Epidemiology of 2009 Pandemic Influenza A (H1N1) in the United States

Michael A. Jhung,[1] David Swerdlow,[2] Sonja J. Olsen,[3] Daniel Jernigan,[1] Matthew Biggerstaff,[1] Laurie Kamimoto,[1] Krista Kniss,[1] Carrie Reed, Alicia Fry,[1] Lynnette Brammer,[1] Jacqueline Gindler, William J. Gregg,[1] Joseph Bresee,[1] and Lyn Finelli[1]

[1]Influenza Division; [2]National Center for Immunization and Respiratory Diseases, Office of the Director, and [3]Division of Emerging Infections and Surveillance Services, Centers for Disease Control and Prevention, Atlanta, Georgia

In April 2009, the Centers for Disease Control and Prevention confirmed 2 cases of 2009 pandemic influenza A (H1N1) virus infection in children from southern California, marking the beginning of what would be the first influenza pandemic of the twenty-first century. This report describes the epidemiology of the 2009 H1N1 pandemic in the United States, including characterization of cases, fluctuations of disease burden over the course of a year, the age distribution of illness and severe outcomes, and estimation of the overall burden of disease.

On 15 April 2009, the first case of 2009 pandemic influenza A (H1N1) (pH1N1) virus infection in the United States was identified in a 10-year-old boy in southern California; 2 days later, a second case of infection with the same virus was confirmed in a 9-year-old girl in an adjacent county in California [1]. During the subsequent 2 weeks, additional cases of infection with this new virus were detected in Mexico, California, Texas, and other states [2, 3].

The pH1N1 influenza virus contained a combination of gene segments that had not been previously reported in animals or humans. The pH1N1 virus' hemagglutination (HA) gene, which codes for an important viral surface antigen, was most closely related to the HA found in contemporary influenza viruses circulating among North American swine. The pH1N1 HA had evolved from the avian-origin 1918 pandemic influenza H1N1 virus, which is thought to have entered human and swine populations at about the same time, but to have evolved into distinct lineages in pigs and in humans [1]. Early serologic data suggested, consistent with the evolutionary origin of the HA, that many older adults had some cross-reactive immunity to the pH1N1 HA due to prior infection with antigenically related strains [4]. Children and most young adults, however, were immunologically naive.

The 2009 pandemic virus quickly spread globally, and on 11 June 2009, the World Health Organization (WHO) declared the first influenza pandemic since 1968–1969 [5]. As of April 2010, laboratory-confirmed infections with pH1N1 influenza virus have been identified in 212 countries and overseas territories, and >15,000 laboratory-confirmed deaths have been reported to the WHO worldwide [6]. In this report, we summarize the epidemiology of pH1N1 influenza in the United States, including timing of the outbreak, geographic distribution, characteristics of cases, and epidemiologic parameters, such as attack rates, generation time, and reproductive rate.

TEMPORAL AND GEOGRAPHIC PATTERNS OF DISEASE

In the United States, the pandemic was characterized by 2 distinct waves (Figure 1), with lower levels of activity that persisted between waves and through the end of April 2010. The first wave began in April 2009 with the

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Correspondence: Michael A. Jhung, M.D., 1600 Clifton Rd, MS-A32, Atlanta, GA 30333 (mjhung@cdc.gov).

Clinical Infectious Diseases 2011;52(S1):S13–S26
Published by Oxford University Press on behalf of the Infectious Diseases Society of America 2011.
1058-4838/2011/52S1-0001$37.00
DOI: 10.1093/cid/ciq008

Downloaded from https://academic.oup.com/cid/article/52/suppl_1/S13/498323 by U.S. Department of Justice user on 16 August 2022

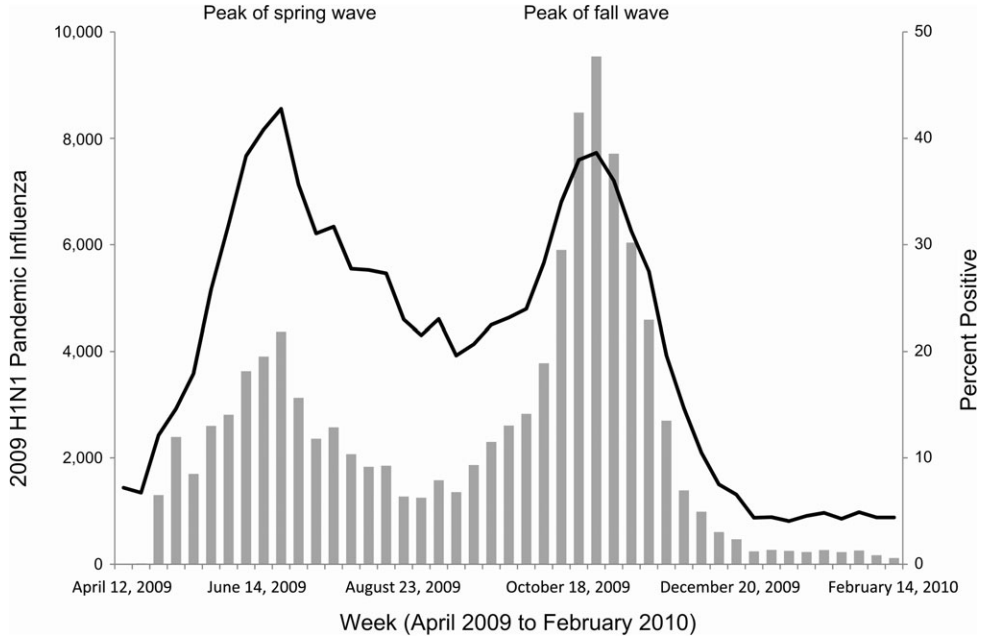

Figure 1. Number of pH1N1 viral isolates tested by week and overall percent positive for all influenza, reported to the Centers for Disease Control and Prevention by World Health Organization/National Respiratory and Enteric Virus Surveillance System laboratories from April 2009 through March 2010 in the United States [7].

identification of the first US cases. Within 1 week, 10 cases had been confirmed in 3 states, and investigations of probable cases were underway in 6 additional states [2]. This first wave peaked during June 2009, and by August influenza activity levels had decreased substantially in most states, although activity was sustained throughout the summer months at levels substantially above what is normally seen during the summer for seasonal influenza [8]. Although pH1N1 infections were observed in all US states during the first wave, the largest numbers of cases were reported from California, Connecticut, Florida, Hawaii, Illinois, Texas, New Jersey, New York, Pennsylvania, and Wisconsin (Figure 2a) and were largely confined to major cities within states (differences in the number of cases reported to the Centers for Disease Control and Prevention (CDC) among states were partly due to differences in state testing and reporting practices). Alaska, Connecticut, Delaware, Hawaii, Illinois, Massachusetts, Texas, Utah, Wisconsin, and Wyoming reported the highest rates of infection during the first wave (Figure 2b). In addition, outbreaks of disease among children attending summer camps were widely reported [9], and many camps that primarily served children with chronic medical conditions were cancelled. The second pandemic wave began in the Southeastern United States as children returned to school in mid-August and early September. Over the following 2 months, disease became geographically widespread throughout the United States. Illness occurring during this fall wave ultimately accounted for the majority of US cases seen during the pandemic. The fall wave peaked in late October, and since that time, although circulation of pH1N1 virus has continued, influenza activity has decreased and remained below what is expected in the winter months [8].

The geographic spread of pH1N1 virus and the timing of the 2 pandemic waves can be visualized using national outpatient illness data. The US Outpatient Influenza-Like-Illness (ILI) Surveillance Network (ILINet) is a system of >3000 sentinel health care providers who report the weekly percentage of outpatient visits for ILI to CDC [10]. ILI is defined as temperature >37.8°C accompanied by cough or sore throat in the absence of other known causes. ILI surveillance correlates well with the number of weekly positive influenza test results and has historically been used to monitor influenza activity (CDC, unpublished data). To facilitate smaller scale visualization of national ILINet data, the CDC and colleagues at the Johns Hopkins Applied Physics Lab (Baltimore, MD) derived threshold statistics describing influenza activity at a core-based statistical area (CBSA) geographic level. This methodology allowed assessment of CBSA-specific influenza activity, measured by the number of standard deviations (SDs) above a weighted mean baseline of ILINet provider ratios within each CBSA (CDC, unpublished data). During the peak of the spring wave, ILI activity was predominately focal (Figure 3, Map 1), and this focal pattern continued throughout the summer and the beginning of the fall wave (Figure 3, Map 2). By mid-September, activity was widespread throughout the Southeastern United States, and by October 2009, during the peak of the second wave, ILI activity was widespread throughout the United

Downloaded from https://academic.oup.com/cid/article/52/suppl_1/S13/498323 by U.S. Department of Justice user on 16 August 2022

