

## INFLUENZA AND THE RATES OF HOSPITALIZATION FOR RESPIRATORY DISEASE AMONG INFANTS AND YOUNG CHILDREN

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### ABSTRACT

**Background** Young children may be at increased risk for serious complications from influenza virus infection. However, in population-based studies it has been difficult to separate the effects of influenza virus from those of respiratory syncytial virus. Respiratory syncytial virus often circulates with influenza viruses and is the most frequent cause of hospitalization for lower respiratory tract infections in infants and young children. We studied the rates of hospitalization for acute respiratory disease among infants and children during periods when the circulation of influenza viruses predominated over the circulation of respiratory syncytial virus.

**Methods** For each season from October to May during the period from 1992 to 1997, we used local viral surveillance data to define periods in Washington State and northern California when the circulation of influenza viruses predominated over that of respiratory syncytial virus. We calculated the rates of hospitalization for acute respiratory disease, excess rates attributable to influenza virus, and incidence-rate ratios for all infants and children younger than 18 years of age who were enrolled in either the Kaiser Permanente Medical Care Program of Northern California or the Group Health Cooperative of Puget Sound.

**Results** The rates of hospitalization for acute respiratory disease among children who did not have conditions that put them at high risk for complications of influenza (e.g., asthma, cardiovascular diseases, or premature birth) and who were younger than two years of age were 231 per 100,000 person-months at Northern California Kaiser sites (from 1993 to 1997) and 193 per 100,000 person-months at Group Health Cooperative sites (from 1992 to 1997). These rates were approximately 12 times as high as the rates among children without high-risk conditions who were 5 to 17 years of age (19 per 100,000 person-months at Northern California Kaiser sites and 16 per 100,000 person-months at Group Health Cooperative sites) and approached the rates among children with chronic health conditions who were 5 to 17 years of age (386 per 100,000 person-months and 216 per 100,000 person-months, respectively).

**Conclusions** Infants and young children without chronic or serious medical conditions are at increased risk for hospitalization during influenza seasons. Routine influenza vaccination should be considered in these children. (N Engl J Med 2000;342:232-9.)

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**A** NNUAL vaccination against influenza is recommended for all persons six months of age or older who have chronic conditions that increase their risk of complications from influenza.<sup>1-5</sup> During past epidemics of influenza, hospitalization rates among high-risk children have ranged from 200 to 500 per 100,000 persons.<sup>1,6,7</sup> During the 1970s and 1980s, Mullooly and Barker<sup>6</sup> and Glezen et al.<sup>7</sup> showed that hospitalization rates for children younger than five years of age who had no known high-risk conditions were elevated during winter months when influenza viruses were in circulation. However, these studies did not address the possibility that some of the hospitalizations resulted from other respiratory virus infections, most notably respiratory syncytial virus. Respiratory syncytial virus frequently circulates with influenza viruses in the winter,<sup>6-11</sup> is the primary cause of lower respiratory tract disease among young children,<sup>8-11</sup> and results in an estimated 84,000 to 144,000 hospitalizations annually for lower respiratory tract disease among U.S. children younger than five.<sup>12</sup>

Our objective was to determine the effect of influenza on hospitalizations for acute respiratory disease in young children. We studied a period of several years because the impact of influenza can vary substantially between seasons depending on several factors, including the overall prevalence of infections, the proportion of circulating influenza virus types and subtypes, the virulence of circulating strains, and the protective antibody levels in the population.<sup>1,2,13</sup> We studied hospitalizations for acute respiratory disease because influenza virus infections frequently remain undiagnosed, even in hospitalized patients, and can precipitate secondary complications, including bacterial infections and exacerbations of chronic conditions that lead to hospitalization.<sup>1,2,13</sup>

### METHODS

#### Study Period and Population

We evaluated data for the period from 1992 to 1997 and included children younger than 18 years of age who had been en-

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rolled continuously for at least one year before the start of the study or since birth in either the Kaiser Permanente Medical Care Program of Northern California, Oakland (Northern California Kaiser), or the Group Health Cooperative of Puget Sound, Seattle (Group Health Cooperative). The average annual numbers of participants from Northern California Kaiser and Group Health Cooperative were 250,892 and 71,705, respectively.

