

California
Influenza and Respiratory Disease
Surveillance Report
2011-2012 Season

July 2012

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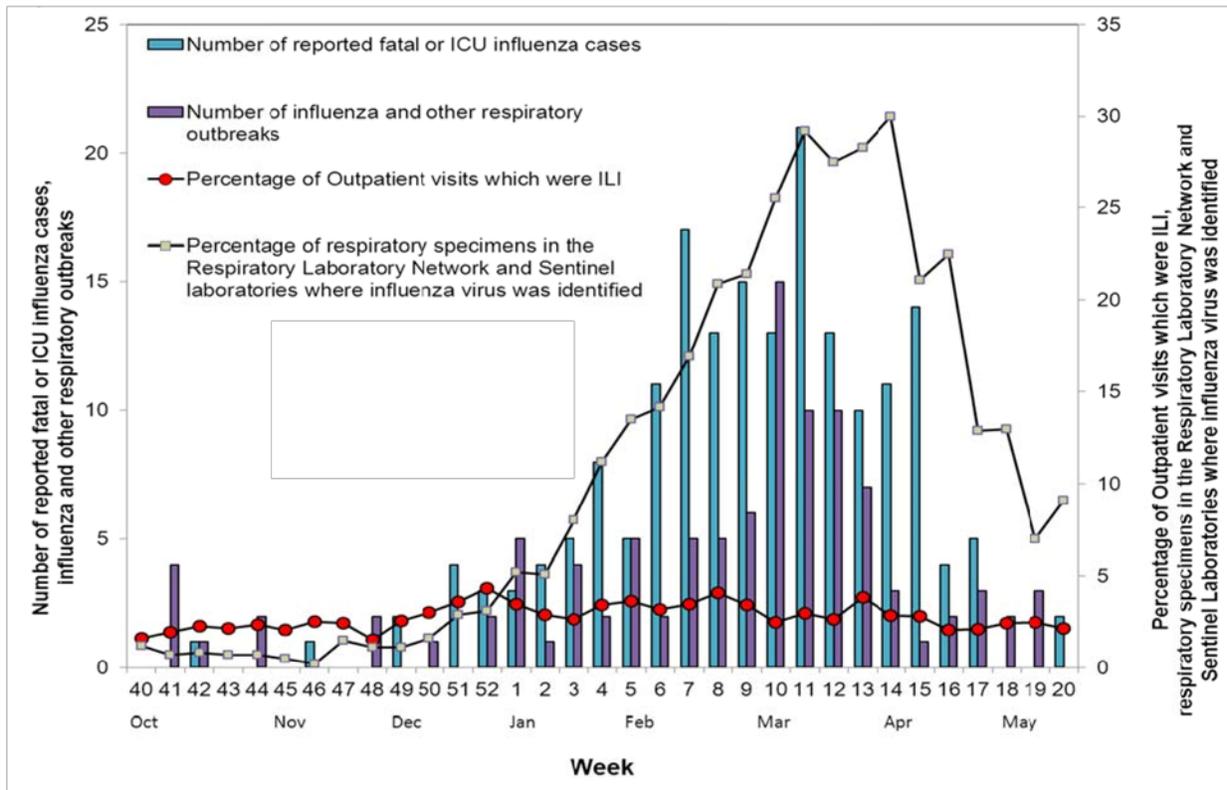
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Synopsis

The 2011-12 influenza season in California began late and was mild to moderate compared to previous seasons for which surveillance data are available. Influenza peak activity was seen in Centers for Disease Control and Prevention (CDC) weeks 10-14 (March 4, 2012- April 7, 2012) as measured by most clinical and laboratory parameters (Figure 1). Seasonal influenza A (H3) [influenza A (H3N2)] was the predominant virus; however, influenza A (H1N1) pdm09 [(influenza A (2009 H1N1))] and influenza B viruses circulated widely.

Figure 1. CDPH selected influenza surveillance parameters, 2011-12 season



Outpatient influenza-like illness (ILI) activity fluctuated greatly with sporadic increases occurring from January through May. The ILI case definition is fever (temperature of 100°F [37.8°C] or greater) and a cough and/or a sore throat in the absence of a known cause other than influenza. The percentage of laboratory tests that were positive for influenza peaked in April (approximately 30%), and was comparable to levels seen in previous years.

As of June 1, 2012, seven fatal influenza cases in children less than 18 years of age occurring during the 2011-2012 season were reported to CDPH. This number is within the range reported since surveillance for these cases was first initiated in 2003. Since that time, the number has ranged from a low of 5 fatal pediatric cases during the 2007-2008 season, to a high of 28 fatal pediatric cases reported during the 2009-2010

pandemic season. It's possible that additional deaths will be reported for the 2011-2012 season as delays in reporting occur.

A total of 196 severe and/or fatal cases of influenza in person less than 65 years of age were reported to CDPH by local health jurisdictions (LHJ). In contrast, 392 severe and/or fatal cases in persons less than age 65 were reported in the 2010-2011 season. More data are needed to interpret these numbers given there is no established baseline; the surveillance for critically ill cases requiring intensive care (ICU) and fatal cases was only recently initiated in 2009; and reporting of cases requiring ICU admission is voluntary. In addition, the proportion of severely ill cases in persons less than 65 years of age may fluctuate greatly in the first few years post pandemic. In the typical influenza season, >95% of severe and fatal illnesses due to influenza occur in the elderly (>65 years) (1). The shift in mortality toward younger age groups observed during the 2009 pandemic is a common feature of influenza pandemics and was observed during all of the 20th century influenza pandemics. Over the next few years, as the newly introduced influenza A (2009 H1N1) virus circulates and becomes established in the community, more of the population will be exposed. Once a relatively high level of population immunity is established, historical patterns suggest that the burden of severe and fatal illness due to influenza will gradually shift to occur predominately in more vulnerable populations such as the elderly and chronically ill, similar to the typical seasonal influenza patterns (1).

Finally, a high number of respiratory outbreaks were reported this season, with CDPH assisting in investigation of several outbreaks occurring in correctional and long term care facility settings. The large number reported may be due in part to heightened awareness post-pandemic of influenza-associated morbidity and mortality, as well as improvements in reporting as more jurisdictions begin using the new statewide electronic surveillance system, CalREDIE.

Influenza Surveillance Data

A. CDPH Virologic Surveillance

CDPH obtains data on laboratory-confirmed influenza and other respiratory viruses from a number of laboratories throughout the state. These laboratories include 27 public health laboratories, collectively known as the Respiratory Laboratory Network (RLN), and 12 clinical, commercial, academic and hospital laboratories, which are referred to as sentinel laboratories.

