The Impact of Influenza Epidemics on Hospitalizations

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The traditional method for assessing the severity of influenza seasons is to estimate the associated increase (i.e., excess) in pneumonia and influenza (P&I) mortality. In this study, excess P&I hospitalizations were estimated from National Hospital Discharge Survey Data from 26 influenza seasons (1970–1995). The average seasonal rate of excess P&I hospitalization was 49 (range, 8–102)/100,000 persons, but average rates were twice as high during A(H3N2) influenza seasons as during A(H1N1)/B seasons. Persons aged <65 years had 57% of all influenza-related hospitalizations; however, the average seasonal risk for influenza-related P&I hospitalizations was much higher in the elderly than in persons aged <65 years. The 26 pairs of excess P&I hospitalization and mortality rates were linearly correlated. During the A(H3N2) influenza seasons after the 1968 pandemic, excess P&I hospitalizations declined among persons aged <65 years but not among the elderly. This suggests that influenza-related hospitalizations will increase disproportionately among younger persons in future pandemics.

Influenza epidemics occur seasonally in temperate climates and result in substantial morbidity and mortality. Since William Farr's [1] studies of influenza-related mortality in London (1847–1848), various statistical models have been used to assess the severity of such epidemics. In particular, models have been used to estimate "excess" numbers of pneumonia and influenza (P&I) deaths (i.e., above an expected baseline of P&I deaths in the absence of influenza) during periods when influenza viruses are in circulation [2–8].

However, mortality is a relatively rare outcome of influenza infection and represents only a fraction of influenza's total health burden in a population [2, 9, 10]. In addition, although influenza A(H3N2) epidemics usually result in increased excess hospitalizations and deaths, some influenza A(H1N1) and influenza B epidemics result only in increased hospitalizations and not increased mortality [9]. Because of these considerations, some investigators have suggested that measurements of excess P&I mortality alone may inadequately reflect the severity of an influenza season [11].

Our primary objective was to determine national estimates of excess P&I hospitalizations and the relationship between such hospitalizations and excess P&I deaths during influenza seasons characterized by all currently circulating influenza virus types and subtypes. A second objective was to determine whether excess P&I hospitalizations among persons aged <65 years declined over time in the influenza A(H3N2) seasons after the 1968 influenza A(H3N2) pandemic. We previously observed a pattern of declining excess P&I deaths among this age group, but not in elderly persons, following each of the 20th century's 3 pandemics [12].

Methods

Definition of P&I hospitalizations and deaths. A P&I hospitalization was defined as a hospitalization for which an International Classification of Diseases (ICD) code for pneumonia or influenza (ICD-8 codes 474 or 480–486 for 1970–1978 and ICD-9 codes 480–487 for 1979–1995) was listed as the first diagnosis on the discharge record. These codes include bacterial and viral pneumonia of known and unknown etiology [13, 14]. A P&I death was defined as one in which an ICD code for pneumonia or influenza was coded as the underlying cause of death.

Definition of influenza seasons. Because influenza seasons usually include winter months, they typically bridge consecutive calendar years (e.g., 1970–1971). We used national influenza virus surveillance data from the Centers for Disease Control and Prevention (CDC) to define an influenza season. The average weekly number of influenza virus identifications was calculated for each October during 1969–1995. An influenza season was defined as the months in which the number of virus identifications for ⩾1 week was more than twice the weekly average number of virus identifications for the preceding October. The remaining months were considered outside the influenza season.

Each influenza season was further defined on the basis of the predominant circulating viruses. An influenza A(H3N2) season was defined as a season in which A(H3N2) viruses comprised ⩾75% of that season's total influenza isolates. An influenza A(H1N1)/influenza B season was defined as a season in which one or both of these viruses together comprised ⩾75% of the season's influenza isolates. A mixed season was defined as one in which neither influenza A(H3N2) virus nor the combined number of influenza

