Centers for Disease Control and Prevention
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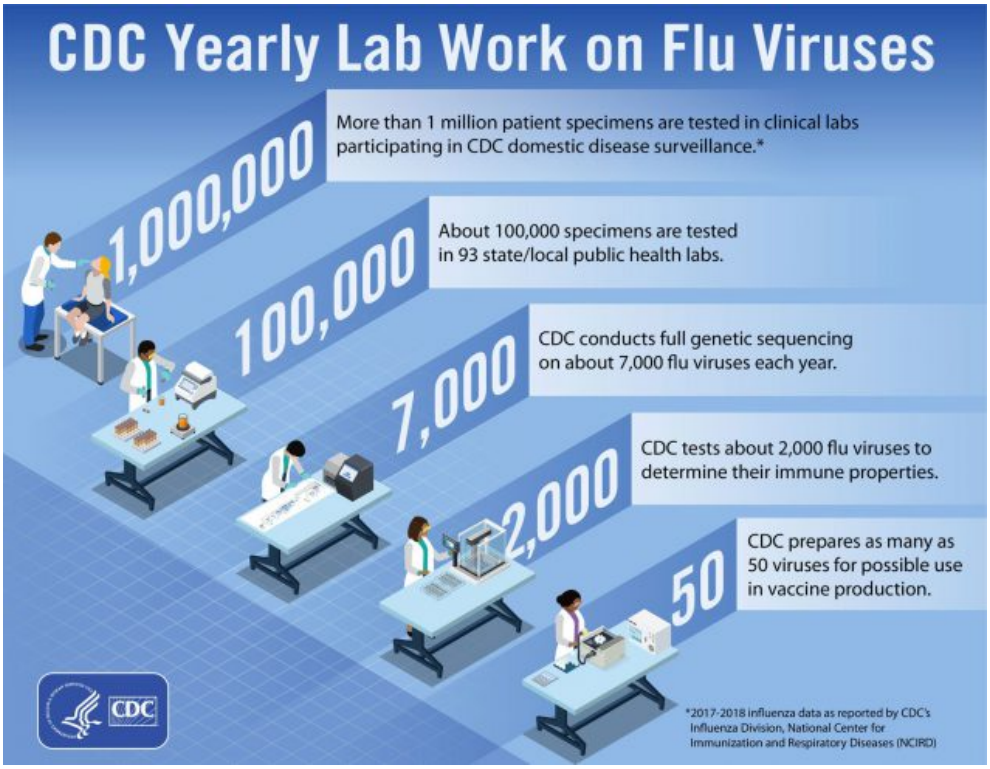
FLUVIEW

U.S. Influenza Surveillance System: Purpose and Methods



Full Sized Infographic and Text Version

The Influenza Division at CDC collects, compiles and analyzes information on influenza activity year-round in the United States. FluView, a weekly influenza surveillance report, and FluView Interactive, an online application which allows for more in-depth exploration of influenza surveillance data, are updated each week. **The data presented each week are preliminary and may change as more data is received.**

The U.S. influenza surveillance system is a collaborative effort between CDC and its many partners in state, local, and territorial health departments, public health and clinical laboratories, vital statistics offices, healthcare providers, clinics, and emergency departments. Information in five categories is collected from eight data sources in order to:

- Find out when and where influenza activity is occurring;
- Determine what influenza viruses are circulating;
- Detect changes in influenza viruses; and
- Measure the impact influenza is having on outpatient illness, hospitalizations and deaths.

It is important to maintain a comprehensive system for influenza surveillance for the following reasons:

- Influenza viruses are constantly changing (referred to as antigenic drift), and thus ongoing data collection and

characterization of the viruses are required;

- Influenza viruses can also undergo an abrupt, major change (referred to as antigenic shift) that results in a virus that is different than currently circulating influenza viruses; surveillance of viruses will detect these changes and inform the public health response;
- Vaccines must be administered annually and are updated regularly based on surveillance findings;
- Treatment for influenza is guided by laboratory surveillance for antiviral resistance; and
- Influenza surveillance and targeted research studies are used to monitor the impact of influenza on different segments of the population (e.g. age groups, underlying medical conditions).

