Mass Vaccination of Schoolchildren against Influenza and Its Impact on the Influenza-Associated Mortality Rate among Children in Japan

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Background. Influenza control based on mass vaccination of schoolchildren was implemented in Japan in the 1960s and was associated with a decrease in the overall mortality rate. The program was discontinued in 1994. The discontinuation was followed by a seasonal increase in the mortality rate. Lately, young children and elderly persons have been receiving influenza vaccines. The purpose of this study was to investigate changes in influenza-related mortality among young children before and after discontinuation of mass vaccination of schoolchildren.

Methods. We calculated the monthly all-cause mortality rates during 1972–2003 and the pneumonia and influenza (P&I) mortality rates during 1972–1999 for young children (age, 1–4 years). We estimated the excess mortality rates attributable to influenza by computing the baseline annual mortality rate as a centered, 3-year moving average of the number of deaths reported during the 2 preceding and the following Decembers.

Results. Prominent winter peaks in monthly all-cause mortality rates among young children occurred in the 1990s. They coincided with the winter peaks in monthly P&I mortality rates among young children and were very similar to the winter peaks observed among elderly persons. The number of excess deaths of young children was estimated to be 783 in the 11 winter seasons from 1990 to 2000, whereas no winter peaks in the number of deaths were seen after 2000.

Conclusions. It is likely that discontinuation of mass vaccination of schoolchildren was responsible for the increase in influenza-associated deaths among young children in the 1990s. The recent increase in influenza vaccinations among young children, together with the routine therapeutic use of neuraminidase inhibitors, has led to a decrease in the influenza-associated mortality rate.

Japan's initial strategy for controlling influenza was designed to maximally protect Japanese society as a whole [1–3]. This strategy was implemented by means of mass vaccination of schoolchildren aged 6–15 years, who are the principle channel through which influenza is introduced into households [4, 5]. Influenza vaccination was required by law for Japanese schoolchildren from the mid-1970s through the late 1980s, during which time vaccine coverage ranged from 50% to 85% [3]. However, in 1987, new legislation allowed parents to refuse influenza vaccination of their children, and vaccine coverage decreased rapidly (figure 1). The annual number of vaccine doses administered in Japan decreased by ~50% between 1987 and 1990. Because of growing doubts about the effectiveness of the vaccine, the government formally discontinued mass vaccination of schoolchildren in 1994, and in that year, the number of doses distributed decreased to almost 0 [3].

The effectiveness of the schoolchild vaccination program was demonstrated only recently [3]. There was a decrease in the overall number of excess deaths between 1962 and 1987, followed by an increase after 1987 and a very large increase after 1994. The most likely explanation for this pattern is that herd immunity resulting from the mass vaccination of schoolchildren reduced the spread of influenza to elderly persons.

The distribution of influenza vaccine in Japan has increased substantially since 1994, and by 2003, the number of doses administered reached ~30 million, the same level as in 1987 (figure 1). After 1994, influenza-associated encephalopathy was widely publicized as a complication of influenza in young Japanese children,

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with 50–100 deaths due to encephalopathy reported each year during 1995–1999 [6–8]. Although not clearly associated with such reports, the rate of vaccination among children 1–6 years of age has increased rapidly, with 40.1% of young Japanese children estimated to have received influenza vaccine in 2003 [9].

Repeated outbreaks of influenza have been reported in nursing homes since 1994, and the Japanese government inaugurated a special vaccination program for elderly persons (age, ⩾65 years) in 2001. The cost of influenza vaccine for this age group is partially subsidized, and the vaccination rate was estimated to be 52.7% in 2003 [9].

Although it is well-known that influenza is responsible for excess hospitalization among children [10, 11], it is less well appreciated that influenza is a significant cause of child mortality during the winter season. In addition to the above reports of influenza-associated encephalopathy, excess mortality rates among young Japanese persons aged 0–4 years and 5–25 years have been detected every winter season since 1993–1994 [12]. Similarly, it was widely reported that 143 children died of influenza in the United States during the 2003–2004 epidemic caused by variant influenza virus strain A/Fujian/411/2002 (subtype H3N2). On the basis of a recent model of influenza-related death, it was estimated that a mean of 92 deaths occurred among children <5 years of age each year during the 1990s [13].

We decided to investigate whether mass vaccination of Japanese schoolchildren protected their younger siblings against influenza-associated death. We also estimated the impact of the recent increase in the distribution of influenza vaccine doses on the mortality rate for young children.