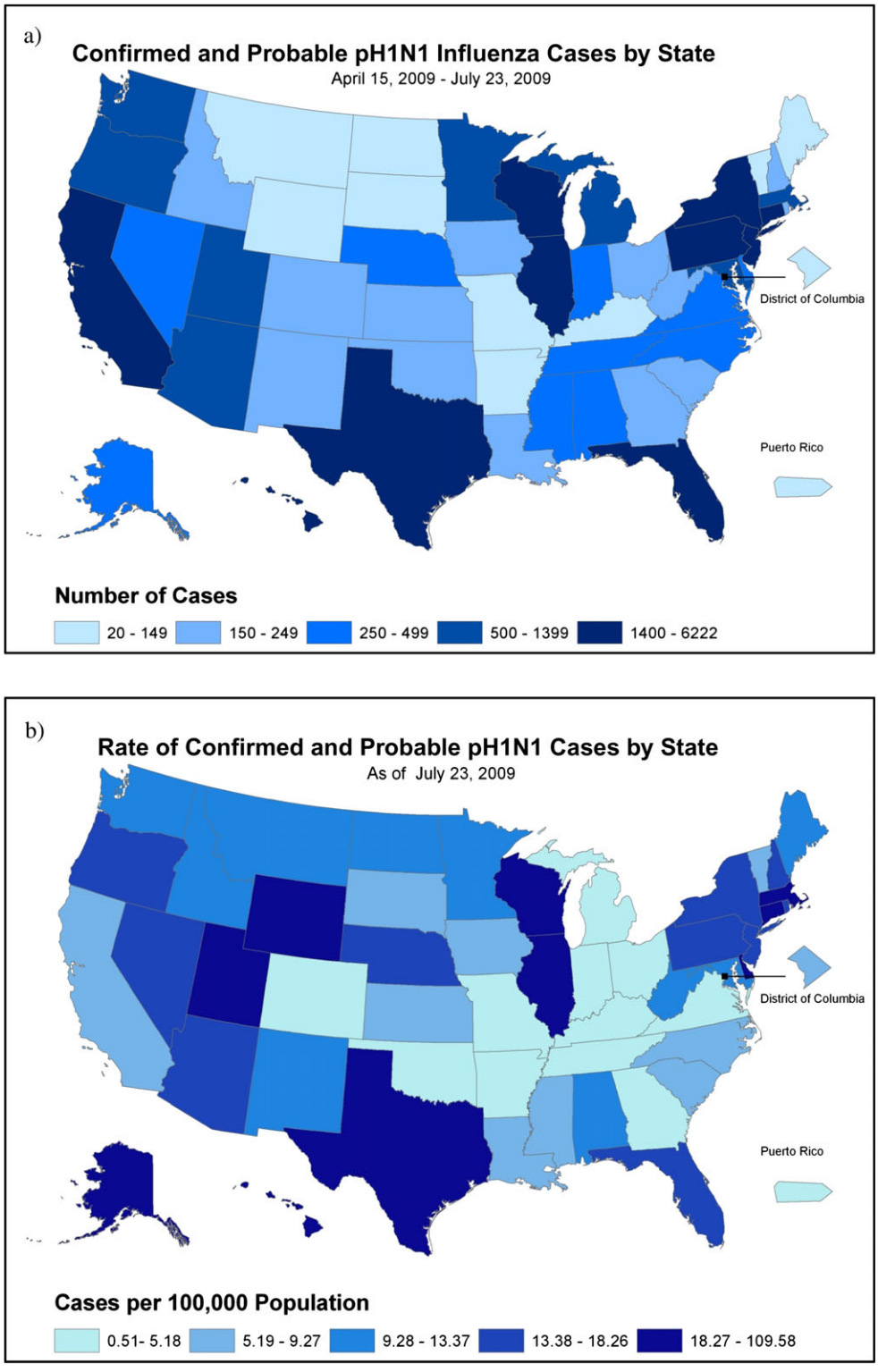

Figure 2. **a)** pH1N1 influenza infections, number of cases by state—United States, 15 April–23 July 2009. **b)** pH1N1 influenza infections, rate of cases by state—United States, 15 April–23 July 2009.

States (Figure 3, Map 3). By February 2010, ILI activity had once again become focal (Figure 3, Map 4). By March 2010, influenza activity had decreased to the lowest levels measured during the pandemic in most states; however, elevated activity persisted briefly in the Southeastern United States before also decreasing by April 2010 in that region [11].

Downloaded from https://academic.oup.com/cid/article/52/suppl_1/S13/498323 by U.S. Department of Justice user on 16 August 2022

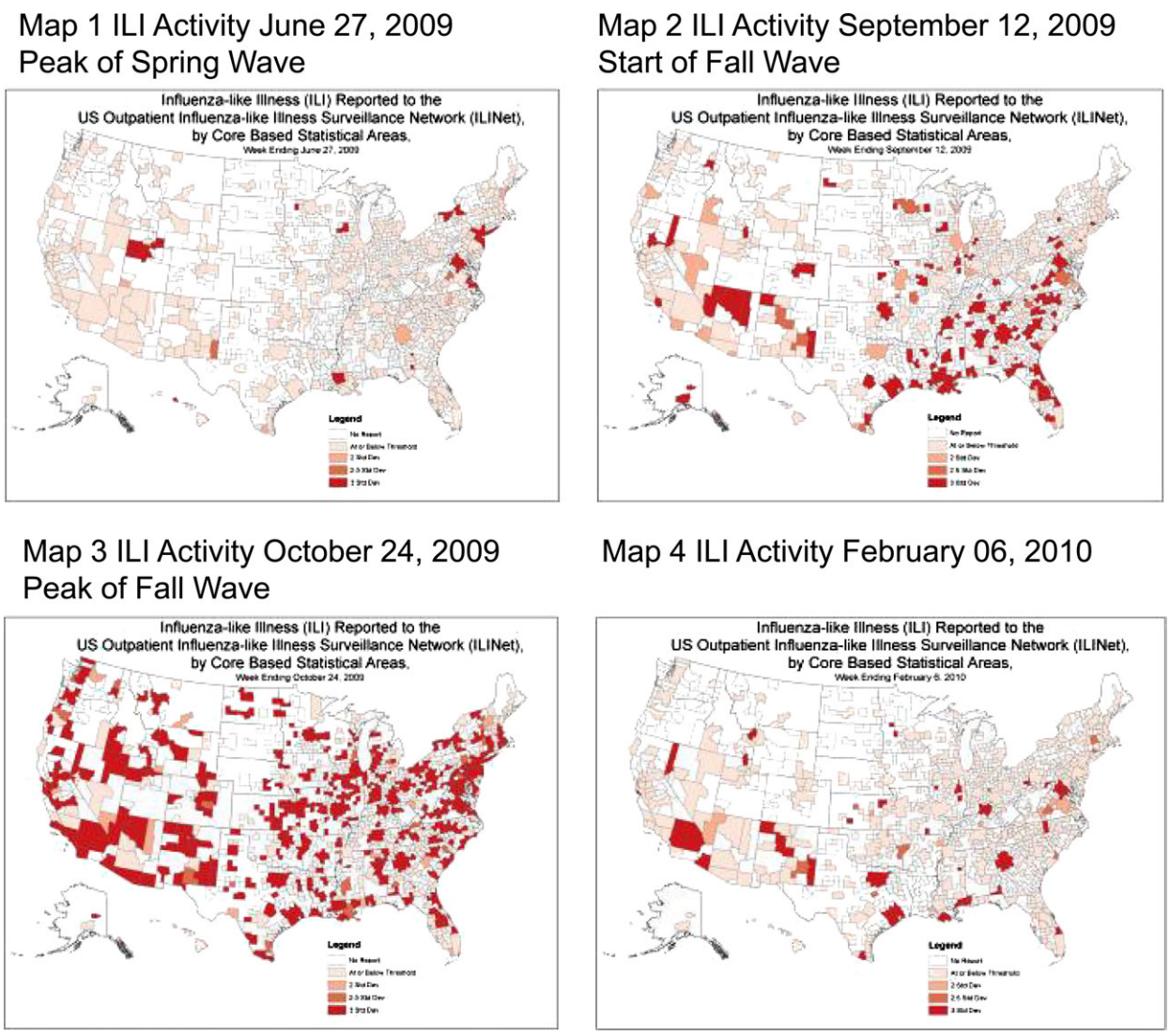

Figure 3. Influenza-like illness activity at different stages of the pH1N1 influenza pandemic—United States, 27 June 2009–6 February 2010.

