Influenza

Influenza is not a reportable disease in Louisiana. However, novel strains and influenza deaths should be reported to the state health department. Cases of influenza-like illness (ILI) are monitored through sentinel sites as a proxy measure of influenza activity.

Influenza is a viral infection of the lungs characterized by fever, cough and severe muscle aches. In younger adults and children, influenza causes debilitating, short-term illness. In the elderly and high risk individuals, it is a major cause of disability and death (often as a result of secondary infection of the lungs by bacteria).

Individuals at high risk of complications are:

- aged six months to four years or, 65 and older
- pregnant women
- residents of chronic-care facilities
- those who are in long-term aspirin therapy
- those who have chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, hematological or metabolic disorders (including diabetes)
- those who are immunosuppressed (immunosuppression caused by meds or by HIV)
- those who are morbidly obese (body-mass index >40)

Influenza Sentinel Surveillance Program

It is estimated that between 450,000 and 900,000 Louisiana residents become infected with influenza each year. Because influenza infections are so common, the reporting system could not rely on the passive case reporting of confirmed cases as done with most infectious diseases. Estimating the number of individual flu cases in the United States is very challenging because:

1. many people with influenza don’t seek medical care and
2. only a small number of those that do seek care are tested
3. more people who are hospitalized or die of influenza-related causes are tested and reported, but under-reporting of hospitalizations and deaths occurs as well.

For this reason the Centers for Disease Control and Prevention (CDC) monitors influenza activity levels and trends and virus characteristics through a nationwide surveillance system, and uses statistical modeling to estimate the burden of flu illness (including hospitalizations and deaths) in the United States.

Reporting is done on suspected cases from sentinel sites. These sentinel surveillance sites are physicians’ offices and hospital emergency departments. Currently, there are about 60 sites participating in the influenza sentinel surveillance system in Louisiana.

Suspected cases are called "Influenza-Like Illnesses" or ILI. To meet the definition of ILI, a case must
1. Have a fever (≥100°F),
2. Have upper respiratory tract infection symptoms (cough, sore throat)
3. No other obvious cause for this infection.

The numbers of ILI and denominator data (number of visits to the facility) are reported weekly by the sentinel facilities to the Office of Public Health (OPH). Cases are categorized into five age groups (in
Influenza seasons: newborn to four; five to 24; 25 to 49; 50 to 64; 65 and older. For physicians, the denominator is the number of patients seen that week; for hospitals, it is the weekly total of all emergency department visits.

Influenza season begins between October and December each year and ends between December and March. The duration of influenza season varies between nine and 17 weeks. The intensity of the season (defined as the proportion of patient visits due to ILI in the physicians’ offices) ranges from 2% to 10% (Figures 1, 2 and 3, and Table 1).

**Figure 1: Percent influenza-like illness visits in emergency departments and physicians’ offices Louisiana, October – March.**

<table>
<thead>
<tr>
<th>Weeks of Year</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td>OCT</td>
</tr>
<tr>
<td>50-53</td>
<td>NOV</td>
</tr>
<tr>
<td>54-56</td>
<td>DEC</td>
</tr>
<tr>
<td>57-59</td>
<td>JAN</td>
</tr>
<tr>
<td>60-62</td>
<td>FEB</td>
</tr>
<tr>
<td>63-65</td>
<td>MAR</td>
</tr>
</tbody>
</table>

Table 1 displays the weeks of the year, starting at week 40, which is usually at the beginning of October. In the second column, the month is displayed. Depending on the year, the beginning of the month may be a row above or below. The following columns display the seasons 1998-1999 to 2011-2014. The indicator of the intensity of the influenza season is the combined percentage of ILI (Influenza-like illness) among the patients that visit the sentinel emergency rooms and physicians' offices.

In the early years (1998 to 2004) the surveillance was limited to the estimated transmission season. Starting in 2005, surveillance was carried year-round.

