State of Wyoming

Department of Health

Wyoming Influenza Summary Report
2018-2019 Season

November 2019

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Public Health Division
Public Health Sciences Section
Wyoming Department of Health
Alexia Harrist, MD, PhD
State Epidemiologist and State Health Officer

Additional information and copies may be obtained from:
Reginald C. McClinton
Infectious Disease Epidemiology Unit
Wyoming Department of Health
6101 Yellowstone Road, Suite 510
Cheyenne, WY 82002
307-777-8640
307-777-5573
reginald.mcclinton@wyo.gov

WYOMING INFLUENZA SUMMARY REPORT, 2018-2019 SEASON
(September 30, 2018 - May 18, 2019)

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 2018-2019 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 influenza cases and hospitalizations were reported. Most of the United States experienced a similar phenomenon during the 2018-2019 influenza season. Overall, influenza A viruses were the predominant influenza viruses circulating in Wyoming. For most of the 2018-2019 influenza season, influenza A (H1N1) pandemic 2009 viruses were the predominant influenza viruses circulating in Wyoming. Throughout the influenza season, influenza A (H1N1) pandemic 2009 viruses co-circulated across Wyoming with influenza A (H3N2) viruses and influenza B viruses. There was a notable transition in February 2019 to influenza A (H3N2) viruses as the predominant circulating viruses in Wyoming. The surge in influenza A (H3N2) viruses towards the end of the season protracted influenza activity across the state. The extended period of elevated influenza activity exacerbated the adverse effects of the influenza season.

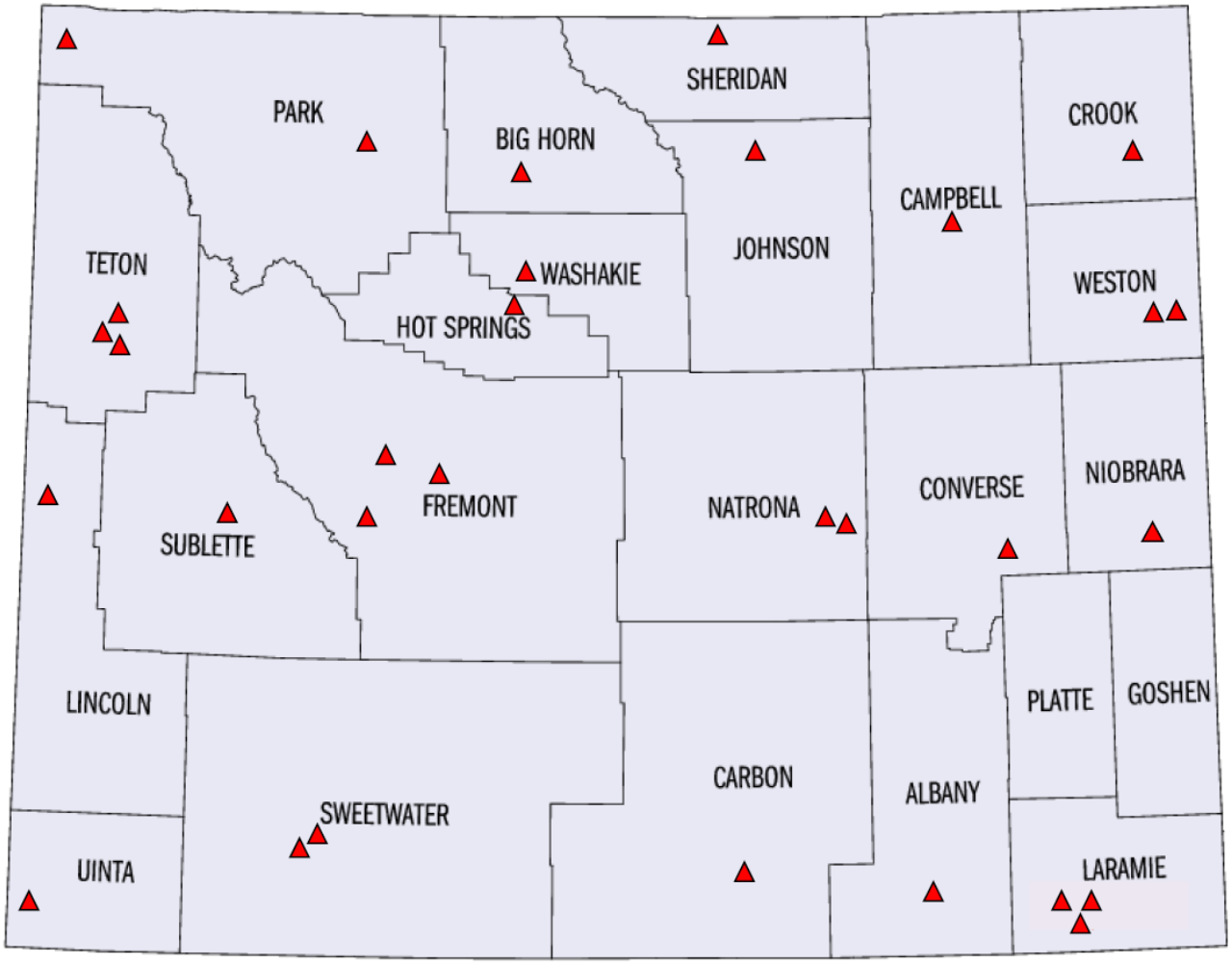
The epidemiology of influenza seasons are unpredictable; however, there are traditional expectations common to most influenza seasons. Like most influenza seasons, influenza A viruses were the predominant circulating viruses. Statistically, the 2018-2019 influenza season, was one of the most severe influenza 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 late December 2018. The number of cases in Wyoming peaked during the week ending February 23, 2019, Morbidity and Mortality Weekly Report Week 08 (MMWR Week 08). Healthcare providers and laboratories concurrently reported high levels of influenza A viruses during the 2018-2019 influenza peak. The state experienced an extended period of high activity beginning in late January 2019, and the high-levels of activity continued until late March 2019. During the elevated period, influenza A (H1N1) pandemic 2009 viruses and influenza A (H3N2) viruses were the predominant viruses in Wyoming. Activity throughout the state remained elevated until March 2019 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 (ID Epi) collects, compiles, and analyzes key indicators associated with influenza activity from multiple datasets. Specifically, datasets from various units, sections, and divisions within the WDH 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 on 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 with 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 2018-2019 influenza season.

