Influenza Vaccination of Schoolchildren and Influenza Outbreaks in a School

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Background. The objective of this retrospective descriptive study was to determine whether the universal influenza vaccination for schoolchildren was effective in controlling influenza outbreaks in a school. A universal vaccination program for schoolchildren was started in Japan in the 1960s, but the government abandoned the program in 1994 because of lack of evidence that the program was effective in preventing influenza in schoolchildren.

Methods. Influenza vaccine coverage rates, total numbers of class cancellation days, and absentee rates were reviewed in a single elementary school during the 24-year period during 1984–2007.

Results. The mean number of class cancellation days and the mean absentee rate in the compulsory vaccination period (1984–1987; mean vaccine coverage rate, 96.5%) were 1.3 days and 2.5%, respectively, and they increased to 8.3 days and 3.2% during the quasi-compulsory vaccination period (1988–1994; vaccine coverage, 66.4%). In the no-vaccination period (1995–1999; vaccine coverage, 2.4%), they were 20.5 days and 4.3%, respectively, and in the voluntary vaccination period (2000–2007; vaccine coverage, 38.9–78.6%), they were 7.0–9.3 days and 3.8%–3.9%. When minor epidemics were excluded, there was a significant inverse correlation between the vaccine coverage rates and both the number of class cancellation days and absentee rates.

Conclusions. The universal influenza vaccination for schoolchildren was effective in reducing the number of class cancellation days and absenteeism in the school.

In the past, Japan’s influenza control strategy was to vaccinate schoolchildren on the basis of the theory it would prevent influenza epidemics in the community [1–3]. A nationwide universal influenza vaccination program for schoolchildren (elementary and junior high school, 6–15 years) was started in 1962, and during an ~20-year period from the early 1970s through the late 1980s, the vaccine coverage rate among schoolchildren was 50%–85% in Japan [4]. During this period, schoolchildren were compulsorily vaccinated with influenza vaccine together at their schools by school doctors. On the other hand, influenza vaccination was not recommended for older patients and patients at high risk. In 1987, however, new legislation allowed parents to refuse to have their children vaccinated against influenza, because of possible adverse effects, and the use of influenza vaccine decreased to low levels. The Japanese government abandoned the universal vaccination program for schoolchildren in 1994, mainly because of lack of evidence that it was effective in preventing influenza among schoolchildren.

It recently emerged that excess deaths decreased in Japan during the period when the universal vaccination program for schoolchildren was in effect [2]. Because >90% of the excess deaths occurred in the older population, the most probable cause to be protection of the older population by the herd immunity generated by the universal vaccination of schoolchildren. Another important report supported the effectiveness of the universal vaccination program for schoolchildren [3]. Until the 1980s, the reports of influenza-associated encephalopathy were rare in Japan. However, after 1994, when universal vaccination was stopped, the incidence of

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influenza encephalopathy increased sharply, and >100 encephalopathy deaths were reported annually during 1995–1999 [5–7]. A total of 783 young children were estimated to die of influenza encephalopathy during the 11 years from 1990 through 2000 [3]. The increased mortality among young children was attributable to the reduction in vaccine coverage rates among schoolchildren. Therefore, the Japanese universal vaccination program for schoolchildren not only protected older persons against influenza-associated mortality, but also protected younger siblings of schoolchildren.

Nevertheless, the prime question of whether the universal vaccination program was effective in controlling influenza outbreaks in schools has never been answered, even though failure to control them was the main reason that the Japanese government gave for abandoning the universal vaccination program. To demonstrate the effectiveness of the universal vaccination program for schoolchildren in controlling outbreaks in schools, we investigated influenza vaccine coverage rates, total number of class cancellation days, and absentee rates in a single elementary school during the 24-year period from 1984 through 2007.

**SUBJECTS AND METHODS**

**School**

The school that was the subject of this study is located in the urban area of Tokyo, Japan. Approximately 800 pupils (range, 780–846 children) aged 6–12 years were enrolled in the school each year during the period from 1984 through 2007, and there were 6 grades. Each grade consisted of 3 classes of 44 students each.

**Vaccine Coverage Rate**

Until 1994, the children attending the school were vaccinated against influenza at school twice per year—in November and again in December. The vaccine coverage rate each year was recorded at the school. We investigated the vaccine coverage rates during 1995–2007 based on the vaccination certificates submitted to the school by the parents; children were vaccinated by their own physicians during this period.

