

# Impact of the Novel Influenza A (H1N1) during the 2009 Autumn-Winter Season in a Large Hospital Setting in Santiago, Chile

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(See the editorial commentary by Glezen, on pages XXX–XXX.)

**Background.** In Chile, the novel influenza A (H1N1) epidemic began in the middle-high income area of Santiago. Clinical and laboratory surveillance was intensified with the aim to characterize the epidemic and determine its impact in a large hospital setting.

**Methods.** Demographic and clinical data were obtained from all patients whose symptoms met the clinical definition of influenza A (H1N1) infection during the epidemic period. Laboratory confirmation was obtained by use of a nasopharyngeal antigen detection test for influenza A and/or influenza A (H1N1) polymerase chain reaction (PCR). A case was considered confirmed if the antigen detection test result for influenza A and/or the PCR test result were positive.

**Results.** The total number of emergency department (ED) visits increased by 88.5% from a mean of 14,489 ED visits in 2006–2008 to a mean of 27,308 ED visits in 2009, during the epidemic period. There were 10,048 patients who were clinically diagnosed with influenza A (H1N1), and they represented 78% of all visits, of which 4591 (45.6%) were laboratory confirmed. The median time from symptom onset to diagnosis was 1 day, and 99.7% of individuals received antiviral treatment. School-aged children represented 67% of ED visits at the beginning of the epidemic and 24% of ED visits at the end of the epidemic. Only 2% of cases were hospitalized; of these, 70% of cases occurred in patients 6–50 years of age, and 32% of cases occurred in patients who had an underlying medical condition. Eleven patients (age range, 1–53 years) required admission to the intensive care unit (ICU); 6 of these patients had pneumonia with or without hemodynamic shock. No influenza-associated deaths occurred.

**Conclusions.** Many cases of influenza A (H1N1) occurred in school-aged and adult individuals who required an ED visit; these visits resulted in a low impact on the use of hospital beds. Aggressive ICU management and/or experience in extracorporeal membrane oxygenation significantly improved outcomes. Early antiviral treatment may have played an important role in the low number of severe cases. Vaccines targeted for school-aged children and young adults may modify the first epidemic wave in the northern hemisphere.

The novel influenza A (H1N1) virus was first identified in Mexico in April 2009 [1]. The initiation of the epidemic in the northern hemisphere coincided with the onset of the spring, when seasonal influenza

virus circulation tends to decrease [2]. The first case of influenza A (H1N1) in the southern hemisphere was reported in New Zealand, on 28 April [3]. In countries in the Southern Cone of America, the novel virus was introduced during the fall [4]. The impact of the new human influenza virus epidemic could thus be assessed throughout the fall and winter flu season. Chile is a country with a population of 16.6 million, and 5 million reside in Santiago. On 17 May, the first case of influenza A (H1N1) was detected in a young woman returning from the Dominican Republic, followed 2 days later by a 6-year-old boy with a mild case of influenza A (H1N1) [5].

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The government response was rapid and included a number of measures supported by a panel of experts in infectious diseases. Initial measures were intended to contain the epidemic wave in accordance with the World Health Organization recommendations. Nevertheless, within the next 2 weeks, a rapid progression of reported cases occurred among schools within the eastern area of the city. By the end of May, 13 schools within this area reported several cases, with 276 confirmed cases in the country [6].

The eastern area of Santiago contains most of the middle-high income population of Chile. The Clínica Las Condes (CLC) is 1 of 3 large private hospitals that provide medical care for individuals living in this area. The hospital rapidly implemented the government recommendations and, in addition, adopted an intensified plan for segregating, evaluating, testing, and tabulating patients with influenza-like illness (ILI).

This report provides relevant clinical and laboratory information on the 10,048 patients diagnosed with influenza A (H1N1), with and without laboratory confirmation, who received medical care as outpatients or inpatients in the CLC throughout the epidemic wave.

## METHODS

**Population and hospital attributes.** The eastern area of Santiago has a population of nearly 400,000 people, 95% of whom belong to the ABC1 socioeconomic classification that represents the upper 10% of the country in terms of socioeconomic status (eg, family income over US\$5000 per month, living in a house  $\geq 100$  square meters in size, and owning  $\geq 1$  car). Individuals living in the area seek medical attention at 3 private hospitals (95% of the population) and at 1 public hospital (5%). The CLC is the second largest private hospital in the area, with 204 adult beds and 51 pediatric beds. The hospital has had the most experience in treating patients with extracorporeal membrane oxygenation (ECMO) in Chile.

