

ORIGINAL ARTICLE

## Influenza-Associated Deaths among Children in the United States, 2003–2004

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### ABSTRACT

#### BACKGROUND

Although influenza is common among children, pediatric mortality related to laboratory-confirmed influenza has not been assessed nationally.

#### METHODS

During the 2003–2004 influenza season, we requested that state health departments report any death associated with laboratory-confirmed influenza in a U.S. resident younger than 18 years of age. Case reports, medical records, and autopsy reports were reviewed, and available influenza-virus isolates were analyzed at the Centers for Disease Control and Prevention.

#### RESULTS

One hundred fifty-three influenza-associated deaths among children were reported by 40 state health departments. The median age of the children was three years, and 96 of them (63 percent) were younger than five years old. Forty-seven of the children (31 percent) died outside a hospital setting, and 45 (29 percent) died within three days after the onset of illness. Bacterial coinfections were identified in 24 of the 102 children tested (24 percent). Thirty-three percent of the children had an underlying condition recognized to increase the risk of influenza-related complications, and 20 percent had other chronic conditions; 47 percent had previously been healthy. Chronic neurologic or neuromuscular conditions were present in one third. The mortality rate was highest among children younger than six months of age (0.88 per 100,000 children; 95 percent confidence interval, 0.52 to 1.39 per 100,000).

#### CONCLUSIONS

A substantial number of influenza-associated deaths occurred among U.S. children during the 2003–2004 influenza season. High priority should be given to improvements in influenza-vaccine coverage and improvements in the diagnosis and treatment of influenza to reduce childhood mortality from influenza.

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IT HAS BEEN ESTIMATED BY THE CENTERS for Disease Control and Prevention (CDC) that more than 200,000 hospitalizations and 36,000 deaths attributable to influenza occur annually in the United States.<sup>1,2</sup> Although most influenza-related deaths occur among elderly persons, rates of influenza-related hospitalization among young children are similar to those among the elderly.<sup>3-5</sup> Each year an estimated average of 92 influenza-related deaths occur among U.S. residents younger than five years of age,<sup>2</sup> but the clinical features of such deaths have been described in only a few cases,<sup>6-8</sup> and national data concerning pediatric mortality associated with laboratory-confirmed influenza have been unavailable.

During late November 2003, the CDC began receiving reports of sporadic cases of severe or fatal influenza in children. On December 12, 2003, the CDC requested that all state, territorial, and local health departments report deaths associated with laboratory-confirmed influenza in children.<sup>9,10</sup> In this report, we describe the results of enhanced surveillance for deaths associated with laboratory-confirmed influenza in children during the 2003–2004 influenza season.

## METHODS

### CASE DEFINITION AND CONFIRMATION OF INFLUENZA-VIRUS INFECTION

A case was defined as a death during the 2003–2004 influenza season (September 28, 2003, through May 22, 2004) that was associated with laboratory evidence of influenza-virus infection in a U.S. resident younger than 18 years of age. Confirmation of influenza-virus infection before or after death required a positive finding by one or more of the following methods: a rapid diagnostic test or enzyme immunoassay, isolation of the virus in tissue-cell culture, direct or indirect immunofluorescent-antibody staining, reverse-transcriptase–polymerase-chain-reaction (RT-PCR) analysis, or immunohistochemistry.<sup>11</sup>

Respiratory specimens were collected from patients during their illness or after death. Most specimens were tested for influenza virus by point-of-care testing or other methods at hospital, local, or state laboratories, and some were tested at the CDC by RT-PCR or viral culture. Available viral isolates were typed, and influenza A viruses were subtyped at local, state, or CDC laboratories. Antigenic and genetic characterizations of some influenza viruses

were performed at the CDC.<sup>12</sup> When available, upper-airway and lung-tissue samples obtained at autopsy from children with confirmed influenza-virus infection or from those who had died of undiagnosed illnesses clinically compatible with influenza were tested for influenza-virus infection at the CDC by RT-PCR and immunohistochemistry.