**Class Cancellations**

School policy was to cancel a class when >20% of the pupils in the class were absent. Class cancellation was usually continued for 3 days. The total number of class cancellation days was calculated as follows: If 1 class was cancelled for a total of 3 days, and the other 2 classes at the time were also cancelled for 3 days each, then the total number of class cancellation days that season was 9 days.

The only influenza season when a large outbreak occurred in the school was the 1994–1995 season, and because the class cancellation policy was temporarily suspended, we excluded the 1994–1995 season from the calculation of class cancellation days. The entire school was never closed because of an influenza outbreak during the 24-year study period.

Because the number of class cancellation days is smaller when the scale of influenza epidemics is small, regardless of the vaccine coverage rate in the school, we excluded small-scale epidemics based on the Tokyo surveillance data [8], in addition to excluding the 1994–1995 season, when we tested the correlation between the number of class cancellation days and vaccine coverage rates. As a result, we excluded a total of 6 seasons in which the peak reported number of influenza cases/week/sentinel was <20 (ie, 1986–1987, 1993–1994, 1995–1996, 1996–1997, 2000–2001, and 2001–2002 seasons) (Table 1).

**Absentee Rates**

The number of absent pupils because of influenza was estimated on the basis of the school’s attendance records. The weekly absentee rate (the number of absentees/total number of pupils/school days of the week) during the period from December through March was calculated every season. The week with the highest absentee rate was considered to be the peak week of an influenza outbreak in the school, and we assumed that most absent pupils were absent because they had influenza.

We compared the vaccination rates and the peak absentee rates in the school during the 24-year period. Except in the 2000–2001 season, the weeks with the highest absentee rates from school coincided with the peak weeks of the influenza epidemics in Tokyo [8] (Figures S1–S4; online only). Although our study was not laboratory confirmed, the method that we used in this study likely largely excluded the impact of other infectious diseases on the absentee rate. We checked the absentee rate during the third week of October of the same season as a control.

Because the absentee rate is lower, regardless of the vaccine coverage rate, when the scale of an influenza epidemic is small, the same as the number of the class cancellation days, we excluded the 6 small-scale epidemics based on the Tokyo surveillance data [8]—the same as described in the Class Cancellation section (Table 1)—and calculated the correlation between the absentee rates and the vaccine coverage rates.

**Statistical Methods**

We used paired t test for all statistical comparisons of mean values. Data were expressed as mean values ± standard deviation [SD]. The vaccine coverage rates and both the numbers of class cancellation days and absentee rates were analyzed for correlations by using Pearson’s coefficients.

**RESULTS**

**Vaccine Coverage Rates at the School**

The vaccine coverage rates at the school reflected vaccine production in Japan (Figure 1). We divided the 24 influenza seasons
into 5 periods (Table 1). During 1984–1987, which was the compulsory vaccination period, mean vaccine coverage was 96.5%. In 1987, new legislation allowed parents to refuse influenza vaccination of their children, and during 1988–1994, the quasi-compulsory vaccination period, the mean vaccine coverage rate was 66.4%. The government abandoned the mass vaccination of schoolchildren in 1994, and the mean vaccine coverage rate decreased to only 2.4% during 1995–1999, the no-vaccination period. There was a large decrease in the vaccination rate, and during 1996, only 1 of the 786 pupils received influenza vaccine (Table 1). After 2000, the mean vaccine coverage rate rebounded to 38.9% in the low voluntary vaccination period during 2000–2003, and in the high voluntary vaccination period during 2004–2007, the mean rate increased to 78.6%.

### Class Cancellation

Classes were cancelled in 13 of the 24 influenza seasons during 1984–2007, and the total number of days a year that class was cancelled during that period ranged from 2 to 59 days (Table 1, Figure 2). The mean number of days that class was cancelled was 1.3 days in the compulsory vaccination period, compared with 8.3 days in the quasi-compulsory vaccination period, and the number peaked at 20.5 days in the no-vaccination period. The mean number of class cancellation days then decreased in the voluntary vaccination period. These data show that vaccination of the schoolchildren against influenza, whether compulsory or voluntary, was effective in reducing class cancellations at the school.

The correlation between the vaccine coverage rates and the number of class cancellation days in the 24 seasons overall was not statistically significant ($r = -0.359; P = .0924$). However, when the 1994–1995 season and the 6 seasons in which there were only minor epidemics were excluded (Table 1), there was a significant inverse correlation between the vaccine coverage rates and number of class cancellation days in the 17 remaining influenza seasons ($r = -0.644; P = .0042$) (Figure 3).

