The second wave of influenza A(H1N1)pdm09 virus occurred in the United States from September 2009 through April 2010, had a prolonged duration, and was associated with high rates of pediatric hospitalizations and pediatric mortality [1-4]. The US national public health response to the influenza A(H1N1)pdm09 virus pandemic, led by the Centers for Disease Control and Prevention (CDC), was altogether extraordinary in its extent and effectiveness. The characterization of a novel pandemic influenza virus—and the development and distribution of diagnostic testing protocols, antiviral drug resistance information, and vaccine—occurred at unprecedented speed [5]. An important part of this response was the characterization of the total burden of influenza A(H1N1)pdm09 virus among persons of all ages, which may be important as future epidemic response plans are prepared and refined. Recent epidemics—including Severe Acute Respiratory Syndrome, pandemic influenza A(H1N1)pdm09, Middle East Respiratory Syndrome, Enterovirus 68, and Ebola—have highlighted the need to measure disease burden [1, 4, 6-17]. Multiple approaches can be used to measure disease burden: passive surveillance, active surveillance, capture-recapture analysis, and administrative databases.

Passive surveillance often counts physician-ordered, clinical laboratory-confirmed cases [18]. This approach utilizes available data with laboratory confirmation, which is relatively inexpensive. However, it can underestimate disease burden if disease is not clinically suspected, if clinicians do not order specific testing, or if a test with low sensitivity is ordered.

Active surveillance includes systematically testing persons who meet prespecified criteria regardless of whether disease is clinically suspected. This approach often requires enrolling patients and is much more costly, but it generally detects more disease, including milder forms of illness. Active surveillance is often performed during limited time periods, based on the assumption that disease rates and presentation are similar during time periods with and without active surveillance.

Estimating the Burden of Pandemic Infectious Disease: The Case of the Second Wave of Pandemic Influenza H1N1 in Forsyth County, North Carolina

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BACKGROUND Understanding the burden of influenza A(H1N1)pdm09 virus during the second wave of 2009–2010 is important for future pandemic planning.

METHODS Persons who presented to the emergency department (ED) or were hospitalized with fever and/or acute respiratory symptoms at the academic medical center in Forsyth County, North Carolina were prospectively enrolled and underwent nasal/throat swab testing for influenza A(H1N1)pdm09. Laboratory-confirmed cases of influenza A(H1N1)pdm09 virus identified through active surveillance were compared by capture-recapture analysis to those identified through independent, passive surveillance (physician-ordered influenza testing). This approach estimated the number of total cases, including those not captured by either surveillance method. A second analysis estimated the total number of influenza A(H1N1)pdm09 cases by multiplying weekly influenza percentages determined via active surveillance by weekly counts of influenza-associated discharge diagnoses from administrative data. Market share adjustments were used to estimate influenza A(H1N1)pdm09 virus ED visits or hospitalizations per 1,000 residents.

RESULTS Capture-recapture analysis estimated that 753 residents (95% confidence interval [CI], 424–2,735) with influenza A(H1N1)pdm09 virus were seen in the academic medical center from September 2009 through mid-April 2010; this result yielded an estimated 4.7 (95% CI, 2.6–16.9) influenza A(H1N1)pdm09 virus ED visits or hospitalizations per 1,000 residents. Similarly, 708 visits were estimated using weekly influenza percentages and influenza-associated discharge diagnoses, yielding an estimated 4.4 influenza A(H1N1)pdm09 virus ED visits or hospitalizations per 1,000 residents.

CONCLUSION This study demonstrates that the burden of influenza A(H1N1)pdm09 virus in ED and inpatient settings by capture-recapture analysis was 4–5 per 1,000 residents; this rate was approximately 8-fold higher than that detected by physician-ordered influenza testing.
Capture-recapture methods are statistical methods that can be used to estimate the burden of disease, including influenza [9, 19-21]. This epidemiological approach combines data from 2 independent surveillance methods, and it can overcome the biases toward underestimation of disease burden that are inherent in each method when used separately. If passive and active surveillance are independently performed in overlapping time periods, then these results can be combined to estimate the total burden. An important strength is that capture-recapture analysis accounts for time periods when active surveillance was not performed during the study period.