### SURVEILLANCE

Health care providers contacted state and local health departments to report cases, except for those detected by postmortem testing at the CDC. Members of the health-department staff completed a standardized report form for each case; the form included the patient's demographic information, influenza-vaccination history from current and previous seasons, prior health status, and clinical course and the results of selected laboratory tests. To enhance surveillance, the health departments of all states and some large metropolitan areas were contacted at least once by the CDC to inquire about possible cases. Case reports and copies of available medical records, death certificates, and autopsy reports were sent to the CDC. Clinical data and the results of microbiologic tests in each case were abstracted and reviewed by one of three pediatricians (each of whom is an author of this report). Because the surveillance applied to deceased persons and was considered to be a public health activity, the Privacy Rule of the Health Insurance Portability and Accountability Act did not apply to data collection.

### DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

Children with a chronic medical condition recognized by the Advisory Committee on Immunization Practices (ACIP) during the 2003–2004 season as a factor that increased the risk of influenza-related complications<sup>13</sup> were classified as having a high-risk condition. Children without an ACIP-defined high-risk condition or any other chronic underlying medical condition were classified as having been “previously healthy.” In our analyses, a child was considered to have received influenza vaccine if a dose had been administered at least 14 days before the onset of illness. Children who were six months of age or older on December 1, 2002, were considered to have been eligible for influenza vaccination in a previous season. Children who were admitted to an inpatient ward or intensive care unit were classified as “hospitalized.” Those who died in an emergency department were classified as “not hospitalized.”

All diagnoses were abstracted from medical records or autopsy reports. To distinguish clinically important infections from probable contamination, a team of clinicians and pathologists (each of whom is an author of this report) assessed all the reported results of bacterial and fungal cultures of specimens obtained before or after death from normally sterile sites (i.e., blood, cerebrospinal fluid, lung tissue, and pleural fluid). Findings were evaluated for the known pathogenicity of the organism, specimen-collection conditions, the results of repeated culture, the interval between death and postmortem specimen collection, and histopathological findings. Influenza-associated encephalopathy was defined as altered mental status lasting at least 24 hours and occurring as long as five days after the onset of fever but did not include acute stroke or hypoxic brain injury; all potential cases were reviewed by a neurologist and two other clinicians (each of whom is an author of this report).

**STATISTICAL ANALYSIS**

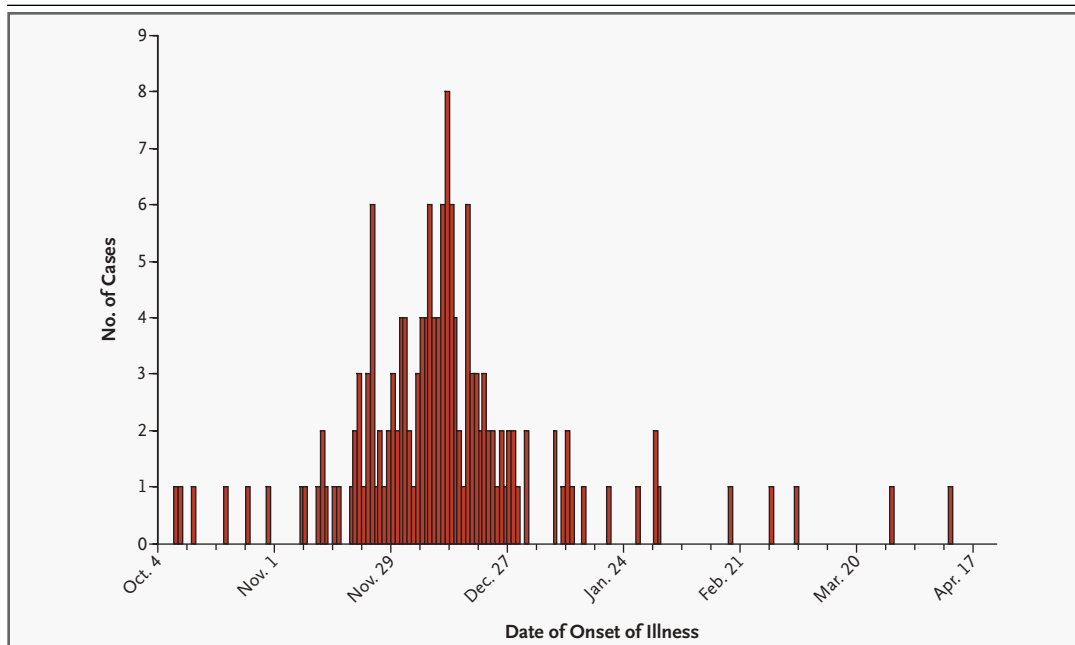
Data were entered and analyzed with the use of Microsoft Access 2002 and SAS statistical software (version 8.1). The denominators used to calculate proportions for the reported data varied on the basis of available information. Population-based mortality rates were calculated according to 2003