Northern California Kaiser has sites in the San Francisco Bay area and serves over 2,300,000 members annually. Twenty-five percent of this population is younger than 18 years of age; 40 percent are white, 19 percent Hispanic, 19 percent of mixed racial or ethnic background, 13 percent Asian, and 8 percent black; the racial or ethnic background of 1 percent is unknown. Most Group Health Cooperative sites are located in the Seattle area, and the organization serves over 340,000 members. Twenty-six percent of this population is younger than 18 years; 81 percent are white, 1 percent Hispanic, 8 percent Asian, 7 percent black, and 1 percent Native American; the racial or ethnic background of 2 percent is unknown.

### Hospitalization and Medical Data

Hospitalization data were obtained through the Vaccine Safety Datalink. This project connects automated clinical data bases from Northern California Kaiser, Group Health Cooperative, and two other West Coast managed-care organizations and was started in 1991 by the National Immunization Program, Centers for Disease Control and Prevention (CDC).<sup>14</sup>

Data on patients included demographic characteristics, vaccination status, prescribed medications, hospital discharges, emergency room visits, and visits to outpatient clinics. Complete data were obtained for Group Health Cooperative participants for the entire study period. For Northern California Kaiser participants, complete data were available for the influenza seasons from 1995 to 1996 and from 1996 to 1997. For the influenza seasons from 1993 to 1994 and from 1994 to 1995, data were limited to children who were younger than seven years of age and who were seen at three clinics (that serve about 15 percent of the total membership); no data were available for the period from 1992 to 1993.

### Determination of Health Status

Children were considered to be at high risk for serious complications from influenza if they had been hospitalized or had visited an outpatient clinic or emergency room during the previous year for any chronic or serious condition (including chronic pulmonary, cardiovascular, metabolic, rheumatic, renal, neurologic, immunosuppressive, and hematologic diseases and premature birth).<sup>1-4,15</sup> Pharmacologic data, which were available for Group Health Cooperative members for the entire study period and for Northern California Kaiser members for the period from 1993 to 1996, were used to identify children with asthma.<sup>16</sup> We considered children without identifiable high-risk conditions at the time of hospitalization to be otherwise healthy.

### Definition of Study Periods

Local virologic surveillance data were used to determine when influenza viruses and respiratory syncytial virus were in circulation at each site. Data for the San Francisco Bay area were obtained from the National Respiratory and Enteric Virus Surveillance System of the CDC,<sup>17</sup> the Northern California Kaiser virology laboratory, Stanford Health Services, and the University of California, San Francisco, Mt. Zion Medical Center. Data for the Seattle area were obtained from the National Influenza Virologic Surveillance System of the CDC<sup>18</sup> and the National Respiratory and Enteric Virus Surveillance System.

#### Period When Influenzavirus Predominated

For each season from October to May during the study period, we identified all periods of two or more consecutive weeks in which each week accounted for at least 5 percent of the season's total number of influenza virus isolates and less than 5 percent of the total number of positive tests for respiratory syncytial virus. All such

weeks during the entire study were combined and together were defined as the period in which influenza virus was predominant.

#### Period of Extended Influenzavirus Circulation

We also identified a longer period during which influenza viruses were in circulation and the circulation of other respiratory viruses was not considered. We identified all periods of two or more consecutive weeks in which each week accounted for at least 5 percent of the season's total number of influenza virus isolates. All such weeks during the entire study were combined and together were defined as the extended period of influenza virus.

#### Period When Respiratory Syncytial Virus Predominated

For each season from October to May during the study period, we identified all periods of two or more consecutive weeks in which each week accounted for at least 5 percent of the season's total number of positive tests for respiratory syncytial virus and less than 5 percent of the season's total number of influenza virus isolates. All such weeks during the entire study were combined and together were defined as the period in which respiratory syncytial virus predominated.