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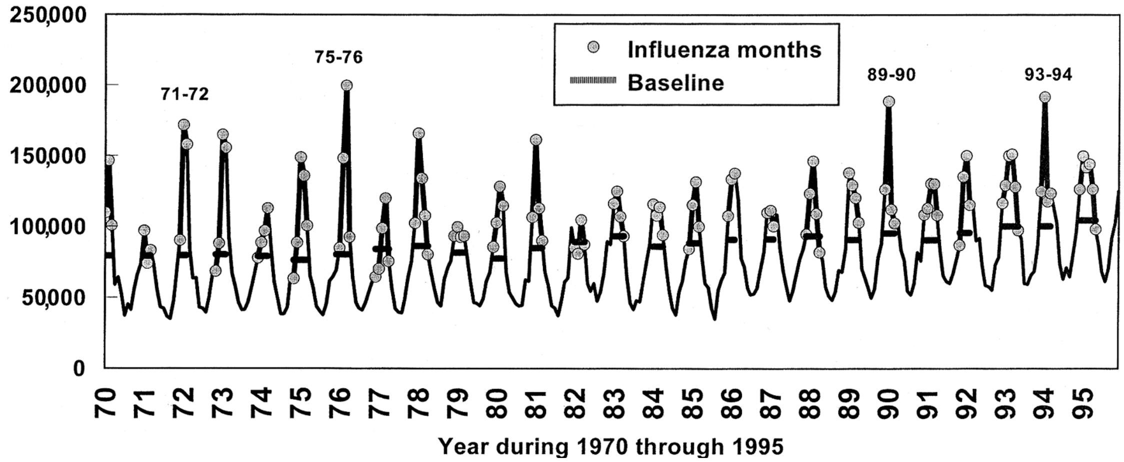

Figure 1. US pneumonia and influenza monthly hospitalizations, all ages, 1970–1995. Laboratory-confirmed influenza periods and baseline levels are indicated for each season.

A(H1N1) and influenza B viruses accounted for ⩾75% of the season's isolates.

Data source for P&I hospitalizations. National Hospitalization Discharge Survey (NHDS) data were obtained for 1970–1995 from the National Center for Health Statistics (NCHS) [15]. Although NHDS data were not available before 1970, we were able to analyze 26 consecutive influenza seasons including the 1969–1970 influenza season, because the first month of that season was January 1970.

NHDS data are collected from ∼200,000 hospital discharge records, representing a sample of ∼1% of all US hospitalizations [15]. The hospital discharge records are collected by a stratified multistage probability sampling design in which each record is assigned a weight. The national total of hospitalizations can be estimated from the sum of the weights. Each NHDS record contains up to 7 ICD-coded discharge diagnoses, usually listed in the order of their appearance on the original hospital discharge record. We extracted all hospital discharge records fitting our definition of a P&I hospitalization and retained the weight variable, the patient's age, and a hospital admission date (month and year). For each of the 26 years studied, national monthly numbers of P&I hospitalizations were calculated for all ages and for 2 age groups (<65 and ⩾65 years).

Validation of NHDS data for estimating monthly hospitalizations. In 1987, a sizable fraction of NHDS hospitals began providing discharge records for only a subset of months each year [15]. Since this potentially introduced a bias for the analysis of seasonal data, we validated the use of monthly NHDS data for estimating excess P&I hospitalizations during influenza seasons. A special NHDS data set was provided by the NCHS for 1988–1993 that included a variable (not found in the publicly available database) identifying "partially" participating hospitals (i.e., those submitting records for some months) and "fully" participating hospitals (i.e., those submitting records for all months). We determined that the monthly P&I hospitalization records submitted by the partially participating hospitals accounted for 10%–25% of the yearly total P&I records from NHDS for those 6 years (corresponding to 9%–22% of US yearly total P&I hospitalizations). The monthly data from the partially participating hospitals exhibited a seasonal pattern of P&I hospitalizations, similar to the public data set, including peaks during the same months within the influenza seasons. We concluded that the potential bias was minimal and that the NHDS public use data were suitable for analysis of monthly P&I hospitalization data.