Finally, administrative databases have been used to estimate the burden of disease. Like passive surveillance, this approach uses data collected for other purposes, making it less costly. However, this method is dependent on discharge diagnosis patterns in the population. For diseases that can have multiple clinical presentations and discharge diagnoses, such as influenza, administrative databases are sensitive but lack specificity. An approach that has been used to better measure disease burden is to estimate disease rates by combining discharge diagnosis data from administrative databases with data from active surveillance [9, 22]. This approach can estimate the number of cases during an epidemic that are not specifically diagnosed and can account for changes in disease prevalence over time.

The first wave of influenza A(H1N1)pdm09 during the 2009–2010 season began in April 2009, and most reports of high disease burden in the United States in the spring and summer were from large cities [23-25]. According to the North Carolina Department of Health and Human Services, the state had a small increase in influenza-like illness in the spring and summer of 2009, and then a dramatic increase was seen in the first week of September. Similarly, the distribution of the 107 influenza-associated deaths reported in North Carolina illustrates the predominant second wave: 8% of deaths occurred before September 1, 2009; 58% occurred during the peak (September 1, 2009 to December 4, 2009); and 34% occurred after the peak (December 5, 2009 to May 8, 2010) [26].

Throughout the second wave of the influenza A(H1N1)pdm09 season, we prospectively conducted active surveillance of patients presenting with fever or acute respiratory symptoms to the emergency department (ED) or inpatient settings of the academic medical center serving persons of all ages in Forsyth County, North Carolina. Forsyth County encompasses Winston–Salem, the 4th largest city in North Carolina. According to the 2010 US census, Forsyth County had an estimated population of 350,670 persons, 65% of whom resided within Winston–Salem. The county’s population was 64% white, 27% black, and 9% other races; 12% of the population was Hispanic [27]. Simultaneously and independently, a detailed compilation of passive surveillance from clinical laboratory-confirmed cases of influenza A(H1N1)pdm09 virus was performed for purposes of hospital infection control.

The availability of these 2 independent data sources allowed us to perform a capture-recapture analysis to estimate the total burden of influenza A(H1N1)pdm09 virus among Forsyth County residents who were seen in the ED or inpatient setting. We also performed a separate analysis to estimate influenza A(H1N1)pdm09 virus ED visits and hospitalizations by combining hospital discharge diagnoses (administrative data) with the proportion of persons with study-confirmed influenza from active surveillance. Thus, we used 2 different methods to combine data collected from passive surveillance, active surveillance, and administrative data to estimate the total disease burden in Forsyth County.

Methods

Active Surveillance

We prospectively enrolled Forsyth County residents of all ages who were evaluated in the ED and/or admitted to an inpatient unit of Wake Forest Baptist Health with fever and/or acute respiratory symptoms. Active surveillance was performed from September 1, 2009 through April 12, 2010, the date of the last laboratory-confirmed case of influenza from active or passive surveillance. Eligible persons were identified based on presenting symptoms and were prospectively enrolled 4 days per week. Identification of eligible patients was independent of the clinical laboratory testing and influenza surveillance performed by the hospital’s infection control service.

After obtaining written informed consent (and child assent, if appropriate), a standardized questionnaire was administered, nasal and throat swabs were obtained, and a chart review of that visit was performed. Nasal and throat swabs from each patient were placed in 1 tube of viral transport media and transported to the laboratory on ice. Laboratory results of the active surveillance were not shared with patients or their treating physicians.

RNA was extracted from these nose/throat specimens and analyzed using real-time, reverse-transcriptase polymerase chain reaction (RT-PCR) assays to detect influenza A(H1N1)pdm09 virus. RT-PCR analysis protocols, probe sequences, and primer sequences were provided by the CDC. Human RNase P gene RNA was detected in parallel for each specimen, which confirmed adequate sample collection.