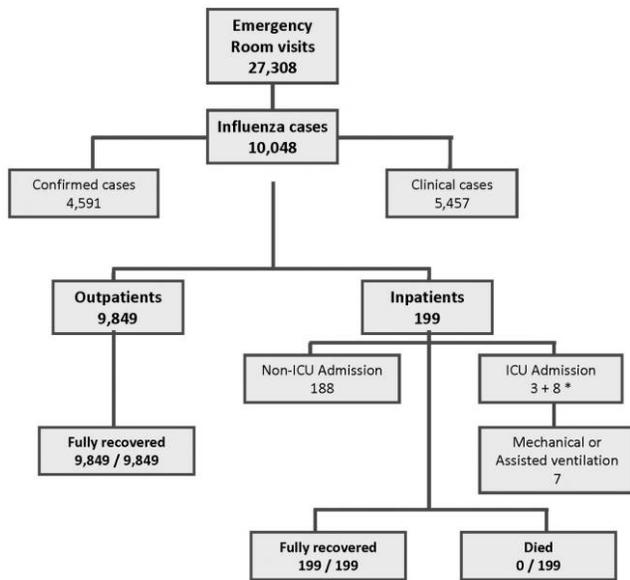
**Influenza A (H1N1) surveillance.** The CLC followed the guidelines recommended by the Health Ministry for case identification and reporting as follows: From 29 April to 28 May, all individuals visiting the emergency department (ED) whose symptoms met the clinical definition of influenza A (H1N1) were isolated and tested for influenza A by use of a rapid antigen detection test and, if the test result was negative, by use of a direct fluorescence antibody (DFA) test; on 15 May, real-time polymerase chain reaction (PCR) for the novel influenza A (H1N1) was developed and standardized at the CLC. Parallel testing of the first 196 samples showed 100% concordance with the influenza A (H1N1) PCR implemented at the Chilean Institute of Public Health. From 18 May to 28 May, all presumptive patients were studied by use of the rapid test and influenza A (H1N1) PCR. From 28 May, patients with ILI were

studied using the rapid test and PCR for influenza A (H1N1) only when the rapid test had a negative result. From 25 June onward, the epidemic was considered widespread within the metropolitan region, and laboratory confirmation was no longer mandatory. The ongoing surveillance for respiratory viruses in the National Surveillance System indicated that  $>90\%$  of cases of ILI that occurred in individuals  $>5$  years of age were caused by influenza A (H1N1), and that  $\approx 50\%$  of cases of ILI that occurred in children  $<5$  years of age were caused by influenza A (H1N1). On the basis of these findings, the new guidelines allowed the prescription of oseltamivir for all individuals  $>5$  years of age whose symptoms met the newly defined, more stringent criteria for ILI [7]. The guidelines also recommended that children  $<5$  years of age with fever and cough be tested for influenza A (H1N1) before receiving treatment. Testing for individuals whose symptoms did not meet the clinical criteria for ILI was discouraged.

**Sample collection and laboratory tests used for identification of cases.** Nasopharyngeal aspirate samples resuspended on 4 mL of phosphate-buffered saline were obtained for all viral testing techniques. A rapid antigen detection test for influenza A and B (Quickvue; Quidel) was performed according to the manufacturer's instructions [8]. In-house real-time PCR for influenza A (H1N1) virus [RealTime ready Influenza A/ (H1N1) Detection Set; Roche] was based on the detection of the conserved matrix protein 2 gene, and subtype identification was based on the detection of the H1 hemagglutinin gene. The test was performed according to the manufacturer's instructions, with secondary confirmation of positive samples at the Chilean Institute of Public Health [9]. A DFA test for influenza A and B, respiratory syncytial virus (RSV), adenovirus, and parainfluenza viruses 1, 2, and 3 (Light Diagnostics; Millipore) [10] was performed for a subset of individuals.

**Case definition of influenza A (H1N1).** A laboratory confirmed case of influenza A (H1N1) required a positive rapid test result or a positive DFA test result for influenza A and/or a positive PCR result for influenza A (H1N1) virus from a nasopharyngeal sample. A positive rapid test result for influenza A was considered diagnostic since parallel testing by PCR documented that 97% of the first 196 samples obtained during the outbreak were positive using both methods (data not shown). A case of ILI was considered clinical influenza A (H1N1) if the patient's symptoms met the standardized clinical criteria, even though a viral diagnostic test had not been performed.

**Data collection and analysis.** We collected data on (1) the number of daily ED visits during the outbreak; (2) the age, sex, number of days from symptom onset to diagnosis, and type of antiviral treatment of patients with confirmed or clinical influenza A (H1N1) infection; (3) the disease burden among hospitalized individuals; and (4) cocirculating respiratory vi-



**Figure 1.** Flowchart of influenza-associated emergency department visits for the 2-month influenza epidemic period (from 17 May to 17 July 2009). \*Three cases were admitted directly from the emergency department, and 8 cases were referred from outside hospitals. ICU, intensive care unit.

rus. Differences between groups were tested using the *t* test or the Mann-Whitney test, according to data distribution. The  $\chi^2$  test with Yates correction for continuity or the Fisher exact test was used for associations between categorical variables. All tests were 2 tailed, and a *P* value of  $<.05$  was considered to be statistically significant. For all statistical analyses, Sigma Stat

