CDC Influenza Division Key Points
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Summary Key Messages

- The current FluView report indicates that flu activity is low and continues to decline across the United States, though flu viruses are still causing illness.
- CDC continues to recommend vaccination as long as influenza viruses are circulating.
- At this point in the season, people may have to check with more than one vaccine provider in order to locate vaccine, but supplies of vaccine should still be available.
- And remember that flu antiviral drugs are a second line of defense to treat flu illness.
- Influenza vaccination and rapid antiviral treatment are especially important for people in the groups at high risk for flu complications.
- People at high risk for serious flu complications include: people with underlying chronic medical conditions such as asthma, diabetes, heart disease, or neurological conditions; pregnant women; those younger than 5 years or older than 65 years of age; or anyone with a weakened immune system. A full list of high risk factors is available at http://www.cdc.gov/flu/about/disease/high_risk.htm.
- As always, people who are at high risk for influenza complications should see their health care provider promptly if they get flu symptoms, even if they have been vaccinated this season.
- A health care provider can determine if the patient needs influenza antiviral drugs. Antiviral drugs can treat flu illness and prevent serious flu complications. These drugs work best when started soon after influenza symptoms begin (within 2 days), but persons with high-risk conditions can benefit even when antiviral treatment is started after the first two days of illness.
- Flu symptoms include fever, cough, sore throat, runny or stuffy nose, muscle or body aches, headache, chills and fatigue.

FluView Activity Update

- According to the latest FluView report, seasonal influenza activity is low and declining nationally, though flu viruses continue to cause illness in the United States.

- Below is a summary of the key indicators for the week ending March 22, 2014:
    - For the week ending March 22, the national proportion of people seeing their health care provider for influenza-like illness (ILI) decreased and remains below the national baseline of 2.0% for the second week. ILI was above or at baseline for 15 weeks this season. Four of 10 regions continue to report ILI activity at or above their region-specific baseline levels. Additional information regarding regional activity is available through FluView Interactive.
    - No states experienced high ILI activity. One state (Texas) and New York City experienced moderate ILI activity. Two states (Minnesota and Utah) experienced low ILI activity. Forty-seven states experienced minimal ILI activity. The District of Columbia did not have sufficient data to calculate an activity level. ILI activity data indicate the amount of flu-like illness that is occurring in each state.
    - Four states reported widespread geographic influenza activity. The same number of states reported widespread activity during the previous week. Guam and seven states reported regional activity. Washington, D.C. and 17 states reported local activity. Puerto Rico and 22 states reported sporadic influenza activity. The U.S. Virgin Islands reported no influenza activity. Geographic spread data show how many areas within a state or territory are seeing flu activity.
    - 8,405 laboratory-confirmed influenza-associated hospitalizations have been reported since October 1, 2013. This translates to a cumulative overall rate of 31.1 hospitalizations per 100,000 people in the United States. The cumulative hospitalization rate for the same week last season (week 12) was 41.9 per 100,000. More data on hospitalization rates are available through FluView Interactive.
        - The highest hospitalization rates are among people 65 and older (70.3 per 100,000), followed by people 50-64 years (48.8 per 100,000) and children younger than 5 years (42.7 per 100,000). During most seasons, children younger than 5 years and adults 65 years and older have the highest hospitalization rates.
        - Of the 8,405 influenza-associated hospitalizations that have been reported this season, more than 60% have been in people 18 to 64 years old. This trend of increased hospitalizations among younger people was also seen during the 2009 H1N1 pandemic.
        - Hospitalization data are collected from 13 states and represent approximately 8.5% of the total U.S. population. The number of hospitalizations reported does not reflect the actual total number of influenza-associated hospitalizations in the United States.