MAP 1: NETWORK OF ILINET PROVIDERS BY COUNTY
WYOMING, 2018-2019 INFLUENZA SEASON



Thirty-one healthcare organizations enrolled as ILINet providers during the 2018-2019 influenza season. A major goal of ID Epi 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, 21 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 (≥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 September 30, 2018 (MMWR Week 40); reporting continued until September 28, 2019 (MMWR Week 39), but some Wyoming ILINet providers discontinued reporting on May 18, 2019 (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 transcription-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 10,009 laboratory-confirmed (RIDT or PCR positive test results) influenza case reports during the 2018-2019 influenza season. Healthcare providers reported the first positive case reports of the influenza season during the week ending October 6, 2018 (MMWR Week 40). Reporting of influenza peaked the week ending February 23, 2019 (MMWR Week 08), when healthcare providers reported 1,211 cases. In comparison, during the 2017-2018 influenza season, reporting of influenza peaked the week ending February 3, 2018 (MMWR Week 05), when healthcare providers reported 914 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, (2013-2014 TO 2018-2019)

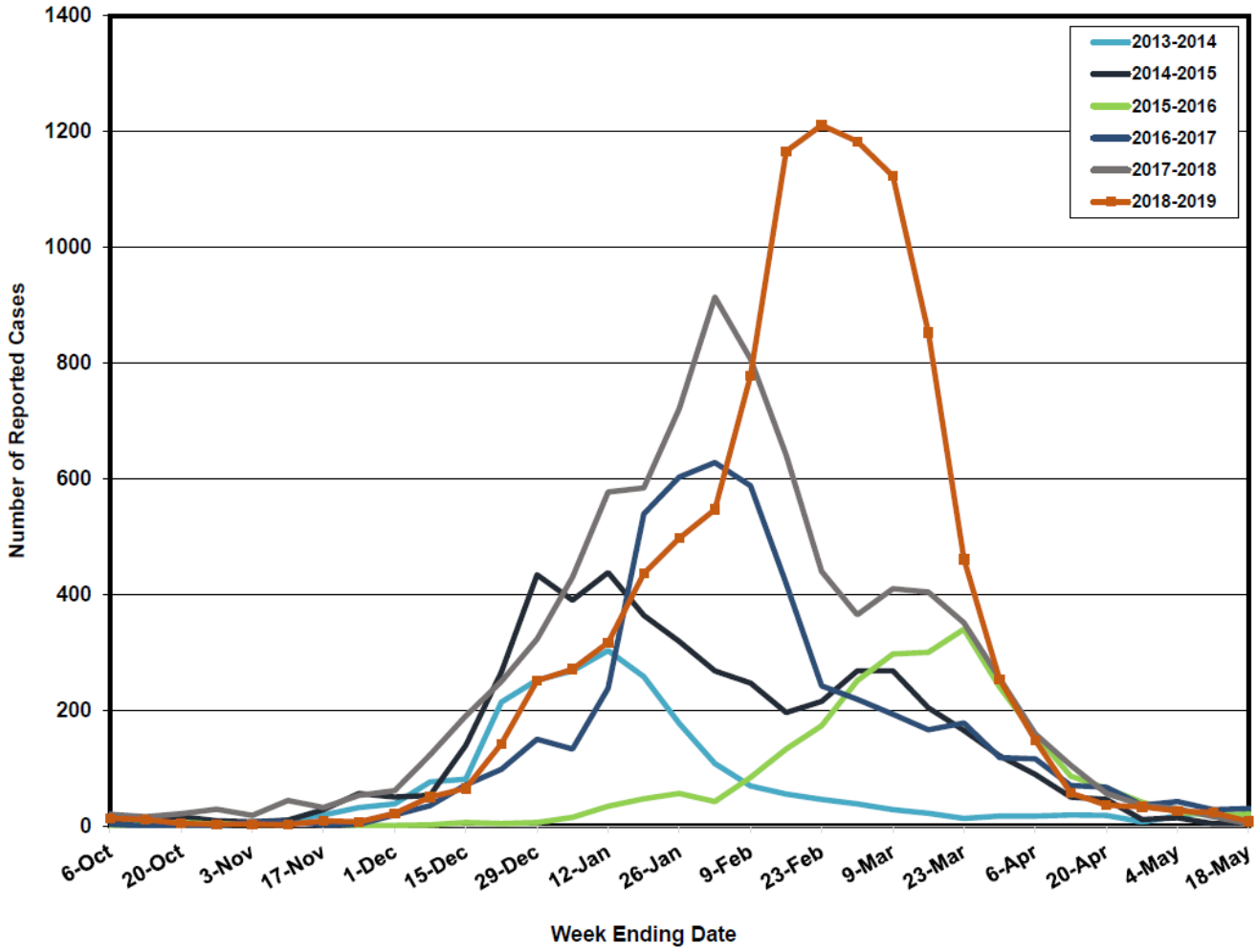


TABLE 1: REPORTED CASES OF INFLUENZA; WYOMING, 2018-2019 INFLUENZA SEASON

Week Ending	Number
06-Oct	13
13-Oct	11
20-Oct	04
27-Oct	03
03-Nov	03
10-Nov	02
17-Nov	09
24-Nov	07
01-Dec	22
08-Dec	50
15-Dec	65
22-Dec	142
29-Dec	251
05-Jan	271
12-Jan	317
19-Jan	436
26-Jan	497
02-Feb	547
09-Feb	778
16-Feb	1166
23-Feb	1211
02-Mar	1183
09-Mar	1123
16-Mar	853
23-Mar	461
30-Mar	253
06-Apr	148
13-Apr	57
20-Apr	36
27-Apr	33
04-May	26
11-May	23
18-May	8
Total	**10,009**

County	Number
Albany	685
Big Horn	155
Campbell	811
Carbon	310
Converse	328
Crook	59
Fremont	711
Goshen	129
Hot Springs	58
Johnson	43
Laramie	1452
Lincoln	143
Natrona	2200
Niobrara	32
Park	305
Platte	159
Sheridan	706
Sublette	63
Sweetwater	958
Teton	230
Uinta	349
Washakie	103
Weston	20
Unknown	0
Total	**10,009**

Lineage (B)	Number
B/ Yamagata	3
B/ Victoria	3
B/ Not Tested	338
B/ Unknown	1
Total	**345**

Age	Number
0-4	1931
5-10	2569
11-19	1849
20-39	1602
40-59	1085
60+	973
Unknown	0
Total	**10,009**

Gender	Number
Male	4946
Female	5063
Total	**10,009**

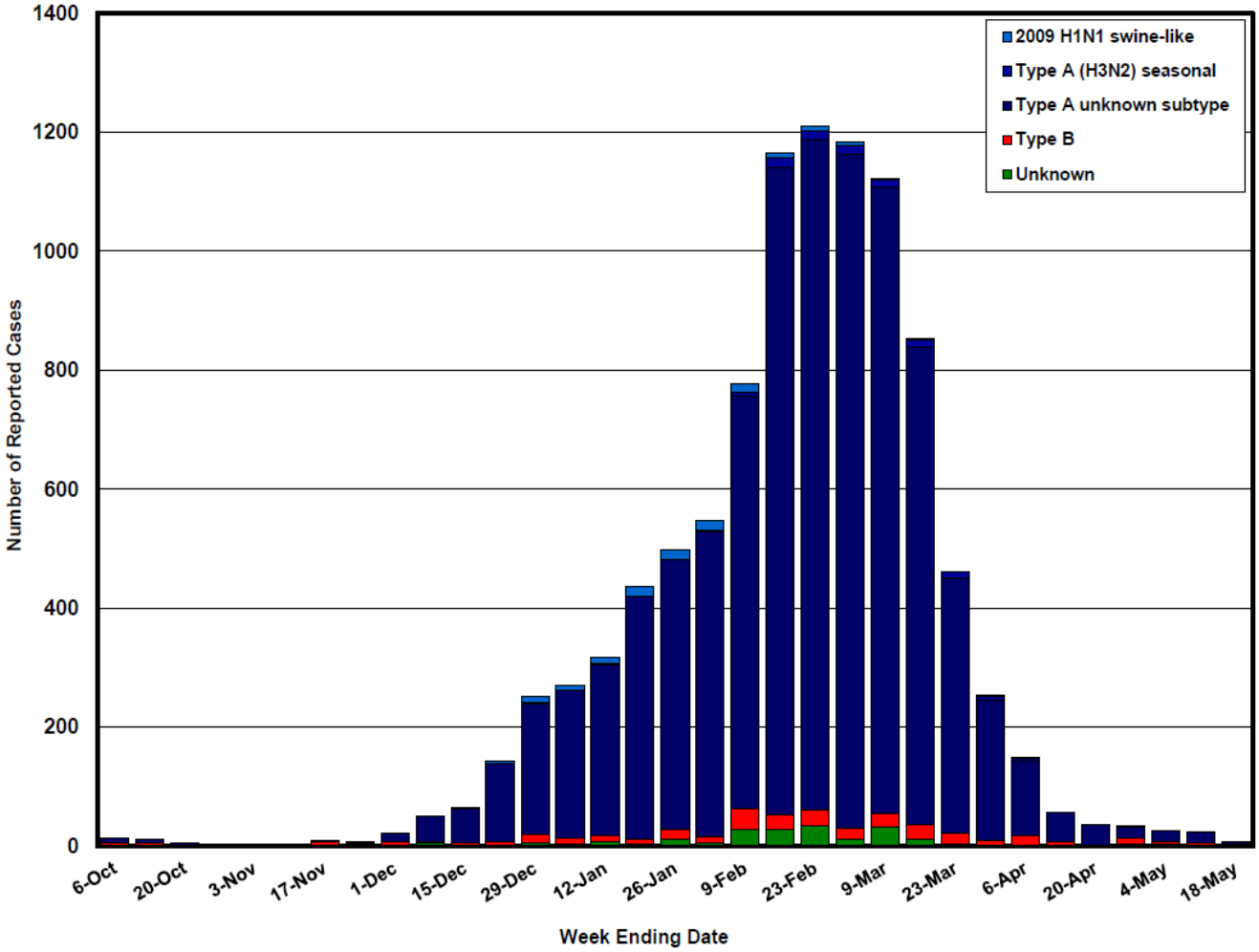
Type	Number
A	9470
B	345
A & B Dual	0
Unknown	194
Total	**10,009**