CHARACTERISTICS OF pH1N1 INFLUENZA CASES

When the pH1N1 outbreak was first detected in April 2009, the CDC worked with state and local health departments to collect and analyze information describing early cases. From 15 April through 16 June 2009, individual laboratory-confirmed cases were reported [12, 13], and from 17 June through 23 July 2009, aggregate data on cases, hospitalizations, and deaths in 5 age groups (0–4 years, 5–24 years, 25–49 years, 50–64 years, and ≥65 years) were collected [14, 15]. From 15 April through 23 July 2009, there were a total of 43,771 laboratory-confirmed cases reported. Case reports accelerated quickly in the early weeks of the pandemic, peaked at >6000 cases per week in late June and early July, and decreased to 3000 cases per week in late July, after which time individual case reporting was discontinued and aggregate reporting was initiated for laboratory-confirmed hospitalizations and deaths only (Figure 4). Of cases reported, 37,030 (85%) were reported with age group information. The majority (73%) of reported cases were in individuals who were ≤24 years of age: 4816 (13%) were in individuals 0–4 years of age, 22,080 (60%) were in individuals 5–24 years of age, 7434 (20%) were in individuals 25–49 years of age, 2187 (6%) were in individuals 50–64 years of age, and 213 (1%) were in individuals ≥65 years of age. This age distribution of cases is consistent with age distributions for cases of pH1N1 virus infection worldwide [16], as well as with serologic studies that demonstrate pre-existing cross-reactive immunity in adults over the age of 60 years, limited levels of immunity in younger adults, and essentially no pre-existing immunity in children [12, 17, 18]. Case reports likely underestimate the true number of cases, because testing was not routinely conducted for all

Downloaded from https://academic.oup.com/cid/article/52/suppl_1/S13/498323 by U.S. Department of Justice user on 16 August 2022

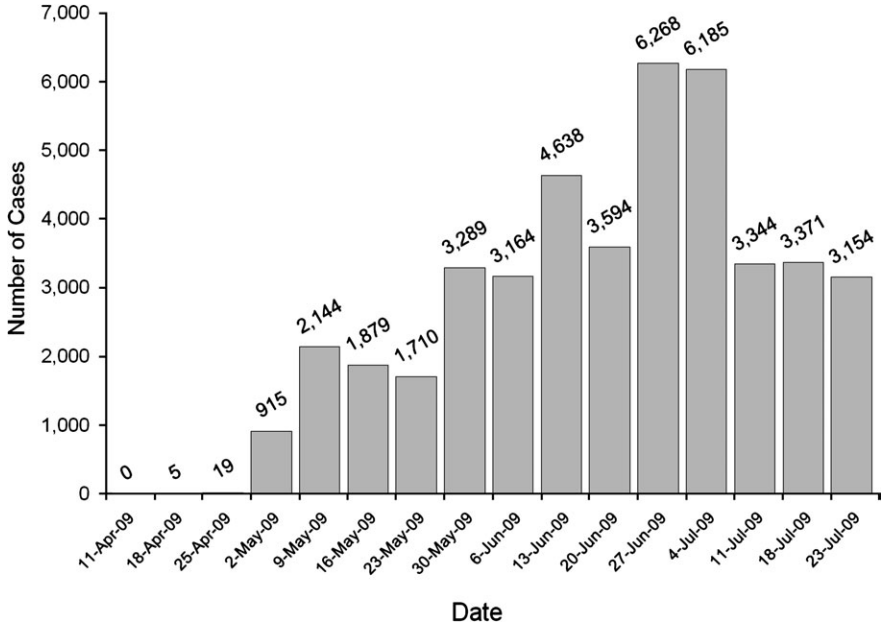

Figure 4. Laboratory-confirmed cases of pH1N1 influenza reported by state and local health departments to the Centers for Disease Control and Prevention by week—United States, 15 April–23 July 2009.

medically attended influenza visits, even early in the pandemic, reflecting a bias toward testing more-severely ill, hospitalized patients. Furthermore, differences in laboratory capacity and testing recommendations among states may have contributed to variability in case-based reporting.

Descriptive epidemiologic and clinical characteristics of early cases are available from data submitted on 931 cases using a standardized case report form. Case reports were submitted from 15 April through 16 June 2009 by state and local health departments [12, 13]. Of those initial cases reported, 52% were in male patients, who ranged in age from <1 month to 86 years. Of the 818 patients (88%) for whom race and ethnicity were reported, just over one-half were white non-Hispanic, and approximately one-third were Hispanic (Table 1). The proportion of cases in individuals of Hispanic ethnicity decreased from 37% in the first few weeks of reporting to 21% in June, possibly reflecting an initial association of cases with travel to Mexico, which may have led to increased testing of Hispanics or persons that had travelled to Mexico. As the pandemic continued, attack rates for self-reported ILI were similar among white non-Hispanics, blacks, non-Hispanics, and Hispanics (CDC, unpublished data from the Behavioral Risk Factor Surveillance System).

Generally, the signs and symptoms reported among the initial 931 cases were similar to those observed in patients with seasonal influenza infection [19]. The most common symptoms were fever or feverishness (93%), cough (86%), sore throat (58%), rhinorrhea (49%), myalgia (48%), vomiting (21%), and diarrhea (17%). However, because fever was often used as part of the case definition, a higher proportion of patients had fever than was reported in other studies that tested persons with a wider range of symptoms [20]. In some case series in which fever was not required as part of screening criteria, the proportion of persons with laboratory-confirmed pH1N1 influenza who had fever ranged from 58% to 67% [20, 21].Vomiting was more frequently reported among children (27%) than among adults (13%); however, other symptoms were reported with similar frequency by adults and children. The frequency of diarrhea was greater than that seen among seasonal influenza cases [22] but was similar to that described in a case series of sporadic swine influenza virus infections that occurred before the pandemic [23]. The overall type and frequency of symptoms among cases in this series is consistent with other studies of pH1N1-infected persons both in the United States and abroad [16, 24, 25].

SEVERE OUTCOMES—HOSPITALIZATIONS

Hospitalizations associated with the pH1N1 virus were monitored using data from 3 surveillance activities: (1) the case-based and aggregate reporting described above, (2) the Emerging Infections Program, and (3) a new aggregate system implemented in August 2009 to monitor influenza-associated hospitalizations and deaths, referred to as the Aggregate Hospitalizations and Deaths Reporting Activity (AHDRA).

From 15 April through 30 August 2009, case-based and aggregate reporting identified 9079 pH1N1 virus–associated hospitalizations. Of the 931 detailed case report forms received from patients with early cases, 883 (95%) gave data on

Downloaded from https://academic.oup.com/cid/article/52/suppl_1/S13/498323 by U.S. Department of Justice user on 16 August 2022

Table 1. Demographic and Clinical Information for 931 Laboratory-Confirmed Cases of pH1N1 Influenza Infection reported to the Centers for Disease Control and Prevention, 15 April–16 June 2009

Characteristic		No. (%) of cases (n =931)		US population, %[a]
Sex	Male sex	484	(52)	49
Race/ethnicity[b]	White non-Hispanic	425	(52)	66
	Black non-Hispanic	52	(6)	12
	Hispanic	278	(34)	15
	Native Hawaiian/Pacific Islander	6	(<1)	<1
	Asian	21	(3)	4
	American Indian/Alaskan Native	32	(4)	1
	Multiracial	4	(<1)	2
Symptoms	Fever/feverishness	864	(93)	—
	Cough	801	(86)	—
	Sore throat	539	(58)	—
	Rhinorrhea	452	(49)	—
	Myalgia	445	(48)	—
	Vomiting	195	(21)	—
	Diarrhea	158	(17)	—

NOTE. Laboratory testing for influenza during the study period was more frequently conducted for patients who presented with influenza-like illness, which included temperature $\geq$ 37.8°C.

[a] Annual estimates of the resident population by sex, race, and Hispanic origin for the United States, 1 April 2000 to 1 July 2008.

[b] Race and/or ethnicity data available for 818 (88%) of cases.

hospitalization status. Of patients for whom this data was known, 56 (6%) required hospitalization, and 11 (23%) of 47 hospitalized patients were admitted to the intensive care unit (ICU).

Beginning in August 2009, the CDC requested that all 50 states submit data on hospitalizations and deaths due to influenza using either a laboratory-confirmed or syndromic case definition through the AHDRA reporting system [7, 10]. Laboratory confirmation included rapid influenza tests, reverse-transcriptase polymerase chain reaction (RT-PCR), direct fluorescent antigen testing, immunofluorescent antigen testing, or viral culture; reporting by specific type or subtype was not required. Syndromic reporting included cases of pneumonia and influenza based on clinical syndrome, hospital admission or discharge data, or a combination of data elements that could include laboratory testing and presence of ILI. From 30 August 2009 through 3 April 2010, a median of 36 states each week reported a cumulative total of 41,914 laboratory-confirmed, pH1N1-associated hospitalizations; the remaining states reported a total of 134,441 syndromic hospitalizations. Although the total AHDRA laboratory-confirmed hospitalization count is likely a substantial underestimate of the number of pandemic-associated hospitalizations, the data on laboratory-confirmed cases was helpful in monitoring trends in the distribution of cases and patient age groups over time. Laboratory-confirmed influenza-associated hospitalization and death rates in AHDRA were calculated using only the populations of states reporting using a laboratory-confirmed case definition as denominators. Based on the laboratory-confirmed cases, the total weekly hospitalization rate peaked in October 2009 at 2.42 hospitalizations per 100,000 persons and decreased to <.25 hospitalizations per 100,000 persons by January 2010 (Figure 5). This peak rate occurred much earlier than the typical peak for seasonal influenza activity, which most often occurs during January or February each year [26].