The main circulating virus in 6 of the 13 seasons in which classes was cancelled was influenza B virus, and it was influenza A (H3N2) virus during 5 seasons (Table 1). The number of class cancellation days was highest, 59 days, during the 1998–1999 influenza B epidemic, and second highest, 37 days, during the 1992–1993 influenza B epidemic.

### Table 1. Vaccine Coverage, Numbers of Class Cancellation Days and Absentee Rates in the School, and Reported Number of Influenza Patients and Epidemic Virus in Tokyo, 1984–2007

<table>
<thead>
<tr>
<th>Period</th>
<th>Year</th>
<th>Vaccine coverage, %</th>
<th>No. of class cancellation days</th>
<th>Absentee rate, %</th>
<th>No. of influenza cases/wk/sentinel</th>
<th>Epidemic virus</th>
<th>Mean vaccine coverage rate, %</th>
<th>Mean no. of class cancellation days</th>
<th>Mean absentee rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Compulsory vaccination period</strong></td>
<td>1984</td>
<td>96.5</td>
<td>0</td>
<td>2.3</td>
<td>23.6</td>
<td>A (H1N1)</td>
<td>96.5</td>
<td>1.3</td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td>1985</td>
<td>96.0</td>
<td>5</td>
<td>3.8</td>
<td>53.0</td>
<td>B</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>1986</td>
<td>96.7</td>
<td>0</td>
<td>2.2</td>
<td>40.2</td>
<td>A (H3N2)</td>
<td>62.0</td>
<td>9.3</td>
<td>3.9</td>
</tr>
<tr>
<td></td>
<td>1987</td>
<td>96.7</td>
<td>0</td>
<td>1.9</td>
<td>14.8</td>
<td>A (H1N1)</td>
<td>66.4</td>
<td>20.5</td>
<td>4.3</td>
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<td>1988</td>
<td>81.0</td>
<td>4</td>
<td>3.6</td>
<td>29.3</td>
<td>B</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>1989</td>
<td>67.0</td>
<td>0</td>
<td>1.9</td>
<td>27.7</td>
<td>A (H1N1)</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>1990</td>
<td>67.1</td>
<td>0</td>
<td>3.5</td>
<td>43.3</td>
<td>A (H3N2)</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
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<tr>
<td></td>
<td>1991</td>
<td>60.1</td>
<td>17</td>
<td>5.1</td>
<td>28.5</td>
<td>A (H3N2)</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>1992</td>
<td>68.1</td>
<td>0</td>
<td>2.4</td>
<td>32.3</td>
<td>A (H1N1)</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>1993</td>
<td>63.0</td>
<td>37</td>
<td>4.6</td>
<td>32.4</td>
<td>B</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>1994</td>
<td>62.0</td>
<td>0</td>
<td>1.3</td>
<td>8.7</td>
<td>A (H3N2)</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
</tr>
<tr>
<td><strong>Quasi-compulsory vaccination period</strong></td>
<td>1995</td>
<td>0.4</td>
<td>Not Done(^c)</td>
<td>5.3</td>
<td>36.3</td>
<td>A (H3N2)</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>1996</td>
<td>0.1</td>
<td>0</td>
<td>2.6</td>
<td>18.1</td>
<td>A (H1N1)</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
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<tr>
<td></td>
<td>1997</td>
<td>0.3</td>
<td>2</td>
<td>2.6</td>
<td>19.0</td>
<td>B</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>1998</td>
<td>0.3</td>
<td>21</td>
<td>4.7</td>
<td>47.8</td>
<td>A (H3N2)</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
</tr>
<tr>
<td><strong>No vaccination period</strong></td>
<td>1999</td>
<td>11.0</td>
<td>59</td>
<td>6.3</td>
<td>27.6</td>
<td>B</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>2000</td>
<td>31.0</td>
<td>7</td>
<td>4.6</td>
<td>22.3</td>
<td>A (H1N1)</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>2001</td>
<td>37.9</td>
<td>4</td>
<td>2.2</td>
<td>4.7</td>
<td>A (H1N1)</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>2002</td>
<td>42.0</td>
<td>3</td>
<td>2.9</td>
<td>13.8</td>
<td>B</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
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<td></td>
<td>2003</td>
<td>44.6</td>
<td>23</td>
<td>5.9</td>
<td>28.1</td>
<td>A (H3N2)</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
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<td></td>
<td>2004</td>
<td>71.3</td>
<td>15</td>
<td>3.0</td>
<td>25.6</td>
<td>A (H3N2)</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
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<tr>
<td></td>
<td>2005</td>
<td>80.6</td>
<td>0</td>
<td>4.4</td>
<td>43.3</td>
<td>B</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
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<tr>
<td></td>
<td>2006</td>
<td>83.6</td>
<td>13</td>
<td>4.2</td>
<td>25.8</td>
<td>A (H3N2)</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>2007</td>
<td>78.7</td>
<td>0</td>
<td>3.6</td>
<td>23.0</td>
<td>B</td>
<td>66.4</td>
<td>8.3</td>
<td>3.2</td>
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\(^b\) The peak reported number of influenza cases/wk/sentinel in Tokyo.