METHODS

Data on all-cause deaths were extracted from *Vital Statistics of Japan* [14]. The following codes from the *International Classification of Diseases* were used to indicate death due to pneumonia and influenza (P&I): codes 470–474 and 480–486 (*Eighth Revision,* 1972–1977), codes 487 and 480–486 (*Ninth Revision,* 1978–1993), and codes J10–J11 and J12–J18 (*Tenth Revision,* 1994–2000). Data for age-specific P&I deaths during 1972–1999 were obtained by application to the Ministry of Health, Labor, and Welfare, because these data had not been officially released.

We calculated the age-specific monthly mortality rates during 1972–2003 that were associated with all causes and with P&I among infants (age, <1 year), young children (age, 1–4 years), schoolchildren (age, 5–9 years and 10–14 years), and elderly persons (age, 65–69 years). In Japan, children in the first year of elementary school are usually 6 years old. This group of children was divided into 3 age groups because the mortality rate for infants is 10–15 times that for young children, which,

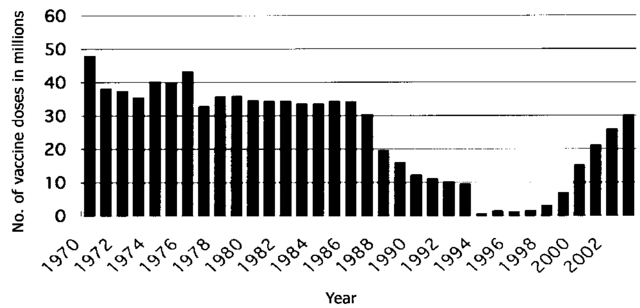

Figure 1. Annual numbers of doses of influenza vaccine distributed in Japan during 1970–2003. Between 1970 and 1994, almost all vaccine doses were used for mass vaccination of schoolchildren (age, 6–15 years), whereas after 1994, vaccine doses were mainly used for vaccination of young children (age, 1–4 years) and of elderly persons (age, 60–69 years).

in turn, is 3–5 times that for schoolchildren. Annual estimates for the population of persons in each age group were made.

There are no validated methods for estimating excess mortality rates among children. Such estimates are complicated by the fact that the excess mortality rate is likely to be low and that other pathogens, such as respiratory syncytial virus and rotavirus, are major causes of pediatric hospitalizations during the winter [10, 11]. Thus, influenza may not be the only contributor to the excess mortality rate during the winter. The peak months for the number of pediatric hospitalizations for influenza and for the P&I mortality rate among children are January and February. According to the sentinel reports of Japan, most influenza-like illnesses occur from January through March [15]. Because of these findings, we estimated the excess influenza-associated mortality rate as the algebraic sum of the differences between the number of deaths observed in January, February, and March for each year and a baseline level. The baseline annual mortality rate was calculated as a centered, 3-year moving average of the number of reported during the 2 preceding and the following Decembers.

This procedure deliberately underestimates excess mortality for children, especially infants and young children, because influenza-attributable deaths probably occur in December in children as in older age groups, and more importantly, there is a respiratory syncytial virus epidemic every December in Japan. We confirmed that, when November was used as a baseline level, excess mortality was greatly increased in all age groups, clearly leading to an overestimation of excess mortality (data not shown).

Virus surveillance data were obtained from the Annual Report of National Epidemiological Surveillance of Vaccine-Preventable Diseases [16].

RESULTS

Mortality rates among young Japanese children aged 1–4 years. Between 1972 and 1989, the all-cause mortality rate

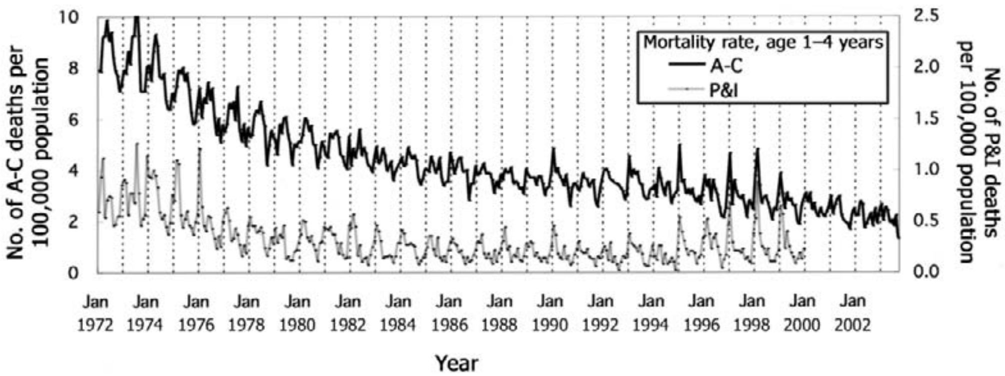

Figure 2. Monthly all-cause (A-C) and pneumonia and influenza (P&I) mortality rates among young Japanese children aged 1–4 years. *Vertical dotted lines,* January of the specified year.

among young Japanese children peaked during the spring or summer (figure 2). In the 1980s, the peak all-cause mortality rates during the spring and summer gradually decreased, becoming indistinguishable from the rates during the rest of the year. In 1990, a peak in the all-cause mortality rate suddenly reappeared, but it had shifted to winter. Distinct peaks were seen in January of the following years: 1990, 1993, 1995, 1997, and 1999. In 1998, the most prominent peak occurred in February. After 1999, distinct peaks in all-cause mortality rates were no longer seen.