U.S. population estimates from the U.S. Census Bureau and preliminary 2003 natality files from the National Center for Health Statistics.<sup>14,15</sup> Exact 95 percent confidence intervals for mortality rates were calculated with the Poisson distribution. A chi-square test for trend was performed to evaluate mortality rates according to age group. All P values are two-sided.

**RESULTS**

**CHARACTERISTICS OF THE PATIENTS**

One hundred fifty-three influenza-associated deaths among children from October 11, 2003, through April 13, 2004, were reported to the CDC by 40 state health departments. Cases occurred throughout the 2003–2004 influenza season and peaked in mid-December (Fig. 1). The median age of the children was 3 years (range, 2 weeks to 17 years), and 76 (50 percent) were boys. Race, which was determined on the basis of data from medical charts and state health departments, was reported for 146 of the children, of whom 98 (67 percent) were white, 32 (22 percent) black, 9 (6 percent) Asian, and 5 (3 percent) Native American or Alaskan Native and of whom 2 (1 percent) were reported as “other”; ethnic background was reported for 134, of whom 32 (24 percent) were Hispanic. Sixty-



**Figure 1.** Timing of 153 Cases of Fatal Influenza in Children — United States, 2003–2004 Season.

one of the 153 children (40 percent) were younger than two years of age, and 96 (63 percent) were younger than five years of age (Table 1). The overall influenza-related mortality rate among the children was 0.21 death per 100,000. The rate varied according to geographic region and was highest among those younger than six months of age and generally declined with increasing age (P for trend <0.001) (Table 1 and Fig. 2).

#### Underlying Health Status

Among the 149 children for whom information on underlying health status was available, 70 (47 percent) had previously been healthy, 49 (33 percent) had an ACIP-defined high-risk medical condition, and 30 (20 percent) had other chronic medical conditions not defined as conferring a high risk (Table 2). Of the 49 children with a high-risk condition, 16 had more than one such condition. Of the 30 children with chronic pulmonary disease, 12 had asthma but no other pulmonary disease, 7 bronchopulmonary dysplasia, and 3 a history of recurrent pneumonia. Thirteen of 14 children in whom a chronic cardiovascular condition had been diag-

nosed had a congenital heart defect. Of the six children with one or more metabolic disorders, three had hypothyroidism, two panhypopituitarism, one diabetes mellitus, and one diabetes insipidus. Thirty-four children at high risk had at least one additional chronic medical disorder not recognized by the ACIP as conferring a high risk.

Chronic neurologic or neuromuscular conditions (including developmental delay in 42 children, seizure disorder in 23, and cerebral palsy in 14) were present in 49 of 149 children (33 percent), 34 of whom had more than one neurologic condition, and 21 of whom had no ACIP-defined high-risk conditions. Of the 14 children with cerebral palsy, 9 had no reported ACIP high-risk conditions. All 42 children with developmental delay had at least one other major coexisting disorder; among them were 23 who had an ACIP-defined high-risk condition.