Passive Surveillance

Throughout the influenza A(H1N1)pdm09 season, the infection control service at Wake Forest Baptist Health conducted passive influenza surveillance, based on physician-ordered testing, of all patients seen in the ED or admitted to inpatient settings. We identified all patients with laboratory-confirmed, physician-ordered influenza testing in outpatient or inpatient settings or referred from an outside clinic or hospital with a positive influenza test result.
Physician-ordered influenza testing included rapid influenza antigen testing, viral culture, and molecular diagnosis for influenza A(H1N1)pdm09 virus using RT-PCR assays. All of these assays had been validated for use with clinical samples and were being used for routine clinical testing. Physician-ordered influenza diagnostic testing was consistent with CDC recommendations; specifically, it focused on hospitalized patients with suspected influenza and on “patients for whom a diagnosis of influenza will inform decisions regarding clinical care, infection control, or management of close contacts” [28].

**Capture-Recapture Analysis**

We used capture-recapture analysis to estimate the total burden of influenza A(H1N1)pdm09 seen in the ED and inpatient settings at Wake Forest Baptist Health from September 1, 2009 through April 12, 2010, using data from 2 independent surveillance systems: active surveillance and passive surveillance (physician-ordered influenza testing) [29, 30].

The capture-recapture data were summarized using Table 1. The number of persons detected by both active surveillance and passive surveillance was denoted as $a$; the number of persons detected by passive surveillance only was denoted as $b$; the number of persons detected by active surveillance only was denoted as $c$; and the unknown number missed by both active and passive surveillance was denoted as $z$. The total number of cases is expressed by the formula $N = [(a+b+1)(a+c+1)/(a+1)] - 1$ [30]. A 95% profile likelihood confidence interval (CI) for the total number of cases is derived based on the 2 × 2 table data under a multinomial model assuming stochastic independence and enrollment probabilities that may differ between the surveillance procedures [29].

**Estimates From ICD-9 Discharge Diagnostic Codes**

Discharge diagnoses associated with influenza have been previously described to estimate hospital influenza burden [18]. All Forsyth County residents discharged from the ED or inpatient settings at Wake Forest Baptist Health who were assigned influenza-associated ICD-9 codes (487, 480–486, 460–466, 490–519, 422, and 427–428) were captured for each week from September 1, 2009 through April 17, 2010 and were grouped by age (0–17 years, 18–49 years, or 50 years or older). These ICD-9 discharge diagnosis codes were evaluated in hierarchical order as listed above (influenza, pneumonia, and other respiratory diagnoses and cardiac diagnoses) so that each visit with 1 or more of these discharge codes was counted only once. This data was used to estimate the weekly total for the number of residents discharged from Wake Forest Baptist Health with influenza-associated discharge diagnoses.

For ED visits and hospitalizations, the proportions of all influenza-associated discharge codes with an influenza-specific discharge diagnosis by age group were compared by Pearson’s chi-square analysis. The 95% CIs for the proportion of all influenza-associated discharge diagnoses for each hierarchical category were computed using Wilson’s intervals for binomial distributions [31].

To estimate the burden of influenza A(H1N1)pdm09 virus from influenza-associated discharge codes, we multiplied the weekly proportion of enrolled patients who underwent active surveillance and had laboratory-confirmed influenza A(H1N1)pdm09 times the weekly number of patients with influenza-related discharge diagnoses. These products were then summed across weeks to estimate the total number of residents who visited the ED or were hospitalized at Wake Forest Baptist Health with influenza A(H1N1)pdm09 infection.

For 2 nonconsecutive weeks when active influenza surveillance was not performed, we estimated the proportion of patients with laboratory-confirmed influenza A(H1N1)pdm09 by averaging the proportions from the week before and after the week for which data were missing [9, 22]. We compared the estimated total burden of influenza A(H1N1)pdm09 virus on ED visits and hospitalizations based on the influenza-associated discharge codes and surveillance to the 95% CIs for the capture-recapture estimate.

**Computation of Population-Based Estimates**

Regional health care market share data were used to estimate the population-based burden of influenza A(H1N1)pdm09 disease in Forsyth County, North Carolina. Inpatient and ED hospital market share data for county residents were derived from data compiled by the North Carolina Hospital Association.

