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Original Article

A primary school outbreak of pandemic 2009 influenza A (H1N1) in China

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Background We investigated the first known outbreak of pandemic 2009 influenza A (H1N1) at a primary school in China.

Objectives To describe epidemiologic findings, identify risk factors associated with 2009 H1N1 illness, and inform national policy including school outbreak control and surveillance strategies.

Methods We conducted retrospective case finding by reviewing the school's absentee log and retrieving medical records. Enhanced surveillance was implemented by requiring physicians to report any influenza-like illness (ILI) cases to public health authorities. A case–control study was conducted to detect potential risk factors for 2009 H1N1 illness. A questionnaire was administered to 50 confirmed cases and 197 age-, gender-, and location-matched controls randomly selected from student and population registries.

Results The attack rate was 4% (50/1314), and children from all grades were affected. When compared with controls, confirmed cases were more likely to have been exposed to persons with respiratory illness either in the home or classroom within 7 days of symptom onset (OR, 4·5, 95% CI: 1·9–10·7). No cases reported travel or contact with persons who had traveled outside of the country.

Conclusions Findings in this outbreak investigation, including risk of illness associated with contacting persons with respiratory illness, are consistent with those reported by others for seasonal influenza and 2009 H1N1 outbreaks in school. The outbreak confirmed that community-level transmission of 2009 H1N1 virus was occurring in China and helped lead to changes in the national pandemic policy from containment to mitigation.

Keywords Outbreak, pandemic 2009 influenza H1N1, school.

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Introduction

On April 15 and 17, 2009, the United States Centers for Disease Control and Prevention confirmed the first two cases of human infection with pandemic 2009 influenza A (H1N1) virus.[1] On May 11, the first confirmed case of 2009 H1N1 infection in mainland China was identified.[2] Following this initial report, the number of confirmed 2009 H1N1 cases in China rose steadily. On June 11, 2009, the World Health Organization (WHO) declared that the first influenza pandemic of the 21st century had begun.[3]

By mid-June, a total of 265 confirmed sporadic 2009 H1N1 cases had been reported across China through national surveillance, but community-level transmission of the virus was not believed to have been established and, therefore, national policy was focused on containment. On June 18, 2009, a primary school in Dongguan City, Guangdong Province, China reported 20 students absent from one class because of fever and acute respiratory symptoms. This unusually high absentee rate during the early stage of the pandemic prompted the school teacher to notify the local health department, and a joint investigation team from the Chinese Center for Disease Control and Prevention and local CDC arrived at the school that same day to initiate an epidemiologic investigation. Among students absent from school, six were laboratory-confirmed as 2009 H1N1 on June 19 by a positive real-time reverse transcription polymerase chain reaction (rRT-PCR) test. As the pandemic evolved in China, we conducted an epidemiological investigation of the first known outbreak of 2009 H1N1 to describe epidemiologic findings, identify risk factors associated with 2009 H1N1 illness, and inform national policy including school outbreak control and surveillance strategies.

Methods

The investigation team conducted retrospective case finding by reviewing the school's absentee log and retrieving medical records from the local hospitals. We also implemented enhanced surveillance in the local hospital and the community clinic by requiring physicians to report any influenza-like illness (ILI) and suspect 2009 H1N1 cases. A case–control study was conducted to detect potential risk factors for 2009 H1N1 illness.

Setting

The town contains nine villages with 12 primary schools, one middle school, and 15 kindergartens. Medical care for residents of the nine villages is provided by one community clinic and one hospital. The outbreak occurred in the only primary day school of village A. The school has an enrollment of 1314 students aged 6–13 in 32 classes with six grades and 97 teachers and staff. The school does not provide a bus for transportation and does not have a cafeteria.

