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J.TWMU 2: 21-30, 2018

Original

Predicting Influenza Outbreak in One Nursery and in the Community Using the Nursery and School Absenteeism Surveillance System

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(Accepted October 11, 2018)
(Advance Publication by J-STAGE November 22, 2018)

Since 2013, all nurseries and elementary/junior high schools (schools hereinafter) in Sumida ward, Tokyo participate in the Nursery and School Absenteeism Surveillance System (NaSASSy). Nurseries and schools report the number of absentees in each class by diagnosis and by symptom every business day via the web system. We predicted the date of seasonal influenza outbreak in a nursey using real-time data of influenza in nurseries and schools in Sumida ward directly accessible from NaSASSy, which would allow the nursery to plan preventive measures. Outbreak was defined as occurrence of the second case in a school or nursery. Incidence rates and epidemic curves of influenza for Nursery H (150 children in 2013) were compared with those for all nurseries (4,460 children) and all schools in Sumida during four seasons (2013/2014 to 2016/2017). In three seasons, the initial case in Nursery H occurred at a minimum of 41 days and a maximum of 89 days after detection of the second case in schools. In four seasons, the initial case in Nursery H occurred at a minimum of 21 days after detection of the second case in all nurseries. Season with high incidence rate alternated with season with low rate. In seasons when Nursery H had high incidence rates, the 5-year-old class always had high rates. In conclusion, real-time detection of influenza outbreak in the community by NaSASSy and using the second case in schools as an indicator of outbreak is useful for nurseries to predict the coming outbreak and plan preventive measures.

Key Words: Nursery and School Absenteeism Surveillance Systems (NaSASSy), outbreak, infection, surveillance, influenza

Introduction

Effective countermeasures to avoid infectious disease outbreak and to minimize its size require early detection, information sharing, and immediate response. Syndromic surveillance is utilized globally to identify disease outbreak early before diagnoses are confirmed[1)2)], and has contributed to public health. The most important information source for syndromic surveillance is electronic medical records both in Japan[3)] and overseas[4)5)]. However, electronic medical records have limited usage for syndromic surveillance in Japan, because patient behavior differs even among people with similar symptoms due to personal preferences; some visit medical doctors, others purchase over-the-counter (OTC) drugs at a pharmacy or do nothing[6)]. For syndromic surveillance in Japan, information sources from outside medical facilities have been utilized, such as ambulance transfer[7)],

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doi: 10.24488/twmuj.2018009

OTC drug sales[8], and prescriptions presented to pharmacies[9)10)]. Prescription surveillance at pharmacies contributed to real-time monitoring of seasonal influenza activity and information sharing nationwide during the 2009 influenza season[9)]. However, its application is still limited to influenza, varicella, and herpes zoster, because the system monitors only prescriptions and not diagnosis.

Innovative method for the prediction of influenza epidemic using search trends of big data, the Google Flu Trends, was reported[11)], which attracted attention. However, the method has limitations. Since health seeking behavior differs among individuals due to personal preferences, health conscious healthy people may be the ones who search heavily. Google Flu Trends has been pointed out to overestimate flu prevalence and that only increasing the quantity of data does not improve the quality of analysis[12)]. Search trends cannot be superior to the real data surveillance.

Many countries have implemented surveillance systems in nurseries and schools[13)-21)], which record total absenteeism of all causes or illnesses, but do not reveal the reasons of absence. In Japan, the Nursery and School Absenteeism Surveillance System (NaSASSy) was developed in 2007 by a research group, funded by the Ministry of Health, Labour and Welfare. The system for elementary schools and junior high schools was released in 2009 and utilized in all schools in nine prefectures as a prevention measure for pandemic influenza. In 2010, it was updated for nurseries. The NaSASSy is used by both schools and nurseries. Currently, NaSASSy is operated by the Japanese Society of School Health. At the end of 2016, NaSASSy covered approximately 37,000 schools (60% of all schools) and 10,000 nurseries (40% of all nurseries) in Japan. It monitors the health conditions of approximately four million children younger than eighteen years of age on a daily basis. Sumida ward introduced NaSASSy to all nurseries in August 2013, and then to all schools on April 1, 2014.