#### Peri-Seasonal Base-Line Period

For each season from October to May during the study period, we identified all periods of two or more consecutive weeks in which each week accounted for less than 5 percent of the season's total number of influenza virus isolates and less than 5 percent of the total number of positive tests for respiratory syncytial virus and in which no isolates of parainfluenza virus type 1 or 3 were identified. All such weeks during the entire study were combined and together were defined as the peri-seasonal base-line period.

#### Summer Base-Line Period

For each interval from June to September during the study period, we identified all periods of two or more consecutive weeks in which no isolates of influenza virus, respiratory syncytial virus, or parainfluenza virus type 1 or 3 were detected. All such weeks during the entire study were combined and together were defined as the summer base-line period.

### Study Outcomes

The main outcomes of the study were hospitalizations for acute respiratory disease in which codes 460 to 496 or 510 to 519 from the *International Classification of Diseases, 9th revision, Clinical Modification* were listed as a discharge diagnosis.<sup>19</sup> These codes excluded respiratory tract diseases resulting from the inhalation of asbestos, dust, or chemical fumes or the aspiration of food.

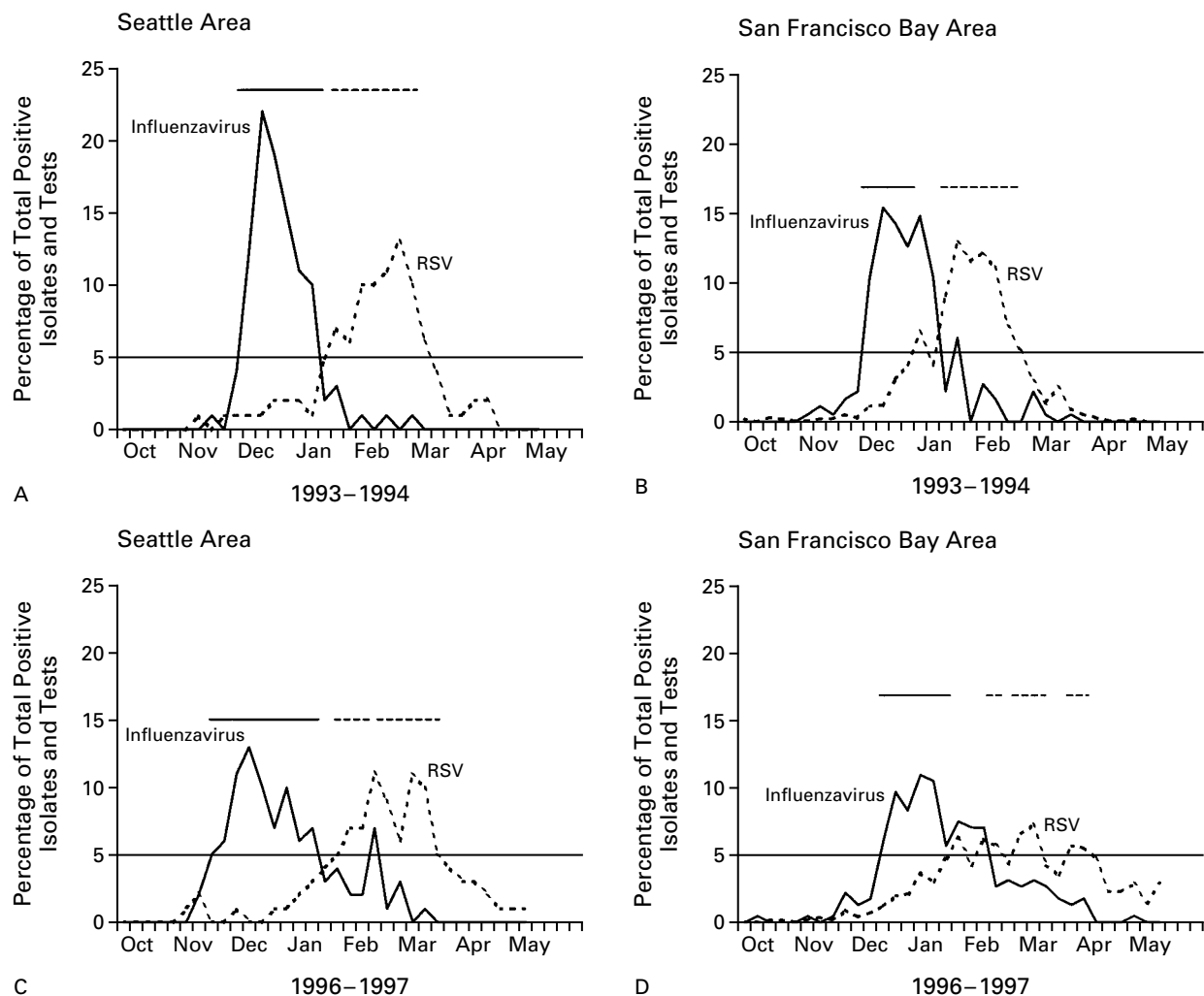
### Statistical Analysis

For each study site and year, we computed rates of hospitalization for acute respiratory disease and incidence-rate ratios per 100,000 person-months according to age and health status for periods in which influenza virus predominated and periods in which respiratory syncytial virus predominated. As reference values, we used hospitalization rates for children 5 to 17 years of age who had no identifiable high-risk conditions during the same period. We used exact two-sided P values and 95 percent confidence intervals to evaluate differences between the groups.<sup>20</sup> For each age group, we also calculated the excess rates of hospitalization attributable to influenza virus by subtracting peri-seasonal rates and rates during the summer base-line period from the rates during periods in which influenza virus predominated. We performed statistical analyses using StatXact software.<sup>21</sup>