The highest rates of hospitalizations were observed among the 0–4-year-old age group, which had rates 2- to 3-fold higher than those observed in the other age groups (Figure 6). Age-specific hospitalization rates for all age groups for the 2009–2010 season were higher than rates for the 2008–2009 season, when seasonal H1N1 viruses predominated, and their distribution was markedly different from that in typical influenza seasons, when hospitalizations are more common among persons >65 years of age [10, 27, 28]. The majority of hospitalizations (>70%) reported to AHDRA were in patients <50 years of age, and <10% were in patients ≥65 years of age. Other studies corroborate this age distribution, showing that nearly one-half of all patients in the United States hospitalized with pH1N1 influenza were 25 years of age, and <10% were ≥65 years of age [10, 29]. The age distribution of hospitalized patients found by national surveillance is also consistent with data from field investigations in Chicago (where the median age of 205 hospitalized patients was 16 years [24]), New York City (where 60% of 99 admitted patients were under 18 years of age [30]), and in California (where the median age of 30 hospitalized patients was 27 years [31]).

Downloaded from https://academic.oup.com/cid/article/52/suppl_1/S13/498323 by U.S. Department of Justice user on 16 August 2022

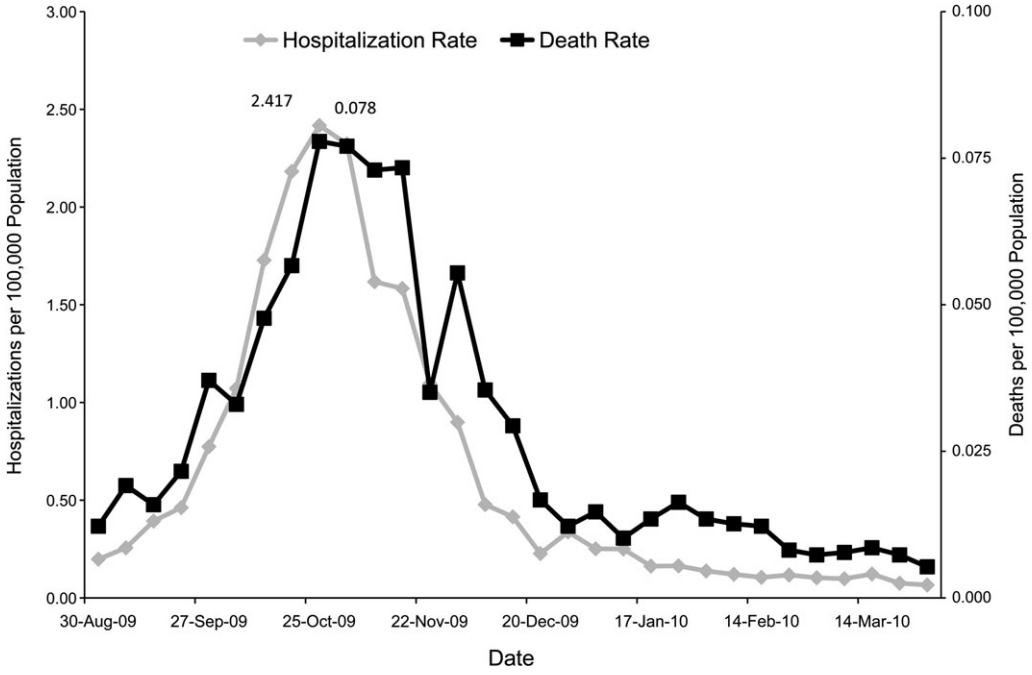

Figure 5. Aggregate hospitalization and death reporting activity (AHDRA) hospitalization and death rates per 100,000 population by week of report, laboratory-confirmed pH1N1 influenza infection—United States, April 2009–February 2010.

More than one-half of patients hospitalized with pH1N1 infection were likely to have at least 1 underlying medical condition [29–31]. In a study of 272 hospitalized patients early in the pandemic in the United States, Jain et al [29] found that respiratory comorbidities (eg, asthma and chronic obstructive pulmonary disease), diabetes, and immunosuppressive conditions were most common in adult patients, whereas asthma and neurologic disorders were most common in patients <18 years of age. From 15 April 2009 through 16 February 2010, hospitals in the Emerging Infections Program (EIP) [32] identified 4987 adult and 2600 pediatric hospitalizations associated with pH1N1 infection. Full analysis of these data is pending, but preliminary results indicate that the majority of adults (85%) and children (58%) hospitalized with pH1N1 infections had at least 1 underlying medical condition (Figure 7).

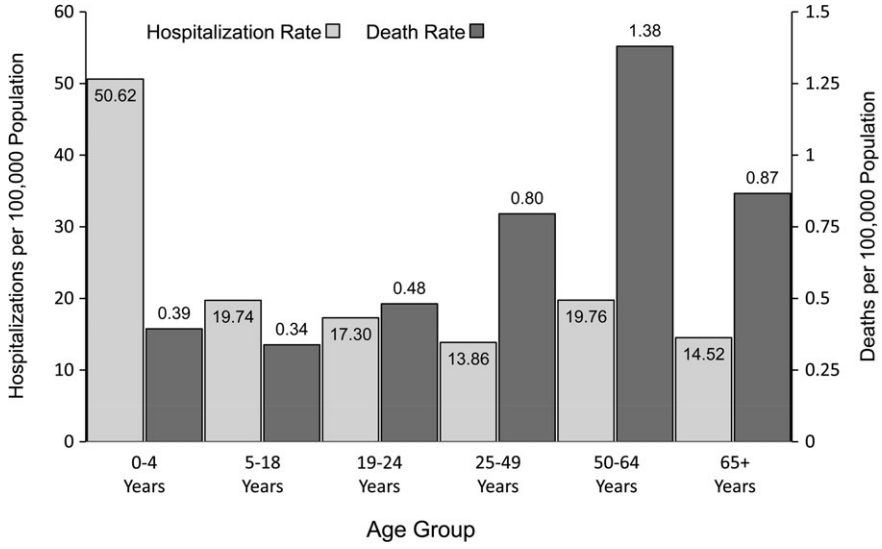

Figure 6. Aggregate hospitalization and death reporting activity (AHDRA) hospitalization and death rates per 100,000 population by age group, laboratory-confirmed pH1N1 influenza infection—United States, August 2009–February 2010.

Downloaded from https://academic.oup.com/cid/article/52/suppl_1/S13/498323 by U.S. Department of Justice user on 16 August 2022

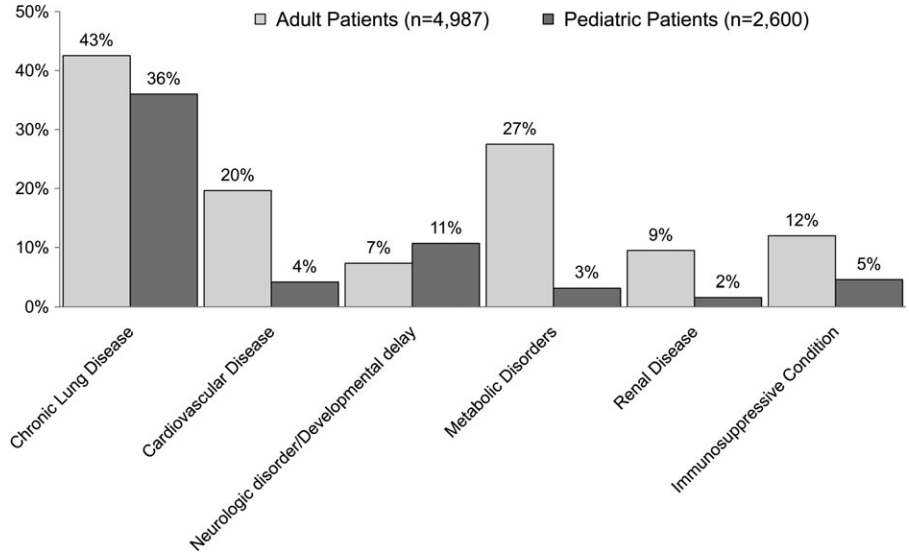

Figure 7. Prevalence of selected underlying medical conditions in adult and pediatric patients hospitalized with pH1N1 influenza infections, Emerging Infections Program, April 2009–February 2010.

In many studies of hospitalized patients in the United States, 20%–25% of patients required ICU admission [24, 29–31]. Early reports suggest that, although the majority of patients hospitalized with pH1N1 virus infection had underlying medical conditions, some hospitalized patients who became critically ill and required ventilator or vasopressor support were previously healthy young adults or adolescents in whom clinical decline after hospital admission was extremely rapid [33–35] (CDC, unpublished data).

In addition to previously recognized risk factors for severe influenza, such as pregnancy, chronic heart and lung disease, neurologic disease, and diabetes [36], obesity and morbid obesity were identified as possible independent risk factors for hospitalization [29], ICU admission [33], and critical illness and death [34, 35] associated with pH1N1virus infection. In a study of 361 hospitalizations and 233 deaths, Morgan et al [37] noted a statistically significant association between morbid obesity (body mass index [BMI], calculated as weight in kilograms divided by the square of height in meters, of $\geqslant$40) and hospitalization in adults, irrespective of the presence of an Advisory Committee on Immunization Practices (ACIP)–recognized chronic medical condition, as well as a significant relationship between obesity (BMI $\geqslant$30) and death in adults. However, obesity was not associated with either hospitalization or death in children in this study [37].