Designated staff at schools and nurseries inputs data on every business day. The input items are: absences, fever, headache, acute respiratory symptoms, diarrhea/abdominal pain, nausea/vomiting, rash, influenza-like symptoms, class closure, and attendance suspension due to (influenza, infectious gastroenteritis, others). The data are updated real-time. The updated marked area map (https://scl11.953862.net/schoolkoukai/view_all.php) is then shown, and feedback can be obtained on the screen immediately. It is a computerized system with detailed real-time data comprising integrated information regarding children's health conditions and network of information sharing among organizations and individuals. When a child is affected by infectious disease and is absent from a nursery, usually the child's caregiver gives information of the cause of absence to the nursery. Nurseries require caregivers to report physical conditions, symptoms, visit to medical institution and diagnosis based on the Guidelines for Infection Control at Nursery School from the Ministry of Health, Labor, and Welfare[22)]. Then, nurses and teachers at the nursery report the information to NaSASSy via the web system. The importance of recording physical conditions of children and recognizing the situation in the community are emphasized in the guidelines[22)].

Information sharing via NaSASSy promotes early awareness of infectious diseases, leading to immediate responses at the initial stage of outbreak in nurseries[23)]. Nurseries utilize the real-time information provided by NaSASSy to recognize the situation in the surrounding community. The information can be disseminated to teachers, students, and caregivers, as well as shared among doctors associated with nurseries, educational board members in the community, local government officers responsible for nurseries, public health center, and local medical association, thereby promoting precautions when an outbreak is detected in the surrounding community.

Influenza outbreak occurs almost every winter and has the highest incidence rate in nursery children. In the 2014/2015 influenza season, the NaSASSy data for Sumida ward revealed that influenza outbreak started in junior high school students first, then in younger school children, and finally in children attending nurseries during the latter half of the season[24)]. Children who attend nurseries usually live in the neighborhood, and since they cannot go out by themselves, their area of activity is narrow. On the other hand, school children go out and meet more people in the community, and their area of activity is wider. However, the relation of influenza outbreak in a specified nursery and that in all schools in Sumida ward has not been examined. Consequently, the present study

focused on one nursery in Sumida ward, where we previously investigated the absence days per year by age of children to estimate the days of leave required for working mothers to nurse a sick child[25]. All nurseries and schools in Sumida ward participate in NaSASSy.

In this study, we examined the incidence curves of influenza in that nursery in relation to those in all schools and nurseries in the same school district during four consecutive influenza seasons, in an attempt to predict the date of seasonal influenza outbreak using real-time data of influenza in nurseries and schools in Sumida ward directly accessible from the NaSASSy database, which would allow the nursery to plan preventive measures.

Methods

In 2017, Nursery H in Sumida ward had 19 0-year-old children, 24 1-year-old children, 25 2-year-old children, 28 3-year-old children, 28 4-year-old children and 28 5-year-old children, with a total of 152 children. Sumida ward initiated NaSASSy in all nurseries in August 2013, and then in all elementary and junior high schools (schools hereinafter), and kindergartens on April 1, 2014. At the end of the study period (2017), the number of 0 to 5-year-old children in all nurseries in Sumida ward was 6,716, while the number of elementary school students was 9,557 and that of junior high school students was 4,005.

The data for this study was obtained from NaSASSy using the ID number and password assigned to Nursery H. In NaSASSy, influenza is defined as showing symptoms such as influenza-like illness or a diagnosis of influenza. Hence, a child who has influenza-like symptoms but negative result by rapid diagnostic test is counted as a case of influenza. The influenza season is defined from the beginning of September to the end of March of the next year. The study period covered four seasons from 2013/2014 to 2016/2017. Since schools started NaSASSy from April 1, 2014, the study period for schools was limited to three seasons, excluding the 2013/2014 season.

All the dates of influenza detection as well as the numbers of children in all nurseries including Nursery H, elementary schools, and junior high schools in Sumida ward were downloaded from NaSASSy on March 31, 2017. We extracted the time of case detection and calculated the incidence rate by season for Nursery H, all nurseries, and all schools in Sumida ward. The time intervals between detection of cases in all schools and all nurseries were calculated. The time interval between the first case and second case (in another class) in Nursery H was also calculated. In this study, the start of influenza outbreak was defined as the time of occurrence of "the second case in a class or in a nursery or school during the season".

Results

In three seasons, the shortest interval from the second case of all schools in Sumida Ward [A] to the first case in Nursery H [C] was 41 days in 2016/2017 season, from the second case of all nurseries [B] to [C] was 21 days in 2013/2014 season, and from [C] to the second case (other class) in Nursery H [D] was 7 days (**Table 1**).