Peaks in P&I mortality rates consistently occurred during the winter (figure 2). Tall peaks were seen during 1972–1976, and the peak values decreased thereafter. High peaks in P&I mortality rates reappeared in the 1990s, especially during 1995–2000.

Monthly distributions of peak mortality rates due to all causes and to P&I are shown in figures 3*A* and 3*B*. During 1972–1989, peaks of P&I mortality rates occurred mainly during the winter (December–March). On the other hand, peaks in all-cause mortality rates occurred during the spring and the summer (figure 3*A*). In the 1990s, peaks of all-cause deaths shifted to winter (figure 3*B*), and as a result, synchronous increases in both all-cause deaths and P&I deaths occurred during the winter, particularly in 1989–1990, 1992–1993, 1994–1995, 1996–1997, 1997–1998, and 1998–1999. During these 6 winters, influenza type A (due to influenza virus subtype H3N2) was

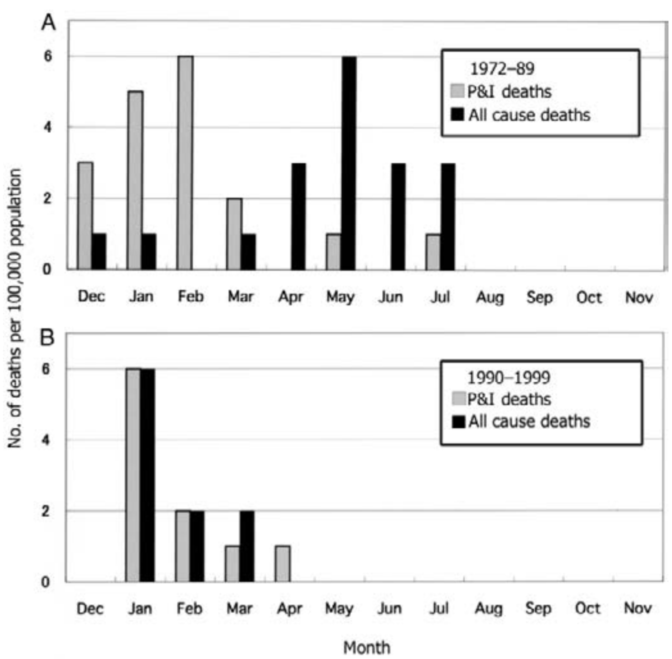

Figure 3. Peak monthly all-cause and pneumonia and influenza (P&I) mortality rates during 1972–1989 (*A*) and 1990–1999 (*B*)

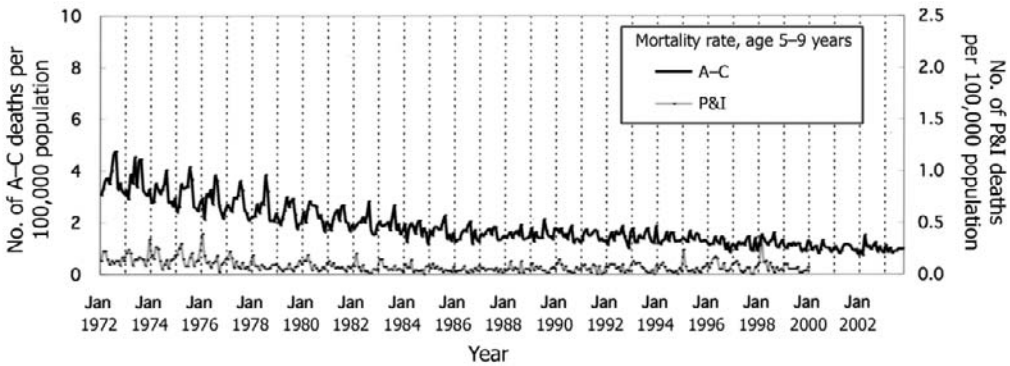

Figure 4. Monthly all-cause (A-C) and pneumonia and influenza (P&I) mortality rates among Japanese children aged 5–9 years. *Vertical dotted lines,* January of the specified year.

epidemic in January and February, and influenza type B was epidemic in February and March. The peaks in the mortality rates were concordant with the influenza type A epidemics (due to influenza virus subtype H3N2) in January, except in 1998, when a variant influenza virus strain (A/Sidney/5/97 [subtype H3N2]) was detected in Japan for the first time. The peaks for both all-cause deaths and P&I deaths in 1998 occurred in February.

