

# Impact of Type A Influenza on Children: A Retrospective Study

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**Abstract:** Excess morbidity was studied during influenza A epidemics (1968–69, 1972–73) among children in a large prepaid group practice program. Excess rates of hospitalization for influenza-related conditions, primarily pneumonia and bronchitis, ranged from 5 per 10,000 (95 per cent confidence limits (CL): 1 to 9) for non-high-risk children to 29 per 10,000 (95 per cent CL: 5 to 53) for children with high-risk conditions. The relative increases in hospitalization rates were greatest for 5–14 year old boys: 278 per cent and

104 per cent increases for high-risk and non-high-risk boys, respectively. The absolute increase was greatest for 0–4 year olds. The excess rate of ambulatory medical care contacts, 2.6 per 100 (95 per cent CL: –1.6 to 6.8 per 100) was not statistically significant. Excess hospitalization rates among 0–14 year olds during epidemics were three to five times larger than those for persons between 15 and 64 years of age but only one-fifth the rate of persons over age 65. (*Am J Public Health* 1982; 72:1008–1016.)

## Introduction

The impact of influenza epidemics in causing excess morbidity and mortality among adults has been well documented.<sup>1,2</sup> Various surveys have demonstrated high influenza attack rates among children during epidemics<sup>3–7</sup>; however, there is little population-based data to estimate how much excess morbidity (over usual rates of acute respiratory viral disease) occurs among children during influenza epidemics. Because children, in contrast to adults, are particularly susceptible and exposed to a number of other acute respiratory virus infections, an epidemic of influenza may show less of an incremental impact upon childhood morbidity rates than has been the case among adults. Among children, those with high-risk conditions are at greatest risk of complications from acute influenza. Since the rate of chronic diseases is low among children, the impact of influenza may best be discerned by studying this group separately.

This study has measured the rates of medical care utilization for influenza-related problems among the pediatric population of a large prepaid group practice during influenza epidemics and contrasted these with rates of medical care utilization during comparable time periods that were free of epidemic influenza. Particular attention has been given to assessing the impact of influenza on children with underlying chronic disease.

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A previous report<sup>2</sup> documented the experience of the adult members of this population during the 1968–1969 and 1972–1973 influenza epidemics compared with the 1970–1971 non-epidemic reference period. The hospitalization rate for influenza-related morbidities increased 140 per cent, and the rate of ambulatory medical care services for acute respiratory diseases increased 35 per cent. The impact of influenza was greatest among the high risk population.

## Materials and Methods

### Population and Setting

All persons 0–14 years of age enrolled in the Kaiser-Permanente Medical Care Program (KPMCP), Oregon Region, during one or more of the study periods (see below) were eligible for inclusion.

The Oregon Region KPMCP was founded in 1943 and officially certified as a health maintenance organization in 1977; it currently enrolls approximately 250,000 persons in the Portland, Oregon metropolitan area. The Health Plan population, approximately 30 per cent of whom are in the 0–14 year old age group, is broadly representative of the metropolitan Portland population.<sup>8</sup> Comprehensive medical care is provided by a multispecialty medical staff. Viral diagnostic studies are not routinely available through KPMCP clinical laboratories, but specimens are sent to the Oregon State Health Department laboratory.

### Study Periods

The study was based upon the four-month period from December to March during two influenza epidemic periods (1968–1969 and 1972–1973) and four non-epidemic reference periods (1967–1968, 1969–1970, 1970–1971 and 1971–1972).

These study periods were selected on the basis of the following indices of epidemic influenza in the Portland area:

- Pneumonia and Influenza (P&I) mortality rates, estimated by the Centers for Disease Control, showed marked excess in the first two periods listed and no evidence of excess in the other four periods.

- Epidemic H3N2 strains of Influenza A virus were frequently isolated from throat cultures referred to the Oregon State Health Department virus laboratory in 1968–1969 and 1972–1973, but infrequently or not at all during the other four periods. The dominant strains isolated in 1968–1969 and 1972–1973 were A/Hong Kong/68 and A/England/72, respectively.

#### Data Collection

*Outpatient*—Computerized outpatient utilization records are available on a 5 per cent probability sample of Health Plan subscribers plus spouse and dependents. Prevalence of high-risk conditions in the population was estimated by identifying all persons in the 5 per cent sample with a record of contact with the Health Plan for treatment of one or more high-risk conditions during the 12 months prior to each study period. The list of high-risk conditions used was developed from the Annual US Public Health Service Influenza Vaccination Recommendations, with the addition of two categories of chronic illness of particular significance to the pediatric age group: congenital anomalies and cystic fibrosis. (See Appendix A for list of high-risk conditions by ICDA codes.)

All diagnoses recorded for a medical care service were used to ascertain high-risk status. High-risk individuals were identified in a cumulative manner. For individuals who met the study population criteria in more than one study period, high-risk status was based on their outpatient morbidity experience from December 1, 1966 to the beginning of the latest study period. For example, if a child was a Health Plan member during the December 1967–March 1968 and December 1968–March 1969 study periods, his/her high-risk status for the first period was determined by reviewing the morbidities for which services were rendered during the period December 1966 through November 1967, whereas the December–November periods for 1966–1967 and 1967–1968 were used to define high risk status for period 2.