\(^c\) The class cancellation policy was not in effect in the 1994–1995 season.
Absentee Rate

The mean absentee rate (±SD) in the third week of October in the 24 seasons was 0.81% ± 0.27%, and the mean absentee rate (±SD) during the peak week of the influenza epidemics in the 24 seasons was 3.54% ± 1.38%. The difference in the mean absentee rate between the peak week of the influenza epidemics and the third week of October as a control was 2.7% (95% confidence interval [CI], 2.1–3.3; P < .0001). Thus, when an influenza outbreak occurred in the school, the absentee rate increased to ~4 times the usual rate.

The mean absentee rate in the compulsory vaccination period was 2.5%, compared with 4.3% in the no-vaccination period (Table 1), and thus, had increased by 1.7 fold (2.5% vs 4.3%) during the same period as the vaccine coverage rate decreased from 96.5% to 2.4% (Table 1, Figure 4). The absentee rate decreased slightly from 4.3% in the no-vaccination period to 3.8% in the high voluntary vaccination period, despite a marked increase in vaccine coverage rate from only 2.4% to 78.6%.

There was no statistically significant correlation between the vaccine coverage rates and the absentee rates in the 24 seasons overall (r = −0.348; P = .0957), but when the 6 seasons in which there were minor epidemics were excluded (Table 1), there was a statistically significant inverse correlation between the vaccine coverage rates and the absentee rates in the 18 remaining influenza seasons (r = −0.668; P = .0018) (Figure S5; available online).

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**Figure 1.** Vaccine production in Japan and vaccine coverage rates in the school during the period from 1984 through 2007.

**Figure 2.** Vaccine coverage rates and numbers of class cancellation days in the school during the period from 1984 through 2007.
High absentee rates of >4% were recorded in 9 of the 24 seasons. In 5 of the 9 seasons, the cause was influenza A (H3N2), and in 3 seasons, it was influenza B (Table 1).

Relation Between the Numbers of Class Cancellation Days and Absentee Rates
Figure 5 shows the changes in the mean absentee rates and the mean class cancellation days. The mean number of class cancellation days varied markedly and inversely reflected the vaccine coverage rate. By contrast, the mean absentee rate varied minimally, with the highest absentee rate (6.3%) being recorded during the 1998–1999 epidemic, which was caused by influenza B. The total number of class cancellation days was also highest (59 days) during that season (Table 1).

Vaccine Strains and Epidemic Strains
During the compulsory vaccination period, there was a good match between the vaccine strains and the circulating viruses. However, in the influenza B epidemic of 1984–1985, class cancellations occurred (Table 1). During the 1992–1993 season, the epidemic influenza B virus was antigenically almost identical to the vaccine strain [9, 10], but a severe influenza outbreak occurred in the school. High absentee rates were recorded during 2004–2005 and 2006–2007, although the circulating influenza B viruses closely matched the vaccine strains.


DISCUSSION
We reviewed the influenza outbreaks over a 24-year period in a single elementary school, where the dramatic changes in mean vaccine coverage rates from a high of 96.5% in the compulsory vaccination period to only 2.4% in the no-vaccination period and the rebound to 78.6% in the voluntary vaccination period (Table 1, Figure 1) provided a golden opportunity to verify the effectiveness of the mass vaccination of schoolchildren. The results of our study revealed that the mass vaccination of schoolchildren was effective in reducing both the number of class cancellation days and absenteeism in the school.

An influential report in which the authors concluded that the universal vaccination of schoolchildren was much less effective in reducing absenteeism in schools during influenza epidemics convinced the Japanese government to stop its mass vaccination program for schoolchildren [11]. The authors compared the absentee rates during 2 consecutive influenza
seasons (1983–1985) in schools in Maebashi City, where mass vaccination had been totally abandoned, and schools in a neighboring city, Takasaki City, where vaccination was strongly recommended (vaccine coverage rate, 85%). The results revealed that the effectiveness of influenza vaccination in reducing school absenteeism was only 5% during the influenza B epidemic of 1983–1984 and 27% in the influenza A (H3N2) epidemic of 1984–1985. It was a large study that included the >40,000 pupils in all of the elementary schools in the 2 cities.