- The proportion of deaths attributed to pneumonia and influenza (P&I) based on the 122 Cities Mortality Reporting System increased slightly to 7.2% but remains below the epidemic threshold.
- Four influenza-associated pediatric deaths were reported to CDC during the week of March 16-22 (week 12). One death was associated with a 2009 H1N1 virus, two deaths were associated with an influenza A virus for which no subtyping was performed, and one death was associated with an influenza B virus. A total of 79 influenza-associated pediatric deaths have been reported for the 2013-2014 season at this time. Additional information about the pediatric deaths from this season and previous seasons is available through FluView Interactive.
- Nationally, the percentage of respiratory specimens testing positive for influenza viruses in the United States during the week ending March 22, 2014 increased slightly to 11.5%. Averaged over the last three weeks, the regional percentage of respiratory specimens testing positive for influenza viruses ranged from 4.5% to 22.1%.
- Influenza A (H3N2), 2009 H1N1, and influenza B viruses have all been identified in the U.S. this season. To date, 2009 H1N1 viruses have predominated. This is the H1N1 virus that emerged in 2009 to cause a pandemic. 2009 H1N1 viruses have continued to circulate among people since that time, but this is the first season that the virus has circulated at such high levels since the pandemic. During the week ending March 22, 348 (61%) of the 571 influenza-positive tests reported to CDC were influenza A viruses and 223 (39%) were influenza B viruses. Of the 169 influenza A viruses that were subtyped, 40% were H3 viruses and 60% were 2009 H1N1 viruses.
- CDC has antigenically characterized 1,914 influenza viruses; 1,562 2009 H1N1 viruses, 229 influenza A (H3N2) viruses, and 123 influenza B viruses, collected since October 1, 2013.
    - 1,561 (99.9%) of the 1,562 2009 H1N1 viruses tested were characterized as A/California/7/2009-like. This is the influenza A (H1N1) component of the Northern Hemisphere quadrivalent and trivalent vaccines for the 2013-2014 season.
    - 224 (97.8%) of the 229 influenza A (H3N2) viruses tested were characterized as Texas/50/2012-like. This is the influenza A (H3N2) component of the Northern Hemisphere quadrivalent and trivalent vaccines for the 2013-2014 season.
    - 84 (68%) of the 123 influenza B viruses tested belonged to the B/Yamagata lineage of viruses, and were characterized as B/Massachusetts/02/2012-like. This is an influenza B component for the

2013-2014 Northern Hemisphere quadrivalent and trivalent influenza vaccines.

- The 39 (32%) other influenza B viruses belonged to the B/Victoria lineage of viruses, and were characterized as B/Brisbane/60/2008-like. This is the recommended influenza B component of the 2013-2014 Northern Hemisphere quadrivalent influenza vaccine.

- Since October 1, 2013, CDC has tested 4,624 2009 H1N1, 334 influenza A (H3N2), and 200 influenza B virus samples for resistance to the neuraminidase inhibitor influenza antiviral drugs. While the vast majority of the 2009 H1N1 viruses that have been tested are sensitive to oseltamivir and zanamivir, eleven additional 2009 H1N1 virus showed resistance to oseltamivir and were reported during the week ending March 22. So far this season 54 (1%) 2009 H1N1 viruses have shown resistance to oseltamivir. No influenza A (H3N2) or influenza B viruses have shown resistance to oseltamivir. No viruses have shown resistance to zanamivir.

  - The neuraminidase inhibitors oseltamivir and zanamivir are currently the only recommended influenza antiviral drugs.
  - As in recent past seasons, high levels of resistance to the adamantanes (amantadine and rimantadine) continue to persist among 2009 H1N1 and influenza A (H3N2) viruses. Adamantanes are not effective against influenza B viruses. Adamantanes are not recommended for use against influenza this season.

FluView is available – and past issues are archived – on the CDC website.

Note: Delays in reporting may mean that data changes over time. The most up to date data for all weeks during the 2013-2014 season can be found on the current FluView.

Influenza-Associated Pediatric Deaths

- Four influenza-associated pediatric deaths were reported to CDC for the week of March 16-22, 2014 (Week 12).
- This brings the total of influenza-related pediatric deaths that have been reported for the 2013-2014 flu season to 79.
- Additional information regarding pediatric deaths is available through FluView Interactive.
- A pediatric death is a death in a person who is a U.S. resident and younger than 18 years old from an illness associated with infection with an influenza virus.