Subtype (A)	Number
A (H3N2)	106
A (H1N1) 2009	134
A & B Dual	0
A Unknown	9230
Total	**9470**

LABORATORY DATA

Of the 10,009 influenza case reports, 9,470 (94.6%) were influenza A virus-positive, 345 (3.5%) were influenza B virus-positive, and 194 (1.9%) were positive for influenza viruses not typed for influenza A or influenza B. Healthcare providers and laboratories confirmed 1,327 cases by PCR and 8,682 cases by RIDT only. The WPHL tested a total of 302 specimens for influenza viruses, and 171 (56.6%) were positive. However, six were out-of-state residents not counted in the Wyoming database. The WPHL confirmed the first positive PCR specimen during the week ending October 6, 2018 (MMWR Week 40), and confirmed the last positive specimen during the week ending April 20, 2019 (MMWR Week 16). Among the 171 positive influenza specimens tested at the WPHL: 88 (51.5%) were 2009 influenza A (H1N1) pandemic viruses; 74 (43.3%) were influenza A (H3N2) viruses; one (0.5%) was an unknown subtype of an influenza A virus; and eight (4.7%) were influenza B viruses (see chart 2). The influenza B viruses were both B/Victoria-lineage and B/Yamagata-lineage viruses.

CHART 2: REPORTED CASES OF INFLUENZA BY VIRUS TYPE & SUBTYPE WYOMING, 2018-2019 INFLUENZA SEASON



On a national level, clinical laboratories tested a total of 1,138,283 specimens for influenza viruses during the 2018-2019 influenza season, and 176,732 (15.5%) were positive. Among the positive influenza viruses, 167,352 (94.7%) were influenza A viruses, and 9,380 (5.3%) were influenza B viruses. Additionally, public health laboratories participating as United States - WHO collaborating laboratories submitted a subset of influenza-positive respiratory specimens to CDC for virus characterization through three National Influenza Surveillance 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 (NREVSS) collaborating laboratories tested 79,889 specimens during the 2018-2019 influenza season; 41,837 (52.4%) of the 79,889 were positive for influenza viruses. The collaborating laboratories subtyped 38,639 (92.6%) of the influenza A viruses: 21,951(56.8%) were influenza A (H1N1) pandemic 2009 viruses and 16,688 (43.2%) were influenza A (H3N2) viruses.

This influenza season, both subtypes of influenza A viruses and both lineages of 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 influenza season, and influenza A (H1N1) pandemic 2009 viruses were the overall predominant influenza subtype circulating across the United States. Influenza A (H1N1) pandemic 2009 viruses were predominant in Region 8 of the Department of Health and Human Services (DHHS) during the weeks preceding the influenza peak; Wyoming is located within DHHS Region 8. Influenza A (H3N2) viruses became the predominant circulating virus in the middle of February 2019. Therefore, the viruses were the predominant circulating influenza virus subtype in Wyoming before peak influenza activity. Influenza A (H3N2) viruses were more commonly reported, but influenza A (H1N1) pandemic 2009 viruses circulated at high levels during the weeks of peak influenza activity. Beginning October 1, 2018, CDC antigenically characterized 2,637 influenza viruses collected by laboratories in the United States during the 2018-2019 influenza season. Phylogenetic analysis of the hemagglutinin genes from the 1,207 influenza A (H1N1) pandemic 2009 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, 296 (97.0%) of 305 antigenically characterized viruses, were well inhibited by ferret antisera raised against cell culture-propagated 6B.1 virus A/Michigan/45/2015, the influenza A (H1N1) pandemic 2009 component of the 2018-2019 Northern Hemisphere influenza vaccine.

Phylogenetic analysis of the hemagglutinin genes from 990 influenza A (H3N2) viruses revealed extensive genetic diversity with multiple clades and subclades co-circulating across the United States. The hemagglutination genes of circulating viruses belonged predominantly to clade 3C.3a (n = 728); however, clade 3C.2a (n = 66) and subclade 3C.2a1 (n = 196) also circulated within the United States. Viruses with the 3C.3a hemagglutinin began to surge in several countries in late 2018; specifically, the surge occurred in the United States and Western European countries. The hemagglutinin genes experienced genetic diversification during this influenza season. Three hundred eighty-eight influenza A (H3N2) viruses were antigenically characterized, and 169 (43.6%) of the influenza A (H3N2) viruses tested were well-inhibited by ferret antisera raised against A/Singapore/INFIMH-16-0019/2016 (3C.2a1), a cell-propagated reference virus representing the influenza A (H3N2) component of the 2018-2019 Northern Hemisphere influenza vaccines. The remaining 219 (56.4%) of the influenza A (H3N2) viruses reacted poorly. The majority, 217 (99.1%) of the 219 influenza A (H3N2) viruses, that reacted poorly belonged to the 36.3a clade.