Small epidemics caused by influenza type A (viral subtype H3N2) occurred in other seasons in the 1990s, and a clear peak in the all-cause mortality rate was seen in March 1994. Influenza type A (due to influenza virus subtype H1N1) was epidemic in January and February 1996, and a high peak in the P&I mortality rate was observed. A major epidemic caused by a variant influenza virus strain, A/Fujian/411/2002 (subtype H3N2), occurred during the 2002–2003 winter, but there was no increase in the all-cause mortality rate.

Mortality rates among Japanese schoolchildren aged 5–14 years. Peaks in the all-cause mortality rate among schoolchildren invariably occurred during the summer (figures 4 and 5). These summer peaks became relatively less prominent, because the mean all-cause mortality rate decreased by approximately one-half from the 1970s to the 1990s.

In contrast, the peaks in P&I mortality rates consistently occurred during the winter (figures 4 and 5). The peaks in P&I mortality rates were prominent during the 1970s, especially in January 1976, when a variant influenza virus strain, A/Victoria/3/75 (subtype H3N2), appeared. Similar peaks in the P&I mortality rate were again seen in 1995 and 1998 among children aged 5–9 years.

Infants. The baseline all-cause and P&I mortality rates among infants are much higher (approximately 10–12-fold) than the rates in other groups. Prominent peaks in all-cause mortality rates occurred in both winter and summer during the 1970s, especially from 1972 through 1976 (figure 6). The summer peaks disappeared in the 1980s, and the winter peaks disappeared in the second half of the 1980s.

There were peaks in P&I mortality rates in both winter and summer during 1972–1976. From 1977 through 1986, the peaks in P&I mortality rates occurred only in winter, and from 1987 onward the winter peaks were no longer seen.

All-cause and P&I mortality rates increased synchronously

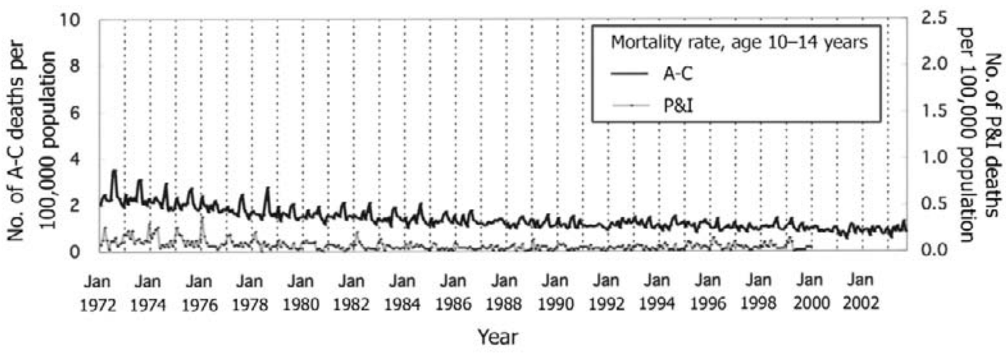

Figure 5. Monthly all-cause (A-C) and pneumonia and influenza (P&I) mortality rates among Japanese children aged 10–14 years. *Vertical dotted lines,* January of the specified year.

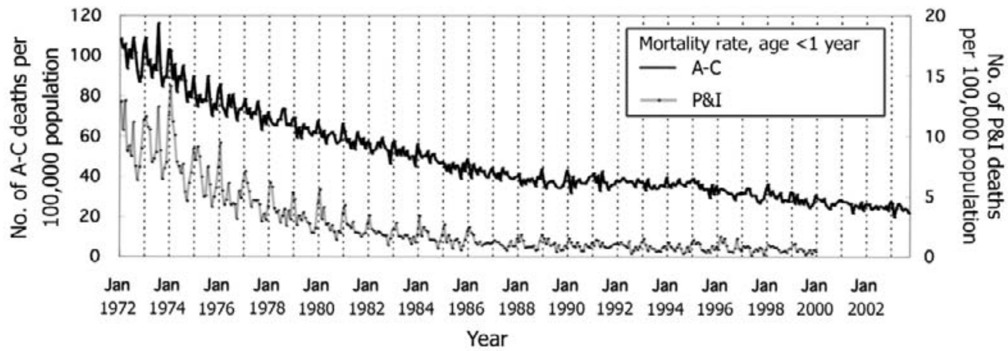

Figure 6. Monthly all-cause (A-C) and pneumonia and influenza (P&I) mortality rates among Japanese infants aged <1 year. *Vertical dotted lines,* January of the specified year.

in winter and summer from 1972 through 1976. From 1976 through 1987, both all-cause and P&I mortality rates increased during the winters only.