#### Influenza-Vaccination Status

Information about influenza-vaccination status was available for 111 of the 135 children at least six months of age (82 percent). Of these 111 children, 18 (16 percent) had received at least one dose of vaccine during the 2003–2004 season. Among the 39 children whose influenza-vaccination status was known and who had an ACIP-defined high-risk condition that prompted a recommendation for annual vaccination, 10 (26 percent) had received at least one dose. Among 21 children 6 to 23 months of age whose influenza-vaccination status was known and who did not have an ACIP-defined high-risk condition, 4 (19 percent) had received at least one dose. Of 107 children who had been eligible for influenza vaccination during prior seasons, information was reported for 47, and vaccine receipt was documented in 12.

The ACIP recommends that children six months to eight years of age receive two doses of influenza vaccine during the first year of vaccination and one dose in each subsequent season.<sup>16</sup> According to these criteria, only 8 of the 18 children who had received at least one dose during the 2003–2004 season had documentation of full influenza vaccination during that season: 5 had been vaccinated in a previous season, and 3 were older than nine years of age.

#### CLINICAL COURSE

Data on signs and symptoms at the time of presentation for medical care were available for 141 of

**Table 1. Distribution of Cases and Mortality Rates According to Geographic Location and Age Group among 153 Children with Fatal Influenza — United States, 2003–2004 Season.**

Variable	No. of Children (%)	Deaths per 100,000 Children (95% CI)*
<b>Overall</b>	153 (100)	0.21 (0.18–0.24)
<b>Geographic census region</b>		
Northeast	13 (8)	0.10 (0.05–0.17)
Midwest	36 (24)	0.22 (0.15–0.31)
South	67 (44)	0.25 (0.20–0.32)
West	37 (24)	0.21 (0.15–0.29)
<b>Age group†</b>		
<6 mo	18 (12)	0.88 (0.52–1.39)
6–11 mo	12 (8)	0.59 (0.30–1.02)
1 yr	31 (20)	0.77 (0.52–1.09)
2 yr	14 (9)	0.35 (0.19–0.58)
3 yr	9 (6)	0.23 (0.11–0.44)
4 yr	12 (8)	0.31 (0.16–0.54)
5–10 yr	26 (17)	0.11 (0.07–0.16)
11–17 yr	31 (20)	0.11 (0.07–0.15)

\* CI denotes confidence interval.

† Ages are those on the date of the onset of illness or, if that information was unavailable, at the date of death. P for trend <0.001 by a chi-square test of age-specific mortality rates.

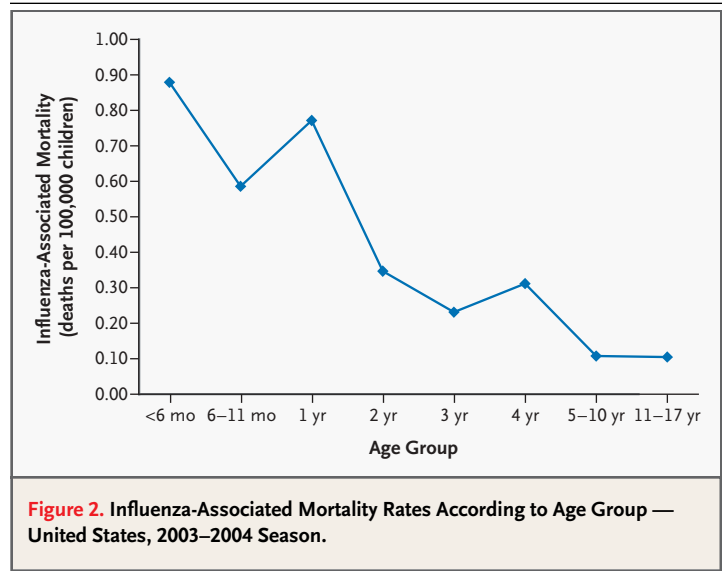
the 153 children (92 percent) (Table 3). Among the 108 children with fever, 36 had a temperature of 40.0°C or higher, and 3 had a temperature of 42.2°C or higher. Fifteen additional children had a temperature below 35.0°C during their clinical course. Respiratory symptoms were most common (86 percent) and were followed in frequency by gastrointestinal symptoms (46 percent). Autopsies were performed in 101 of the 153 cases (66 percent), and results were available for review in 85. Diagnoses in addition to influenza were reported before or after death in 146 cases and included pneumonia in 71 (49 percent) and sepsis or shock in 50 (34 percent) (Table 3).