Estimation of excess P&I hospitalizations. A method recently developed for analyzing monthly P&I mortality data was used to estimate excess P&I hospitalizations during each influenza season [12]. In brief, a baseline was constructed of the number of expected P&I hospitalizations in winter months in which influenza was absent. First, a 3-month moving average of P&I hospitalizations was calculated for 24 Novembers between January 1970 and December 1995 that were not considered part of any influenza season. We then raised this November baseline to best fit the level of P&I hospitalizations in the month of December during 6 seasons in which the influenza period started in January or later. This was achieved by iteratively adding a constant to the November baseline level until the squared distance between the increased November baseline and the December estimates was minimized. The sum of P&I hospitalizations above the December baseline during an influenza season was considered excess hospitalizations attributable to influenza.

Seasonal numbers and rates of excess P&I hospitalizations were calculated for the total population and for the age groups <65 and ⩾65 years by use of US census data (e.g., the 1970 census for the 1970–1971 season). We also conducted a sensitivity analysis: when the baseline levels of expected P&I hospitalizations were varied upward or downward by 30%, there was a 14% decrease and increase, respectively, in the estimated numbers of excess P&I hospitalizations.

Comparison of excess P&I hospitalizations and deaths during influenza seasons. US multiple-cause-of-death data tapes were obtained from the NCHS for 1970–1995 [16]. The same methods for calculating excess P&I hospitalizations were used to estimate excess P&I deaths for the 26 influenza seasons during 1970–1995. We used the restricted least squares method to compare seasonal estimates of excess P&I hospitalizations rates and excess P&I death rates [17]. Separate comparisons were made for persons aged <65 and

Table 1. Pneumonia and influenza (P&I) excess hospitalizations for United States influenza epidemics, 1970–1995.

Season	Season type on basis of influenza virus surveillance[a]	Epidemic period[b]	Severity index[c] category	Excess P&I hospitalizations[d]		
				All ages	⩾65 years	<65 years
1969–1970	A(H3N2)	January–March	4	119 (58)	34 (170)	85 (47)
1970–1971	Mixed	January–March	1	16 (8)	0	28 (15)
1971–1972	A(H3N2)	December–February	5	182 (88)	60 (292)	122 (66)
1972–1973	A(H3N2)	November–February	4	159 (76)	33 (159)	125 (66)
1973–1974	B	December–March	1	56 (26)	13 (58)	43 (22)
1974–1975	A(H3N2)	November–March	4	143 (67)	61 (278)	81 (42)
1975–1976	A(H3N2)	January–April	6	220 (102)	68 (299)	152 (79)
1976–1977	Mixed	December–April	1	28 (13)	1 (6)	26 (14)
1977–1978	Mixed	December–April	5	171 (78)	54 (227)	116 (59)
1978–1979	A(H1N1)	December–March	1	35 (16)	0	53 (27)
1979–1980	B	December–March	3	105 (47)	34 (136)	71 (35)
1980–1981	A(H3N2)	December–March	6	161 (71)	59 (229)	102 (51)
1981–1982	B and A(H1N1)	January–April	2	19 (8)	6 (23)	13 (6)
1982–1983	A(H3N2)	January–April	3	85 (37)	25 (94)	59 (29)
1983–1984	B and A(H1N1)	January–April	2	58 (25)	38 (140)	20 (10)
1984-1985	A(H3N2)	December–March	5	88 (37)	49 (175)	38 (18)
1985–1986	B	December–February	4	114 (48)	60 (210)	54 (26)
1986–1987	A(H1N1)	December–February	1	49 (20)	17 (58)	32 (15)
1987–1988	A(H3N2)	December–April	4	100 (41)	58 (194)	42 (20)
1988–1989	A(H1N1) and B	January–April	3	118 (48)	72 (240)	45 (21)
1989–1990	A(H3N2)	December–March	6	167 (68)	107 (348)	60 (28)
1990–1991	B	December–April	3	114 (46)	81 (262)	32 (15)
1991–1992	A(H3N2)	November–February	4	126 (50)	68 (214)	58 (26)
1992–1993	Mixed	December–May	4	200 (78)	133 (411)	66 (30)
1993–1994	A(H3N2)	December–March	5	157 (61)	93 (283)	63 (28)
1994–1995	Mixed	December–May	3	187 (73)	52 (154)	123 (53)

[a] Based on prevalence of circulating viruses (see Methods section).
[b] Epidemic period was based on Centers for Disease Control and Prevention laboratory surveillance data for virus activity.
[c] Influenza epidemic severity index category ranks severity of individual seasons in a linear index based on excess P&I deaths, ranging from category 1 (mild) to 6 (severe) [8].
[d] In thousands (rate per 100,000 population). Estimates for each age group were based on separate analyses of monthly P&I hospitalization data. Negative values were replaced with zero.