During the 2011-2012 season, these 39 participating laboratories reported results from a total of 50,733 specimens tested for influenza; 7,451 (14.7%) were positive for influenza. Of the positive specimens, 1,257 (16.9%) were influenza B and 6,194 (83.1%) were influenza A. Of the 6,194 specimens that tested positive for influenza A, 2,219 (35.8%) had further subtyping performed. Among these, 634 (28.6%) were subtyped as influenza A (2009 H1N1) and 1,585 (71.4%) were subtyped as influenza A

(H3N2). These virologic surveillance data are similar to national findings (<http://www.cdc.gov/flu/weekly/>).

The proportion of specimens testing positive for influenza during the 2011-2012 season first exceeded 10% during the week ending January 28, 2012, indicating higher levels of virus circulation. The proportion peaked at 30% during the week ending April 7, 2012, and declined to <10% during the week ending May 12, 2012.

Although influenza A (H3N2) viruses predominated, influenza A (2009 H1N1) and influenza B viruses also circulated widely. While the relative proportion of each type and subtype of influenza virus varied by week, the early part of the season was characterized by circulation of mostly influenza A (H3N2) viruses, while in the latter half of the season (weeks 10-20), influenza B was also reported with high frequency. There was no clear regional pattern of circulation for the three influenza types/subtypes, although more influenza A (2009 H1N1) and influenza B viruses were reported in Southern California compared to other regions.

1. Respiratory Laboratory Network (RLN) Surveillance Results

The RLN laboratories offer polymerase chain reaction (PCR) testing for influenza A and B, including influenza A subtyping, and testing using the R-Mix shell vial culture system to identify five other common respiratory viruses [respiratory syncytial virus (RSV), adenovirus, and parainfluenza virus type 1-3].

Of 4,068 specimens tested by the RLN from October 2, 2011 through May 19, 2012, 2,155 (53.0%) were positive for influenza; of these, 2,042 (94.8%) were influenza A and 113 (5.2%) were influenza B (Table 1). Of the 2,042 influenza A specimens, 1,457 (71.4%) were influenza A (H3N2), 575 (28.2%) were influenza A (2009 H1N1), 5 were not subtyped, and 5 are pending subtyping results. There were no detections of non-pandemic influenza A (H1N1).

Table 1. RLN surveillance results, October 2, 2011–May 19, 2012

| | Total RLN* No. (%) | Northern CA No. (%) | Central CA No. (%) | Southern CA No. (%) |
|---|---------------------------------|-------------------------------|-------------------------------|---------------------------------|
| Number of specimens tested by PCR | 4,068 | 1,476 | 316 | 2,276 |
| Number of specimens negative for influenza | 1,913 (47.0)[†] | 786 (53.3)[†] | 213 (67.4)[†] | 914 (40.2)[†] |
| Number of specimens positive for influenza | 2,155 (53.0)[†] | 690 (46.7)[†] | 103 (32.6)[†] | 1,362 (59.8)[†] |
| Influenza A | 2,042 (94.8) [‡] | 659 (95.5) [‡] | 98 (95.1) [‡] | 1285 (94.3) [‡] |
| <i>H3N2</i> | 1,457 (71.4) [§] | 521 (79.1) [§] | 77 (78.6) [§] | 859 (66.8) [§] |
| <i>2009 H1N1</i> | 575 (28.2) [§] | 133 (20.2) [§] | 16 (16.3) [§] | 426 (33.2) [§] |
| <i>Not subtyped</i> | 5 (0.2) [§] | 4 (0.6) [§] | 1 (1.0) [§] | 0 (0.0) |
| <i>Subtyping pending</i> | 5 (0.2) [§] | 1 (0.2) [§] | 4 (4.1) [§] | 0 (0.0) |
| Influenza B | 113 (5.2) [‡] | 31 (4.5) [‡] | 5 (4.9) [†] | 77 (5.7) [†] |
| Number of specimens tested by R-mix | 504 | 44 | 273 | 187 |
| RSV | 31 (6.2) [¶] | 7 (15.9) [¶] | 17 (6.2) [¶] | 7 (3.7) [¶] |
| Other respiratory viruses | 23 (4.6) ^{¶,††} | 1 (2.3) [¶] | 6 (2.2) [¶] | 16 (8.6) [¶] |

* Participating laboratories:

Northern California: Alameda, Contra Costa, El Dorado, Humboldt, Marin, Placer, Sacramento, San Francisco, San Mateo, Santa Clara, Shasta, Solano, Sonoma.

Central California: Monterey, San Joaquin, Stanislaus, Tulare.

Southern California: Long Beach, Los Angeles, Orange, Riverside, San Bernardino, San Diego, San Luis Obispo, Santa Barbara.

[†] Percent of total specimens tested for influenza by PCR

[‡] Percent of specimens positive for influenza

[§] Percent of influenza A positives

[¶] Percent of total specimens tested by R-mix

^{††} Adenovirus (12), parainfluenza type 1 (10), parainfluenza type 3 (1)

2. Sentinel Laboratory Surveillance

The 12 sentinel laboratories use various testing methods, including rapid test, direct fluorescent assay, viral culture and PCR.

From October 2, 2011–May 19, 2012, the sentinel laboratories tested a total of 46,665 specimens for influenza; 5,296 (11.3%) were positive. Of the specimens that tested positive for influenza, 4,152 (78.4%) were influenza A and 1,144 (21.6%) were influenza B (Table 2). The highest weekly percentage of influenza detections in the sentinel laboratories occurred during week 11 (March 11, 2012 – March 17, 2012), when 24.0% (575/2,399) of specimens were positive for influenza. Of 43,729 specimens tested for RSV by the sentinel laboratories, 5,369 (12.3%) were positive.

Table 2. Influenza and RSV detections in Sentinel Laboratories*, October 2, 2011–May 19, 2012

| | No. (%) |
|---|----------------------------------|
| Total specimens tested for influenza | 46,665 |
| Number of specimens negative for influenza | 41,369 (88.7)[†] |
| Number of specimens positive for influenza | 5,296 (11.3)[†] |
| Influenza A | 4,152 |
| H3N2 | 128 (3.1) [†] |
| 2009 H1N1 | 59 (1.4) [†] |
| Influenza B | 1,144 (21.6) [†] |
| Total specimens tested for RSV | 43,729 |
| RSV | 5,369 (12.3) [†] |

* Participating laboratories

3. Combined RLN and Sentinel Laboratory Surveillance Results

Figures 2 and 3 summarize the combined laboratory data from both the RLN and the sentinel laboratories. The overall level of activity seen during the 2011–2012 season was comparable to that of previous non-pandemic influenza seasons while the time course of activity was late (Figure 2). The majority of influenza detections identified by the RLN and sentinel laboratories during the 2011–2012 season were influenza A (H3N2) and influenza B (Figure 3). RSV also played a prominent role in ILI during the influenza season (Figures 4, 5).