The numerator for influenza A(H1N1)pdm09 visits equaled the sum of the estimated number of influenza A(H1N1)pdm09 ED visits and hospitalizations divided by the market share for that hospital. The denominator was the Forsyth County population from the 2010 US census [27]. The rate per 1,000 persons was the estimated number of influenza A(H1N1)pdm09 visits adjusted for market share, divided by the county population and multiplied...
by 1,000. Statistical analyses were performed with S+ version 9.1 for Windows and with SAS version 9.2.

Approval

All components of this study were reviewed and approved by the Wake Forest School of Medicine institutional review board.

Results

Active surveillance with influenza confirmed by RT-PCR was performed from September 1, 2009 through April 12, 2010 in the pediatric and adult EDs and inpatient settings at Wake Forest Baptist Health. During this period, 40 of 696 (6%) enrolled persons who resided in Forsyth County had confirmed influenza A(H1N1)pdm09. Few persons with influenza A(H1N1)pdm09 were hospitalized (3 of 40; 8%). Demographic characteristics of enrolled persons with influenza A(H1N1)pdm09 who were identified via active surveillance are shown in Table 2.

Passive surveillance (physician-ordered testing) for influenza A(H1N1)pdm09 was independently conducted at Wake Forest Baptist Health throughout the influenza season. Passive surveillance captured all patients seen in pediatric or adult EDs and inpatient settings who had a positive result for a physician-ordered influenza test (see Table 2). From September 1, 2009 through April 12, 2010, a total of 91 Forsyth County residents had physician-ordered diagnostic laboratory testing that was positive for influenza A(H1N1)pdm09. Almost all patients identified by passive surveillance were hospitalized during the peak of the influenza epidemic (September 1, 2009 through December 4, 2009).

A total of 127 persons were positive for influenza A(H1N1)pdm09 by either active or passive surveillance (see Table 3). Four persons were identified by both systems; 36 persons were identified by active surveillance only; and 87 persons were identified by passive surveillance only. Using the capture-recapture formula, we estimated that 753 persons were hospitalized during the peak of the influenza epidemic (September 1, 2009 through December 4, 2009).

A second method for estimating the influenza A(H1N1)pdm09 burden was also used, and these results were compared with those of the capture-recapture analysis. First, we estimated the total number of patients discharged from the ED or inpatient settings with 1 or more influenza-associated ICD-9 discharge code. A total of 6,999 ED visits and 3,580 hospitalizations associated with these ICD-9 codes were identified from September 1, 2009 through April 17, 2010 (see Table 4). Children accounted for 49% of these ED visits, with a progressive decline with increasing age, and adults 50 years or older accounted for 69% of these hospitalizations, with a progressive decline with decreasing age ($P < .001$). An influenza-specific discharge diagnosis was identified for 9% of ED visits and 1% of hospitalizations. The proportion of persons with an influenza-specific discharge diagnosis as compared to any influenza-associated discharge diagnosis was highest for children and progressively decreased with increasing age; this trend held true both in the ED (11% for patients 0–17 years, 9% for patients 18–49 years, and 3% for patients 50 years or older; $P < .001$) and in the inpatient setting (6%, 2%, and 1% respectively; $P < .001$).

The summation of the product of weekly influenza-associated discharge diagnoses times the proportion of persons with influenza A(H1N1)pdm09—were missed by both active and passive surveillance were hospitalized during the peak of the influenza epidemic (September 1, 2009 through December 4, 2009).

