

Epidemiology of Seasonal Influenza: Use of Surveillance Data and Statistical Models to Estimate the Burden of Disease

William W. Thompson,¹ Lorraine Comanor,² and David K. Shay¹

¹Centers for Disease Control and Prevention, Atlanta, Georgia; ²Independent Clinical Research Consultant, Truckee, California

The US Centers for Disease Control and Prevention (CDC) uses a 7-component national surveillance system for influenza that includes virologic, influenza-like illness, hospitalization, and mortality data. In addition, some states and health organizations collect additional influenza surveillance data that complement the CDC's surveillance system. Current surveillance data from these programs, together with national hospitalization and mortality data, have been used in statistical models to estimate the annual burden of disease associated with influenza in the United States for many years. National influenza surveillance data also have been used in suitable models to estimate the possible impact of future pandemics. As part of the public health response to the 2003–2004 influenza season, which was noteworthy for its severe effect among children, new US surveillance activities were undertaken. Further improvements in national influenza surveillance systems will be needed to collect and analyze data in a timely manner during the next pandemic.

Over the past century, US systems to estimate the health burden associated with circulation of influenza viruses have grown from reporting of spikes in wintertime mortality in a few cities to an integrated surveillance system made up of many components, including detailed characterization of circulating viruses. By use of current surveillance data with national hospitalization and mortality data, models have been developed to estimate the annual burden of influenza. In addition, models have been used to estimate the possible economic impact and health care needs of future pandemics, by using data available from the 3 pandemics of the 20th century. This review describes current human

US influenza surveillance programs and modeling efforts; their role in the public health response to both seasonal epidemics, caused by well-characterized influenza A and B viruses, and pandemics, caused by novel influenza A subtypes, is emphasized. (Veterinary surveillance will be discussed elsewhere in this supplement [1].) The accompanying review by Monto et al. [2] examines how surveillance data have provided insight into the 3 pandemics of the 20th century and how they might assist preparations for a future pandemic.

CURRENT NATIONAL PROGRAMS

The Centers for Disease Control and Prevention (CDC) has developed a 7-component surveillance system that collects and reports weekly data concerning influenza activity, with a focus on the months of October through May (table 1). The goals of the system include (1) determining the location and timing of influenza activity, (2) defining the types and subtypes of circulating influenza viruses, (3) detecting antigenic changes in circulating viruses, (4) tracking influenza-like illnesses, (5) determining rates of influenza-associated hospitalizations among children, and (6) tracking influenza-associated mortality [3, 4].

These 7 complementary components are designed to

Presented in part: Seasonal and Pandemic Influenza 2006: At the Crossroads, a Global Opportunity, Washington, DC, 1–2 February 2006 (for a list of sponsors and funding, see the Acknowledgments).

Potential conflicts of interest: none reported.

Financial support: supplement sponsorship is detailed in the Acknowledgments.

The findings and conclusions of this commentary are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

Reprints or correspondence: Dr. William W. Thompson, MS-A32, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333 (wct2@cdc.gov).

The Journal of Infectious Diseases 2006;194:S82–91

© 2006 by the Infectious Diseases Society of America. All rights reserved.
0022-1899/2006/19409S2-0005\$15.00

Table 1. Summary of the Centers for Disease Control and Prevention (CDC) national influenza surveillance system, with examples from week 6 of the 2006 calendar year.

Component of surveillance	Tracking mechanism	Tracking goal	Data collected and reported weekly	Example of report from week 6, 2006
State and territorial epidemiologists' reports	State health departments	Influenza activity by state	Estimated level of influenza activity by week, in 5 categories	Activity level by state: widespread, 13 states; regional, 21 states; local, 11 states; sporadic, 5 states
ILI surveillance ^a	CDC influenza sentinel providers' surveillance network of ~1000 health care providers	Influenza activity by state and nationally	Total no. of patients seen and no. of those patients with ILIs, by age group, in representative US locations, weighted on the basis of state population	2.5% of patient visits to sentinel providers due to ILIs (0.3% above national baseline level)
Influenza-associated pediatric mortality	Nationally Notifiable Disease Surveillance System	Influenza A--related pediatric deaths	Laboratory-confirmed influenza deaths in children <18 years of age	No deaths reported from week 6 but 12 deaths reported to date for season
Laboratory-confirmed hospitalizations for children <5 years of age in 3 counties in OH, TN, NY ^b	New Vaccine Surveillance Network	Influenza-related hospitalizations in children <5 years of age	Population-based estimates of laboratory-confirmed, influenza-associated hospitalizations for children <5 years of age	No hospitalizations reported from week 6 or 7
Mortality from influenza or pneumonia in 122 cities	122 cities' mortality reporting systems; vital statistics offices in 122 cities	Deaths resulting from influenza and pneumonia in representative US cities	Total no. of death certificates filed and no. where pneumonia or influenza was underlying or contributing cause of death; comparison with baseline and epidemic threshold value	7% of deaths reported due to pneumonia or influenza—below the 8.3% epidemic threshold for week 6
WHONREYSS	~75 WHO and 50 NREYSS collaborating laboratories in the US (includes sentinel laboratories)	No. of respiratory tract specimens testing positive for influenza in representative US laboratories	No. of respiratory specimens tested and no. positive for influenza A or B	455 (18.7%) of 2438 specimens tested positive for influenza: 136 A(H3N2), 6 A(H1N1), 280 A with A not subtyped, 33 B; antigenic characterization of 189 influenza viruses since Oct 2005

NOTE. NREYSS, National Respiratory and Enteric Virus Surveillance System; NY, New York; OH, Ohio; TN, Tennessee; WHO, World Health Organization.