Case definitions

A case of ILI was defined as a resident of the town that had sudden onset of fever ≥38°C and either cough or sore throat. To estimate the impact of outbreak in the school, we defined, for this investigation, a suspect 2009 H1N1 case as a student or staff member of the school with ILI. A confirmed 2009 H1N1 case was defined as a person with ILI and laboratory evidence of 2009 H1N1 virus infection diagnosed by rRT-PCR testing of a throat swab.

Retrospective case finding and prospective enhanced surveillance

The parents of initial six confirmed 2009 H1N1 influenza cases were interviewed. The earliest date of symptom onset for these cases was June 16. We reviewed the school's absentee log to identify any student or staff member who was absent since June 9 to account for an estimated incubation period of up to 7 days before the earliest case's symptom onset date. We then administered a brief questionnaire to all students and staff who were absent during this time to identify additional suspect cases.

From the date of school closure (June 19) until 14 days later (July 2, 2009), prospective enhanced surveillance was implemented immediately in the hospital and the community clinic using the ILI and suspect case definitions to detect more cases from community transmission and from the school outbreak, respectively. Physicians were asked to identify and report any ILI and suspect 2009 H1N1 cases.

Specimen collection and laboratory testing

Throat swabs obtained from suspect cases and patients with ILI had been placed in sterile viral transport medium and tested by rRT-PCR following the WHO standard protocol.[4] These assays were performed in biosafety level two facilities of Dongguan CDC laboratory.

Data collection

All suspect cases reported by physicians were interviewed using a brief questionnaire that asked about demographics and symptoms. All confirmed cases were later interviewed using a structured questionnaire that collected more detailed information, including potential exposure to patients with respiratory illness within 7 days before symptom onset and clinical presentations.

Case management

All suspected case–patients who were evaluated by a physician were immediately admitted to the hospital for isolation, consistent with national policy at the time of the outbreak. Patients who tested negative for 2009 H1N1were discharged, while those tested positive were isolated in the hospital until 48 hours after resolution of symptoms.

Matched case–control study

One week after the outbreak was detected, a case–control study was conducted to identify potential risk factors for 2009 H1N1 illness. All confirmed cases were eligible to be enrolled in the study. Up to four randomly selected controls, including two school controls and two community controls, were matched to each case by gender, age (±1 year) and location. Student registries from the school and population registries from each case's village were used to identify eligible age- and gender-matched school and community controls, respectively; the two potential controls were selected using randomly generated numbers from the list of eligible controls. Eligible school control subjects were pupils at the same school but not in the same class with any suspected or confirmed cases, while community control subjects were pupils from the same village, if possible, who neither in the same family nor in the same primary school with the matched case. Because most confirmed cases were residents of village A, an additional four community controls matched to two cases living in village A were recruited from adjacent village B. Controls were not eligible if they reported any history of ILI since June 9. Beginning June 27, 2009, the parents or grandparents of cases and controls were interviewed in person or by telephone using the structured questionnaire described earlier.

Statistical analysis

Questionnaire data were entered in duplicate and verified by using EpiData software. Descriptive statistics included frequency analysis for categorical variables and medians and ranges for continuous variables. The Wilcoxon rank-sum test was used to compare continuous variables, and chi-square test or Fisher's exact test was used for discrete variables in bivariate analyses.

Baseline characteristics of cases and controls and independent associations between potential risk factors and 2009 H1N1 illness were compared using an exact conditional logistic regression model. Matched odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. For multivariable exact conditional logistic analyses, we initially included variables that had $P \leq 0{\cdot}10$ in the bivariate matched analyses. Backward conditional logistic regression was performed by excluding variables with $P > 0{\cdot}10$.

Statistical analysis was performed using SPSS (v13.0, SPSS Inc., Chicago, IL, USA). For all analyses, probabilities were 2-tailed and a P-value of <0·05 was considered statistically significant.

Ethical review

Cases and controls provided verbal consent to participate in this investigation. Because both the enhanced system and the case–control study were conducted by public health authorities as part of an emergency outbreak investigation, this study was designated as public health response by the China CDC without a need for institutional review board approval.