### Table 2.

**Characteristics of Forsyth County Residents With Influenza A(H1N1)pdm09 Identified Through Active or Passive Surveillance**

|                      | Active surveillance\(a\) | Passive surveillance\(b\) | P-value\(c\) |
|----------------------|--------------------------|--------------------------|--------------|
| Total                | 40                       | 91                       |              |
| Age                  |                          |                          |              |
| 0–17 years           | 18 (45%)                 | 42 (46%)                 | .17          |
| 18–49 years          | 16 (40%)                 | 24 (26%)                 |              |
| 50 years or older    | 6 (15%)                  | 25 (27%)                 |              |
| High-risk conditions\(d\) |                      |                          |              |
| Yes                  | 20 (50%)                 | 70 (77%)                 | .004         |
| No                   | 20 (50%)                 | 21 (23%)                 |              |
| Time of enrollment\(e\) |                      |                          |              |
| Peak                 | 27 (68%)                 | 82 (90%)                 | .004         |
| After peak           | 13 (33%)                 | 9 (10%)                  |              |
| Sex                  |                          |                          |              |
| Male                 | 15 (38%)                 | 44 (48%)                 | .26          |
| Female               | 25 (63%)                 | 47 (52%)                 |              |
| Race/ethnicity       |                          |                          |              |
| Non-Hispanic white   | 15 (38%)                 | 29 (32%)                 | .90          |
| Non-Hispanic black   | 16 (40%)                 | 42 (46%)                 |              |
| Hispanic             | 8 (20%)                  | 18 (20%)                 |              |
| Other/unknown        | 1 (3%)                   | 2 (2%)                   |              |
| Health insurance     |                          |                          |              |
| Public               | 22 (55%)                 | Not collected —          |              |
| Any private          | 12 (30%)                 | 6 (7%)                   |              |
| None/unknown         | 6 (15%)                  | 6 (7%)                   |              |

\(a\)Active surveillance was determined by influenza detection from prospective, population-based, laboratory-confirmed surveillance.

\(b\)Passive surveillance was determined by influenza detection from physician-ordered influenza testing.

\(c\)P-values are for comparison of each characteristic between the 2 surveillance groups based on Pearson’s chi-square and Fisher’s exact tests.

\(d\)High-risk conditions include those medical conditions associated with increased risk for complications from influenza (cardiac, hematologic, metabolic, neurological, pulmonary and renal disorders; primary and secondary immunodeficiencies; and pregnancy) [35].

\(e\)Peak influenza A(H1N1)pdm09 season spanned the dates September 1, 2009 through December 4, 2009. After-peak influenza A(H1N1)pdm09 season spanned the dates December 5, 2009 through April 12, 2010.
enrolled in active surveillance with confirmed influenza yielded an estimated 708 influenza A(H1N1)pdm09 visits (data not shown). Of these 708 visits, an estimated 573 (81%) were ED visits, and 135 (19%) were hospitalizations.

We used these 2 estimates to determine influenza A(H1N1)pdm09 visit rates for the Forsyth County population using hospital market share data from the North Carolina Hospital Association. Using the summation of the product of weekly influenza-associated discharge diagnoses multiplied by the proportion of persons enrolled in active surveillance with confirmed influenza, we estimated 4.4 influenza A(H1N1)pdm09 visits per 1,000 residents, with 3.5 ED visits and 0.9 inpatient visits per 1,000 residents. Using the results from the capture-recapture analysis, we estimated 4.7 influenza A(H1N1)pdm09 visits per 1,000 residents (95% CI, 2.6–16.9).

Discussion

Two complementary methods to estimate rates of ED visits and hospitalizations due to influenza A(H1N1)pdm09 among residents of Forsyth County, North Carolina yielded similar results; 753 ED visits or hospitalizations were estimated using capture-recapture analysis, and 708 ED visits or hospitalizations were estimated using administrative data and active surveillance. After adjusting for hospital market share, we estimated that there are 4–5 influenza A(H1N1)pdm09 ED visits or hospitalizations per 1,000 Forsyth County residents. The influenza A(H1N1)pdm09 burden was much higher in the ED than in the inpatient setting.