Surveillance System Components

1. Virologic Surveillance

U.S. World Health Organization (WHO) Collaborating Laboratories System and the **National Respiratory and Enteric Virus Surveillance System (NREVSS) –** Approximately 100 public health and over 300 clinical laboratories located throughout all 50 states, Puerto Rico, Guam, and the District of Columbia participate in virologic surveillance for influenza through either the U.S. WHO Collaborating Laboratories System or NREVSS. Influenza testing practices differ between public health and clinical laboratories and each network provides valuable information for monitoring influenza activity. Clinical laboratories primarily test respiratory specimens for diagnostic purposes and data from these laboratories provide useful information on the timing and intensity of influenza activity. Public health laboratories primarily test specimens for surveillance purposes to understand what influenza virus types, subtypes, and lineages are circulating and the age groups affected.

All public health and clinical laboratories report each week to CDC the total number of respiratory specimens tested for influenza and the number positive for influenza viruses, along with age or age group of the person, if available. Data presented from clinical laboratories include the weekly total number of specimens tested, the number of positive influenza tests, and the percent positive by influenza virus type. Data presented from public health laboratories include the weekly total number of specimens tested and the number positive by influenza virus type and subtype/lineage. In order to obtain specimens in an efficient manner, public health laboratories often receive samples that have already tested positive for influenza at a clinical laboratory. As a result, monitoring the percent of specimens testing positive for influenza in a public health laboratory is less useful (i.e., we expect a higher percent positive). In order to use each data source most appropriately and to avoid duplication, reports from public health and clinical laboratories are presented separately in both FluView and FluView Interactive.

The age distribution of influenza positive specimens reported from public health laboratories is visualized in FluView Interactive. The number and proportion of influenza virus-positive specimens by influenza A subtype and influenza B lineage are presented by age group (0-4 years, 5-24 years, 25-64 years, and ≥65 years) each week and cumulative totals are provided for the season.

Additional laboratory data for current and past seasons and by geographic level (national, Department of Health and Human Services (HHS) region, and state) are available on FluView Interactive.

Virus Characterization – This includes genetic characterization and antigenic characterization. Most U.S. viruses submitted for virus characterization come from state and local public health laboratories. Due to Right Size considerations, specimen submission guidance to public health laboratories for the 2020-2021 season is that, if available, 2 influenza A(H1N1)pdm09, 3 influenza A(H3N2), and 2 influenza B viruses be submitted every other week. Therefore, the

numbers of each virus type/subtype characterized should be more balanced across subtypes/lineages but will not reflect the actual proportion of circulating viruses. The goal of antigenic and genetic characterization is to compare how similar the currently circulating influenza viruses are to the reference viruses representing viruses contained in the current influenza vaccines and to monitor evolutionary changes that continually occur in influenza viruses circulating in humans. For genetic characterization, all influenza-positive surveillance samples received at CDC undergo next-generation sequencing to determine the genetic identity of circulating influenza viruses and to monitor the evolutionary trajectory of viruses circulating in our population. Virus gene segments are classified into genetic clades/subclades based on phylogenetic analysis. However, genetic changes that classify the clades/subclades do not always result in antigenic changes.

Antigenic characterization is performed using hemagglutination inhibition and/or neutralization based focus reduction assays to compare antigenic properties of cell-propagated reference viruses representing currently recommended vaccine components with those of cell-propagated circulating viruses. Antigenic characterization is used to detect "antigenic drift", a term used to describe gradual antigenic change that occurs as viruses evolve to escape host immune pressure.