The 1972–1973 cumulative prevalence estimates for treated diseases were used to derive denominators for comparing rates of influenza-related hospitalization among high-risk and non-high-risk populations during epidemic and non-epidemic periods. While the cumulative treated prevalence measure may be affected by selected enrollment and termination of high-risk children, the effect would be expected to be similar in computing hospitalization rates for epidemic and non-epidemic periods.

All contacts for acute respiratory disease (ARD) during the study periods were used to derive rates of utilization of medical services. These included both direct contacts with health service providers and indirect telephone contacts and are comparable to the category “medically attended condition” used in the National Health Survey.<sup>9</sup> Because influenza virus has been causally implicated in a wide spectrum of

ARD in children,<sup>10</sup> a comprehensive list of ARDs was used (see Appendix B). For purposes of analysis, these have been considered in the aggregate.

*Inpatient*—Computerized medical discharge records, available for all hospitalizations in the Health Plan, were used to identify members between 0–14 years of age discharged from the pediatric service during a study period and having an influenza-related morbidity listed among their discharge diagnoses. For purposes of analysis, influenza-related morbidities were both aggregated together and divided into several broad mutually exclusive diagnostic categories as shown in Appendix C.

The high-risk status of children who were hospitalized for influenza-related morbidities was defined in terms of the diagnoses noted at discharge. All ten discharge diagnostic fields were reviewed to ascertain an individual’s status with respect to the list of high risk ICDA codes shown in Appendix A.

#### Data Analysis

The impact of influenza on the rate of hospitalization among high-risk and non-high-risk children was estimated by the excess of the hospitalization rate during epidemic years over non-epidemic years. The estimated hospitalization rate for influenza-related morbidities among the high-risk group is based on two data sources. The denominator, the number of high-risk children in the Health Plan, is estimated by multiplying the number of such children in the 5 per cent sample by 20. The numerator is the number of influenza-related hospital discharges in the entire pediatric Health Plan population for which a high-risk condition was noted as a discharge diagnosis, either primary or secondary. Similar definitions apply to the non-high-risk group. Comparisons between aggregated epidemic and non-epidemic periods are given. Statistical significance of excess rates was tested by a standard normal *Z* statistic described in Appendix D. Statistical methods for the type of design used in this study, the hybrid retrospective design, have been discussed elsewhere.\*

The impact of influenza epidemics on ARD among high-risk and non-high-risk children was estimated by comparing the medical care utilization rates for ARD during epidemic and non-epidemic periods. These comparisons are given for aggregated epidemic and non-epidemic periods. T-tests are used for statistical comparisons of medical care contact rates.

#### Results

The numbers of children in the 5 per cent sample who were Health Plan members for at least one month of the December–March study periods are shown in Table 1. The study population increased from 1,694 in 1967–1968 to 2,806 in 1972–1973 and included approximately equal numbers of males and females.

The cumulative prevalence per cent of treated high-risk conditions for the six study periods is also shown in Table 1.

\*Mullooly JP: Statistical properties of relative risk for hybrid retrospective designs. Submitted to *Amer J Epid* (under revision).

**TABLE 1—Cumulative Prevalence of Treated High-Risk Conditions, among Persons 0–14 Years Old, Kaiser-Permanente Medical Care Program, Oregon**