These estimates of the influenza A(H1N1)pdm09 burden in Forsyth County are higher than those reported by the North Carolina Department of Health and Human Services. This is an expected result, since the state laboratory performed RT-PCR testing on only a small subset of patients presenting with influenza-like illness in 2009–2010. Specifically, the state laboratory identified a total of 487 influenza A(H1N1)pdm09 isolates during this season [26]. Further, capture-recapture analysis provided the opportunity to estimate the total burden of disease, since many patients were likely missed by both active and passive surveillance. Active surveillance was systematically performed only during weekdays, and thus it did not capture cases that presented on weekends or evenings. Passive surveillance was continuously available, but testing recommendations were focused on patients needing hospitalization or at risk for severe disease [28]; thus many patients with suspected disease were not tested. As expected, the proportion of patients hospitalized with influenza A(H1N1)pdm09 was much lower in groups enrolled in active surveillance than in patient groups identified via passive surveillance (8% versus 93%, respectively). These data indicate that a large proportion of patients with influenza were seen in the ED but were not captured by passive surveillance, while many (but not all) hospitalized influenza patients were captured by this method. Hence, the estimated burden using capture-recapture methodology was approximately 8-fold higher than the disease burden estimated using passive surveillance alone.

Our findings are comparable with those of several published studies. Jules and colleagues used similar methodology and estimated a rate of 0.94 hospitalizations per 1,000 residents of Davidson County, Tennessee in 2009–2010 [9]. This result is similar to our overall estimate of 0.9 hospitalizations per 1,000 residents of Forsyth County, North Carolina. The first wave of influenza A(H1N1)pdm09 varied geographically and was included in their estimates but not in our estimates. They noted that studies reporting clinical testing data consistently show lower hospitalization rates, likely due to under-testing for influenza [32–34]. This observation was supported by our findings.

In another study, Self and colleagues estimated influenza A(H1N1)pdm09 ED visit rates to be approximately 10 visits per 1,000 residents of Davidson County, Tennessee in 2009–2010 [21]. We had a lower estimate of 3.5 ED visits per 1,000 residents of Forsyth County, North Carolina, which may reflect geographic variation in disease burden, geographic variation in health care utilization, or differences associated with inclusion of the first wave. However, our data were consistent with their pattern showing higher rates of influenza A(H1N1)pdm09 ED visits in children than in older adults.

Our results compared and contrasted with the estimates from 10 states in the CDC’s Emerging Infections Program [7]. Using multi-state, physician-ordered, and hospital-confirmed influenza surveillance data, Cox and colleagues estimated 0.33 influenza A(H1N1) hospitalizations per 1,000 persons [7], which is lower than the estimated 0.9 hospitalizations per 1,000 persons found in both the study

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**TABLE 3. Estimating the Total Burden Based on Results of 2 Independent Influenza A(H1N1)pdm09 Surveillance Systems**

| Surveillance Method | Observed Influenza A(H1N1)pdm09 | Detected | Missed | Total |
|---------------------|---------------------------------|----------|--------|-------|
| Active surveillance | Influenza A(H1N1)pdm09 Detected | 4        | 87     | 91    |
|                     | Influenza A(H1N1)pdm09 Missed    | 36       | 626    | 662   |
| Total               |                                 | 40       | 713    | 753 (95% CI, 424–2,735) |

Note. CI, confidence interval.

*Active surveillance enrolled patients with fever and/or acute respiratory illness in the emergency department or inpatient setting and prospectively tested all for influenza A(H1N1)pdm09 to determine their influenza A(H1N1)pdm09 status.

Passive surveillance identified patients who had a positive physician-ordered influenza test.

The total estimated burden is 753; the 95% confidence interval is based on profile likelihood.

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Because of the limitations of passive surveillance, we estimated using capture-recapture analysis, and 708 ED visits or hospitalizations were estimated using administrative data and active surveillance. After adjusting for hospital market share, we estimated that there are 4–5 influenza A(H1N1)pdm09 ED visits or hospitalizations per 1,000 Forsyth County residents. The influenza A(H1N1)pdm09 burden was much higher in the ED than in the inpatient setting.