CDC also tests a subset of the influenza viruses collected by public health laboratories for susceptibility to the neuraminidase inhibitor antivirals (oseltamivir, zanamivir, and peramivir) and the PA cap-dependent endonuclease inhibitor (baloxavir). Susceptibility to the neuraminidase inhibitors is assessed using next-generation sequencing analysis and/or a functional assay. Neuraminidase sequences of viruses are inspected to detect the presence of amino acid substitutions previously associated with reduced or highly reduced inhibition by any of three neuraminidase inhibitors. In addition, a subset of viruses is tested using the neuraminidase inhibition assay with three neuraminidase inhibitors. The level of neuraminidase activity inhibition is reported using the thresholds recommended by the World Health Organization Expert Working Group of the Global Influenza Surveillance and Response System (GISRS). These samples are routinely obtained for surveillance purposes rather than for diagnostic testing of patients suspected to be infected with an antiviral-resistant virus. Susceptibility to baloxavir is assessed using next-generation sequencing analysis to identify PA protein changes previously associated with reduced susceptibility to this medication; a subset of representative viruses is also tested phenotypically using a high-content imaging neutralization test.

Results of the genetic and antigenic characterization and antiviral susceptibility testing are presented in the virus characterization and antiviral resistance sections of the FluView report.

Surveillance for Novel Influenza A Viruses – In 2007, human infection with a novel influenza A virus became a nationally notifiable condition. Novel influenza A virus infections include all human infections with influenza A viruses that are different from currently circulating human seasonal influenza H1 and H3 viruses. These viruses include those that are subtyped as nonhuman in origin and those that cannot be subtyped with standard laboratory methods and reagents. Rapid detection and reporting of human infections with novel influenza A viruses – viruses against which there is often little to no pre-existing immunity – is important to facilitate prompt awareness and characterization of influenza A viruses with pandemic potential and accelerate the implementation of public health responses to limit the transmission and impact of these viruses.

Newly reported cases of human infections with novel influenza A viruses are reported in FluView and additional information, including case counts by geographic location, virus subtype, and calendar year, are available on FluView Interactive.

2. Outpatient Illness Surveillance

Information on outpatient visits to health care providers for influenza-like illness is collected through the **U.S. Outpatient Influenza-like Illness Surveillance Network (ILINet)**. ILINet consists of outpatient healthcare providers in all 50 states, Puerto Rico, the District of Columbia and the U.S. Virgin Islands reporting approximately 60 million patient visits during the 2019-20 season. Each week, approximately 3,000 outpatient healthcare providers around the country report data to CDC on the total number of patients seen for any reason and the number of those patients with influenza-like illness (ILI) by age group (0-4 years, 5-24 years, 25-49 years, 50-64 years, and ≥65 years). For this system, ILI is defined as fever (temperature of 100°F [37.8°C] or greater) and a cough and/or a sore throat without a known cause other than influenza. Sites with electronic health records use an equivalent definition as determined by public health authorities.

Additional data on medically attended visits for ILI for current and past seasons and by geographic level (national, HHS region, and state) are available on FluView Interactive.

The national percentage of patient visits to healthcare providers for ILI reported each week is calculated by combining state-specific data weighted by state population. This percentage is compared each week with the national baseline of 2.6% for the 2020-21 influenza season. The baseline is developed by calculating the mean percentage of patient visits for ILI during non-influenza weeks for the previous three seasons and adding two standard deviations. A non-influenza week is defined as periods of two or more consecutive weeks in which each week accounted for less than 2% of the season's total number of specimens that tested positive for influenza in public health laboratories. Region-specific baselines are calculated using the same methodology. Due to the wide variability in regional level data, it is not appropriate to apply the national baseline to regional data.