Results

Retrospective case finding and prospective surveillance

From June 9 to 17, school's absentee log and brief questionnaire helped us to identify 9 (0·7%) of 1314 students as suspect H1N1 cases with illness onset dates ranging from June 10–17 (Figure 1). All nine suspected cases attended the school while symptomatic except for the day of symptom onset.

Throat swabs were taken from 13 (65%) of the 20 absent students on June 18, and six were confirmed with 2009 H1N1 infection. After the school closed on June 19, an additional 76 (97%) swabs were obtained from 78 suspect student cases identified during following enhanced surveillance, and 44 were confirmed with 2009 H1N1 infection. Thus, a total of 50 were confirmed with 2009 H1N1 virus infection. There were no suspect H1N1 cases found among staff members. The median age of confirmed cases was 8 years (range: 6–11). Thirty-three (66%) were men, and all were previously healthy, except for one who reported asthma. More than half of the confirmed cases lived in village A where the school was located. The median household size of confirmed cases was 4 (range: 2–8). None of the confirmed cases reported traveling outside the town within the week before symptom onset (Table 1).

Illness onset dates of confirmed cases from the school ranged from June 16 to June 20 and the peak occurred on June 18 and 19. All confirmed patients experienced fever, by definition, with a median axillary temperature recorded as 38·6°C (range: 38·4–39·8°C). All confirmed patients were evaluated by physicians in a hospital or a clinic within a median of 0 days (range: 0–2) after illness onset and were admitted to hospital for respiratory isolation within a

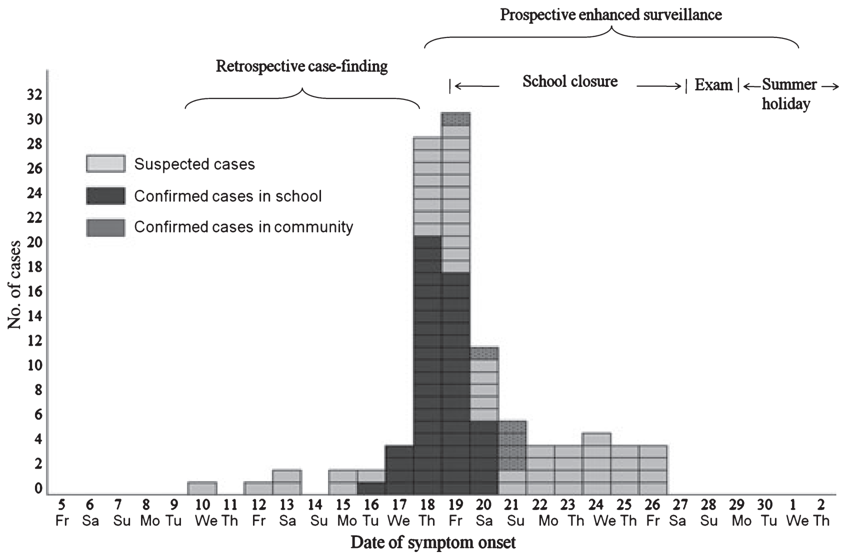

Figure 1. Epidemiologic curve of the first detected 2009 H1N1 school outbreak in China, 2009.

Table 1. Demographic, clinical characteristics, and exposures of cases in school outbreak in China, 2009

Characteristics	Suspect cases (*N* = 48)	Confirmed cases (*N* = 50)
Demographic characteristics		
Age (year), Median(range)	8 (6–13)	8 (6–11)
Men (%)	18 (38)	33 (66)
Residence (%)		
Village A where school located	33 (69)	37 (74)
Other villages	15 (31)	13 (26)
Population size of household		
Median no. of family members (range)	4 (2–12)	4 (2–8)
Medical history (%)		
With underlying medical conditions	0	1 (2)
Influenza vaccination within the past year	N/A	9 (18)
Signs and symptoms (%)		
Fever	48 (100)	50 (100)
Cough	19 (40)	41 (82)
Sore throat	6 (13)	16 (32)
Running nose	10 (21)	5 (10)
Diarrhea	1 (2)	0
Medical consultation (%)		
Consult with physicians	43 (90)	50 (100)
Exposure history (%)		
Contact with person with respiratory illness or laboratory-confirmed cases	6 (13)	31 (62)
Relationship with the contacted person		
Classmate	3 (6)	21 (68)
Sibling	1 (2)	8 (26)
Parents	1 (2)	1 (3)
Neighbor	1 (2)	1 (3)

