State of Wyoming

Department of Health

Wyoming Influenza Summary Report
2017-2018 Season

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WYOMING INFLUENZA SUMMARY REPORT, 2017-2018 SEASON
(October 1, 2017 - May 19, 2018)

SYNOPSIS

Influenza activity was high in severity as determined by the number of influenza-associated deaths, the number of laboratory-diagnosed influenza cases, and the percentage of visits to outpatient clinics or hospitals for influenza-like illness (ILI) during the 2017-2018 influenza season. During this high severity season, influenza surveillance and other influenza activity indicators were notable for the intensity and volume of reported cases throughout the state. A record number of reported cases, along with elevated rates of influenza-associated outbreaks, hospitalizations, and deaths were reported. Most of the United States experienced a similar phenomenon during the 2017-2018 influenza season. Overall, influenza A (H3N2) viruses and influenza B/Yamagata-lineage viruses were the predominant influenza viruses circulating in Wyoming. Throughout the influenza season, the 2009 influenza A (H1N1) pandemic virus co-circulated with influenza A (H3N2) viruses and influenza B viruses across Wyoming. The extended period of elevated influenza activity across the state exacerbated the traditional adverse effects of influenza seasons. The surge in influenza B viruses in the middle of the season protracted influenza activity across the state. Influenza B viruses predominated the influenza season from late January 2018 onward.

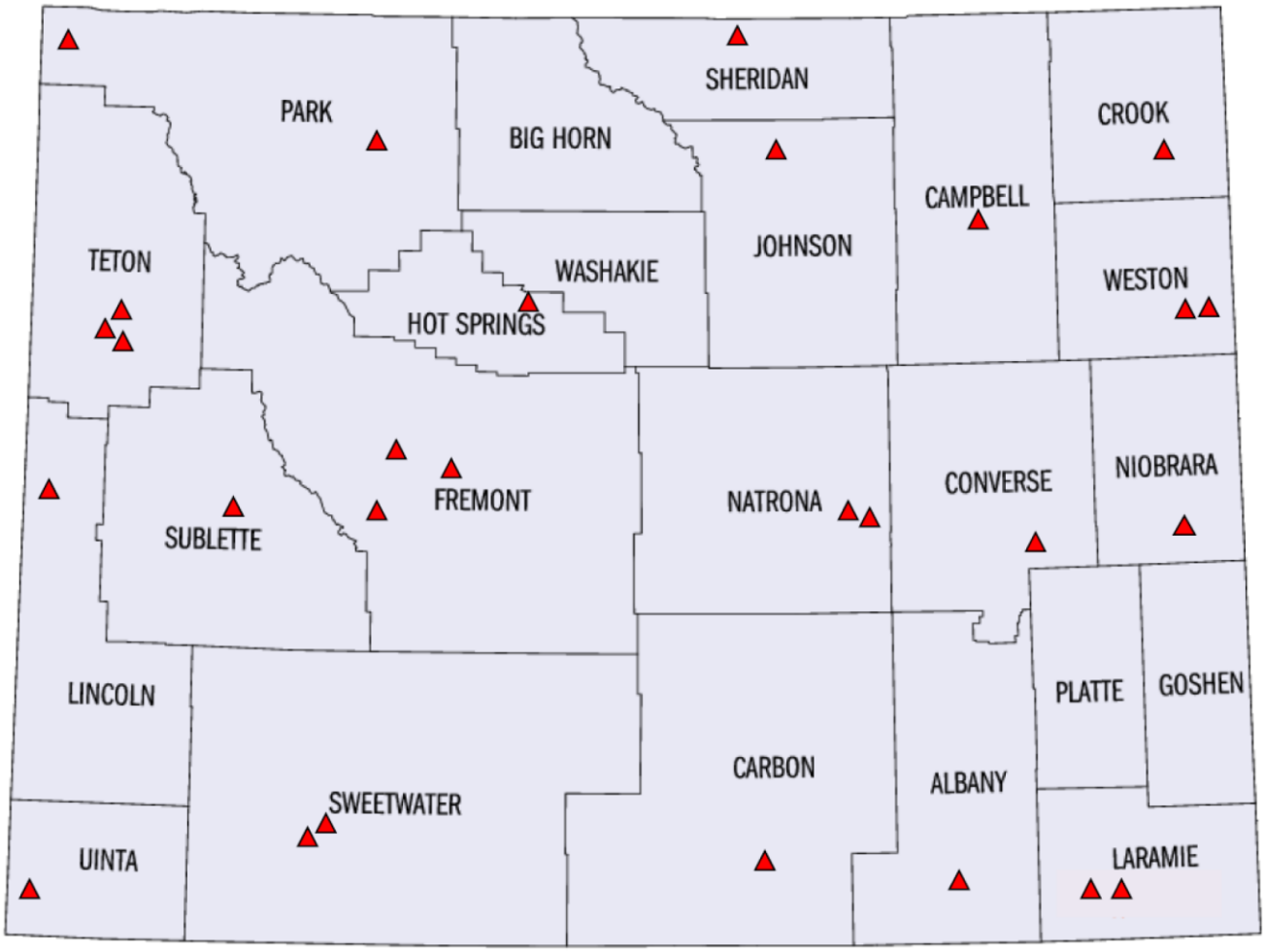
The epidemiology of influenza seasons are unpredictable; however, there are usually traditional expectations common to most influenza seasons. Like most influenza seasons, there was a transition to influenza B viruses as the predominating circulating virus. The transition occurred approximately during the midpoint of the 2017-2018 influenza season. Statistically, the 2017-2018 influenza season, was one of the most severe influenza seasons experienced over the past 15 years. At the start of the influenza season, healthcare providers across Wyoming reported low levels of influenza activity. The number of cases and the percentage of outpatient visits for ILI significantly increased in December 2017. The number of cases in Wyoming peaked during the week ending February 3, 2018, Morbidity and Mortality Weekly Report Week 05 (MMWR Week 05). Healthcare providers and laboratories concurrently reported high levels of influenza A viruses and peak levels of influenza B viruses during the 2017-2018 influenza peak. The state experienced an extended period of high activity during January and February 2018. Furthermore, influenza activity mirrored what were traditional influenza peak levels from previous influenza seasons through the middle of March 2018. Activity throughout the state remained elevated until April 2018 when influenza activity began gradually decreasing. For the remainder of the season, Wyoming experienced decreasing levels of influenza activity.

SURVEILLANCE AND THE INFLUENZA SENTINEL PROVIDER NETWORK

Influenza is a reportable disease in the State of Wyoming. Each year, the Wyoming Department of Health (WDH) receives laboratory reports of rapid influenza diagnostic test (RIDT), direct fluorescent antibody (DFA), indirect fluorescent antibody (IFA), polymerase chain reaction (PCR), and cell culture results from clinics, hospitals, and laboratories across the state and the nation. The surveillance program relies on these sectors to report all positive test results. Healthcare providers and laboratories submit influenza reports in multiple formats, including electronic submissions. However, laboratory data is only one of the surveillance tools utilized as a key indicator to monitor influenza activity. The reported cases of influenza do not accurately portray the burden of disease experienced by the residents of Wyoming during each influenza season. Influenza seasons are complex, and many factors influence the severity and geographic spread of the disease. Therefore, the Infectious Disease Epidemiology Unit collects, compiles, and analyzes key indicators associated with influenza activity from multiple datasets. Specifically, datasets from various units, sections, and divisions within the Wyoming Department of Health comprise the key influenza activity indicators utilized for influenza surveillance each season. The datasets include laboratory reports, Medicaid data, immunization records, mortality surveillance, and reports from hospitals and Emergency Medical Services (EMS). The collection of datasets provides public health officials with a robust influenza surveillance system.

