

ORIGINAL ARTICLE

Outbreak of 2009 Pandemic Influenza A (H1N1) at a New York City School

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ABSTRACT

BACKGROUND

In April 2009, an outbreak of novel swine-origin influenza A (2009 H1N1 influenza) occurred at a high school in Queens, New York. We describe the outbreak and characterize the clinical and epidemiologic aspects of this novel virus.

METHODS

The New York City Department of Health and Mental Hygiene characterized the outbreak through laboratory confirmation of the presence of the 2009 H1N1 virus in nasopharyngeal and oropharyngeal specimens and through information obtained from an online survey. Detailed information on exposure and the onset of symptoms was used to estimate the incubation period, generation time, and within-school reproductive number associated with 2009 H1N1 influenza, with the use of established techniques.

RESULTS

From April 24 through May 8, infection with the 2009 H1N1 virus was confirmed in 124 high-school students and employees. In responses to the online questionnaire, more than 800 students and employees (35% of student respondents and 10% of employee respondents) reported having an influenza-like illness during this period. No persons with confirmed 2009 H1N1 influenza or with influenza-like illness had severe symptoms. A linkage with travel to Mexico was identified. The estimated median incubation period for confirmed 2009 H1N1 influenza was 1.4 days (95% confidence interval [CI], 1.0 to 1.8), with symptoms developing in 95% of cases by 2.2 days (95% CI, 1.7 to 2.6). The estimated median generation time was 2.7 days (95% CI, 2.0 to 3.5). We estimate that the within-school reproductive number was 3.3.

CONCLUSIONS

The findings from this investigation suggest that 2009 H1N1 influenza in the high school was widespread but did not cause severe illness. The reasons for the rapid and extensive spread of influenza-like illnesses are unknown. The natural history and transmission of the 2009 H1N1 influenza virus appear to be similar to those of previously observed circulating pandemic and interpandemic influenza viruses.

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IN APRIL 2009, CLUSTERS OF CASES OF 2009 H1N1 influenza involving potential human-to-human transmission were reported in multiple countries.¹ One of the earliest and largest clusters identified in the United States was an acute outbreak of 2009 H1N1 influenza at a New York City high school.² This outbreak prompted an immediate and rapid investigation by the New York City Department of Health and Mental Hygiene. This report describes the clinical and epidemiologic findings from this investigation.

On Thursday, April 23, 2009, a nurse from a high school in Queens, New York, that had an enrollment of 2686 students notified the Department of Health and Mental Hygiene that approximately 100 students were being sent home because they had symptoms that included fever, headache, dizziness, sore throat, and respiratory symptoms. In a conference call earlier that afternoon, the Centers for Disease Control and Prevention (CDC) had updated state and local health officials on reports of emerging novel H1N1 infections in the United States.³ By Friday morning, April 24, the Department of Health and Mental Hygiene suspected that the high-school outbreak might be related to the 2009 H1N1 virus and dispatched staff members to interview students and collect specimens.

Nasopharyngeal and oropharyngeal specimens were collected from nine students who had symptoms resembling those of seasonal influenza, including fever, cough, rhinorrhea, body aches, sore throat, and headache. None had symptoms that suggested a need for hospitalization. The Department of Health and Mental Hygiene provided nasopharyngeal test kits to selected physicians in the vicinity of the high school for testing of symptomatic students or employees. A school event scheduled for April 24, which would typically have been attended by more than 1000 people, was canceled at the recommendation of the Department of Health and Mental Hygiene.

Specimens from the nine students were tested for influenza virus at the Department of Health and Mental Hygiene Public Health Laboratory with the use of a real-time polymerase-chain-reaction (PCR) assay. Results on April 25 showed that eight of the specimens were positive for influenza A. Human H1 or H3 subtypes were not detected, indicating that the virus was probably 2009 H1N1 influenza. Specimens were transported to the CDC for additional testing.

On April 26, the CDC confirmed that seven of the nine specimens were positive for 2009 H1N1 influenza as assessed with the use of a real-time PCR assay, and one result was inconclusive. The illness in the person whose specimen had an inconclusive result was subsequently classified as a confirmed case. After consultation with the Department of Health and Mental Hygiene, the principal of the high school decided not to reopen the school until Wednesday April 29 and subsequently extended the school closure through May 3. The school was effectively closed for 9 days (April 25 through May 3).

