Population-based surveillance for 2009 pandemic influenza A (H1N1) virus in Guatemala, 2009

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Background In April 2009, 2009 pandemic influenza A H1N1 (2009 H1N1) was first identified in Mexico but did not cause widespread transmission in neighboring Guatemala until several weeks later.

Methodology and principle findings Using a population-based surveillance system for hospitalized pneumonia and influenza-like illness ongoing before the 2009 H1N1 pandemic began, we tracked the onset of 2009 H1N1 infection in Guatemala. We identified 239 individuals infected with influenza A (2009 H1N1) between May and December 2009, of whom 76 were hospitalized with pneumonia and 11 died (case fatality proportion: 4.6%, 95% confidence interval [CI] 2.3–8.1%). The median age of patients infected with 2009 H1N1 was 8.8 years, the median age of those hospitalized with pneumonia was 4.2 years, and five (45.5%) deaths occurred in children <5 years old. Crude rates of hospitalization between May and December 2009 were highest for children <5 years old. Twenty-one (27.6%) of the patients hospitalized with 2009 H1N1 were admitted to the intensive care unit and eight (10.5%) required mechanical ventilation. Underlying chronic conditions were noted in 14 (18.4%) of patients with pneumonia hospitalized with 2009 H1N1 infection.

Conclusions and significance Chronic illnesses may be underdiagnosed in Guatemala, making it difficult to identify this risk group for vaccination. Children 6 months to 5 years old should be among priority groups for vaccination to prevent serious consequences because of 2009 H1N1 infection.

Keywords Epidemiology, Guatemala, influenza, pandemic influenza, population-based.

Introduction On April 24, 2009, the World Health Organization (WHO) announced transmission of a novel influenza A H1N1 subtype in Mexico, the United States and Canada (http://www.who.int/csr/don/2009_04_24/en/index.html), and three days later raised the global pandemic alert level declaring an international health emergency. By December 30, 2009, more than 280 countries had reported laboratory-confirmed cases of 2009 pandemic influenza A (H1N1) virus (2009 H1N1) and more than 12,220 deaths had been reported to WHO (http://www.who.int/csr/don/2009_12_30/en/index.html).

Although bordering Mexico, there was no evidence of increased pneumonia or influenza-like illness (ILI) in the Republic of Guatemala in April 2009 and no reported cases of 2009 H1N1 until May 5 when an infection was confirmed in an 11-year-old girl returning from a vacation in Mexico. Since that time, 720 laboratory-confirmed cases and 12 deaths have been reported by the Guatemala Ministry of Public Health and Social Assistance (MSPAS in the Spanish acronym) (http://portal.mspas.gob.gt/index.php?ID=6128&action=display&ID_BOLETIN=151). In Guatemala, influenza surveillance is conducted through sentinel surveillance in selected ambulatory clinics for ILI and hospitals for severe acute respiratory infection (SARI) following guidelines developed by the Pan American Health Organization (PAHO) and the United States Centers for Disease Control and Prevention (CDC) (http://www.paho.org/English/AD/DPC/CD/flu-snl-gpis.pdf). In November 2007, CDC’s International Emerging Infections Program (IEIP), in collaboration with the MSPAS and the Universidad del Valle de Guatemala (UVG), began population-based surveillance for ILI and hospitalized pneumonia in the Department of Santa Rosa. This surveil-
lance system was extended to the Department of Quetzaltenango in February of 2009. Within this system, all individuals meeting the case definitions for either hospitalized pneumonia or ILI are asked for consent to participate, and appropriate biological samples are taken for laboratory diagnostics. Real-time reverse transcriptase polymerase chain reaction (rRT-PCR) analysis for a range of respiratory viruses, including influenza, has been continuously conducted on all samples from patients meeting the case definition. This population-based surveillance system was established to complement the MSPAS sentinel surveillance system by comprehensively including all age groups and cases who met the case definition.