⩾65 years and for influenza A(H3N2), influenza A(H1N1)/influenza B, and mixed influenza seasons.

Results

Seasonality and trends in P&I hospitalizations. The average influenza season in this study was 4 months (range, 3–6 months; table 1). P&I hospitalizations exhibited a seasonal pattern (similar to P&I deaths), with peaks during winter months and troughs during summer months (figure 1). The largest absolute monthly numbers of P&I hospitalizations occurred during the 1975–1976 and 1989–1990 influenza seasons (figure 1), which are considered 2 of the most severe influenza seasons since the 1968 A(H3N2) pandemic on the basis of excess P&I mortality estimates [8].

We also observed a significant increase in the monthly numbers of P&I hospitalizations during periods outside the influenza seasons over the study period (figure 1). This upward secular trend was due to an almost 2-fold increase in the incidence rate of P&I hospitalizations outside influenza seasons among persons aged ⩾65 years during the study period. By contrast, P&I hospitalizations among persons aged <65 years outside the influenza seasons declined by 12% during the study period (data not shown).

Excess P&I hospitalizations by virus (sub)type. The average number of excess P&I hospitalizations per influenza season was 114,000 (range, 16,000–220,000), corresponding to an average incidence rate of 49 excess P&I hospitalizations per 100,000 persons (range, 8–102; table 1). These figures varied substantially by season depending on the predominating influenza virus(es).

During the 12 influenza A(H3N2) seasons, the average number of excess P&I hospitalizations per season was 142,000 (incidence rate of 63 excess P&I hospitalizations per 100,000 population). Among these A(H3N2) seasons, the lowest excess P&I hospitalization incidence rate (all are per 100,000 population) was 37 in 1982–1983 and 1984–1985, and the highest (102) was in 1975–1976 (table 1). During the 9 influenza A(H1N1) or influenza B seasons, the average number of excess P&I hospitalizations was 74,000 (rate of 32 excess P&I hospitalizations). The lowest rate of excess P&I hospitalizations for these seasons occurred in 1981–1982 (8), whereas the highest rates occurred during the 1985–1986 and 1988–1989 seasons (48). During the