Among the 153 children, the median duration of illness was 5 days (range, 1 to 74; interquartile range, 3 to 8). Forty-five children (29 percent) died within three days after the onset of illness, and eight (5 percent) died within one day. Ninety children (59 percent), including 85 who had been admitted to an intensive care unit, died after hospital admission; 16 (10 percent) died in an emergency department; and 47 (31 percent) died at home or in transit to a health care facility. In two of the children, influenza-like symptoms had begun more than 48 hours after hospital admission, suggesting nosocomial acquisition. Clinical information for those who had received no medical attention was limited, but the available data showed a symptom profile similar to that of the children who had been hospitalized: 31 of the 47 children who died outside a hospital (66 percent) had a temperature of 38°C or higher, 35 (74 percent) had respiratory symptoms, and 18 (38 percent) had gastrointestinal symptoms.

#### LABORATORY TESTING

Influenza-virus infection was determined by multiple testing methods in 63 of the 153 cases (41 percent). Rapid diagnostic or enzyme immunoassay testing was the sole method of diagnosis for influenza in 58 (38 percent). Influenza was detected by viral culture alone in 17 cases and by RT-PCR, immunofluorescence, or postmortem immunohistochemical analysis alone in 5 cases each.

Of the 126 cases in which the influenza-virus type was determined, 123 (98 percent) involved influenza A viruses and 3 (2 percent) influenza B viruses. All 39 influenza A viruses that were subtyped were subtype A (H3N2). Among 33 influenza A (H3N2) viruses that were antigenically characterized, 3 (9 percent) were A/Panama/2007/99-like, and 30 (91 percent) were A/Fujian/411/2002-like



or A/Korea/770/2002-like and had drifted antigenically from the A/Panama/2007/99 virus, the H3N2 component of the 2003–2004 influenza vaccine. One influenza B virus was characterized and was B/Shanghai/361/2002-like and antigenically distinct from the B/Hong Kong/330/2001 component of the vaccine.

Clinically significant laboratory-confirmed bacterial coinfections were identified in 24 of 102 cases (24 percent) for which there were reported culture results; among them were *Staphylococcus aureus* infection, found in 11 cases (6 of which involved a methicillin-resistant strain) (Table 4). Bacterial-culture testing was reported in 52 children in whom pneumonia had been diagnosed and 40 in whom sepsis or shock had been diagnosed, and an invasive bacterial cause was identified in 21 and 18 children, respectively. Of 81 children tested for viral pathogens other than influenza virus, coinfections with respiratory syncytial virus (5 patients), adenovirus (3), and hepatitis B virus (1) were identified. *Aspergillus fumigatus* was cultured from an endotracheal aspirate and fungal elements were identified in lung and brain autopsy tissue from one additional child who was considered immunosuppressed as a result of long-term corticosteroid therapy.

#### DISCUSSION

This report describes results from a national assessment of pediatric mortality associated with laboratory-confirmed influenza. One hundred fifty-three deaths among children during the 2003–2004