Low levels of Influenza B viruses circulated across the United States and Wyoming during the 2018-2019 influenza season. Influenza B viruses from the B/Victoria-lineage and the B/Yamagata-lineage co-circulated during the 2018-2019 influenza season. The influenza B/Victoria-lineage viruses were the predominant influenza B viruses circulating in the United States. There was a small number of B/Victoria-lineage viruses antigenically characterized during the 2018-2019 influenza season. Phylogenetic analysis of 244 B/Victoria-lineage viruses indicates that all hemagglutinin genes belonged to the genetic clade V1A. However, antigenically distinct genetic subclades also emerged. The majority, 129 (79.1%) of the 163 B/Victoria-lineage viruses were antigenically similar using post-infection ferret antisera raised against cell propagated B/Colorado/06/2017-like V1A.1 reference virus for the 2018-2019 influenza season. The remaining 34 (20.9%) viruses reacted poorly and belonged to the V1A clade or the V1A-3Del subclade. Despite the viral changes, the reference vaccine virus representing the influenza B/Victoria-lineage component for the upcoming 2019-2020 Northern Hemisphere quadrivalent vaccines will remain the same as the previous influenza season. In contrast, phylogenetic analysis of 196 influenza B/Yamagata-lineage viruses indicates that all hemagglutinin genes belonged to the genetic clade Y3. All of the 178 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 2018-2019 Northern Hemisphere quadrivalent vaccines. Therefore, the reference vaccine virus representing the influenza B/Yamagata-lineage component for the upcoming 2019-2020 Northern Hemisphere quadrivalent vaccines will remain the same as the previous influenza season.

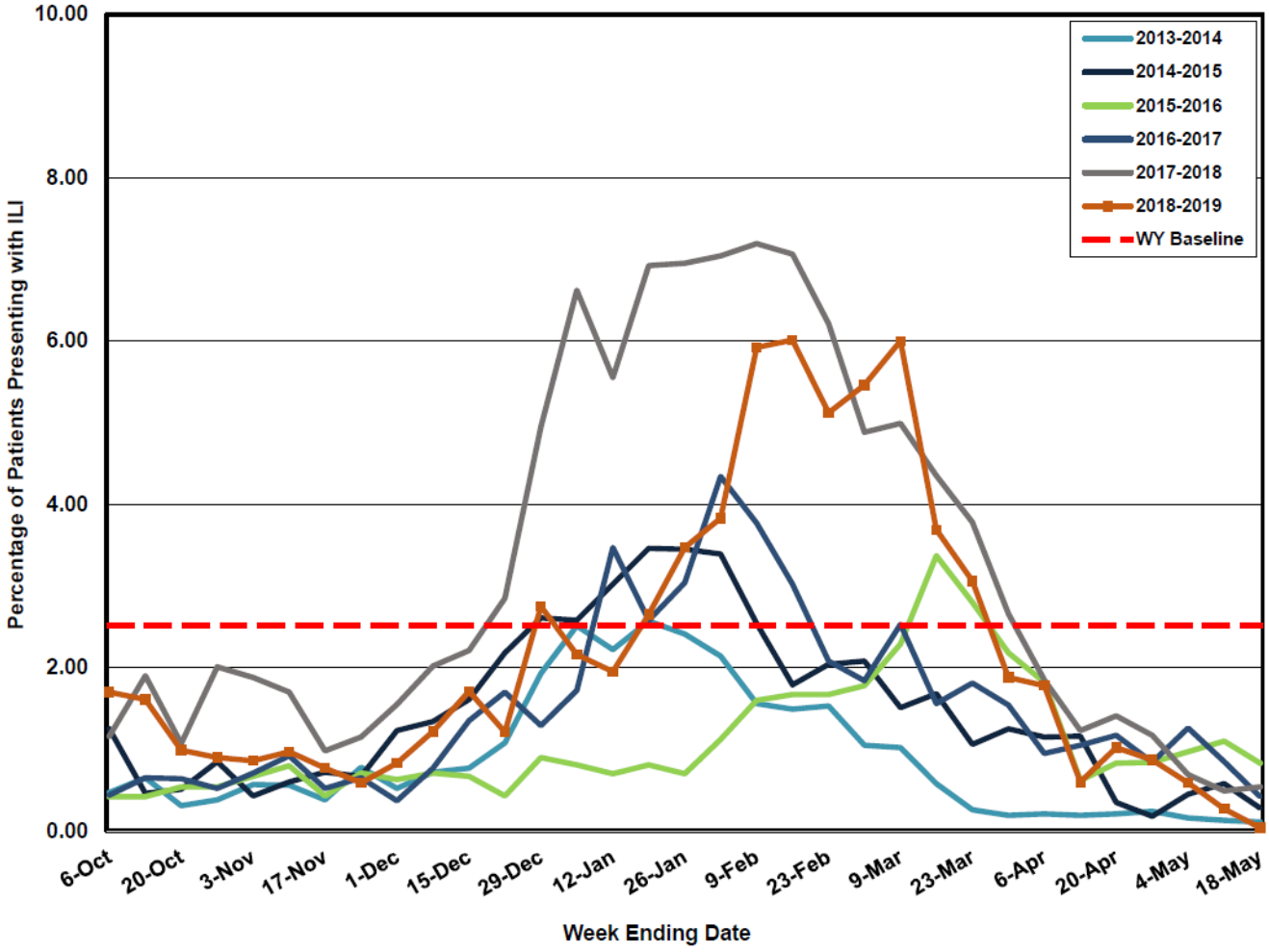
Laboratorians at CDC routinely use hemagglutination inhibition assays to antigenically characterize influenza viruses year-round to compare how similar currently circulating influenza viruses are to those included in the influenza vaccine and to monitor for changes in circulating influenza viruses. The 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 in determining the potential for influenza viruses in animals infecting human populations. During the 2018-2019 influenza season, there was considerable genetic diversification of hemagglutinin and neuraminidase genes within influenza A (H3N2) viruses. The genetic diversity and the increase in 3C.3a clade viruses caused a delay in selecting the influenza A (H3N2) virus component for the 2019-2020 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. Accordingly, the laboratory data evaluates whether the changes in the viruses impacted vaccine effectiveness. The laboratory data for influenza A (H1N1) pandemic 2009 viruses exhibited increasing genetic diversity of the hemagglutinin gene sequences belonging to the 6B.1 subclade. Consequently, the influenza A (H1N1) pandemic 2009 virus component of the 2019-2020 Northern Hemisphere trivalent influenza vaccine was updated from the A/Michigan/45/2015 pdm09-like virus to an A/Brisbane/02/2018 (H1N1) pdm09-like virus. As previously stated, the predominance of influenza A (H3N2) viruses in the 3C.3a clade contributed to the decrease in vaccine effectiveness. Laboratory data indicated possible gaps in protection with the influenza A (H3N2) viruses vaccine component. Consequently, the 2019-2020 Northern Hemisphere influenza vaccine components for the influenza A (H3N2) virus was updated from the A/Singapore/INFIMH-16-0019/2016 (H3N2)-like virus to an A/Kansas/14/2017 (H3N2)-like virus. The majority of circulating influenza B/Victoria-lineage and influenza B/Yamagata-lineage viruses tested were antigenically similar to the referenced vaccine viruses in the 2018-2019 Northern Hemisphere influenza vaccines. Consequently, the B/Victoria-lineage virus component and the B/Yamagata-lineage virus component remained unchanged for the 2019-2020 Northern Hemisphere influenza vaccine. 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 below the baseline level (0 - 2.52%); ILI activity among the network of ILINet providers exceeded the baseline in January and remained elevated until early April 2019. The 2018-2019 influenza season was a high severity influenza season. The peak percentage of patient visits for ILI was 6.01%, which occurred the week ending February 16, 2019 (MMWR Week 7). The number of reported cases peaked the following week, the week ending February 23, 2019 (MMWR Week 8). ILI activity among the ILINet providers remained above the baseline until the week ending March 30, 2019 (MMWR Week 13). In comparison, during the 2017-2018 influenza season, the peak percentage of patient visits for ILI was 7.19%, which occurred the week ending February 10, 2018 (MMWR Week 6).