| High-Risk Conditions                                     | 1967–68 |      |           | 1968–69 |      |           | 1969–70 |      |           | 1970–71 |      |           | 1971–72 |      |           | 1972–73 |      |           |
|--|---------|------|-----------|---------|------|-----------|---------|------|-----------|---------|------|-----------|---------|------|-----------|---------|------|-----------|
|  | N       | %    | Rate/1000 | N       | %    | Rate/1000 | N       | %    | Rate/1000 | N       | %    | Rate/1000 | N       | %    | Rate/1000 | N       | %    | Rate/1000 |
| Cardiovascular   | 2       | 4.7  | 1.2       | 6       | 8.3  | 2.9       | 12      | 11.9 | 5.2       | 14      | 10.5 | 5.8       | 15      | 9.6  | 5.6       | 17      | 9.5  | 6.1       |
| Asthma   | 16      | 37.2 | 9.4       | 27      | 37.0 | 13.1      | 38      | 37.6 | 16.4      | 54      | 40.6 | 22.3      | 61      | 39.1 | 22.7      | 76      | 42.5 | 27.1      |
| Bronchitis-<br>Emphysema                                 | 3       | 7.0  | 1.8       | 4       | 5.5  | 1.9       | 5       | 5.0  | 2.2       | 10      | 7.5  | 4.1       | 11      | 7.1  | 4.1       | 13      | 7.3  | 4.6       |
| Renal  | 6       | 14.0 | 3.5       | 7       | 9.6  | 3.4       | 7       | 6.9  | 3.0       | 11      | 8.3  | 4.5       | 11      | 7.1  | 4.1       | 12      | 6.7  | 4.3       |
| Metabolic Nutritional                                    | 0       |      |           | 0       |      |           | 1       | 1.0  | 0.4       | 2       | 1.5  | 0.8       | 5       | 3.2  | 1.9       | 5       | 2.8  | 1.8       |
| Neurological   | 10      | 23.3 | 5.9       | 15      | 20.5 | 7.3       | 17      | 16.8 | 7.4       | 20      | 15.0 | 8.3       | 22      | 14.1 | 8.2       | 22      | 12.3 | 7.8       |
| Malignant Disease  | 1       | 2.3  | 0.6       | 3       | 4.1  | 1.5       | 4       | 4.0  | 1.7       | 2       | 1.5  | 0.8       | 3       | 1.9  | 1.1       | 4       | 2.2  | 1.4       |
| Congenital<br>Anomalies                                  | 7       | 16.3 | 4.1       | 17      | 23.3 | 8.2       | 28      | 27.7 | 12.1      | 34      | 25.6 | 14.1      | 47      | 30.1 | 17.5      | 51      | 28.5 | 18.2      |
| Cystic Fibrosis  | 0       |      |           | 0       |      |           | 0       |      |           | 0       |      |           | 0       |      |           | 0       |      |           |
| TOTAL  | 45      |      |           | 79      |      |           | 112     |      |           | 147     |      |           | 175     |      |           | 200     |      |           |
| No. of Children w/<br>at Least 1 High-<br>Risk Condition | 43      |      |           | 73      |      |           | 101     |      |           | 133     |      |           | 156     |      |           | 179     |      |           |
| Average Number<br>Conditions per<br>Child                | 1.05    |      |           | 1.08    |      |           | 1.11    |      |           | 1.11    |      |           | 1.12    |      |           | 1.12    |      |           |
| Population   | 1694    |      |           | 2064    |      |           | 2312    |      |           | 2419    |      |           | 2692    |      |           | 2806    |      |           |
| Rate per 1000<br>Population                              |         |      | 25.4      |         |      | 35.4      |         |      | 43.7      |         |      | 55.0      |         |      | 57.9      |         |      | 63.8      |

A review of medical care services rendered from December 1966 to November 1967 disclosed that 43 children (2.5 per cent of the population) in the 1967–1968 study population were treated for high-risk conditions. The identification of high-risk children in the 1972–1973 population was based on review of medical care contacts during the preceding six December–November periods. One hundred seventy-nine (179) children (6.4 per cent) were identified as having a high-risk condition. This procedure of ascertaining high-risk status for a given study period by reviewing medical care experience during one or more December–November periods resulted in prevalence rates that increased over the study periods.

As seen from the cumulative data for 1972–1973, 42.5 per cent of the 1979 high-risk children received a diagnosis of asthma sometime during the six-year period. The second most common high-risk condition was congenital anomaly (28.5 per cent). High-risk children had an average of 1.12 high-risk conditions per child.

Table 2 displays the number of person-periods in the Health Plan aggregated over epidemic (1968–1969, 1972–1973) and non-epidemic periods (1967–1968, 1969–1970, 1970–1971, 1971–1972) by age, sex, and high-risk status. There were 97,400 and 182,340 person-periods of experience during aggregated epidemic and non-epidemic periods, respectively. Individual children generally contributed to both the epidemic and non-epidemic counts of person-periods.

The 1972–1973 age/sex specific cumulative prevalence rates of treated high-risk conditions were used to estimate the total number of person-periods of experience for high-risk children in the Health Plan. The cumulative prevalence rate was greater in males than in females (7.2 per cent versus

5.5 per cent). The sex difference was greater for 0–4 year olds, 7.4 per cent for males versus 3.7 per cent for females.

Table 3 indicates that the rate of influenza-related hospitalizations for the entire population was significantly higher during the combined epidemic periods than during the combined non-epidemic periods. The rate of influenza-related hospitalizations was eight and 12 times higher for 0–4 year than for 5–14 year olds, during epidemic and non-epidemic periods. The overall excess hospitalization rate was seven per 10,000 population. A statistically significant excess of 29 influenza-related hospitalizations per 10,000 occurred in the high-risk population during the epidemic periods compared with non-epidemic periods; a small but statistically significant excess of five hospitalizations per 10,000 occurred in the non-high-risk population. Although the excess for 0–4 year old high-risk children (47 per 10,000) was higher than that of 5–14 year old high-risk children (21 per 10,000), only the latter excess was statistically significant. The discharge rates were high for 0–4 year old high-risk children during epidemic and non-epidemic periods (190 and 143 per 10,000 respectively). The corresponding rates for 5–14 year old high-risk children were 32 and 11 per 10,000, respectively. The sample size was inadequate for analysis of the impact of influenza A epidemics among children in their first year of life.