**Table 2. Underlying Health Status of 149 of 153 Children with Fatal Influenza — United States, 2003–2004 Season.\***

Underlying Health Status	No. of Children (%)	
	Age <6 Mo (N=17)	Age ≥6 Mo (N=132)
<b>Prior good health, according to age</b>		
All ages	7 (41)	63 (48)
6–23 mo	—	20 (15)
2–4 yr	—	22 (17)
5–17 yr	—	21 (16)
<b>ACIP-defined high-risk condition†</b>		
All high-risk conditions	5 (29)	44 (33)
Asthma (without other pulmonary disease)	—	12 (9)
Chronic pulmonary disease (with or without asthma)	2 (12)	16 (12)
Chronic cardiovascular disease	4 (24)	10 (8)
Metabolic or endocrine disorder	—	6 (5)
Immunosuppression‡	—	5 (4)
Long-term aspirin therapy	—	5 (4)
Hemoglobinopathy	—	2 (2)
Renal disease	—	2 (2)
Pregnancy	—	1 (1)
<b>Other chronic condition</b>		
All chronic conditions	10 (59)	54 (41)
Chronic condition without a concurrent ACIP-defined high-risk condition	5 (29)	25 (19)
Neurologic or neuromuscular disorder§	4 (24)	45 (34)
Gastrointestinal disorder¶	3 (18)	15 (11)
Upper-airway abnormality	1 (6)	8 (6)

\* Underlying health status was unknown for four children. The categories shown are not mutually exclusive, since some children had more than one condition. Dashes denote no cases or not applicable.

† High-risk conditions are those defined as such by the ACIP.<sup>16</sup>

‡ Four of the five children were considered immunosuppressed as a result of systemic corticosteroid use lasting more than two weeks. The fifth child had received long-term rituximab therapy.

§ Neurologic and neuromuscular disorders included developmental delay, cerebral palsy, seizure disorders, congenital neurologic disorders, and other chronic central nervous system disorders.

¶ Gastrointestinal disorders included hepatobiliary disease, gastroesophageal reflux disease, the presence of a gastrostomy tube, and a history of Nissen gastric fundoplication.

|| Upper-airway abnormalities included a tracheostomy, a cleft lip or palate, laryngomalacia, and the Pierre Robin syndrome.

influenza season were reported by 40 U.S. state health departments. The reported deaths peaked in December, as did the national level of influenza activity.<sup>17</sup> Mortality rates were highest among children younger than six months of age, but cases were reported among children of all ages. Twenty-nine percent of the children died within three days after the onset of illness, and 59 percent died after

admission to a hospital. Although one third of the deaths occurred in children who had an ACIP-defined high-risk condition, nearly half occurred in children who did not have any documented underlying medical disorders.

These fatal cases involved a range of clinical complications similar to those associated with nonfatal influenza,<sup>6,18</sup> including pneumonia,<sup>6</sup> laryngotracheobronchitis,<sup>6,7,19</sup> bronchiolitis,<sup>18</sup> and encephalopathy.<sup>20</sup> These complications can be grouped into at least three categories: exacerbation of chronic underlying disease, invasive bacterial infection, and fulminant progression to death after an initially mild illness. The mechanisms of these sudden deaths are unknown but could include an exaggerated inflammatory response to influenza-virus infection or complications of an unrecognized metabolic disorder.

Our findings suggest that younger children and those with ACIP-defined high-risk conditions may be at increased risk for influenza-related death. These groups have previously been shown to have elevated rates of hospitalization attributable to influenza.<sup>3,4,18,21,22</sup> In our study, mortality rates were highest among children younger than 6 months of age and next highest among those 6 to 23 months of age. At least one ACIP-defined high-risk condition was present in 33 percent of the children, as compared with an estimated prevalence of 7 percent among U.S. residents younger than 18 years of age.<sup>23</sup> In the 2002–2003 and 2003–2004 seasons, influenza vaccination of all children 6 to 23 months of age was encouraged when feasible.<sup>13</sup> Beginning with the 2004–2005 season, the ACIP formally recommended annual influenza vaccination for all children in this age group.<sup>16</sup> However, the prevention of influenza-related complications among infants younger than six months of age remains an ongoing challenge, because influenza vaccination and antiviral agents are not approved for children in this age group. During the 2003–2004 season, these young infants had the highest mortality rate of any age group, highlighting the importance of ACIP recommendations that promote influenza vaccination of pregnant women and of all household contacts and caregivers of children younger than six months of age.

