



Effectiveness of vaccination and wearing masks on seasonal influenza in Matsumoto City, Japan, in the 2014/2015 season: An observational study among all elementary schoolchildren

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ABSTRACT

Measures of seasonal influenza control are generally divided into two categories: pharmaceutical and non-pharmaceutical interventions. The effectiveness of these measures remains unclear, because of insufficient study sample size and/or differences in study settings. This observational epidemiological study involved all elementary schoolchildren in Matsumoto City, Japan, with seasonal influenza during the 2014/2015 season. Questionnaires, including experiences with influenza diagnosis and socio-demographic factors, were distributed to all 29 public elementary schools, involving 13,217 children, at the end of February 2015. Data were obtained from 10,524 children and analyzed with multivariate logistic regression analysis. The result showed that vaccination (odds ratio 0.866, 95% confidence interval 0.786–0.954) and wearing masks (0.859, 0.778–0.949) had significant protective association. Hand washing (1.447, 1.274–1.644) and gargling (1.319, 1.183–1.471), however, were not associated with protection. In the natural setting, hand washing and gargling showed a negative association, which may have been due to inappropriate infection control measures or aggregating infected and non-infected children to conduct those measures. These results may indicate a pathway for influenza transmission and explain why seasonal influenza control remains difficult in school settings. The overall effectiveness of vaccination and mask wearing was 9.9% and 8.6%, respectively. After dividing children into higher (grades 4–6) and lower (grade 1–3) grade groups, the effectiveness of vaccination became greater in the lower grade group, and the effectiveness of wearing masks became greater in the higher grade group. These results may provide valuable information about designing infection control measures that allocate resources among children.

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1. Introduction

Measures of seasonal influenza control are generally divided into two categories: pharmaceutical interventions, such as vaccination, and non-pharmaceutical interventions (NPIs), not involving drugs (CDC, 2016b; WHO, 2005). Although vaccination is regarded as the most effective method of controlling the spread of influenza (CDC, 2016a; WHO, 2016), studies are needed to explore the effectiveness of vaccination and to determine the optimal type of vaccine, age at vaccination, and matching of vaccine to virus subtype (DiazGranados et al., 2012).

Moreover, the effectiveness of vaccination has been found to differ among age groups (Shinjo et al., 2015). Longitudinal epidemiological studies focused on the effectiveness of vaccines, including over several generations, are necessary.

In contrast to pharmaceutical methods, NPIs, which include wearing masks, hand washing and gargling, are designed to interfere with virus transmission (WHO, 2005). NPIs are used for infection control when pharmaceutical interventions such as vaccines are unavailable or inappropriate. Examples include the lack of vaccine to address a novel type of pandemic influenza virus or hypersensitivity to drugs. In addition, combinations of NPIs with pharmaceutical intervention may be more effective than either alone. However, studies assessing the effectiveness of NPIs have yielded inconsistent results (Aiello et al., 2010a; Smith et al., 2015), which may be caused by poor statistical power due to sample

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size or selection bias. Alternatively, randomized controlled trials may not always reflect the natural setting of an influenza epidemic.

Observational studies at the community level are required to clarify these issues. These studies should include an entire community in a natural setting, with all individuals, both those with and without influenza, evaluated to determine the effectiveness of vaccines and NPIs. This epidemiological study therefore evaluated seasonal influenza control methods in all elementary school children in Matsumoto City, Nagano Prefecture, Japan.

2. Methods

2.1. Study subjects

Before conducting the current study, a prospective first survey was performed to evaluate the dynamics of seasonal influenza during the 2014/2015 season (Uchida et al., 2016). At the end of the prospective survey period, questionnaires were administered to all subjects to obtain information about their experience with influenza infection. Briefly, the study subjects included all 13,217 schoolchildren attending all 29 public elementary schools in Matsumoto City, Nagano, Japan. Matsumoto City is a suburban area, with a population of about 240,000 individuals, located in the middle of Japan. Teachers and guardians were not included in the analysis. Questionnaires were distributed to all 13,217 schoolchildren, with answers returned by 11,390 children (response rate, 86.2%). After excluding questionnaires with missing data, 10,524 questionnaires were analyzed. To comprehensively determine the protective association and effectiveness of NPIs, all subjects were analyzed as a single group. Subjects were regarded as having seasonal influenza if they were diagnosed by physicians at medical institutions. Thus, 2149 schoolchildren (20.4%) were considered to have had influenza, a proportion similar to that in our first prospective survey in the same season (20.1%) (Uchida et al., 2016).