Wyoming is also part of a network of influenza sentinel providers located across the nation. An influenza sentinel provider, or Influenza-like Illness Surveillance Network (ILINet) provider, conducts surveillance for ILI in collaboration with state health departments and the Centers for Disease Control and Prevention (CDC). The structure of the network is useful in identifying when and where influenza activity is occurring, determining what influenza viruses are circulating, tracking influenza-related illnesses, and detecting changes in influenza viruses. The network is also integral in measuring the impact of influenza with morbidity and mortality. However, one of the main focuses of the network of providers involves outpatient illness surveillance. The ILINet providers submit reports each week, even when they observe no influenza or ILI activity. The ILINet providers also collect samples from a small number of patients with ILI. The providers submit the samples to the Wyoming Public Health Laboratory (WPHL) or other state public health laboratories for specialized influenza testing. This information provides public health officials the earliest identification of circulating influenza virus types, subtypes, lineages, and strains during the influenza season. Map 1 indicates the locations of healthcare providers enrolled in the ILINet Provider - Influenza Surveillance Program during the 2017-2018 influenza season.

MAP 1: NETWORK OF ILINET PROVIDERS BY COUNTY
WYOMING, 2017-2018 INFLUENZA SEASON



Twenty-eight healthcare organizations enrolled as ILINet providers during the 2017-2018 influenza season. A major goal of the WDH-Infectious Disease Epidemiology Unit is to recruit and maintain ILINet providers from every county in the state, including multiple municipalities and various types of practices within each county. This season, 19 of the 23 counties in Wyoming participated in the program, including ILINet providers at the Wind River Indian Reservation and Yellowstone National Park. Data from the network of ILINet providers are critical for monitoring the impact of influenza. Additionally, public health officials can utilize the data, in combination with other influenza surveillance data, to guide prevention and control activities, vaccine strain selection, and patient care. Providers of any specialty (e.g., pediatrics) in any practice (e.g., emergency department) are eligible to be ILINet providers. The ILINet sentinel provider program involves two major components: weekly ILI reporting and laboratory specimen collection.

The first component, weekly ILI reporting, consists of recording and reporting summary data (total number of patient visits for any reason and the number of patient visits for ILI by age group) each week to CDC via the ILINet website. The influenza sentinel provider program, also known as the ILINet provider program, consists of approximately 3,000 healthcare providers in all 50 states and several United States Territories. The program provides public health officials with a source of outpatient illness surveillance during the influenza season. The ILI case definition used for national surveillance is {1} a fever ($\geq$100.0° F or 37.8° C) and {2} a cough and/or a sore throat in the absence of a known cause other than influenza. The ILI case definition intends to capture patients with influenza-like illnesses; consequently, providers may capture other diseases that are not influenza cases. Therefore, some patients will meet the ILI case definition without having the disease of influenza. Wyoming ILINet providers submitted reports weekly through the ILINet website beginning October 1, 2017 (MMWR Week 40); reporting continued until September 29, 2018 (MMWR Week 39) but some Wyoming ILINet providers discontinued reporting on May 19, 2018 (MMWR Week 20). Historically, the twentieth week of the year marks the end of the influenza season. However, after the 2009 pandemic, CDC requested that the national network of ILINet providers continue to report throughout the summer. Year-round influenza surveillance provides a baseline level of influenza activity; this process functions to establish the annual epidemic thresholds of influenza.

The second component, laboratory specimen collection, involves collecting specimens from a small number of patients with ILI each influenza season. Healthcare providers submit specimens to the WPHL for specialized influenza testing. The WPHL performs reverse transcriptase – polymerase chain reaction (RT-PCR) testing to detect the various influenza virus types, subtypes, and lineages circulating in Wyoming. Also, WPHL forwards a subset of the specimens submitted by Wyoming ILINet providers to CDC for additional testing. This testing often provides the earliest identification of circulating influenza virus types, subtypes, lineages, and strains during the current influenza season. During a typical influenza season, laboratory and epidemiology officials will utilize the ILINet provider program as a major part of influenza surveillance for the WDH. Also, the WPHL is a World Health Organization (WHO) Collaborating Laboratory. As a WHO Collaborating Laboratory, the WPHL reports the total number of respiratory specimens tested and the number of positive influenza specimens to CDC each week. The participating ILINet providers receive exclusive summaries of state and national influenza data, free subscriptions to CDC journal publications, influenza outbreak assistance, and viral isolation test kits for free influenza testing at the WPHL. Finally, it is important to note that data provided by ILINet providers are critical to monitoring and protecting the public's health.

REPORTED CASES

The WDH received 8,485 laboratory-confirmed (RIDT, DFA, or PCR positive test results) influenza case reports during the 2017-2018 influenza season. Healthcare providers reported the first positive case reports of the influenza season during the week ending October 7, 2017 (MMWR Week 40). Reporting of influenza peaked the week ending February 3, 2018 (MMWR Week 05) when healthcare providers reported 914 cases. In comparison, during the 2016-2017 influenza season, reporting of influenza peaked the week ending February 4, 2017 (MMWR Week 05) when healthcare providers reported 628 case reports. Chart 1 and Table 1 display the number of cases reported by week. The WDH requires healthcare providers and laboratories to report all positive influenza laboratory tests; however, not all providers report these results. Additionally, many ill persons do not seek medical care, and not all healthcare providers test for the disease during medical visits. Therefore, comparing reported cases of influenza from week-to-week or season-to-season may not be valid, as many factors influence both the testing and reporting of influenza.

CHART 1: REPORTED CASES OF INFLUENZA (RIDT, DFA, PCR, & LAB CULTURE) WYOMING, (2012-2013 TO 2017-2018)

