Estimating the Burden of 2009 Pandemic Influenza A (H1N1) in the United States (April 2009–April 2010)

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To calculate the burden of 2009 pandemic influenza A (pH1N1) in the United States, we extrapolated from the Centers for Disease Control and Prevention's Emerging Infections Program laboratory-confirmed hospitalizations across the entire United States, and then corrected for underreporting. From 12 April 2009 to 10 April 2010, we estimate that approximately 60.8 million cases (range: 43.3–89.3 million), 274 304 hospitalizations (195 086–402 719), and 12 469 deaths (8868–18 306) occurred in the United States due to pH1N1. Eighty-seven percent of deaths occurred in those under 65 years of age with children and working adults having risks of hospitalization and death 4 to 7 times and 8 to 12 times greater, respectively, than estimates of impact due to seasonal influenza covering the years 1976–2001. In our study, adults 65 years of age or older were found to have rates of hospitalization and death that were up to 75% and 81%, respectively, lower than seasonal influenza. These results confirm the necessity of a concerted public health response to pH1N1.

INTRODUCTION

The 2009 pandemic influenza A (H1N1) virus (pH1N1) was first reported in the United States on 12 April 2009 [1, 2]. By 23 July 2009, a total of 43,677 laboratory-confirmed cases, 5009 hospitalizations, and 302 deaths had been reported to the Centers for Disease Control and Prevention (CDC), but early investigations indicated that the number of reports had notably underestimated the true burden of the pandemic to date [3]. As the influenza season rapidly approached, to aid public health planning and response, there was a critical need for a method to rapidly assess the evolving burden of pH1N1.

We built a model that enabled us to produce interim estimates of cases, hospitalizations, and deaths that could be frequently updated as new information became available. Beginning 14 November 2009, the CDC published online monthly estimates of deaths, hospitalizations, and cases attributed to pH1N1 in the entire United States. We describe here the full details of how these estimates were calculated for different time periods in the United States as well as how we validated the method. We also compared the rates of hospitalizations and deaths from pH1N1 to the average rates from seasonal influenza. These data helped public health officials and the public assess the magnitude of the pandemic and the success of the response effort. Furthermore, the methods used here will help public health officials plan the production of similar data during the next pandemic and could also be used for seasonal influenza.

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.

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Clinical Infectious Diseases 2011;52(S1):S75–S82
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/ciq012

METHODS

Overview

To model the impact of pH1N1, we used weekly surveillance reports of laboratory-confirmed pH1N1-related hospitalizations to calculate a range of rates of hospitalizations per 100,000 population. We then extrapolated those hospitalization rates to the 50 states. During extrapolation, we adjusted for different levels of influenza activity by dividing the United States into 3 groups based on levels of physician visits for influenza-like illness (ILI). We then corrected for underreporting of hospitalizations using previously published multiplication factors [3] and then calculated numbers of cases using a previously estimated hospitalization-to-cases multiplier [3]. Finally, we calculated deaths as a percentage of hospitalizations using reports of laboratory-confirmed pH1N1-related hospitalizations and deaths collected by State Health Departments.

Data Sources

To estimate the burden of the pH1N1 influenza virus in the United States, we used data from 3 influenza surveillance systems. To estimate hospitalizations, we used reports of laboratory-confirmed influenza-related hospitalizations from the CDC's Emerging Infections Program (EIP). The EIP conducts surveillance for laboratory-confirmed influenza-related hospitalizations, in both children and adults, in 60 counties covering 12 metropolitan areas of 10 states (approximately 22 million people; for details see: http://www.cdc.gov/ncpdcid/deiss/eip/index.html). For outpatient visits, we used weekly data collected through the US Outpatient Influenza-Like-Illness Surveillance Network (ILINet: http://www.cdc.gov/flu/weekly/fluactivity.htm#OIS). This system records the percentage of outpatients who present to physicians with ILI, and comprises more than 3000 healthcare providers in all 50 states. Influenza-like illness is defined as having a fever of at least 100°F, with either a cough or sore throat, in the absence of a known cause other than influenza. Note that causative pathogens of the ILI visits, when known, are not reported as part of this surveillance system.