## RESULTS

### Periods When Influenzavirus Predominated and Extended Periods of Influenzavirus

In the San Francisco Bay area from 1993 to 1997, a total of 3638 respiratory viruses were identified,



**Figure 1.** Isolates of Influenzavirus and Positive Tests for Respiratory Syncytial Virus (RSV) as a Percentage of All Positive Isolates and Tests in the Seattle Area (Panels A and C) and the San Francisco Bay Area (Panels B and D) from October 1993 to May 1994 and October 1996 to May 1997.

The horizontal lines over the graphs represent the consecutive periods in which influenza virus and respiratory syncytial virus predominated (i.e., accounted for at least 5 percent of all viral isolates in a season).

of which 515 were influenza virus isolates (ranging from 41 in the period from 1994 to 1995 to 228 in the period from 1996 to 1997) and 3029 were identified as respiratory syncytial virus (mostly through the use of rapid antigen tests). During the entire period from 1993 to 1997, there were 13 weeks during which the circulation of influenza viruses predominated relative to that of respiratory syncytial virus. During individual seasons from October to May, the length of the periods in which influenza virus predominated ranged from two weeks in the period from 1994 to 1995 (data not shown) to six weeks in the period from 1993 to 1994 (Fig. 1).

For the Seattle area from 1992 to 1997, a total of 4883 respiratory viruses were identified, of which 1285 were influenza virus isolates (ranging from 101 in the period from 1994 to 1995 to 454 in the period from 1996 to 1997) and 2584 were respiratory syncytial virus. During the entire period from 1992 to 1997, there were 24 weeks during which the circulation of influenza viruses predominated relative to that of respiratory syncytial virus. The length of the periods in which influenza virus predominated ranged from two weeks in the period from 1994 to 1995 (data not shown) to nine weeks in the period from 1996 to 1997 (Fig. 1).

When data from both sites were combined, the av-

TABLE 1. DISTRIBUTION OF HIGH-RISK CONDITIONS IN THE STUDY POPULATIONS.