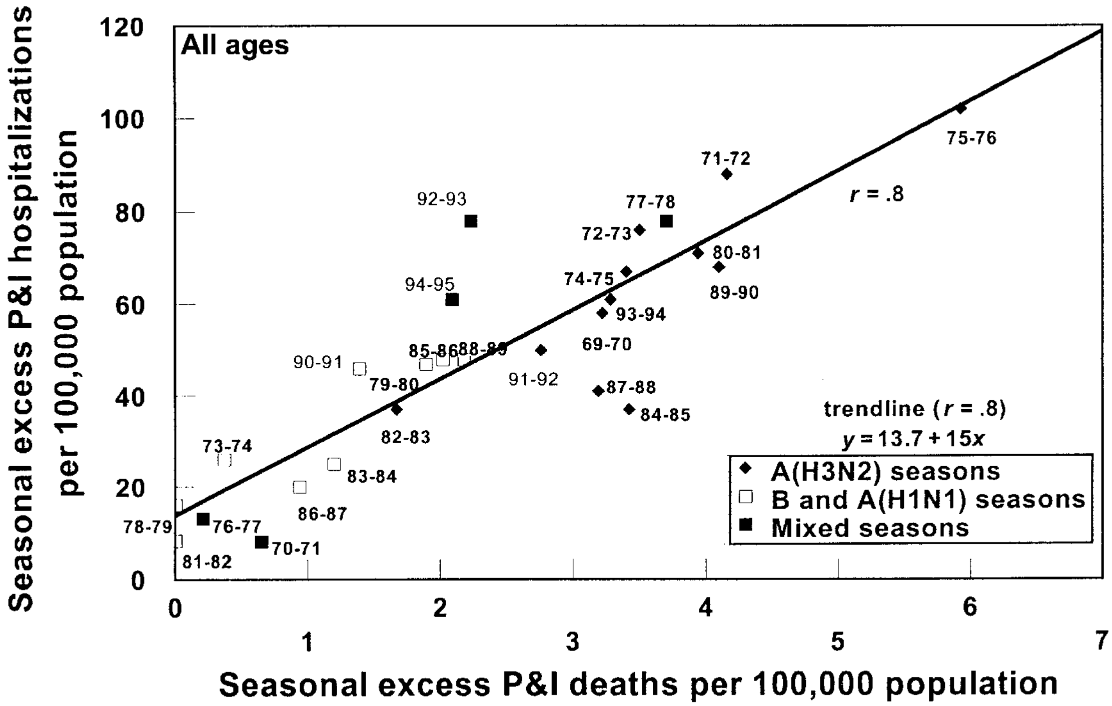

Figure 2. Linear relationship between US seasonal incidences of pneumonia and influenza (P&I) hospitalizations and deaths for 26 influenza seasons, 1970–1995. Year and season type (as defined for this study) are indicated.

5 mixed influenza virus seasons, the average number of excess P&I hospitalizations was 120,000 (rate of excess P&I hospitalizations, 48). The figures for the mixed seasons and the proportion of influenza A(H3N2) viruses varied considerably (table 1).

Excess P&I hospitalizations by age group. Among persons <65 years of age, the average number of excess P&I hospitalizations per season was 64,000, corresponding to an incidence rate of 33 excess P&I hospitalizations per 100,000 population. In persons aged ⩾65 years, the average number of excess P&I hospitalizations each season was 48,000 (174 excess P&I hospitalizations per 100,000 elderly; table 1).

For all seasons, the median and mean relative risks of influenza-related P&I hospitalizations among persons aged ⩾65 years compared with those aged <65 years were 4.1 and 6.4, respectively. In absolute numbers, however, 57% of all excess P&I hospitalizations each season occurred among persons <65 years of age. This proportion was similar when seasons were stratified by circulating virus (sub)types. For both younger and older age groups, excess P&I hospitalization rates were ~2 times higher during A(H3N2) seasons than in A(H1N1)/B seasons (table 2).

Five influenza seasons (1970–1971, 1973–1974, 1976–1977, 1978–1979, and 1986–1987) associated with little or no excess in P&I mortality had an average rate (± SD) of 16.7 ± 6.2 excess P&I hospitalizations per 100,000 population; almost all of these hospitalizations occurred among people aged <65 years (table 1). These influenza seasons were category 1 seasons with respect to a mortality-based influenza severity index [8].

Relationship of excess P&I hospitalizations to excess P&I deaths. During the 26 seasons studied, the pairs of excess P&I hospitalization and excess P&I mortality rates were strongly correlated (Pearson's $r = 0.8$, $P < .05$; figure 2). The linear relationship was described by the following equation: P&I excess hospitalizations per 100,000 population = [13.7 + (15 × P&I excess mortality per 100,000 population)].

However, 2 influenza A(H3N2) seasons (1984–1985 and 1987–1988) decreased significantly under the trend line, suggesting that those seasons were associated with a higher ratio of excess deaths to excess hospitalizations. One mixed virus season (1992–1993) was significantly above the trend line, suggesting a lower ratio of excess deaths to excess hospitalizations for that season.

Age-specific pattern of influenza A(H3N2) hospitalization after the 1968 pandemic. Excess P&I hospitalizations during the 1968–1969 influenza A(H3N2) pandemic could not be estimated because NHDS data were not collected before 1970. However, we studied the excess P&I hospitalizations during the subsequent 12 influenza A(H3N2) seasons. Among persons aged <65 years, the average excess P&I hospitalization rate during the first 5 influenza A(H3N2) seasons (1969–1976) was 60 per 100,000 population and decreased by about half during

Table 2. Absolute and relative impact of influenza on hospitalization and deaths, stratified by type of season and age, United States, 1969–1995.