Chronic neurologic or neuromuscular disorders have not previously been recognized to increase the risk of influenza-related complications, and none were indications for influenza vaccination during the 2003–2004 season. In our surveillance, condi-

tions in this category were reported in one third of children; however, this category includes several dissimilar disorders that may not confer the same risk. The ACIP recently recommended annual influenza vaccination for all persons with conditions that “can compromise respiratory function or the handling of respiratory secretions, or that can increase the risk of aspiration.”<sup>24</sup> This recommendation supports the use of influenza vaccination in persons with many of the underlying neurologic disorders identified in this study.

In addition to improved identification and vaccine coverage among high-risk persons, influenza prevention also depends on the degree of match between the circulating and vaccine strains of influenza virus. Eighty-nine percent of the influenza A (H3N2) viruses characterized in the United States during the 2003–2004 season, and most of the viruses characterized in this study, were similar to the A/Fujian/411/2002 variant, which was antigenically distinct from the 2003–2004 influenza A (H3N2) vaccine strain.<sup>17</sup> Although one investigation of the 2003–2004 season reported the influenza vaccine to be 25 to 49 percent effective in children 6 to 23 months of age,<sup>25</sup> further studies will be necessary to determine the overall significance of antigenic drift with respect to vaccine effectiveness and the prevention of influenza-associated death.

Our findings are subject to several limitations. Some influenza-related deaths may have been missed, since influenza testing may not have been performed in all cases of fatal respiratory illness in children. In particular, surveillance started at the peak of the influenza season in some areas, and less testing may have been done before that time. In addition, influenza was diagnosed by rapid diagnostic tests alone in almost 40 percent of the cases, and potential cases may have been missed by this relatively insensitive method. Conversely, some rapid-test results may have been false positive during periods of low influenza activity.<sup>26</sup> Retrospectively collected medical records varied in availability and completeness and were particularly limited in cases involving children who had not been hospitalized. Similarly, neither influenza testing nor the clinical evaluation of the children was standardized. Thus, some complications and other contributing causes of death may not have been identified.

The number and characteristics of the deaths reported here represent data from only one season, and therefore must be interpreted with caution. The predominant viruses circulating in the 2003–

**Table 3. Clinical Features of Fatal Influenza in Children — United States, 2003–2004 Season.\***

Clinical Feature	No. of Children (%)
<b>Signs or symptoms at presentation for medical care</b>	
Fever	108 (77)
Cough	93 (66)
Respiratory distress	83 (59)
No respiratory symptoms	19 (13)
Vomiting	55 (39)
Vomiting with fever	46 (33)
Vomiting without respiratory symptoms	8 (6)
Vomiting and diarrhea without respiratory symptoms	2 (1)
Diarrhea	20 (14)
Diarrhea without vomiting	5 (4)
Altered mental status	23 (16)
Seizures	14 (10)
<b>Diagnoses†</b>	
Any acute respiratory tract disorder	99 (68)
Pneumonia	71 (49)
Pneumonitis	13 (9)‡
Bronchiolitis	11 (8)
Laryngotracheobronchitis or tracheobronchitis	22 (15)
Croup	7 (5)§
Tracheitis	4 (3)‡
Bronchitis	3 (2)‡
Sepsis or shock	50 (34)
Disseminated intravascular coagulopathy	18 (12)
Encephalopathy	9 (6)
Myocarditis or pericarditis	6 (4)
Myositis or rhabdomyolysis	5 (3)
Myocardial infarction	2 (1)
Hemophagocytosis syndrome	3 (2)

\* Data on signs and symptoms were available for 141 children, and data on diagnoses were available for 146 children.

† Multiple diagnoses before and after death were possible.

‡ The diagnosis was made at autopsy.

§ The diagnosis was made before death. In one child with croup, laryngotracheobronchitis was also diagnosed at autopsy.