METHODS

INVESTIGATION OF THE OUTBREAK

Detection and Follow-up of Confirmed Cases

We used two methods to detect confirmed cases of 2009 H1N1 influenza associated with the high-school outbreak. First, during the initial investigation, nine students were tested for the 2009 H1N1 virus as described above. Second, from April 26 through May 8, New York City health care providers were asked to submit nasopharyngeal samples from persons with severe cases of influenza-like illness to the Department of Health and Mental Hygiene for testing for the 2009 H1N1 virus. Samples from mildly or moderately ill patients with a link to the high school were also accepted. Samples were tested at the Public Health Laboratory with the use of a real-time PCR assay; those that were positive for influenza A but for which the subtype could not be determined were sent to the CDC or to the New York State Department of Health Wadsworth Center Laboratory to determine whether the virus was the 2009 H1N1 virus.

The staff at the Department of Health and Mental Hygiene attempted to interview by telephone all persons with confirmed 2009 H1N1 influenza or their proxies to obtain demographic, epidemiologic, and clinical information, including information about whether the person was a student or an employee or was otherwise linked to the high school. Those who reported such a link are included in this report.

Because the testing was part of an active public health response, the Department of Health and Mental Hygiene allocated resources on a priority basis to test persons who were severely ill and was unable to test all high-school students and employees. Therefore, the number of persons who were

seen by a physician but were never tested or who were tested for influenza with the use of rapid tests only is unknown.

Surveillance of Symptoms and Characterization of the Outbreak

The Department of Health and Mental Hygiene and high-school officials collaborated in developing two online surveys to administer to 2934 students and employees in the school (both faculty and staff). The surveys were administered on April 26 and on May 2. Students and employees were recruited by means of a mass e-mail message to all students, parents, and employees. The e-mail message contained a secure link to the online survey, which remained active for 4 days. Two reminder e-mail messages were sent after each survey. The surveys required students and employees to enter their name and a valid identification. Each survey included questions about demographic characteristics, clinical symptoms, the course of illness during the preceding 24 hours, medical history, status with respect to the 2008–2009 seasonal influenza vaccination, household illnesses, and travel since April 8. An influenza-like illness was defined as reported fever (subjective or measured) accompanied by cough or sore throat on or after April 18. Vaccination status with respect to 2008–2009 seasonal influenza was verified by a check of the records in the New York Citywide Immunization Registry. Respondents who reported a worsening of their symptoms during the previous 24 hours were contacted by telephone to monitor the course of their illness. Structured telephone interviews were conducted with students and employees who reported that they had traveled to Mexico. Destinations, travel dates, and contacts with other travelers were ascertained. All information from patient interviews, as well as tracking data for specimens, were entered into secure databases.

NATURAL HISTORY AND TRANSMISSION OF 2009 H1N1 INFLUENZA

Incubation Period

We estimated the incubation period of 2009 H1N1 influenza (i.e., the time between infection and the onset of symptoms) by identifying the earliest and latest possible dates of exposure and the date of the onset of symptoms in persons with confirmed cases.⁴ A log-normal distribution was

fit to the resulting data with the use of regression techniques for the analysis of time-to-event data.

Generation Time

The generation time for 2009 H1N1 influenza (i.e., the time between successive onsets of symptoms in a chain of transmission) was estimated with the use of data from infector–infected pairs among confirmed cases when a single person who was likely to have been the infector could be identified and the dates of symptom onset for both the infector and the infected person were known. Infector–infected pairs were either persons in the high school (students or employees) along with secondary contacts in their households or other persons in the community who had contact with a single, identified, ill high-school student or employee. For each pair, the longest and shortest generation times that were consistent with the data were calculated. Parametric distributions were fit to the censored data with the use of maximum-likelihood techniques.

Duration of Illness

The duration of illness was estimated with the use of information on the dates of onset and recovery reported by persons with confirmed 2009 H1N1 influenza. In the case of persons who reported at the time of the interview that they were still having symptoms, we treated the data as right censored (i.e., censoring when the event had not yet occurred at the time of measurement). Persons who had recovered but who did not provide a date of recovery were treated as left censored (i.e., censoring when the event had occurred before the time of measurement but the exact time it had occurred was not known). We fit a nonparametric Kaplan–Meier distribution to the data using techniques for left and right censored data.⁵ A parametric log-logistic distribution was fit to the interval-censored data for comparison.