These estimates of the influenza A(H1N1)pdm09 burden in Forsyth County are higher than those reported by the North Carolina Department of Health and Human Services. This is an expected result, since the state laboratory performed RT-PCR testing on only a small subset of patients presenting with influenza-like illness in 2009–2010. Specifically, the state laboratory identified a total of 487 influenza A(H1N1)pdm09 isolates during this season [26]. Further, capture-recapture analysis provided the opportunity to estimate the total burden of disease, since many patients were likely missed by both active and passive surveillance. Active surveillance was systematically performed only during weekdays, and thus it did not capture cases that presented on weekends or evenings. Passive surveillance was continuously available, but testing recommendations were focused on patients needing hospitalization or at risk for severe disease [28]; thus many patients with suspected disease were not tested. As expected, the proportion of patients hospitalized with influenza A(H1N1)pdm09 was much lower in groups enrolled in active surveillance than in patient groups identified via passive surveillance (8% versus 93%, respectively). These data indicate that a large proportion of patients with influenza were seen in the ED but were not captured by passive surveillance, while many (but not all) hospitalized influenza patients were captured by this method. Hence, the estimated burden using capture-recapture methodology was approximately 8-fold higher than the disease burden estimated using passive surveillance alone.

Our findings are comparable with those of several published studies. Jules and colleagues used similar methodology and estimated a rate of 0.94 hospitalizations per 1,000 residents of Davidson County, Tennessee in 2009–2010 [9]. This result is similar to our overall estimate of 0.9 hospitalizations per 1,000 residents of Forsyth County, North Carolina. The first wave of influenza A(H1N1)pdm09 varied geographically and was included in their estimates but not in our estimates. They noted that studies reporting clinical testing data consistently show lower hospitalization rates, likely due to under-testing for influenza [32–34]. This observation was supported by our findings.

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Our results compared and contrasted with the estimates from 10 states in the CDC’s Emerging Infections Program [7]. Using multi-state, physician-ordered, and hospital-confirmed influenza surveillance data, Cox and colleagues estimated 0.33 influenza A(H1N1) hospitalizations per 1,000 persons [7], which is lower than the estimated 0.9 hospitalizations per 1,000 persons found in both the study.
systems had low sensitivity. However, this low overlap was just 4 persons, highlighting the fact that both surveillance rates of influenza ED and hospital visits based on administrative data and active surveillance. The agreement of active and passive surveillance having a larger proportion of influenza A(H1N1)pdm09 that were identified using both inpatient burden of influenza A(H1N1)pdm09 were at least 5-fold higher than the reported historical mean (0.1–0.16 per 1,000 for seasonal influenza) from 4–6 years prior to 2009–2010.

Given the large disease burden of undiagnosed influenza, accurate measurement of the disease burden is increasingly important, and this measurement is enhanced by the use of capture-recapture methods [9, 19-21]. We have used this statistical approach to overcome limitations inherent in active surveillance (limited sampling and high expense) and limitations in passive surveillance based on physician-ordered testing (disease under-recognition and under-testing). We also used a complementary analysis to determine rates of influenza ED and hospital visits based on administrative data and active surveillance. The agreement of results from these independent statistical analyses provides further confidence in these estimates.

This study has important limitations. First, case capture overlap between active and passive surveillance was just 4 persons, highlighting the fact that both surveillance systems had low sensitivity. However, this low overlap was expected both because active surveillance was not continuous and because passive surveillance followed the recommendations to test only those with severe disease or those at risk of complications [28]. Second, the use of influenza-associated ICD-9 codes to estimate the burden of influenza relies on appropriate discharge coding. Significant variations in hospital ICD-9 coding practices were not observed, but bias due to this effect is a possibility. For example, if patients were assigned influenza A(H1N1)pdm09 codes other than the ICD-9 codes that we considered to be influenza-associated, this could lead to underestimation of influenza ED and hospital visit rates. However, we used hospital ICD-9 codes that have been previously reported. A third limitation is that the clinical performance of hospital laboratory testing for influenza A(H1N1)pdm09 improved throughout the 2009–2010 season as testing methods were refined, and this may have led to relative under-ascertainment of influenza cases early in the season. Fourth, groups with influenza A(H1N1)pdm09 that were identified using both active and passive surveillance had a larger proportion of blacks and Hispanics compared to the county population. This difference could represent a selection bias, leading to either an overestimation or underestimation of disease rates in these groups, or it could reflect differences in health care utilization. For example, there could be systematic differences between groups in terms of seeking influenza H1N1