When influenza incidence rates by age in Nursery H were compared to those in all nurseries in Sumida ward, Nursery H had higher incidence rates of influenza than all nurseries in Sumida ward in the 2014/2015 and 2016/2017 seasons (every other season) (**Fig. 1**). In the 2013/2014 season, the incidence rates were 15.3% (23 children) in Nursery H and 20.1% (898 children) in all nurseries in Sumida ward. In the 2014/2015 season, the rates were 23.3% (35 children) in Nursery H and 14.8% (962 children) in all nurseries. In the 2015/2016 season, the rates were 13.2% (20 children) in Nursery H and 15.9% (1,074 children) in all nurseries. In the 2016/2017 season, the rates were 29.3% (44 children) in Nursery H and 19.2% (1,289 children) in all nurseries (**Table 1**).

Figure 2-5 show the dynamics of incidence rates of influenza by age in Nursery H compared to all nurseries and all schools in Sumida Ward for the four seasons. Since the time of outbreak started differently every season, the horizontal axes of the graphs showed slightly different periods; from November to February in the 2013/2014, 2014/2015 and 2016/2017 seasons, and from December to March in the 2015/2016 season.

In the 2013/2014 season (**Table 1** and **Fig. 2**), outbreak in nurseries was detected on December 24, and the initial case in Nursery H was detected on January 14, with an interval of 21 days. The second case in Nursery H (different class from the first case) was detected on January 23, nine days after the initial case. The time of

Table 1 Outbreak of influenza by season: dates of outbreak start, intervals and incidence in Nursery H, all nurseries, and all elementary and junior high schools in Sumida ward

	Date of influenza detection				Time interval (days)			Incidence (%)			
	Second case in all schools in Sumida ward [A]	Second case in all nurseries in Sumida ward [B]	First case in Nursery H [C]	Second case (other class) in Nursery H [D]	Between [A] and [C]	Between [B] and [C]	Between [C] and [D]	All junior high schools in Sumida ward	All elementary schools in Sumida ward	All nurseries in Sumida ward	Nursery H
2013/2014 Season	*	December 24	January 14	January 23	*	21	9	*	*	20.1	15.3
2014/2015 Season	October 19	November 15	December 26	January 2	78	41	7	10.7	10.7	14.8	23.3
2015/2016 Season	October 20	October 20	January 18	January 25	89	89	7	10.3	15.2	15.9	13.2
2016/2017 Season	October 18	October 18	Novermber 28	December 5	41	41	7	9.5	14.6	19.2	29.3

*Data not available because schools in Sumida ward had not yet participated in NaSASSy in 2013.