Another report, however, suggested that the mass vaccination of schoolchildren in Japan was effective [4, 12]. The authors of that report investigated the vaccine coverage rates and the percentages of class cancellation in every school in Nara City during the influenza B epidemic of 1981–1982, and the results showed a definite decrease in the percentage of class cancellations in schools in which the vaccine coverage rate was >50%. However, even this study reported only slight effectiveness of influenza vaccination in reducing absenteeism in the schools.

Some reports in the English-language literature suggest that influenza vaccination is not effective in reducing school absenteeism. King et al [13] reported finding no significant differences in rates of school absenteeism between schools that participated in a vaccination program with trivalent live attenuated influenza vaccine (CAIV-T), in which 47% of pupils were vaccinated, and control schools. However, Piedra et al [14] found good protection in vaccinated children, but the small proportion vaccinated (<20%) did not reduce the medically attended acute respiratory illness rate in their invaccinated school contacts.

If the effectiveness of mass vaccination for schoolchildren were assessed on the basis of absenteeism in a school, it would probably be low or, sometimes, questionable. The changes in absentee rates were small in comparison with the changes of the numbers of class cancellation days in our study (Figure 5). However, the 24-year observation period allowed us to demonstrate the effectiveness of the mass vaccination program in reducing absenteeism in the school.

Recently, it was shown that influenza vaccine provides 2 kinds of effectiveness: conventionally recognized effectiveness in protecting against illness and a newly recognized effectiveness in protecting against transmission [13, 15–17]. It is suggested that the protection against infectiousness or transmission of infection by vaccines is greater than their protection against illness [14]. Although the absentee rates in our study directly paralleled the rates of protection against illness, there were no clear differences between the no-vaccination period and the vaccination period (Figure 4, and 5), and explosive outbreaks that lead to class cancellation were prevented in the vaccination period, probably because of protection against transmission (Figure 2, and 5).

In the 1960s, Monto et al [18] reported that mass vaccination of schoolchildren was effective in protecting young children, adults, and schoolchildren against respiratory illness. The vaccine coverage rate was high (>86%) in their study, and in our own study, when the mean vaccine coverage was 96.5% in the compulsory vaccination period, the mean absentee rate was the lowest (2.5%) (Table 1, Figure 4). Thus, a much higher vaccine coverage rate, such as 80–90%, is necessary to lower the absentee rate in a school.

In the United States, routine influenza vaccination is recently recommended for all persons aged ≥6 months [17]. On the basis of the experience with vaccination of schoolchildren in Japan, however, it will be rather difficult to reduce absence from school. Instead, if there is a moderate increase in the vaccination rate in schools, by protection against transmission (ie, by herd immunity), the impact of influenza epidemics on the community may decrease [1, 2].

An important feature of school influenza outbreaks became clear in this study: Influenza B virus plays a major role in school
outbreaks. Both the largest and the second largest outbreaks during the 24-year period were caused by influenza B virus strains (Table 1). Of interest, influenza B outbreaks occurred in the school even when vaccine coverage was high and antigen match was good. This finding is at least partially attributable to the fact that current influenza vaccine is less effective against influenza B [9]. It was also reported that influenza B epidemics were an important cause of illness among schoolchildren in a multiyear study in New York City [19]. By contrast, school outbreaks caused by influenza A, mostly A (H3N2) virus strains, always occurred when antigenically drifted strains appeared. Thus, mass vaccination programs can efficiently prevent influenza A outbreaks in schools, if the vaccine strains match the circulating viruses.

In conclusion, the mass influenza vaccination of schoolchildren was effective in reducing the number of class cancellation days and absenteeism in the school. It was reported that the universal vaccination program in Japan for schoolchildren protected older persons [2] and younger siblings of the schoolchildren [3] by the vaccine-generated protection against transmission. However, the universal vaccination did not have a clear-cut effect in decreasing the absentee rates in schools, and that led to discontinuation of the program in 1994 by the Japanese government. The indirect protection of the older population and young siblings against influenza by the universal vaccination program for schoolchildren was not recognized in Japan at that time.

**Supplementary Data**

Supplementary materials are available at Clinical Infectious Diseases online (http://www.oxfordjournals.org/our_journals/cid/). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyrighted. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

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Potential conflicts of interest. N. S. has been an advisor to Shionogi and a technical advisor to Daiichi Sankyo and has received speaker’s honoraria from Chugai and Taisho-Toyama. All other authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed in the Acknowledgments section.

**References**