^a Influenza-like illness (ILI) defined as fever $\geq 37.8^{\circ}\text{C}$ plus either cough or sore throat.

^b Reported biweekly during the influenza season.

provide a national picture of influenza activity. They include reports from >120 laboratories, >2000 sentinel health care providers, vital statistics offices in 122 cities, public health researchers from the New Vaccine Surveillance Network (NVSN) and Emerging Infections Program (EIP), and influenza surveillance coordinators and state epidemiologists from all 50 state health departments, in addition to the New York City and District of Columbia Health Departments. The CDC collects, compiles, and analyzes the data and posts a report on its Web site every Friday [4].

Although comprehensive in its goals, the CDC's existing surveillance system has a number of limitations. State and health care provider reporting of influenza activity is voluntary. Although the national indices together give an indication of where, when, and what influenza viruses are circulating, they do not provide the actual number of influenza infections during an influenza season. The only state-level data available from all areas are general, qualitative reports from state and territorial epidemiologists summarizing weekly influenza activity. Although the EIP and NVSN systems provide population-based estimates of the rates of laboratory-confirmed influenza virus infections from several geographic areas, they have thus far provided data only on children. Finally, current influenza-associated mortality estimates are made only on a national level, and region- or state-specific estimates are not routinely provided [3]. This review describes, in greater detail, some important features of existing US surveillance programs and how they are used nationally and internationally and provides an overview of several state- and organization-based influenza surveillance systems.

INTERNATIONAL USES OF US VIRAL SURVEILLANCE DATA

The ability to identify new strains of influenza viruses and describe their circulation has expanded in recent years. National virologic data are obtained through weekly reports from ~75 World Health Organization (WHO) and 50 National Respiratory and Enteric Virus Surveillance System laboratories. Global viral surveillance involves 115 national influenza centers in 84 countries that analyze 175,000–200,000 samples and characterize 4000–8000 viruses annually. Viruses submitted for detailed antigenic and genetic characterization to WHO centers in Atlanta, London, Melbourne, and Tokyo are used in formulating annual influenza vaccines [4]. A recent initiative to strengthen the influenza surveillance infrastructure in Asia and elsewhere is expected to lead to enhanced viral surveillance and to provide a better early-warning system for viruses with pandemic potential [5].

STATE- AND ORGANIZATION-BASED SURVEILLANCE PROGRAMS

Although all states conduct influenza virologic surveillance, funded in part by CDC, some cities, states, and other groups, such as the Veterans Administration and certain health maintenance organizations, have added additional influenza surveillance programs. For example, laboratory-confirmed influenza virus infections or hospitalizations have been made reportable conditions by some states [6–9] (table 2). In California, several surveillance programs are coordinated by the California Department of Health Services (CDHS) and provide more detailed local data ([10] and J. Louie, personal communication). Two large health maintenance organizations, Kaiser Permanente Northern California and Kaiser Permanente Southern California, have well-developed influenza-reporting mechanisms, which contribute to the CDHS system, but also include additional health plan-specific features (R. Baxter, Kaiser Permanente, personal communication). Another example of expanded surveillance is in New York City, where the multipronged approach to influenza surveillance includes several unique elements. In this system, nosocomial and long-term-care facility outbreaks of influenza-like illnesses (ILIs) also have been incorporated into influenza surveillance. City laboratories provide weekly data on positive influenza test results, either by electronic transmission or in response to calls by the city surveillance coordinator. Syndromic surveillance for influenza in New York City includes tabulating emergency room visits for ILIs, sales of antiviral and over-the-counter influenza medications, and employee absenteeism at one large city agency ([11, 12] and S. Harper, New York City Department of Health and Mental Hygiene, personal communication).

THE BURDEN OF INFLUENZA

Estimating the burden of influenza-related disease is useful for determining the risk of morbidity and mortality in different segments of the population, guiding vaccination programs, evaluating the use of diagnostic tests and antiviral drugs, and planning for seasonal epidemics and future pandemics. Efforts to understand the burden of influenza began more than a century ago in the United States, when Massachusetts began tracking influenza- and pneumonia-related deaths [13]. Modern data facilitate the appreciation of the persistent patterns first recognized more than a century ago. Overlaying graphs of the circulation of influenza viruses with those of pneumonia and influenza hospitalizations and deaths demonstrates that, when circulation of influenza A(H3N2) viruses peaked from 1990 through 2000, so did death and hospitalization rates for pneumonia and influenza (figure 1). The recognition of this fact underpins all efforts to estimate the impact of influenza.

Table 2. Selected examples of state and nongovernment influenza surveillance programs as of January 2006.