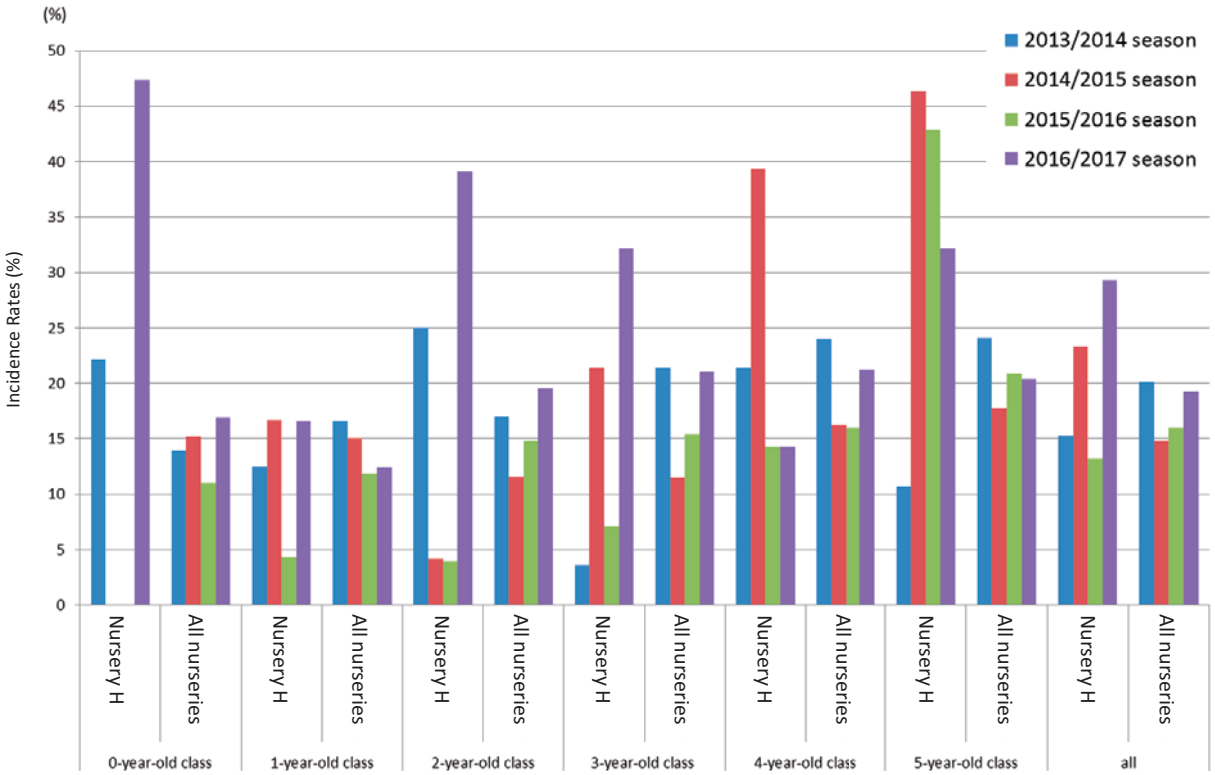

Fig. 1 Incidence rates of influenza by season and by age in Nursery H and in all nurseries in Sumida ward.
Note: Data not available because schools in Sumida ward had not participated NaSASSy in 2013/2014 season yet.

occurrence of the first case of influenza in each class in Nursery H was in ascending order of 2-year-old, 4-year-old, 1-year-old class, and 0-year-old. The incidence rate was the highest in the 2-year-old class. The 0-year-old class had the latest start of outbreak but relatively high incidence rate.

In the 2014/2015 season (**Table 1** and **Fig. 3**), outbreak started in schools on October 19 and in nurseries on November 15. In Nursery H, the first case was detected on December 26, and was 78 and 41 days later than the outbreak in all schools and nurseries, respectively (**Table 1**). The second case (different class from

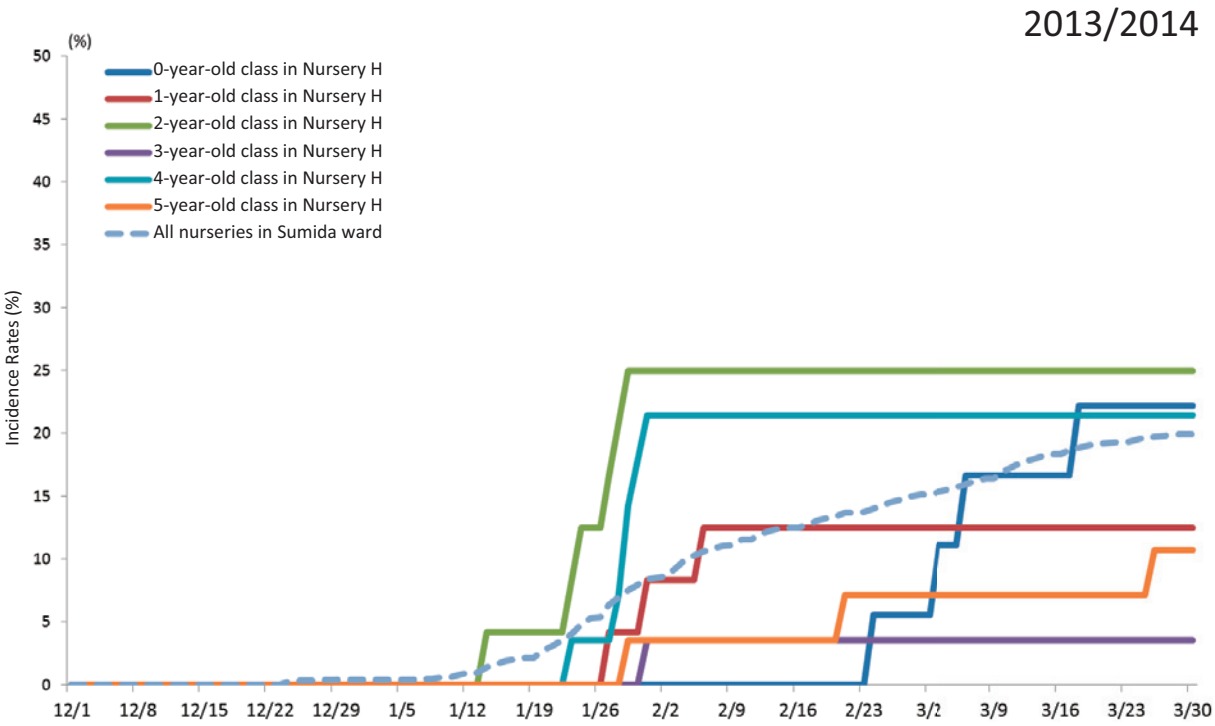

Fig. 2 Dynamics of incidence rates of influenza by age in Nursery H compared with all nurseries in Sumida Ward in the 2013/2014 season. Data of all elementary and junior high schools are not available because schools in Sumida ward had not yet participated in NaSASSy in 2013.