Comparison of all-cause deaths between elderly persons and young children. The monthly all-cause mortality rates among elderly persons (age, 65–69 years) and young children (age, 1–4 years) are shown in figure 7. The mean monthly all-cause mortality rate for elderly persons was 20 times that for young children during 1972–2002.

The peaks in the monthly mortality rate among elderly persons always occurred in winter, whereas the peaks in the monthly mortality rate among young children were observed between April and July until 1990, when there was a sudden shift in the peak to the winter. During the 1990s, the all-cause mortality rate patterns were very similar for elderly persons and young children. After 1999, the winter peaks among young children disappeared again.

Estimated all-cause and P&I excess mortality rates. Epidemic viruses and estimated excess mortality rates during the winters of 1975–2003 are shown in table 1. In the 1990s, prominent excess all-cause mortality rates appeared among young children. During 1997–1998, when infection with the variant influenza virus strain A/Sidney/5/97 (subtype H3N2) was epidemic in Japan, excess all-cause mortality rates were observed not only among young children (age, 1–4 years), but also among infants (age, ⩽1 year) and schoolchildren aged 5–9 years. In total, 202 children died of causes attributable to influenza. Among schoolchildren aged 10–14 years, the all-cause mortality rate was high during 1998–1999, with 55 influenza-attributable deaths observed. The excess P&I mortality rates also increased among infants, young children, and schoolchildren aged 5–9 years during 1998–1999.

Annual excess all-cause mortality rates among young children and the annual numbers of doses of vaccine produced in Japan during 1975–2004 are shown in figure 8*A*. No significant excess mortality rates were observed during 1975–1989, except in 1980. Excess mortality rates clearly appeared in 1990. In 1998, when influenza virus strain A/Sidney/5/97 (subtype

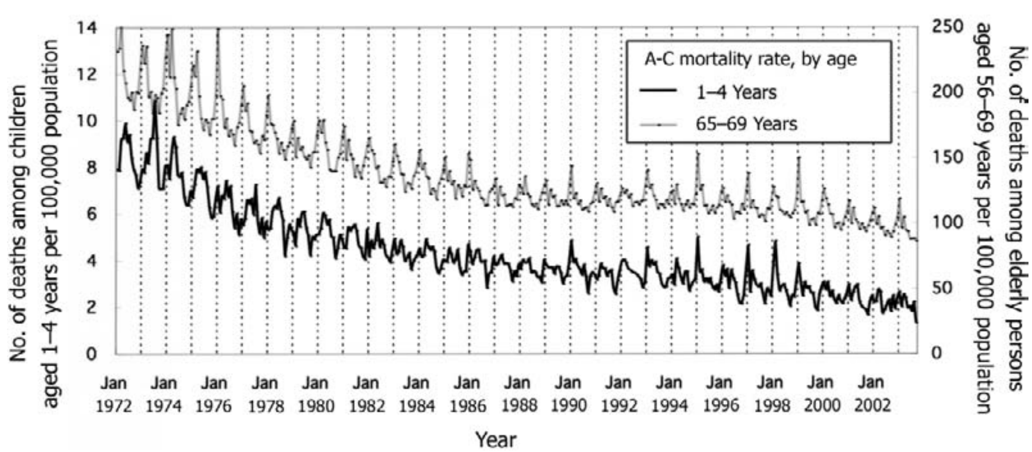

Figure 7. Monthly all-cause (A-C) mortality rates among Japanese children (age, 1–4 years) and elderly persons (age, 65–69 years). *Vertical dotted lines,* January of the specified year.

Table 1. Influenza virus types and subtypes and excess mortality rates associated with influenza epidemics in Japan, 1974–2003.