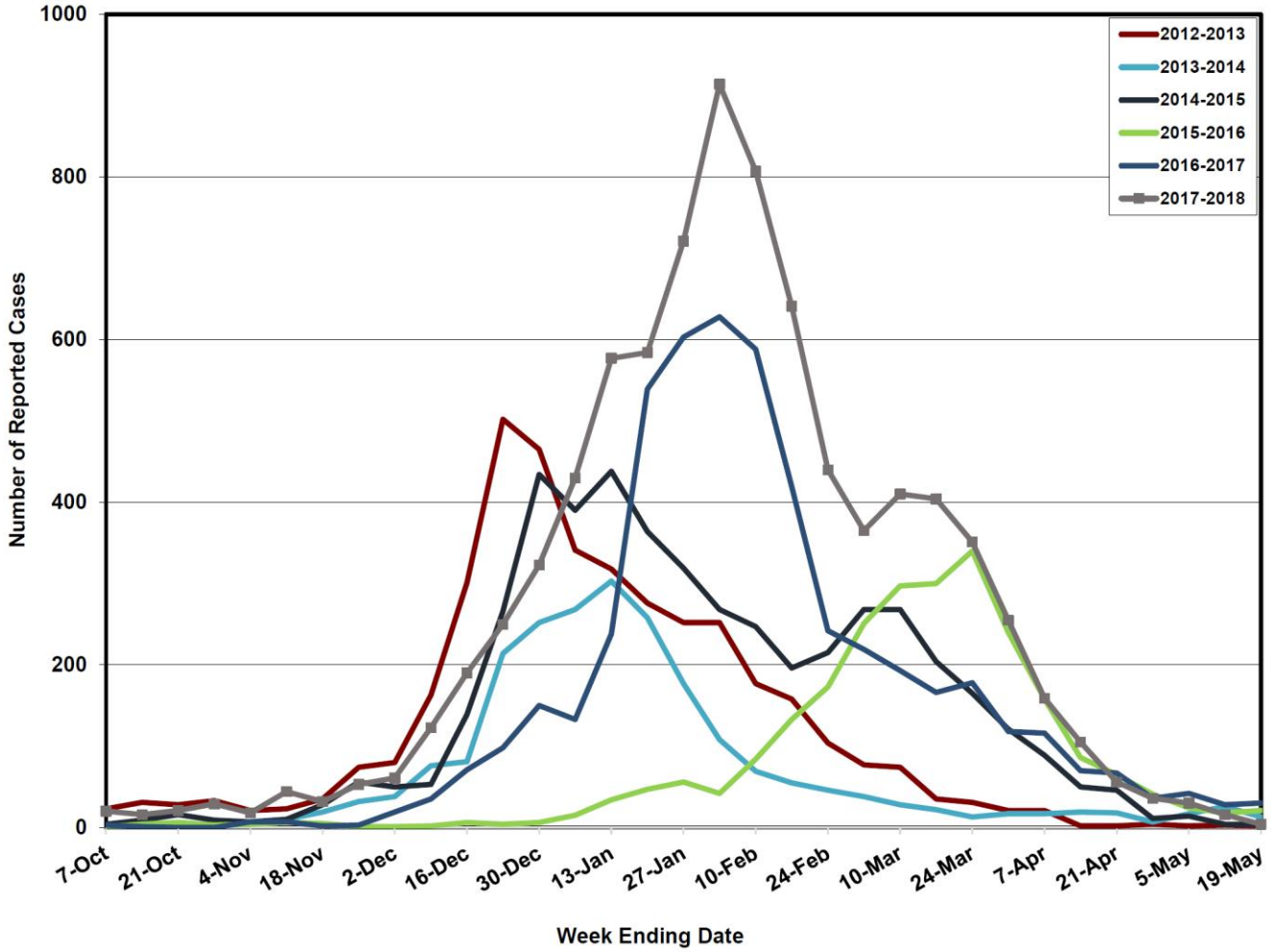


TABLE 1: REPORTED CASES OF INFLUENZA; WYOMING, 2017-2018 INFLUENZA SEASON

Week Ending	Number
07-Oct	20
14-Oct	16
21-Oct	21
28-Oct	29
04-Nov	18
11-Nov	44
18-Nov	32
25-Nov	53
02-Dec	61
09-Dec	123
16-Dec	190
23-Dec	250
30-Dec	323
06-Jan	430
13-Jan	577
20-Jan	584
27-Jan	721
03-Feb	914
10-Feb	807
17-Feb	641
24-Feb	440
03-Mar	365
10-Mar	410
17-Mar	404
24-Mar	351
31-Mar	255
07-Apr	159
14-Apr	105
21-Apr	56
28-Apr	36
05-May	30
12-May	16
19-May	4
Total	**8485**

County	Number
Albany	428
Big Horn	143
Campbell	801
Carbon	151
Converse	273
Crook	48
Fremont	470
Goshen	191
Hot Springs	45
Johnson	64
Laramie	1416
Lincoln	271
Natrona	1696
Niobrara	8
Park	357
Platte	134
Sheridan	531
Sublette	133
Sweetwater	665
Teton	220
Uinta	369
Washakie	62
Weston	9
Unknown	0
Total	**8485**

Lineage (B)	Number
B/ Yamagata	93
B/ Victoria	1
B/ Not Tested	4003
B/ Unknown	0
Total	**4097**

Age	Number
0-4	1268
5-10	1775
11-19	1416
20-39	1403
40-59	1392
60+	1231
Unknown	0
Total	**8485**

Gender	Number
Male	4224
Female	4261
Total	**8485**

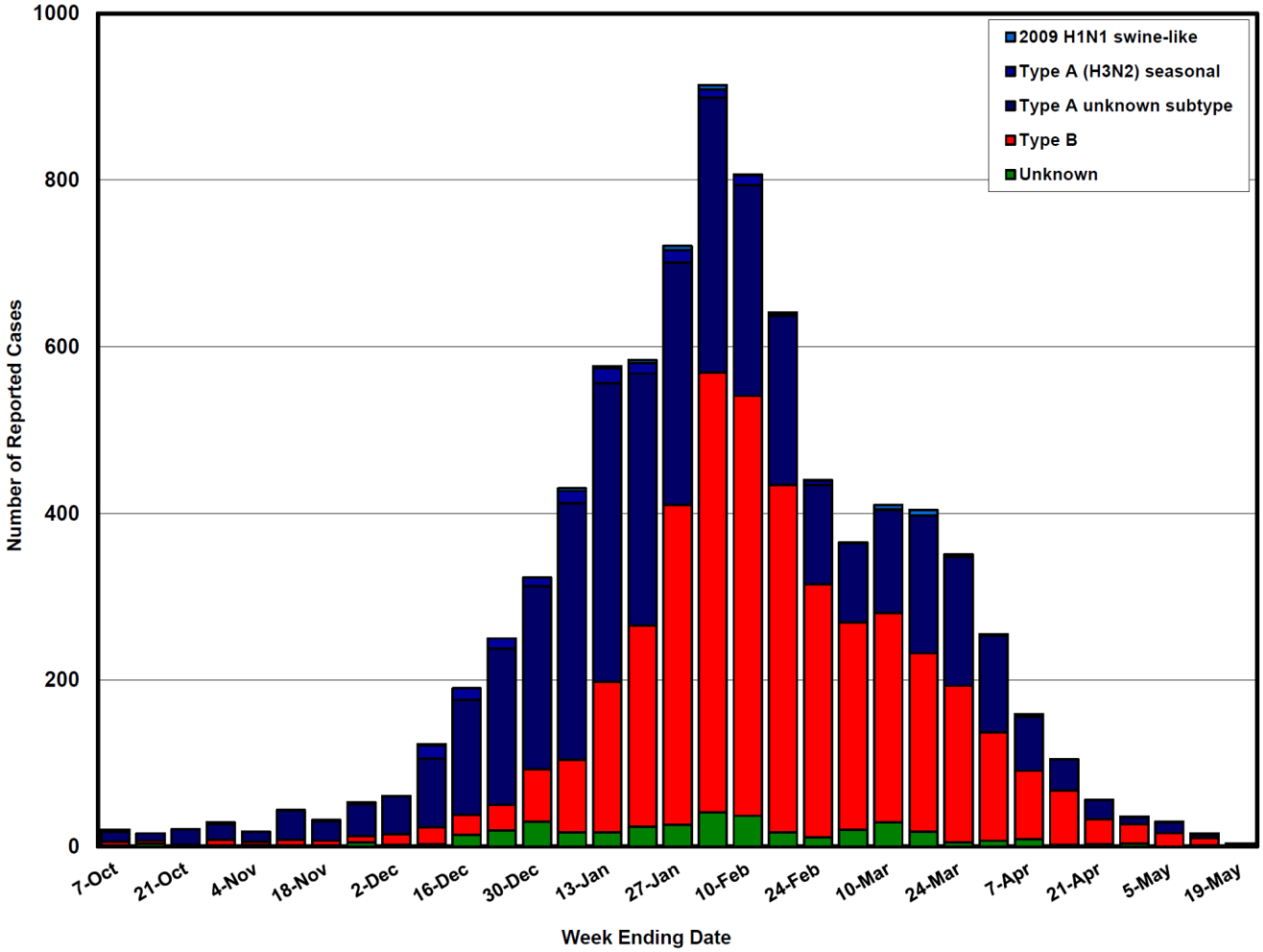
Type	Number
A	4015
B	4097
A & B Dual	0
Unknown	373
Total	**8485**

Subtype (A)	Number
A (H3N2)	154
A (H1N1) 2009	46
A & B Dual	0
A Unknown	3815
Total	**4015**

LABORATORY DATA

Of the 8,485 influenza case reports, 4,015 (47.3%) were influenza A virus positive, 4,097 (48.3%) were influenza B virus positive, and 373 (4.4%) were positive for influenza viruses not typed for influenza A or influenza B. Healthcare providers and laboratories confirmed two cases by DFA; 1,305 cases by PCR; and 7,178 cases by RIDT only. The WPHL tested a total of 619 specimens for influenza viruses, and 260 (42.0%) were positive. However, 19 were out-of-state residents not counted in the Wyoming database. The WPHL confirmed the first positive PCR specimen during the week ending October 7, 2017 (MMWR Week 40), and confirmed the last positive specimen during the week ending April 18, 2018 (MMWR Week 16). Among the 260 positive influenza specimens tested at the WPHL: 34 (13.0%) were 2009 influenza A (H1N1) pandemic viruses; 126 (48.5%) were influenza A (H3N2) viruses; and 100 (38.5%) were influenza B viruses (see chart 2). The influenza B viruses were both B/Victoria-lineage and B/Yamagata-lineage viruses; the overwhelming majority of influenza B viruses were B/Yamagata-lineage viruses.