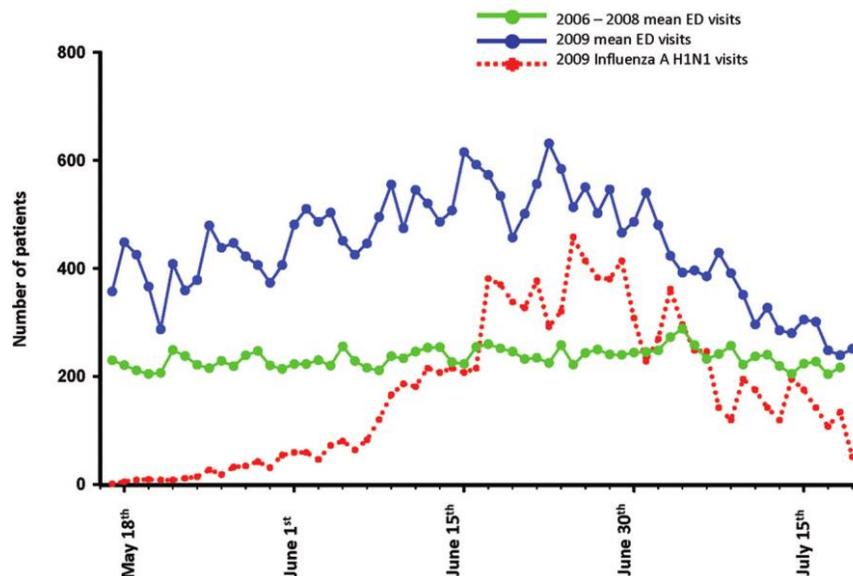
software, version 3.0 (SPSS Science), was used. The study was approved by the ethics committee of the CLC.

## RESULTS

**ED visits during the influenza epidemic.** From 17 May to 17 July 2009, a total of 27,308 individuals were seen in the hospital ED, ranging from 357 individuals per day at the beginning of the epidemic to 631 individuals per day at the peak of the epidemic (22 June) to 251 individuals per day at the end of the epidemic (Figures 1 and 2). The total number of ED visits increased by 88.5%, compared with the mean number of visits for 2006–2008 during the same 2-month period. During the peak of the epidemic, the number of ED visits per day tripled the mean value, compared with the previous 3 years (Figure 2). During the epidemic, a total of 10,048 patients received a final diagnosis of influenza A (H1N1) representing 36.8% of all ED visits for the 2009 epidemic period and 78% of all excess visits, compared with the mean ED visits for the previous 3 years during the same period of time. Except for a slight delay in the onset, the curve for influenza-associated ED visits per day paralleled the curve of increase in the 2009 ED visits per day (Figure 2).

### Characterization of cases diagnosed as influenza A (H1N1).

A total of 4591 (45.6%) of 10,048 patients who received a diagnosis of influenza A (H1N1) had their diagnosis confirmed in the laboratory according to the following distribution: positive test result by influenza A rapid antigen testing for only 3110 patients (67%), by DFA test for only 67 patients (1.4%),



**Figure 2.** Line graph showing comparison of daily emergency department (ED) visits occurring during the 2-month epidemic period for years 2006–2008 and year 2009, including influenza-associated visits for 2009.

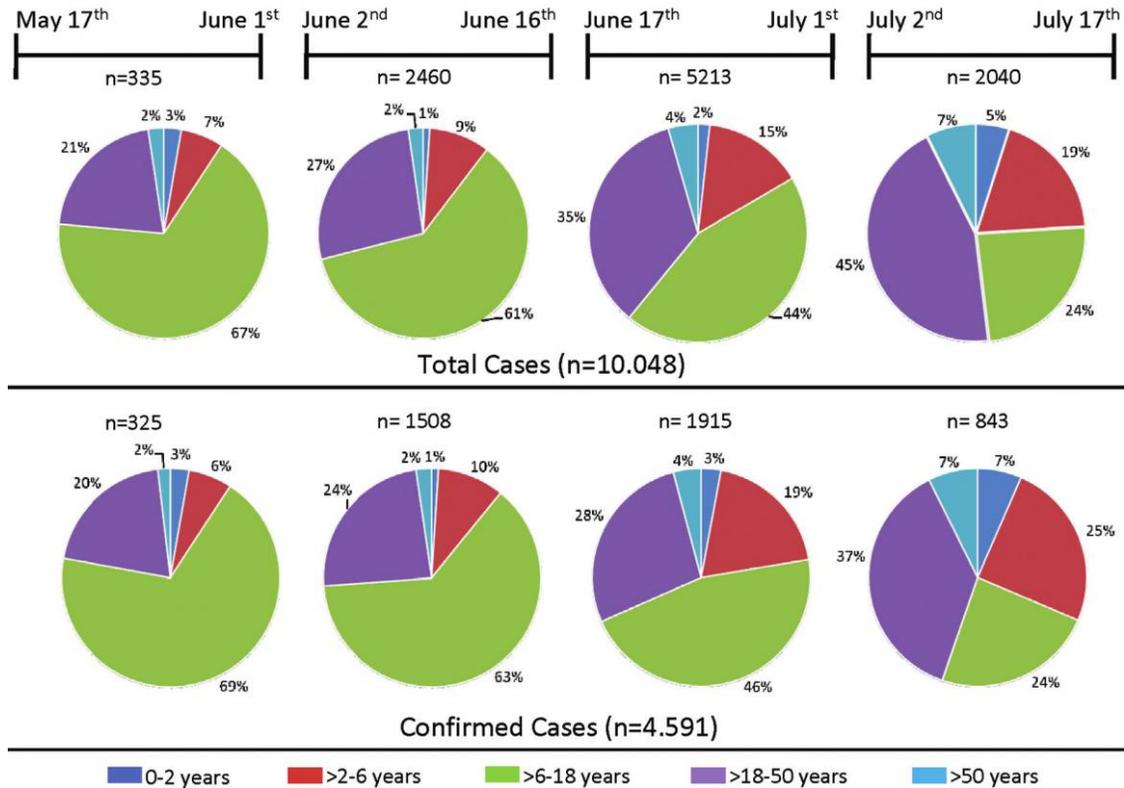
**Table 1. Demographic and Clinical Characteristics of Patients with a Confirmed or Clinical Case of Influenza A (H1N1)**