The male influenza-related discharge rates were higher than the female rates in both high-risk and non-high-risk categories. The excesses for 5–14 year old males, 25 and five per 10,000 for high-risk and non-high-risk categories respectively, reached statistical significance. The small excesses experienced by 5–14 year old females were not statistically significant.

**TABLE 2—Distribution of Pediatric Population by Age, Sex, and High-Risk Status for Epidemic and Non-Epidemic Periods, Kaiser-Permanente Medical Care Program, Oregon**

| Age        | Sex Risk Status | 1972-73 Percent Cumulative Prevalence | Combined Epidemic Periods | Combined Non-Epidemic Periods |
|------------|-----------------|---------------------------------------|---------------------------|-------------------------------|
| 0-4        | Male            | 7.4                                   | 1190                      | 2210                          |
|            | with HR         |                                       |                           |                               |
|            | without HR      |                                       |                           |                               |
|            | Total           | 14890                                 | 27650                     |                               |
|            | Female          | 3.7                                   | 569                       | 1030                          |
|            | with HR         |                                       |                           |                               |
|            | without HR      |                                       |                           |                               |
|            | Total           | 14811                                 | 26810                     |                               |
|            | Both            | 5.7                                   | 1793                      | 3289                          |
| with HR    |                 |                                       |                           |                               |
| without HR |                 |                                       |                           |                               |
| Total      | 29667           | 54411                                 |                           |                               |
| 5-14       | Male            | 7.1                                   | 2323                      | 4402                          |
|            | with HR         |                                       |                           |                               |
|            | without HR      |                                       |                           |                               |
|            | Total           | 30397                                 | 57598                     |                               |
|            | Female          | 6.3                                   | 2093                      | 3946                          |
|            | with HR         |                                       |                           |                               |
|            | without HR      |                                       |                           |                               |
|            | Total           | 31127                                 | 58694                     |                               |
|            | Both            | 6.7                                   | 4418                      | 8351                          |
| with HR    |                 |                                       |                           |                               |
| without HR |                 |                                       |                           |                               |
| Total      | 61522           | 116289                                |                           |                               |
| All Ages   | Male            | 7.2                                   | 3513                      | 6614                          |
|            | with HR         |                                       |                           |                               |
|            | without HR      |                                       |                           |                               |
|            | Total           | 45287                                 | 85246                     |                               |
|            | Female          | 5.5                                   | 2673                      | 4976                          |
|            | with HR         |                                       |                           |                               |
|            | without HR      |                                       |                           |                               |
|            | Total           | 45927                                 | 85504                     |                               |
|            | Both            | 6.4                                   | 6234                      | 11670                         |
| with HR    |                 |                                       |                           |                               |
| without HR |                 |                                       |                           |                               |
| Total      | 91166           | 170670                                |                           |                               |
|            |                 |                                       | 97400                     | 182340                        |

Three of the children with influenza-related discharges died during the hospitalization. Two of the fatalities occurred during non-epidemic periods and one during an epidemic period. The fatalities included an infant with bronchopneumonia and multiple congenital anomalies, a one-year old with viral encephalitis, and a two-year old with acute bronchitis and bronchiolitis. The overall case fatality rate was 5.2 per 1,000 influenza-related hospitalizations.

Table 4 presents discharge rates for specific influenza-related morbidities. The categories were defined in a hierarchical manner and are mutually exclusive, i.e., if bronchitis-pneumonia and laryngitis-tracheitis were both listed as discharge diagnoses, the hospitalization was included only in the former category. There were generally positive excesses during the epidemic periods among the various diagnostic categories; bronchitis-pneumonia accounted for most of the excess.

Table 5 examines the impact of epidemic influenza on the rate of ambulatory medical care utilization for ARD

among high-risk and non-high-risk children. In both epidemic and non-epidemic periods the rates for 0-4 year olds were three to four times the rates for 5-14 year olds. Overall there were 2.6 more contacts per 100 person-periods during epidemic periods with excesses of 6.9 per 100 for high-risk children and 2.2 per 100 for non-high-risk children. None of the differences shown in Table 5 achieved statistical significance when compared with their standard errors (SE).

### Discussion

The pediatric population, especially 5-14 year old males, experienced excess influenza-related hospitalizations, primarily for bronchitis and pneumonia, during epidemic periods compared with non-epidemic periods. The higher influenza-related hospitalization rate in boys than in girls is consistent with the sex differences reported for respiratory illness incidence.<sup>11</sup> High-risk children had a statistically significant excess of 29 influenza-related hospi-