CHART 2: REPORTED CASES OF INFLUENZA BY VIRUS TYPE & SUBTYPE
WYOMING, 2017-2018 INFLUENZA SEASON



On a national level, clinical laboratories tested a total of 1,210,053 specimens for influenza viruses during the 2017-2018 influenza season, and 224,113 (18.5%) were positive. Among the positive influenza viruses, 151,413 (67.6%) were influenza A viruses, and 72,700 (32.4%) were influenza B viruses. Additionally, public health laboratories participating as United States (U.S.) WHO collaborating laboratories submitted a subset of influenza-positive respiratory specimens to CDC for virus characterization through three National Influenza Reference Centers coordinated through the state public health laboratories in California, New York, and Wisconsin. CDC characterizes influenza viruses through genomic sequencing and antigenic characterization, using hemagglutination inhibition or neutralization assays). The process evaluates whether genetic changes in circulating viruses have led to antigenic drift away from the reference vaccine virus. The WHO and the National Respiratory and Enteric Virus Surveillance System collaborating laboratories tested 98,446 specimens during the 2017-2018 influenza season; 53,790 (54.6%) of the 98,446 were positive for influenza viruses. The collaborating laboratories subtyped 37,578 (24.8%) influenza A viruses: 31,977 (84.9%) were influenza A (H3N2) viruses, and 5,704 (15.1%) were 2009 influenza A (H1N1) pandemic viruses.

This influenza season, influenza A (H3N2) viruses, 2009 influenza A (H1N1) pandemic viruses, and influenza B viruses co-circulated in the United States. However, the relative proportion of each type and subtype of influenza virus varied by region and week. Influenza A viruses were the most commonly reported influenza virus type throughout the first half of the influenza season, and influenza A (H3N2) viruses were the overall predominant influenza subtype circulating across the United States. Additionally, influenza A (H3N2) viruses were predominant in Region 8 of the U.S. Department of Health and Human Services (DHHS) during the weeks preceding the influenza peak; Wyoming is located within DHHS Region 8. Influenza B viruses were more commonly reported from early March to late May (MMWR Weeks 9-20). In contrast, influenza B viruses in Wyoming became the predominant viruses in late January 2018. Therefore, influenza B viruses were the predominant circulating influenza viruses in Wyoming before peak activity. Beginning October 1, 2017, CDC antigenically characterized 3,329 influenza viruses collected by laboratories in the United States during the 2017-2018 influenza season: 832 influenza A (H1N1) 2009 pandemic viruses were characterized as A/California/7/2009-like. Phylogenetic analysis of the hemagglutinin genes from the 832 influenza A (H1N1) 2009 pandemic viruses showed that all belong to clade 6B.1, the predominant hemagglutinin clade in the United States since the 2015-2016 influenza season. The majority, 735 (99.9%) of 736, were well inhibited by ferret antisera raised against cell culture-propagated 6B.1 virus A/Michigan/45/2015, the recommended influenza A (H1N1) pandemic 2009 component of the 2017-2018 Northern Hemisphere influenza vaccine.

Influenza A (H3N2) viruses were associated with outbreaks in multiple countries across the world. Phylogenetic analysis of the hemagglutinin genes from the 1,313 influenza A (H3N2) viruses revealed extensive genetic diversity with multiple clades/subclades co-circulating across the United States. The hemagglutination genes of circulating viruses belonged predominantly to clade 3C.2a (n = 1,057); however, subclade 3C.2a1 (n = 145) and clade 3C.3a (n = 93) also circulated within the United States. Viruses with the 3C.2a hemagglutinin emerged at the end of the 2013-2014 influenza season and remained the predominant clade since the 2014-2015 influenza season. The hemagglutinin genes have experienced continued genetic diversification each season. Six hundred fifty-five influenza A (H3N2) viruses were antigenically characterized, and 612 (93.4%) of the influenza A (H3N2) viruses tested were well-inhibited by ferret antisera raised against A/Michigan/15/2014 (3C.2a), a cell-propagated A/Hong Kong/4801/2014-like reference virus representing the influenza A (H3N2) component of 2017-2018 Northern Hemisphere influenza vaccines. A small percentage (6.6%) of the influenza A (H3N2) viruses, the majority belonging to genetic clade 3C.3a, showed evidence of antigenic drift. The remaining 93.4% of the influenza A (H3N2) viruses were well inhibited by ferret antisera raised against cell-propagated A/Michigan/15/2014. Only 48.2% of the viruses tested were well inhibited by ferret antiserum raised against the egg-propagated A/Hong Kong/4801/2014 reference virus representing the influenza A (H3N2) vaccine component. Researchers identified a higher proportion (77.3%) of viruses tested were well inhibited by ferret antisera raised against the egg-propagated A/Singapore/INFIMH-16-0019/2016 reference virus, the upcoming influenza A (H3N2) component representing the 2018-2019 Northern Hemisphere influenza vaccines.

Influenza B viruses from the B/Victoria-lineage and the B/Yamagata-lineage co-circulated during the 2017-2018 influenza season. The influenza B/Yamagata-lineage viruses were the predominant influenza B viruses circulating in the United States and Wyoming. The overwhelming majority (98.9%) of typed influenza B viruses in Wyoming were B/Yamagata-lineage viruses. Additionally, U.S. laboratories antigenically characterized 896 (75.7%) of the 1,184 influenza B viruses as B/Yamagata-lineage viruses. Phylogenetic analysis of the 896 influenza B/Yamagata-lineage viruses indicates that the hemagglutinin genes belonged to clade Y3, the predominant influenza B viruses during the 2017-2018 influenza season. All of the antigenically characterized B/Yamagata-lineage viruses were antigenically similar to cell-propagated B/Phuket/3073/2013, the reference vaccine virus representing the influenza B/Yamagata-lineage component of the 2017-2018 Northern Hemisphere quadrivalent vaccines. Therefore, the reference vaccine virus representing the influenza B/Yamagata-lineage component for the upcoming 2018-2019 Northern Hemisphere quadrivalent vaccines will remain the same as the previous influenza season.

There was a small number of B/Victoria-lineage viruses antigenically characterized during the 2017-2018 influenza season. Additionally, public health researchers identified an increasing proportion of amino acid deletions within the hemagglutinin proteins. Laboratories antigenically characterized 288 (24.3%) of the 1,184 influenza B viruses as B/Victoria-lineage viruses. The 288 B/Victoria-lineage viruses were antigenically characterized using post-infection ferret antisera. All hemagglutinin genes belonged to the genetic clade V1A, the same genetic clade as the vaccine reference virus, B/Brisbane/60/2008. However, 234 (81.3%) of the B/Victoria-lineage viruses had a six-nucleotide deletion in the hemagglutinin gene segment encoding amino acids 162 and 163. The viruses were abbreviated as V1A-2Del and currently designated as V1A.1. The V1A.1 influenza B viruses were first reported during the 2016-2017 influenza season, but the V1A.1 influenza B viruses became prominent during the 2017-2018 season. Only 53 (19.6%) of the 288 B/Victoria-lineage viruses were well-inhibited by ferret antisera raised against the cell-propagated B/Brisbane/60/2008 reference virus, representing the recommended B virus component of the 2017-2018 Northern Hemisphere influenza vaccines. The majority of recent viruses tested during the 2017-2018 influenza season were inhibited well by post-infection ferret antisera raised against B/Brisbane/60/2008-like cell culture-propagated viruses in hemagglutinin inhibition assays; however, a substantial proportion of viruses were poorly inhibited by these antisera.