2.2. Ethics statement

The study was reviewed and approved by the Medical Ethics Board of Shinshu University School of Medicine (approval number 2715). Because this study was performed anonymously and questionnaires were returned voluntarily, informed consent was not obtained from study subjects.

2.3. Questionnaire and data sampling

Before the survey, study aims were explained to administrators of the board of education, the medical associations, public health centers and each school in Matsumoto City, with all providing approval. At the end of February 2015, questionnaires were distributed to school nurses. The nurses distributed questionnaires to class teachers, who, in turn, handed them to the guardians of all schoolchildren and requested their return within 1 week. Guardians were asked to answer questionnaires by themselves anonymously. Class teachers subsequently collected the questionnaires and gave them to the school nurses.

The questionnaire included questions about children's experiences with seasonal influenza during the 2014/2015 season (yes/no); if yes, the date of onset (calendar month), and diagnosis by a medical institution (yes/no). Because self-reported diagnosis at a medical institution is generally accepted criteria for infectious disease statistics at schools, we relied on and used this information. Sociodemographic factors for each child included sex (male/female), grade in school (description), and class (description). In Japan, as elementary school grades 1–6 correspond to ages 7–12 years old, their grade was used as the factor for age in this study. Questions also asked about any underlying disease associated with influenza-related complications (CDC, 2015) including cardiovascular disease, pulmonary disease, kidney disease, liver disease, nerve disease, muscle disease, blood disease and diabetes (description).

To determine associations with household-related infections, questions were asked about family members in the household (e.g. father, mother, grandfather, grandmother, brother, sister, others) and number of siblings (description). To assess the possibility of transmission among children, the questionnaire asked about places the child regularly goes at least once per week (description). Questions about interventions included vaccination during that influenza season (yes/no), and if yes, the date of vaccination (calendar month). To analyze individual infection control measures, questions asked about each child's use of NPIs at any place or time, including wearing a mask, hand washing, or gargling with water (yes/no). To determine prior experience with influenza, questions included whether the child had been diagnosed with seasonal influenza (yes/no) or vaccinated against influenza (yes/no) during the previous influenza season. All the questions included in this study were based on our previous survey (Uchida et al., 2016).

Guardians who had already filled out questionnaires in our first prospective study were specifically asked to fill out this questionnaire also. Data were input to a database by researchers or trained operators using standardized sorting methods.

2.4. Statistical analysis

Categorical data were compared by Chi-square tests. To determine the associations of infection control measures for individuals, the associations were evaluated by multiple logistic regression analysis and expressed as odds ratios (ORs) and 95% confidence intervals (95% CIs). In this multivariate analysis, explanatory variables were adjusted for each other and subjects with or without diagnosis were regarded as objective variables. To avoid multi-collinearity, Spearman's correlation analysis was used for the correlation matrix. If multi-collinearity was found, insignificant variables were not included in further analysis.

The simultaneous effects of infection control measures were not determined in this study. All analyses were performed with SPSS ver.22 (Chicago, IL, USA) and $P < 0.05$ was regarded as statistically significant.

This study gathered vaccination and diagnosis information about all subjects. In general, to assess the effect of infection control measures at the group level, the effectiveness of vaccination was calculated as follows:

$$1 - RR \text{ (Relative Risk).}$$

In this study, this formula was modified appropriately and expressed as follows:

$$1 - \left(\frac{\text{the number of vaccinated children with influenza}}{\text{the number of non-vaccinated children with influenza}} \right).$$

In addition, information was obtained about mask wearing at any place or time by all subjects. Because the equation was utilized to assess the effectiveness of NPIs (Aiello et al., 2008), it was applied to assess the effectiveness of wearing a mask:

$$1 - \left(\frac{\text{the number of children with influenza who wore a mask}}{\text{the number of children with influenza who did not wear a mask}} \right).$$

Furthermore, to evaluate whether effectiveness differed by age groups, elementary school children were subdivided into those in higher (grades 4–6) and lower (grades 1–3) grades. The above equations applied to each subgroup.