### Table 4
Number of Forsyth County Residents by Age Group With an Emergency Department or Hospital Visit With an Influenza-Associated Discharge Diagnosis, in Hierarchical Order

| Age group      | Influenza* N (row %) | Pneumonia* N (row %) | Other respiratory diagnoses N (row %) | Cardiac diagnoses N (row %) | Total N |
|----------------|----------------------|----------------------|--------------------------------------|-----------------------------|---------|
|                | Emergency department |                      | Hospitalization                      |                             |         |
| 0–17 years     | 21 (6%)              | 86 (25%)             | 229 (66%)                           | 12 (3%)                     | 348     |
| 18–49 years    | 16 (2%)              | 189 (25%)            | 406 (54%)                           | 140 (19%)                   | 751     |
| 50 years or older | 16 (1%)              | 494 (20%)            | 1,111 (45%)                         | 860 (35%)                   | 2,481   |
| Total          | 53 (1%)              | 769 (21%)            | 1,746 (49%)                         | 1,012 (28%)                 | 3,580   |
| Total 95% CI*  | 1–2%                 | 20–23%               | 47–50%                              | 27–30%                      |         |

Note. CI, confidence interval.

*Influenza is defined as an ICD-9 discharge diagnosis of 487.x.

*Pneumonia is defined as an ICD-9 discharge diagnosis of 480.x–486.x and without a discharge diagnosis of influenza.

*Other acute or chronic respiratory conditions are defined as at least 1 ICD-9 discharge diagnosis of 460.x–466.x (which includes nasopharyngitis, sinusitis, pharyngitis, tonsillitis, laryngitis or tracheitis, acute respiratory infection or bronchiolitis) or ICD-9 discharge diagnoses of 490.x–519.x (which includes acute or chronic bronchitis, emphysema, asthma, bronchiectasis, chronic obstructive pulmonary disease not elsewhere classified, pneumonitis, empyema, pleurisy, pulmonary congestion, and other diseases of the lung or respiratory system) and without a discharge diagnosis of influenza or pneumonia.

*Cardiac diagnoses include at least 1 discharge diagnosis of acute myocarditis (excluding rheumatic myocarditis [422.x] or cardiac dysrhythmias [427.x]) or heart failure (excluding rheumatic and pregnancy-related [428.x]) and without any discharge diagnoses of influenza, pneumonia, or other acute or chronic respiratory conditions.

*95% confidence intervals for total row percentages are calculated as Wilson intervals for a binomial proportion.
vaccination, limiting potential exposures, or seeking care for acute respiratory illness symptoms. Finally, estimates of overall rates of ED and hospital visits for all persons in Forsyth County, North Carolina depended on hospital market share data, and the use of these data could introduce bias.

Conclusion

We used complementary statistical methods to estimate rates of ED visits and hospitalization caused by influenza A(H1N1)pdm09 throughout the second wave of the 2009–2010 season. Using both methods, we estimated 4–5 influenza A(H1N1)pdm09 ED visits or hospitalizations per 1,000 residents. This capture-recapture approach led to an 8-fold higher estimate than the estimate generated using passive surveillance data alone, and our estimate highlighted the large burden of disease in the ED. Thus, capture-recapture analysis provides better estimates than passive surveillance when large numbers of visits occur in a short period of time, when diagnostic testing is performed infrequently or has low sensitivity, or when a significant proportion of disease is not clinically suspected. These results highlight the benefit of active surveillance, which provided important data that enabled both the capture-recapture analysis and the estimate derived from ICD-9 discharge codes from administrative data. It may be feasible to combine data from 2 independent surveillance systems between health care settings—such as hospitals, health departments, or community practice—in order to estimate the community-wide impact using capture-recapture analysis. Since 2010, influenza A(H1N1)pdm09 has continued to circulate and remains an important cause of influenza disease. Efforts to develop more effective vaccines and treatments, as well as control strategies informed by accurate estimates of influenza burden, will be important as we work to control influenza as well as other epidemics.

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