The great majority of these poorly reacting viruses, the circulation of which has expanded in Europe and the Americas, had the two amino acid deletion (amino acids 162 and 163) in the hemagglutinin proteins and were well inhibited by antisera raised against B/Colorado/06/2017, a V1A.1 reference virus representing the influenza B component recommended for the upcoming 2018-2019 Northern Hemisphere influenza vaccine. Additionally, viruses circulating in Asia had three amino acid deletions (amino acids 162, 163, and 164). Therefore, the overall majority of B/Victoria-lineage viruses that were poorly inhibited by antisera raised to B/Brisbane/60/2008 had the V1A.1 hemagglutinin segment. According to WHO, serology studies using human serum panels yielded geometric mean hemagglutinin inhibition titers of antibodies against representative recent B/Victoria/2/87 lineage viruses that were somewhat reduced when compared to hemagglutinin inhibition titers against egg or cell culture-propagated B/Brisbane/60/2008-like reference viruses. Antibodies induced by B/Brisbane/60/2008-like vaccine viruses in very young children reacted with reduced titers against viruses of the B/Victoria/2/87 lineage with the two and three amino acid deletions in hemagglutinin proteins. Additionally, studies using serum panels from recipients of the quadrivalent vaccines indicated that the geometric mean titers against most representative recent B/Yamagata/16/88 lineage viruses were similar to those against cell culture-propagated B/Phuket/3073/2013-like reference viruses.

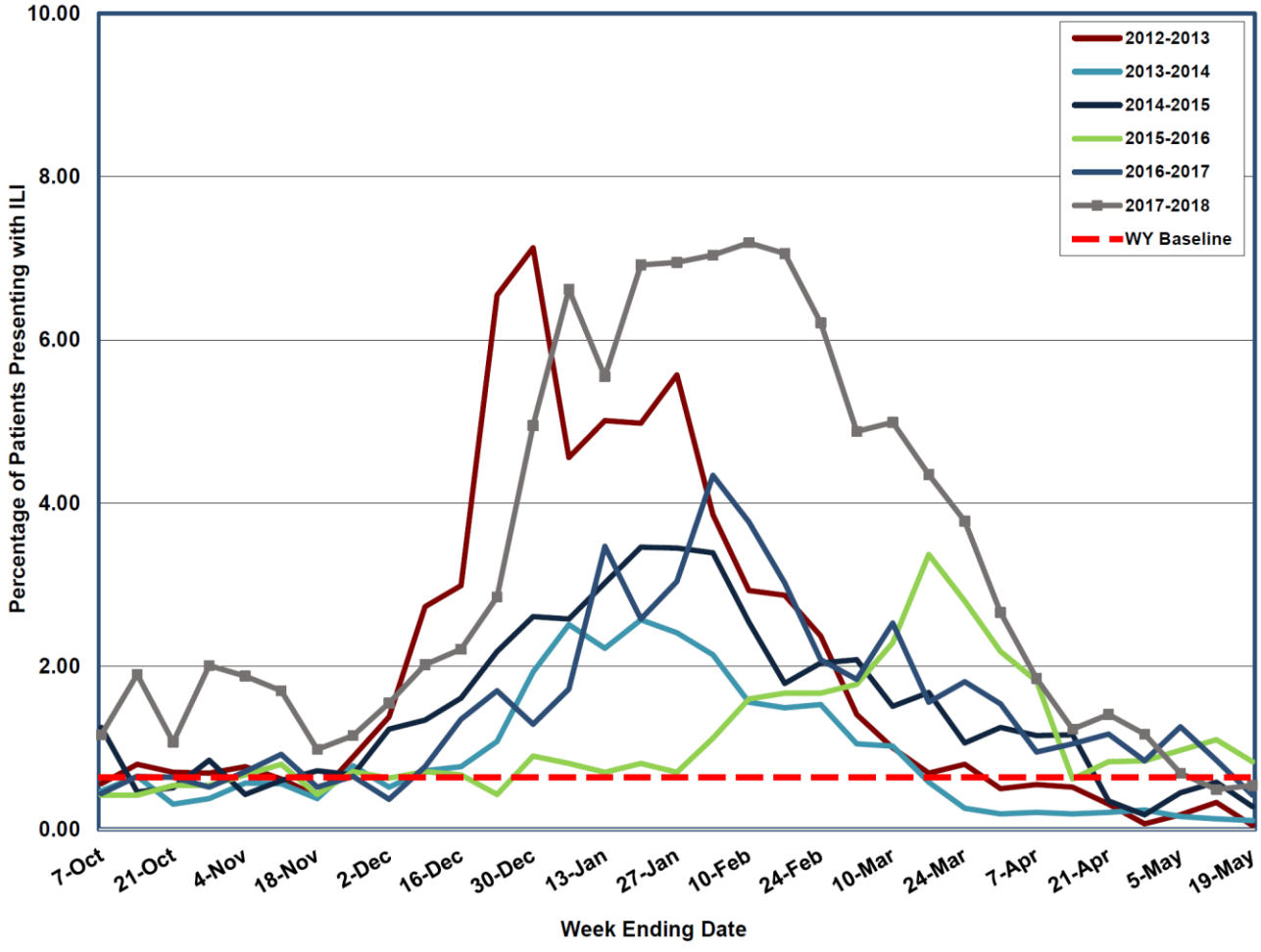
Laboratorians at CDC routinely use hemagglutination inhibition assays to antigenically characterize influenza viruses year-round to compare how similar currently circulating influenza viruses are to those included in the influenza vaccine and to monitor for changes in circulating influenza viruses. The information CDC collects from studying genetic changes in viruses (substitutions, variants, or mutations) are an important part of public health. The information assists public health officials in determining whether existing vaccines and medical countermeasures such as antiviral drugs are effective against influenza viruses. Additionally, the information is useful to determine the potential for influenza viruses in animals to infect humans. During the 2017-2018 influenza season, there was considerable genetic diversification of hemagglutinin and neuraminidase genes within influenza A (H3N2) viruses. Additionally, a substantial portion of B/Victoria-lineage viruses were antigenically distinguishable from the reference virus components of the 2017-2018 Northern Hemisphere influenza vaccine.