Surveillance outcome, tracking organization(s)	State used	Data collected	Data distribution	Reference
Outpatient visits, hospitalizations Kaiser Permanente NCAL and SCAL, CDHS	CA	No. of outpatient visits for ILI; no. of hospitalizations with admitting diagnosis of influenza or pneumonia	Weekly memo to Kaiser NCAL physicians; weekly update from CDHS to local health departments posted on CDHS Web site	R. Baxter and J. Louie, personal communication
State of Wisconsin Pediatric admissions to ICU with laboratory-confirmed influenza CDHS	WI	No. of patients seen per week with ILI	WI DPH	[9]
Phone calls to HMO for ILI Kaiser Permanente NCAL and SCAL	CA	No. of pediatric admissions to ICU with laboratory-confirmed influenza	Weekly update from CDHS to local health departments and participating hospitals	J. Louie, personal communication
Antiviral prescriptions Kaiser Permanente NCAL CDHS	CA	No. of phone calls for ILI	Weekly Kaiser NCAL and SCAL memo	R. Baxter, personal communication
NY state and NYC	NY	No. of prescriptions filled for influenza antiviral drugs	Kaiser memo; weekly update from CDHS to local health departments posted on CDHS Web site	R. Baxter and J. Louie, personal communication
Nosocomial respiratory outbreaks NYC	NY	NY Medicaid system and retail pharmacies	NY DOHMH receives daily data from retail pharmacies	[12] and S. Harper, personal communication
Influenza-related emergency department visits NYC	NY	No. of acute and long-term-care facilities reporting nosocomial respiratory outbreaks and the no. with ≥ 1 laboratory-positive influenza cases	NYC DOHMH	[11] and S. Harper, personal communication
CDHS	CA	No. of emergency department visits for ILI	NYC DOHMH	[11] and S. Harper, personal communication
NYC labs performing influenza testing	NY	No. of influenza-related emergency department visits seen by CA Emergency Physicians Group	Weekly update from CDHS to local health departments posted on CDHS Web site	J. Louie, personal communication
~20 sentinel public health and clinical laboratories in California	CA	Rapid antigen and culture-positive results reported electronically or in response to call by city coordinator	NYC DOHMH	[11] and S. Harper, personal communication
Worker absenteeism NYC	NY	Confirmed influenza- and RSV-positive results	Weekly update from CDHS to local health departments; weekly update posted on CDHS Web site	J. Louie, personal communication
School-reported ILIs CDHS pilot project	NY	No. and cause of absences at 1 NYC agency year round	NYC DOHMH	[11] and S. Harper, personal communication
ILI	CA	No. and location of schools with ILI outbreaks	Weekly update from CDHS to participating schools	J. Louie, personal communication
Early Warning Infectious Disease Surveillance, Border Infectious Disease Surveillance, CDHS	CA-Mexican Baja border	No. of ILI reported cases weekly at clinics located in San Diego and Imperial County	CDHS	[10] and J. Louie, personal communication

NOTE. CA, California; CDHS, California Department of Health Services; DOHMH, Department of Health and Mental Hygiene; DPH, department of health; HMO, health maintenance organization; ICU, intensive care unit; ILI, influenza-like illness; NCAL, northern California; NYC, New York City; RSV, respiratory syncytial virus; SCAL, southern California; WI, Wisconsin.