A mild influenza season would be characterized by low percentages of ILI: from 1% to 3%. A high intensity season would show percentages of at least 5% and above.
**Table 1:** Seasonal distribution of influenza–like illnesses as percentage of visits among sentinel sites
Louisiana, 1998 to 2014

<table>
<thead>
<tr>
<th>Wk</th>
<th>Mo</th>
<th>9899</th>
<th>0001</th>
<th>0102</th>
<th>0203</th>
<th>0304</th>
<th>0405</th>
<th>0506</th>
<th>0607</th>
<th>0708</th>
<th>0809</th>
<th>0910</th>
<th>1011</th>
<th>1112</th>
<th>1213</th>
<th>1314</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>Oct</td>
<td>0.8</td>
<td>0.2</td>
<td>0.2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0.8</td>
<td>0.9</td>
<td>2.4</td>
<td>2.9</td>
<td>2.3</td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td>41</td>
<td>Nov</td>
<td>0.9</td>
<td>0.2</td>
<td>0.3</td>
<td>1.2</td>
<td>0.1</td>
<td>0</td>
<td>1.4</td>
<td>1.5</td>
<td>0.8</td>
<td>9.1</td>
<td>2</td>
<td>3</td>
<td>2.6</td>
<td>2.1</td>
<td></td>
</tr>
<tr>
<td>42</td>
<td>Dec</td>
<td>1</td>
<td>0.1</td>
<td>0.7</td>
<td>1</td>
<td>0.9</td>
<td>0.5</td>
<td>0.7</td>
<td>1.4</td>
<td>0.6</td>
<td>9.5</td>
<td>2.6</td>
<td>2.6</td>
<td>2.6</td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td>43</td>
<td>Jan</td>
<td>1</td>
<td>0.4</td>
<td>0.4</td>
<td>1</td>
<td>1.5</td>
<td>0</td>
<td>0.2</td>
<td>2.2</td>
<td>2.5</td>
<td>1.2</td>
<td>5.3</td>
<td>3.2</td>
<td>2.6</td>
<td>2.8</td>
<td></td>
</tr>
</tbody>
</table>

(Continued)
The season 1998/1999 was unusual with a very slow start and a large peak (up to 8%) from February to April.

- Season 1999/2000 data is missing.
- From 2000 to 2002, seasonal transmission was low.
- The season 2003/2004 was very short with an early high peak at 5% in early November.
- The season 2005/2006 was a mild influenza season but was marked with some moderate activity in early September of 2006. It is important to remember that this surveillance is not specific for influenza. Outbreaks of other respiratory infections may also be shown as increased ILI.
- From 2006 on, the seasons became more intense, starting early in October and lasting until March. Changes in surveillance may be responsible for such shifts in intensity. As more attention is focused on influenza surveillance, health care provider may become more concerned and suspect influenza more frequently than before.
- Season 2008/2009 is the season when the 2009 H1N1 pandemic occurred. At first the new strain was called “Swine Origin Influenza Virus” (SOIV). Recognizing that besides the swine component there were other important component, the name of the strain was later renamed “H1N1pdm9” to highlight the difference with other seasonal H1N1. The initial rows of column 0809 show an early and intense seasonal influenza starting at the beginning of October 2008 and lasting until the end of March 2009. By Mid-April and May 2009 a small high peak is detected, that is the initial surge of the novel virus. From May to August 2009 the percentage of ILI was higher than expected for the season, resulting from a continuous moderate transmission of the novel virus.
- Season 2009/2010 was a continuation of the pandemic of H1N1pdm9. A few weeks after school started, in October 2009 an intense transmission took place with ILI percent reach 9%. The pandemic lasted until August 2010. The season 2010/2011 showed a late onset but reaching a very high peak at above 10% ILI in February.
- Season 2011/12 was a very mild season with no ILI percentage above 3.6%.
- Season 2012/13 and 2013/14 were high influenza seasons starting in mid-November /mid-December, peaking at above 8% ILI for the last week of December and continuing at rates above 4% until mid-February.
Figure 2: Seasonal distribution of influenza – Louisiana, 2006-2011

Figure 3: Distribution of the Influenza Pandemic of 2009 in Louisiana
Age Distribution

Sentinel surveillance data from physicians and hospitals show major differences between the age group distribution of ILI and the population (Table 2).

The proportion of ILI:
- is much higher among children under four years
- is similar among the 5-24 years age group
- is much lower among the 25-64 years age group
- is lower among the elderly (65+)

<table>
<thead>
<tr>
<th>Age Group (Years)</th>
<th>0-4</th>
<th>5-24</th>
<th>25-64</th>
<th>65+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cases</td>
<td>29.7</td>
<td>34.9</td>
<td>29.0</td>
<td>6.4</td>
</tr>
<tr>
<td>Population</td>
<td>7.2</td>
<td>29.5</td>
<td>51.5</td>
<td>11.8</td>
</tr>
</tbody>
</table>

The age group distribution of the proportion of cases shows some slight variations from year to year (Figure 4).