CHART 3: WEEKLY ILI REPORTING BY ILINET PROVIDERS WYOMING, (2013-2014 TO 2018-2019)



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 23 influenza-associated deaths (3.98 per 100,000). In contrast, during the 2017-2018 influenza season, the WDH-Vital Statistics Services reported 27 influenza-associated deaths (4.66 per 100,000). The number of reported deaths during the 2018-2019 influenza season was less than the number of influenza-associated deaths reported during the previous influenza season. The median age of the 23 influenza-associated deaths was 77 years, with 16 (69.6%) of the deaths occurring in individuals 65 years of age or older. The remaining seven (30.4%) influenza-associated deaths occurred in individuals under the age of 65 years. In comparison, during the 2017-2018 influenza season, the median age of influenza-associated deaths was 75 years, with 18 (66.7%) of the deaths occurring in individuals over the age of 65 years. This influenza season was unique, influenza A (H1N1) pandemic 2009 viruses predominated with influenza A (H3N2) viruses during the peak level period of influenza activity. Influenza A (H1N1) pandemic 2009 viruses primarily predominated during the first half of the elevated period, and influenza A (H3N2) viruses predominated during the latter half of the peak level period. Consequently, public health officials linked the majority of reported influenza-associated deaths with influenza A viruses. The majority of the influenza-associated deaths occurred during peak levels of influenza activity when the influenza viruses co-circulated. Therefore, it is not clear which subtype of influenza A was responsible for the majority of influenza-associated deaths. More than two-thirds of the influenza-associated deaths occurred in Wyoming residents over the age of 65 years. 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. Therefore, it is likely that the majority of the influenza-associated deaths in individuals over the age of 65 years involved influenza A (H3N2) viruses.

COMPOSITION OF THE 2019-2020 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-two National Influenza Centers (NIC), located in 115 different countries, gather circulating influenza strains and information on disease trends. The five 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) typically makes final decisions on vaccine strains in February. Manufacturers grow vaccine strains based on these recommendations.