**TABLE 3—Pediatric Discharge Rates with Influenza-Related Diagnoses by Age, Sex, and High-Risk Status for Epidemic and Non-Epidemic Periods, Kaiser-Permanente Medical Care Program, Oregon**

| Age        | Sex/Risk Status | Combined Epidemic Periods |     | Combined Non-Epidemic Periods |     | Excess Rate/10,000 | SE    | Per Cent Difference |
|------------|-----------------|---------------------------|-----|-------------------------------|-----|--------------------|-------|---------------------|
|            |                 | Rate/10,000               | SE  | Rate/10,000                   | SE  |                    |       |                     |
| 0-4        | Male            |                           |     |                               |     |                    |       |                     |
|            | with HR         | 193                       | 40  | 149                           | 26  | 44                 | 48    | 29.5                |
|            | without HR      | 66                        | 7   | 54                            | 4   | 12                 | 8     | 22.2                |
|            | Total           | 75                        | 7   | 61                            | 5   | 14                 | 9     | 23.0                |
|            | Female          |                           |     |                               |     |                    |       |                     |
|            | with HR         | 193                       | 58  | 136                           | 36  | 57                 | 68    | 41.9                |
|            | without HR      | 40                        | 5   | 32                            | 3   | 8                  | 6     | 25.0                |
|            | Total           | 46                        | 5   | 36                            | 4   | 10†                | 6     | 27.8                |
|            | Both            |                           |     |                               |     |                    |       |                     |
| with HR    | 190             | 32                        | 143 | 21                            | 47  | 38                 | 32.9  |                     |
| without HR | 53              | 4                         | 43  | 3                             | 10* | 5                  | 23.3  |                     |
| Total      | 61              | 4                         | 49  | 3                             | 12* | 5                  | 24.5  |                     |
| 5-14       | Male            |                           |     |                               |     |                    |       |                     |
|            | with HR         | 34                        | 12  | 9                             | 5   | 25†                | 13    | 277.8               |
|            | without HR      | 9                         | 2   | 5                             | 1   | 5*                 | 2     | 104.4               |
|            | Total           | 11                        | 2   | 5                             | 1   | 6**                | 2     | 129.2               |
|            | Female          |                           |     |                               |     |                    |       |                     |
|            | with HR         | 29                        | 12  | 13                            | 6   | 16                 | 13    | 123.1               |
|            | without HR      | 3                         | 1   | 3                             | 1   | 0                  | 1     | 10.3                |
|            | Total           | 5                         | 1   | 4                             | 1   | 1                  | 1     | 37.1                |
|            | Both            |                           |     |                               |     |                    |       |                     |
| with HR    | 32              | 8                         | 11  | 4                             | 21* | 9                  | 190.9 |                     |
| without HR | 6               | 1                         | 4   | 1                             | 2*  | 1                  | 50.0  |                     |
| Total      | 8               | 1                         | 4   | 1                             | 4** | 1                  | 100.0 |                     |
| All Ages   | Male            |                           |     |                               |     |                    |       |                     |
|            | with HR         | 88                        | 16  | 56                            | 9   | 32†                | 18    | 57.1                |
|            | without HR      | 28                        | 2   | 21                            | 2   | 7*                 | 3     | 33.3                |
|            | Total           | 32                        | 3   | 23                            | 2   | 9*                 | 4     | 39.1                |
|            | Female          |                           |     |                               |     |                    |       |                     |
|            | with HR         | 64                        | 15  | 38                            | 9   | 26                 | 17    | 68.4                |
|            | without HR      | 15                        | 2   | 12                            | 1   | 3                  | 2     | 25.0                |
|            | Total           | 17                        | 2   | 13                            | 1   | 4*                 | 2     | 30.8                |
|            | Both            |                           |     |                               |     |                    |       |                     |
| with HR    | 77              | 11                        | 48  | 6                             | 29* | 12                 | 60.4  |                     |
| without HR | 21              | 2                         | 16  | 1                             | 5*  | 2                  | 31.3  |                     |
| Total      | 25              | 2                         | 18  | 1                             | 7** | 2                  | 38.9  |                     |

†:p &lt; .10

\*:p &lt; .05

\*\*:p &lt; .01

talizations per 10,000, compared to an excess rate of five for non-high-risk children. This suggests a substantial potential benefit may result from prophylactic immunization of high-risk children.

Children aged 0-4 had higher hospitalization rates than 5-14 year olds during both epidemic and non-epidemic periods; and, although their absolute excess rate was higher than that of 5-14 year olds, the relative excess among 0-4 year olds was smaller. This observation is compatible with several reports which have noted that the characteristically high incidence of pneumonia among children under five years of age (both during influenza epidemics and other times) is primarily caused by non-influenza respiratory viruses such as respiratory syncytial virus.<sup>4,12,13</sup>

An impact of epidemic influenza on the rate of ambulatory medical care for acute respiratory illness was suggested

by the overall excess rate of 2.6 contacts per 100 children. However, the overall excess was not statistically significant and there was not a consistent trend among age, sex, and high-risk groups.

The lack of clear-cut evidence of excess ambulatory care during influenza epidemics contrasts with the observed significant increase in hospitalizations. This may be explained by the fact that the characteristically high rate of ambulatory medical services for ARD among children in winter due to various respiratory viruses (e.g., type B influenza, RSV) masks the relatively small incremental effect of an influenza A epidemic. However, influenza A infections being of greater severity than those due to other respiratory viruses may have a greater likelihood of leading to hospitalization.