Figure 4: Proportion of cases in age groups by season-year - Louisiana, 1998-2011

ILI activity does not show differences between males and females.
Mortality Data

Note on Influenza mortality from the CDC Website: Questions and Answers Regarding Estimating Deaths from Influenza in the United States.
http://www.cdc.gov/flu/about/disease/us_flu-related_deaths.htm#exact-number

The CDC does not know exactly how many people die from seasonal flu each year. There are several reasons for this. First, states are not required to report individual seasonal flu cases or deaths of people older than 18 years of age to CDC. Second, seasonal influenza is infrequently listed on death certificates of people who die from flu-related complications. Third, many seasonal flu-related deaths occur one or two weeks after a person’s initial infection, either because the person may develop a secondary bacterial co-infection (such as bacterial pneumonia) or because seasonal influenza can aggravate an existing chronic illness (such as congestive heart failure or chronic obstructive pulmonary disease). Also, most people who die from seasonal flu-related complications are not tested for flu, or they seek medical care later in their illness when seasonal influenza can no longer be detected from respiratory samples. Sensitive influenza tests are only likely to detect influenza if performed within a week after onset of illness. In addition, some commonly used tests to diagnose influenza in clinical settings are not highly sensitive and can provide false negative results (i.e. they misdiagnose flu illness as not being flu.) For these reasons, many flu-related deaths may not be recorded on death certificates. These are some of the reasons that CDC and other public health agencies in the United States and other countries use statistical models to estimate the annual number of seasonal flu-related deaths. Flu deaths in children were made a nationally notifiable condition in 2004, and since then, states have reported flu-related child deaths in the United States through the Influenza Associated Pediatric Mortality Surveillance System.

CDC feels it is important to convey the full burden of seasonal flu to the public. Seasonal flu is a serious disease that causes illness, hospitalizations, and deaths every year in the United States. CDC estimates of annual influenza-associated deaths in the United States are made using well-established scientific methods that have been reviewed by scientists outside of CDC.

The number of seasonal influenza-associated (i.e., seasonal flu-related) deaths varies from year to year because flu seasons are unpredictable and often fluctuate in length and severity. Therefore, a single estimate cannot be used to summarize influenza-associated deaths. Instead, a range of estimated deaths is a better way to represent the variability and unpredictability of flu. An August 27, 2010 MMWR report entitled “Thompson MG et al. Updated Estimates of Mortality Associated with Seasonal Influenza through the 2006-2007 Influenza Season. MMWR 2010; 59(33): 1057-1062.” provides updated estimates of the range of flu-associated deaths that occurred in the United States during the three decades prior to 2007. CDC estimates that from the 1976-1977 season to the 2006-2007 flu season, flu-associated deaths ranged from a low of about 3,000 to a high of about 49,000 people. Death certificate data and weekly influenza virus surveillance information was used to estimate how many flu-related deaths occurred among people whose underlying cause of death was listed as respiratory or circulatory disease on their death certificate.

The CDC uses underlying respiratory and circulatory (R&C) deaths in its mortality modeling because R&C deaths provide an estimate of deaths associated with respiratory infections that is more sensitive than underlying pneumonia and influenza (P&I) deaths and more specific than all-cause deaths (Table 3).

CDC does not base its seasonal flu mortality estimates only on death certificates that specifically list influenza. Seasonal influenza may lead to death from other causes, such as pneumonia, congestive heart failure, or chronic obstructive pulmonary disease. It has been recognized for many years that influenza is infrequently listed on death certificates and testing for seasonal influenza infections is usually not done, particularly among the elderly who are at greatest risk of seasonal influenza complications and death. Some deaths — particularly in the elderly — are associated with secondary complications of seasonal
influenza (including bacterial pneumonias). Influenza virus infection may not be identified in many instances because influenza virus is only detectable for a short period of time and/or many people don’t seek medical care until after the first few days of acute illness. For these and other reasons, statistical modeling strategies have been used to estimate seasonal flu-related deaths for many decades, both in the United States and the United Kingdom. Only counting deaths where influenza was included on a death certificate would be a gross underestimation of seasonal influenza’s true impact.

There is a lot of variability from year-to-year, though, with a low of 3,349 deaths during the 1986-87 flu season to a high of 48,614 in 2003-04, which was considered a severe flu season.

The estimated ranges of cases, hospitalizations and deaths generated by this method provide a sense of scale in terms of the burden of disease caused by influenza. Quoting from CDC: "It may never be possible to validate the accuracy of these figures. The true number of cases, hospitalizations and deaths may lie within the range provided or it’s also possible that it may lie outside the range. The underlying assumption in this method is that the level of influenza activity (based on hospitalization rates) in EIP sites matches the level of influenza like illness (ILI) activity across the states".