Characteristics of Transmission

To characterize transmission among students, we estimated the within-school reproductive number. This analysis was based on the rate of increase in the number of student cases of influenza-like illness during the initial period of exponential increase in incident cases (which was determined to be between April 18 and April 24).^{6,7} We performed a sensitivity analysis of estimates of the

Table 1. Characteristics of Persons with Confirmed Cases of 2009 H1N1 Influenza and with Suspected Cases of Influenza-like Illnesses among 2686 High-School Students and 248 Employees.*

Characteristic	Confirmed Cases of 2009 H1N1 Influenza		Suspected Cases of Influenza-like Illnesses	
	Students (N=115) †	Employees (N=4)	Students (N=694)	Employees (N=18)
Age (yr)				
Median	16	25	16	35
Range	14–19	20–47	14–19	23–55
Female sex (%)	61	75	60	50
Clinical symptoms (%)				
Fever	93‡	100	100	100
Cough	90	100	94	78
Headache	79	75	80	83
Sore throat	76	75	76	67
Muscle pain	76	75	38	56
Fatigue	73	75	59	61
Rhinorrhea	69	75	60	39
Chills	67	75	62	50
Nausea	46	50	24	22
Diarrhea	26	25	16	22
Vomiting	17	50	10	11
Maximum reported body temperature (°C)				
Mean	38.8	39.0	38.7	38.6
Range	36.1–40.5	38.1–40.0	36.7–40.6	37.3–41.1
Reported receipt of 2008–2009 seasonal influenza vaccine (%)	30	75	20	33
Reported travel to Mexico within 7 days before onset of illness (no.)	1	0	4	1
Household contacts (no.)				
Mean	4.3	2.8	3.0	3.0
Range	2–8	1–4	1–10	0–10
Household contacts with reported influenza-like illness (no.)				
Mean	1.4	1.0	1.0	0.6
Range	1–3	1–1	0–4	0–1

* An influenza-like illness was defined as self-reported fever with cough, sore throat, or both.

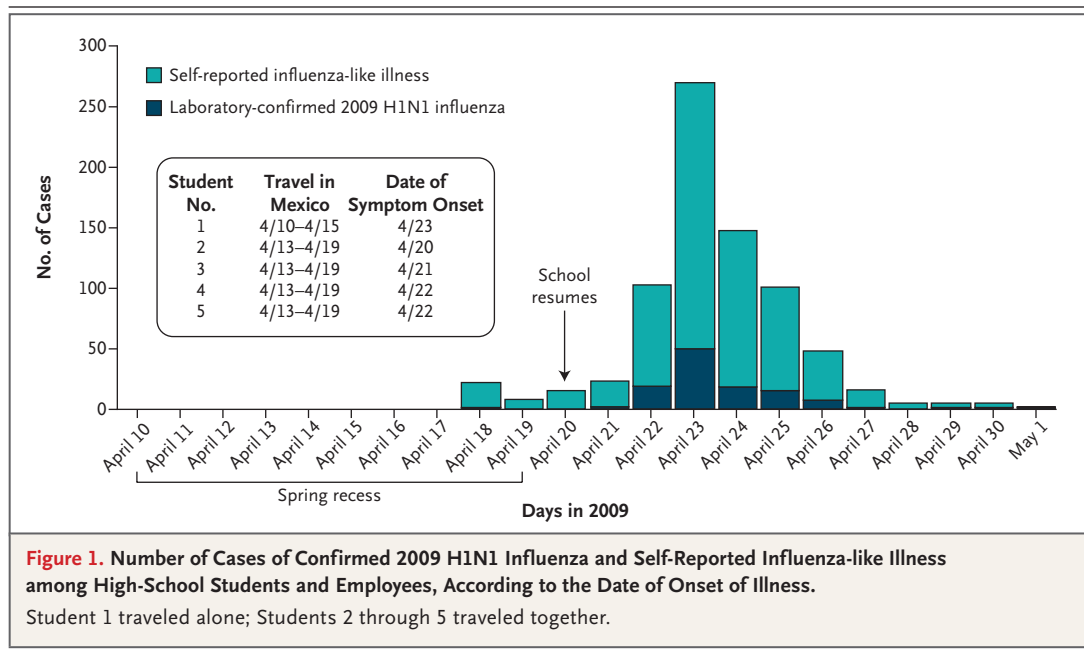
† The total number of confirmed cases among students was 120; however, 5 students could not be contacted.

‡ Some of the students in whom infection with the H1N1 virus was confirmed by laboratory testing did not report having fever.

within-school reproductive number assuming different periods of exponential growth.