VARIABLE	1992-1993 SEASON		1993-1994 SEASON		1994-1995 SEASON		1995-1996 SEASON		1996-1997 SEASON	
	NO. OF CHILDREN	RATE/100,000 CHILDREN	NO. OF CHILDREN*	RATE/100,000 CHILDREN	NO. OF CHILDREN*	RATE/100,000 CHILDREN	NO. OF CHILDREN	RATE/100,000 CHILDREN	NO. OF CHILDREN	RATE/100,000 CHILDREN
<b>Northern California Kaiser</b>										
Total no. of children	—	—	24,669		24,755		461,148		477,175	
No. with at least one high-risk condition†	—	—	2,147	8703	4,076	16,465	47,275	10,252	48,661	10,198
Asthma	—	—	1,874	7597	3,841	15,516	41,768	9,057	42,008	8,803
Cardiovascular diseases	—	—	52	211	60	242	1,174	255	2,494	523
Other conditions‡	—	—	293	1188	269	1,087	10,084	2,187	5,916	1,240
Average no. of conditions per child	—	—	1.03		1.02		1.12		1.04	
<b>Group Health Cooperative</b>										
Total no. of children	70,108		70,078		69,089		71,324		77,926	
No. with at least one high-risk condition†	5,428	7742	5,402	7709	5,181	7,499	5,597	7,847	6,613	8,486
Asthma	4,287	6115	4,415	6300	4,168	6,033	4,517	6,333	5,394	6,922
Cardiovascular diseases	266	379	306	437	239	346	287	402	304	390
Other conditions‡	1,128	1609	934	1333	1,007	1,458	945	1,325	1,161	1,490
Average no. of conditions per child	1.05		1.05		1.04		1.05		1.04	

\*The Northern California Kaiser population includes only children younger than seven years of age.

†Some children had more than one high-risk condition.

‡This category includes other pulmonary diseases, metabolic diseases, immunosuppression (from all causes), cancer, prematurity, chronic renal diseases, hemoglobinopathies, and neurologic diseases.

erage annual duration of the extended period of influenza virus was 7.3 weeks (51 days).

**Prevalence of High-Risk Conditions**

Among all participants at both sites, 9.7 percent had at least one identifiable high-risk condition (Table 1). Asthma was the most common condition and was diagnosed in 8.3 percent of all participants (Table 1).

**Hospitalization Rates during Periods When Influenzavirus Predominated**

During the periods in which influenza virus predominated, hospitalization rates for acute respiratory disease among children with high-risk conditions at Northern California Kaiser sites were 1181 per 100,000 person-months for children younger than 2 years of age, 713 per 100,000 person-months for children 2 to 4 years of age, and 386 per 100,000 person-months for children 5 to 17 years of age. The rates among high-risk children at Group Health Cooperative sites were 772 per 100,000 person-months for children younger than 2 years of age, 458 per 100,000 person-months for children 2 to 4 years of age, and 216 per 100,000 person-months for children 5 to 17 years of age.

During the periods in which influenza virus predominated, hospitalization rates for acute respiratory disease among children without high-risk conditions at Northern California Kaiser sites were 231 per 100,000 person-months for children younger than 2 years of age, 53 per 100,000 person-months for children 2 to

4 years of age, and 19 per 100,000 person-months for children 5 to 17 years of age (Table 2). The rates among children without high-risk conditions at Group Health Cooperative sites were 193 per 100,000 person-months for children younger than 2 years of age, 21 per 100,000 person-months for children 2 to 4 years of age, and 16 per 100,000 person-months for children 5 to 17 years of age (Table 2).

At each site, rates of hospitalization for acute respiratory disease among children without high-risk conditions who were younger than 2 years of age were 12 times as high as those for children who were 5 to 17 years of age, and these differences were statistically significant (Table 3). Among children without high-risk conditions who were 2 to 4 years of age, hospitalization rates were significantly higher than those among children 5 to 17 years of age at Northern California Kaiser sites but not at Group Health Cooperative sites (Table 3). There were no significant differences between the sexes in the relative risk of hospitalization at any age (data not shown).