Currently, there are primarily three types of influenza viruses circulating in humans: influenza A (H1N1) pandemic 2009 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 2018-2019 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/Brisbane/02/2018 (H1N1) pandemic 2009-like virus, an A/Kansas/06/2017 (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 (H1N1) pandemic 2009 virus and the influenza A (H3N2) virus components of the vaccine compared with the composition of the 2018-2019 influenza vaccine. Samples of influenza A (H1N1) pandemic 2009 viruses during the 2018-2019 influenza season indicated the majority of sequenced hemagglutinin genes belonged to the phylogenetic subclade 6B.1. Researchers observed an increasing amount of genetic diversity of the hemagglutinin genes within this subgroup that spurred the emergence of several genetic subgroups. Likewise, researchers noticed increasing amounts of genetic diversity within phylogenetic clades and subclades of the influenza A (H3N2) viruses. The genetic diversity caused the WHO to postpone the influenza A (H3N2) vaccine-strain selection decision for the 2019-2020 influenza vaccine to allow additional time to study the candidate vaccine viruses.

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 vary across the population and depend on the 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 2018-2019 influenza season to evaluate the effectiveness of the influenza vaccine for preventing laboratory-confirmed influenza infections. The dataset is complete, and researchers have published the final report that examines the vaccine effectiveness for the 2018-2019 influenza season.

In June 2019, CDC presented vaccine effectiveness estimates for the 2018-2019 influenza season during the Advisory Committee on Immunization Practices (ACIP) meeting. As referenced earlier, influenza A (H1N1) pandemic 2009 viruses were the predominant circulating viruses for most of the season; however, the epidemiological patterns shifted, and influenza A (H3N2) viruses became the predominant circulating viruses in the United States and Wyoming. Consequently, vaccine effectiveness estimates decreased significantly from the estimates provided earlier in the season because of the vaccine's performance against influenza A (H3N2) viruses. The estimates reported by the United States Influenza Vaccine Effectiveness Network for the 2018-2019 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 2018-2019 influenza season. Overall, the end of season estimated vaccine effectiveness against influenza A and influenza B was 29% (95% confidence interval [CI]: 21% to 35%). The vaccine effectiveness estimate for the 2018-2019 influenza season is similar to previous seasons in which circulating viruses and vaccine viruses are not well matched. Consequently, this illustrates the fact that one or more of the circulating influenza viruses during the 2018-2019 influenza season were antigenically and genetically different from the influenza vaccine virus components of the 2018-2019 Northern Hemisphere seasonal influenza vaccines.

The research associated with vaccine effectiveness estimates suggests that the 2018-2019 Northern Hemisphere seasonal influenza vaccine marginally reduced outpatient influenza visits and provided protection against hospitalizations. Influenza activity remained relatively low in most regions of the United States from the start of the season until December 2018. However, in December, influenza activity gradually began to increase until it peaked in February 2019. Also, public health officials noted a transition to influenza A (H3N2) viruses as the predominant circulating virus in February 2019; the transition contributed to prolonged influenza activity during the 2018-2019 influenza season. The CDC recommended ongoing influenza vaccinations to help prevent infections with the predominant circulating influenza A viruses and infections with the low levels of influenza B viruses circulating throughout most of the influenza season. The end of season vaccine effectiveness estimates indicated that the 2018-2019 Northern Hemisphere seasonal influenza vaccine provided limited protection against circulating influenza viruses, specifically, influenza A (H3N2) viruses. The CDC sponsored interim analysis of the 2018-2019 influenza season indicated an overall typical vaccine effectiveness rate among individuals. The emergence of influenza A (H3N2) viruses impacted the overall vaccine effectiveness estimates for the 2018-2019 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 ten thousand outpatients enrolled during the 2018-2019 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. This influenza season, the New Vaccine Surveillance Network, contributed inpatient influenza data on children 18 years of age and younger to vaccine effectiveness studies. The study estimated the effectiveness of influenza vaccines for the prevention of influenza hospitalizations among children.

This influenza season, influenza A (H1N1) pandemic 2009 viruses, influenza A (H3N2) viruses, and influenza B viruses co-circulated in the United States and Wyoming. Influenza A (H1N1) pandemic 2009 viruses and Influenza A (H3N2) viruses were the predominant viruses in Wyoming during the 2018-2019 influenza season. The end of season vaccine effectiveness estimates for the 2018-2019 Northern Hemisphere influenza vaccine for the prevention of influenza virus-associated outpatient acute respiratory illness visits, identified limited protection against influenza virus illnesses. The circulating influenza A (H3N2) viruses blunted the overall impact of the 2018-2019 Northern Hemisphere influenza vaccine. The end of season estimated vaccine effectiveness against influenza A (H3N2) viruses was 9% (95% CI: - 4% to 20%). 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 influenza A (H1N1) pandemic 2009 viruses was 44% (95% CI: 36% to 51%). Overall, influenza A (H1N1) pandemic 2009 virus component had the highest estimated vaccine effectiveness of the influenza A virus components.