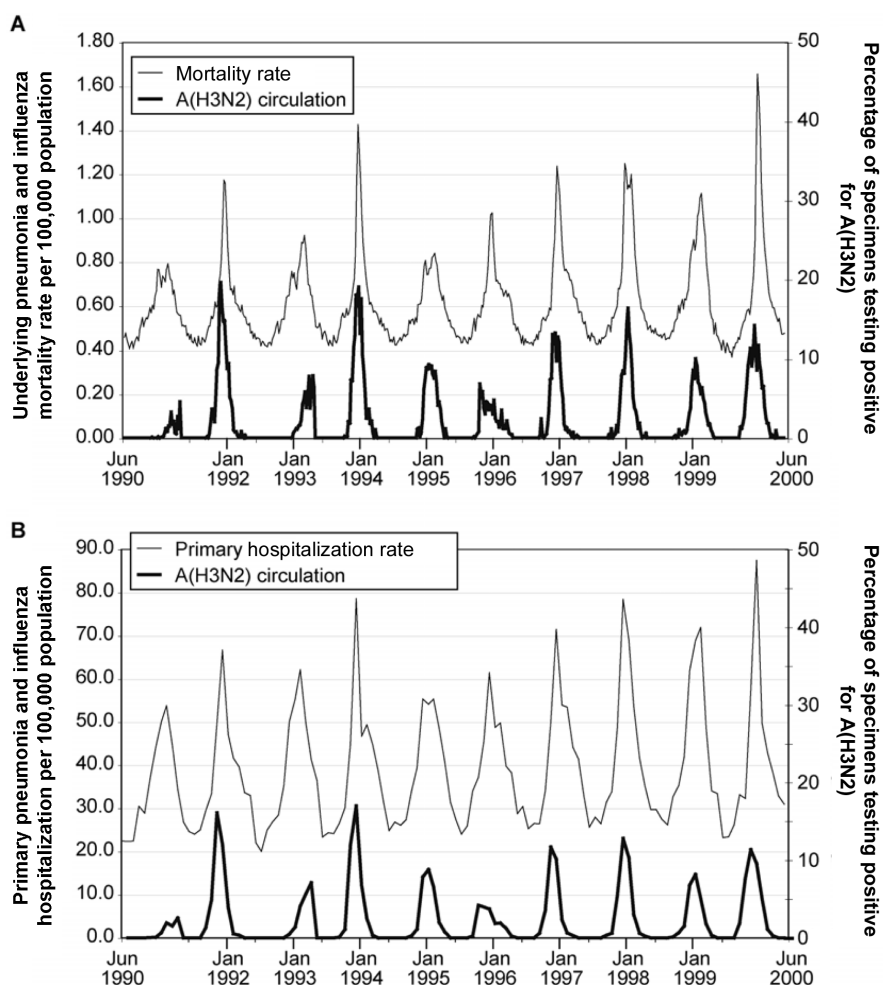


Figure 1. A, Pneumonia and influenza mortality rate and circulation of influenza A(H3N2) viruses, 1990–2000. B, Primary pneumonia and influenza hospitalization rate and circulation of influenza A(H3N2) viruses, 1990–2000.

THE ROLE OF INFLUENZA-ASSOCIATED MORTALITY AND HOSPITALIZATION ESTIMATES IN ESTABLISHING THE BURDEN OF INFLUENZA

Mortality statistics were used to provide the most comprehensive record of the impact of the 1889–1892 and 1918 pandemics, because reports of influenza-related morbidity were sparse and not standardized. Massachusetts was a pioneer in these efforts and has maintained and published mortality rates continuously since 1887 [13, 14]. During the 1918 pandemic, inspectors from the Public Health Service conducted house-to-house surveillance for influenza, pneumonia, and deaths in 10 geographically diverse US cities with populations of 25,000–600,000, as well as in several smaller cities and rural areas [13]. In the surveyed populations, inspectors recorded basic demographic data on each individual in a household, along with whether each person had been sick with pneumonia, influenza, or suspected influ-

enza since September 1918. They also recorded the numbers of rooms in each household and an impression of the family's economic status. This ambitious surveillance program documented the wide range of illnesses caused by the pandemic virus across the United States and suggested a relationship between crowding and increased attack rates. Massachusetts records demonstrated an ~1-week lag between peaks in case incidence and mortality, a finding that has been noted in influenza epidemics and pandemics since this initial report [14].

During seasonal influenza epidemics, the impact of influenza on annual death and hospitalization rates is more difficult to estimate. During interpandemic periods, the health effects of infection are usually less severe, the symptoms of infection are similar to those caused by other respiratory tract infections, illnesses consistent with influenza are often not confirmed by virologic testing, and influenza is rarely specifically recorded on death certificates [15]. Attempts to confirm influenza di-

agnoses by testing for influenza virus have limitations, because many adults tested after 6–8 days of illness are no longer shedding virus and, hence, are likely to test negative [16].

CONTRIBUTION OF STATISTICAL MODELS IN ESTIMATING THE BURDEN OF EPIDEMIC DISEASE

Because a broad range of respiratory and cardiac diagnoses have been associated with influenza virus infections and these infections are often not confirmed by virologic testing, statistical models based on vital statistics data have been used for decades to estimate the overall burden of influenza in the United States. Several different types of models have been developed to estimate this illness burden (table 3). In general, the estimates from each of these models suggest that seasonal influenza epidemics from 1976 through 2000 were associated with substantial morbidity, including >200,000 annual hospitalizations and an annual average of >30,000 influenza-associated all-cause US deaths. These estimates also highlight the increased morbidity and mortality in older age groups and the pronounced variability in disease burden between seasons. For example, the 1984–1985 influenza season was severe, with an estimated 50,789 influenza-associated deaths, compared with a season of moderate severity (1978–1979 season), when only 7608 influenza-associated deaths were estimated to have occurred [17].

Several methods of estimating the “excess deaths” associated with the circulation of influenza viruses are based on a linear-regression approach first developed by Serfling and published in 1963 [18]. Recently, Simonsen et al. [19] developed a Serfling-type linear-regression model to estimate underlying pneumonia and influenza and all-cause deaths on the basis of weekly death data from 1972–1992 collected by the National Center of Health Statistics (NCHS). The initial step in making estimates with models of this type involves removing the annual peaks in wintertime deaths. Then, by use of mortality statistics from several years (e.g., 5 years of data) with these seasonal peaks removed, a curve is fit to establish a sinusoidal baseline for the subsequent season (i.e., the number of deaths expected in the absence of influenza circulation). The excess deaths estimated to occur each season are defined as the numbers of deaths that exceeded a baseline (or “epidemic threshold”) value during ≥ 2 consecutive weeks. A newer version of this type of model was developed in 2005 by use of a best-fitting curve derived from a subset of baseline values from 33 years of data [20]. Although neither of these models makes use of influenza virus surveillance data, their estimates of influenza-associated deaths are similar to those obtained from models that do incorporate viral data: ~30,000 annual influenza-associated all-cause deaths from 1976 through 2000 [18, 19].