Influenza season	Predominant influenza virus type (subtype)	Excess all-cause mortality rate, by age group				Excess pneumonia and influenza mortality rate, by age group			
		0 years	1–4 years	5–9 years	10–14 years	0 years	1–4 years	5–9 years	10–14 years
1974–1975	A (H3N2)	−40.7	0.2	−0.5	0.2	−2.7	0.4	0.0	0.1
1975–1976	A (H3N2)	−14.7	0.6	−0.1	0.9	−3.4	0.5	0.1	0.3
1976–1977	B	−6.7	−0.2	0.2	0.2	0.7	0.2	0.0	0.1
1977–1978	A (H3N2), A (H1N1)	−15.6	0.1	0.1	0.1	0.1	0.2	0.0	0.2
1978–1979	A (H1N1)	−16.0	−0.5	−0.3	0.3	−3.1	0.1	−0.2	0.0
1979–1980	A (H1N1), A (H3N2), B	−17.5	1.2	0.6	0.3	−0.6	0.4	0.1	0.1
1980–1981	A (H1N1)	−13.7	−0.9	−0.2	0.0	−1.2	0.1	0.0	0.0
1981–1982	B	−19.8	−1.2	−0.2	0.0	−0.7	0.2	0.1	0.2
1982–1983	A (H3N2)	−8.4	−0.5	0.3	−0.1	0.0	0.1	0.2	0.0
1983–1984	A (H1N1)	−7.8	0.1	0.2	−0.1	1.7	0.3	0.1	0.1
1984–1985	B	−16.8	−0.6	0.6	−0.1	−0.1	0.2	0.0	0.1
1985–1986	A (H3N2), A (H1N1)	−8.7	−0.6	−0.1	−0.3	1.2	0.2	−0.1	0.0
1986–1987	A (H1N1)	−10.7	−1.0	0.2	−0.4	−1.0	0.2	0.0	0.0
1987–1988	A (H3N2), B	−12.6	−0.5	0.3	−0.4	−0.1	0.2	0.0	0.1
1988–1989	A (H1N1)	−18.2	−0.6	0.0	0.0	0.0	0.1	0.1	0.1
1989–1990	A (H3N2), B	−14.8	1.5	0.7	0.0	−0.1	0.2	0.2	0.1
1990–1991	A (H1N1), A (H3N2), B	−2.2	−0.5	0.4	0.1	0.7	0.0	0.0	0.0
1991–1992	A (H3N2), A (H1N1)	−0.8	1.9	0.0	0.1	−0.3	0.0	0.1	0.0
1992–1993	A (H3N2), B	−6.1	2.4	−0.6	0.5	0.1	0.3	0.1	0.0
1993–1994	A (H3N2)	−7.7	0.9	−1.1	−0.6	−0.2	−0.1	0.1	0.0
1994–1995	A (H3N2), B	−0.3	2.5	−0.5	−0.2	1.2	0.4	0.1	0.2
1995–1996	A (H1N1)	−6.7	0.9	−0.3	−0.7	1.0	0.2	0.1	0.2
1996–1997	A (H3N2), B	−3.4	1.7	0.0	−0.4	0.7	0.0	0.0	0.0
1997–1998	A (H3N2)	1.7	2.9	0.7	0.1	1.0	0.7	0.4	0.0
1998–1999	A (H3N2), B	−7.4	1.0	−0.3	0.8	0.8	0.6	0.1	0.2
1999–2000	A (H3N2), A (H1N1)	−7.2	0.4	−0.4	0.0	…	…	…	…
2000–2001	A (H1N1), A (H3N2), B	−4.1	−0.1	−0.2	−0.5	…	…	…	…
2001–2002	A (H1N1), A (H3N2), B	−6.8	−0.3	0.6	0.0	…	…	…	…
2002–2003	A (H3N2), B	−11.9	−0.3	0.5	−0.4	…	…	…	…

NOTE. Data are no. of deaths per 100,000 population. See Methods for an explanation of how data were calculated.

H3N2) emerged, the excess mortality rate reached 2.94 deaths/10^5 population, with 140 young children dying of causes attributable to influenza (table 2). We estimated that a total of 783 young children died of such causes during the 11-year period from 1990 through 2000. By contrast, no increase in the all-cause mortality rate was observed in 2003, the year when influenza virus strain A/Fujian/411/2002 (subtype H3N2) first appeared and caused a severe epidemic in Japan. The excess P&I mortality rates among young children and the annual numbers of doses of vaccine produced during 1975–2004 are shown in figure 8*B*. Excess P&I mortality rates were prominent in 1998 and 1999.

Monthly peaks in the numbers of influenza-like illnesses and deaths among young children. Monthly peaks in the numbers of influenza-like illnesses and all-cause and P&I deaths during the winters from 1989–1990 through 1999–2000 are shown in table 2. During the 9 winters that significant numbers of excess all-cause deaths were observed (>40 deaths), months in which the number of influenza-like illnesses and all-cause deaths peaked coincided. In 7 of these 9 winters, months in which the number of P&I deaths peaked are also consistent with months in which the number of influenza-like illnesses peaked. These data also support the likelihood that peaks in the numbers of all-cause deaths among young children during the 1990s were attributable to influenza.