Finally, there is preliminary evidence suggesting that some racial or ethnic groups may have been at increased risk for severe outcomes after pH1N1 virus infection in the United States.

Table 2. Secondary Household Attack Rates for Confirmed and Probable Cases of Acute Respiratory Illness and Influenza-like Illness by Age and State–California and Texas, April–May 2009

Cases	Percentage (proportion) of households Acute respiratory illness[a]	Influenza-like illness[b]	Confirmed and probable
Overall	17.6 (72/408)	8.1 (33/408)	3.9 (16/408)
By state			
California	23.9 (28/117)	12.8 (15/117)	6.0 (7/117)
Texas	15.1 (44/291)	6.2 (18/291)	3.1 (9/291)
By age[c]			
$\leqslant$18 years	19.5 (34/174)	12.1 (21/174)	6.9 (12/174)
>18 years	17.0 (38/224)	5.4 (12/224)	1.8 (4/224)

NOTE. Cases are from 38 households in San Diego County, CA, and 86 households primarily in Bexar and Guadelupe Counties, TX (Centers for Disease Control and Prevention, unpublished data).

[a] Acute respiratory illness is defined as having at least 2 of the following signs or symptoms: fever or feverishness, cough, runny nose, and sore throat.

[b] Influenza-like-illness is defined as having fever (temperature, $\geqslant$37.8°C) and either cough or sore throat.

[c] Ten non-ill household members with missing age data are excluded.

Downloaded from https://academic.oup.com/cid/article/52/suppl_1/S13/498323 by U.S. Department of Justice user on 16 August 2022

Enhanced surveillance in Chicago, Illinois, showed that pH1N1-associated hospitalization rates were higher for non-Hispanic blacks, Asian/Pacific Islanders, and Hispanics, compared with non-Hispanic whites, during the spring wave of the pandemic [24], and an elevated pH1N1-associated mortality rate was found in American Indian/Alaska Natives in 12 states, compared with all other racial/ethnic populations combined [38]. Further assessment of the risk of severe pH1N1 infection associated with race and ethnicity is pending.

SEVERE OUTCOMES—DEATHS

Deaths associated with pH1N1 virus were monitored using data from 3 surveillance activities: (1) the case-based and aggregate reporting described above, (2) AHDRA, and (3) the CDC's influenza-associated pediatric mortality surveillance system [10].

From 15 April through 30 August 2009, case-based and aggregate reporting identified 593 pH1N1-associated deaths. From 30 August 2009 through 3 April 2010, the CDC received 2125 laboratory-confirmed death reports from a median of 39 states each week via AHDRA. Syndromic deaths totaling 13,983 were reported by the remaining states during this time. The AHDRA weekly laboratory-confirmed death rate peaked in October 2009 at .078 and decreased to <.015 deaths per 100,000 persons by January 2010. Overall, the age distribution of laboratory-confirmed pH1N1 influenza–associated death rate was markedly different from that seen in typical influenza seasons. In contrast to typical influenza seasons, when 90% of deaths occur in the elderly population [39, 40], 86% of pH1N1 deaths reported to AHDRA were in persons <65 years of age, with the highest rates found in persons aged 50–64 years (Figure 6).

Fowlkes et al [41] identified a wide geographic distribution in 377 deaths reported during the first 3 months of the pandemic, as well as a tendency for fatal cases to occur in patients with at least 1 underlying illness. In patients for whom information was available, 69% of those <18 years of age and 80% of those ⩾18 years of age had at least one co-morbid condition [41]. Chronic lung disease (including asthma), metabolic disorders, and cardiovascular disease were most common in adults who died, whereas neurologic disorders and chronic lung conditions (48% of which were asthma) were most common among pediatric patients who died [41].

Laboratory-confirmed influenza-associated pediatric deaths have been a nationally notifiable condition since 2004, and surveillance data, including demographic information, virus characteristics, underlying medical conditions, and vaccination history, have been collected for pediatric deaths since that time. Using data from this surveillance system, Cox et al [42] described 272 confirmed and 45 probable pH1N1-associated pediatric deaths that were reported from 15 April 2009 through 31 January 2010. The 317 reported pediatric deaths represented ~4 times the average annual number reported during the previous 6 influenza seasons. Among children for whom information was available, 68% had a pre-existing condition that placed them at higher risk of complication from influenza infection, as defined by the ACIP. Neurological disorders and pulmonary disease were the most common high-risk medical conditions [42].

SEVERE OUTCOMES—PREGNANCY

Changes in immunosuppression and in respiratory and cardiovascular system physiology during pregnancy may increase the risk of severe outcomes from influenza illness [43–48]. Increased mortality during previous influenza pandemics and a greater risk of complications from seasonal influenza have been reported in pregnant women [45, 49–53], and reports from early in the 2009 pandemic suggest a similar risk associated with pH1N1 infection [54–56]. In a study involving 94 pregnant women hospitalized with pH1N1 infection in the state of California, Louie et al [56] estimated an influenza-specific maternal mortality ratio (the number of maternal deaths per 100,000 live births) of 4.3 (95% confidence interval [CI], 1.8–8.4), which was nearly one-fourth of the maternal mortality ratio for death from any cause (19.3) in the state. Jamieson et al [55] identified a similar risk of severe outcome in a study involving 34 pregnant women with pH1N1 virus infection, estimating that pregnant women were 4.3 times more likely (95% CI, 2.3–7.8) than the general population to be hospitalized with pH1N1 virus infection. Siston et al [57] estimate that 5.8% of all pH1N1 influenza–associated deaths reported to the CDC from 14 April–21 August 2009 were in pregnant women, whereas only 1% of the population is pregnant at any time.

COMMUNITY AND SECONDARY HOUSEHOLD ATTACK RATES, REPRODUCTIVE RATE, AND GENERATION TIME

Knowledge of community and household attack rates, reproductive rate, and generation time were crucial for understanding the epidemiology of the pandemic and informing control measures. Early in the pH1N1 pandemic, the impact on communities was largely unknown, and investigators estimated community impact using several methods. In May 2009, a telephone survey was conducted in 10 states using Behavioral Risk Factor Surveillance System (BRFSS) methodology to estimate ILI prevalence [58, 59]. Although 4.7% of primary respondents (persons >18 years of age) reported ILI overall during April 2009, prevalence was higher among persons aged 18–64 years (range, 4.9%–5.9%) than it was among those ⩾65 years of age (1.9%). Among household members of primary respondents, ILI prevalence was 23.1% among children <5 years of age and 10.2% among children aged 5–17 years. ILI prevalence ranged

Downloaded from https://academic.oup.com/cid/article/52/suppl_1/S13/498323 by U.S. Department of Justice user on 16 August 2022

from a low of 1.5% in New York State to 8.4% in New Mexico and 9.2% in Tennessee, reflecting the focal nature of illness during the spring wave. These survey results were similar to the ILI attack rate of 4.9% found in a household survey in a heavily affected Chicago community following an outbreak of laboratory-confirmed pH1N1 virus infection at a neighborhood elementary school [60]. During the spring wave, in a New York City telephone survey conducted among a random sample of community households in May 2009, 6.9% of respondents or their household members reported ILI; prevalence rates were highest among persons <18 years of age (11.7%) and were 5.7% and 4.3% among 18–64-year-olds and persons ≥65 years of age, respectively. Rates were higher in Queens and Brooklyn than in other boroughs [61, 62] (M. Layton, personal communication). In a subsequent follow-up New York City survey conducted to include May and June, the reported ILI prevalence rates increased to 12.1% overall; the highest rates were among children <5 years of age (19.5%) and school-aged children aged 5–17 years (21.8%), and the lowest rate was among adults ≥65 years of age (5.7%) [61, 62] (M. Layton, personal communication). An investigation of the first reported US university pH1N1 outbreak, which occurred in Delaware during April 2009, found that 10% of students and 5% of faculty reported ILI; 3 hospitalizations were reported during this outbreak [63].

Community ILI rates were significantly higher in the fall than they were in the spring. In September 2009, questions about ILI symptoms that occurred during the month preceding the telephone interview were added to BRFSS surveys in 49 states, Washington DC, and Puerto Rico. Among the ILI questions was included a query regarding symptom onset date, thereby allowing calculation of cumulative incidence. Interviews conducted between 1 September 2009 and 17 January 2010 indicated that the cumulative incidence of ILI was 17% (95% CI, 12%–26%) for adults and 64% (95% CI, 58%–75%) for children (CDC, unpublished data). Although some persons reporting ILI were probably not infected with pH1N1 virus, the low prevalence of other circulating respiratory pathogens during both the spring and early fall suggests that the majority of ILI was caused by pH1N1 [10]. Community attack rates of influenza symptoms during previous pandemics have been estimated using a variety of survey methods to approach 25% in 1957 (H2N2), 30% in 1918 (H1N1), and 35%–40% in 1968 (H3N2) [64].