**Hospitalization Rates of Children without High-Risk Conditions during Other Periods**

During the periods of extended influenza virus circulation, the rates of hospitalization for acute respiratory disease among children without high-risk conditions who were younger than 2 years of age were 350 per 100,000 person-months at Northern California Kaiser sites and 225 per 100,000 person-months at Group Health Cooperative sites. During the periods in which respiratory syncytial virus predominated,

**TABLE 2. RATES OF HOSPITALIZATION FOR ACUTE RESPIRATORY DISEASE AMONG CHILDREN WITHOUT HIGH-RISK CONDITIONS.**

PERIOD AND AGE GROUP	NORTHERN CALIFORNIA KAISER, 1993-1997			GROUP HEALTH COOPERATIVE, 1992-1997		
	NO. HOSPITALIZED	NO. OF PERSON-MONTHS	RATE/100,000 PERSON-MONTHS (95% CI)*	NO. HOSPITALIZED	NO. OF PERSON-MONTHS	RATE/100,000 PERSON-MONTHS (95% CI)*
Period when influenza virus predominated						
0-1 yr	155	66,964	231 (197-271)	86	44,589	193 (154-238)
2-4 yr	42	79,280	53 (38-72)	11	52,137	21 (11-38)
5-17 yr	74	384,887	19 (15-24)	54	327,652	16 (12-22)
Period when respiratory syncytial virus predominated						
0-1 yr	360	116,332	309 (278-343)	193	51,944	372 (321-428)
2-4 yr	72	141,725	51 (40-64)	28	63,630	44 (29-65)
5-17 yr	171	741,451	23 (19-27)	39	395,600	10 (7-13)
Peri-seasonal base-line period						
0-1 yr	355	296,514	120 (108-133)	79	73,874	107 (85-133)
2-4 yr	138	366,685	38 (32-44)	21	87,603	24 (14-37)
5-17 yr	264	1,898,072	14 (12-16)	55	555,915	10 (7-13)
Summer base-line period						
0-1 yr	324	401,902	81 (72-90)	50	75,469	66 (49-87)
2-4 yr	134	494,327	27 (23-32)	16	102,065	16 (8-25)
5-17 yr	510	2,672,879	19 (17-21)	75	642,685	12 (9-14)

\*CI denotes confidence interval.

**TABLE 3. RELATIVE RISK OF HOSPITALIZATION FOR ACUTE RESPIRATORY DISEASE AMONG CHILDREN WITHOUT HIGH-RISK CONDITIONS DURING PERIODS IN WHICH INFLUENZAVIRUS PREDOMINATED.**

STUDY SITE AND AGE GROUP	NO. HOSPITALIZED	NO. OF PERSON-MONTHS	RATE/100,000 PERSON-MONTHS	RELATIVE RISK (95% CI)*	P VALUE
Northern California Kaiser					
0-1 yr	155	66,964	231	12.1 (9.1-16.1)	<0.001
2-4 yr	42	79,280	53	2.8 (1.8-4.1)	<0.001
5-17 yr	74	384,887	19	1.0†	—
Group Health Cooperative					
0-1 yr	86	44,589	193	11.7 (8.2-16.8)	<0.001
2-4 yr	11	52,137	21	1.3 (0.7-2.4)	0.455
5-17 yr	54	327,652	16	1.0†	—

\*CI denotes confidence interval.

†This group served as the reference group.

ed, the respective rates were 309 and 372 per 100,000 person-months.

**Comparison of Hospitalization Rates**

In each age group, children with high-risk conditions were significantly more likely to be hospitalized than children without high-risk conditions. During the periods in which influenza virus predominated, relative risks of hospitalizations for acute respiratory disease among children with high-risk conditions, as compared with children without high-risk conditions, were 5 (95 percent confidence interval, 4 to 7) at Northern California Kaiser sites and 4 (95 percent confidence interval, 3 to 6) at Group Health Coop-

erative sites for children younger than 2 years of age; 13 (95 percent confidence interval, 9 to 19) and 21 (95 percent confidence interval, 11 to 41), respectively, for children 2 to 4 years of age; and 20 (95 percent confidence interval, 15 to 26) and 13 (95 percent confidence interval, 9 to 19), respectively, for children 5 to 17 years of age.