To estimate deaths as a percentage of hospitalizations, we used reports of laboratory-confirmed pH1N1-related hospitalizations and deaths collected each week by state health departments and reported to the CDC via the Aggregate Hospitalization and Death Reporting Activity (AHDRA) surveillance system. AHDRA was established during the pandemic to monitor laboratory-confirmed hospitalizations and deaths in the United States. In any given week, there were approximately 35 states reporting into the system. From the ADHRA data, we calculated deaths as a percentage of hospitalizations (note: this percentage also includes deaths of pH1N1 outside of hospitals). For our first report of estimates of burden (released 12 November 2009), we used the data from the week ending 7 November 2009, when deaths as a percentage of hospitalizations in the ADHRA system were: 0–17 years of age, 1.48%; 18–64 years of age, 5.79%; and 65 years of age and older, 5.76%. To simplify the process, we used the following percentages in our calculations: 0–17 years of age, 1.5%; adults (all ages), 6.0%. We then applied these percentages to all hospitalizations for all time periods covered in this paper.

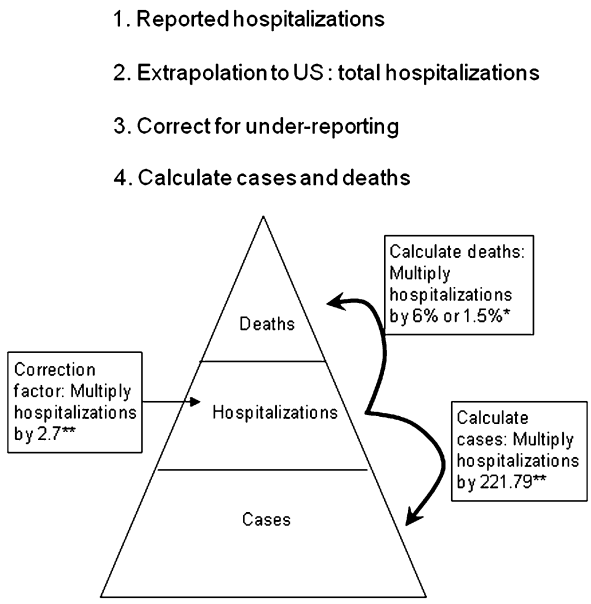

Figure 1. An illustration of the methodology used to extrapolate from reported laboratory-confirmed 2009 pandemic influenza A (H1N1) hospitalizations to total US cases, hospitalizations, and deaths. *Deaths are calculated as a percentage of hospitalizations using data from the Aggregate Hospitalization and Death Reporting Activity (AHDRA) surveillance system. The factor for calculating deaths among children aged 0–17 years is 1.5% of estimated hospitalizations for that age group. For all adults, deaths are calculated as 6% of all hospitalizations. Note, however, that not all deaths occurred in hospitals. Hospitalizations, and thus cases and deaths, are divided into 3 age groups (0–17 years, 18–64 years, and 65+ years) by using the age-based proportions of pH1N1 hospitalizations reported by the EIP sites. See main text for further details. **Factors to correct for underreporting of hospitalizations and to calculate number of cases from Reed et al. [3]. The same factors are used for all 3 age groups.

Estimation

April–July 2009. For this initial time frame, we used the estimated hospitalizations and cases by age group from Reed et al. [3]. We then estimated the number of deaths using the laboratory-confirmed deaths as a percentage of laboratory-confirmed hospitalizations as calculated from the ADHRA system (described above).

2 August 2009–10 April 2010. Our system for extrapolation and correction for underreporting is illustrated in Figure 1. For this period, we extrapolated the numbers of

laboratory-confirmed hospitalized US patients reported by the 10 EIP sites. Simple extrapolation to all 50 states of the average rate of hospitalization as measured across all EIP sites would not adjust for the fact that, in any given week, influenza attack rates differ by region. To allow for geographic variability by week of the impact of 2009 H1N1, we estimated the numbers as follows.

Estimation of Hospitalization Rates at EIP Sites. For each EIP site, we first estimated the weekly rate of laboratory-confirmed hospitalizations per 100 000 population as follows: Rate of laboratory-confirmed 2009 H1N1 hospitalizations per EIP site = (number of confirmed cases hospitalized / site population) × 100 000.

Categorization of EIP Sites. We then categorized, for each week, the 10 EIP sites into low, midrange, and high categories of hospitalizations rates, using <33 percentile, ⩾33 and <67 percentile, and ⩾67 percentile of hospitalization rates, respectively. For each category and each reporting week, we calculated the median rate in that category and recorded the minimum and maximum rates.