median of 1 day (range: 0–7) after illness onset. None of the confirmed patients developed signs or symptoms of lower respiratory tract disease such as tachypnea and all had normal CXRs. Twelve (24%) confirmed patients were treated for 5 days with oral oseltamivir (75 mg twice daily for nine patients, 45 mg twice daily for two, and 60 mg twice daily for two, respectively) beginning at a median of 2 days (range: 0–6) after illness onset. As of July 4, all confirmed patients recovered fully and were discharged.

In addition to the suspected cases identified in the school, 173 ILI cases were identified from the community that sought medical consultation in the town from June 19 to July 2. Throat swabs were obtained from 15 (9%) of them because of limited testing resources, and six were confirmed with 2009 H1N1 infection. Of these, two were adults (aged 32 and 47), and four were children (aged 6, 3, 3, and 2), respectively.

Attack rates

Children in all grades were affected by the outbreak. Twenty-six (81%) classes were affected, while four (13%) had only confirmed cases and seventeen (65%) had only suspect cases. Both suspect and confirmed cases were identified in five (16%) classes. Neither suspect nor confirmed cases were identified in six (19%) classes. The overall ILI attack rate was 7% (98/1314) among all pupils. The attack rate for confirmed cases was 4% (50/1314), including 4% (33/780) among boys and 3% (17/534) among girls. The suspected and confirmed case attack rates among the pupils were also calculated by school year and class (Figure 2), ranging from 2% (1/43) to 59% (24/41) for confirmed cases and 2% (1/42) to 18% (9/51) for suspected cases.

School closure

The primary school affected by the outbreak was closed from Friday, June 19, until Sunday, June 28, and all schools in the town were closed from Monday, June 22 until Sunday, June 28. All students were required to stay home. Teachers and parents were required to promptly report to the local CDC about any students with ILI symptoms. Before school closure, few school children attended extracurricular classes together after school, and, of those that did, these activities only involved students in the same school year. Extracurricular classes were canceled as soon as the outbreak was identified. Persons with ILI were advised to stay home for 7 days after symptom onset or until 48 hours after fever resolution whichever was longer, to cover their cough, and to wash their hands frequently.