3. Results

Of the 10,524 children included in this survey, 2149 (20.4%) were diagnosed with influenza. None died of influenza. Almost all children were diagnosed using rapid diagnosis kits (96.4%), and the remainder were diagnosed based on symptoms of influenza-like illness as reported in a previous report (Uchida et al., 2016). There were no laboratory confirmed cases. During this influenza season, there were no major outbreaks in schools requiring school closure, but classes in 26 schools were temporarily closed. These closures may affect the study result, however, the closure effect was not evaluated in this study because data was limited and could not be linked with study subjects.

We found that 5063 (48.1%) children were vaccinated at least once during the 2014/2015 influenza season. Three strains of inactivated virus were included in the vaccine; A/California/7/2009(H1N1)pdm09, A/New York/39/2012(H3N2) and B/Massachusetts/2/2012 (National Institute of Infectious Diseases of Japan, 2015). NPIs included wearing masks by 5474 (52.0%) children, hand washing by 8322 (79.1%) and gargling by 7268 (69.1%). Sex distribution, and the percentages of children vaccinated during the influenza season, wearing a mask, hand washing and gargling differed significantly in children with and without influenza (Table 1). To evaluate the associations of individual infection control measures, factors were analyzed using a multiple logistic regression method (Table 2). Because multi-collinearity was observed between hand washing and gargling ($\rho(\text{rho}) > 0.7$, $P < 0.001$), and between vaccination during the current and previous seasons ($\rho > 0.7$, $P < 0.001$), only hand washing and vaccination during the current season were included in the analysis. There were no correlations between other variables ($\rho < 0.3$). Vaccination during the influenza season (OR 0.866, 95% CI 0.786–0.954) and wearing a mask (OR 0.859, 95% CI 0.778–0.949) showed significant protective association. In contrast, hand washing was not associated with protection (OR 1.447, 95% CI 1.274–1.644). A similar finding was observed when hand washing was replaced by gargling (OR 1.319, 95% CI 1.183–1.471).

As the questionnaires included information about vaccination and diagnosis at medical institutions, the effectiveness of vaccination was

Table 1

Characteristics of the study population and difference between cases and non-cases in Matsumoto City, Japan, in the 2014/2015 season.

Factors	Respondents n = 10,524	Cases n = 2,149	(%) 20.4	Non-cases n = 8,375	(%) 79.6	#P value
Sex	Male	5372	1139	21.2	4233	78.8
	Female	5152	1010	19.6	4142	80.4
Grade	1	1844	408	22.1	1436	77.9
	2	1795	366	20.4	1429	79.6
	3	1756	344	19.6	1412	80.4
	4	1734	377	21.7	1357	78.3
	5	1692	323	19.1	1369	80.9
	6	1703	331	19.4	1372	80.6
Underlying disease	Yes	1116	219	19.6	897	80.4
	No	9408	1930	20.5	7478	79.5
Number of siblings	1	1584	313	19.8	1271	80.2
	2	5673	1144	20.2	4529	79.8
	3	2797	599	21.4	2198	78.6
	≥4	470	93	19.8	377	80.2
Regularly go out	Yes	9392	1897	20.2	7495	79.8
	No	1132	252	22.3	880	77.7
Vaccination in this season	Yes	5063	978	19.3	4085	80.7
	No	5461	1171	21.4	4290	78.6
Mask wearing	Yes	5474	1069	19.5	4405	80.5
	No	5050	1080	21.4	3970	78.6
Hand washing	Yes	8322	1778	21.4	6544	78.6
	No	2202	371	16.8	1831	83.2
Gargling	Yes	7268	1561	21.5	5707	78.5
	No	3256	588	18.1	2668	81.9
Influenza in previous season	Yes	3359	689	20.5	2670	79.5
	No	7165	1460	20.4	5705	79.6
Vaccination in previous season	Yes	5374	1135	21.1	4239	78.9
	No	5150	1014	19.7	4136	80.3

Chi-square test.

Table 2

Protective association of vaccination and NPIs using multivariate model in Matsumoto City, Japan, in the 2014/2015 season.