Categorization of 50 States by of Influenza Activity. We next used the ILINet data to categorize the 50 states into low, midrange, and high categories, using <33 percentile, ⩾33 and <67 percentile, and ⩾67 percentile of percentages of weekly reported ILI-related physician outpatient visits, respectively.

Matching States to Rates of Hospitalization. For each reporting week, to calculate state-level rates of hospitalizations, we matched each state to the appropriate category of hospitalization rate. For example, states categorized as having a midrange level of ILI activity were matched to the rate of hospitalization for EIP sites categorized as having midrange rates of 2009 H1N1-related hospitalizations. We then used the matched EIP estimated hospitalization rates to estimate the state-specific number of hospitalizations. For example, for states categorized as having had midrange-level activity based on ILI rates:

> Median number of hospitalizations = (median hospitalization rates from EIP sites categorized as having midrange level of hospitalizations × population of the state categorized as having "mid" level of influenza activity) / 100,000

We repeated this calculation for each of the 50 states and then summed the estimated hospitalizations across all states to provide a weekly national total. We also calculated, using the same method, the national minimum and maximum number of hospitalizations for each week.

Correcting for Under-Reporting. The four steps described above extrapolated the rate of hospitalizations at the EIP sites to the 50 states, providing a national estimate of reported hospitalizations. However, because hospitalizations for pH1N1 are underreported [3], we multiplied the extrapolated EIP hospitalizations (median, minimum, and maximum estimates) by a factor of 2.74 (Reed et al.) to obtain a corrected number of hospitalizations.

Estimation of Cases. We estimated the median weekly national number of pH1N1 cases by multiplying the estimated number of median national hospitalizations by a factor of 221.79. This factor was calculated by Reed et al. [3] based on the number of pH1N1 laboratory-confirmed hospitalizations as a proportion of cases.

Estimation of the Age-Specific Hospitalizations and Cases. We distributed the weekly estimates of median national hospitalizations and cases into 3 age groups by using the age-based proportions of pH1N1 hospitalizations reported by the EIP sites. As of 10 April 2010, the age-based breakdown of pH1N1 hospitalizations at the EIP sites was: 0–17 years of age, 31%; 18–64 years of age, 59%; 65 years of age or older, 10%. These percentages were used to calculate the age-based breakdown from 2 August 2009, through to 10 April 2010 (age-based breakdown of cases and hospitalizations for the April–July 2009 period were previously calculated [3]).

Estimation of Deaths. We then estimated the median national number of deaths by the 3 age groups using age-specific deaths as percentage of hospitalizations derived from ADHRA (see earlier).

Estimation of Ranges: Cases and Deaths. We calculated the lower and upper total number of cases and deaths by multiplying the estimated median estimates by a factor of .71 and 1.47, respectively. These factors are the minimum and maximum hospitalizations as proportions of the median hospitalizations (for the period 2 August 2009, to 10 April 2010).

Adjustments for August 2009. For the month of August 2009 (weeks 31–34), there was insufficient state-level differentiation of influenza activity to readily divide states into 3 categories (as defined by ILI-related visits; see http://www.cdc.gov/flu/weekly/weeklyarchives2008-2009/weekly34.htm). Also, for this period, many of the EIP sites reported fewer than 3 pH1N1-related hospitalizations per week, making it difficult to categorize the sites and calculate median, minimum, and maximum values. We therefore adjusted the estimation methodology for August by calculating the simple average, minimum, and maximum rates of hospitalizations across all 10 EIP sites, and then we extrapolated those to all the 50 states (without any categorization). We corrected for underreporting, proportioned into the 3 age groups, and calculated national cases and deaths using the methods described above.

Method Validation

We did not have a census or a statistically valid laboratory-confirmed sampling of all relevant cases, hospitalizations, or deaths with which to compare our estimates. We therefore validated our methodology by using it to estimate hospitalizations

for the 2007/2008 and 2008/2009 nonpandemic influenza seasons and then compared those estimates to previously published estimates of hospitalizations due to seasonal influenza. We used the number of laboratory-confirmed influenza hospitalizations for those 2 seasons as reported to the CDC from the EIP sites and then extrapolated to the 50 states and corrected for underreporting using the methodology and correction factors described earlier. Then we compared our estimates of 2007/2008 hospitalizations (in which cases were caused predominantly by influenza A H3N2 strains) with Thompson et al. (Table 2, ref. [4]) estimates of hospitalizations due to pneumonia and influenza (any listed cause of hospitalization) from 14 seasons during a 21-season period (1979–2001) when H3N2 strains were predominately circulating. Similarly, we compared our estimates of 2008/2009 hospitalizations with Thompson et al. (Table 2, ref. [4]) estimates of pneumonia and influenza hospitalizations (any listed cause of hospitalization) during the 5 seasons when H1N1 nonpandemic strains predominately circulated (during the period 1979–2001).[1]