To characterize the extent of transmission within the households of students, we estimated the secondary attack rate within households as

the number of persons in the household of a person with confirmed 2009 H1N1 influenza who reported influenza-like illness divided by the total number of persons in that household. We estimated the probability of household transmission



(i.e., the probability that one susceptible household member would become infected as a result of contact with a single infectious household member) with the use of a Reed–Frost chain binomial model.⁸ Households with two to five members in which there was at least one member with a confirmed case were included. We assumed that all transmission to household members after the first confirmed case was the result of household contact.

Details of the methods and the data used for all analyses are available in the Supplementary Appendix, available with the full text of this article at NEJM.org. The investigation of this novel strain of influenza in April–May 2009 was considered by the Department of Health and Mental Hygiene to be public health practice and therefore did not require review by an institutional review board or written informed consent; response to the survey was voluntary.

RESULTS

OUTBREAK AND PRELIMINARY EPIDEMIOLOGY

By May 8, the Department of Health and Mental Hygiene had received 348 specimens from health care providers in New York City (including the 9 samples collected by the Department of Health and Mental Hygiene during the initial investigation). A total of 179 of these samples were positive for influenza A, and all of them were subse-

quently confirmed to be positive for the 2009 H1N1 virus. Of these, 124 were specimens from students (120) or employees (4) of the high school. Telephone interviews were conducted with 119 of the 124 persons with confirmed cases of 2009 H1N1 influenza. Of these 119, only 2 had been hospitalized: a 14-year-old student who had received a diagnosis of a viral syndrome and a 17-year-old student who had been hospitalized after an episode of syncope. Both had been discharged after 1 day. Symptoms and selected demographic characteristics of persons with confirmed cases of 2009 H1N1 influenza are shown in Table 1. One person with a confirmed case reported having traveled to Mexico in the 7 days before the onset of illness; none reported having traveled to California or Texas during that period.

A total of 83% of the students (2225 of 2686) and 92% of the employees (228 of 248) responded to at least one of the two online surveys, and 780 students (35% of respondents) and 22 employees (10% of respondents) reported that they currently had or had recently had an influenza-like illness. The dates of the onset of symptoms ranged from April 18 through May 1 (Fig. 1). A total of 86 students and 4 employees who reported an influenza-like illness on the survey were also among those who were confirmed through testing as having 2009 H1N1 influenza. Among suspected cases (in 694 students and 18 employees), the symptoms reported on the survey were similar to those re-

ported by persons with confirmed cases of 2009 H1N1 influenza (Table 1). A total of 20 students with confirmed 2009 H1N1 influenza who responded to the survey did not report in the survey that they had had an influenza-like illness; however, in telephone interviews, all but 5 of these persons reported having had an influenza-like illness; the symptoms in the 5 persons who did not report having had an influenza-like illness are listed in Table 2.

Among 155 employees who reported their age on the online survey, the attack rate was significantly higher among those who were younger than 60 years of age (14 of 124 [11%]) than among those 60 years of age or older (0 of 31) ($P=0.04$ with the use of a two-sided Fisher's exact test).

A total of 25% of students reported that they had received the 2008–2009 seasonal influenza vaccination, and receipt of the vaccination was confirmed in the case of 6% of these students by a check of the records in the Citywide Immunization Registry. Neither self-reported nor confirmed receipt of seasonal influenza vaccination, as compared with no vaccination, was associated with a significant difference in reported influenza-like illness (risk ratio with self-reported receipt, 1.1; 95% confidence interval [CI], 0.9 to 1.2; risk ratio with confirmed receipt, 1.2; 95% CI, 1.0 to 1.5).

Several high-school students reported on the online survey that they had recently traveled to Mexico. Follow-up interviews verified that 14 students had traveled to Mexico (all but 1 to Cancun) during the school's spring recess (April 8 through 19). Return dates ranged from April 14 to April 21. None of the students who had traveled to Mexico reported that they had attended large social gatherings between the time of their return from Mexico and the resumption of classes on April 20, although some reported that they had met in small groups at private homes.

Five students who had traveled to Mexico reported influenza-like illness in the online survey, with onset dates ranging from April 20 to 23. One had confirmed 2009 H1N1 influenza, with an onset of symptoms on April 22. All had returned to New York City by April 19.

NATURAL HISTORY OF 2009 H1N1 INFLUENZA

Among persons with confirmed cases of 2009 H1N1 influenza, we estimated that the median incubation period was 1.4 days (95% CI, 1.0 to 1.8), with symptoms developing in 95% of the persons

Table 2. Reported Symptoms in Five Students Who Had Confirmed 2009 H1N1 Influenza but Who Did Not Meet the Criteria for Influenza-like Illness.