Regional baselines for the 2020-21 influenza season are:

Region 1 — 2.0%
Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont

Region 2 — 3.3%
New Jersey, New York, Puerto Rico, and the U.S. Virgin Islands

Region 3 — 2.0%
Delaware, District of Columbia, Maryland, Pennsylvania, Virginia, and West Virginia

Region 4 — 3.1%
Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, and Tennessee

Region 5 — 1.9%
Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin

Region 6 — 3.9%
Arkansas, Louisiana, New Mexico, Oklahoma, and Texas

Region 7 — 1.7%
Iowa, Kansas, Missouri, and Nebraska

Region 8 — 2.8%
Colorado, Montana, North Dakota, South Dakota, Utah, and Wyoming

Region 9 — 2.4%
Arizona, California, Hawaii, and Nevada

Region 10 — 1.6%
Alaska, Idaho, Oregon, and Washington

ILI Activity Indicator Map: — Activity levels are based on the percent of outpatient visits due to ILI in a jurisdiction compared with the average percent of ILI visits that occur during weeks with little or no influenza virus circulation (non-influenza weeks) in that jurisdiction. The number of sites reporting each week is variable, therefore baselines are adjusted each week based on which sites within each jurisdiction provide data. To perform this adjustment, provider level baseline ILI ratios are calculated for those that have a sufficient reporting history. Providers that do not have the required reporting history are assigned the baseline ratio for their practice type. The jurisdiction level baseline is then calculated using a weighted sum of the baseline ratios for each contributing provider.

The activity levels compare the mean reported percent of visits due to ILI for the current week to the mean reported percent of visits due to ILI for non-influenza weeks. The 13 activity levels correspond to the number of standard deviations below, at, or above the mean for the current week compared with the mean of the non-influenza weeks. Activity levels classified as minimal (levels 1-3), low (levels 4-5), moderate (levels 6-7), high (levels 8-10), and very high (levels 11-13). An activity level of 1 corresponds to values that are below the mean, level 2 corresponds to an ILI percentage less than 1 standard deviation above the mean, level 3 corresponds to ILI more than 1, but less than 2 standard deviations above the mean, and so on, with an activity level of 10 corresponding to ILI 8 to 11 standard deviations above the mean. The very high levels correspond to ILI 12 to 15 standard deviations above the mean for level 11, 16 to 19 standard deviations above the mean for level 12, and 20 or more standard deviations above the mean for level 13.

The ILI Activity Indicator map reflects the intensity of ILI activity, not the extent of geographic spread of flu, within a jurisdiction. Therefore, outbreaks occurring in a single area could cause the entire jurisdiction to display high or very high activity levels. In addition, data collected in ILINet may disproportionally represent certain populations within a jurisdiction, and therefore, may not accurately depict the full picture of influenza activity for the whole jurisdiction. Differences in the data presented here by CDC and independently by some health departments likely represent differing levels of data completeness with data presented by the health department likely being more complete.

The ILI Activity Indicator Map displays state-specific activity levels for multiple seasons and allows a visual representation of relative activity from state to state. More information is available on FluView Interactive.

3. Summary of the Geographic Spread of Influenza

State and territorial health departments report the estimated level of geographic spread of influenza activity in their jurisdictions each week through the **State and Territorial Epidemiologists Report**. This level does not measure the severity of influenza activity; low levels of influenza activity occurring throughout a jurisdiction would result in a classification of "widespread". Jurisdictions classify geographic spread as follows:

- **No Activity:** No laboratory-confirmed cases of influenza and no reported increase in the number of cases of ILI.
- **Sporadic:** Small numbers of laboratory-confirmed influenza cases or a single laboratory-confirmed influenza outbreak has been reported, but there is no increase in cases of ILI.
- **Local:** Outbreaks of influenza or increases in ILI cases and recent laboratory-confirmed influenza in a single region

of the state.

- **Regional:** Outbreaks of influenza or increases in ILI and recent laboratory confirmed influenza in at least two but less than half the regions of the state with recent laboratory evidence of influenza in those regions.
- **Widespread:** Outbreaks of influenza or increases in ILI cases and recent laboratory-confirmed influenza in at least half the regions of the state with recent laboratory evidence of influenza in the state.