2004 season were influenza A (H3N2) virus,<sup>17</sup> a subtype associated with increased morbidity and mortality,<sup>1,2</sup> and several indicators suggest that this season was more severe than the previous three seasons.<sup>27</sup> These indicators included estimates of outpatient visits, pediatric hospitalizations, and influenza-related mortality. Comparable data on pediatric mortality associated with laboratory-confirmed influenza in previous years are unavailable, however, and influenza seasons have varied widely

**Table 4. Bacterial Coinfections in 24 Children with Fatal Influenza — United States, 2003–2004 Season.\***

Bacterial Agent	No. of Children
<i>Staphylococcus aureus</i>	11
Methicillin-resistant	6
Methicillin-susceptible	1
Unknown sensitivity	4
<i>Staphylococcus</i> , species not specified	1
<i>Streptococcus pneumoniae</i> †	2
Group A streptococcus	3
<i>Bordetella pertussis</i> ‡	1
<i>Haemophilus influenzae</i>	4
Nontypeable	2
Type a	1
Type b	1
<i>Pseudomonas aeruginosa</i>	1
<i>Enterococcus faecalis</i>	1
<i>Neisseria meningitidis</i>	1
<i>Mycoplasma pneumoniae</i> §	1

\* All organisms were isolated by culture from normally sterile sites, except for *B. pertussis* and *M. pneumoniae*. In addition, *Escherichia coli* and *Enterobacter cloacae* were isolated from one child each but were of uncertain clinical significance, and 15 other positive cultures were classified as probable contaminants on the basis of clinical and pathological review. Polymicrobial infections were considered likely in two children.

† *S. pneumoniae* was isolated from a cerebrospinal fluid specimen in one case.

‡ *B. pertussis* infection was diagnosed on the basis of the result of PCR analysis of a nasopharyngeal specimen.

§ *M. pneumoniae* infection was diagnosed on the basis of the result of latex-agglutination testing of a serum specimen. This child also had a methicillin-resistant *S. aureus* coinfection.

in severity over the past three decades.<sup>2,28</sup> Despite substantial methodologic differences among the studies, our findings are similar to two previous estimates of 0.48 and 0.77 excess influenza-attributable death from respiratory and cardiac causes per 100,000 person-years in children.<sup>2,4</sup> Therefore, continued surveillance is needed for multiple seasons to allow better assessment of the effect of influenza on childhood mortality. Toward this goal, influenza-associated death in children was made a nationally reportable condition in October 2004.<sup>29</sup>

It is well established that influenza causes substantial illness among children in the United States each year and results in school absenteeism, outpatient and emergency department visits, and hospitalizations.<sup>1,22,30</sup> By comparison, influenza-associated death among children appears to be rare. However, the 153 influenza-associated deaths reported here exceed recently published estimates of childhood mortality associated with several other conditions, including invasive pneumococcal disease (120 deaths in 2003),<sup>31</sup> varicella (39 from 1999 through 2001),<sup>32</sup> pertussis (101 from 1990 through 1999),<sup>33</sup> and measles (none from 1993 through 2002).<sup>34</sup> It is likely that, during the 2003–2004 season, more deaths among children were associated with influenza than with any other currently vaccine-preventable disease in the United States. Therefore, increased influenza-vaccine coverage and early identification and effective treatment of influenza among children should be key goals.

Dr. Greenberg reports that he is currently employed by Glaxo-SmithKline Biologicals.

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#### APPENDIX

In addition to the authors, the members of the Influenza Special Investigations Team are M. Amundson, B.S. Baughman, E. Belay, C. Borkowf, L. Brammer, R.A. Bright, T. Do, T. Farris, M. Fischer, T. Fischer, A. Foust, H.E. Hall, M. Kuehnert, M.M. Patel, L.J. Podewils, A.S. Postema, S.J. Schrag, J.S. Sekhar, M.W. Shaw, I. Shui, K.S. Teates, S. Wang, M.A. Weideman, C. Whitney, and X. Xu.

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