Age group, outcome[a] (excess in outcome/ 100,000 population)	12 A(H3N2) seasons during 1969–1995, mean (95% CI)	9 A(H1N1)/B seasons during 1969–1995, mean (95% CI)	Significance of difference *(P)* between means[b]
All ages			
P&I hospitalizations	63.00 (51.10–74.90)	31.60 (21.40–41.90)	.001
P&I deaths	3.60 (3.00–4.10)	1.10 (0.60–1.70)	.0001
⩾65 years of age			
P&I hospitalizations	228.00 (191.00–265.00)	125.00 (62.00–188.00)	.01
P&I deaths	26.40 (21.30–31.50)	8.40 (4.10–12.80)	.001
<65 years of age			
P&I hospitalizations	41.80 (30.00–53.50)	19.80 (13.70–25.80)	.01
P&I deaths	0.75 (0.39–1.10)	0.14 (0.07–0.21)	.01

NOTE. CI, confidence interval; P&I, pneumonia and influenza.
[a] Excess P&I hospitalizations may capture majority of influenza-related hospitalizations [10], whereas excess P&I mortality captures only ~25% of all influenza-related deaths [8].
[b] Two-tailed *t* test.

the last 4 influenza A(H3N2) seasons, 1987–1994 ($P = .002$; table 3). In contrast, among persons aged ⩾65 years, there was no significant decline ($P > .4$) in excess P&I hospitalization rates over the same seasons (table 3).

An analysis of excess P&I mortality showed a similar pattern of declining excess mortality rates in the younger age group during A(H3N2) seasons following the 1968 pandemic (table 3). Compared with the average excess mortality rate for the 4 most recent A(H3N2) seasons, rates of excess P&I mortality were 19 times higher during the 1968–1969 pandemic and ~6 times higher during the next 5 A(H3N2) seasons. In contrast, among the elderly, rates of excess P&I mortality were only 2 times higher during the 1968 pandemic than during the most recent A(H3N2) seasons, and the pattern did not decline over time.

Discussion

The national impact of influenza on hospitalizations has been documented less well than the impact on mortality. We estimate that during 26 consecutive influenza seasons from 1969–1970 through 1994–1995, ~3 million excess P&I hospitalizations occurred in the United States. Although average rates of excess P&I hospitalizations were higher in the elderly (174/100,000 population) than in those aged <65 years (33/100,000 population), the younger age group accounted for more than half of the total number of influenza-related P&I hospitalizations. In addition, the average number of excess P&I hospitalizations was twice as high during seasons dominated by influenza A(H3N2) viruses as during those dominated by influenza B/ A(H1N1) viruses.

Our findings are consistent with those reported by other investigators. In a study of influenza-related hospitalizations that was also based on NHDS data, the authors estimated an average seasonal number of 172,000 excess P&I hospitalizations for 5 severe influenza A seasons between 1970 and 1978 [10]. Although we used an entirely different statistical approach, we estimated an average of 175,000 excess P&I hospitalizations for the same 5 seasons. Previous studies also showed that excess hospitalizations but not excess mortality could be documented in some seasons dominated by influenza B and A(H1N1) viruses [2, 9, 11]. We found that an average of 16.7 excess P&I hospitalizations per 100,000 population occurred during the influenza seasons without measurable excess in P&I mortality and that most of those hospitalizations were among persons aged <65 years. A key finding was that the overall seasonal numbers

Table 3. Impact of early A(H3N2) season after 1968 pandemic vs. recent A(H3N2) seasons on hospitalization and deaths, United States, 1969–1995.