This report describes the spread of 2009 H1N1 in a well-defined population of a tropical country and provides important information on the incidence of mild and severe disease and the clinical and epidemiological characteristics of severe cases of 2009 H1N1.

**Materials and methods**

**Ethics statement**

Verbal consent was requested from patients to screen them for eligibility for the study. Patients who met the surveillance case definition for pneumonia or ILI were asked for written, informed consent to participate in the study. Parents or guardians of children <18 years old were requested to provide written, informed consent for the participation of their children, and children aged 7 through 17 were asked for written, informed assent. The protocol received approval from the institutional review boards of the UVG (Guatemala City, Guatemala) and CDC (Atlanta, GA, USA) and approval from the MSPAS. All positive 2009 H1N1 results were reported immediately to the MSPAS, who informed the public health authorities and patients in each site. The policy of the MSPAS was to provide oseltamivir treatment free of charge to all patients confirmed with 2009 H1N1 infection, although reporting delays and distribution challenges meant that not all patients received oseltamivir treatment promptly.

**Study areas**

The surveillance study was carried out in the Departments of Santa Rosa (total population: 319,963), located 50 km south-east of Guatemala City, and Quetzaltenango (total population: 705,301), 120 km north-west of the capital (Figure 1). These locations were chosen previously as sites for an integrated population-based surveillance study that also includes surveillance for diarrhea, infectious neurologic disease and febrile illnesses of unknown origin because, in part, they had referral hospitals with basic laboratory capacity, represented different populations of Guatemala and had willing and interested MSPAS counterparts.

In Santa Rosa, surveillance for hospitalized pneumonia began in November 2007 and is conducted at the only hospital in the department, the National Hospital of Cuilapa (NHC), a 176-bed regional referral government hospital with a four-bed pediatric intensive care unit (ICU) and a four-bed adult ICU. In Quetzaltenango, hospital surveillance for pneumonia began in February 2009 and is conducted at the Western Regional Hospital (WRH), a large government facility with 425 beds, including 22 pediatric and six adult ICU beds, and one of only two general-purpose hospitals in the department.

Health care through government hospitals and clinics is free to everyone, but utilization of these services is generally low. In two cross-sectional healthcare utilization surveys carried out in Santa Rosa (2006) and Quetzaltenango (2009), utilization of the surveillance hospitals by participants who self-reported pneumonia was 13.4% in Santa Rosa overall, 26.1% in the urban part of Quetzaltenango and 18.0% in the rural area. Utilization of government health centers and health posts for patients who self-reported ILI was 32.6% in Santa Rosa, 23.6% in the urban area of Quetzaltenango and 15.1% in the rural area. In general, children are more likely than adults to use government health services; adults are more likely to seek care from private physicians (A. Johnson and O. Morgan, personal communication).

**Identification of cases**

Surveillance for ILI cases presenting to selected ambulatory clinics began in November 2007 in the Health Center of Nueva Santa Rosa (total population: 29,657), one of 14 municipios (similar to a county) in the Department of Santa Rosa. Surveillance for ILI was extended to all remaining (5) government health clinics in this municipio in June 2009 in response to the pandemic. In July 2009, in the Department of Quetzaltenango, surveillance for ILI was extended to the health centers and health posts of three municipios out of 24 (combined population: 72,817). Collectively, all health centers and health posts involved in ILI surveillance are referred to as ambulatory clinics.

In all sites, surveillance nurses prospectively identified patients admitted with a respiratory disease or presenting with respiratory symptoms by reviewing ward registers for respiratory-related admission diagnoses and by determining the chief complaints of patients waiting to be admitted from the emergency department or treated at ambulatory clinics. In addition, patients presenting or admitted for reasons related to diarrhea, febrile or neurologic disease were screened to determine whether they might also meet the case definition for pneumonia or ILI. A case of pneumonia was defined as a patient admitted to the hospital with at least one sign of acute infection and one respiratory symptom (Table 1). A case of ILI was defined according to
PAHO/CDC guidelines as a patient presenting to an ambulatory health clinic with a documented fever >38°C and either cough or sore throat. A laboratory-confirmed case of influenza was defined as a case of pneumonia or ILI with rRT-PCR confirmed influenza virus.