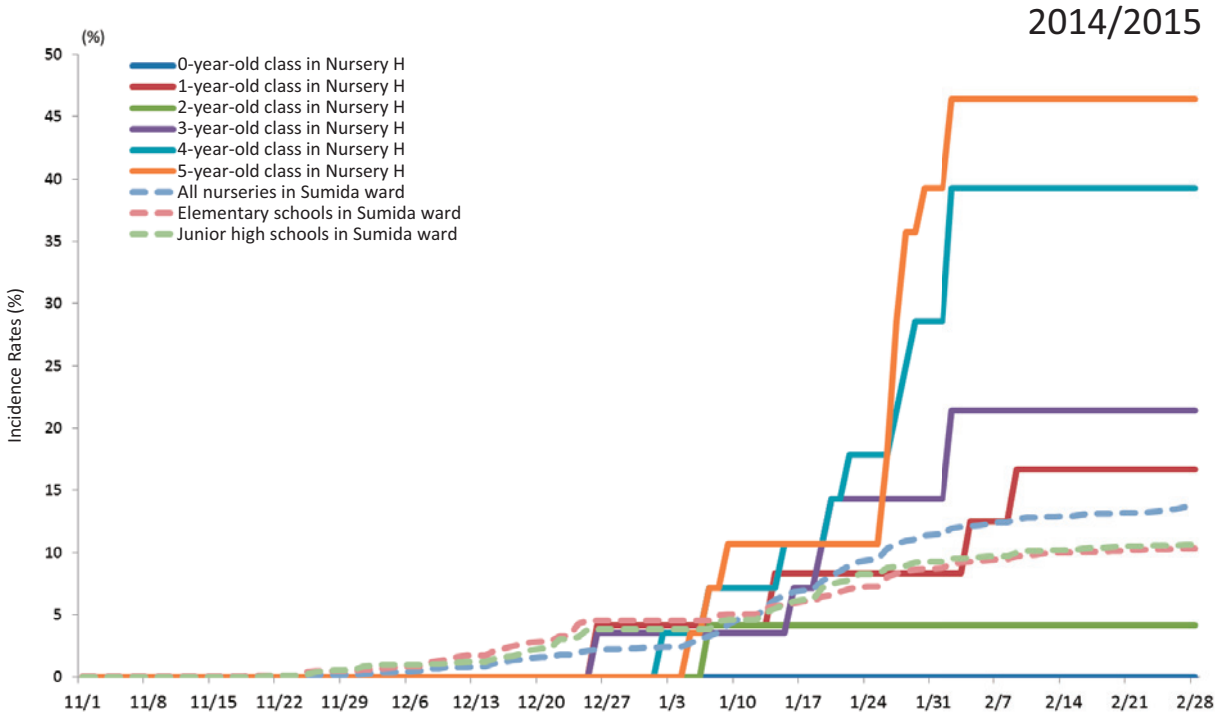

Fig. 3 Dynamics of incidence rates of influenza by age in Nursery H compared with all nurseries, and all elementary and junior high schools in Sumida Ward in the 2014/2015 season