Characteristic	Patients with a confirmed case (n = 4591)	Patients with a clinical case (n = 5457)	All patients (n = 10,048)
<b>Age groups</b>			
<1 year	16 (0.3)	13 (0.2)	29 (0.3)
1–2 years	119 (2.6)	78 (1.4)	197 (1.9)
3–5 years	752 (16.4)	662 (12.1)	1414 (14.1)
6–18 years	2255 (49.1)	2264 (41.5)	4519 (45)
19–50 years	1267 (27.6)	2178 (39.9)	3445 (34.3)
>50 years	182 (4.0)	262 (4.8)	444 (4.4)
Age, median years	11	14	13
Female sex	2266 (49.4)	2875 (52.7)	5141 (51.2)
<b>Time from symptom onset to diagnosis, days</b>			
Mean	1.6	1.2	1.4
Median (range)	1 (0–22)	1 (0–10)	1 (0–22)
Antiviral treatment	4563 (99.4)	5452 (99.9)	10,015 (99.7)

**NOTE.** Data are no. (%) of patients, unless otherwise indicated.

by influenza A (H1N1) PCR for only 1289 patients (28%), and by both antigen testing and PCR for 125 patients (2.7%). The remaining 5457 patients fulfilled the clinical definition and received a diagnosis of clinical influenza A, but they were not tested (Figure 1).

Overall, there was a mild predominance of female patients (51.2%), and the median age of affected individuals was 13 years (Table 1). Only 54% of children <5 years of age underwent viral diagnostic testing, despite the recommendation of laboratory confirmation for this age range. Compared with the



**Figure 3.** Pie charts showing the age stratification of total and confirmed cases of influenza that required a visit throughout the 2-month epidemic period.

**Table 2. Demographic and Clinical Characteristics of Individuals Hospitalized for Management of Influenza A (H1N1) Infection**

Characteristic	Individuals (n = 99)
Laboratory confirmation	187 (94)
Age, <sup>a</sup> median (range), years	26 (<1–82)
Age groups	
<1 year	3 (1.5)
1–2 years	4 (2.0)
3–5 years	21 (10.6)
6–18 years	42 (21.1)
19–50 years	99 (49.7)
>50 years	30 (15.1)
Female sex	122 (61.3)
Symptoms at admission <sup>b</sup>	
Fever	162 (81.4)
Cough	148 (74.4)
Myalgia	119 (59.8)
Odynophagia	89 (44.7)
Dehydration	28 (14.1)
Underlying disease <sup>c</sup>	63 (31.7)
Pregnant	12 (6.0)
Pneumonia	26 (13.1)
Received seasonal influenza vaccine <sup>d</sup>	59 (29.6)
Received antiviral treatment	
Oseltamivir	168 (84.4)
Zanamivir	10 (5.1)
Total	178 (89.5)
Median days (range) of hospitalization	2 (1–57)
Duration of hospitalization	
0–2 days	125 (62.8)
3–5 days	53 (26.6)
6–10 days	12 (6.0)
>10 days	9 (4.6)

**NOTE.** Data are no. (%) of patients, unless otherwise indicated.

<sup>a</sup> The youngest child was 1 month and 1 day of age.

<sup>b</sup> With regard to the proportion of individuals presenting with any of the symptoms indicated, the patients with a confirmed case (n = 187) did not differ from the patients with a clinical case (n = 12).

<sup>c</sup> The following underlying conditions were diagnosed: asthma (17 patients), chronic obstructive pulmonary disease (6 patients), other respiratory conditions (2 patients), diabetes mellitus (6 patients), hypothyroidism (6 patients), hypertension (5 patients), coronary disease (4 patients), dyslipidemias (2 patients), genetic disease (5 patients), malignancies (3 patients), and/or some other conditions (10 patients).