Influenza B viruses accounted for less than five percent of viruses included in vaccine effectiveness estimates. Furthermore, influenza B viruses accounted for less than five percent of viruses reported by healthcare providers in Wyoming during the 2018-2019 influenza season. The majority of influenza B viruses included in the vaccine effectiveness study were B/Victoria-lineage viruses. Consequently, because of the low number of cases, researchers were unable to determine an adjusted vaccine effectiveness rate for influenza B viruses. Nationally, the 2018-2019 influenza season was a moderately high severity season. The end of season vaccine effectiveness estimate for the 2018-2019 influenza vaccine for prevention of influenza A (H3N2) virus-associated outpatient acute respiratory illness visits identified no significant protection against influenza A (H3N2) virus illnesses. The end of season estimated vaccine effectiveness against influenza A (H3N2) viruses was 9% (95% CI: -4% to 20%). A drifted influenza A (H3N2) virus from the 3C.3a clade emerged as the predominant circulating virus towards the end of the 2018-2019 influenza season. The emergence of the drifted influenza A (H3N2) virus decreased protection from the 2018-2019 Northern Hemisphere influenza vaccine. The vast majority of influenza A (H3N2) viruses sequenced were from the 3C.3a clade. Influenza researchers released the preliminary data to the WHO showing the surge of influenza A (H3N2) viruses from the 3C.3a clade before the selection of vaccine strains for the 2019-2020 Northern Hemisphere influenza vaccine. The information delayed the selection for the 2019-2020 influenza season. Eventually, the selection of the influenza A (H3N2) vaccine strain component for the 2019-2020 Northern Hemisphere influenza vaccine came from the 3C.3a clade. The complications associated with the vaccine illustrates the importance of developing better influenza vaccines.

ANTIVIRAL AGENTS FOR INFLUENZA

The FDA approved and recommended four antiviral drugs for use against influenza: oseltamivir, zanamivir, peramivir, and baloxavir marboxil, or just baloxavir. 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. Baloxavir is also active against influenza A and B viruses but has a different mechanism of action compared to neuraminidase inhibitors. Baloxavir inhibits cap-dependent endonuclease by interfering with the initiation of messenger ribonucleic acid (mRNA) synthesis of influenza viruses. The clinical benefits of antiviral treatment are greatest with early administration, especially within 48 hours of influenza illness onset. For additional information on antiviral medications, 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, 2018-2019 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	, months and older	Not Applicable	
Zanamivir (Relenza®)	**Influenza A and B**	**Treatment**	vary 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	
Baloxavir Marboxil (Xofluza®)	**Influenza A and B**	**Treatment**	12 years and older	Not Applicable	**Adverse events:** none more common than placebo in clinical trials.
		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 2018-2019 influenza season, the WHO reported a human infection with a highly pathogenic avian influenza A (H5N1) virus. The case was the first reported case of an avian influenza A (H5N1) virus since 2017. The virus is highly contagious among birds, especially domestic poultry. Highly pathogenic avian influenza A (H5N1) viruses in humans are rare and typically do not spread easily from person-to-person. Most of the cases are severe, with death occurring in over half of the reported cases. Since 2003, the WHO received approximately 860 reports of human infections with avian influenza A (H5N1) viruses. The reported cases span four continents and seventeen countries. Influenza A (H5N1) viruses have been detected in the United States poultry population; however, the viruses are different from the Asian-lineage viruses. The infection occurred in a resident of the country of Nepal. The case was the first reported human infection of the highly pathogenic avian influenza A (H5N1) virus in their country. Nepal reported avian influenza A (H5N1) virus outbreaks in poultry preceding the diagnosis of the confirmed case. Public health officials in Nepal did not find evidence of avian influenza A (H5N1) virus transmission in other humans; moreover, public health officials, along with CDC, monitored the region for additional cases. There is limited information about the case; however, reports of highly pathogenic avian influenza A (H5N1) viruses are usually associated with exposures to bird-contaminated environments or infected birds. The viruses do not appear to spread easily from person-to-person.

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, city, and 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 2018-2019 influenza season, a *Health Advisory*. A *Health Advisory* provides important information for a specific incident or situation. The *Health Advisory* may contain 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 00419), was an official CDC *Health Advisory* released on March 28, 2019. The CDC Health Advisory, *Influenza Season Continues with an Increase in Influenza A (H3N2) Activity*, provided recommendations for the remainder of the 2018-2019 influenza season.

The CDC issued HAN alerted healthcare providers and public health officials of elevated levels of influenza A (H3N2) activity across the country. During the 2018-2019 influenza season, CDC received reports that influenza A (H3N2) viruses transitioned to the predominant circulating virus subtype. The influenza A (H1N1) pandemic 2009 viruses were the predominant circulating viruses for most of the influenza season. Influenza A (H1N1) pandemic 2009 viruses and low levels of influenza B viruses continued co-circulating around the country during the surge of influenza A (H3N2) viruses as the predominant circulating virus. Also, public health researchers were aware of the genetic diversity within phylogenetic clades and subclades of the influenza A (H3N2) viruses when the HAN was issued. The information may have contributed to the distribution of the *Health Advisory* by CDC. Historically, influenza seasons during which influenza A (H3N2) viruses predominate are associated typically with higher rates of hospitalizations and deaths among the elderly, compared to the other age groups. The *Health Advisory* reminded clinicians to maintain a high suspicion of influenza and to treat suspected influenza in high-risk outpatients, those with progressive disease, and all hospitalized patients with antiviral medications as soon as possible, regardless of vaccination status or laboratory results. Although the HAN was issued late in the influenza season, it specifically emphasized the importance of early antiviral treatment to help reduce influenza morbidity and mortality. Studies from previous influenza seasons proved that treatment with antiviral medications has the clinical benefits of treating influenza and reducing complications; and the public health benefits of reducing illness and severe outcomes of influenza. 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/.