We also tested whether our estimation methodology provided less variability than merely extrapolating the average weekly hospitalization rates from all the EIP sites to all the 50 states (ie, without adjustments for differences in influenza activity). We repeated the estimation of the hospitalizations in 2007/2008 and 2008/2009 as described above but without dividing either the EIP sites or the 50 states into 3 groups. We then calculated for each method the range of estimates (maximum minus minimum) as a percentage of the mean. The method with the lowest percentage indicates less variability.

Comparison of Impact to Seasonal Influenza

We converted our estimates of deaths and hospitalizations due to pH1N1 to rates per 100 000 population and compared those rates to previously published estimates of rates of death and hospitalizations caused by influenza for periods 1976–1999 and 1979–2001, respectively [4, 5]. To allow for a direct comparison, we regrouped the previously published rates into the same 3 age groups that we used. We did this by weighting the published rates by the proportions of each age group of the appropriate population using 1995 population estimates [6].

RESULTS

When corrected for underreporting, for the periods 12 April–23 July, August 2009, and 1 September 2009–10 April 2010, there were 13 764, 7 240, and 253 300 estimated hospitalizations, respectively (Table 1). The estimates from 1 September 2009, to 10 April 2010 were based on the EIP-reported laboratory-confirmed hospitalizations (approximately 6 400 cases). This was equivalent to approximately 93 800 reported hospitalizations (range: 66 721–137 734) in the 50 states (Table 2).

For the entire period of 12 April 2009–10 April 2010 there were approximately 274 300 hospitalizations (range: 195 100–402 700) (Table 1). Approximately 92% of these hospitalizations occurred from 1 September 2009 to 10 April 2010, of which 115 000 (42%) occurred from 16 October 2009 through 14 November 2009 (see http://cdc.gov/h1n1flu/estimates/April_November_14.htm).

The distribution over time of cases and deaths followed a similar pattern (Table 1). There were a total of 12 469 deaths (range: 8 868–18 306), with the majority occurring from 1 September through 10 April 2010. Of the approximate 12 500 deaths, 77% occurred in the 18–64-year-old age group and 10% in children (Table 2). The estimate of 60.8 million cases (Table 1) gave a gross, total population clinical attack rate of approximately 20.0% (range: 14.2%–29.4%).[2] The estimated attack rates by age group were: 0–17 years, 26.4% (range: 18.8%–38.7%); 18–64 years, 18.5% (range: 13.2%–27.2%); and 65 years or older, 18.5% (range: 10.9%–22.5%).

Method Validation

Our methodology, when applied to data from the 2007/2008 and 2008/2009 (nonpandemic) influenza seasons, provided estimates that were very similar to estimates of hospitalizations due to pneumonia or influenza (any listed cause of hospitalization) for seasons during 1979 through 2001 when H3N2 or seasonal H1N1 predominated [4] (Table 3). Our method of dividing both the EIP sites and the 50 states into 3 groups (to reduce variability) provided ranges that were approximately 3 times smaller than those calculated by simply extrapolating the average hospitalization rate from all 10 EIP sites to all 50 states, without any allowance for differences between states in levels of weekly influenza activity (Appendix Table A1).

Comparison of Impact to Seasonal Influenza

Children were hospitalized due to pH1N1 at a rate of approximately 117 per 100 000 (Table 4). This is approximately 7 times greater than previously published rates of seasonal influenza–related hospitalization during the years 1979–2001 as estimated by Thompson et al. [4] (Table 4). Adults aged 18–64 years had approximately 4 times greater risk of being hospitalized compared to these published estimated rates. Adults 65 years of age

[1]Note that, because EIP sites only started reporting the relevant data in 2005, and the most recent year in the Thompson et al. study (4) was 2001, we could not do a direct year-to-year comparison with Thompson et al. (i.e., we had to compare results using EIP data from a nonpandemic season to a strain-appropriate average of Thompson et al.)