In 2003, Thompson et al. further modified Serfling-type

models, using Poisson regression techniques and directly incorporating influenza surveillance data, to estimate influenza-associated deaths. Using NCHS weekly death certificate data from 1976–2000 together with WHO influenza virus surveillance data, this model was fit to 3 death categories: underlying pneumonia and influenza deaths, underlying respiratory and circulatory deaths, and all-cause deaths [17]. Thompson et al. use 3 terms in the regression models to represent the percentage of specimens submitted to influenza surveillance laboratories that test positive for influenza A(H1N1), A(H3N2), or B viruses during each week for which estimates were made. Thus, these models provide specific estimates of outcomes associated with each of the commonly circulating influenza strains each season.

Simpler models, based on rate differences, have been used for many years to estimate influenza-associated morbidity and mortality. In these models, influenza-associated outcomes are estimated by subtracting rates of events occurring during a baseline period from the rates occurring during an influenza period. Rate-difference models often make use of viral surveillance data, but only to establish periods of influenza circulation. For example, the influenza period can be defined as the period (in weeks) during which the proportion of respiratory tract specimens that test positive for influenza exceeds a preset threshold (e.g., 10%). A winter rate-difference model, first developed by Barker and Mullooly [21], has been used to estimate influenza-related rates occurring from January through March. Izurieta et al. [22] estimated influenza-associated hospitalization rates among healthy children by use of a peri-season baseline period (the weeks during October–May when influenza circulation is uncommon but other respiratory viral pathogens are circulating) and a summer baseline period (weeks when circulation of all respiratory viruses is uncommon). In general, annual estimates of influenza-associated events made by use of summer baselines are substantially higher than those made by use of the Simonsen or Thompson model. However, estimates made by use of peri-season models, although often greater than those derived from either the Simonsen or the Thompson model, are highly correlated with estimates from these models [23]. Similarly, estimates of influenza-associated hospitalizations from all 3 of these models are roughly comparable [23]. Because the rate-difference models are simple and require fewer assumptions, they have been used in a wide range of situations. For example, rate-difference models have been used to make estimates of influenza-associated mortality by 5-year age intervals.

In addition to estimating influenza-associated mortality, Thompson et al. [24] used their models to estimate influenza-associated hospitalization rates. Employing nationally representative monthly data from the National Hospital Discharge Survey and WHO influenza viral surveillance data from 1979–2001, they estimated influenza-associated hospitalizations for

Table 3. Impact of influenza on all-cause deaths in the United States, estimated by various models.

Model (year published) [reference]	Technique	Requirements and limitations	Appropriate application	Data modeled	Examples of events estimated	All-cause death estimates for US (1976–2000)
Serfling (1963) [18]	Linear regression	Baseline data required; viral surveillance data not required	Temperate countries; influenza epidemics; influenza pandemics	108 US cities	Pneumonia and influenza deaths; cardiovascular-renal deaths; all-cause deaths	NA
Simonsen et al. (1997) [19]	Linear regression	5 years of baseline data required; viral surveillance data not required	Temperate countries; influenza epidemics; influenza pandemics	NCHS weekly death data, 1976–2000	Underlying pneumonia and influenza deaths; all-cause deaths	31,467
Thompson et al. (2003) [17]	Poisson regression	Viral surveillance data incorporated; type- and subtype-specific estimates provided; circulation of RSV controlled for; cannot be used for pandemics	Temperate countries; influenza epidemics	NCHS weekly death data, 1976–2000	Underlying pneumonia and influenza deaths; underlying respiratory and cardiovascular deaths; all-cause deaths	35,463
Simonsen et al. (2005) [20]	Linear regression	Viral data not required	Temperate countries; influenza epidemics; influenza pandemics	Monthly NCHS death data 1976–2000	Underlying pneumonia and influenza deaths; all-cause deaths	32,748 ^a
Barker and Mullooly winter season excess rate ^b (1980) [21]	Influenza period rate; winter season baseline rate	Viral data not required; defining seasons as “influenza free” required; difficulty in identifying seasons with no influenza activity	Any country; influenza epidemics; influenza pandemics	Hospitalizations 1968–1969 and 1972–1973 seasons	Deaths; hospitalizations; outpatient visits	NA
Izurieta et al. peri-season excess rate ^b (2000) [22]	Influenza period rate; peri-season baseline rate	Peri-season baseline rate when influenza is not circulating defined and required	Any country; influenza pandemics	Weekly NCHS death data 1976–2000	Deaths; hospitalizations; outpatient visits	43,958
Izurieta et al. summer season excess rate (2000) [22]	Influenza period rate; summer-season baseline rate	Summer season baseline rate when influenza is not circulating defined and required	Any country; influenza pandemics	Weekly NCHS death data 1976–2000	Deaths; hospitalizations; outpatient visits	73,635

NOTE. All-cause deaths was the only outcome analyzed in all studies. NA, not applied; NCHS, National Center for Health Statistics; RSV, respiratory syncytial virus.

^a Estimate adjusted on the basis of 90% of deaths occurring among the elderly.

^b Excess rate = (influenza rate) – (non-influenza baseline rate).