Data and sample collection
In the hospital, clinical, epidemiologic and travel history data were collected both from patient interviews and chart reviews. Clinical data included admission diagnosis, general signs and symptoms of illness, measured temperature upon admission and highest temperature in the first 24 hours of admission, hematology results, history of chronic illness, HIV/AIDS status, if known, admission to ICU, use of mechanical ventilation and discharge diagnoses. Epidemiological data included demographic characteristics of the patient, general risk factor data related to living conditions and personal habits, treatment history prior to admission and indicators of socioeconomic status. Upon admission to the hospital, patients with a clinical diagnosis of pneumonia received a chest radiograph, which was reviewed by a study radiologist who reported findings on a standardized report form. A study physician performed a pulmonary physical exam on all enrolled individuals. Surveillance nurses measured saturation of peripheral oxygen using a pulse oximeter. We determined the vital status of all hospitalized patients at 3–6 weeks after discharge through patient convalescent visits or phone calls.

In the ambulatory clinics, axillary temperature was measured by surveillance nurses and all other clinical and epidemiologic data on ILI cases were collected through patient interview. Clinical data collected from patients with ILI included general signs and symptoms of illness; epidemiologic data was as for patients with pneumonia.

Trained surveillance nurses took nasopharyngeal swabs from patients enrolled as pneumonia and ILI cases, whereas oropharyngeal (OP) swabs were also taken from individuals enrolled with pneumonia.

Laboratory diagnostics
Nasopharyngeal and OP swabs were put into one tube with viral transport media and sent to the IEIP Laboratory at the UVG, where they were tested by rRT-PCR using standardized CDC protocols for adenovirus, parainfluenza 1–3, respiratory syncytial virus (RSV), influenza A and B and human metapneumovirus (hMPV). Subtyping for influenza A to detect 2009 H1N1 was conducted using a standardized CDC protocol (http://www.who.intcsr/
Samples positive for influenza A collected before May 19, 2009, when the IEIP laboratory at the UVG received primers for 2009 H1N1, were tested retrospectively; thereafter, all influenza A positive samples were subtyped within 2–3 days of receipt of sample. Any sample positive for influenza A that could not be subtyped was sent to the WHO Reference Center Laboratory at CDC in Atlanta for further characterization.

Data management and analysis
Data were collected primarily using questionnaires and data collection forms on hand-held personal digital assistants (PDAs) with pre-programmed range and logic checks and skip patterns. Unique identifiers linked laboratory results with clinical and epidemiological data to facilitate data merging. Data were managed and stored using Microsoft SQL Server v.2008 (Redmond, VA, USA) and imported into SAS v. 9.1 (Cary, NC, USA) for descriptive analysis; exact confidence intervals (CI) for the case fatality proportion (CFP) were calculated using PROC FREQ, and the Chi-square or Fisher’s exact statistic was used to test for differences in categorical variables.

Calculation of attack and hospitalization rates
Only individuals with laboratory-confirmed 2009 H1N1 infection from the municipio of Nueva Santa Rosa in the Department of Santa Rosa were included in the numerator for calculation of attack rates as this was the only municipio with surveillance ongoing for both ILI and hospitalized pneumonia at the beginning of the pandemic. The denominator for the calculation of attack rates was the age-specific total population of the municipio obtained from the 2002 national census (http://www.ine.gob.gt), adjusted for population growth (Nueva Santa Rosa catchment area population: 29 657). Included in the numerator of hospitalization rates were only those persons residing in the hospital surveillance catchment areas and hospitalized for pneumonia with confirmed 2009 H1N1 infection. The surveillance catchment area for each hospital was determined by reviewing the emergency department registers and identifying the municipios that contributed at least 80% of the visits for pneumonia and diarrhea (NHC catchment population: 238 204; WRH catchment population: 336 761).