Figure 2. Percentage of specimens from which influenza was detected in Respiratory Laboratory Network and Sentinel Laboratories, 2007–2012

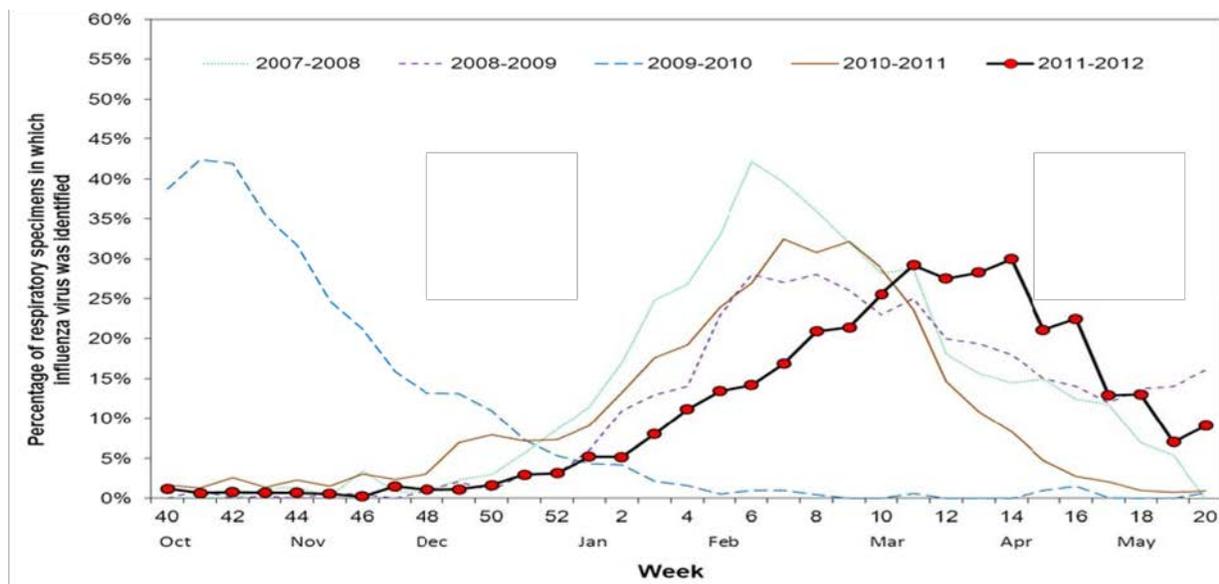


Figure 3. Percentage of influenza types and subtypes in Respiratory Laboratory Network and Sentinel Laboratories, 2011–2012

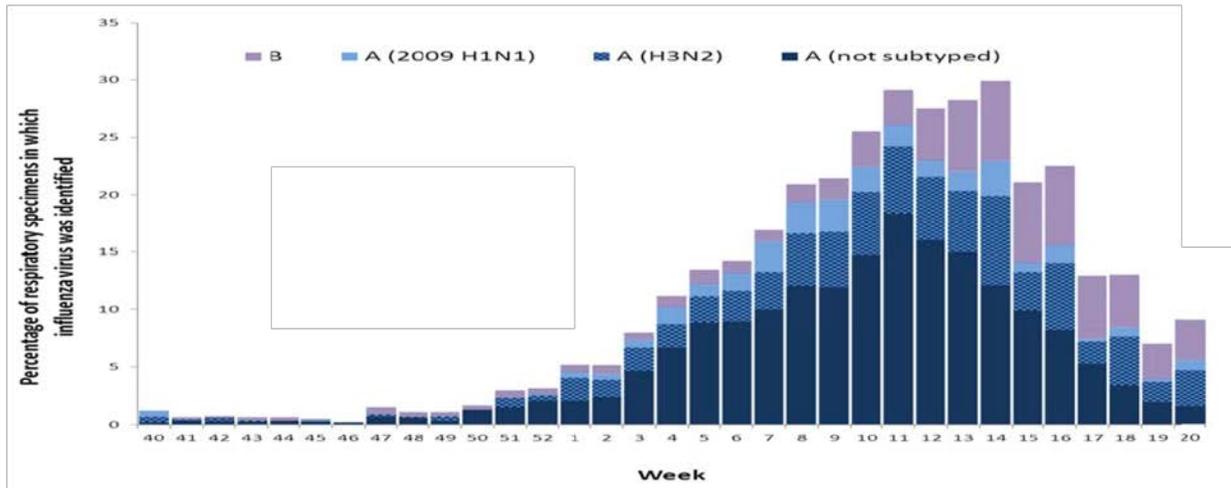


Figure 4. RSV detections in Sentinel Laboratories/Respiratory Laboratory Network, 2007-2012

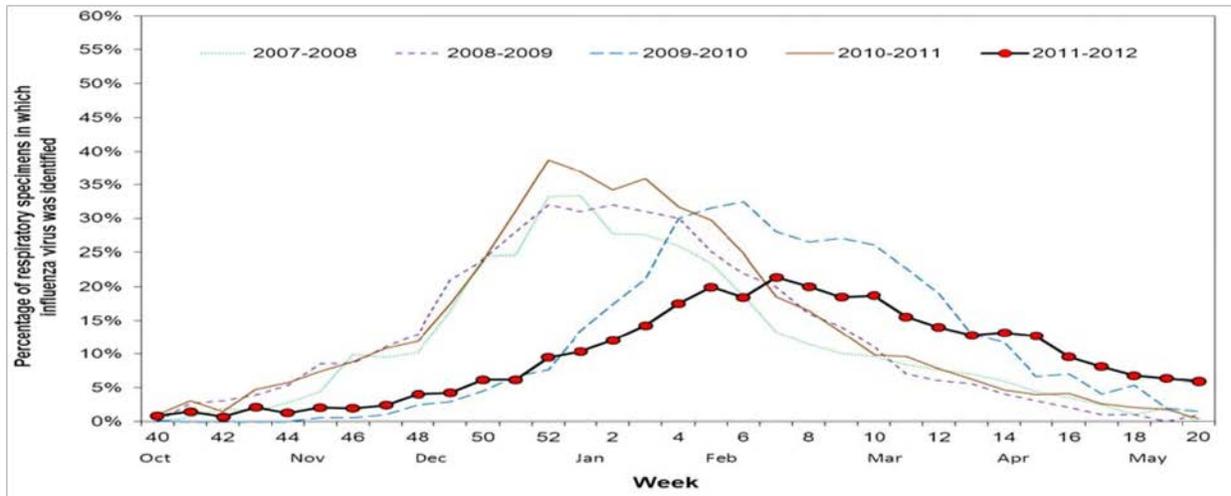
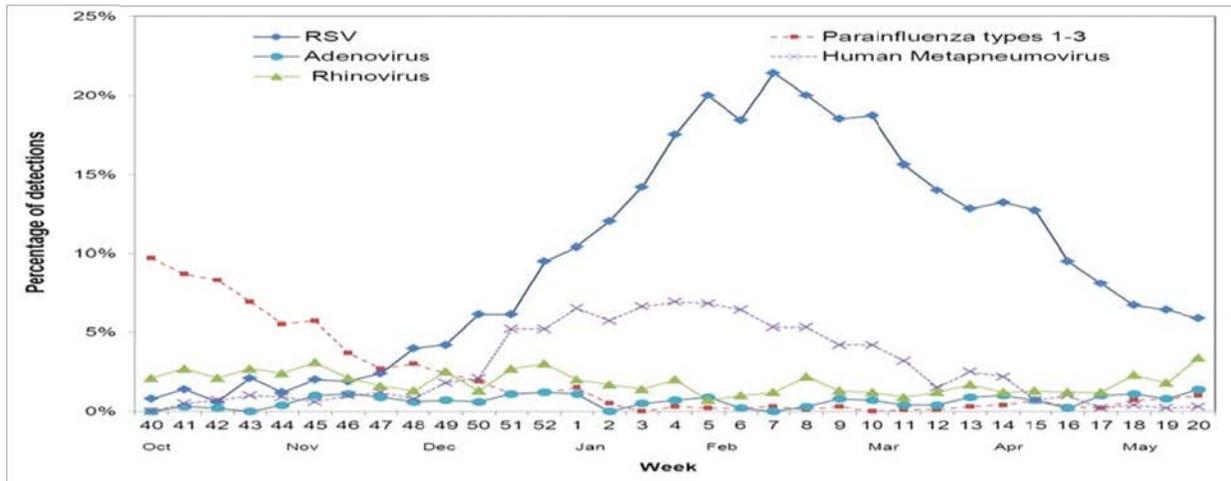