To put the impact of influenza among the pediatric

**TABLE 4—Number, Rate, and Excess Rate of Pediatric Hospitalization for Influenza-Related Diagnosis by Age and Sex, for Epidemic and Non-Epidemic Periods, Kaiser-Permanente Medical Care Program, Oregon**

|                                       | 0-4 years   |         |          | 5-14 years |         |         | All Ages 0-14 years |          |          |
|---------------------------------------|-------------|---------|----------|------------|---------|---------|---------------------|----------|----------|
|                                       | Male        | Female  | Total    | Male       | Female  | Total   | Male                | Female   | Total    |
| <b>Total Flu-Related Discharges</b>   |             |         |          |            |         |         |                     |          |          |
| Epi Periods                           | 75* (121)** | 46 (70) | 61 (191) | 11 (36)    | 5 (16)  | 8 (52)  | 32 (157)            | 17 (86)  | 25 (243) |
| Non-Epi Periods                       | 61 (183)    | 36 (99) | 49 (282) | 5 (30)     | 4 (22)  | 4 (52)  | 23 (213)            | 13 (121) | 18 (334) |
| Excess Rate                           | 14          | 10      | 12       | 6          | 1       | 4       | 9                   | 4        | 7        |
| <b>Bronchitis-Pneumonia</b>           |             |         |          |            |         |         |                     |          |          |
| Epi Periods                           | 40 (64)     | 25 (39) | 32 (107) | 7 (22)     | 2 (6)   | 4 (28)  | 18 (86)             | 9 (45)   | 13 (131) |
| Non-Epi Periods                       | 32 (97)     | 18 (49) | 25 (146) | 2 (14)     | 2 (14)  | 2 (28)  | 12 (111)            | 7 (63)   | 10 (174) |
| Excess Rate                           | 8           | 7       | 7        | 5          | 0       | 2       | 6                   | 2        | 3        |
| <b>Laryngitis-Tracheitis</b>          |             |         |          |            |         |         |                     |          |          |
| Epi Periods                           | 18 (29)     | 9 (14)  | 14 (43)  | 3 (9)      | 0 (0)   | 1 (9)   | 8 (38)              | 3 (14)   | 5 (52)   |
| Non-Epi Periods                       | 13 (40)     | 6 (16)  | 10 (56)  | 1 (9)      | 0.5 (3) | 1 (12)  | 5 (49)              | 2 (19)   | 4 (68)   |
| Excess Rate                           | 5           | 3       | 3        | 2          | -0.5    | 0       | 3                   | 1        | 1        |
| <b>Uri-Influenza</b>                  |             |         |          |            |         |         |                     |          |          |
| Epi Periods                           | 9 (15)      | 3 (5)   | 6 (20)   | 0.6 (2)    | 2 (5)   | 1 (7)   | 3 (17)              | 2 (10)   | 3 (27)   |
| Non-Epi Periods                       | 6 (19)      | 5 (15)  | 6 (34)   | 0.6 (4)    | 0       | 0.3 (4) | 3 (23)              | 2 (15)   | 2 (38)   |
| Excess Rate                           | 3           | -2      | 0        | 0          | 2       | 0.7     | 0                   | 0        | 1        |
| <b>Asthma</b>                         |             |         |          |            |         |         |                     |          |          |
| Epi Periods                           | 6 (9)       | 1 (2)   | 3 (11)   | 0.3 (1)    | 1 (4)   | 0.8 (5) | 2 (10)              | 1 (6)    | 2 (16)   |
| Non-Epi Periods                       | 4 (13)      | 3 (7)   | 3 (20)   | 0 (0)      | 0 (0)   | 0 (0)   | 1 (13)              | 1 (7)    | 1 (20)   |
| Excess Rate                           | 2           | -2      | 0        | 0.3        | 1       | 0.8     | 1                   | 1        | 1        |
| <b>Other Flu-Related Diagnoses***</b> |             |         |          |            |         |         |                     |          |          |
| Epi Periods                           | 2 (4)       | 7 (10)  | 4 (14)   | 0.6 (2)    | 0.3 (1) | 0.5 (3) | 1 (6)               | 2 (11)   | 2 (17)   |
| Non-Epi Periods                       | 5 (14)      | 4 (12)  | 5 (26)   | 0.5 (3)    | 0.8 (5) | 0.6 (8) | 2 (17)              | 2 (17)   | 2 (34)   |
| Excess Rate                           | -3          | 3       | -1       | 0.1        | -0.5    | -0.1    | -1                  | 0        | 0        |

\*Hospitalizations/10<sup>4</sup>

\*\*Number of Hospitalizations in parenthesis

\*\*\*Other diagnoses: see appendix

population in perspective, we compare excess influenza-related hospitalization rates among various age groups in Table 6. The estimates for the population over 14 years of age are derived from the previous report of the impact of influenza in the adult population of the Health Plan.<sup>2</sup> The

excess of 7.0 hospitalizations per 10,000 experienced by 0-14 year olds was three to five times larger than the excess rates of 2.6 and 1.5 observed among 15-44 and 45-64 year olds, respectively, but only a fifth of the 33.0 per 10,000 excess among the age 65+ population. The greatest impact