- During the 2012-2013 influenza season, a total of 171 influenza-associated pediatric deaths were reported to CDC.
- A review of the available pediatric death reports from the 2012-2013 season indicates that:
    - Of the 164 deaths in which the child's medical history was known, 55% occurred in children who had underlying medical conditions that placed them at high risk of developing serious flu-associated complications. However, 45% had no recognized underlying health problems.
    - The proportions of pediatric deaths that occurred in unvaccinated children and among children with underlying medical conditions that placed them at high risk from flu complications are largely consistent with what has been seen in the past.
- Since 2004, when flu-associated pediatric deaths became a nationally notifiable condition, the number of deaths reported to CDC each season has ranged from 35 (2011-2012 season) to 171 (2012-2013 season).
- During the 2009 H1N1 pandemic — April 15, 2009 to October 2, 2010 — 348 pediatric deaths were reported to CDC.
- These deaths are a somber reminder of the danger flu poses to children.
- The single best way to protect children against seasonal flu and its potential severe consequences is to have them receive a seasonal flu vaccine each year.
- Among children, vaccination is especially important for those younger than 5 years of age and those of any age with an underlying medical condition like asthma; a neurological, neuromuscular or neurodevelopmental disorder; or immune suppression. These children are at higher risk of serious complications if they get the flu.
- Yearly vaccination also is especially important for people who come in contact with high risk children in order to protect the child (or children) from the flu.
- Even previously healthy children can become seriously ill if they get the flu. Data on laboratory-confirmed influenza hospitalizations during the 2012-2013 flu season indicated that 46% of children hospitalized with the flu had no identified underlying medical conditions.
- Flu-associated deaths in children younger than 18 years old should be reported through the Influenza-Associated Pediatric Mortality Surveillance System. The number of flu-associated deaths among children reported during the 2013-2014 flu season will be updated each week and can be found at http://www.cdc.gov/flu/weekly/.
- Additional information about the pediatric deaths, including basic demographics, underlying conditions and week and place of death, for the 2013-2014 season as well

as past influenza seasons, is available through the Influenza Associated Pediatric Mortality application of FluView Interactive at http://gis.cdc.gov/GRASP/Fluview/PedFluDeath.html.

Oseltamivir-Resistant Influenza Viruses

- Influenza viruses can sometimes develop resistance to antiviral medications.
- Antiviral resistance means that a virus has changed in such a way that the antiviral drug is less effective in treating or preventing illnesses caused by the virus.
- Influenza viruses constantly change as the virus makes copies of itself. Some changes can result in the viruses being resistant to one or more of the antiviral drugs that are used to treat or prevent influenza.
- Resistance of influenza A viruses to antiviral drugs can occur spontaneously or emerge during the course of antiviral treatment.
- Antiviral resistance is detected through laboratory testing.
- CDC reports specimens collected and tested through national surveillance as well as additional specimens tested at public health laboratories who share testing results with CDC.
- For the week of March 16-22, 2014 (Week 12), eleven oseltamivir-resistant 2009 H1N1 virus were reported, bringing the total number of oseltamivir-resistant viruses to 54 for this season.
- Oseltamivir resistance among 2009 H1N1 viruses is rare.
- The majority of 2009 H1N1 viruses circulating in the United States remain susceptible to the neuraminidase inhibitor antiviral medications, oseltamivir and zanamivir.
- Oseltamivir-resistant viruses often have a single known substitution in the neuraminidase protein of the virus (H275Y) that seems to confer oseltamivir resistance. All the oseltamivir-resistant H1N1 viruses reported this season have had this substitution.
- CDC and state and local partners will continue to watch influenza viruses closely for possible emerging patterns of antiviral resistance in addition to watching for antigenic changes.
- Two FDA-approved influenza antiviral medications are recommended for use in the United States during the 2013-2014 influenza season: oseltamivir (Tamiflu®) and zanamivir (Relenza®). More information about antiviral drug resistance can be found at http://www.cdc.gov/flu/about/qa/antiviralresistance.htm and http://www.cdc.gov/flu/antivirals/index.htm.

- Information on the monitoring of antiviral resistance of influenza viruses to oseltamivir and zanamivir is updated weekly in the CDC FluView surveillance report, which is available at: http://www.cdc.gov/flu/weekly/.