Factors	Respondents	n = 10524	OR	95% CI	P value
Sex	Female	5152	1.000		
	Male	5372	1.091	0.990	1.203
Grade	Lower grade	5395	1.000		
	Higher grade	5129	0.973	0.884	1.071
Underlying disease	No	9408	1.000		
	Yes	1116	0.959	0.819	1.122
Sibling	No	1584	1.000		
	Yes	8940	1.037	0.907	1.186
Regularly go out	No	1132	1.000		
	Yes	9392	0.881	0.758	1.024
Vaccination in this season	No	5461	1.000		
	Yes	5063	0.866	0.786	0.954
Mask wearing	No	5050	1.000		
	Yes	5474	0.859	0.778	0.949
Hand washing	No	2202	1.000		
	Yes	8322	1.447	1.274	1.644
Influenza in previous season	No	7165	1.000		
	Yes	3359	0.996	0.899	1.103

#Factors adjusted for each other using a multiple logistic regression model.

determined. Of all children, 20.4% had been diagnosed, including 20.1% in the higher grade (grades 4–6) group and 20.7% in the lower grade (grades 1–3) group. The effectiveness of vaccination in all children was 9.9% (Table 3a), 1.5% in children in higher grades and 17.4% in children in lower grades (Table 3b, c). Similarly, the effectiveness of wearing a mask was 8.6% in all schoolchildren (Table 4a), 12.0% in children in grades 4–6 and 5.3% in children in grades 1–3 (Table 4b, c).

4. Discussion

This study was conducted to evaluate the association between seasonal influenza and individual infection control measures among schoolchildren in Matsumoto City, Japan, using observational epidemiological methods. In general, cross-sectional methods are inappropriate in evaluating infectious diseases because some indirect effects, such as herd immunity, cannot be considered in sampling and a cause-and-effect relationship cannot be determined. However, as this survey evaluated all schoolchildren attending all 29 public elementary schools in Matsumoto City, this was a census with reduced likelihood of sampling bias. This study showed that vaccination and wearing a mask reduced the likelihood of developing seasonal influenza. In contrast, hand washing and gargling were associated with a greater likelihood of developing seasonal influenza. Moreover, when schoolchildren were divided by grade, the effectiveness of vaccination and wearing a mask differed between higher and lower grade schoolchildren.

The seasonal influenza epidemic of 2014/2015 started at the end of November 2014 in Japan and peaked during the fifth week of 2015 (National Institute of Infectious Diseases of Japan, 2015), with similar start and peak times in Nagano Prefecture, in which Matsumoto City is located (Nagano Prefecture, 2015). In the national survey and the local survey, the epidemic curve showed an immediate decline after the

Table 3a

Effectiveness of vaccination in all schoolchildren in Matsumoto City, Japan, in the 2014/2015 season.

All schoolchildren	Not vaccinated	Vaccinated	Effectiveness
Non-case	4290	4085	
Case	1171	978	
Total	5461	5063	
Proportion (%)	21.4	19.3	9.9

Table 3b
Effectiveness of vaccination in higher grade (grades 4–6) schoolchildren.

Higher grade group	Not vaccinated	Vaccinated	Effectiveness
Non-case	2263	1835	
Case	574	457	
Total	2837	2292	
Proportion (%)	20.2	19.9	1.5

fifth week. At the end of February, few cases were found from reports of schools, therefore, almost all elementary schoolchildren cases in Matsumoto City were able to be analyzed. Most people affected had influenza virus subtype AH3 (National Institute of Infectious Diseases of Japan, 2015), with over 95% of symptomatic individuals diagnosed with subtype A, as determined by rapid diagnosis kits. Infection with influenza subtype B virus was rare during this period.

The main aim of this study was to explore factors preventing seasonal influenza among schoolchildren. A logistic regression model was used to analyze the association between children affected by influenza and individual influenza control measures. Vaccination (OR 0.866) and wearing a mask (OR 0.859) showed protective association against seasonal influenza. Vaccination has shown efficacy against seasonal influenza (DiazGranados et al., 2012; Luksic et al., 2013), especially when compared with placebo, in studies conducted in school settings (Cowling et al., 2010, 2014). Because vaccine strain was not matched fully with the virus type during this season (National Institute of Infectious Diseases of Japan, 2015), protective association was not greater than that in a season when strain and virus type was matched. This lack of protective association may also have been due to the disparity between timing of vaccination and the period of seasonal influenza. Because the influenza season of 2014/2015 started earlier than other years, the vaccination schedule was relatively late. In addition, because individuals who had been vaccinated at least once were included in the vaccination group, the protective association of vaccine might have been underestimated in this study.