Figure 5. Non-influenza respiratory virus detections in Respiratory Laboratory Network and Sentinel Laboratories, 2011-2012



4. Antigenic Characterization

Most of the viruses tested this season were well-matched to the vaccine viruses (the viruses the vaccine is designed to protect against). Of the 103 California specimens that have been strain-typed to date, all influenza A viruses and 13 influenza B viruses (61.9%) matched with components of the 2011-2012 vaccine for the Northern Hemisphere.

Table 3. Influenza virus antigenic characterization, 2011-2012 Season

| | California (N=103) | United States (N=1,887) |
|--|-------------------------------|------------------------------------|
| Influenza A (2009 H1N1) | 30 | 527 |
| A/California/07/2009-like (H1N1)* | 30 (100%) | 503 (95.4%) |
| Influenza A (H3N2) | 52 | 1,058 |
| A/Perth/16/2009-like (H3N2)* | 52 (100%) | 864 (81.7%) |
| Influenza B | 21 | 302 |
| B/Brisbane/60/2008-like* (B/Victoria lineage) | 13 (61.9%) | 139 (46.0%) |
| B/Wisconsin/01/2010-like (B/Yamagata lineage) | 8 (38.1%) | 155** (51.3%) |

* Matches components of the 2011-12 Northern Hemisphere influenza vaccine

** Reported by CDC as B/Yamagata lineage only (specific stain not identified)

The California findings are similar to national findings, where the predominant mismatch occurred with the influenza B viruses (<http://www.cdc.gov/flu/weekly/>).

While 38% of California influenza B viruses tested this season differed from the influenza B component in the 2011-2012 influenza vaccine, influenza B viruses accounted for <20% (1,256/7,432) of influenza positive tests reported this season.

5. Antiviral Resistance

Surveillance for antiviral resistance is performed by CDPH-VRDL. During the 2011-2012 influenza season, as part of a CDC national surveillance effort, CDPH-VRDL implemented a functional assay to survey circulating influenza strains for resistance to neuraminidase inhibitors. In addition, selected influenza A (2009 H1N1) clinical specimens were tested using pyrosequencing for a single known mutation that confers oseltamivir resistance (H275Y). Since high levels of resistance to adamantanes (amantadine and rimantadine) are observed among circulating influenza A viruses (influenza A (2009 H1N1) and A (H3N2)), adamantane resistance testing was not performed at the CDPH-VRDL on a routine basis.

Since October 1, 2011, CDPH-VRDL has tested 140 influenza specimens for neuraminidase inhibitor resistance; all but one influenza A (2009 H1N1) have been sensitive (Table 4).

Table 4. Number of specimens tested for antiviral resistance, California, 2011-2012 season

| | Neuraminidase Inhibitors Resistance |
|--------------------------------|--|
| Influenza A (2009 H1N1) | 1/35 |
| Influenza A (H3N2) | 0/105 |

Nationally, 2,756 specimens were tested by CDC during the 2011-12 season as part of routine surveillance; 16 viruses (<1%) resistant to the neuraminidase inhibitor drugs were identified. Eleven of the 16 oseltamivir-resistant viruses were collected from Texas. Oseltamivir resistance remains quite low nationally and in Texas; the percentage of oseltamivir-resistant influenza A (2009 H1N1) viruses in Texas (2.6%) was higher than the national percentage (<http://www.cdc.gov/flu/weekly/>).

6. Novel Influenza A Viruses

Neither the RLN nor the CDPH-VRDL identified any influenza viruses by polymerase chain reaction (PCR) typing or subtyping that were suggestive of a novel virus infection.

B. Case-Based Surveillance

1. Influenza-Associated Critical Illness and Mortality in Californians <65 years old

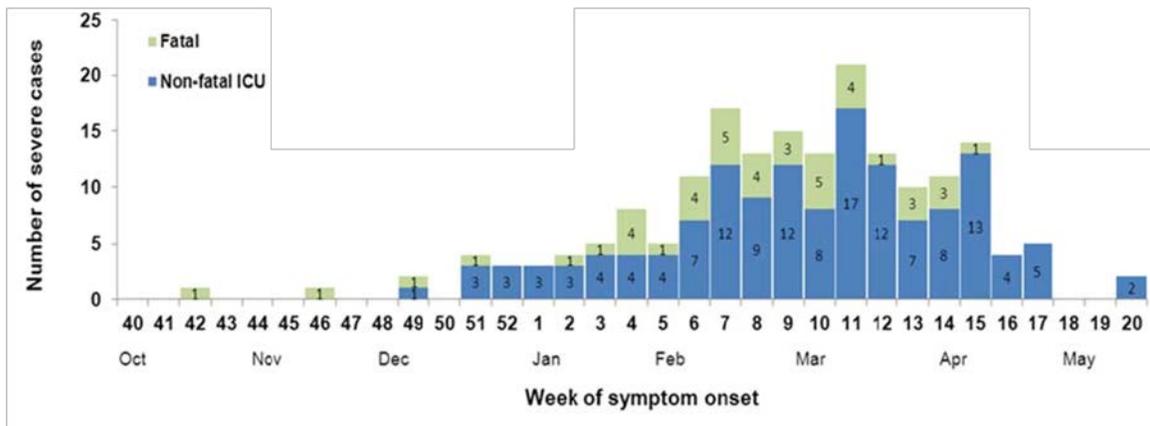
During the 2011-2012 influenza season, CDPH requested that LHJs report all laboratory confirmed influenza cases <65 years with severe illness requiring intensive care or who died. This surveillance was initiated in 2009 during the pandemic in recognition that strong pandemic influenza preparedness requires maintenance of strong inter-pandemic influenza surveillance, and that previous pandemics have historically most severely affected children and young adults (1). In September 2011, all fatal cases <65

years due to influenza were made reportable [Title 17, California Code of Regulations (CCR) §2500].