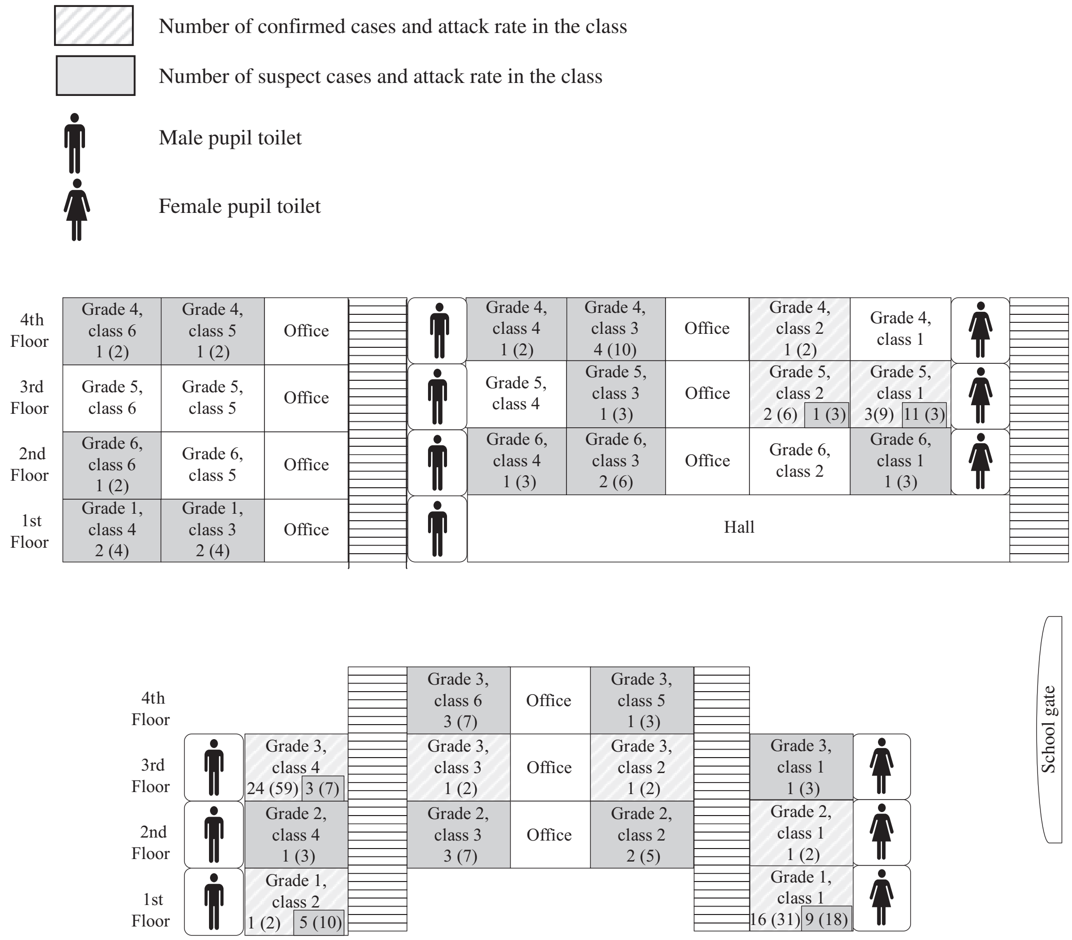

Figure 2. Map of the school, with number of confirmed and suspected cases and attack rate by class in the first detected 2009 H1N1 school outbreak in China, 2009.

All the schools re-opened on Monday, June 29 for pupils to take examinations and closed for a scheduled 2-month summer break after July 2, 2009.

Case–control study

In bivariate analyses, when combining school controls and community controls together, the only significant risk factor associated with 2009 H1N1 illness was exposure either to family members (OR 5·4, 95% CI: 1·9–15·0) or to classmates (OR 5·1, 95% CI: 2·0–13·1) with respiratory illness (Table 2). The candidate variables considered in the multivariable analysis included exposure to persons with respiratory illness either at home or in the classroom and personal hygiene behaviors, the latter included covering the mouth while coughing or sneezing and washing hands frequently. In the final multivariable model, the only significant risk factor was exposure to persons with respiratory illness either in the home or classroom within 7 days of symptom onset (OR, 4·5, 95% CI: 1·9–10·7, $P = 0.001$).

Discussion

We report the first known school outbreak of 2009 H1N1 in China, about 1 month after the first confirmed 2009 H1N1 case was identified in the country.[2] At the time of this outbreak, community-level transmission of the virus was not believed to have been established. The initial six confirmed cases reported no travel history before symptom onset and they did not report contact with any person who had a travel history, suggesting that community-level transmission of the virus had already been established before identification of the outbreak. It is likely that many ILI cases detected through retrospective review were caused by 2009 H1N1 virus infection, and one of these was the source of the school outbreak. The suspected cases detected through retrospective review all had returned to school one day after their symptom onset. Therefore, transmission of 2009 H1N1 virus from some of these symptomatic suspect cases to other exposed students is believed to have occurred.