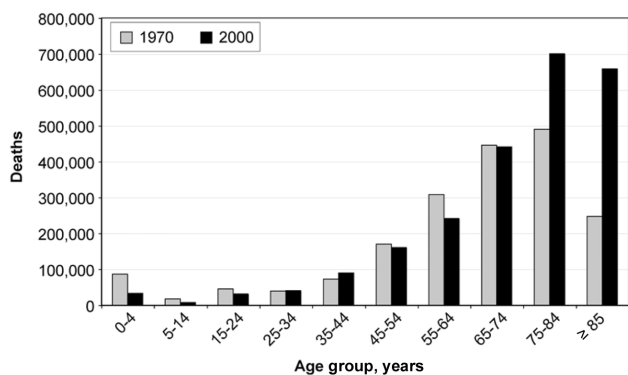


Figure 2. All-cause deaths in the United States, by age group and year, 1970 and 2000.

4 sets of discharge diagnoses: primary pneumonia and influenza, any-listed pneumonia and influenza, primary respiratory and circulatory, and any-listed respiratory and circulatory hospitalizations. The age-specific hospitalization rates formed a J shape, in which the rates of hospitalization were high among children <5 years of age, declined for those 5–49 years of age, and increased among those ≥ 50 years of age, although not as steeply as mortality rates did. In terms of absolute numbers, the model estimates $\sim 20,000$ hospitalizations for children <5 years of age and $\sim 40,000$ hospitalizations for individuals ≥ 85 years of age, who are 6 times more likely to be hospitalized for influenza than are people in the 65- to 69-year age group. The need for age-specific estimates of morbidity and mortality will be great during a pandemic. For example, age-specific curves of hospitalization and mortality rates during the first wave of a future pandemic will be important in the prioritization of medical interventions. It is expected that supplies of pandemic vaccines will be limited during a first wave, but, as supplies of vaccine increase during second and possibly later waves, it will be important to prioritize groups at greatest risk of morbidity and mortality for early receipt of vaccine.

The 2003–2004 influenza season provided an opportunity to compare mortality estimates derived from statistical models with those obtained by an enhanced surveillance effort for influenza deaths among children. An estimate of an average of 92 influenza-related deaths among children <5 years of age, derived from the Poisson regression model [17], was similar to the 96 deaths in that age group reported by state, local, and territorial health departments to the CDC during the 2003–2004 influenza season. This influenza season, which may have received more media attention than usual, provided a comparative opportunity, because it began early (in October in some states) and did not overlap substantially with the seasons for other viral respiratory pathogens in most areas, particularly respiratory syncytial virus [25].

DEMOGRAPHIC TRENDS AND INFLUENZA-ASSOCIATED DEATH AND HOSPITALIZATION RATES

Examining demographic trends among the US population and patterns in influenza-associated mortality provides useful information concerning the future effects of seasonal and pandemic influenza. The substantial increases in the numbers of elderly people in the United States have important implications for planning. From 1970 through 2000, the number of individuals 65–74 years of age increased from 12 to 18 million, the number 75–84 years of age increased from 6 to 12 million, and the number ≥ 85 years of age increased from 1.5 to 4.5 million. These changes in demographics led to large differences in the numbers of deaths by age group in 1970 and 2000 (figure 2). Moderate increases in deaths among those 55–64, 65–74, and 75–84 years of age must be contrasted with the almost tripled estimated number of deaths among those ≥ 85 years of age [23]. These data help to explain the great burden of influenza documented over the past several decades in the United States (figure 3). The continued aging of the US population also sug-

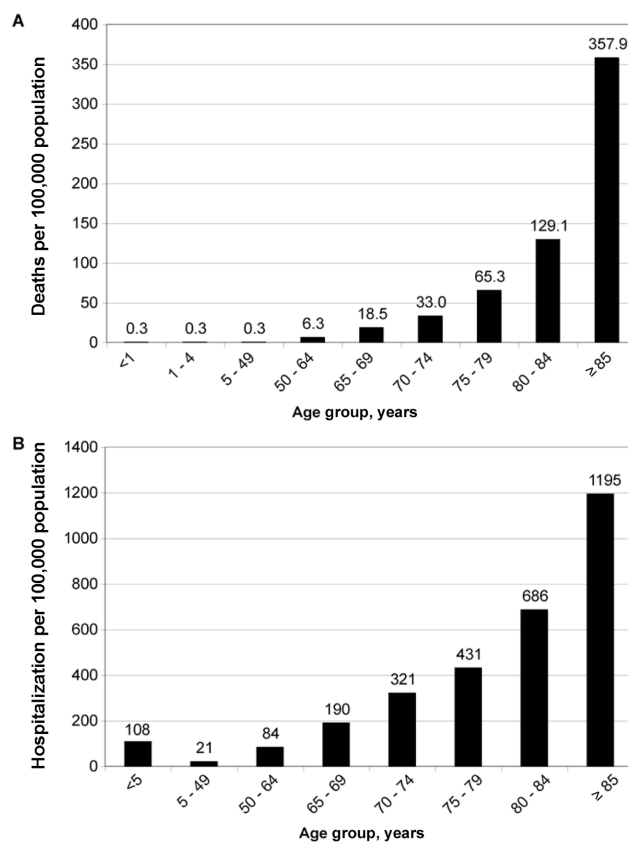


Figure 3. A, Influenza-associated mortality rates, by age group, during 1976–2000. B, Influenza-associated hospitalization rates, by age group, during 1979–2001.

gests that influenza-associated deaths can be expected to increase in the future. If the next pandemic is similar in its epidemiological profile to the 1957 and 1968 pandemics, it could be particularly devastating in the elderly.