**TABLE 5—Number and Rate of Pediatric Medical Care Contacts for Acute Respiratory Disease by Age and High-Risk Status for Epidemic and Non-Epidemic Periods, Kaiser-Permanente Medical Care Program, Oregon**

| Age and Risk Status | Combined Epidemic Periods |          |      | Combined Non-Epidemic Periods |          |      | Excess Rate/100 | SE   |
|---------------------|---------------------------|----------|------|-------------------------------|----------|------|-----------------|------|
|                     | N                         | Rate/100 | SE   | N                             | Rate/100 | SE   |                 |      |
| <b>0-4 years</b>    |                           |          |      |                               |          |      |                 |      |
| with HR             | 119                       | 160.8    | 28.7 | 171                           | 127.6    | 15.9 | 33.2            | 32.8 |
| without HR          | 1245                      | 83.1     | 39.1 | 2318                          | 84.3     | 3.2  | -1.2            | 39.2 |
| TOTAL               | 1364                      | 86.7     | 4.0  | 2489                          | 86.3     | 3.1  | 0.4             | 5.1  |
| <b>5-14 years</b>   |                           |          |      |                               |          |      |                 |      |
| with HR             | 141                       | 79.2     | 14.8 | 246                           | 82.3     | 14.2 | 3.1             | 20.5 |
| without HR          | 799                       | 25.6     | 1.4  | 1339                          | 22.6     | 1.0  | 3.0             | 1.7  |
| TOTAL               | 940                       | 28.5     | 1.6  | 1585                          | 25.4     | 1.2  | 3.1             | 2.0  |
| <b>0-14 years</b>   |                           |          |      |                               |          |      |                 |      |
| with HR             | 260                       | 103.2    | 13.6 | 417                           | 96.3     | 11.0 | 6.9             | 17.5 |
| without HR          | 2044                      | 44.3     | 1.6  | 3657                          | 42.1     | 1.3  | 2.2             | 2.1  |
| TOTAL               | 2304                      | 47.3     | 1.7  | 4074                          | 44.7     | 1.3  | 2.6             | 2.1  |

**TABLE 6—Excess Influenza-Related Hospitalizations per 10<sup>4</sup> during Influenza A Epidemic, by Age and High-Risk Status, Kaiser-Permanente Medical Care Program, Oregon**

| Age/Risk Status | Epidemic Periods | Non-Epidemic Periods | Excess |
|-----------------|------------------|----------------------|--------|
| 0–14 years      |                  |                      |        |
| with HR         | 77.0             | 48.0                 | 29.0   |
| without HR      | 21.0             | 16.0                 | 5.0    |
| TOTAL           | 25.0             | 18.0                 | 7.0    |
| 15–44 years     |                  |                      |        |
| with HR         | 16.2             | 7.5                  | 8.7    |
| without HR      | 3.0              | 0.6                  | 2.4    |
| TOTAL           | 3.6              | 1.0                  | 2.6    |
| 45–64 years     |                  |                      |        |
| with HR         | 65.3             | 16.6                 | 48.7   |
| without HR      | 7.7              | 5.9                  | 1.8    |
| TOTAL           | 9.1              | 7.6                  | 1.5    |
| 65+ years       |                  |                      |        |
| with HR         | 84.3             | 26.0                 | 58.3   |
| without HR      | 23.0             | 6.9                  | 16.1   |
| TOTAL           | 48.3             | 15.3                 | 33.0   |

of high-risk conditions occurred among 45–64 year olds, the ratio of high-risk and non-high-risk excess rates being 27, whereas it was four to six for the other age groups.

The results of this study contribute to the information base required for cost/benefit analysis of influenza immunization of children.

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**APPENDIX A  
HIGH RISK CONDITIONS**