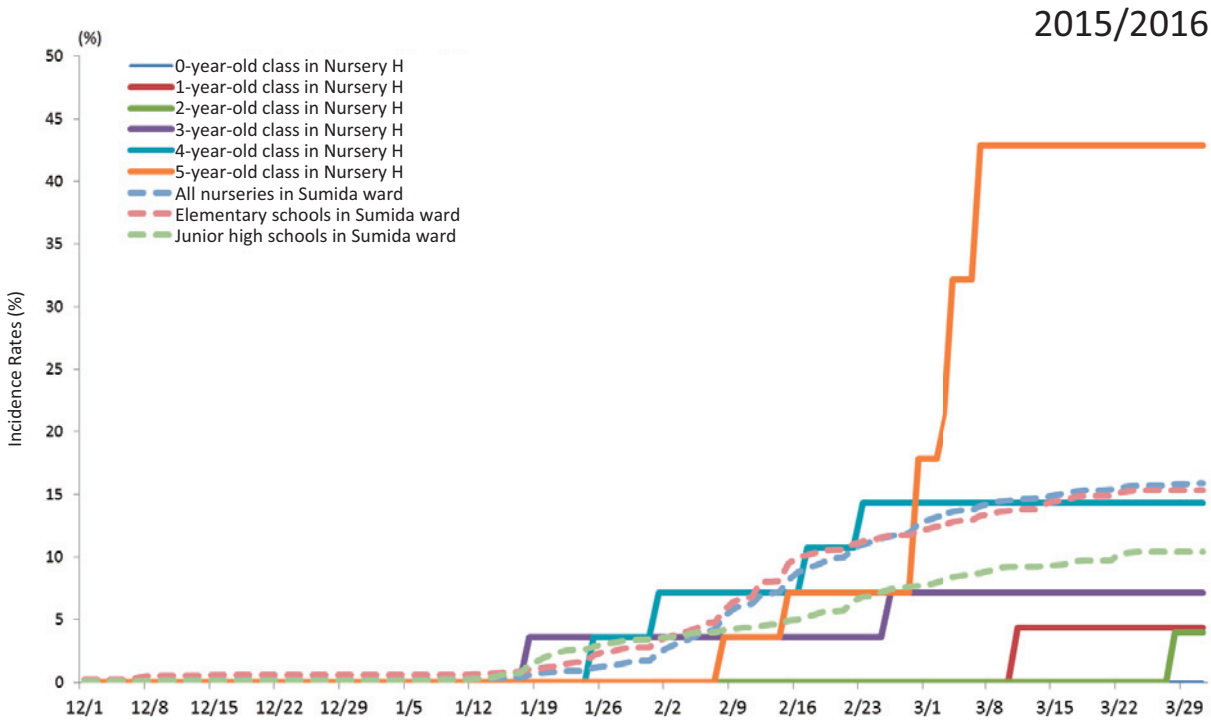

Fig. 4 Dynamics of incidence rates of influenza by age in Nursery H compared with all nurseries, and all elementary and junior high schools in Sumida Ward in the 2015/2016 season

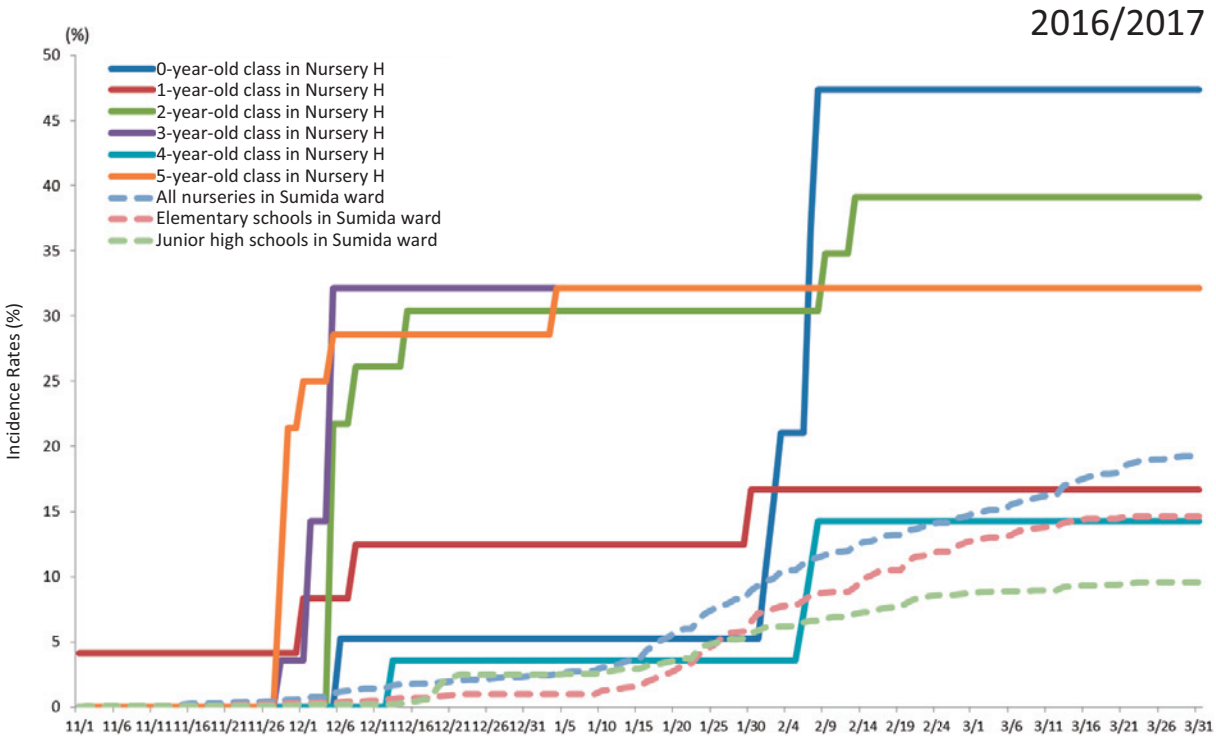

Fig. 5 Dynamics of incidence rates of influenza by age in Nursery H compared with all nurseries, and all elementary and junior high schools in Sumida Ward in the 2016/2017 season

the first case) in Nursery H was detected on January 2, seven days after the initial case. In Sumida ward, outbreak started in schools and then spread to nurseries. In Nursery H, outbreak occurred in 3-year-old class first followed by 4-year-old and 5-year-old classes. For the whole season, 5-year-old class had the highest incidence rate compared to the average incidence rate in all nurseries in Sumida ward, followed by 4-year-old and 3-year-old classes.