Age group, outcome[a] (excess in outcome/ 100,000 population)	1968–1969 A(H3N2) pandemic	Average of 5 early A(H3N2) seasons, 1969–1976 (95% CI)	Average of 4 recent A(H3N2) seasons, 1987–1994 (95% CI)	Significance of difference *(P)* between means[b]
⩾65 years				
P&I hospitalizations	No data	240.0 (179.0–300.0)	260.00 (219.00–301.00)	.5
P&I deaths	44	28.0 (17.4–38.5)	27.00 (23.00–29.90)	.4
<65 years				
P&I hospitalizations	No data	60.0 (46.9–73.4)	26.00 (21.70–29.30)	.002
P&I deaths	4.3	1.4 (1.04–1.72)	0.23 (0.19–0.28)	.0005

NOTE. CI, confidence interval; P&I, pneumonia and influenza.
[a] Excess P&I hospitalizations may capture majority of influenza-related hospitalizations [10], whereas excess P&I mortality captures only ~25% of all influenza-related deaths [8].
[b] Two-tailed *t* test.

of excess P&I deaths and excess P&I hospitalizations were linearly correlated, regardless of the predominant circulating types or subtypes of influenza virus. This observation is useful, because it suggests that rates and numbers of excess P&I hospitalizations can be extrapolated from national excess P&I mortality estimates, which are calculated routinely in the United States by the CDC.

Although some investigators have suggested that influenza-related hospitalizations might provide a more sensitive index than mortality for assessing the severity of individual influenza epidemics [11], the direct annual estimation of excess P&I hospitalizations poses some difficulties. First, hospitalization discharge coding can be sensitive to changes in billing practices. Second, NHDS data are derived from a 1% sample of US hospitalizations, and estimates of seasonal excess P&I hospitalizations derived from the sample are subject to considerable random error. Although Health Care Financial Administration data cover most hospitalizations for persons aged ⩾65 years in the United States and could be utilized (see [18]), such studies would allow only estimates of influenza-related hospitalizations for the elderly population. By contrast, annual national estimates of excess P&I mortality are based on complete mortality records for the United States. Extrapolating hospitalization estimates from mortality estimates on the basis of the linear relationship between overall excess P&I hospitalizations and excess P&I mortality and the other considerations would be a reasonable approach for most years. In addition, the CDC's ongoing surveillance for national P&I mortality data could be used to generate timely preliminary estimates of P&I hospitalizations after each influenza season [19]. However, for influenza seasons in which an unusual relationship between mortality and hospitalizations is suspected or for pandemic years in which the introduction of a novel influenza virus is expected to result in substantially elevated morbidity and mortality, direct calculations of P&I hospitalizations would be preferable.

It is important to note that the analysis in this study was limited to hospitalizations in which either pneumonia or influenza (P&I) was listed as the first condition on the discharge records. We did not attempt to estimate the total increase in hospitalizations attributable to influenza. Rates of hospitalizations for other conditions, including acute bronchitis, chronic respiratory disease, and congestive heart failure, may increase during influenza seasons [18]. Another study would be needed to estimate the total impact of influenza on hospitalizations.

The large overall increase in P&I hospitalization rates among persons aged ⩾65 years during periods outside influenza seasons was consistent with a general increase in infectious disease hospitalization rates among the elderly during the 1980s [20]. The basis for the increase is uncertain. It could reflect a true increase in hospitalizations among the elderly, perhaps as a result of the aging of that cohort, or, alternatively, changing hospital reimbursement practices [20]. Regardless, our method for establishing a baseline of expected P&I hospitalizations in the absence of influenza adjusted for this secular trend in the data.

A final observation of particular interest was the significant decline in rates of excess P&I hospitalization among persons aged <65 years during the influenza A(H3N2) seasons following the 1968 pandemic. During the study period, persons aged <65 years accounted for a gradually declining proportion of excess P&I hospitalizations from ~70% to 40% in the influenza A(H3N2) seasons after the 1968 pandemic. No similar decline was seen in the elderly age group (table 3). In a previous study, we described a similar, but even more dramatic, pattern for influenza-related mortality following all 3 pandemics in this century [12]. The major implication of these observations is that excess hospitalizations and deaths during the next influenza pandemic probably will increase substantially beyond rates in recent A(H3N2) seasons among persons aged <65 years. By contrast, rates of influenza-related hospitalizations and deaths among the elderly are almost always higher than in the younger age group, and our findings suggest that rates of influenza-related hospitalizations and deaths may increase only marginally during the next pandemic. The potential for a disproportionate increase in rates of influenza-related hospitalizations and deaths among persons aged <65 years during the next pandemic is important and should be taken into consideration by those developing plans to diminish the health impact of the next pandemic.

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