Results
Participation rates
Between May and December 2009, 528 (95.7%) of 553 eligible hospitalized patients with pneumonia and 366 (90.4%) of 405 patients with ILI identified in Santa Rosa provided written, informed consent to participate in the study. In Quetzaltenango, 574 (95.2%) of 603 hospitalized patients with pneumonia and 177 (84.7%) of 209 patients with ILI agreed to participate. Among hospitalized patients, children aged 2–4 and adults >60 years old had the lowest rates of participation (90.1% and 90.5%, respectively); there were no differences in participation rates by age for patients with ILI.

2009 Influenza A (H1N1)
By the end of December 2009, 239 cases of 2009 H1N1 infection had been identified from both Santa Rosa and Quetzaltenango, of which 76 occurred among patients hospitalized with pneumonia and 163 in patients with ILI (Figure 2). Three of 134 hospitalized patients with pneumonia with 2009 H1N1 infection in Santa Rosa died...
(CFP: 2.2%, 95% CI 0.5–6.4%), as did eight of 105 individuals hospitalized with 2009 H1N1 infection in Quetzaltenango (CFP: 7.6%, 95% CI 3.3–14.5%). The difference in CFP of hospitalized patients between the two sites was not statistically significant ($P = 0.06$); we, therefore, report the CFP among hospitalized cases as 4.6% (95% CI 2.3–8.1%).

The first case of 2009 H1N1 found in the surveillance system was in a person living on the border with Mexico who was hospitalized with pneumonia on May 1 (week 17; the case was not detected until May 20). Persons in the community with ILI confirmed with 2009 H1N1 infection were not detected until week 24 (June 14–20), almost 2 months later (Figure 3). Whereas the first person with confirmed 2009 H1N1 infection came from a community on the border with Mexico, none of the subsequent individuals with 2009 H1N1 reported having traveled outside of Guatemala in the month prior to illness. The number of cases per week peaked at 43 in week 33, 9 weeks after the first community ILI case was identified. By week 7, influenza transmission was minimal.

The median age of patients with confirmed 2009 H1N1 infection was 8.8 years (range: 17 days to 82 years). Overall, 136 (56.9%) cases of 2009 H1N1 influenza infection occurred in men.

**Figure 2.** Distribution of cases of influenza A (2009 H1N1) in population-based surveillance, Guatemala, May–December 2009.

**Time to presentation, admission and death**

The median time from the onset of illness to presentation at an ambulatory clinic among patients with ILI with 2009 H1N1 infection was two days (range: 0–50 days). The median time from illness onset to admission in the hospital with pneumonia was five days (range: 1–90 days), and the median hospital stay was five days (range: 1–27 days). The 11 patients with 2009 H1N1 influenza infection who died did so between five and 17 days of the onset of symptoms, with a median time of nine days.
from onset of illness to death. Nine of the 11 deaths occurred during hospitalization, and two occurred within one day of discharge.

**Influenza A virus subtypes**

The predominant influenza A virus subtype circulating before the first 2009 H1N1 case was detected was seasonal...
influenza A (H1N1) with sporadic cases of influenza A (H3N2). Once significant community transmission of 2009 H1N1 virus began in week 24, 2009 H1N1 began replacing seasonal influenza subtypes until week 34 after which all influenza A viruses that could be subtyped were identified as 2009 H1N1 (Figure 4).

Age distribution of 2009 H1N1 cases
We compared the age distributions of persons with ILI and hospitalized pneumonia and those who died with laboratory-confirmed 2009 H1N1 infection (Figure 5). The 2009 H1N1 infections detected in the ILI surveillance were most likely to occur in school-age children 5–14 years old (49.1%). Among persons hospitalized with pneumonia, the age group most affected by 2009 H1N1 infection was children <5 years old, who accounted for 51.3% of hospitalized cases of 2009 H1N1 infection. Children <5 years old represented the largest proportion (45.5%) of the deceased individuals with 2009 H1N1 infection.