Antigenic characterization continues to provide important data for assessing the similarity between reference viruses and circulating viruses. Field studies on vaccine effectiveness are conducted to determine how well vaccines work. Consequently, the laboratory data evaluates whether the changes in the viruses impacted vaccine effectiveness. The laboratory data for 2009 influenza A (H1N1) pandemic viruses were antigenically indistinguishable from the vaccine virus component for the 2017-2018 Northern Hemisphere influenza vaccine. Likewise, the majority of circulating influenza B/Yamagata-lineage viruses were inhibited by post-infection ferret antisera raised against cell culture and egg propagated component of the 2017-2018 Northern Hemisphere influenza vaccine. Consequently, the 2009 influenza A (H1N1) pandemic virus component and the B/Yamagata-lineage virus component remained unchanged for the 2018-2019 Northern Hemisphere influenza vaccine. As previously stated, laboratory data indicated possible gaps in protection with the influenza A (H3N2) viruses and the B/Victoria-lineage viruses. The laboratory data displayed evidence of antigenic drift among both viruses. Consequently, the 2018-2019 Northern Hemisphere influenza vaccine components for the influenza A (H3N2) virus was updated from the A/Hong Kong/4801/2014 (H3N2)-like virus to an A/Singapore/INFIMH-16-0019/2016 (H3N2)-like virus. Likewise, the influenza B component of the 2018-2019 Northern Hemisphere trivalent influenza vaccine was updated from the B/Brisbane/60/2008-like virus to a B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage). For the vast majority of viruses characterized at CDC laboratories, next-generation whole genome sequencing was performed to determine the genetic identity of circulating viruses. For the subset of viruses that did not yield sufficient hemagglutination titers, antigenic properties were inferred using results obtained from viruses within the same genetic group as those that have been characterized antigenically.

OUTPATIENT INFLUENZA-LIKE ILLNESS (ILI) REPORTS FROM WYOMING SENTINEL SITES

The ILINet website is a data repository for healthcare providers to record aggregated data on patients with ILI symptoms. Each week, ILINet providers reported the total number of patients seen and the number of those patients with ILI by age group. Chart 3 illustrates ILI reported by Wyoming ILINet providers. Influenza and ILI morbidity started the influenza season above the baseline level (0 - 0.64%); ILI activity among the network of ILINet providers extensively remained above the baseline throughout most of the influenza season. The 2017-2018 influenza season was a high severity influenza season. The peak percentage of patient visits for ILI was 7.19%, which occurred the week ending February 10, 2018 (MMWR Week 6). The number of reported cases peaked the previous week, the week ending February 3, 2018 (MMWR Week 5). ILI activity among the ILINet providers remained above the baseline until the week ending May 12, 2018 (MMWR Week 19). In comparison, during the 2016-2017 influenza season, the peak percentage of patient visits for ILI was 4.34%, which occurred the week ending February 4, 2017 (MMWR Week 5).

CHART 3: WEEKLY ILI REPORTING BY ILINET PROVIDERS WYOMING, (2012-2013 TO 2017-2018)



REPORTED INFLUENZA-ASSOCIATED DEATHS

Influenza-associated deaths are reportable in the State of Wyoming. Influenza-associated deaths are defined as deaths occurring in Wyoming residents, in which an influenza infection was the primary cause or a contributing cause of mortality listed on an individual's death certificate. Currently, tracking death certificates is the best surveillance system to capture and identify influenza-associated deaths in Wyoming. However, according to the CDC, influenza is infrequently listed on death certificates. Also, testing for seasonal influenza infections is not frequently performed, particularly among the elderly who are at greatest risk for seasonal influenza complications and death. Therefore, public health officials may not identify influenza-associated deaths in many instances; consequently, this surveillance system may underestimate the true impact of influenza-associated deaths in the state.

This season, the WDH-Vital Statistics Services reported 27 influenza-associated deaths (4.66 per 100,000). In contrast, during the 2016-2017 influenza season, the WDH-Vital Statistics Services reported 15 influenza-associated deaths (2.56 per 100,000). The number of reported deaths during the 2017-2018 influenza season was greater than the number of influenza-associated deaths reported during the previous influenza season. The median age of the 27 influenza-associated deaths was 75 years, with 18 (66.7%) of the deaths occurring in individuals 65 years of age or older. The remaining nine (33.3%) influenza-associated deaths occurred in individuals under the age of 65 years, with one of those being a pediatric influenza-associated death (0-18 years). In comparison, during the 2016-2017 influenza season, the median age of influenza-associated deaths was 88 years, with thirteen (86.7%) of the deaths occurring in individuals over the age of 65 years. Similar to the previous influenza season, influenza A (H3N2) viruses were one of the predominant circulating influenza viruses in Wyoming during the 2017-2018 influenza season. Consequently, public health officials linked the majority of reported influenza-associated deaths with influenza A viruses, specifically, influenza A (H3N2) virus infections. However, multiple influenza-associated deaths were also linked with the 2009 influenza A (H1N1) pandemic viruses and influenza B viruses. According to CDC, influenza seasons during which influenza A (H3N2) viruses predominate are associated typically with higher rates of hospitalizations and deaths among the elderly. Although influenza viruses co-circulated throughout the season, all of the influenza-associated deaths linked by Wyoming public health officials to 2009 influenza A (H1N1) pandemic virus infections and influenza B virus infections, occurred after the influenza peak. Additionally, the majority of influenza-associated deaths, 18 (66.7%), occurred after the influenza peak, the week ending February 3, 2018 (MMWR Week 05).

COMPOSITION OF THE 2018-2019 VACCINE

Researchers study the various strains of influenza viruses infecting humans and how they are changing. Public health officials select influenza viruses for the seasonal influenza vaccines each year based on information gathered over previous influenza seasons. One hundred forty-three National Influenza Centers (NIC), located in 113 different countries, gather circulating influenza strains and information on disease trends. The six WHO Collaborating Centers for Reference and Research on Influenza analyze the combined data. Based on this information, experts forecast which viruses are likely to circulate during upcoming influenza seasons, and the WHO recommends specific virus strains to make the vaccine. Each February, the WHO makes the final recommendations for vaccines produced for the Northern Hemisphere. Each country then uses the recommendations made by the WHO to assist with national decisions of what virus strains to include in the influenza vaccine supply for their country. In the United States, an advisory committee convened by the Food and Drug Administration (FDA) makes the final decision about vaccine strains in February. Manufacturers grow vaccine strains based on these recommendations.

Currently, there are primarily three types of influenza viruses circulating in humans: 2009 influenza A (H1N1) pandemic viruses, influenza A (H3N2) viruses, and influenza B viruses. Each year, vaccine manufacturers use influenza virus strains from each of the three circulating viruses to produce the trivalent seasonal influenza vaccine. The WHO recommended the influenza vaccine virus strains for the 2017-2018 Northern Hemisphere Trivalent Influenza Vaccine. The FDA - Vaccines and Related Biological Products Advisory Committee (VRBPAC) agreed with the recommendations for the United States influenza vaccine supply. Both agencies recommend that the trivalent vaccine contain an A/Michigan/45/2015 (H1N1) pandemic 2009-like virus; an A/Singapore/INFIMH-16-0019/2016 (H3N2)-like virus; and a B/Colorado/06/2017-like (B/Victoria-lineage) virus. The upcoming vaccine formulation represents a change in the influenza A (H3N2) virus and the Influenza B (Victoria-lineage) virus components of the vaccine compared with the composition of the 2017-2018 influenza vaccine. Recent samples of influenza A (H3N2) viruses indicated that a higher proportion of the circulating viruses were well inhibited by the reference virus included in the 2018-2019 Northern Hemisphere influenza vaccines. The B/Victoria-lineage viruses were detected in low numbers across the Northern Hemisphere and the United States. However, an increasing portion of the B/Victoria-lineage viruses contained a two amino acid deletion with hemagglutination inhibition testing and were antigenically distinguishable from the B/Victoria-lineage vaccine virus component (B/Brisbane/60/2008) from the 2017-2018 influenza season. Ultimately, the viruses were updated because they showed evidence of antigenic drift.