Epidemiologic curve of ICU and fatal cases under age 65 years

Since October 2, 2011, CDPH has received 196 reports of influenza-associated severe illness or deaths among persons <65 years old; 152 (77.6%) were non-fatal ICU cases and 44 (22.4%) were fatal cases. Figure 6 shows the number of fatal and non-fatal ICU cases by week of symptom onset. The 2011-2012 influenza season began late compared to most previous seasons. Fewer than 5 cases were reported each week until week 3 (January 15–21, 2012), when the number of cases began increasing. The peak of the season occurred during weeks 7 through 11 (February 12–March 17, 2012), with an average of 16 cases reporting illness onset per week.

Figure 6. Number of fatal and non-fatal ICU cases of all laboratory-confirmed influenza reported to the California Department of Public Health, by week of symptom onset, October 2, 2011 - May 19, 2012



Demographic characteristics and clinical features of ICU and fatal cases

A little over one-third (38.3%) of all the ICU or fatal cases reported to CDPH were among children under 18 years of age. The median age among all cases was 31 years (range: 3 weeks-64 years); fatal cases (median age: 44 years; range: 2-62 years) were significantly (p=0.0006) older than non-fatal ICU cases (median: 24 years; range: 3 weeks-64 years), (data not shown).

The CDPH case-based surveillance data should be interpreted with caution due to the following limitations: exclusion of cases 65 years of age and older, voluntary reporting of ICU cases, differing degrees of participation by the LHJs, and biases in testing practices. These numbers are also provisional as some cases are not yet reported or are still being investigated and the surveillance is conducted year-round.

Table 5. Number of non-fatal ICU and fatal cases with laboratory-confirmed influenza reported to the California Department of Public Health and ICU hospitalization and death rates (per 100,000 population), by age-group, October 2, 2011 – May 19, 2012

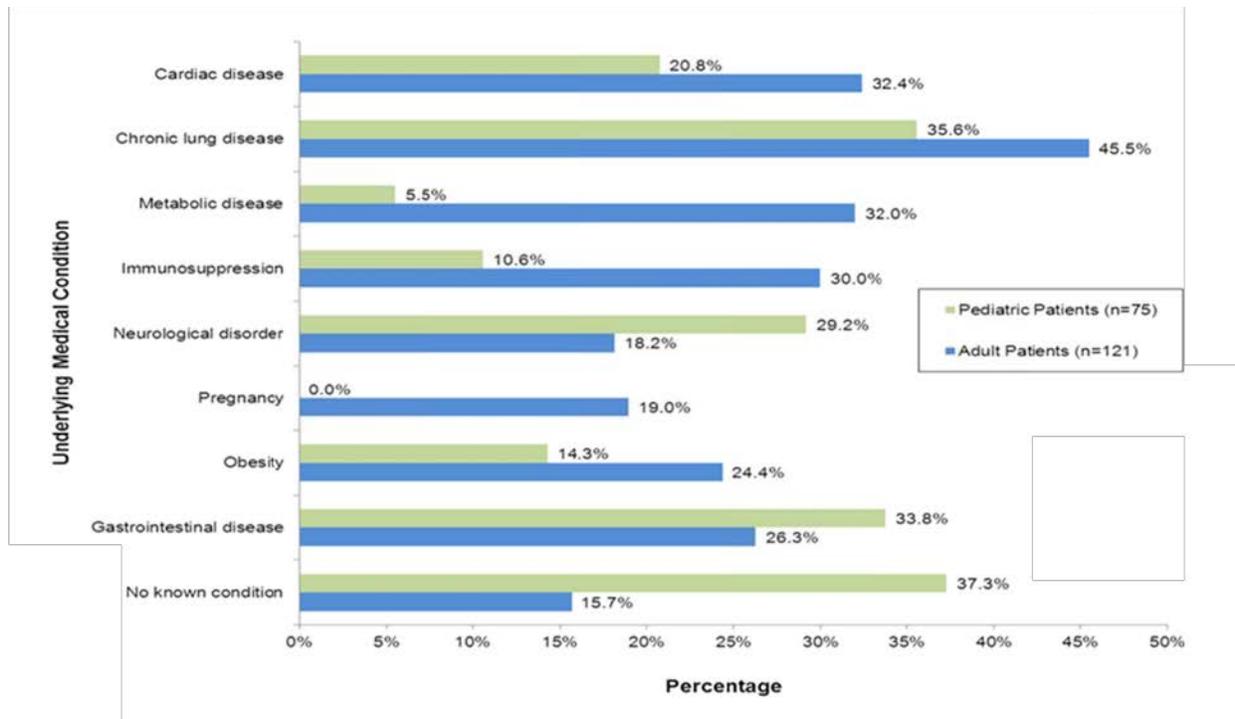
| | NON-FATAL ICU CASES* No. (%) | FATAL CASES No. (%) |
|-----------------------------|--|-------------------------------|
| Total | 152 | 44 |
| Age group, in years (0-4) | 36 (23.7) | 6 (13.6) |
| Age group, in years (5-17) | 32 (21.1) | 1 (2.3) |
| Age group, in years (18-49) | 51 (33.6) | 18 (40.9) |
| Age group, in years (50-64) | 33 (21.7) | 19 (43.2) |

* Excludes counties not participating in the voluntary reporting of influenza-associated ICU hospitalizations.

ICU - intensive care unit

Figure 7 shows the percentage of selected underlying medical conditions reported in the critically ill and fatal cases. Among the 121 adults age 18-64 years with known information, 92 (76.0%) had an underlying condition defined by the Advisory Committee for Immunization Practices (ACIP) as being associated with severe influenza (3). The most frequent underlying medical conditions were chronic lung disease (46/101; 45.5%), cardiac disease (33/102; 32.4%), and metabolic disease (32/100; 32.0%). Among the 75 pediatric cases less than 18 years old with known information, the most frequent underlying medical condition was chronic lung disease (26/73; 35.6%); 14 (53.8%) of the 26 children with chronic lung disease had underlying asthma. Twenty-eight (37.3%) of the children were previously healthy. These findings are similar to previous California data published during the 2009 pandemic (4,5).