Understanding the secondary household attack rate following introduction by an index patient with influenza infection is an important indicator of the overall transmissibility of a newly emerged influenza virus [65]. Secondary household ILI attack rates were estimated during field investigations in Texas, California, and New York City (Table 2). In San Antonio, Texas, one of the first areas in the United States to be affected, transmission was investigated in 77 households between 15 April and 8 May 2009 in which at least 1 person in the household had laboratory-confirmed pH1N1 virus infection. The date of the index household case was defined as the earliest onset date of acute respiratory infection (ARI), ILI, or laboratory-confirmed pH1N1 virus infection. The secondary household attack rate was 13% for ARI, 9% for ILI, and 4% for laboratory-confirmed pH1N1 virus infection, and it was highest for children aged 0–4 years (ranging from 19% for ARI to 8% for laboratory-confirmed pH1N1 virus infection) and was lowest for adults ≥ 50 years of age (ranging from 12% for ARI to 4% for laboratory-confirmed pH1N1 virus infection) [66]. In San Diego County, California, 117 contacts in 38 households in which at least 1 person had laboratory-confirmed influenza were investigated at the onset of the pandemic. The secondary attack rate was 24% for ARI, 13% for ILI, and 6% for laboratory-confirmed pH1N1 virus infection (CDC, unpublished data). In New York City, following the first large school outbreak of laboratory-confirmed pH1N1 virus infection in the United States, 222 households of high school students with ILI were evaluated. Overall, 11% of household contacts (79 of 702) reported ILI. There was a progressive negative correlation between age and secondary ILI attack rate, ranging from 31% in household contacts <5 years of age to 2.1% in household contacts ≥55 years of age [67]. Finally, Cauchemez et al [12] reported on illness among 216 index case patients with laboratory-confirmed pH1N1 virus infection and 600 household members reported to the CDC from April through 11 June 2009. ARI was reported in 78 (13%) of household contacts (10% reported ILI), a rate thought to be at the lower range of attack rates for seasonal influenza (10%–40%) and lower than that reported during previous pandemics. Household contacts ≤18 years of age were twice as likely to report ARI or ILI as those 19–50 years of age, and those older than 50 years of age were the least likely to have ARI [12]. Results from studies to assess the proportion of ILI that was attributable to laboratory-confirmed pH1N1 virus infection are pending.

Two additional metrics are useful in understanding the dynamics of an influenza pandemic and were analyzed during the early field investigations: the basic reproduction number and the generation time (serial interval). The basic reproductive number R_0 is defined as the mean number of secondary cases per typical case in an otherwise susceptible population [14]. Although estimates of R_0 from past pandemics vary, the R_0 of previous pandemic influenza viruses generally range from 1.5 to 1.8 for the 1957 H2N2 and 1968 H3N2 pandemic viruses, and 1.8–2.4 for 1918 H1N1 influenza A strain, with a high estimate of 5.4 by Andreasen et al [68, 69]. During the current pandemic, White et al [14] used CDC case-based data from 1368 confirmed and probable cases with a date of report on or before 8 May 2009 and estimated the reproductive number of pH1N1 virus to be between 2.2 and 2.3. Estimates decreased to 1.7–1.8 after adjustment for increased case ascertainment during the initial pandemic period. In a sensitivity analysis making use of previous

Downloaded from https://academic.oup.com/cid/article/52/suppl_1/S13/498323 by U.S. Department of Justice user on 16 August 2022

estimates of the mean serial interval, White et al [14] estimated that the reproductive number was between 1.5 and 3.1. Fraser et al [69] used data from the initial outbreak in Mexico to estimate R_0 in the range of 1.2–1.6. Yang et al [70] used reported case clusters in the United States to estimate R_0 to be 1.3–1.7. Most estimates of R_0 for pH1N1 virus, therefore, have indicated that the virus was at the low end of transmissibility, compared with the strains that caused the 1918 pandemic, and was comparable to or slightly less transmissible than the strains that caused the 1957 and 1968 pandemics.

The time period between successive generations of infected persons is called the generation time, which can be measured indirectly by using the serial interval (the time between onset of symptoms in successive generations) and incubation period (the time between exposure and onset of symptoms) associated with a disease [71, 72]. The mean serial interval for seasonal influenza has been estimated in one study to be 3.6 days with standard deviation 1.6 days [74]. The serial interval of pH1N1 virus infection was estimated to be a mean ($\pm$SD) of 2.6 $\pm$ 1.3 days by Cauchemez et al [12], to be between 2.2 and 2.3 days by White et al [14], and to be between 2.6 and 3.2 days by Yang et al [70]. Thus, the estimated generation time of pH1N1 virus infection may be less than that of seasonal influenza, possibly because of higher proportions of susceptible persons. The distribution of the serial interval determines, along with R_0, the rate at which an epidemic can spread and can inform recommendations for control measures, such as school closure, isolation of infected persons, and use of non-pharmaceutical interventions [12, 14].

ESTIMATES OF OVERALL DISEASE BURDEN

By 23 July 2009, 43,677 laboratory-confirmed cases, 5009 hospitalizations, and 304 deaths had been reported to the CDC. However, laboratory-confirmed cases were believed to represent only a fraction of the total cases, because not all persons with influenza illness sought care, not all patients had specimens collected, not all specimens were sent to public health laboratories for confirmatory PCR tests, and not all confirmed cases were reported. To estimate the burden of pH1N1 virus infection in the United States from April through July 2009, Reed et al [75] created a model that adjusted for these sources of under-ascertainment via multipliers that were calculated using a Monte Carlo approach incorporating data from field studies [60, 63], a BRFSS telephone survey conducted in 2007 (CDC, unpublished data), and a similar BRFSS survey conducted in 2009 [59]. Using their model, the authors estimated that, for every pH1N1 case reported to the CDC, 79 cases likely occurred (90% probability range, 47–148 cases). For every hospitalization reported, 2.7 persons were estimated to be hospitalized (90% probability range, 1.9–4.3 hospitalizations) [75].

Because individual case-based reporting was discontinued on 23 July 2009, different models were needed to estimate the impact of the pandemic in the fall. One method combined influenza-associated hospitalization data from EIP, hospitalization-to-death ratio data from AHDRA, and ILI estimates obtained using multipliers derived from Reed et al [75]. Using these methods, the CDC estimated that, from April 2009 through 13 March 2010, pH1N1 virus was associated with 60 million cases (upper and lower range estimates, 43–88 million cases), 270,000 hospitalizations (range, 192,000–398,000 hospitalizations), and 12,270 deaths (range, 8720–18,050 deaths) occurred [76, 77]. The estimate of 60 million cases represents a cumulative attack rate in the United States of ~19.9%. In contrast to typical influenza seasons, in which the majority of influenza-associated hospitalizations and deaths occur in elderly persons [27], 90% of pH1N1 virus–associated hospitalizations and 87% of deaths were estimated to occur in persons younger than 65 years of age [76, 77]. Finally, although disease estimates through 13 March 2010 are substantially lower than pandemic planning assumptions, overall impact among persons younger than 65 years of age was substantial.

SUMMARY

Overall, influenza activity during the 2009 H1N1 pandemic occurred in 2 distinct waves and differed substantially from the pattern seen in a typical influenza season. Notably, secondary household attack rates and overall disease burden were lower than pandemic planning assumptions, in part due to limited impact on persons 65 years of age and older and low case fatality ratios. A key feature of the 2009 pandemic was relative sparing of health impact on older adults, compared to both seasonal influenza and prior pandemics, and a disproportionate impact on children. Compared to seasonal influenza outbreaks, in which >90% of deaths and over one-half of hospitalizations occur among persons ≥65 years of age, only 13% of deaths and 10% of hospitalizations are estimated to have occurred among those ≥65 years of age [77]. Thus, although the overall health impact was lower among the elderly population, the impact of pH1N1 virus infection in children, young adults, and specific risk groups (such as pregnant women) was substantial.

The "2-wave" pattern observed during the 2009 H1N1 pandemic is reminiscent of the temporal distribution of disease seen in the 1918–1919 H1N1 virus pandemic in the United States and other countries [68, 78, 79]. The H2N2 pandemic in 1957–1958 also spread in the United States in 2 distinct waves and reportedly affected older persons disproportionately. In contrast, only a single peak was observed during the first year after the emergence of H3N2 virus in 1968. The variability in patterns of circulation of the 4 pandemics in the last 100 years is a reminder of the unpredictable nature of influenza pandemics. Novel

Downloaded from https://academic.oup.com/cid/article/52/suppl_1/S13/498323 by U.S. Department of Justice user on 16 August 2022

influenza A viruses may arise at any time of the year and on any continent, reinforcing the need for sustained improvements in global year-round surveillance to maximize the potential for early disease detection and deployment of counter measures. The association between waves of community transmission and school years seen during the 2009 pandemic is intriguing and should be considered in future pandemic planning.

Early recognition that the highest rates of disease and complications occurred in non-elderly persons in the United States was critical to creating pandemic vaccine policies, focusing surveillance strategies, and communicating risks to the public and clinicians. The relatively high burden of disease in younger age groups has been observed worldwide and may be due in part to the presence of prior exposure to antigenically similar viruses among older adults but not among children. Similar to seasonal influenza epidemics, the risk of severe outcomes during this pandemic has been associated with very young age and with the presence of comorbid conditions [36]. Although confirmation that these groups were at higher risk of severe disease through focused field investigations was important, the recognition of new risk factors (eg, obesity) and risk groups demonstrated that detailed data collection and well-designed epidemiologic studies remain critical components of the early response to the emergence of novel influenza A viruses. Special studies also helped better understand the risk that pH1N1 posed to pregnant women [55, 56, 80]. Finally, pandemic investigations helped characterize the risk associated with groups not traditionally targeted for annual seasonal vaccination and informed the recent ACIP recommendation for universal influenza vaccination in the United States [81].