DISCUSSION

Since 1990, the monthly all-cause mortality rates among young children have peaked in the winter and have coincided with the peaks in P&I mortality rates, suggesting that the influenza-associated mortality rate among young children increased significantly during the 1990s (figure 2). On the basis of annual all-cause mortality rates, the total number of excess deaths of young children was estimated to be 783 during the 11-year period from 1990 through 2000 (table 2).

The all-cause mortality rate reflects the impact of influenza epidemics on children more accurately than does the mortality

Table 2. Monthly peaks of influenza-like illness (ILI) cases, all-cause deaths, and pneumonia and influenza (P&I) deaths among young children.

Influenza season	Predominant influenza virus type (subtype)	Peak month of ILI cases	Peak month of all-cause deaths	Peak month of P&I deaths	No. of excess all–cause deaths	No. of excess P&I deaths
1989–1990	A (H3N2), B	January	January	January	77	13
1990–1991	A (H1N1), A (H3N2), B	February	March	January	0	1
1991–1992	A (H1N1), A (H3N2)	February	February	April	94	0
1992–1993	A (H3N2), B	January	January	January	117	14
1993–1994	A (H3N2)	March	March	March	46	0
1994–1995	A (H3N2), B	January	January	January	120	20
1995–1996	A (H1N1)	January	January	February	41	11
1996–1997	A (H3N2), B	January	January	January	82	0
1997–1998	A (H3N2)	February	February	February	140	35
1998–1999	A (H3N2), B	January	January	January	49	30
1999–2000	A (H3N2), A (H1N1)	February	January	January	18	No data

rate attributed to P&I (figure 8*A* and 8*B*), because the symptoms and signs of influenza virus infection in children are protean. Although influenza viruses are classified as respiratory viruses, lower respiratory tract infection accounts for only approximately one-half of all illnesses due to influenza virus in children that result in hospitalization [10, 17].

The monthly mortality rates for all-cause deaths and P&I deaths in the elderly groups (age, >65 years) peak at the same time (during the winter), and the increase in the all-cause mortality rate is principally attributable to the influenza epidemic during the winter [17]. Beginning in approximately 1990, the monthly all-cause mortality rates among elderly persons in Japan peaked synchronously during the winter with the all-cause mortality rates among young children (figure 6). Moreover, months in which the peak numbers of influenza-like illnesses were reported from sentinels during the 1990s coincided with months in which the all-cause mortality rates were observed among young children (table 2). Thus, the increase in the number of all-cause deaths of young children that occurred in the 1990s was also likely attributable to influenza.

It has been reported that the magnitude of the influenza-associated mortality rate is significantly larger during seasons

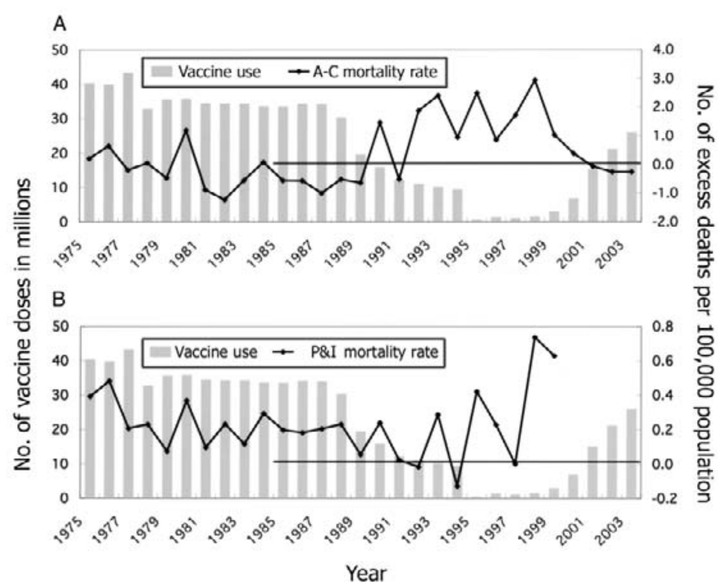

Figure 8. *A,* Estimated annual numbers of influenza vaccine doses administered versus annual excess all-cause (A-C) mortality rates among young children (age, 1–4 years; *A*) and annual excess pneumonia and influenza (P&I) mortality rates among young children (*B*) in Japan. During 1975–1994, almost all influenza vaccine doses were used for mass vaccination of schoolchildren, whereas after 1994, most influenza vaccine doses were used for young children and for elderly persons (age, >65 years). See Methods for an explanation of how data were calculated.

