved by the AAVSB RACE program for 1.2 hours of continuing education in jurisdictions which recognize AAVSB RACE approval. Please contact the AAVSB RACE program if you have any comments/concerns regarding this program's validity or relevancy to the veterinary profession.

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Those who participate in the COCA Conference Calls and who wish to receive CE credit/contact hours and will complete the online evaluation by **February 13, 2015** will use the course code **WC2286**. Those who wish to receive CE credits/contact hours and will complete the online evaluation between **February 14, 2015** and **December 13, 2015** will use course code **WD2286**. CE certificates can be printed immediately upon completion of your online evaluation. A cumulative transcript of all CDC/ATSDR CE's obtained through the CDC Training & Continuing Education Online System will be maintained for each user.

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