This study also showed that wearing a mask reduced the likelihood of seasonal influenza. A randomized clinical trial found that medical staff members who used a mask correctly had a decrease in virus transmission (MacIntyre et al., 2015). Although less is known about the efficacy of wearing a mask in community settings, wearing a mask showed efficacy in young adults (Aiello et al., 2010b, 2012). This study found that wearing a mask had significant protective association among schoolchildren in a community setting.

Hand washing and gargling showed significant increases in OR for seasonal influenza. In contrast, hand washing and gargling were efficacious in laboratory and experimental settings (Grayson et al., 2009; Satomura et al., 2005). A meta-analysis also showed that hand washing had efficacy in a community setting (Aiello et al., 2008). These inconsistent results may have been due to study design, in that previous analyses included only interventional studies, not natural observational studies. Subjects in interventional studies may be more careful in use of NPIs, by, for example, using correct methods of hand washing and water gargling. However, in natural settings, infection control measures are left to subjects to perform, and it is possible that they might not perform them appropriately. This observational study in a natural setting found that hand washing and gargling increased the likelihood of seasonal influenza, suggesting that hand washing and gargling in schools

Table 3c
Effectiveness of vaccination in lower grade (grades 1–3) schoolchildren.

Lower grade group	Not vaccinated	Vaccinated	Effectiveness
Non-case	2027	2250	
Case	597	521	
Total	2624	2771	
Proportion (%)	22.8	18.8	17.4

Table 4a
Effectiveness of mask wearing in all schoolchildren in Matsumoto City, Japan, in the 2014/2015 season.

All schoolchildren	Without mask	With mask	Effectiveness
Non-case	3970	4405	
Case	1080	1069	
Total	5050	5474	
Proportion (%)	21.4	19.5	8.6

were not performed appropriately. For example, if schoolchildren washed their hands or gargled together with infected children, influenza may have spread within schools. Because influenza virus can survive on materials (Bean et al., 1982), transmission through faucets and knobs may have occurred, making it important to prevent virus transmission through materials (Collignon and Carnie, 2006). Moreover, those measures aggregated children including infected and non-infected children and the virus might have transmitted easily among children, instead. Thus, NPIs performed individually, such as wearing a mask, tend to be protective, whereas NPIs performed in groups, such as hand washing and gargling, result in the spread of infection. These results may explain why seasonal influenza is not always controlled, despite implementation of hand washing and water gargling in school settings. Thus, because NPIs have been considered a single category, interpretation of efficacy was difficult (Aiello et al., 2010a, 2012; Cowling et al., 2009; Simmerman et al., 2011; Smith et al., 2015), suggesting that NPIs should be evaluated individually. However, because this study was cross-sectional in design, cause-and-effect relationships could not be determined. In addition, the frequency of NPI was not included in this study. This lack of information remains a validity issue of the study result. Further research evaluating effects of frequency of NPIs performed in groups is necessary.

Information was obtained from all schoolchildren in Matsumoto City, both those with and without seasonal influenza. Because vaccination and wearing a mask showed protective association in these children, their effectiveness was further evaluated. Vaccination had an effectiveness of about 10%, suggesting that vaccination provides little protection. In general, vaccine effectiveness is thought to be around 50%, and it ranges from 10% to 60%. The variation is considered due to differences in study design, outcomes measured, population studied, and the season in which the flu vaccine was studied (CDC, 2016a). Because vaccinated individuals in this study were defined as those vaccinated at least once, and each influenza case was based on symptomatic information, the effectiveness of vaccination may have been underestimated. Moreover, vaccination may not have been fully matched to the virus during that influenza season (National Institute of Infectious Diseases of Japan, 2015). However, the 10% effectiveness we observed was similar to that of a study, performed two years earlier, reporting that the effectiveness of vaccination in a community setting was 13% (Suzuki et al., 2014). Taken together, these results indicate that influenza vaccination may have about 10% effectiveness in natural settings. Other experimental studies have reported higher effectiveness in hospital (Treanor et al., 2012) and community (Loeb et al., 2010) settings. These discrepancies may have been due to differences in study methods.

To evaluate the effects of vaccination and NPIs on different age groups, the study population was divided into of children in higher

Table 4b
Effectiveness of mask wearing in higher grade (grades 4–6) schoolchildren.