JID Article: Effectiveness of influenza vaccine against life-threatening RT-PCR-confirmed influenza illness in US children, 2010-2012

- A study released today in the *Journal of Infectious Diseases* examined the effectiveness of the flu vaccine to reduce a child's risk of flu-related pediatric intensive care unit (PICU) admission.
- The article is available online at http://jid.oxfordjournals.org/content/early/2014/03/23/infdis.jiu185.abstract.
- This observational, case-control study – the first to estimate vaccine effectiveness (VE) against life-threatening outcomes of influenza infection in children – shows that flu vaccine reduces children's risk of PICU flu admission by three-fourths.
- Researchers analyzed the medical and immunization records of 216 children aged 6 months through 17 years who had been admitted to 21 U.S. PICUs with acute severe respiratory illness during the 2010-11 and 2011-12 flu seasons. RT-PCT was used to confirm that 44 children were influenza-positive ("cases") and 172 were influenza-negative ("PICU controls").
    - In addition, ninety-three "community controls" who had similar flu exposure and underlying medical conditions as the cases were enrolled from a population of children who had received inpatient or outpatient care at facilities associated with the study sites in the two years prior to the study.
- Compared to unvaccinated children, children who were fully vaccinated were **74%** (95% CI: 19-91%) or **82%** (95% CI: 23-96%) less likely to be admitted to a PICU for influenza illness compared to PICU controls and community controls, respectively.
- These seasonal influenza VE estimates suggest that flu vaccination was associated with reduced influenza PICU admissions during the 2010-2012 flu seasons.
    - Similar estimates for VE against outpatient flu visits are not available (e.g, same age group and combined years). However, as a comparison, during the 2010-2011 flu season, the VE against outpatient flu visits was 58% (95% CI: 31-74%) and 69% (95% CI: 56-77%) for children aged 6 months to 2 years and 3 to 8 years, respectively. In 2011-2012, the estimated VE against outpatient flu visits for children aged 6 months to 8 years and 9 to 17 years were 45% (95% CI:20-62%) and 58% (95% CI:27-76%), respectively.

  - Since the PICU study and the outpatient study results have wide confidence intervals, and were from different systems and study sites, it is not possible to say one VE estimate is statistically different than the other.

- In the PICU study, flu vaccination was not protective for children for whom two influenza vaccine doses were recommended, but had only received one dose.
- Vaccine coverage among enrollees in this study was low; only 18% of cases, 31% of PICU controls and 51% of community controls were fully vaccinated against flu.
  - A child was considered "fully vaccinated" if they had received the recommended number of flu vaccine doses required for his/her age based on the ACIP recommendations for the influenza season in which they were enrolled in the study.
- Children younger than 5 years and children of any age with certain underlying chronic medical conditions, like asthma, diabetes or developmental delays, are at high risk of serious flu complications. (A full list of these conditions that increase the risk of flu-related complications is available at http://www.cdc.gov/flu/about/disease/high_risk.htm.)
- Among the cases and PICU controls with at least one underlying chronic condition that increased their risk for influenza complications, only 37% had been fully vaccinated.

Vaccine Effectiveness Background

- CDC typically conducts studies throughout the influenza season to measure the benefits of seasonal flu vaccination to help determine how well flu vaccines are working. These studies are called "vaccine effectiveness" studies or "VE" studies, for short.
- How well the flu vaccine works can vary by season, virus type/subtype, the vaccine, and age and other host factors of the people being vaccinated.
- VE is difficult to measure and study results can vary widely based on the study design, the outcome being measured and the population being studied.
- CDC has worked with researchers at universities and health systems since 2003-2004 to estimate VE in non-randomized, observational studies.
- The U.S. Flu VE Network consists of five study sites across the United States that measure the flu vaccine's effectiveness at preventing outpatient medical visits due to laboratory-confirmed influenza.
- CDC's observational studies at U.S. Flu VE Network sites measure outpatient visits for laboratory-confirmed influenza infection using a highly accurate lab test called RT-PCR to verify the outcome.

- Data for the current *JID* study was obtained from the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network, a collaboration of pediatric clinical researchers in North America.

Other Study Details

- One shortcoming of observational, case-controlled studies of vaccine effectiveness is that they are at risk for confounding due to participants' health status.
- Children with underlying health conditions are both more likely to be vaccinated and more likely to have severe complications of influenza, which is a potential confounder for influenza vaccine effectiveness studies, and tends to falsely lower VE.
- Researchers in this study attempted to minimize confounders based on the health status of children enrolled in the study by including PICU controls and community controls.
- However, some unmeasured confounders and biases may still exist.