Attack rates
From May through December, 87 cases of laboratory-confirmed 2009 H1N1 infection, including 4 (4.8%) individuals hospitalized with pneumonia, but no deaths, were detected from the municipio of Nueva Santa Rosa for a crude attack rate of 3.1 per 1000 (Figure 2 and Table 2). The crude age-specific attack rates were highest for school-age children 5–14 years old.

Rate of hospitalization
Among the 76 cases that occurred in hospitalized patients, 28 were identified by the hospital in Santa Rosa and 21 (75.0%) were residents of the hospital surveillance catchment area (Figure 2 and Table 3). There were 48 patients hospitalized

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**Table 2.** Number and rate of laboratory-confirmed influenza-like illness cases of 2009 pandemic influenza A (H1N1) virus by patient age group, Nueva Santa Rosa, Guatemala, May–December 2009

| Age group | 2009 Population* | No. of cases | Crude rate † |
|-----------|------------------|-------------|--------------|
| 0–4       | 4230             | 17          | 4.0          |
| 5–14      | 8180             | 50          | 6.1          |
| 15–24     | 7653             | 16          | 2.1          |
| 25–44     | 4562             | 2           | 0.4          |
| 45–59     | 2651             | 4           | 1.5          |
| 60+       | 2381             | 2           | 0.8          |
| Total     | 29,657           | 91          | 3.1          |

*Based on the 2002 national census and updated using official growth rate estimates.
†Crude rates are per 1000 population.
with 2009 H1N1 infection in Quetzaltenango, of whom 22 (45.8%) were from the hospital surveillance catchment area. The crude rate for hospitalization with 2009 H1N1 between May and December (weeks 17–43) was 8.8 per 100 000 in Santa Rosa and 7.1 per 100 000 in Quetzaltenango (Table 3). In both sites, we found the rate of hospitalizations for children <5 years of age to be the highest.

Characteristics of hospitalized and fatal 2009 H1N1 cases
The median age of patients hospitalized with 2009 H1N1 was 4.2 years (range: 17 days to 82 years). The 11 patients who died were all detected through hospital surveillance and included five males and six females; four of the deceased persons were <1 year old, and the rest were 1, 14, 25, 35, 50, 53 and 57 years old. Forty-four (60.3%) of the patients hospitalized for pneumonia with confirmed 2009 H1N1 infection were men. The most common symptom among patients hospitalized with 2009 H1N1 was cough (98.7%), followed by difficulty breathing (86.8%) and subjective fever (86.8%; Figure 6). Diarrhea, defined as three or more loose stools in a 24-hour period during the last seven days, was found in 17.1% of patients. Among 38 hospitalized pneumonia patients with 2009 H1N1 who had a chest radiograph reviewed by a study radiologist, 27 (71.1%) had an infiltrate consistent with pneumonia. An oxygen saturation level <90% was noted in 52.9% of patients. Twenty-one (27.6%) patients were admitted into the ICU, for a median length of stay in the ICU of two days (range: 1–7 days), and eight (10.5%) required mechanical ventilation (median days on ventilation: 1, range: 1–3 days). Eight (72.7%) of the 11 deaths occurred in patients who required mechanical ventilation.

Documented temperature ≥38°C within the first 24 hours of admission was measured in 61.8% of patients hospitalized for pneumonia with 2009 H1N1, whereas 86.8% reported subjective fever. More than 10% of the patients had neither a documented fever nor a reported subjective fever. Use of an antipyretic for fever, headache or body aches in the 72 hours before admission was reported by 57.5% of the hospitalized pneumonia patients with laboratory-confirmed 2009 H1N1 infection. The proportion of hospitalized pneumonia patients who had a measured fever ≥38°C in the first 24 hours of admission was not different between those who had taken an antipyretic (57.5%) and those who had not (63.6%; P = 0.59). Among the patients who reported subjective fever during their illness, the proportion (73.1%) of those febrile within 24 hours of admission was higher among those who had not taken an antipyretic than among those who had (59.5%), but the difference was not statistically significant (P = 0.26).