<sup>d</sup> Information obtained retrospectively for 175 individuals.

patients who had received a clinical diagnosis, patients with confirmed influenza A (H1N1) were predominantly male and had a lower median age ( $P < .01$  for sex and age, respectively). For the first 1093 individuals with confirmed influenza A (H1N1), a more detailed clinical history was available that indicated the following findings: fever (83% of patients), cough (72%), odynophagia (54%), myalgia (48%), and dehydration (4%). Diagnosis occurred mostly within the first 2 days of symptom onset with a median of 1 day. Records on antiviral

treatment were available for 9271 patients (92.3%), of whom 9218 (99.4%) received oseltamivir, 29 (0.3%) received zanamivir, and 24 (0.3%) received no treatment. Ninety-eight percent of patients with influenza A were managed as outpatients, and there were no deaths attributed to this novel virus.

The age distribution of patients who required a visit shifted throughout the course of the epidemic (Figure 3). At the beginning, both total and confirmed cases of influenza A (H1N1) occurred mostly in school-aged children, followed by a progressive increase among adults 18–50 year of age and preschool children 2–6 years of age. Young infants and older adults represented only 5% of the total number of patients who received a diagnosis at the beginning of the epidemic, but they represented 12% of the total toward the end of the epidemic.

**Influenza A (H1N1)-associated hospitalizations.** The great majority (94%) of individuals hospitalized with influenza A (H1N1) had their diagnoses confirmed in the laboratory (Table 2). The ages of hospitalized individuals ranged from 6 to 50 years, with more female patients when compared with all influenza cases (61.3% vs 51.1%;  $P < .001$ ). Symptoms on admission were compatible with an ILI. Thirty-two percent of patients had an identifiable underlying medical condition, the most common being a respiratory disorder (12.5%); 12 pregnant women (6%) required hospitalization. Nearly 30% of individuals had received the seasonal influenza vaccine, and most (83.4%) received an antiviral drug after diagnosis. Hospitalizations were mostly short stays, with only 9.5% of hospitalized individuals staying >6 days. The most significant complication observed among individuals with influenza A (H1N1) was pneumonia. Eleven patients required medical care in the intensive care unit (ICU), 8 of whom were referrals from outside hospitals. Thus, only 3 patients representing 1.5% and 0.03% of hospitalized and total influenza cases seen at the hospital's ED, respectively, had a severe clinical course (Figure 1 and Table 3). Severe disease characterized mostly by the presence of pneumonia (6 individuals) with or without hemodynamic shock occurred similarly in all age groups except for the elderly; 2 individuals had severe bronchial obstruction, and 2 developed neurological symptoms. All 11 ICU patients recovered completely. The most severe case occurred in a 38-year-old woman, without a recognized underlying condition. The patient required intense ventilatory support, including 13 days of ECMO. She was discharged after 57 days of hospitalization without any identifiable sequelae.

**Respiratory virus detection during the influenza epidemic.** During the 2 months of the study, a total of 22,585 viral tests were performed for 12,281 individuals with the following overall positivity: 4591 (38.3%) of 11,972 test results were positive for influenza A (by use of any of the 3 methods described); 630 (19.8%) of 3189 test results were positive for RSV; 90 (2.9%) of 3115 test results were positive for adenovirus; 108

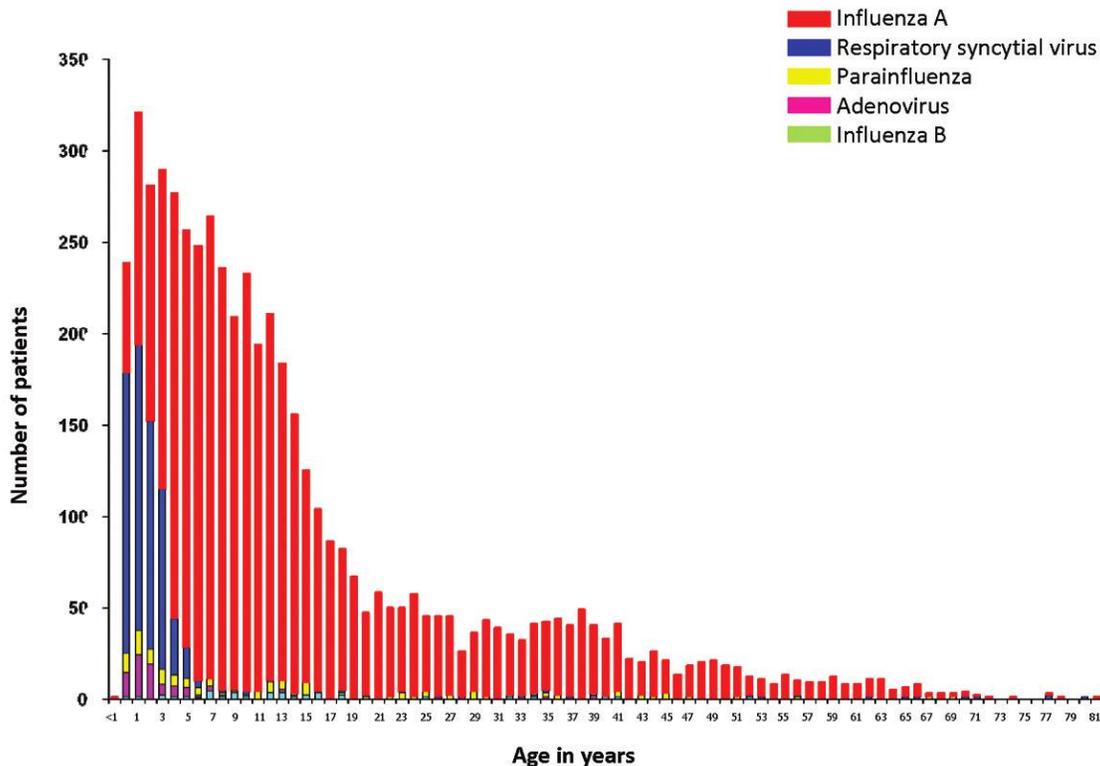
**Table 3. Relevant Characteristics of 11 Patients with Influenza A (H1N1) That Required Medical Care in the Intensive Care Unit**