During the pandemic, the CDC periodically produced estimates of the total disease burden associated with pH1N1 infection. This has not been routinely possible during annual seasonal influenza epidemics; rather, the overall burden has been estimated using retrospective national data sets, with significant time delay between season's end and when data become available. The ability to produce estimates of illness, hospitalizations, and deaths at frequent intervals was helpful in understanding and communicating the severity of the pandemic and was made possible by the existence of greater capacity for influenza laboratory confirmation and improved surveillance data on laboratory-confirmed outcomes, including death and hospitalization.

The experience during the past year with the pH1N1 virus has produced important lessons for public health. First, robust influenza surveillance combining the interests and resources of state and national public health agencies is critical for ensuring an early and appropriate response. Moreover, the realization that additional data were needed required flexibility and frequent, productive communication among state and federal partners. Second, influenza epidemiology is difficult to predict. Because the age distribution, severity, and transmission parameters of pH1N1 differed from prior pandemics and from patterns of recent seasonal epidemics, pandemic plans and exercises based on previous experience had limitations. Thus, the value of rapid field investigations in addressing public health needs related to a newly emerged infectious disease was reaffirmed during the pH1N1 pandemic. Finally, given the difficulty in predicting changes in influenza epidemiology and virus characteristics, using this experience to improve US and global epidemiology and surveillance capacity for influenza will be important. And time is of the essence—with the continued endemicity of avian influenza H5N1 in many parts of the world, the persistence of sporadic human cases of H9N2 virus infection, and the dynamic nature of influenza viruses circulating among animal populations, the next pandemic of the twenty-first century may be 10–40 years away.

Acknowledgment

Supplement Sponsorship. Published as part of a supplement entitled "The 2009 H1N1 Influenza Pandemic: Field and Epidemiologic Investigations," sponsored by the Centers for Disease Control and Prevention.

Potential conflicts of interest. All authors: no conflicts.

References

1. Centers for Disease Control and Prevention. Swine influenza a (H1N1) infection in two children–Southern California, March-April 2009. MMWR Morb Mortal Wkly Rep **2009**; 58:400–402.
2. Centers for Disease Control and Prevention. Update: Swine influenza a (H1N1) infections–California and Texas, April 2009. MMWR Morb Mortal Wkly Rep **2009**; 58:435–437.
3. Centers for Disease Control and Prevention. Update: Infections with a swine-origin influenza a (H1N1) virus–United States and other countries, April 28, 2009. MMWR Morb Mortal Wkly Rep **2009**; 58:431–433.
4. Hancock K, Veguilla V, Lu X, et al. Cross-reactive antibody responses to the 2009 pandemic H1N1 influenza virus. N Engl J Med **2009**; 361:1945–1952.
5. New influenza a (H1N1) virus: global epidemiological situation, June 2009. Wkly Epidemiol Rec **2009**; 84:249–257.
6. Pandemic (H1N1) 2009 update http://www.who.int/csr/don/2010_02_12/en/index.html. Accessed 15 February 2010.
7. Brammer L, Blanton L, Epperson S, et al. Surveillance for influenza during the 2009 influenza A (H1N1) pandemic – United States April 2009 – March 2010. Placeholder Brammer. Clin Infect Dis.
8. Update: influenza activity – United States, August 30, 2009-January 9, 2010. MMWR Morb Mortal Wkly Rep; 59:38–43.
9. Centers for Disease Control and Prevention, Oseltamivir-resistant 2009 pandemic influenza a (H1N1) virus infection in two summer campers receiving prophylaxis–North Carolina, 2009. MMWR Morb Mortal Wkly Rep **2009**; 58:969–972.
10. Flu view http://www.cdc.gov/flu/weekly/. Accessed 26 April 2010.
11. Update: influenza activity - United States, August 30, 2009-March 27, 2010, and composition of the 2010-11 influenza vaccine. MMWR Morb Mortal Wkly Rep **2010**; 59:423–430.
12. Cauchemez S, Donnelly CA, Reed C, et al. Household transmission of 2009 pandemic influenza a (H1N1) virus in the United States. N Engl J Med **2009**; 361:2619–2627.
13. Dawood FS, Jain S, Finelli L, et al. Emergence of a novel swine-origin influenza a (H1N1) virus in humans. N Engl J Med **2009**; 360: 2605–2615.
14. White LF, Wallinga J, Finelli L, et al. Estimation of the reproductive number and the serial interval in early phase of the 2009 influenza a/H1N1 pandemic in the USA. nfluenza Other Respi Viruses **2009**; 3:267–276.

Downloaded from https://academic.oup.com/cid/article/52/suppl_1/S13/498323 by U.S. Department of Justice user on 16 August 2022