Fourteen (18.4%) patients hospitalized with 2009 H1N1 infection had a known underlying condition that could have put them at increased risk for severe disease: four individuals had asthma, two had hypertension and one had hypertension with heart disease; one had heart disease alone and one had heart disease, diabetes and kidney disease; one patient

| Location     | Age group (years) | 2009 Population* | Total cases identified in the hospital | From surveillance catchment area | Crude rate† |
|--------------|-------------------|------------------|----------------------------------------|---------------------------------|-------------|
| Santa Rosa   | 0–4               | 34 465           | 18                                     | 12                              | 34.8        |
|              | 5–14              | 66 239           | 3                                      | 3                               | 4.5         |
|              | 15–24             | 61 567           | 4                                      | 4                               | 6.5         |
|              | 25–44             | 36 430           | 2                                      | 1                               | 2.7         |
|              | 45–59             | 22 097           | 1                                      | 1                               | 4.5         |
|              | 60+               | 17 407           | 0                                      | 0                               | 0           |
| Total        |                   | 238 204          | 28                                     | 21                              | 8.8         |
| Quetzaltenango| 0–4              | 42 473           | 21                                     | 6                               | 14.1        |
|              | 5–14              | 91 229           | 2                                      | 2                               | 2.2         |
|              | 15–24             | 91 407           | 6                                      | 5                               | 5.5         |
|              | 25–44             | 56 444           | 7                                      | 5                               | 8.9         |
|              | 45–59             | 32 645           | 7                                      | 4                               | 12.3        |
|              | 60+               | 22 563           | 5                                      | 2                               | 8.9         |
| Total        |                   | 336 761          | 48                                     | 22                              | 7.1         |

*Based on the 2002 national census and updated using official growth rate estimates.
†Crude rates are per 100 000 population.

Table 3. Number and rate of laboratory-confirmed hospitalized cases of 2009 pandemic influenza A (H1N1) virus by location and patient age group, Guatemala, May–December 2009
reported liver cirrhosis, one had tuberculosis and another had chronic obstructive pulmonary disease. Two women (16.7% of the 11 women between 14 and 45 years old) with pneumonia associated with 2009 H1N1 infection were in the second trimester of their pregnancy. One of the patients with underlying illness died.

Seventeen (22.4%) patients infected with 2009 H1N1 virus had a coinfection with another respiratory virus (nine with RSV alone, one coinfected with RSV, parainfluenza-2 and parainfluenza-3, one with RSV and adenovirus, five with adenovirus alone, and one with both adenovirus and hMPV). Four of the five children <5 years old who died had viral coinfections (three with RSV and one with adenovirus).

We were able to determine the vital status after discharge of 45 (67.2%) of the 67 hospitalized patients with 2009 H1N1 infection who were discharged alive. Between three and six weeks after discharge, 43 (95.6%) were found alive: 24 (53.3%) were completely recovered, 16 (35.6%) recovered with sequelae and three (6.6%) were in a worse condition than before they were admitted to the hospital.

**Discussion**

Guatemala, which borders Mexico, the epicenter of the 2009 H1N1 pandemic, did not see widespread, sustained community transmission for approximately two months after the first cases of 2009 H1N1 infection were reported, and transmission peaked approximately two months after community transmission began. There was great interest in monitoring countries in the tropics, whose influenza seasons started after the onset of the pandemic, to determine whether the virus might become more lethal. We report a CFP (4.6%) within the range of estimates from other countries.

Attack rates of laboratory-confirmed 2009 H1N1 infections were highest in school-age children 5–14 years old, but the hospitalization rates were highest for children <5 years old. Age-specific hospitalization rates have been difficult to obtain during the pandemic from other countries, but at least one area in the United States has also found hospitalization rates to be highest in children <5 years old. The attack and hospitalization rates

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**Figure 6.** Clinical characteristics of patients hospitalized with laboratory-confirmed 2009 pandemic influenza A (H1N1) from population-based surveillance in Guatemala, May–December 2009.
presented in this report are clear underestimates of the true rate of disease in this population as usage of government healthcare facilities in Guatemala is low. Therefore, the rates of attack and hospitalization that we report here should be taken as the minimum rates of disease associated with 2009 H1N1 infection.