SURVEILLANCE AND POLICY DEVELOPMENT

Seasonal influenza epidemics that are especially severe, or perceived as severe, may lead to the development of additional surveillance systems and the collection of new data and may subsequently lead to policy change. In the relatively severe and early influenza epidemic of 2003–2004, large numbers of deaths among healthy children were noted in a variety of reports. As a result, the CDC and state and local public health authorities implemented surveillance for childhood deaths associated with influenza. Through case reports, medical records, and autopsy reports received through state and local health authorities, a total of 153 deaths among children <18 years of age with laboratory evidence of influenza virus infections were reported to the CDC [25]. Forty-four (29%) of the 153 deaths occurred within 3 days of illness onset, and 72 (47%) occurred in children without evidence of underlying medical conditions [25]. Partly on the basis of these reports, the Council of State and Territorial Epidemiologists voted to make laboratory-confirmed influenza-associated deaths in children <18 years of age a nationally notifiable condition during the subsequent 3 years [26].

Additional surveillance activities regarding children are now part of CDC's influenza surveillance system. These include reports of laboratory-confirmed influenza hospitalizations among children <18 years of age through the EIP sites and reports of hospitalizations and outpatient visits due to influenza virus infection among children <5 years of age through the 3 sites participating in the NVSN. Burden-of-disease data from the EIP and the NVSN have provided additional statistics to support the ACIP recommendation to expand annual influenza vaccination campaigns to include children 6–23 months of age and, subsequently, to include those 24–59 months of age [27–29]. Both surveillance systems are being used to conduct assessments of vaccine effectiveness in pediatric populations.

EVALUATION OF CURRENT SURVEILLANCE ACTIVITIES AND PLANNING FOR FUTURE NEEDS

The uses of influenza surveillance data extend beyond the estimation of the burden of seasonal disease. These data also contribute to decisions regarding the influenza strains selected for annual vaccine production, the use of antivirals, and groups for whom annual vaccination is recommended [30].

Effective surveillance activities cannot be developed during a crisis, such as during a pandemic, but must be in place beforehand. Newer surveillance activities, such as tracking lab-

oratory-confirmed influenza outpatient and inpatient visits among children, have enhanced our understanding of the epidemiological profile of influenza. Although the current US surveillance systems are reasonably effective for describing seasonal influenza activity, improvements are needed in influenza surveillance in anticipation of a pandemic. For example, more rapidly available data on hospitalization rates among persons of all ages would not only better describe the variable burden of seasonal epidemics but also improve current efforts to estimate medical surge capacity needs during a future pandemic. Plans are under way to evaluate the CDC's influenza surveillance system, with the assistance of the states that provide data and the Council of State and Territorial Epidemiologists. It is hoped that improvements to the current influenza surveillance systems will provide increasingly accurate estimates of the burden of influenza and help the United States to better prepare for a future pandemic.

Acknowledgments

We thank Lynnette Brammer and Eric Weintraub (Centers for Disease Control and Prevention, Atlanta, Georgia), for providing surveillance data and conducting analyses for this work, and Kristina Whitfield (PosterDocs, Oakland, California), for assistance with graphics. The "Seasonal and Pandemic Influenza 2006: At the Crossroads, a Global Opportunity" conference was sponsored by the Infectious Diseases Society of America, the Society for Healthcare Epidemiology of America, the National Institute of Allergy and Infectious Diseases, and the Centers for Disease Control and Prevention. Funding for the conference was supplied through an unrestricted educational grant from Gilead Sciences, GlaxoSmithKline, Roche Laboratories, MedImmune, Sanofi Pasteur, Biota Holdings, and BioCryst Pharmaceuticals.

Supplement sponsorship. This article was published as part of a supplement entitled "Seasonal and Pandemic Influenza: At the Crossroads, a Global Opportunity," sponsored by the Infectious Diseases Society of America, the Society for Healthcare Epidemiology of America, the National Institute of Allergy and Infectious Diseases, and the Centers for Disease Control and Prevention.

References

1. Morgan A. Avian influenza: an agricultural perspective. *J Infect Dis* **2006**; 194(Suppl 2):S139–46 (in this supplement).
2. Monto AS, Comanor L, Shay DK, et al. Epidemiology of pandemic influenza: use of surveillance and modeling for pandemic preparedness. *J Infect Dis* **2006**; 194(Suppl 2):S92–7 (in this supplement).
3. Centers for Disease Control and Prevention. Overview of influenza surveillance in the United States. Available at: <http://www.cdc.gov/flu/weekly/fluactivity.htm>. Accessed 10 August 2006.
4. Centers for Disease Control and Prevention. CDC weekly influenza report: influenza summary update 6, 2005–2006 season. Available at: <http://www.cdc.gov/flu/weekly/weeklyarchives2005-2006/weekly06.htm>. Accessed 10 August 2006.
5. Cox N. Enhancing influenza surveillance: from the global to local perspective. Presented at: Institute of Medicine Workshop on Pandemic Influenza: Assessing Capabilities for Prevention and Response (Washington, DC), 16–17 June 2004. Washington, DC: Institute of Medicine Forum on Microbial Threats, **2004**.
6. Centers for Disease Control and Prevention. Surveillance for laboratory-