VACCINE EFFECTIVENESS

Vaccine effectiveness depends on how closely related, or matched, the viruses in the vaccine are to the viruses circulating during the influenza season. It also depends on how well a vaccinated person responds to the vaccine, specifically, producing protective antibody. In years when the vaccine strains and the virus strains are well-matched, public health officials measure substantial benefits from vaccination regarding preventing influenza illness. Even during years when the vaccine is not well matched, the benefits of vaccination varies across the population and depends on characteristics of the person vaccinated and potentially, which vaccine was used. In the United States, public health officials recommend annual vaccinations against influenza for all persons aged six months and older. Since the 2004-2005 influenza season, CDC has conducted studies to estimate how well the seasonal influenza vaccine protects against influenza-associated medical visits. Researchers conducted early season and end of season estimates during the 2017-2018 influenza season to evaluate the effectiveness of the influenza vaccine for preventing laboratory-confirmed influenza infections. Although the dataset is complete, researchers have not published the final report that examines the vaccine effectiveness for the 2017-2018 influenza season.

In June 2018, CDC presented vaccine effectiveness estimates for the 2017-2018 influenza season during the Advisory Committee on Immunization Practices (ACIP) meeting. As referenced earlier, influenza A (H3N2) viruses were the predominant influenza viruses circulating in the United States. Consequently, vaccine effectiveness estimates of the 2017-2018 influenza vaccines were similar to previous seasons in which influenza A (H3N2) viruses were the predominant circulating viruses. The epidemiological patterns shifted during the influenza season, and influenza B viruses became the predominant circulating viruses. The estimates reported by the United States Influenza Vaccine Effectiveness Network for the 2017-2018 influenza season represent complete seasonal activity. The researchers based the vaccine effectiveness estimates on patients enrolled throughout the influenza season. The vaccine effectiveness estimates indicate that seasonal influenza vaccines provided a modicum of protection against influenza viruses circulating during the 2017-2018 influenza season. Overall, the end of season estimated vaccine effectiveness against influenza A and influenza B was 40% (95% confidence interval [CI]: 36% to 46%). The vaccine effectiveness estimate for the 2017-2018 influenza season is similar to previous seasons when circulating viruses and vaccine viruses are matched. Consequently, this illustrates the fact that circulating influenza viruses during the 2017-2018 influenza season were antigenically and genetically similar to the influenza vaccine virus components of the 2017-2018 Northern Hemisphere seasonal influenza vaccines.

The research associated with vaccine effectiveness estimates suggests that the 2017-2018 Northern Hemisphere seasonal influenza vaccine reduced outpatient influenza visits and provided significant protection against hospitalizations. Influenza activity remained relatively low in most regions of the United States from the start of the season until December 2017. However, in December, influenza activity gradually began to increase until activity peaked in February 2018. In January 2018, public health officials noted a surge in influenza B viruses that eventually contributed to prolonged activity throughout the remainder of the 2017-2018 influenza season. The CDC recommended ongoing influenza vaccinations to help prevent infections with the predominant circulating influenza viruses during the majority of the season and infections with influenza B viruses that circulated as the predominant influenza virus later in the season. The end of season vaccine effectiveness estimates indicated that the 2017-2018 Northern Hemisphere seasonal influenza vaccine provided significant protection against circulating influenza viruses, specifically 2009 influenza A (H1N1) pandemic viruses, and influenza B viruses. In contrast, a CDC sponsored interim analysis of the 2017-2018 influenza season indicated a low vaccine effectiveness rate among individuals 65 years and older. The low rate impacted the overall vaccine effectiveness for the 2017-2018 Northern Hemisphere influenza vaccine. The vaccine effectiveness estimates highlight the importance of continued influenza prevention and aggressive treatment measures.

The end of season estimates reported by the United States Influenza Vaccine Effectiveness Network represents outpatient influenza data for individuals of all ages. The design of the study is to determine vaccine effectiveness based on several factors. The study utilizes multivariate logistic regression models adjusted for the site-location, age, race, ethnicity, self-rated general health status, days from illness onset to enrollment, and calendar time of illness onset, to predict vaccine effectiveness. The study reviews medical records, immunization registries, or self-reported immunization data to verify vaccination status for the current influenza season. The vaccine effectiveness study utilizes a test-negative case-control design to determine the odds of PCR-confirmed influenza among immunized enrollees compared to unimmunized enrollees. The study had over eight thousand outpatients enrolled during the 2017-2018 influenza season. During the 2016-2017 influenza season, public health scientists implemented the United States Hospitalized Adult Influenza Vaccine Effectiveness Network to contribute inpatient influenza data on adults to vaccine effectiveness studies. The ongoing CDC funded study estimated the effectiveness of influenza vaccines for the prevention of influenza hospitalizations among adults. The study enrolled ten hospitals with over five thousand acute care beds. The design of the inpatient study was similar to the outpatient version with a few exceptions. Overall, both studies indicated that the rates of vaccine effectiveness were higher in the younger age groups compared to the elderly age group.

This influenza season, influenza A (H3N2) viruses, the 2009 influenza A (H1N1) pandemic viruses, and influenza B viruses co-circulated across the United States and Wyoming. Influenza A (H3N2) viruses and influenza B/Yamagata-lineage viruses were the predominant viruses in Wyoming during the 2017-2018 influenza season. The end of season vaccine effectiveness estimate for the 2017-2018 influenza vaccine for prevention of influenza A (H3N2) virus-associated outpatient acute respiratory illness visits was similar to vaccine effectiveness estimates for seasonal influenza vaccines for prevention of outpatient medical visits associated with influenza A (H3N2) virus infections during previous influenza seasons. The end of season estimated vaccine effectiveness against influenza A (H3N2) viruses was 24% (95% CI: 15% to 33%). The 2009 influenza A (H1N1) pandemic viruses have continued to circulate each season since the 2009 pandemic. The end of season estimated vaccine effectiveness against 2009 influenza A (H1N1) pandemic viruses was 65% (95% CI: 55% to 73%). Overall, the 2009 influenza A (H1N1) pandemic virus component had the highest estimated vaccine effectiveness of both influenza A and influenza B virus components.

Influenza B viruses accounted for approximately 48% of viruses reported by healthcare providers in Wyoming during the 2017-2018 influenza season. The majority of influenza B viruses included in the vaccine effectiveness study were B/Yamagata-lineage viruses. The end of season estimated vaccine effectiveness against influenza B/Yamagata-lineage viruses was 49% (95% CI: 40% to 56%). The B/Victoria-lineage viruses circulated at low levels across the United States during the 2017-2018 influenza season. Therefore, a low number of B/Victoria-lineage viruses were included in the vaccine effectiveness study. Although the data was limited, it did not suggest a major difference in the vaccine effectiveness between the two influenza B virus lineages. However, because of the low number of cases, researchers were unable to determine an adjusted vaccine effectiveness rate for B/Victoria-lineage viruses. The influenza B components of the 2017-2018 Northern Hemisphere vaccines were effective. Nationally, the 2017-2018 influenza season was a high severity season, and influenza A (H3N2) viruses were the predominant circulating viruses. The 2017-2018 Northern Hemisphere influenza vaccine was effective in reducing the outpatient visits for influenza-associated acute respiratory illness by 40% among persons six months and older. The vaccine effectiveness studies also revealed a reduction in influenza-associated hospitalizations among adults by 22% (95% CI: 8% to 35%). Unfortunately, vaccine effectiveness for the $\geq$ 65 years age group was dismal and impacted the overall vaccine effectiveness for the 2017-2018 Northern Hemisphere influenza vaccine. Vaccine effective estimates against 2009 influenza A (H1N1) pandemic viruses and influenza B/Yamagata-lineage viruses were higher than vaccine effectiveness against influenza A (H3N2) viruses. The vaccine effectiveness rates are consistent with previous influenza seasons.