Only a small proportion of deaths in pneumonia and all respiratory and circulatory deaths are estimated to be influenza-related. CDC estimated that

- only 8.5% of all pneumonia and influenza deaths and
- only 2.1% of all respiratory and circulatory deaths were influenza-related.

The CDC has done several studies over the years to estimate the disease burden (cases in the population, cases getting medical care, hospitalizations and deaths), from influenza. These are useful to understand the importance of influenza and justify the recurrent resources spent every year on influenza prevention, primarily immunization.

**CDC Estimates**

The most important references on the CDC estimates are:


A short summary of the numbers estimated by these scientific peer-reviewed articles is presented in the table below. The numbers estimated are number of cases, of hospitalizations and deaths. For each estimate, CDC presented the confidence interval. The lower number would be giving an idea of what to expect in a low season, the higher number for a very active season.

In the column “USA CDC” the estimates for entire US are presented. In the column “LA”, the extrapolation to Louisiana is displayed. The 2012-13 year being very intense one would expect high numbers, close to the higher end of the confidence interval (Table 3).
Table 3: Estimated Cases, Hospitalizations and Deaths due to Influenza in the US and Louisiana

<table>
<thead>
<tr>
<th></th>
<th>USA CDC</th>
<th>LA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Population 2012</strong></td>
<td>311,000,000</td>
<td>4,575,000</td>
</tr>
<tr>
<td><strong>Estimated Cases 2012-2013 Season</strong></td>
<td>31,817,000</td>
<td>454,529</td>
</tr>
<tr>
<td>Confidence interval: Low</td>
<td>20,631,000</td>
<td>294,729</td>
</tr>
<tr>
<td>Confidence interval: High</td>
<td>46,371,000</td>
<td>662,443</td>
</tr>
</tbody>
</table>

Based on the estimated number of hospitalizations and age-specific case-hospitalization ratios for persons aged <65 years, and using a case-hospitalization ratio of 11:1 for persons aged ≥65 years (1)

<table>
<thead>
<tr>
<th><strong>Estimated Medically Attended Cases, 2012-2013 Season</strong></th>
<th>USA CDC</th>
<th>LA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confidence interval: Low</td>
<td>14,431,000</td>
<td>206,157</td>
</tr>
<tr>
<td>Confidence interval: High</td>
<td>22,102,000</td>
<td>315,743</td>
</tr>
</tbody>
</table>

Based on the estimated number of cases and outpatient medically attended ratios by age group (2)

<table>
<thead>
<tr>
<th><strong>Estimated Hospitalization, 2012-2013 Season</strong></th>
<th>USA CDC</th>
<th>LA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confidence interval: Low</td>
<td>381,500</td>
<td>5,450</td>
</tr>
<tr>
<td>Confidence interval: High</td>
<td>568,700</td>
<td>8,124</td>
</tr>
<tr>
<td>Rate per 100,000 population/season 42.0 last year</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Estimated using FluSurv-NET hospitalization rates adjusted for underreporting. The underreporting adjustment multiplier was calculated during the 2009–10 pandemic season and was 2.74 across age categories (1).

<table>
<thead>
<tr>
<th><strong>Estimated Deaths, 1976-2007 seasons</strong></th>
<th>USA CDC</th>
<th>LA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confidence interval: Low</td>
<td>23,607</td>
<td>337</td>
</tr>
<tr>
<td>Confidence interval: High</td>
<td>48,614</td>
<td>694</td>
</tr>
<tr>
<td>Rate per 100,000 population/season 1.4 to 16.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: CDC Estimates were rounded to the 1,000 for clarity

**Pediatric Influenza Deaths**

Unlike influenza deaths in adults, which are just estimates, it is actually known exactly how many children die from influenza each year as it has been a nationally notifiable condition since 2004. The deaths are not all in children with risk factors, for example, having asthma, diabetes, or other chronic medical conditions. Reports have shown that about half of the children who die from the flu each year have no known high-risk factors for flu complications (Figure 5).
Progression in Louisiana

Based on the data collected by OPH influenza surveillance, it is possible to prepare an estimate by week for number of cases, hospitalizations and deaths.

- The ILI surveillance collects ILI data on 20,000 to 30,000 ambulatory care patients week. The proportion of confirmed influenza cases among these ILI is estimated from the confirmation proportion observed by the OPH laboratory. Extrapolating to the total ambulatory care of the entire state is possible by using the National Center for Health Statistics (NCHS) estimate of patient visits at physicians, hospital out-patients clinics, urgent care and emergency departments (220,000 visits /week).
- Using the rate of admission for ILI patients calculated by the Louisiana Early Event Detection System (LEEDS) and CDC data from states with enhanced influenza surveillance, the number of hospitalizations can be estimated,
- Deaths were estimated by CDC using several approaches (population based data, review of mortality from several conditions such as pneumonia and influenza (P&I) causes and respiratory and circulatory (R&C) causes.