| Condition                                     | ICDA 7th Revision          | ICDA 8th Revision       |
|---|----------------------------|-------------------------|
| <b>Cardiovascular</b>                         |                            |                         |
| Rheumatic Heart Disease                       | 410-416                    | 391-398                 |
| Ischemic Heart Disease                        | 420, 422.1, 435.0          | 410-414                 |
| Other Heart Diseases                          | 421, 422.0, 422.9, 430-434 | 420-429                 |
| Hypertension with Heart or Renal Complication | 442-446, 447.6             | 400, 402, 403           |
| Hypertension without Complication (essential) | 447 excluding 447.6        | 401                     |
| Cerebrovascular Disease                       | 330-334                    | 430-438                 |
| <b>Asthma</b>                                 | 241                        | 493                     |
| <b>Bronchitis (chronic) and Emphysema</b>     | 501, 502, 527.1            | 490-492                 |
| <b>Other Chronic Respiratory Disease</b>      | 518-526                    | 510-519                 |
| <b>Renal</b>                                  |                            |                         |
| Nephritis and Nephrosis                       | 590-594                    | 580-584                 |
| Other Chronic Kidney Disease                  | 600, 603                   | 590, 591                |
| <b>Metabolic and Nutritional</b>              |                            |                         |
| Diabetes without Complications                | 260.0                      | 250.9                   |
| Diabetes with Complications                   | 260.1-260.9                | 250.0                   |
| <b>Neurological</b>                           |                            |                         |
| Epilepsy                                      | 353                        | 345                     |
| (Other) Dis. Cent. Nerv. Syst.                | 350-357 (except 354)       | 330-333, 340-344, 347.9 |
| <b>Malignant Diseases</b>                     |                            |                         |
| Lymphatic and Hematopoietic                   | 200-205                    | 200-209                 |
| All Others                                    | 140-199                    | 140-199                 |
| <b>Congenital Anomalies</b>                   |                            |                         |
| C.N.S.  | 750-753                    | 740-743                 |
| Circulatory System                            | 754.0-754.9                | 746, 747                |
| G.I. System                                   | 756.0-756.9                | 750, 751                |
| G.U. System                                   | 757.0, 757.9               | 753                     |
| Resp. System (Cystic Lung)                    | 759.0-759.2                | 748                     |
| Multi-System (Down's, etc.)                   | 308.2                      | 759.0-759.9             |
| <b>Cystic Fibrosis</b>                        | 587.2                      | 273.0                   |

**APPENDIX B  
ACUTE RESPIRATORY DISEASE (ARD)**

| Condition   | ICDA 7 Codes   |
|---|--|
| Respiratory Tract Symptoms: nasal discharge, nasal congestion, sore throat, cough, chest pain, dyspnea            | T-284, T-290, T-311, T-410, T-401, T-417               |
| General Flu Symptoms: generalized pain, fever, chilliness, chill, malaise, headache, myalgia, multiple joint pain | T-001, T-010, T-015, T-016, T-066, T-151, T-701, T-891 |
| Upper Respiratory Illness   | 470-473, 475   |
| Laryngitis, Tracheitis  | 474  |
| Bronchitis  | 500-501  |
| Influenza, Unspecific Respiratory   | 481  |
| Influenza Pneumonia   | 480  |
| Pneumonia   | 490-493  |
| Asthma  | 241  |
| Acute Otitis Media  | 391.0, 391.1, 391.9                                    |



**APPENDIX C  
FLU-RELATED MORBIDITIES\***

| Condition   | ICDA 8th Revision | ICDA 7th Revision |
|---|-------------------|-------------------|
| Influenza   | 470-472           | 480-481           |
| Pneumonia   | 480-486           | 490-493, 763      |
| Acute Laryngitis, Tracheitis                        | 464               | 474               |
| Acute Bronchitis                                    | 466               | 500, 501          |
| Asthma  | 493               | 241               |
| Acute Upper Respiratory Infection                   | 460-463, 465      | 470-473, 475      |
| Acute Heart Disease                                 |                   |                   |
| Congestive Heart Failure & Left Ventricular Failure | 427.0, 427.1      | 434.1, 434.2      |
| Other Symptomatic Heart Disease                     | 427.2-427.9       | 433               |
| Acute Pericarditis and Myocarditis                  | 420, 422, 428     | 431, 432, 434.3   |
| Acute C.N.S.  |                   |                   |
| Viral Encephalitis, unspecified                     | 065               | 082.9             |
| Flu with Neurologic Signs                           | 474               | 483               |
| Infectious Myositis                                 | 732               | 743               |
| Fever of Unknown Origin                             | 788.6             | 788.8             |

\*This list was derived on the basis of a literature review and discussion with Dr. Caroline B. Hall, associate professor and consultant in infectious disease, Department of Pediatrics, University of Rochester Medical Center.

**APPENDIX D  
STANDARD NORMAL Z STATISTIC FORMULA**

The standard errors for the rates shown in Table 3 were estimated assuming the number of hospitalizations is a Poisson variate. When aggregating high-risk and non-high-risk children the population size is known to be  $20n$ , where  $n$  is the size of the 5% sample. In this case the estimated standard error of the rate is given by

$SE = \sqrt{\text{rate}/20n}$ . When computing rates separately for high-risk and non-high-risk children the denominator is unknown and must be estimated from the 5% sample. Letting  $n_1$  denote the number of high-risk children in the 5% sample, it may be shown that the standard error of the rate is approximated by

$$SE \approx \sqrt{\text{rate}/20n_1} \sqrt{1 + \frac{3(n-n_1)}{nn_1}}$$

The significance of observed excess rates was tested using the approximate standard normal statistic

$$Z = \frac{\text{rate}_1 - \text{rate}_2}{\sqrt{SE_1^2 + SE_2^2}}$$

where the subscripts 1 and 2 denote epidemic and nonepidemic periods, respectively.

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