Due to the ongoing COVID-19 pandemic, this system will suspend data collection for the 2020-21 influenza season. Data from previous seasons are available on FluView Interactive.

4. Hospitalization Surveillance

Laboratory confirmed influenza-associated hospitalizations are monitored through the Influenza Hospitalization Surveillance Network (FluSurv-NET). FluSurv-NET conducts population-based surveillance for laboratory-confirmed influenza-related hospitalizations in children younger than 18 years of age (since the 2003-2004 influenza season) and adults (since the 2005-2006 influenza season). The network includes more than 99 counties in the 10 Emerging Infections Program (EIP) states (CA, CO, CT, GA, MD, MN, NM, NY, OR, and TN) and four Influenza Hospitalization Surveillance Project (IHSP) states (IA, MI, OH, and UT). The IHSP began during the 2009-2010 season to enhance surveillance during the 2009 H1N1 pandemic. IHSP sites included IA, ID, MI, OK and SD during the 2009-2010 season; ID, MI, OH, OK, RI, and UT during the 2010-2011 season; MI, OH, RI, and UT during the 2011-2012 season; IA, MI, OH, RI, and UT during the 2012-2013 season; MI, OH, and UT during the 2013-2014 through 2019-20 seasons; and IA, MI, OH, and UT during the 2020-2021 season.

Cases are identified by reviewing hospital laboratory and admission databases and infection control logs for patients hospitalized during the influenza season with a documented positive influenza test (i.e., viral culture, direct/indirect fluorescent antibody assay (DFA/IFA), rapid influenza diagnostic test (RIDT), or molecular assays including reverse transcription-polymerase chain reaction (RT-PCR)). Data gathered are used to estimate age-specific hospitalization rates on a weekly basis and describe characteristics of persons hospitalized with influenza illness. The rates provided are likely to be an underestimate as influenza-related hospitalizations can be missed if testing is not performed.

Patient charts are reviewed to determine if any of the following categories of high-risk medical conditions are recorded in the chart at the time of hospitalization:

- Asthma/reactive airway disease;
- Blood disorder/hemoglobinopathy;
- Cardiovascular disease;
- Chronic lung disease;
- Chronic metabolic disease;
- Gastrointestinal/liver disease;
- Immunocompromised condition;
- Neurologic disorder;
- Neuromuscular disorder;
- Obesity;
- Pregnancy status;

- Prematurity (pediatric cases only);
- Renal disease; and
- Rheumatologic/autoimmune/inflammatory conditions.

During the 2017-18 season, seven FluSurv-NET sites (CA, GA, MN, NM, NYA, OH, OR) conducted random sampling to select cases ≥50 years for medical chart abstraction, while still performing full chart abstractions of all cases <50 years. During the 2018-19 season, six sites (CA, GA, NM, NYA, OH, OR) conducted random sampling of cases ≥65 years for medical chart abstraction. All other sites performed full chart abstractions on all cases. Data on age, sex, admission date, in-hospital death, and influenza test results were collected for all cases. For each season going forward, including 2020-21, sampling for medical chart abstraction may be considered in cases ≥50 years. In early January of each season, observed case counts across all FluSurv-NET sites will be compared against predetermined thresholds to determine whether sampling will be implemented for the season.

Additional FluSurv-NET data including hospitalization rates for multiple seasons and different age groups and data on patient characteristics (such as virus, type, demographic, and clinical information) are available on FluView Interactive. More information is available at Influenza Hospitalization Surveillance Network (FluSurv-NET).

5. Mortality Surveillance

National Center for Health Statistics (NCHS) mortality surveillance data – NCHS collects death certificate data from state vital statistics offices for all deaths occurring in the United States and are aggregated by the week of death occurrence. Deaths are classified based on ICD-10 multiple cause of death codes as associated with influenza, COVID-19, or pneumonia. To allow for collection of enough data to produce a stable percentage, NCHS surveillance data are released one week after the week of death and percentages for earlier weeks are continually revised and may increase or decrease as new and updated death certificate data are received by NCHS.