In the 2015/2016 season (**Table 1** and **Fig. 4**), outbreak in schools and nurseries occurred on the same day; October 20. In Nursery H, the first case was detected on January 18, and was 89 days later than the outbreak in schools and nurseries. The second case in Nursery H (different class from the first) was detected on January 25, seven days after the initial case. In Sumida ward, outbreak started in junior high schools and elementary schools and then spread to nurseries. In Nursery H, influenza occurred in 3-year-old class first, followed by 4-year-old and 5-year-old classes. For the whole season, 5-year-old class had the highest incidence rate, followed by 4-year-old class (**Fig. 4**). The incidence rate in Nursery H was higher than that in all nurseries in Sumida ward.

In the 2016/2017 season (**Table 1** and **Fig. 5**), outbreak in schools and nurseries occurred on the same day; October 18. In Nursery H, the first case was detected on November 28, and was 41 days after the outbreak in schools. Another case in other class of Nursery H was detected on December 5, and was 7 days after the initial case in Nursery H. In Sumida ward, outbreak started in nurseries and elementary schools first, and then spread to junior high schools. In Nursery H, outbreak occurred in 5-year-old class first, followed by 3-year-old children. For the whole season, 0-year-old class had the highest incidence rate, followed by 2-year-old class and then 5-year-old class. Outbreak in 0-year-old class started later but the size was the largest in Nursery H, and the incidence rate was higher than the average incidence rate in all nurseries in Sumida ward.

The cumulative incidence rate in Nursery H was higher than that in all nurseries in the 2014/2015 and 2016/2017 seasons, but lower in the 2013/2014 and 2015/2016 seasons (**Table 1**). When cumulative incidence rate in Nursery H was higher than that in Sumida ward, the rates were particularly higher in 4-year-old and 5-year-old classes (cumulative incidence rates in 0-, 1-, 2-, 3-, 4- and 5-year-old classes were 17.5%, 12.63%, 17.7%, 16.0%, 22.3% and 33.0%, respectively).

Discussion

The present study suggested that nurseries may predict the date of influenza outbreak from NaSASSy that has large data with complete coverage, with sufficient time to plan appropriate protective measures for the children. In this study, we defined the start of influenza outbreak as the time of occurrence of "the second case in a class or in a nursery or school during the season". The reasons for this definition are as follows. First, Dr. Tamie Sugawara who provided insightful suggestions for our study noticed an unpublished phenomenon that the date of occurrence of the second case in schools may be a quantitative indicator for prediction of outbreak in nurseries within the school district. To the best of our knowledge, the present report is the first to use this definition. Second, we did not use the first case for the definition to avoid sporadic cases that do not lead to outbreak.

In each of the four seasons studied, after the second case was detected, the incidence rate increased gradually and was never interrupted. When the third case is detected, the outbreak has already established and there is not sufficient time for effective responses such as recommendation of vaccination for children.

When the second case of influenza occurs in the same class of a nursery as the first case, the second case is possibly infected by the first case when children in the same classroom play together, before the first case is suspended from attending the nursery. On the other hand, when the second case of influenza occurs in another class in a nursery, it is highly possible that the child is infected by the child's family members (parents, siblings, and others) or in the community where the child lives, and that influenza is already prevalent in the community. Therefore, we believe that the occurrence of a second case of influenza in another class of the nursery more realistically reflects the level of influenza activity in the community as a whole, both inside and outside the nursery.

In this study, influenza outbreak started earlier in the community of Sumida ward than in Nursery H during all four seasons, and the outbreak started in older children in

schools before spreading to younger children in nurseries. There was a time lag of approximately two months for nurseries from the time the epidemic was detected in schools, providing enough time for nurseries to take protective measures. Promotion of vaccination and cough etiquette to prevent droplet infection are valuable measures. Disseminating information to children in elementary and junior high schools is indispensable for prevention of outbreak in nurseries. Influenza vaccination for nursery children has to be given twice with an interval of four weeks. After the second case in schools is reported, signifying the start of regional epidemic, there is still time to implement vaccination in nursery children. On the other hand, when the second case in nurseries in Sumida ward is detected, the epidemic is already established, and it is too late to give warning about vaccination, because the shortest duration to outbreak in Nursery H observed in this study was shorter than the interval required for influenza vaccination. The interval of detecting the second case of influenza (in another class) in the same nursery is as short as one week, reflecting rapid spread because children of different classes participate in activities together in the facility. It should be noted that the risk of influenza-associated encephalitis and encephalopathy has been reported, especially in young children[26].