Patient	Diagnostic test(s) used <sup>a</sup>	Age, years	Sex	Comorbidity	Nutritional status	Type of treatment	Hospital-days	Relevant clinical features
1	RAD test and PCR	10	M	Asthma	Overweight	Oseltamivir, bronchodilator, antibiotics	5	Severe bronchial obstruction <sup>b</sup>
2	PCR	13	F	Asthma	Overweight	Oseltamivir, bronchodilator, noninvasive ventilation	4	Severe bronchial obstruction
3	DFA test and PCR	7	M	Asthma	Eutrophic	Oseltamivir, noninvasive ventilation, antibiotics	6	Pleuropneumonia, cardiovascular shock <sup>b</sup>
4	DFA test and PCR	1	M	Bronchopulmonary dysplasia	Eutrophic	Oseltamivir, invasive ventilation, antibiotics	24	Severe bilateral pneumonia, pneumothorax <sup>b</sup>
5	RAD and DFA tests, and PCR	10	F	None	Eutrophic	Oseltamivir	3	Febrile seizure <sup>b</sup>
6	PCR	6	F	Congenital heart disease	Eutrophic	Oseltamivir, antibiotics, noninvasive ventilation	7	Bilateral pneumonia <sup>b</sup>
7	DFA test and PCR	5	M	Asthma	Eutrophic	Oseltamivir, antibiotics	4	Coinfection with pharyngeal group A streptococci
8	RAD test	1	F	Dandy-Walker syndrome	Eutrophic	Oseltamivir	6	Status epilepticus, pneumonia
9	DFA test	8	F	None	Malnutrition	Oseltamivir, antibiotics, invasive ventilation	13	Pleuropneumonia, septic shock <sup>b</sup>
10	PCR	39	F	None	Overweight	Oseltamivir, ECMO, invasive ventilation, antibiotics	57	Respiratory distress, severe bilateral pneumonia, cardiovascular shock <sup>b</sup>
11	RAD test and PCR	54	M	Diabetes mellitus	Malnutrition	Oseltamivir, noninvasive ventilation	12	Chronic liver disease, mild to moderate respiratory distress <sup>b</sup>

**NOTE.** DFA, direct fluorescence antibody; ECMO, extracorporeal membrane oxygenation; PCR, polymerase chain reaction; RAD, rapid antigen detection.

<sup>a</sup> Time from symptom onset to diagnosis for all 11 patients: mean, 2.2 days; median (range), 2 days (1–5 days).

<sup>b</sup> Referrals from outside hospitals.



**Figure 4.** Bar graph showing age distribution of respiratory viruses during the 2-month influenza A epidemic.

(7.2%) of 1493 test results were positive for parainfluenza; and 3 (0.1%) of 2816 test results were positive for influenza B. Distribution of virus positivity by age is displayed in Figure 4. Among individuals >5 years of age, 3682 (96.7%) of 3804 virus-positive cases were associated with influenza A; among children <5 years of age, 964 (56%) of 1716 virus-positive cases were associated with influenza A ( $P < .001$ ). In the latter age group, RSV represented 34.7% of the virus-positive cases, and 596 (29.3%) of the 2030 children tested were positive for RSV, compared with only 2.9% of the 1159 individuals tested who were >5 years of age ( $P < .001$ ). Viral coinfections were detected in 11 (0.9%) of 1197 patients who tested positive for influenza A, of whom 10 had RSV and 1 had parainfluenza.