[2]Attack rates calculated using estimate of residents of U.S. population as at July 01, 2008. 0-17 years - 74.6 million; 18-64 years 190.5 million; 65+ years 38.9 million. Source: Table 1: Annual Estimates of the Resident Population by Sex and Five-Year Age Groups for the United States: April 1, 2000 to July 1, 2008 (NC-EST2008-01) U.S. Census Bureau. Release Date: May 14, 2009. Available at: http://www.census.gov/popest/national/asrh/NC-EST2008-sa.html.

Table 1. Estimates of Cases, Hospitalizations, and Deaths due to 2009 Pandemic Influenza A (pH1N1) in the Entire United States (April 12, 2009 to April 10, 2010)

	Estimates of cases, hospitalizations, and deaths by time period	
	April 12–July 23, 2009[a]	
Deaths[c]		
0–17 years	90	
18–64 years	394	
65+ years	32	
Subtotal	***516***	
Hospitalizations[a]		
0–17 years	6012	
18–64 years	7099	
65+ years	654	
Subtotal	***13,764***	
Cases[a]		
0–17 years	1,580,218	
18–64 years	1,430,258	
65+ years	42,292	
Subtotal	***3,052,768***	
	August 1–31, 2009[b]	
Deaths[c]		
0–17 years	39	
18–64 years	219	
65+ years	35	
Subtotal	***292***	
Hospitalizations[d]		
0–17 years	2611	
18–64 years	3926	
65+ years	703	
Subtotal	***7240***	
Cases[e]		
0–17 years	579,037	
18–64 years	870,804	
65+ years	155,919	
Subtotal	***1,605,760***	
	Sept. 1, 2009–Apr. 10, 2010[b]	
Deaths[c]		
0–17 years	1153	
18–64 years	8952	
65+ years	1554	
Subtotal	***11,660***	
Hospitalizations[d]		
0–17 years	78,190	
18–64 years	149,204	
65+ years	25,906	
Subtotal	***253,299***	
Cases[e]		
0–17 years	17,341,749	
18–64 years	33,091,869	
65+ years	5,745,602	
Subtotal	***56,179,220***	

	TOTALS: April 12, 2009–April 10, 2010[f]
Deaths[c,f]	
0–17 years	1282 *(912–1883)*
18–64 years	9565 *(6,803–14,043)*
65+ years	1621 *(1153–2380)*
Subtotals	**12,469** ***(8,868–18,306)***
Hospitalizations[d,f]	
0–17 years	86,813 *(61,742–127,454)*
18–64 years	160,229 *(113,955–235,239)*
65+ years	27,263 *(19,389–40,025)*
Subtotals	**274,304** ***(195,086–402,719)***
Cases[e,f]	
0–17 years	19,501,004 *(13,869,153-28,630,340)*
18–64 years	35,392,931 *(25,171,524-51,962,026)*
65+ years	5,943,813 *(4,227,252-8,726,391)*
Subtotals	**60,837,748** ***(43,267,929-89,318,757)***

[a] The data for April 12–July 23, 2009, are from Reed et al. [3].

[b] Calculated by extrapolating from the reported laboratory-confirmed hospitalizations of pH1N1 reported to the CDC from the 10 EIP sites.We first calculated the rate per 100,000 per EIP site. To allow for different levels of influenza activity among the sites, for each reporting week we divided the EIP sites, based on rates of hospitalization, into 3 equal groups: low, midrange, high. We then divided the 50 states, based on reported percent of visits that are for ILI, into 3 equal groups: low, midrange, high. We then matched EIP hospitalization rates to states (low to low, etc). We then extrapolated the appropriate EIP hospitalization rate to the populations of those states similarly categorized, arriving at an estimated number of hospitalizations per state. For example, the median number of hospitalizations for a given week and state was calculated as follows: Median estimate of number of hospitalizations in a state categorized as having mid level of influenza activity = (Median rate of hospitalization from EIP sites categorized as midrange level of hospitalization rates) x Population of the state categorized as having midrange level of influenza activity / 100,000. Finally, the estimates for each state were added up to provide a total median estimate for all 50 states for that week. See main text for further details.

[c] Deaths are calculated as a percentage of hospitalizations using data from the Aggregate Hospitalization and Death Reporting Activity (AHDRA) surveillance system. This system has approximately 35 states reporting per week. To simplify the process, we used the following percentages in our calculations: 0–18 years of age, 1.5%; adults (all ages), 6.0%. We applied these percentages to all hospitalizations for all time periods covered in this table.