dominated by influenza type A (caused by influenza virus subtype H3N2) than the influenza-associated mortality rates associated with seasons in which influenza type A (caused by subtype H1N1) and type B predominate [17]. When all-cause mortality rates among young children peaked in the 1990s, most peaks were concordant with the epidemics associated with influenza type A (caused by subtype H3N2) (table 2). However, influenza virus type A (subtype H1N1) also caused significant excess mortality (e.g., during the 1995–1996 epidemic) (table 2). During the 1991–1992 influenza season, the number of excess all-cause deaths peaked at 94 deaths, although influenza type A (caused by subtype H1N1) was dominant. In young children, influenza type A due to subtype H1N1 may be as serious as that due to subtype H3N2.

The increased influenza-associated mortality rate among young children is probably attributable to the reduction in vaccination rates among schoolchildren since 1987 (figures 1, 8*A*, and 8*B*). The complete discontinuation of vaccination of schoolchildren in 1994 was followed by a prominent increase in influenza-associated mortality rates among young children during the second half of the 1990s, and the results of our study suggest that the vaccination of schoolchildren was effective in protecting young children against influenza.

The recent increase in influenza vaccine use may lead to a decrease in the influenza-associated mortality rate among young children (8*A*). In 2003, influenza vaccine use reached the same level as that in 1987, the final year in which the vaccination rate among schoolchildren was high (figure 1). However, the age profile of vaccinees during the 2 seasons was totally different. In 1987, almost all vaccine doses were used for schoolchildren, whereas in 2003, most doses were used for young children and elderly persons. The age-specific vaccination rate in 2003 was estimated to be 9.6% for infants, 40.1% for children aged 1–6 years, 23.6% for schoolchildren aged 7–13 years, 12.1% for persons aged 14–64 years, and 52.7% for persons aged ⩾65 years [9].

No marked changes in mortality rates were seen among schoolchildren in the 1990s, although a small number of schoolchildren died of causes attributable to influenza during 1995–2000 (table 1). It was recently reported that school absenteeism increased 3-fold after the discontinuation of mass vaccination of schoolchildren, suggesting that mass vaccination may have been highly effective in reducing the amount of school absenteeism during influenza epidemics [18].

Since 1995, excess P&I mortality rates have increased annually among infants, and in 1998, the excess all-cause mortality rate was 1.7 deaths/100,000 population, for a total of 20 infant deaths. The discontinuation of mass vaccination of schoolchildren had a smaller effect on the mortality rate among infants, compared with that among young children, although infants (as well as elderly persons) are generally considered to be at high risk for influenza. A Japanese report on pediatric hospitalization for influenza found that most of the hospitalized persons were young children aged 1–6 years of age, rather than infants [10]. However, in our study, the influenza-related mortality rates among infants may have been considerably underestimated, because of the December baseline levels.

The decrease in the all-cause mortality rates observed among young children in Japan since 2000 may in part be attributable to the widespread use of neuraminidase inhibitors. Dramatic advances have been made in the diagnosis and treatment of influenza in Japan in recent years [19]. Most children with influenza-like illness are now tested with rapid diagnostic tests, and if the test results are positive, oseltamivir is routinely administered. A major epidemic caused by a variant influenza virus strain, A/Fujian/411/2002 (subtype H3N2), occurred in Japan during the 2002–2003 influenza season. Although the scale of the epidemic was the third largest in the past 10 years, according to the sentinel report [15], there was no increase in the all-cause mortality rate among young children (table 1). On the other hand, the epidemic caused by the same virus in the United States during the 2003–2004 influenza season had a severe impact on children. This difference between the United States and Japan in child mortality rates due to influenza may be attributable to the high vaccination rate of young Japanese children and to the routine use of neuraminidase inhibitors to treat influenza in Japan.

Since 1995, many deaths of children due to influenza encephalopathy have been reported, and most have been in young children [6–8]. Accordingly, fatal cases of encephalopathy may have significantly contributed to the increase in the number of excess deaths observed among young children, although prominent numbers of excess all-cause deaths have been noted since 1990. The authors of one report hypothesized that the discontinuation of mass vaccination of schoolchildren was responsible for the increase in the incidence of influenza-associated encephalopathy [20], and our results appear to support this hypothesis.

In conclusion, the discontinuation of mass vaccination of schoolchildren probably led to the increase in influenza-associated deaths among young children in the 1990s. Moreover, it is also likely that the recent high rate of vaccination against influenza among young children, together with the widespread use of neuraminidase inhibitors to treat influenza, has led to a decrease in influenza-associated mortality rate among young children since 2001.

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