Table 2. Univariate analyses of potential risk factors associated with 2009 H1N1 illness, overall and stratified by school controls and community controls, China

Characteristics*	Cases (*n* = 50)	Controls					
		Subtotal (*n* = 197))	OR (95 CI), *P*	School controls (*n* = 99)	OR (95 CI), *P*	Community controls (*n* = 98)	OR (95 CI), *P*
Demographic characters**							
Age (year), Median (range)	8 (6–11)	8 (6–12)	NA	8 (6–12)	NA	8 (6–12)	NA
Men	33 (66)	129 (65)	NA	65 (66)	NA	64 (65)	NA
Location of community controls							
Village A	37 (64)	–	NA	83 (84)	NA	68 (69)	NA
Village B	1 (2)	–	NA	0	NA	6 (6)	NA
Village C	1 (2)	–	NA	0	NA	2 (2)	NA
Other villages	11 (22)		NA	16 (16)	NA	22 (22)	NA
Medical history							
Underlying medical condition	1 (2)	4 (2)	1·0 (0·1–8·9), 1·000	2 (2)	1·0 (0·1–11·0), 1·000	2 (2)	1·0 (0·1–11·0), 1·000
Influenza vaccination	9 (18)	32 (16)	1·1 (0·4–2·8), 0·865	19 (19)	0·8 (0·3–2·4), 0·722	13 (13)	1·8 (0·5–6·0), 0·351
No. of family members (person)							
Median(range)	4 (2–8)	5 (2–12)	0·9 (0·7–1·1), 0·357	4 (2–12)	0·9 (0·7–1·2), 0·932	5 (2–10)	0·8 (0·6–1·1), 0·220
Personal hygiene***							
Cover mouth while cough or sneezing†	15/38 (39)	81 (41)	0·8 (0·4–1·9), 0·633	42/88 (48)	0·6 (0·2–1·8), 0·401	39/85 (46)	1·0 (0·4–2·4), 1·000
Wash hands frequently††	31 (62)	106 (54)	1·5 (0·7-3·0), 0·259	58 (59)	1·2 (0·6–2·4), 0·672	48 (49)	2·0 (0·9–4·3), 0·094
Exposure to persons with respiratory illness							
Family member	9 (18)	10 (5)	5·4 (1·9–15·0), 0·001	5 (5)	4·7 (1·5–15·0), 0·010	5 (5)	5·7 (1·6–21·2), 0·009
Teacher	0	2 (1)	NA	1 (1)	NA	1 (1)	NA
Classmate	21 (42)	27 (14)	5·1 (2·0–13·1), 0·001	10 (10)	2·9 (0·9–8·4), 0·057	17 (17)	6·8 (2·0–23·8), 0·003
Neighbor	1 (2)	6 (3)	0·7 (0·1–6·2), 0·767	5 (5)	2·0 (0·1–32·0), 0·624	1 (1)	0·4 (0·1–3·3), 0·373

*Data are presented as no. (%) of participants unless otherwise indicated, and denominators for testing of fewer participants than full group are indicated; and percentages may not total 100 because of rounding.
**Matched factors (age, gender, and location) were excluded in analyses.
***The denominators for calculation in fewer than the full groups were indicated.
†Cover mouth when cough or sneezing: Cover the nose and mouth with a tissue or handkerchief every time cough or sneeze.
††Wash hands frequently: pupils who wash hands more than three times every day.

This large primary school outbreak resulted in an overall suspected case attack rate of 7% and a confirmed 2009 H1N1 case attack rate of nearly 4%, consistent with 2009 H1N1 outbreaks among school children reported in European countries.[5–7] The confirmed case attack rate among students in two classes, located on different floors of a building, was higher than among other classes. While students in all school years experienced illness, there was considerable variation in the attack rate of confirmed cases between classes.