[d] Hospitalizations corrected for underreporting by multiplying by a factor of 2.7 from Reed et al. [3].

[e] Cases estimated as 221.79 of hospitalizations. This factor was calculated using the median estimates of cases (3.052 million) and hospitalizations (13,764) from Reed et al. [3].

[f] Ranges calculated using the same system as calculating the midrange estimate (see earlier footnote), except instead of using the midrange rate of hospitalization we used either the low or high estimate of rates of hospitalization. Upper limits are calculated as 1.47 of the midrange estimate for hospitalizations; the lower limit is calculated as .71 of the midrange estimate for hospitalizations. (See main text for further details.)

Table 2. Number of Actual Laboratory-Confirmed 2009 Pandemic Influenza A (pH1N1)–Related Hospitalizations at 10 EIP Sites and Resultant Extrapolation From Entire United States (Weeks 35–14)[a]

	Hospitalizations: Reported and extrapolated[c]
Reported from 10 EIP sites[b]	
Hospitalizations (lab confirmed)	**6424**
Extrapolated to entire US[d]	
Hospitalizations	**93,815** ***(66,721–137,734)[d]***

[a] Week 35 ends September 5, 2009, and week 14 ends April 10, 2010.

[b] There are 10 Emerging Infections Program (EIP) sites. There are approximately 22 million persons in the catchment areas of the EIP sites. For details about the EIP program and sites, please see http://www.cdc.gov/ncpdcid/deiss/about_eip.html.

[c] The reported hospitalizations are laboratory-confirmed cases of 2009 H1N1 reported to the CDC from the 10 EIP sites.

[d] For a description of the methods used to extrapolate the number of hospitalizations to the 50 US states, please see the footnotes to Table 2 and the main text.

or older, however, were hospitalized at a rate of 70 per 100 000, 75% lower than estimated hospitalization rates for this age group (Table 4).

Children experienced an estimated rate of death due to pH1N1 of 1.7 (range: 1.2–2.5) per 100 000. This is approximately 8 times greater than the average rate of death from seasonal influenza during years 1990–1999 as estimated from data by Thompson et al. [5] (Table 4). The estimated rate of death per 100 000 among adults aged 18–64 years was 5.0 (range: 3.6-7.3), which is approximately 12 times greater than estimated for this age group during 1990–1999. Adults aged 65 years or older experienced an estimated rate of death due to pH1N1 of 4.2 (range: 3.0–6.1), approximately 19% of the average rate estimated rate from 1990–1999 for this age group (Table 4).

Table 3. Validation: Comparison of Previous Estimates of Pneumonia and Influenza-Related Hospitalizations During Nonpandemic H1N1 and H3N2 Seasons vs Our Estimates for 2007/2008 and 2008/2009 Seasons

Predominant nonpandemic subtype	Thompson et al.[a]	Our estimates[b]
	Various seasons[c]	2008/09
A(H1N1)	81,225 (30,757–127,328)	78,173 (61,156–138,346)
	Various seasons[d]	2007/08
A(H3N2)	145,532 (67,710–271,529)	153,511 (120,111–248,841)

[a] Thompson et al. [4], Table 2. Estimates show the median (minimum and maximum) estimated hospitalizations for pneumonia or influenza (any listed in cause of hospitalization) as calculated by Thompson et al.

[b] Our estimates, for 2 years (2007/08 and 2008/09), using reports from the 10 EIP sites to the CDC of laboratory-confirmed influenza-related hospitalizations. We used the methodology described in the main text to both extrapolate the reported hospitalizations to the entire United States and then correct for underreporting.

[c] Seasons included, when an AH1N1, nonpandemic type was predominant: 1981/1982, 1983/1984, 1986/1987, 1988/1989, and 2000/2001.

[d] Seasons included, when an AH3N2, non-nonpandemic type was predominant: 1980/1981, 1982/1983, 1984/1985, 1985/1986, 1987/1988, 1989/1990, 1991/1992, 1992/1993, 1994/1995, 1995/1996, 1996/1997, 1997/1998, 1998/1999, 1999/2000. These seasons include those season in which H3N2 cocirculated predominately with either a B strain or an H1N1 type strain. Note that seasons 1979/1980 and 1990/1991 are not included because during those seasons only B types predominately circulated.