Figure 7. Selected underlying medical conditions in severe cases with laboratory-confirmed influenza reported to the California Department of Public Health, October 2, 2011 – May 19, 2012



Circulating influenza types and subtypes

Of the 196 severe cases reported, 166 (84.7%) were influenza type A and 27 (13.8%) were influenza type B. An additional three cases tested positive by rapid influenza diagnostic tests that detect influenza but are unable to distinguish between influenza A and B viruses. Of the 166 influenza A detections, 70 (42.2%) were subtyped as influenza A (H3), 47 (28.3%) were subtyped as A (2009 H1N1), and 49 (29.5%) were typed as influenza A with no further subtype identified.

The majority of the 166 severe influenza A cases occurred among adults age 18-64 years (107; 64.5%), while the majority of the 27 severe influenza B cases occurred in children (16; 59.3%), (data not shown). The pediatric population has also been disproportionately affected by influenza B compared to influenza A in previous seasons.

C. Syndromic Surveillance

1. ILI Outpatient Surveillance (Sentinel Providers)

Sentinel providers report the number of outpatient visits for ILI and the total number of visits per week. ILI activity levels, as defined by the CDC, are classified as minimal, low, moderate, or high, and are based on the percent of outpatient visits due to ILI compared to the mean percent of ILI visits that occur during spring and fall weeks with

little or no influenza virus circulation. Activity is “minimal” when the ILI percentage is less than 2 standard deviations above the mean, “low” when the ILI percentage is 2-3 standard deviations above the mean, “moderate” when the ILI percentage is 4-5 standard deviations above the mean, and “high” when ILI is 6 or more standard deviations above the mean.

ILI typically begins to increase in late December or early January and most commonly peaks in February. In California this season, 126 sentinel providers reported ILI activity on a regular basis. ILI activity was low through mid- December; from late December through early May, ILI fluctuated greatly without a clear peak (Figures 8 and 9).

Figures 8 and 9 below compare ILI from the past five seasons, including the current season (2011-2012), the 2009 H1N1 pandemic season, and a ‘moderately severe’ influenza season (2007-2008) as defined by CDC.

Figure 8. Percentage of visits for influenza-like illness reported by California Sentinel Providers, 2007-2012

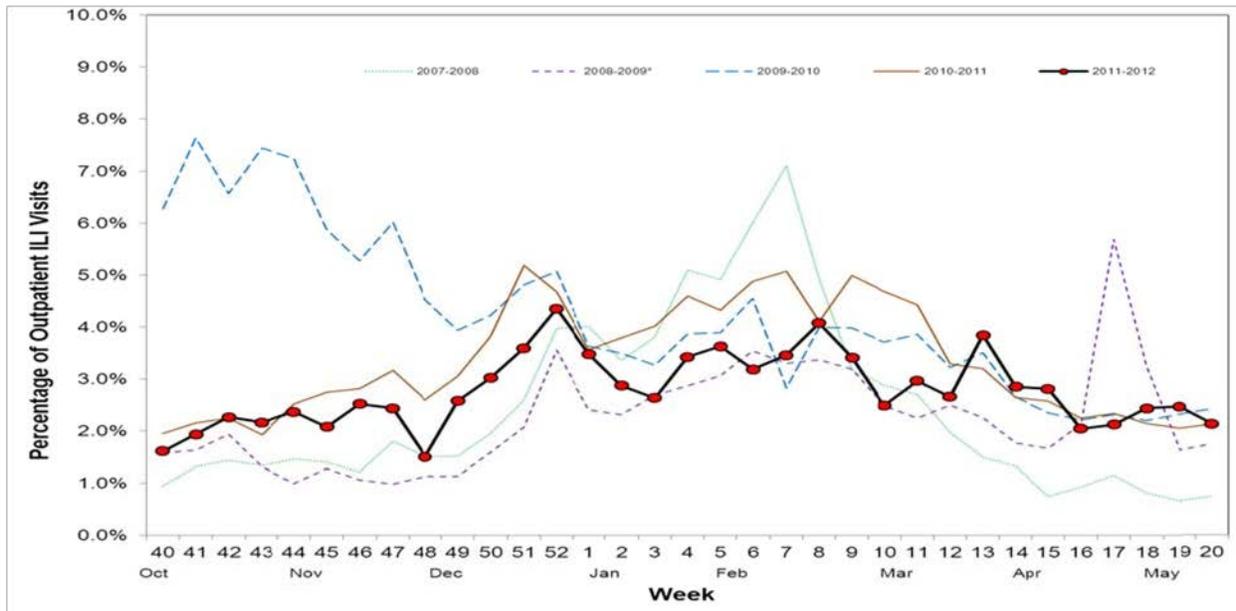
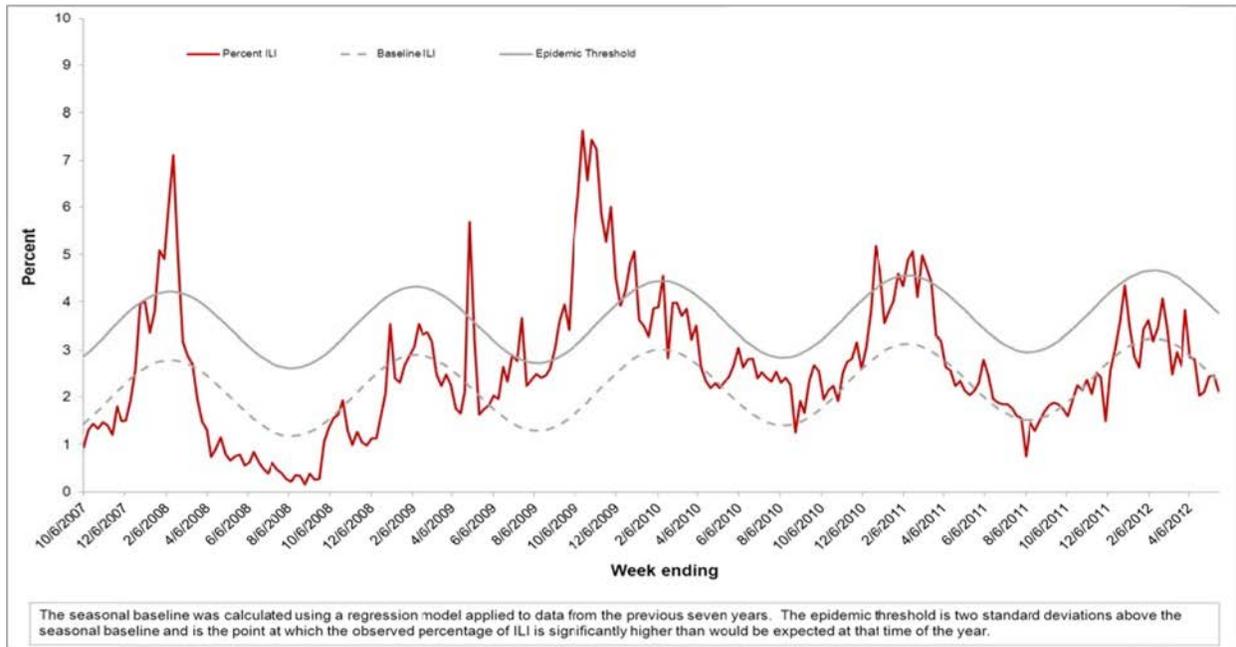