**Excess Rates of Hospitalization Attributable to Influenzavirus**

Among children without high-risk conditions at Northern California Kaiser sites and Group Health Cooperative sites, the excess rates of hospitalization attributable to influenza virus with use of the base-

**TABLE 4.** EXCESS RATES OF HOSPITALIZATION FOR ACUTE RESPIRATORY DISEASE ATTRIBUTABLE TO INFLUENZAVIRUS AMONG CHILDREN WITHOUT HIGH-RISK CONDITIONS DURING PERIODS IN WHICH INFLUENZAVIRUS PREDOMINATED.\*

STUDY SITE AND AGE GROUP	RATE IN PERIOD WHEN INFLUENZAVIRUS PREDOMINATED	RATE IN SUMMER BASE-LINE PERIOD	EXCESS RATE ATTRIBUTABLE TO INFLUENZAVIRUS (95% CI)†	P VALUE	RATE IN PERI-SEASONAL BASE-LINE PERIOD	RATE ATTRIBUTABLE TO INFLUENZAVIRUS (95% CI)‡	P VALUE
	rate/100,000 person-months				rate/100,000 person-months		
Northern California Kaiser							
0-1 yr	231	81	151 (113 to 188)	<0.001	120	112 (73 to 150)	<0.001
2-4 yr	53	27	26 (9 to 42)	<0.002	38	15 (-2 to 33)	<0.081
5-17 yr	19	19	0 (-5 to 5)	0.951	14	5 (1 to 10)	<0.026
Group Health Cooperative							
0-1 yr	193	66	127 (82 to 171)	<0.001	107	86 (39 to 132)	<0.001
2-4 yr	21	16	5 (-9 to 20)	0.468	24	-3 (-19 to 13)	0.727
5-17 yr	17	12	5 (-3 to 10)	0.066	10	7 (1 to 12)	<0.012

\*CI denotes confidence interval.

†Values are the rates during periods in which influenzavirus predominated minus the rates during the summer base-line periods.

‡Values are the rates during periods in which influenzavirus predominated minus the rates during the peri-seasonal base-line periods.

line rates from the summer periods were 151 and 127 per 100,000 person-months, respectively, for children younger than 2 years of age; 26 and 5 per 100,000 person-months, respectively, for children 2 to 4 years of age; and 0 and 5 per 100,000 person-months, respectively, for children 5 to 17 years of age (Table 4). When peri-seasonal base-line rates were used, the excess rates of hospitalization attributable to influenzavirus were significantly elevated for children younger than two years of age at both sites but not children in other age groups (Table 4).

**DISCUSSION**

Seasonal epidemics of influenza cause a disproportionate number of serious complications among the elderly and among persons of any age who have certain chronic conditions.<sup>1-5,22,23</sup> In our study, children with chronic medical conditions were 4 to 21 times as likely to be hospitalized for an acute respiratory disease as children of the same age without such conditions during periods when influenzaviruses predominated. These findings strongly support current recommendations of the Advisory Committee on Immunization Practices and the American Academy of Pediatrics to vaccinate children with high-risk conditions against influenza annually.<sup>1,24</sup> Despite such recommendations, a recent study found that only 8.9 percent of children with asthma, the predominant high-risk condition in children, had received an influenza vaccination in the period from 1993 to 1995.<sup>25</sup>

In contrast to the situation in children with high-risk conditions, it has been uncertain whether young age alone increases the risk of serious complications from influenza.<sup>6,7</sup> Although earlier studies demonstrated increased hospitalization rates among chil-

dren during winter months when influenzaviruses were in circulation, these studies did not consider the possible effect of other respiratory virus infections on population-based rates of hospitalization.

Among the noninfluenza respiratory viruses, respiratory syncytial virus has been associated most frequently with lower respiratory tract disease in children.<sup>8,10,11</sup> The potential confounding effect of the parainfluenza viruses was of less concern to us, because type 1 parainfluenza viruses circulate in odd-numbered years and primarily during the fall,<sup>26</sup> whereas type 3 parainfluenza viruses circulate annually but usually during the early spring.<sup>10</sup> In addition, less than 1 percent of the respiratory viruses identified through local surveillance were type 2 parainfluenza viruses, and most were identified outside the periods in which we defined influenzavirus to be predominant (CDC: unpublished data).