DISCUSSION

We developed a model to determine the impact of the H1N1 pandemic in the United States. For the period 12 April 2009, to 10 April 2010, we estimated that the pandemic caused approximately 61 million symptomatic cases, 274 000 hospitalizations, and 12 500 deaths. Similar to what has been described for seasonal influenza, surveillance systems that report laboratory-confirmed pH1N1-related hospitalizations and deaths provide a significant underestimate of burden imposed by pH1N1 [3]. Our estimates are the first to provide a systematic correction for such underreporting, and the estimates demonstrate the magnitude of the H1N1 pandemic and the importance of a concerted public health response.

The higher estimated rates of hospitalizations and deaths due to 2009 H1N1 among children and adults 18–64 years of age compared to seasonal influenza estimates demonstrate that the pH1N1 imposed a notable burden upon people in these age groups. Equally striking were the lower estimated hospitalization and death rates compared to those for seasonal influenza among those 65 years of age and older.

Using our estimate of the number of symptomatic cases, pH1N1 caused a population-wide clinical attack rate of approximately 20% (range: 14%–29%). Estimates of the population-wide clinical attack rates for the 3 pandemics in the twentieth century range from approximately 25% to 35% [7, 8]. A lower attack rate from pH1N1 compared to previous pandemics could be attributed to lower attack rates among those aged 65 years or older. This decrease in pandemic-related risk of clinical illness among adults aged 65 years or older is likely related, in part, to the existence of immunity from prior exposure to H1N1 viruses that are antigenically more closely related to the pH1N1 strain compared with seasonal influenza [9].

There are a number of limitations associated with our estimates. Although our methodology produced estimates for seasonal influenza that are very similar to previously published estimates from different years of seasonal influenza (Table 4), it is not proof that our estimates are robust. We used single estimates of multipliers [3] that were measured early in the pandemic and applied across age groups and across time periods. These multipliers could have changed during the course of the

Table 4. Comparing Impact: 2009 Pandemic Influenza A (pH1N1) vs Seasonal Influenza: Deaths and Hospitalizations per 100,000 by Age Groups

	Numbers per 100,000 (ranges)			
	Deaths		Hospitalizations	
Age (years)	Median pH1N1[a]	Average 1990 to 1999[b]	Median pH1N1[a]	Average 1979 to 2001[c]
0–17	1.7	0.2	117.4	15.8
	(1.2–2.5)	(.03–.4)	(83.5–172.4)	(3.6–32.3)
18–64	5.0	0.4	83.8	20.8
	(3.6–7.3)	(.07–1.0)	(59.6–123.0)	(4.8–42.4)
65+	4.2	22.1	70.1	282
	(3.0–6.1)	(3.8–54.1)	(49.9–103.0)	(64.8–575.2)
All	4.1	3.1	90.2	52.4
	(2.9–6.0)	(.5–7.6)	(64.2–132.4)	(12.1–107.0)

[a] Median, minimum, and maximum calculated from the total estimates of deaths and hospitalizations, April 12, 2009–April 10, 2010 (cf Table 2). Rates calculated using estimates of US population as at July 1, 2008. 0–17 years, 74.6 million; 18–64 years, 190.5 million; 65+ years, 38.9 million. Source: Table 1: Annual Estimates of the Resident Population by Sex and Five-Year Age Groups for the United States: April 1, 2000, to July 1, 2008 (NC-EST2008-01) US Census Bureau. Release Date: May 14, 2009. Available at http://www.census.gov/popest/national/asrh/NC-EST2008-sa.html.

[b] Underlying pneumonia and influenza deaths, calculated from Table 5 in Thompson et al. 2003 (5). We estimated ranges based on the proportion of the minimum and maximum number of annual deaths to the mean number of deaths (Table 3, ref. [5]). The minimum was .17 of the mean, and the maximum was 2.45 of the mean. We used these proportions to estimate ranges about the mean number of deaths per 100,000 per age group.