- confirmed, influenza-associated hospitalizations—Colorado 2004–05 influenza season. *MMWR Morb Mortal Wkly Rep* **2005**;54:535–7.
7. Hadler JL, Siniscalchi A, Dembek Z. Hospital admissions syndromic surveillance—Connecticut, October 2001–June 2004. *MMWR Morb Mortal Wkly Rep* **2005**;54(Suppl):169–73.
 8. Ritzwoller DP, Kleinman K, Palen T, et al. Comparison of syndromic surveillance and a sentinel provider system in detecting an influenza outbreak—Denver, Colorado 2003. *MMWR Morb Mortal Wkly Rep* **2005**;54(Suppl):151–6.
 9. Department of Health, State of Wisconsin. Influenza surveillance. Available at: <http://www.dhfs.state.wi.us/communicable/influenza/surveillance.htm>. Accessed 31 August 2006.
 10. California Department of Health Services. Pandemic influenza preparedness and response plan. Appendix 1: Influenza and pandemic influenza surveillance and epidemiology. Available at: <http://www.dhs.ca.gov/ps/dcdc/pdf/Draft%20Pandemic%20Influenza%20Plan%201-18-06.pdf>. Accessed 10 August 2006.
 11. Department of Health, City of New York. Influenza surveillance summary, New York City: update of activity through November 12, 2005. Available at: <http://www.nyc.gov/html/doh/downloads/pdf/imm/flu-weekly-surveillance-20051121.pdf>. Accessed 31 August 2006.
 12. Centers for Disease Control and Prevention. Increased antiviral medication sales before the 2005–06 influenza season—New York City. *MMWR Morb Mortal Wkly Rep* **2006**;55:277–9.
 13. Frost WH. The epidemiology of influenza. *Public Health Rep* **1919**;34:1823–36.
 14. Frost WH. Statistics of influenza mortality. Presented at: American Public Health Association Meeting (New Orleans), 31 October 1919. American Public Health Association, **1920**.
 15. Glezen WP, Couch RB. Influenza viruses. In: Evan AS, Kaslow RA, eds. *Viral infections of humans: epidemiology and control*. 4th ed. New York and London: Plenum Medical Book Company, **1997**:492.
 16. Wright PF, Webster RG. Orthomyxoviruses. In: Knipe DM, Howley PM, eds. *Fields virology*, 4th ed. Philadelphia: Lippincott Williams and Wilkins, **2001**:1554.
 17. Thompson W, Shay D, Weintraub E, et al. Mortality associated with influenza and respiratory syncytial virus in the United States. *JAMA* **2003**;289:179–86.
 18. Serfling RE. Methods for current statistical analysis of excess pneumonia-influenza deaths. *Public Health Rep* **1963**;78:494–505.
 19. Simonsen L, Clarke MJ, Williamson GD, Stroup DF, Arden NH, Schonberger LB. The impact of influenza epidemics on mortality: introducing a severity index. *Am J Pub Health* **1997**;87:1944–50.
 20. Simonsen L, Reichert TA, Viboud C, Blackwelder WC, Taylor RJ, Miller MA. Impact of influenza vaccination on seasonal mortality in the US elderly population. *Arch Intern Med* **2005**;165:265–72.
 21. Barker WH, Mullooly JP. Impact of epidemic type A influenza in a defined adult population. *Am J Epidemiol* **1980**;112:798–811.
 22. Izurieta HS, Thompson WW, Kamarz P, et al. Influenza and the rates of hospitalization for respiratory disease among infants and young children. *N Engl J Med* **2000**;342:232–9.
 23. Thompson W. Impact of seasonal influenza. Presented at: Seasonal and Pandemic Influenza 2006: At the Crossroads, a Global Opportunity (Washington, DC), 1–2 February **2006**.
 24. Thompson W, Shay D, Weintraub E, et al. Influenza-associated hospitalizations in the United States. *JAMA* **2004**;292:1333–40.
 25. Bhat N, Wright J, Broder K, et al. Influenza-associated deaths among children in the United States, 2003–2004. *N Engl J Med* **2005**;353:2559–67.
 26. Council of State and Territorial Epidemiologists. Influenza-associated pediatric mortality. Position statement, 9 June **2004**. Available at: <http://www.cste.org/ps/2004pdf/04-ID-04-final.pdf>. Accessed 20 June 2006.
 27. Iwane MK, Edwards K, Szilagyi P, et al. Population-based surveillance for hospitalizations associated with respiratory syncytial virus, influenza virus, and parainfluenza viruses among young children. *Pediatrics* **2004**;113:1758–64.
 28. Schrag SJ, Shay DK, Gershman K, et al. Multisite surveillance for laboratory-confirmed, influenza-associated hospitalizations in children: 2003–2004. *Pediatr Infect Dis J* **2006**;25:395–400.
 29. Smith NM, Bresee JS, Shay DK, Uyeki TM, Cox NJ, Strikas RA. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* **2006**;55(RR-10):1–42.
 30. Knobler SL, Mack A, Mahmoud A, Lemon SM, eds. *The threat of pandemic influenza: are we ready?* Workshop summary. Washington, DC: National Academies Press, **2005**.