Age	Sex	Symptoms
15 yr	Male	Cough, sore throat, rhinorrhea
18 yr	Female	Cough, headache, rhinorrhea
18 yr	Male	Cough, headache, sore throat, fatigue, rhinorrhea, nausea
16 yr	Female	No symptoms reported
17 yr	Female	Cough, headache, sore throat, fatigue, rhinorrhea

by 2.2 days (95% CI, 1.7 to 2.6) (Fig. 2A). We estimated that the median generation time was 2.7 days (95% CI, 2.0 to 3.5), with a generation time of less than 5.1 days (95% CI, 3.6 to 6.5) in 95% percent of persons (Fig. 2B). The median duration of symptoms among persons with confirmed cases was 6 days (95% CI, 5 to 8), and 75% recovered by 9 days after the onset of symptoms (95% CI, 8 to 12) (Fig. 2C). Owing to censoring of the data, we observed only one person who recovered after 9 days; therefore, higher quantiles were not estimated. Data for a patient were censored on the date on which the person completed the second survey or on which the last telephone contact was made with that person — in either case, no later than May 8.

TRANSMISSIBILITY OF 2009 H1N1 INFLUENZA

We estimated that the number of incident cases of influenza-like illness at the high school doubled every 1.3 days from April 18 through April 24. On the basis of this rate of growth, we estimated that the within-school reproductive number was 3.3 (95% CI, 3.0 to 3.6). This estimate is highly sensitive to the assumed period of exponential growth, and estimates ranged from 3.3 to 5.3, depending on the period chosen. The estimated secondary attack rate of influenza-like illness in households in which there was at least one member with a confirmed case was 17.7% (95% CI, 14.1 to 21.8). This rate did not appear to vary according to the size of the family. We estimated that the probability of household transmission was 0.14 (95% CI, 0.11 to 0.18).

DISCUSSION

By May 8, infection with the 2009 H1N1 virus had been confirmed in 124 students and employees. Responses to the online survey suggest that more than 800 students and employees were infected. Although some of the reported influenza-

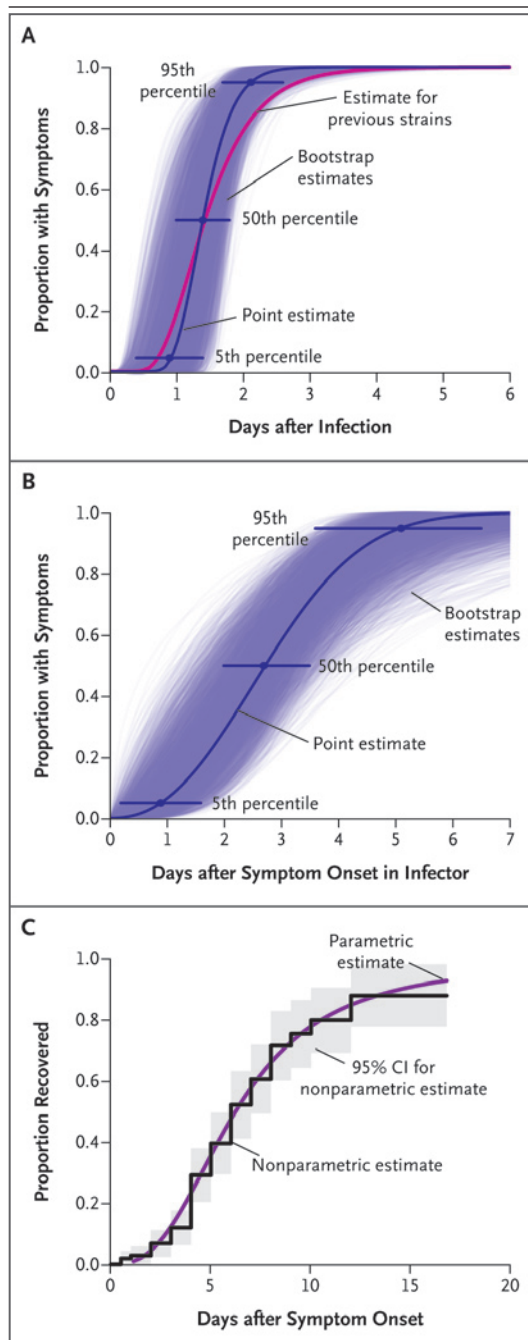


Figure 2. Estimated Cumulative Distribution Functions for the Incubation Period, Generation Time, and Duration of Symptoms.