The population affected by the 2009 H1N1 virus in Guatemala is much younger (median age 8.8) than that reported from South America (median ages: Bolivia, 20; Peru, 13; Chile, 13), North America (median ages: Chicago, 12; Canada, 17), Europe (median age 24) and the Western Pacific (median age 23). The median age of hospitalized patients (4-2 years) is significantly lower than that reported for Chicago (16 years), the US overall (21 years) and Germany (19 years). In addition, five of the 11 deaths (45-5%) identified through the surveillance study were in children <5 years old. There may be several factors contributing to the higher burden of morbidity and mortality associated with 2009 H1N1 infection in children in Guatemala. First, the proportion (22-4%) of hospitalized individuals coinfected with other respiratory viruses was high, related largely to a significant increase in laboratory-confirmed RSV infection beginning in May 2009 and continuing through October 2009. Four of the five children <5 years old who died were coinfected with either RSV or adenovirus. There is some suggestion that coinfection with two or more respiratory viruses might increase severity of respiratory disease in children, perhaps as a result of immune response suppression. Second, Guatemala has the highest rate of chronic malnutrition in Latin America and the Caribbean, and the fourth highest in the world (http://www.who.int/nutgrowthdb/database/countries/who_standards/gtm.pdf). In a national sample in 2002, the proportion of children <5 years old severely underweight was 39%, and the proportion with severe, chronic malnutrition was 26.9%. Although we were not able to analyze anthropometric measurements in this group of patients, it is probable that a high proportion of children <5 were chronically and/or acutely malnourished, which may have affected immune responses to infection with the 2009 H1N1 virus. Third, very few of the results published to date on cases of 2009 H1N1 infection have come from resource-limited countries (Peru and Bolivia being the exceptions). The age distribution in many developing countries is younger than that of more developed countries, which can impact the age distribution of infection. It is also likely that the pattern of disease in developing countries is quite different from those in more developed countries because of differences in access to care, coinfections, disease burden, availability of antiviral medications and nutrition. Finally, most of the published reports on cases of 2009 H1N1 infection have been from convenience samples without a clear population base or have used aggregated data. As such, it can be difficult to identify where there may be biases in the estimated age distributions of 2009 H1N1 cases because of patterns of health care seeking, diagnostic availability or reporting.

Underlying chronic diseases have been commonly reported among patients with severe complications of 2009 H1N1 infection. In the United States, 41% of 22 patients hospitalized during the first months of the pandemic had chronic medical conditions, and a more complete review of 272 hospitalized patients with 2009 H1N1 infection from across the US reported 73% of patients with an underlying medical condition. Of 241 fatal cases from around the world, 90% had documented underlying disease. In the United States, among deaths in children associated with 2009 H1N1 infection, 67% had at least one high risk condition. We report 18-4% of hospitalized individuals with 2009 H1N1 infection in Guatemala with underlying medical conditions. We believe it is likely that in Guatemala there is an under-diagnosis of chronic medical conditions such that many individuals with underlying disease are not identified.

The surveillance case definition used in our population-based surveillance for hospital pneumonia is very broad and does not require documented fever for eligibility. We found that <62% of patients hospitalized with 2009 H1N1 infection had a documented fever ≥38°C within 24 hours of admission. When testing for influenza is routine, 2009 H1N1 infections occurring in sick patients without fever have been reported, but these cases are not generally identified when a documented fever is included in the surveillance case definition. Slightly more than half of the patients with pneumonia with 2009 H1N1 infection reported use of antipyretics in the 72 hours before admission. While use of antipyretics may have lowered the proportion with documented fever, we did not see a significant impact of antipyretics on measured fever in patients who reported a history of subjective fever. As the CDC/PAHO definition for SARI, a widely used generic surveillance case definition, includes documented fever, the burden of pneumonia and ILI with confirmed 2009 H1N1 infection may be underestimated in countries using documented fever as part of the surveillance case definition. Surveillance systems that do not require documented fever in the case definition, such as the system described in this report, may be useful to help correct for the proportion of cases of 2009 H1N1 that are missed.