Environmental management of the facilities is also important. The incidence at Nursery H was certainly higher compared to other nurseries and schools in Sumida ward. The possible reasons are as follows. (1) Nursery H and a facility for after school care are located in the same building, sharing the same staircase and entrance. The after school care facility may influence the incidence of influenza in Nursery H. (2) The capacity of many nurseries in Sumida Ward is about 50 to 70 children, and only a few nurseries has a large capacity of 150 children, like Nursery H. (3) There were many influenza cases at the ages of 4 and 5, and these children may have been infected by their siblings attending elementary schools. Since this study was retrospective, Nursery H did not take extra control measures during the study periods. According to the present findings, Nursery H is expected to plan or reinforce measures in advance for the following influenza season.

It is important to share useful information of the trend of regional epidemic, to disseminate the information to children ahead of time, and to utilize the preventive activities. While it is possible to detect influenza at the early stage by NaSASSy, but when the third case is detected, the epidemic has already begun. Moreover, since the virus type causing epidemic may change, the vaccine sometimes does not match the current seasonal influenza type. Nursery H was chosen as a case study. By comparing the starting dates of influenza outbreak in schools, all nurseries and Nursery H, we found that the outbreak in Nursery H started later than that in schools by more than 40 days. This gives enough time for Nursery H to begin control measures as soon as the first outbreak in schools (defined as the second case) is confirmed. Our data provides initial evidence of the possibility to predict the date of outbreak of influenza for the current season in a nursery using real-time surveillance data, which allows timely implementation of control measures.

The School Health and Safety Act in Japan requires "suspension of attendance due to illness" for students at all levels of schools for the purpose of prevention of spread of infectious diseases such as influenza, varicella, and mumps. Under Japanese law, the schools include kindergarten, elementary school, junior high school, senior high school, and special support school. Students affected by infectious diseases should not attend school but should stay at home, so as not to transmit the disease to other students. Caregivers should notify the school when their children are diagnosed or not yet diagnosed with any of the designated infectious diseases. They usually telephone the school and report their children's symptoms such as fever, vomiting, and diarrhea, even though their children have not visited a doctor, and this system has worked well[23)24)27)28)]. However, nurseries are classified as welfare facilities, and not educational institutions. Therefore, the School Health and Safety Act does not apply to nursery children, and nurseries do not prohibit children from attending even though they have infectious diseases. Therefore, prevention by early detection becomes important.

Based on the Guidelines for Infection Control at Nursery School produced by the Ministry of Health, Labor, and Welfare, when a child is affected by infectious disease and is absent from a nursery, usually the child's caregiver give information of the cause of absence to the nursery. Then, nurses and teachers at the nursery input

the information to NaSASSy via the web system. The guidelines describe the importance of recording the physical conditions of children in their personal "health diary" as a measure against infectious diseases. The guidelines also emphasize the importance of knowing the situation in the community.

This study has some limitations. First, the small sample size in Nursery H does not represent the situation of infectious disease in the whole Sumida ward. Second, the second case of influenza in schools was used as the definition or indicator of outbreak in Sumida ward. We confirmed that this definition was correct within the limited situation of four influenza seasons in Sumida ward. There is a possibility that the second case in Sumida ward could occur at Nursery H. However, if the definition of start of outbreak as "the second case in schools" applies to a small area, the probability of occurrence is possible.

To verify the usefulness of the definition of influenza outbreak used in the study, further prospective study in a large number of nurseries is warranted. In the future, we would like to extend our research using NaSASSy to promote large epidemiological studies of other infectious diseases that require facilities to respond quickly.

Conclusions

Real-time detection of influenza outbreak in the community by NaSASSy and using the second case in schools as an indicator of outbreak are useful for nurseries to predict and prepare for the coming outbreak by disseminating information to children's caregivers to receive vaccination and enhance their preparedness.

Acknowledgments

This study was supported by a Grant-in-Aid for Scientific Research (C) No. 16K08884 from the Japan Society for the Promotion of Science. We also acknowledge Dr. Tamie Sugawara for her insightful suggestions and Dr. Teresa Nakatani for useful discussion.

Conflicts of Interest: The authors indicated no conflicts of interest.

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