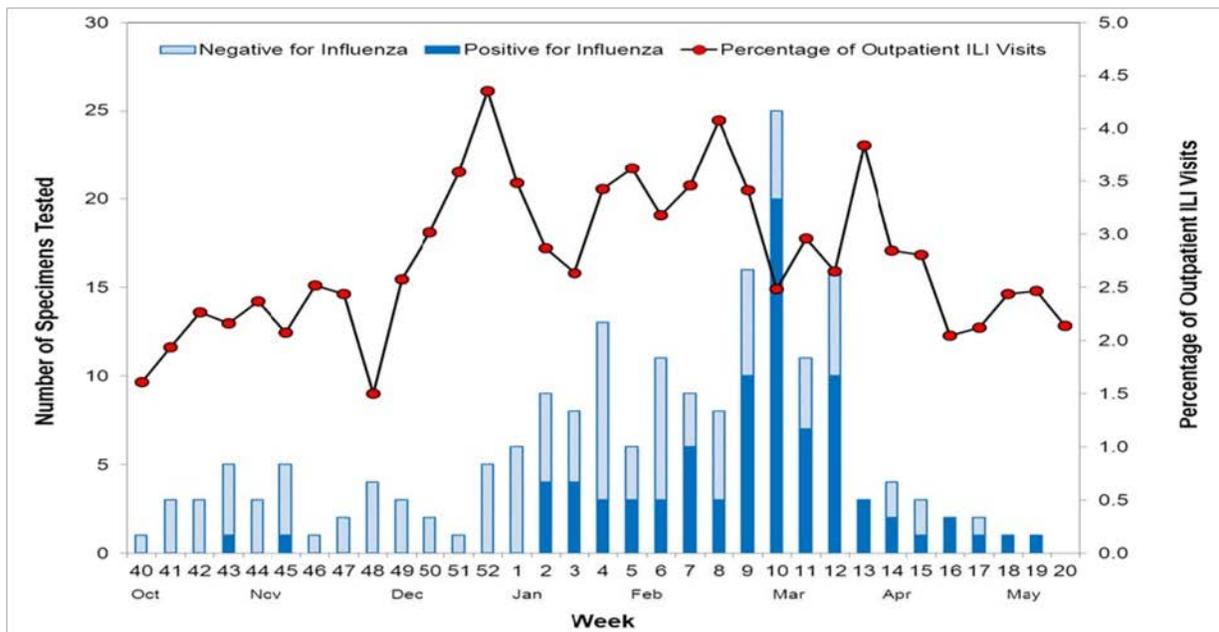
Figure 9. Percentage of influenza-like illness visits among patients seen by California Sentinel Providers, 2007–2012



Sentinel providers voluntarily submit specimens from patients with ILI to CDPH-VRDL for influenza testing. Testing of sentinel provider specimens provides important information about what influenza viruses are circulating and are the primary source of specimens sent for further characterization and strain-typing to the CDC. Between October 2, 2011 to May 19, 2012, 194 respiratory specimens were submitted by sentinel providers; 87 (45%) were positive for influenza, with the majority subtyped as influenza A (H3N2), (51; 59%), followed by influenza B (19; 22%) and influenza A (2009 H1N1), (17; 20%).

Figure 10 shows that the number of specimens submitted by sentinel providers that tested positive for influenza peaked in weeks 9-12 (February 26, 2012-March 24, 2012), and correlated with the peak seen in the same timeframe for RLN and sentinel laboratory influenza positive tests statewide.

Figure 10. California Sentinel Providers - specimens tested at CDPH-VRDL by week of collection and percentage of influenza-like visits by week of visit, October 2, 2011 - May 19, 2012

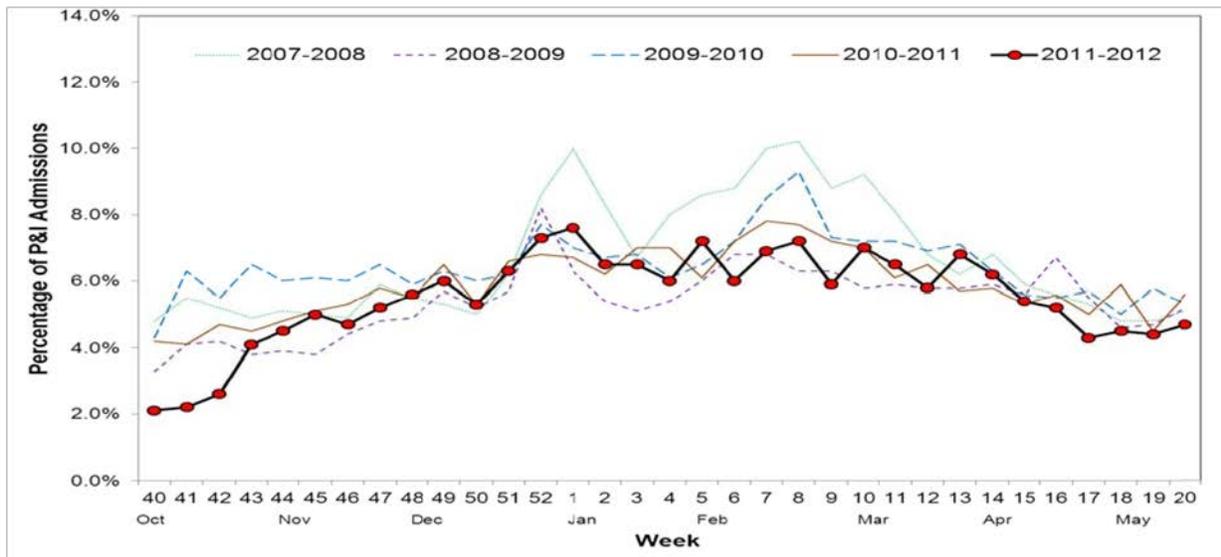


2. Kaiser Permanente Northern California Pneumonia and Influenza Admission Data

Pneumonia and influenza (P&I) admissions are defined as a diagnosis of “flu,” “pneumonia,” or “influenza” recorded in text fields at time of admission to the hospital. Influenza activity is tracked by dividing the number of P&I admissions by the total number of hospital admissions for the same day to obtain a percentage of P&I admissions. Admissions for pregnancy, labor and delivery, birth, and outpatient procedures are excluded from the denominator.