[c] Underlying pneumonia and influenza-related hospitalizations, where pneumonia or influenza was listed as, upon patient discharge, any cause of hospitalization. We estimated ranges based on the proportion of the minimum and maximum number of annual hospitalizations compared to the mean number of hospitalizations (Table 2, ref. [4]). We used these proportions to estimate ranges about the mean number of hospitalizations per 100,000 per age group.

pandemic, altering the estimated number of hospitalizations, cases, and deaths. Furthermore, the method relied upon the extrapolation of data recorded at 10 EIP sites. These sites cover approximately 7% of the US population, and the distribution of such sites is not done on a statistically random basis. Thus the extrapolated rate of hospitalizations may not reflect what was experienced in states without EIP sites. Also, we used a single set of estimates of deaths as a percentage of hospitalizations (from the AHDRA data). These percentages did increase past November (the month in which we fixed the percentages used). Thus we could have underestimated deaths. We believe that our estimates are conservatively low, in that there are larger, published multipliers to correct for underreporting of hospitalizations and calculations of cases [10]. However, the confidence intervals of these larger multipliers greatly overlapped with the confidence intervals of the multipliers that we used [3]. Thus we believe that our estimates are not unrealistically low. Additional analyses using death certificate data from the pandemic period and analytic methods similar to those used by Thompson et al. [4, 5] may help further validate these results. The relevant data from death certificates typically takes 2 to 3 years to become available.

An important advantage of our method is that it allowed for serial estimates of cases, hospitalizations, and deaths to be produced as the pandemic progressed. These ''near real time'' estimates allowed public health officials to refine response plans as the pandemic evolved. Another important feature of our method is that it allowed us to make the best use of all the relevant available data produced by ILINet, AHDRA, and EIP surveillance systems. The use of multipliers calculated from field data collected early in the pandemic [3] helped generate estimates that reflected the unique impact of pH1N1. For example, the actual death rates among those over 65 years of age were much lower than those anticipated in previous publications [8].

We used a method of estimation that is new to the field of influenza, although it has been used in other fields, such as measuring the burden of food-borne diseases [11]. The standard statistical models used to date to estimate influenza-related hospitalizations and deaths [4, 5] require the use of data sets that are only fully assembled some 2 to 3 years after a given season. The method demonstrated here allows a more rapid but still reasonable assessment of impact. Both methods can contribute to a better understanding of the burden imposed by influenza.

Appendix Table A1: Comparing the Difference in Variability Produced by Two Different Methods Used to Derive Estimates

	Influenza seasons	
	2007/2008	*2008/2009*
Method A: Allowing for geographic differences in influenza activity[a]		
Median:	51,490	24,293
Min:	38,880	17,337
Max:	87,271	47,707
Mean:	57,246	28,233
Variability: Range as % of mean[b]	84.5%	107.6%

Method B: No allowance for geographic difference in weighted activity[a]		
Median:	45,930	19,057
Min:	14,874	6,162
Max:	175,843	83,922
Mean:	60,407	26,611
Variability: Range as % of mean[b]	266.5%	292.2%

[a] Method A is the method described in the main text, in which each week the EIP sites are divided into low, medium and high rates of influenza-related hospitalizations, and the 50 states are divided into three groups (low, medium, and high) based on rates of ILI visits to physician offices (as reported to ILI net (see main text for further details). Method B simply takes the weekly average rate of influenza-related hospitalization from all the EIP sites and extrapolates that rate to all 50 states, without any adjustments for different levels of influenza activity between states.

[b] Variability is calculated as follows: Range as % of mean = (Maximum value – minimum value)/mean × 100. The lower the calculated the percent, the less variability generated by the method used.

Additionally, we believe that both methods can be replicated in various forms in other countries that have lacked local measurements of the burden of influenza. In time, this would allow a measurement of the global burden of influenza, which would aid many public health policy decisions regarding the prevention and control of influenza.

Acknowledgments

We wish to thank the following for providing essential data: California Emerging Infections Program, Oakland, California, USA; Colorado Department of Public Health and Environment, Denver, Colorado, USA; Connecticut Emerging Infections Program, Yale University, New Haven, Connecticut, USA; Georgia Emerging Infections Program—a collaboration between Georgia Division of Public Health, Emory University, and the Atlanta Veterans Administration Medical Center, Atlanta, Georgia, USA; Maryland Department of Health and Mental Hygiene, Baltimore, Maryland, USA; Minnesota Department of Health, St. Paul, Minnesota, USA; Emerging Infections Program, New Mexico Department of Health, Santa Fe, New Mexico, USA; New York State Health Department, Albany, New York, USA; Center for Community Health and Department of Medicine, University of Rochester School of Medicine and Dentistry, Rochester, New York, USA; Oregon Public Health Division, Portland, Oregon, USA; Tennessee Department of Health, Nashville, Tennessee; Department of Preventive Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee, USA.

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.

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