Higher grade group	Without mask	With mask	Effectiveness
Non-case	1860	2238	
Case	509	522	
Total	2369	2760	
Proportion (%)	21.5	18.9	12.0

Table 4c
Effectiveness of mask wearing in lower grade (grades 1–3) schoolchildren.

Lower grade group	Without mask	With mask	Effectiveness
Non-case	2110	2167	
Case	571	547	
Total	2681	2714	
Proportion (%)	21.3	20.2	5.3

(grades 4–6) and lower (grades 1–3) grades. Although there were no significant linear effect trends across grades 1–6 when comparing children grouped by school grade, comparison of dichotomous groups (higher grades and lower grades) revealed differences. Therefore, to show differences of effectiveness among grades, we used a simple dichotomous analysis in this study. The effectiveness of vaccination was found to be 1.5% in higher grade and 17.4% in lower grade subjects. This disparity may have been affected by vaccine coverage, which was 44.7% in higher grades and 51.4% in lower grades. Moreover, differences in the effectiveness of vaccination between children in elementary school and kindergarten may reflect differences in activities (Suzuki et al., 2014), suggesting that differences in vaccination effectiveness between higher and lower grade elementary schoolchildren may have been due to differences in activity. In addition, vaccination was recently reported to be less protective in older than in younger schoolchildren (Shinjoh et al., 2015) and this may explain partly the disparity of effectiveness found in the age groups in the present study. We could only report the difference of vaccine effectiveness which this study found without giving a clear explanation of the cause, to which extent this is a limitation and its discussion may be limited. However, we could show actual epidemiological data concerning over 10,000 individuals in the study population. This study may induce a follow-up study to elucidate precise reasons for the difference in effectiveness among generations.

This study also assessed the effectiveness of wearing masks, using a method similar to that used to evaluate the effectiveness of NPIs (Aiello et al., 2008). We found that mask wearing had an effectiveness of 8.6% in all schoolchildren. Similarly, a randomized controlled study found that wearing a mask reduced influenza transmission among outpatients in a medical institution (Cowling et al., 2009). However, another study found that wearing a mask did not reduce the second attack ratio within households (Simmerman et al., 2011). In contrast to vaccination, wearing a mask was found to be much more effective in higher than in lower grade schoolchildren. This difference may be associated with the greater ability of higher grade children to control their own activities. In contrast, the greater effectiveness of vaccination in lower grade schoolchildren may be associated with their lower ability to control their own activities. This finding may be useful in determining the allocation by grade of limited or insufficient resources to infection control measures in case of pandemic influenza.

This study had several limitations. First, because this study was based on a questionnaire survey and rapid diagnosis kits, blood samples were not obtained. This may have reduced the number of children with influenza, by not including asymptomatic or mild symptomatic individuals not diagnosed at medical institutions. However, questionnaires have been regarded as acceptable for large public health epidemiological surveys. Assessing only those symptomatic for influenza is considered acceptable in natural settings when the study results will be used within educational organizations. Better interpretation of study results should also include asymptomatic and mildly symptomatic individuals, as they can transmit influenza virus. Second, this study assessed elementary schoolchildren, but did not include other individuals, including children in kindergarten and junior high school. Because interactions among children of different ages are important in the spread of infectious diseases, future studies should include children in other grades. Third, because this study was cross-sectional and evaluated influenza during only one season, the results may not apply generally. Moreover,

rapid diagnosis kits or school closures which are usually administrated in Japan may not be usual in several countries, therefore, generalization of the present study result may be limited. Fourth, use of NPIs was not evaluated quantitatively, only qualitatively, with answers scored as yes or no; therefore, the effectiveness of each NPI may not have been estimated precisely. This should be clarified in future studies.

5. Conclusion

This observational study of seasonal influenza during the 2014/2015 season among all elementary schoolchildren in Matsumoto City, Japan, found that vaccination and wearing a mask were protective in a natural setting but hand washing and gargling were not. This finding may provide evidence on one method of influenza transmission and explain why seasonal influenza control is still difficult in school organizations. Elementary schoolchildren should receive additional education about appropriate methods of hand washing and gargling, and further studies should evaluate hand washing and gargling in natural community settings. The effectiveness of vaccination and wearing a mask differed between schoolchildren in grades 1–3 and grades 4–6, suggesting that infection control methods in these age groups should also differ. These results may provide valuable information about designing infection control measures that allocate resources among children.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

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