During the 2011-2012 influenza season, the percentage of P&I hospitalizations increased steadily in northern California from October 2011 through the beginning of January 2012, and remained level until the end of March, when the percentage began to decrease. This trend falls within the range of percentages seen for seasonal influenza in previous years.

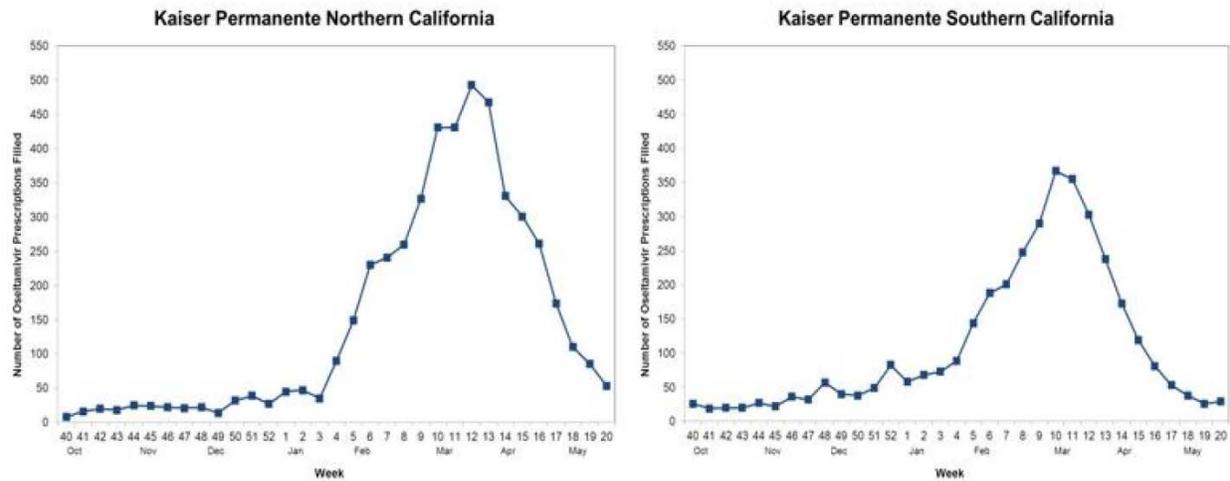
Figure 11. Pneumonia and influenza admissions at Kaiser Permanente Northern California facilities, 2007-2012



3. Kaiser Permanente (Northern and Southern California) Pharmacy Data

The number of outpatient prescriptions filled for oseltamivir is used to serve as a proxy indicator of influenza activity. Figures 12 and 13 show the number of oseltamivir prescriptions filled weekly by Kaiser Permanente outpatient pharmacies in northern and southern California. The number of prescriptions for oseltamivir began to increase significantly at the end of January 2012 in both northern and southern California. It is unknown whether health care providers prescribed oseltamivir in response to an increase in patients seen with ILI, or as a result of widespread recommendations distributed by Kaiser Permanente when influenza was first laboratory confirmed. However, the increase in prescriptions was concurrent with a statewide increase in laboratory detections of influenza. By mid-March, the number of prescriptions for oseltamivir in southern California had peaked, while prescriptions in northern California continued to rise through the end of March.

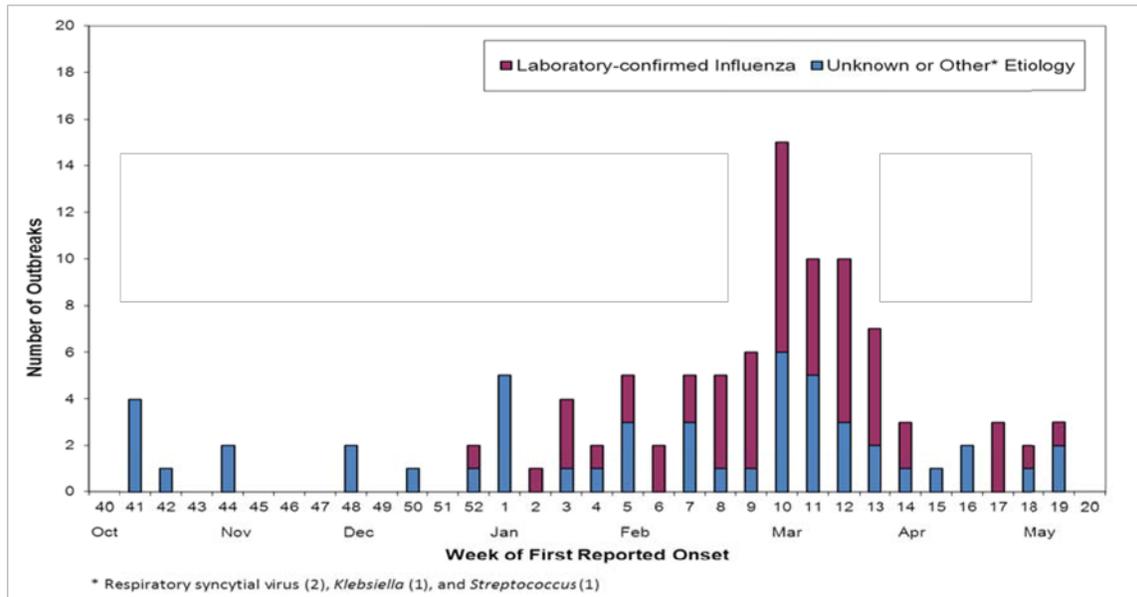
Figures 12 & 13. Oseltamivir prescriptions filled, Kaiser Permanente outpatients, October 2, 2011– May 19, 2012



D. Outbreaks of Respiratory Illness, Including Influenza

CDPH requests that all LHJs voluntarily submit preliminary reports of outbreaks that are suspected or laboratory-confirmed as influenza. CDPH also assists LHJs with management of outbreaks, including facilitating of testing and recommendations for use of antiviral drugs for both treatment and prophylaxis to prevent further spread. Settings where CDPH assistance was requested in the 2011-12 season included long-term care facilities, state prisons, elementary schools and jails. From October 2, 2011–May 19, 2012, a total of 135 preliminary reports of respiratory disease outbreaks were received by CDPH: 60 (39%) included cases with laboratory-confirmed influenza. Outbreaks were reported from the following local health jurisdictions: Alameda (2), Butte (5), Contra Costa (2), Humboldt (1), Imperial (1), Long Beach City (1), Los Angeles (33), Marin (1), Merced (1), Orange (16), Riverside (1), Sacramento (8), San Bernardino (1), San Diego (1), San Francisco (7), San Joaquin (5), San Luis Obispo (2), San Mateo (8), Santa Barbara (6), Santa Clara (16), Santa Cruz (3), Shasta (1), Sonoma (5), Stanislaus (5), Tulare (2), and Tuolumne (1).

Figure 14. Preliminary reports of respiratory and influenza outbreaks, 2011-2012 Season, by week



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