ANTIVIRAL AGENTS FOR INFLUENZA

The FDA approved and recommended three antiviral drugs for use against influenza: oseltamivir, zanamivir, and peramivir. Table 2 presents an overview of the indications, administration, and use of antiviral medications. Oseltamivir, zanamivir, and peramivir are a class of medication known as neuraminidase inhibitors and are active against both influenza A and B viruses. Currently, antiviral resistance to the neuraminidase inhibitors among circulating influenza viruses is low. Additionally, antiviral resistance can emerge during or even after treatment of certain patients with influenza, specifically patients who are immunosuppressed. Clinical trials and observational data show that early antiviral treatment can shorten the duration of fever and illness symptoms, may reduce the risk of complications from influenza, and shorten the duration of hospitalization. Clinical benefit is greatest with early administration of antiviral treatment, especially within 48 hours of influenza illness onset. For additional information on antiviral medications during the 2017-2018 influenza season, please visit http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm.

TABLE 2: RECOMMENDED DOSAGE & SCHEDULE OF INFLUENZA ANTIVIRAL MEDICATIONS FOR TREATMENT OR CHEMOPROPHYLAXIS, 2017-2018 INFLUENZA SEASON

Antiviral Agent	Activity Against	Use	FDA Approved For	Not Recommended for Use in	Adverse Events
Oseltamivir (Tamiflu®)	**Influenza A and B**	**Treatment**	Any age	Not Applicable	**Adverse events:** nausea, vomiting, headache. Post-marketing reports of serious skin reactions and sporadic, transient neuropsychiatric events.
		Chemoprophylaxis	3 months and older	Not Applicable	
Zanamivir (Relenza®)	**Influenza A and B**	**Treatment**	7 years and older	People with underlying respiratory disease (e.g., asthma or COPD)	**Allergic reactions:** skin rash oropharyngeal or facial edema. **Adverse events:** risk of bronchospasm, especially in the setting of underlying airways disease; sinusitis, dizziness, and ear, nose and throat infections. Post-marketing reports of sporadic, transient neuropsychiatric events.
		Chemoprophylaxis	5 years and older	People with underlying respiratory disease (e.g., asthma or COPD)	
Peramivir (Rapivab®)	**Influenza A and B**	**Treatment**	2 years and older	Not Applicable	**Adverse events:** diarrhea. Post-marketing reports of serious skin reactions and sporadic, transient neuropsychiatric events.
		Chemoprophylaxis	Not Applicable	Not Applicable	

AVIAN INFLUENZA A VIRUSES IN HUMANS

Influenza A viruses have been identified in various animal species around the world. Typically, certain subtypes of influenza A viruses are specific to certain species. However, avian species are the exception; birds are hosts to all known subtypes of influenza A viruses. Currently, influenza A H3N2 and H1N1 viruses are the main subtypes of influenza A viruses circulating in humans. Occasionally, public health officials receive reports of sporadic human infections with avian influenza A viruses. The reported illnesses in humans associated with avian influenza A virus infections have ranged from mild to severe. The symptoms are usually similar to infections with human influenza viruses. Therefore, it is difficult for healthcare providers to diagnose avian influenza infections by clinical signs and symptoms alone. Laboratory testing is necessary to confirm suspected cases of avian influenza virus infections. Public health officials continue to monitor and track cases of avian influenza A viruses due to the unpredictable nature of viruses. Specifically, avian influenza A viruses have the potential to change and possibly even gain the ability to spread easily from person-to-person. As avian influenza A viruses continue to evolve in unpredictable ways, it is important for public health officials to monitor the epidemiology of circulating viruses to understand the risk of avian influenza in human populations.

During the 2017-2018 influenza season, the WHO reported a human infection with a highly pathogenic avian influenza A (H7N4) virus. The case was the first reported human case of avian influenza A (H7N4) virus in the world. Genetic analysis of the influenza A (H7N4) virus proved that it is an avian-origin influenza virus. Researchers specifically identified that all the viral segments of the influenza A (H7N4) virus originated from avian influenza viruses. The avian influenza A (H7N4) virus was sensitive to both adamantanes and neuraminidase inhibitor antiviral medications. Information associated with the circulation of the influenza A (H7N4) virus in birds is not currently available. Current evidence indicates that the virus cannot sustain transmission in humans. The report of influenza A (H7N4) viruses in a human is a singular event; however, the viruses do not appear to spread easily from person-to-person. The infection occurred in an elderly resident of Jiangsu Province, an eastern coastal province of the People’s Republic of China. The patient reported a history of exposure to live poultry before the onset of symptoms. Chinese public health officials conducted risk assessments and enhanced control measures. Surveillance and epidemiological investigations concluded that all of the close-contacts of the patient were asymptomatic and influenza testing produced only negative results. The elderly patient was the only reported human case detected in the world; however, public health officials are continuing to monitor the region for additional cases.

HEALTH ADVISORY AND UPDATE

The Health Alert Network (HAN) is CDC's primary method of sharing cleared information about urgent public health incidents with public health partners. The HAN collaborates with federal, state, territorial, and city/county partners to develop protocols and stakeholder relationships that will ensure a robust, interoperable platform for the rapid distribution of public health information. There are several different HAN message types: *Health Alert, Health Advisory, Health Update, and Info Service*. CDC released one influenza-related HAN notice during the 2017-2018 influenza season, a *Health Advisory*. A *Health Advisory* provides important information for a specific incident or situation; contains recommendations or actionable items to be performed by public health officials, laboratorians, and/or clinicians; and it may not require immediate action. The HAN, (HAN 00409), was an official CDC *Health Advisory* released on December 27, 2017. The CDC Health Advisory, *Seasonal Influenza A (H3N2) Activity and Antiviral Treatment of Patients with Influenza*, provided recommendations for the 2017-2018 influenza season.

CDC issued the HAN to alert healthcare providers and public health officials of the increase in influenza A (H3N2) activity across the country. During the 2017-2018 influenza season, CDC received increasing reports of severe influenza illness from around the country. The Health Advisory reminded clinicians to treat suspected influenza in high-risk outpatients, those with progressive disease, and all hospitalized patients with neuraminidase inhibitor antiviral medications as soon as possible, regardless of negative rapid influenza diagnostic test results and without waiting for RT-PCR testing results. The HAN specifically emphasized the importance of early antiviral treatment to help reduce influenza morbidity and mortality. During the 2017-2018 season, the CDC received early reports of severe respiratory illness associated with influenza A (H3N2) viruses among all age-groups. Some of the reported cases required intensive care unit (ICU) admissions, and fatalities were reported. Some of the patients reported being vaccinated with the 2017-2018 Northern Hemisphere influenza vaccine, and some were reportedly unvaccinated. Historically, influenza seasons during which influenza A (H3N2) viruses predominate are associated typically with higher rates of hospitalizations and deaths among the elderly and young children, compared to the other age groups. Consequently, the 2017-2018 influenza season exceeded the previous record for the highest number of pediatric deaths during a single season. The HAN provided three objectives: a summary of influenza antiviral drug treatment recommendations, an update for clinicians about approved treatment drugs and supply for the influenza season, and background information for patients regarding anti-influenza treatment. The Health Advisory is available at the following link: http://emergency.cdc.gov/han/dir.asp.

REPORTING REMINDER

All of the following are reportable to the WDH-Infectious Disease Epidemiology Unit: laboratory-confirmed cases of influenza and influenza-associated deaths. Furthermore, state statutes require attending healthcare providers, clinics, hospitals, and laboratories performing influenza diagnostic testing to report cases of influenza. Healthcare providers can fax reports to the WDH secure fax line at (307) 777-5573. Additionally, WDH requests that hospitals submit respiratory specimens to the WPHL on all hospitalized patients with ILI or clinical suspicion of influenza regardless of the laboratory results. Typically, influenza cases that require hospitalization are severe influenza cases. In an effort to understand the epidemiology of circulating influenza strains in the community, WDH requests respiratory specimens for testing at the state's public health laboratory. Influenza and other infectious diseases listed on the reportable disease list are located at the following link: https://health.wyo.gov/publichealth/infectious-disease-epidemiology-unit/reporting/.