Applying these estimates and using the intensity of ILI morbidity and confirmed influenza it is possible to create a spreadsheet displaying the estimated numbers of cases, hospitalization and death from the onset of the season.

Correlation Between ILI Proportion in Physicians' Offices and Hospital Emergency Departments

Figure 6 shows the correlation between the proportion of ILI among all visits in physicians' offices and emergency departments by region and by week (from week 2009-40 to week 2010-02 i.e from October 2009 to January 2010). Each point in the graph represent a matched pair (% ILI in MD office in the vertical axis, % ILI in emergency departments in the horizontal axis. The slope of the regression line is 0.59, correlation coefficient 0.649, CI 0.323 to 0.837, Costas-Santos measure of disagreement 0.42. In summary there is a good correlation between the two methods.
School Absenteeism Does Not Correlate Well With ILI Data

During the 2009-2010 season data was systematically collected for most of the schools. Schools report daily their absenteeism data (number absent, enrollment) to the department of education in an electronic format. The electronic data was made available to the Infectious Disease Epidemiology Section (IDEpi) for monitoring school absenteeism under the assumption that school absenteeism was a reliable indicator of absenteeism secondary to illness and particularly secondary to influenza during the pandemic. Absenteeism data collected in such a manner does not differentiate between absenteeism due to illness or any other causes.

Figure 7 shows the correlation between school absenteeism by region and by week (from week 2009-40 to week 2010-02 i.e from October 2009 to January 2010). Each point in the graph represent a matched pair (% Absenteeism in the vertical axis, % ILI in the horizontal axis. The slope of the regression line is 0.003, correlation coefficient 0.016, CI -0.174 to 0.204, Costas-Santos measure of disagreement 0.517. In summary, there is an extremely poor correlation between the two methods. Using absenteeism on such a wide scale does not contribute to a better surveillance.
Hospital Discharge Data

Each year, Louisiana hospitals report hospital admission and discharge data to the state Department of Health and Hospitals. This data contains the number and nature of persons admitted to Louisiana hospitals and is contained in a database, LAHIDD. This dataset contains the main diagnosis and up to eight additional diagnoses for each patient, recorded by ICD9 code. Records of patients with influenza were extracted using the following ICD9 codes whether in the main diagnosis or in the eight additional secondary diagnoses: 487.0 = influenza with pneumonia, 487.1 = influenza with other respiratory manifestations, 487.8 = influenza with other manifestations.

The total number of hospitalizations vary from 500 to 1,600 per year, with the rate varying from 15 to 35 per 100,000 population per year. The hospitalization rate and the proportion of ILI are not always parallel. The numbers and rates obtained from the LAHIDD data do not represent the true burden of influenza hospitalizations because:

1-influenza is not systematically diagnosed and
2-there is no reliable way to determine the role of influenza in a hospitalization.

Resistance to Antivirals

The results presented in Table 4 are obtained as part of ongoing influenza virus surveillance for their sensitivity to FDA-approved neuraminidase inhibitors. Assessment of isolates for their susceptibility to neuraminidase inhibitors is done in the fluorescent neuraminidase inhibition assay. For viruses identified as potentially resistant, sequence analysis of the neuraminidase gene is performed to detect molecular markers associated with resistance to the neuraminidase inhibitor(s).
Table 4: Susceptibility of virus isolates, 2013-14 Season

<table>
<thead>
<tr>
<th>Type and Subtype</th>
<th>Oseltamivir</th>
<th></th>
<th>Zanamivir</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Viruses tested</td>
<td>Viruses Resistant</td>
<td>Viruses tested</td>
<td>Viruses Resistant</td>
</tr>
<tr>
<td>Influenza A(H1N1)pdm09</td>
<td>38</td>
<td>10*</td>
<td>38</td>
<td>0</td>
</tr>
<tr>
<td>Influenza A(H3N2)</td>
<td>7</td>
<td>0</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Influenza B</td>
<td>15</td>
<td>0</td>
<td>15</td>
<td>0</td>
</tr>
</tbody>
</table>

* The H275Y substitution, an established marker, was detected in the neuraminidase of the A(H1N1)pdm09 viruses identified as oseltamivir resistant in the neuraminidase inhibition assay.