## DISCUSSION

The impact of the novel influenza A (H1N1) epidemic on this large Chilean hospital during the 2-month autumn-winter period was observed mostly at the ED level, in which visits nearly doubled compared with the previous 3 years. This situation caused significant delays in patient attendance from the regular 10–15 minutes to 2–3 h. The number of individuals hospitalized was low and represented only 2% of the ED visits for ILI and 0.1% of ICU admissions. None of the patients seeking medical care in this hospital died due to influenza, although 1 patient required prolonged treatment in ECMO, a situation that would

have been fatal in many regions of the world where this advanced procedure is not available. The above-described situation occurred in a population that rapidly sought medical care (most within 48 h of symptom onset), the great majority of whom received antiviral treatment. This aggressive approach may have had a favorable impact on the relatively low number of severe cases diagnosed and on the positive outcomes observed during the epidemic. It is noteworthy that none of the 12 pregnant women (who were all treated) had a severe outcome, which differs from reports of an increased lethality for this group in other countries [11].

The distribution of influenza A (H1N1) cases in this population by sex and age group was similar to the distribution of cases observed worldwide, which was characterized by a concentration of cases in the 6–50-year-old age bracket that was predominantly female [3, 12–17]. The observation of a shift in the predominant age distribution of individuals diagnosed with the novel influenza A (H1N1) throughout the epidemic can aid in the preparedness of EDs in northern hemisphere countries; hospital staff should be prepared for an excess of visits for mostly school-aged children and young adults at the beginning of the epidemic, followed by a rapid increase in visits for older individuals and, to a lesser extent, for younger individuals.

Hospitalizations were a consequence of a variety of reasons

and not necessarily due to a strict medical indication; only one-third of hospitalized individuals had an identifiable underlying condition. The majority of hospitalized individuals had mild disease requiring only a few days of hospitalization. Of interest was the higher proportion of women hospitalized, compared with those who seek medical attention in the ED. This observation does not seem to reflect a more severe outcome for women because the distribution of more severe cases requiring ICU management was evenly distributed between women and men. Severe cases requiring management in the ICU occurred in all age groups but mostly in individuals with an underlying condition.

The hospitalization rate in Chile was 503 cases per 100,000 infected individuals, and the lethality rate was 38 cases per 100,000 infected individuals, when considering notified cases [18]. The true hospitalization and lethality rates would have probably been less than half if many of the cases that were not notified were included. In our study, the hospitalization rate was more than double (1980 cases per 100,000 infected individuals), most probably reflecting the increased awareness and laxness of criteria for hospitalization in the private hospital. Overall, deaths attributable to influenza A (H1N1) were low countrywide (38 deaths per 100,000 notified cases), even in high-risk groups such as pregnant women (1 in 65). We believe that this is a consequence of the aggressive strategy implemented in Chile; this strategy included raising awareness, rapid identification of cases, and massive antiviral treatment [19]. The effectiveness of contact treatment could not be measured in our study. Nationwide, although initially proposed by the expert advisory panel, this measure was rapidly discontinued as a result of logistic complications and because of its probable lack of effectiveness.

The influenza epidemic occurred simultaneously with the autumn-winter peak of RSV infection. The latter virus caused the majority of ED visits and hospitalizations (data not shown) among children <3 years of age. In this age range, ILI caused a significant increase in the number of visits to the ED and a relatively moderate impact on the number of hospitalizations. The most significant impact of influenza A (H1N1) on hospitalizations was observed among older children and adults. This situation tends to differ from the overall country report that describes the highest rates of hospitalizations occurring among children <1 year of age [20]. Although countrywide data are not directly comparable to our data, this observation may be the result of differences in timely consultation among parents or caregivers from different socioeconomic settings, or it may be the result of the viral diagnostic testing performed; however, this hypothesis would need to be confirmed. Interestingly, we documented a very low number of viral coinfections among cases of laboratory-confirmed influenza A (H1N1)

and an exceedingly low number of circulating seasonal influenza A or B viruses during the epidemic.

The main limitation of our study is the lack of influenza A (H1N1) virus confirmation for one-half of our patients. Information obtained in parallel provides reasonable certainty that the majority of cases, especially those occurring in patients >3 years of age, were truly influenza A (H1N1). For laboratory-confirmed cases of influenza A by antigen detection, it became clear from our initial pilot study of 196 samples that >97% of test results were positive for the novel virus; at the same time, it became clear that the sensitivity of the antigen detection test was low (56%), similar to other reports [8, 17]. Throughout the epidemic, the parallel national respiratory virus surveillance for ILI demonstrated that the clinical definition used had >90% sensitivity for individuals >5 years of age with influenza A (H1N1) and nearly 50% sensitivity for younger children. Thus, we strongly believe that the great majority of our 10,048 patients had influenza A (H1N1). Nevertheless, the number of non-confirmed ILI cases in children <5 years of age that may have been caused by a different respiratory virus represented a small proportion (13.8%) of the total cases.