In contrast, hospitalizations associated with respiratory syncytial virus infections were of great concern to us.<sup>8-12</sup> In several studies, both respiratory syncytial virus and influenzaviruses have been recovered from young children hospitalized for acute respiratory infections during the same periods.<sup>27-31</sup> In many of these studies, respiratory syncytial virus was detected more often than influenzaviruses; however, none of these studies used population-based denominators. We attempted to minimize the potential confounding from respiratory syncytial virus in our analysis by focusing on periods when the circulation of influenzaviruses predominated over the circulation of respiratory syncytial virus.

During the periods in which influenzaviruses predominated, the rates of hospitalization for acute respiratory disease among children without high-risk conditions were approximately 12 times as high among

those younger than 2 years of age than among older children and were similar to the rates among children with high-risk medical conditions who were 5 to 17 years of age. In contrast, our data did not convincingly demonstrate that children without high-risk conditions who were two to four years of age had an elevated risk of hospitalization.

The validity and strength of our findings are supported by several considerations. We found similar results in two managed-care organizations located in different areas and serving memberships with different racial and ethnic compositions. Data were collected over a period of five years, which was important because the effect of influenza can vary considerably from season to season.<sup>1,2,13,18,32-34</sup> Most of the hospitalizations occurred during the periods from 1993 to 1994 and from 1996 to 1997, when influenza A/Beijing/32/92-like (H3N2) viruses and A/Wuhan/359/95-like (H3N2) viruses, respectively, predominated in the United States.<sup>18,34</sup> Both these viruses have been associated with high levels of influenza-associated morbidity and mortality.<sup>1,2,18,34</sup> Nonetheless, our study design reduced but could not eliminate the effect of hospitalizations associated with noninfluenza virus infections.

To assess the relevance of our findings for influenza-vaccine policy, we estimated the excess rates of hospitalization attributable to influenza virus among children without high-risk conditions. These rates represent hospitalizations that might have been avoided by influenza vaccination. We used both summer and peri-seasonal base-line rates to estimate rates of hospitalization attributable to influenza virus, because the choice of the base-line period can substantially affect such results. Various studies have used summer periods,<sup>7</sup> winter weeks with low levels of influenza virus in circulation,<sup>5,35</sup> or entire winters during years in which the levels of influenza virus in circulation were low as base-line periods.<sup>4,6</sup> On the basis of the rates of hospitalization attributable to influenza virus, the average length of the extended periods of influenza virus, and the estimated number of children without high-risk conditions who were between the ages of 6 and 24 months (according to 1999 U.S. Census Bureau population estimates), we estimate that 8400 (using a peri-seasonal base line) to 11,700 (using a summer base line) children might have been hospitalized annually due to influenza virus infections.

Although these estimates of potentially preventable hospitalizations are compelling, any modification of the national policy of influenza vaccination requires a balanced assessment of all relevant considerations. First, the vaccine schedule for children is already complicated and crowded and may become more so in the future, making it more difficult for all to comply with vaccine recommendations. Second, there are substantial logistic issues surrounding a requirement to vaccinate approximately 5.5 million chil-

dren 6 to 24 months of age with either one or two doses of vaccine during a relatively brief period each fall. Third, issues related to cost effectiveness and safety must be seriously assessed. Discussions of such considerations are ongoing, further prompted by the promising results of efficacy studies of a live attenuated influenza virus vaccine in children.<sup>36</sup> Our study demonstrates increased rates of influenza-related hospitalization among children younger than two years of age and suggests that routine influenza vaccination should be considered in these children.

Supported entirely by the CDC.

*We are indebted to the following persons for providing virologic surveillance data: Lee Schmeltz, Lynnette Brammer, and Sara Lowther (Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, CDC, Atlanta); Dr. Thomas Török (Epidemiology Program Office, CDC, Atlanta); Dr. Ann Warford (Stanford Health Services, Stanford, Calif.); Dr. Larry Drew (University of California, San Francisco, Mt. Zion Medical Center, San Francisco); Karen Fessel (Northern California Kaiser Permanente, San Francisco); and to Drs. Howard Gary, Carolyn Bridges, and Nancy Cox (Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, CDC, Atlanta), and Dr. Robert Chen (National Immunization Program, CDC, Atlanta) for their useful comments.*

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