In contrast to other Latin American countries, in Guatemala men (56.9%) were more affected by 2009 H1N1 virus than women (43.1%) and men (60.3%) were also more likely to be hospitalized with 2009 H1N1 infection than women (39.7%). The reason for the greater burden of disease in men is not clear but appears across all age groups.

Before the appearance of the 2009 H1N1 virus, the influenza subtype circulating most widely was influenza A
(H1N1), in contrast to other areas of the world that experienced more influenza A (H3N2) (http://www.who.int/csr/don/2009_08_21/en/index.html). By the time, the 2009 H1N1 virus was spread widely in the community, seasonal influenza was mostly, but not completely, replaced by the pandemic virus. Cases of seasonal influenza continued to co-circulate with the 2009 H1N1 virus until week 34 (August 24–30) but were not found thereafter. As of the end of 2009, 100% of influenza A viruses circulating in Guatemala were of the 2009 H1N1 subtype.

This surveillance system presents important strengths, including the prospective nature of the surveillance that provides a clear picture of the emergence and spread of a novel flu strain; a sensitive case definition that was unchanged by the onset of the pandemic; inclusion of all age groups; and the ability to calculate population-based rates. One significant limitation is the relatively low utilization of government health care services in the surveillance catchment areas, which means that the rates presented here are underestimates of the true rate of disease.

This surveillance system will continue to monitor the progress and characteristics of the 2009 H1N1 pandemic in the upcoming season. In addition, it will be able to document changes in severity, as measured by hospitalization and ICU admission rates, and community transmissibility, as measured by ILI visits, in addition to the impact of the 2009 H1N1 vaccine, if it is widely introduced. Ongoing, continuous and comprehensive population-based surveillance for diseases of local, regional and global importance can provide critical and reliable information on emerging infections. In the first days of the 2009 H1N1 pandemic, the sites described in this report were able to accurately and rapidly determine that there had not yet been any increase in respiratory infections in the hospital or the community. In addition, the presence of a strong laboratory with standardized and high-quality diagnostic procedures was capable of subtyping all of the respiratory samples positive for influenza A that had been identified since the beginning of 2009 and determine that none was of the pandemic strain. This information was helpful to international and Guatemalan authorities to understand the global limits of the pandemic and track its onset in Guatemala.

In conclusion, our data have implications for vaccine policy for 2009 H1N1 infection in Guatemala. Whereas individuals with chronic, underlying conditions are at risk for significant morbidity and mortality from influenza infection, these diagnoses are probably under-reported in Guatemala and many patients with chronic diseases will not be easily identified. Most significantly, the data we have presented highlight the importance of including young children among the first groups targeted for immunization against 2009 H1N1 infection to prevent severe morbidity and mortality in this age group. The potential role of other viral coinfections and undernutrition need to be examined more closely to understand why young children in Guatemala are particularly vulnerable to severe consequences of 2009 H1N1 infection.

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Disclaimer

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Author contributions

Conceived, designed and supervised the surveillance system: LR, WA, JG, JCM, BG, GF, FA, FM, SJO, AMF, SL, KAL. Conducted diagnostic assays: AE. Analyzed the data: LR, WA, AE, JG, JCM, KAL. Contributed reagents/materials/analysis tools: SL. Wrote the paper: LR, WA, AE, JG, SJO, AMF, KAL. Revised and approved final version of the publication: LR, WA, AE, JG, JCM, BG, GF, FA, FM, SJO, AMF, SL, KAL.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Data S1. Vigilancia Basada en la Población Para el Virus de la Pandemia de Influenza A H1N1 en Guatemala, 2009 (Spanish translation of the paper).

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