In previous seasons, the NCHS surveillance data were used to calculate the percent of all deaths occurring each week that had pneumonia and/or influenza (P&I) listed as a cause of death. Because of the ongoing COVID-19 pandemic, COVID-19 coded deaths were added to P&I to create the PIC (pneumonia, influenza, and/or COVID-19) classification. PIC includes all deaths with pneumonia, influenza, and/or COVID-19 listed on the death certificate. Because many influenza deaths and many COVID-19 deaths have pneumonia included on the death certificate, P&I no longer measures the impact of influenza in the same way that is has in the past. This is because the proportion of pneumonia deaths associated with influenza is now influenced by COVID-19-related pneumonia. The PIC percentage and the number of influenza and number of COVID-19 deaths will be presented in order to help better understand the impact of these viruses on mortality and the relative contribution of each virus to PIC mortality.

The PIC percentages are compared to a seasonal baseline of P&I deaths that is calculated using a periodic regression model incorporating a robust regression procedure applied to data from the previous five years. An increase of 1.645 standard deviations above the seasonal baseline of P&I deaths is considered the “epidemic threshold,” i.e., the point at which the observed proportion of deaths attributed to pneumonia or influenza was significantly higher than would be expected at that time of the year in the absence of substantial influenza-related mortality.

Additional P&I and PIC mortality data for current and past seasons and by geographic level (national, HHS region, and state) are available on FluView Interactive. Data displayed on the regional and state-level are aggregated by the state of residence of the decedent.

Influenza-Associated Pediatric Mortality Surveillance System — Influenza-associated deaths in children (persons less than 18 years of age) was added as a nationally notifiable condition in 2004. An influenza-associated pediatric death is defined for surveillance purposes as a death resulting from a clinically compatible illness that was confirmed to be influenza by an appropriate laboratory diagnostic test. There should be no period of complete recovery between the illness and death. Demographic and clinical information are collected on each case and are transmitted to CDC.

Information on influenza-associated pediatric deaths including basic demographics, underlying medical conditions, bacterial co-infections, and place of death for the current and past seasons, is available on FluView Interactive.

Influenza Surveillance Considerations

It is important to remember the following about influenza surveillance in the United States.

- All influenza activity reporting by public health partners and health-care providers is voluntary.
- The reported information answers the questions of where, when, and what influenza viruses are circulating. It can be used to determine if influenza activity is increasing or decreasing but does not directly report the number of influenza illnesses. For more information regarding how CDC classifies influenza severity and the disease burden of influenza, please see Disease Burden of Influenza.
- The system consists of eight complementary surveillance components in five categories. These components include reports from more than 350 laboratories, approximately 3,000 outpatient health care providers, the National Center for Health Statistics, research and healthcare personnel at FluSurv-NET sites, and influenza surveillance coordinators and state epidemiologists from all state, local, and territorial health departments.
- Influenza surveillance data collection is based on a reporting week that starts on Sunday and ends on the following Saturday. Each surveillance participant is requested to summarize weekly data and submit it to CDC by Tuesday afternoon of the following week. The data are then downloaded, compiled, and analyzed at CDC. FluView and FluView Interactive are updated weekly each Friday.

  The reporting period for each influenza season begins during *Morbidity and Mortality Weekly Report* (MMWR) week 40 and ends week 39 of the following year. MMWR weeks refer to the sequential numbering of weeks (Sunday through Saturday) during a calendar year. This means that the exact start of the influenza reporting period varies slightly from season to season. The 2020-2021 influenza season begins on September 27, 2020 and ends on October 2, 2021.

- "Flu season" — as determined by elevated flu activity – also varies from season to season. During most seasons, activity begins to increase in October, most often peaks between December and February and can remain elevated into May. The flu season is said to have started after consecutive weeks of elevated flu activity is registered in the various CDC influenza surveillance systems.

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