All confirmed 2009 H1N1 cases in this outbreak experienced self-limited, uncomplicated ILI. Their clinical illness was consistent with seasonal influenza illness observed in school outbreaks[8,9] and reported in a WHO clinical summary for 2009 H1N1 infection.[10] Globally, most 2009 H1N1 infections result in self-limited, uncomplicated ILI, although the clinical spectrum of disease ranges from non-febrile, mild upper respiratory tract illness to severe or fatal pneumonia.[11]

During seasonal influenza outbreaks, school-age children experience the highest illness attack rates and play a central role in sustaining influenza transmission in the community.[12] Not surprisingly, schools represent an important source of 2009 H1N1 virus transmission as well.[5–7,13,14] One modeling study[15] predicted that the school classroom and household were two of the most critical settings in terms of duration of exposure to symptomatic persons and risk of virus transmission.

Influenza transmission is thought to occur primarily via droplet spread and potentially via contact transmission, although droplet nuclei transmission also likely occurs.[16] The gathering of school children in class or activities after class can facilitate substantial exposure to infectious diseases and amplify their transmission.[14] In our investigation, the most significant risk factor associated with 2009 H1N1 illness was recent exposure to persons with acute respiratory illness either at home or school. This adds weight to the argument that social activities are important routes of transmission and that, during the containment phase, school closure alone may not be enough to interrupt transmission.

School closure in this outbreak was implemented as soon as the high rate of absenteeism and the first laboratory-confirmed 2009 H1N1 infection were detected, but it might not have been early enough. After the school closure, the number of newly reported suspected and confirmed cases declined rapidly. Closure of all schools in the town and rigorous clinical management, including isolation of all confirmed patients together, may have had an impact on reducing transmission and eliminating a large, successive outbreak peak; it also may have fostered greater public awareness about the need for preventive measures. In seasonal influenza epidemics, the impact of school closings upon influenza transmission has been variable.[17–20] A recent modeling study on 2009 H1N1 suggests that school closure was unlikely to have been effective in reducing transmission but, if closed early and for a prolonged period, may have a useful effect.[21] Our limited findings suggest that school closure did not prevent transmission of influenza in the community. Given that school closure remains a major component of 2009 H1N1 outbreak control efforts, further research is needed to assess its impact on outpatient ILI visits and influenza-related hospital admissions in communities. Further, the 2009 H1N1 influenza pandemic highlights the need for a flexible national policy regarding school closure that can be quickly adapted to reflect current situations.

Our investigation had several limitations. Laboratory testing for influenza was not routinely performed for all residents in the town who presented with ILI and was discontinued when 2009 H1N1 was confirmed among students at the primary school. It is likely that the magnitude of the outbreak in the school and in the community was underestimated because not all ill persons likely sought medical care or were tested. Additionally, we only conducted surveillance for ILI, not for acute respiratory illness or other non-febrile illness. Because fever and cough are highly predictive for the diagnosis of seasonal influenza during out breaks, we used ILI for surveillance and case finding in this investigation. 2009 H1N1 had been found among people without fever or respiratory symptoms. It is possible, therefore, that we failed to identify cases of 2009 H1N1. Although we obtained exposure histories for suspected H1N1 cases and confirmed cases, we were unable to ascertain the epidemiological links among all the cases as well as within household transmission. Interviews for the case–control study were conducted one week after the outbreak was detected, potentially leading to recall bias. Finally, the town was not part of national sentinel virological surveillance and could not provide any evidence to support community transmission of 2009 H1N1 as a source of the school outbreak.

In response to the emergence of the 2009 H1N1 virus, China's Ministry of Health implemented active enhanced surveillance for ILI among travelers returning from affected areas at the very beginning of the pandemic. Amplifying events, such as this school outbreak of 2009 H1N1, helped change China's national prevention and control strategy. These events confirmed that sustained community-level transmission of 2009 H1N1 virus was occurring in China, and, in response, China adapted its surveillance system to focus on detecting community transmission, virologic changes, and hospitalized patients of 2009 H1N1 virus infection, as well as the switch from a containment to mitigation strategy.

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