Many school-aged and adult individuals ( $n = 10,048$ ) developed influenza A (H1N1) and required ED visits in this large Chilean hospital; these visits resulted in a low impact on the use of hospital beds. Aggressive ICU management and/or experience in ECMO significantly improved outcomes of our more severe cases. Indeed, no influenza-associated deaths were documented. For nonvaccinated communities, a similar scenario could be expected for hospitals in the northern hemisphere during the upcoming influenza season. Targeting school-aged children and young adults for vaccination before the first epidemic wave is encouraged in northern hemisphere countries, because this was clearly the most heavily affected age group in Chile, especially during the onset of the epidemic.

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## References

1. Neumann G, Noda T, Kawaoka Y. Emergence and pandemic potential of swine-origin H1N1 influenza virus. *Nature* **2009**;459(7249):931-939.
2. 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(25):2605-2615.
3. Surveillance for the 2009 pandemic influenza A (H1N1) virus and seasonal influenza viruses—New Zealand, 2009. *MMWR Morb Mortal Wkly Rep* **2009**;58(33):918-921.
4. Depoortere E, Mantero J, Lenglet A, Kreidl P, Coulombier D. Influenza A(H1N1)v in the southern hemisphere—lessons to learn for Europe? *Euro Surveill* **2009**;14(24):1-2.
5. Lagos R, Avendaño LF, Levine MM. Systematic surveillance of influ-

- enza, syncytial respiratory, parainfluenza and adenovirus in children with acute respiratory infections [in Spanish]. *Rev Med Chil* **1999**; 127(9):1063–1072.
6. Ministerio de Salud. Reporte diario de situación de influenza A-H1N1. 31 May 2009. <http://www.redsalud.gov.cl/portal/url/item/6b64ba57cbfea979e04001011f01072f.pdf>. Accessed 30 September 2009.
  7. Gobierno de Chile. Ministerio de Salud. Division de Prevención y Control de Enfermedades. Guía clínica para el manejo de casos nueva influenza humana A (H1N1) (IHA H1N1) etapa de mitigación. 9 June 2009. <http://www.redsalud.gov.cl/portal/url/item/6b14a541236acdeae04001011f010eda.pdf>. Accessed 30 September 2009.
  8. Vasoo S, Stevens J, Singh K. Rapid antigen tests for diagnosis of pandemic (swine) influenza A/H1N1. *Clin Infect Dis* **2009**; 49(7):1090–1093.
  9. Panning M, Eickmann M, Landt O, et al. Detection of influenza A(H1N1)v virus by real-time RT-PCR. *Euro Surveill* **2009**; 14(36):1–6.
  10. McIntosh K, Hendry RM, Fahnestock ML, Pierik LT. Enzyme-linked immunosorbent assay for detection of respiratory syncytial virus infection: application to clinical samples. *J Clin Microbiol* **1982**; 16(2): 329–333.
  11. Jamieson DJ, Honein MA, Rasmussen SA, et al. H1N1 2009 influenza virus infection during pregnancy in the USA. *Lancet* **2009**; 374(9688): 451–458.
  12. Rello J, Rodriguez A, Ibanez P, et al. Intensive care adult patients with severe respiratory failure caused by Influenza A (H1N1)v in Spain. *Crit Care* **2009**; 13(5):R148.
  13. Webb SA, Seppelt IM; ANZIC Influenza Investigators. Pandemic (H1N1) 2009 influenza (“swine flu”) in Australian and New Zealand intensive care. *Crit Care Resusc* **2009**; 11(3):170–172.
  14. Gilsdorf A, Poggensee G; Working Group Pandemic Influenza A(H1N1)v. Influenza A(H1N1)v in Germany: the first 10,000 cases. *Euro Surveill* **2009**; 14(34):1–4.
  15. Baker MG, Wilson N, Huang QS, et al. Pandemic influenza A(H1N1)v in New Zealand: the experience from April to August 2009. *Euro Surveill* **2009**; 14(34):1–6.
  16. Lister P, Reynolds F, Parslow R, et al. Swine-origin influenza virus H1N1, seasonal influenza virus, and critical illness in children. *Lancet* **2009**; 374(9690):605–607.
  17. Human infection with pandemic A (H1N1) 2009 influenza virus: clinical observations in hospitalized patients, Americas, July 2009—update. *Wkly Epidemiol Rec* **2009**; 84(30):305–308.
  18. Influenza pandémica (H1N1). Ministerio de Salud de Chile. Reporte 3 November 2009. [http://www.pandemia.cl/pagnew/prensa/REPORTE\\_04\\_11\\_09.pdf](http://www.pandemia.cl/pagnew/prensa/REPORTE_04_11_09.pdf). Accessed 30 September 2009.
  19. Piedra PA, Schulman KL, Blumentals WA. Effects of oseltamivir on influenza-related complications in children with chronic medical conditions. *Pediatrics* **2009**; 124(1):170–178.
  20. Influenza pandémica (H1N1). Ministerio de Salud de Chile. Reporte 9 September 2009. [http://www.pandemia.cl/pagnew/prensa/REPORTE\\_09\\_09\\_09.pdf](http://www.pandemia.cl/pagnew/prensa/REPORTE_09_09_09.pdf). Accessed 30 September 2009.