15. 2009 H1N1 early outbreak and disease characteristics http://www.cdc.gov/H1N1FLU/surveillanceqa.htm. Accessed 15 February 2010.
16. Health Protection Agency, Health Protection Scotland, National Public Health Service for Wales, HPA Northern Ireland Swine influenza investigation teams, Epidemiology of new influenza a (H1N1) virus infection, United Kingdom, April-June 2009. Euro Surveill **2009**; 14:1–3.
17. Centers for Disease Control and Prevention, Serum cross-reactive antibody response to a novel influenza a (H1N1) virus after vaccination with seasonal influenza vaccine. MMWR Morb Mortal Wkly Rep **2009**; 58:521–524.
18. Miller E, Hoschler K, Hardelid P, Stanford E, Andrews N, Zambon M. Incidence of 2009 pandemic influenza a H1N1 infection in England: a cross-sectional serological study. Lancet **2010**; 375:1100–1108.
19. Mandell GL, Bennett JE, Dolin R. Mandell, Douglas, and Bennett's principles and practice of infectious diseases, 7th ed. Philadelphia, PA: Churchill Livingstone/Elsevier, **2010**;1834–1836.
20. Cao B, Li X-W, Mao Y, et al. Clinical features of the initial cases of 2009 pandemic influenza a (H1N1) virus infection in China. New Engl J Med **2009**; 361.
21. Witkop CT, Duffy MR, Macias EA, et al. Novel influenza a (H1N1) outbreak at the U.S. air force academy: epidemiology and viral shedding duration. Am J Prev Med **2010**; 38:121–126.
22. Shinde V, Bridges CB, Uyeki TM, et al. Triple–reassortant swine influenza a (H1) in humans in the United States, 2005-2009. N Engl J Med **2009**; 360:2616–2625.
23. Nicholson KG. Clinical features of influenza. Semin Respir Infect **1992**; 7:26–37.
24. Centers for Disease Control and Prevention, 2009 Pandemic influenza a (H1N1) virus infections - Chicago, Illinois, April-July 2009. MMWR Morb Mortal Wkly Rep **2009**; 58:913–918.
25. Centers for Disease Control and Prevention, Swine-origin influenza a (H1N1) virus infections in a school - New York City, April 2009. MMWR Morb Mortal Wkly Rep **2009**; 58:470–472.
26. Centers for Disease Control and Prevention. Update: Influenza activity–United States, September 28, 2008-April 4, 2009, and composition of the 2009-10 influenza vaccine. MMWR Morb Mortal Wkly Rep **2009**; 58:369–374.
27. Thompson WW, Shay DK, Weintraub E, et al. Influenza-associated hospitalizations in the United States. JAMA **2004**; 292:1333–1340.
28. Molinari NA, Ortega-Sanchez IR, Messonnier ML, et al. The annual impact of seasonal influenza in the Us: measuring disease burden and costs. Vaccine **2007**; 25:5086–5096.
29. Jain S, Kamimoto L, Bramley AM, et al. Hospitalized patients with 2009 H1N1 influenza in the United States, April-June 2009. N Engl J Med **2009**; 361:1935–1944.
30. Patients hospitalized with 2009 pandemic influenza a (H1N1) - New York City, May 2009. MMWR Morb Mortal Wkly Rep **2010**; 58:1436–1440.
31. Centers for Disease Control and Prevention, Hospitalized patients with novel influenza a (H1N1) virus infection - California, April-May, 2009. MMWR Morb Mortal Wkly Rep **2009**; 58:536–541.
32. 2009H1N1 flu: underlying health conditions among hospitalized adults and children http://www.cdc.gov/H1N1flu/eip_underlying_conditions.htm. Accessed 1 March 2010.
33. Centers for Disease Control and Prevention, Intensive-care patients with severe novel influenza a (H1N1) virus infection - Michigan, June 2009. MMWR Morb Mortal Wkly Rep **2009**; 58:749–752.
34. Dominguez-Cherit G, Lapinsky SE, Macias AE, et al. Critically ill patients with 2009 influenza a(H1N1) in Mexico. JAMA **2009**; 302:1880–1887.
35. Kumar A, Zarychanski R, Pinto R, et al. Critically ill patients with 2009 influenza a(H1N1) infection in Canada. JAMA **2009**; 302:1872–1879.
36. Centers for Disease Control and Prevention. Use of influenza a (H1N1) 2009 monovalent vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2009. MMWR Recomm Rep **2009**; 58:1–8.
37. Morgan OW, Bramley A, Fowlkes A, et al. Morbid obesity as a risk factor for hospitalization and death due to 2009 pandemic influenza a(H1N1) disease. PLoS One **2010**;5:e9694.
38. Centers for Disease Control and Prevention, Deaths related to 2009 pandemic influenza a (H1N1) among American Indian/Alaska Natives - 12 States, 2009. MMWR Morb Mortal Wkly Rep **2009**; 58: 1341–1344.
39. Thompson WW, Shay DK, Weintraub E, et al. Mortality associated with influenza and respiratory syncytial virus in the United States. JAMA **2003**; 289:179–186.
40. Simonsen L, Schonberger LB, Stroup DF, Arden NH, Cox NJ. Impact of influenza on mortality in the USA. In: options for the control of influenza iII: proceedings of the 3rd International Conference on options for the control of influenza. Australia. Cairns: Elsevier Science, 1996; 26–33.
41. Fowlkes A, Arguin P, Biggerstaff M, et al. Epidemiology of 2009 pandemic influenza A (H1N1)-associated deaths in the United States, April–July 2009. Placeholder. Fowlkes. Clin Infect Dis.
42. Cox CM, Blanton L, Dhara R, Brammer L, Finelli L. 2009 pandemic influenza A (H1N1) deaths among children—United States, 2009–2010. Placeholder. Cox. Clin Infect Dis.
43. Cox S, Posner SF, McPheeters M, Jamieson DJ, Kourtis AP, Meikle S. Hospitalizations with respiratory illness among pregnant women during influenza season. Obstet Gynecol **2006**; 107:1315–1322.
44. Gonik B. Viral diseases in pregnancy. New York: Springer-Verlag, 1994.
45. Neuzil KM, Reed GW, Mitchel EF, Simonsen L, Griffin MR. Impact of influenza on acute cardiopulmonary hospitalizations in pregnant women. Am J Epidemiol **1998**; 148:1094–1102.
46. Schoenbaum SC, Weinstein L. Respiratory infection in pregnancy. Clin Obstet Gynecol **1979**; 22:293–300.
47. Shahab S, Glezen W. Viral diseases in pregnancy. New York: Springer-Verlag, 1994.
48. Widelock D, Csizmas L, Klein S. Influenza, pregnancy, and fetal outcome. Public Health Rep **1963**; 78:1–11.
49. Freeman DW, Barno A. Deaths from Asian influenza associated with pregnancy. Am J Obstet Gynecol **1959**; 78:1172–1175.
50. Nuzum JW, Pilot I, Stangl FH, Bonar BE. 1918 Pandemic influenza and pneumonia in a large civil hospital. IMJ Ill Med J **1976**; 150:612–616.
51. Dodds L, McNeil SA, Fell DB, et al. Impact of influenza exposure on rates of hospital admissions and physician visits because of respiratory illness among pregnant women. Cmaj **2007**; 176:463–468.
52. Hartert TV, Neuzil KM, Shintani AK, et al. Maternal morbidity and perinatal outcomes among pregnant women with respiratory hospitalizations during influenza season. Am J Obstet Gynecol **2003**; 189:1705–1712.
53. Lindsay L, Jackson LA, Savitz DA, et al. Community influenza activity and risk of acute influenza-like illness episodes among healthy unvaccinated pregnant and postpartum women. Am J Epidemiol **2006**; 163:838–848.
54. Centers for Disease Control and Prevention, Novel influenza a (H1N1) virus infections in three pregnant women - United States, April-May 2009. MMWR Morb Mortal Wkly Rep **2009**; 58:497–500.
55. Jamieson DJ, Honein MA, Rasmussen SA, et al. H1N1 2009 influenza virus infection during pregnancy in the USA. Lancet **2009**; 374:451–458.
56. Louie JK, Acosta M, Jamieson DJ, Honein MA. Severe 2009 H1N1 influenza in pregnant and postpartum women in California. N Engl J Med **2010**; 362:27–35.
57. Siston AM, Rasmussen SA, Honein MA, et al. Pandemic 2009 influenza a(H1N1) virus illness among pregnant women in the United States. JAMA **2010**; 303:1517–1525.
58. Behavioral risk factor surveillance system http://www.cdc.gov/brfss. Accessed 24 February 2010.
59. Reed C, Angulo FJ, Biggerstaff M, Swerdlow D, Finelli L. Influenza-like illness in the community during the emergence of 2009 pandemic influenza A/H1N1 – Ten US States, April 2009. Clin Infect Dis.
60. Janusz KB, Cortes JE, Serdarevic F, et al. Influenza-like illness in a community surrounding a school-based outbreak of 2009 pandemic

Downloaded from https://academic.oup.com/cid/article/52/suppl_1/S13/498323 by U.S. Department of Justice user on 16 August 2022

influenza A (H1N1) virus – Chicago, Illinois, 2009. Emerg Infect Dis 2010.
61. Prevalence of flu-like illness in New York City: May 2009. New York: New York City Department of Health and Mental Hygiene, **2009**.
62. Prevalence of flu-like symptoms in New York City: May/June 2009. New York: New York City Department of Health and Mental Hygiene, **2009**.
63. Iuliano AD, Reed C, Guh A, et al. Notes from the field: outbreak of 2009 pandemic influenza a (H1N1) virus at a large public University in Delaware, April-May 2009. Clin Infect Dis **2009**; 49:1811–1820.
64. Centers for Disease Control and Prevention. Interim pre-pandemic planning guidance: community strategy for pandemic influenza mitigation in the United States **2007.**
65. Longini IM Jr., Koopman JS, Monto AS, Fox JP. Estimating household and community transmission parameters for influenza. Am J Epidemiol **1982**; 115:736–751.
66. Morgan OW, Parks S, Shim T, et al. Household transmission of pandemic (H1N1) 2009, San Antonio, Texas, USA. Emerg Infect Dis **2010**; 16.
67. France AM, Jackson M, Schrag S, et al. Household transmission of 2009 influenza a (H1N1) virus after a school-based outbreak in New York City, April-May 2009. J Infect Dis **2010**; 201:984–992.
68. Andreasen V, Viboud C, Simonsen L. Epidemiologic characterization of the 1918 influenza pandemic summer wave in copenhagen: implications for pandemic control strategies. J Infect Dis **2008**; 197: 270–278.
69. Fraser C, Donnelly CA, Cauchemez S, et al. Pandemic potential of a strain of influenza a (H1N1): early findings. Science **2009**; 324:1557–1561.
70. Yang Y, Sugimoto JD, Halloran ME, et al. The transmissibility and control of pandemic influenza a (H1N1) virus. Science **2009**; 326: 729–733.
71. Anderson RM, May RM. Infectious diseases of humans: dynamics and control, Oxford ; New York: Oxford University Press **1991**.
72. Rothman KJ, Greenland S, Lash TL. Modern epidemiology, 3rd ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, **2008**.
73. Cowling BJ, Fang VJ, Riley S, Malik Peiris JS, Leung GM. Estimation of the serial interval of influenza. Epidemiology **2009**; 20:344–347.
74. White LF, Pagano M. Transmissibility of the influenza virus in the 1918 pandemic. PloS One, **2008**; 3.
75. Reed C, Angulo FJ, Swerdlow DL, et al. estimates of the prevalence of pandemic (H1N1) 2009, United States, April-July 2009. Emerg Infect Dis **2009**; 15:2004–2007.
76. CDC estimates of 2009 H1N1 influenza cases, hospitalizations and deaths in the United States, April 2009 – January 16, 2010 http://www.cdc.gov/h1n1flu/estimates_2009_h1n1.htm. Accessed 3 March 2010.
77. Shrestha SS, Swerdlow DL, Borse RH, et al. Estimating the burden of 2009 pandemic influenza A (H1N1) in the United States (April 2009 – January, 2010). Clin Infect Dis.
78. Chowell G, Ammon CE, Hengartner NW, Hyman JM. Transmission dynamics of the great influenza pandemic of 1918 in Geneva, Switzerland: assessing the effects of hypothetical interventions. J Theor Biol **2006**; 241:193–204.
79. Olson DR, Simonsen L, Edelson PJ, Morse SS. Epidemiological evidence of an early wave of the 1918 influenza pandemic in New York City. Proc Natl Acad Sci U S A **2005**; 102:11059–11063.
80. Siston AM, Rasmussen SA, Honein MA, et al. Pandemic 2009 Influenza a(H1N1) Virus Illness among Pregnant Women in the United States. Jama **2010**; 303:1517–25.
81. ACIP provisional recommendations for the Use of influenza vaccines. Atlanta, GA: Meeting of the Advisory Committee on Immunization Practices (ACIP), **2010**.

Downloaded from https://academic.oup.com/cid/article/52/suppl_1/S13/498323 by U.S. Department of Justice user on 16 August 2022