The maximum-likelihood estimates for the parametric distribution of the cumulative distribution function are shown, along with 10,000 parametric bootstrap estimates of the cumulative distribution function, estimates for previous influenza strains, and nonparametric estimates. Panel A shows estimates of the proportion of case subjects in whom symptoms developed, according to the number of days after infection. We estimated that symptoms developed in 5% of the subjects by 0.9 days (95% CI, 0.4 to 1.4), in 50% by 1.4 days (95% CI, 1.0 to 1.8), and in 95% by 2.2 days (95% CI, 1.7 to 2.6). Panel B shows estimates of the proportion of persons in whom symptoms developed according to the number of days after symptoms developed in the infector (generation time). We estimated that symptoms developed in 5% of the infected persons by 0.9 days (95% CI, 0.2 to 1.6), in 50% by 2.7 days (95% CI, 2.0 to 3.5), and in 95% by 5.1 days (95% CI, 3.6 to 6.5). Panel C shows estimates of the proportion of persons who recovered from illness, according to the number of days after the onset of symptoms. We estimated that 50% recovered by 6 days (95% CI, 5 to 8) and 75% recovered by 9 days (95% CI, 8 to 12). Higher quantiles cannot be estimated since, owing to the censoring of data, only one person was observed to recover after 9 days. A total of 23 observations were censored after 9 days, the latest of which was censored at 20 days.

persons with confirmed cases of 2009 H1N1 influenza. These factors and subsequent evidence of widespread community transmission of 2009 H1N1 influenza in New York City suggest that most reported influenza-like illnesses were likely to have been due to the 2009 H1N1 virus.

The overwhelming majority of students and employees with confirmed or suspected cases of 2009 H1N1 influenza had a self-limited febrile respiratory illness. The median time to recovery was 6 days, and 75% had recovered by 9 days. The high attack rate and rapid increase in the number of cases of influenza-like illness suggest that there was swift and widespread transmission of 2009 H1N1 influenza in the high school after the students' return from spring recess. The incubation period for 2009 H1N1 influenza suggests that students who had traveled in Mexico may have been infected there or while in transit to New York City and that transmission of the virus from these students may have initiated the outbreak. However, the possibility that 2009 H1N1 virus may have been introduced from other sources cannot be excluded.

The estimated natural-history characteristics

like illnesses may have been due to seasonal influenza or other respiratory viruses, 2009 H1N1 influenza was confirmed in 7 of the 9 symptomatic students who were examined by the Department of Health and Mental Hygiene during the initial outbreak investigation, as well as in 117 other persons. The nature and timing of the symptoms reported by persons with influenza-like illnesses were consistent with those reported by

of this outbreak are consistent with those seen in the case of previously circulating influenza viruses. The median incubation period of 1.4 days is the same as that of other influenza A viruses observed during pandemic and inter pandemic periods,⁹ and the time by which symptoms developed in 95% of cases is within the confidence limits of previous estimates. The median generation time of 2.7 days is also consistent with previous estimates for influenza^{10,11} but is slightly longer than early estimates from Mexico.¹² The consistency with previous estimates suggests that findings regarding the natural history of previous influenza strains may be relevant to the 2009 H1N1 virus. We estimate that the within-school reproductive number in this outbreak was 3.3, which is at the high end of the range estimated for pandemic and inter pandemic influenza outbreaks¹³ and higher than estimates for the transmission of 2009 H1N1 influenza in Mexico.¹⁴ However, it is generally assumed that transmission is more efficient among schoolchildren than it is in the general population.^{15,16} The rapid growth of this epidemic is consistent with a high reproductive number, but the total number of students infected over the course of the entire outbreak is consistent with a lower transmission rate than that suggested by the estimated within-school reproductive number of 3.3, a finding that may be due to a high rate of asymptomatic cases. (The estimated within-school reproductive number as calculated from the percentage infected over the course of the entire outbreak is 1.2 [see the Supplementary Appendix].) School closure may have helped control the outbreak; however, the number of incident cases of influenza-like illness began declining before the school was closed on April 25, suggesting that the epidemic was already receding.

Our estimate of the probability of household transmission (0.14) is lower than estimates in the case of inter pandemic influenza A (estimates of 0.21 to 0.48,¹⁴ 0.42,¹⁷ and 0.17 to 0.40¹⁸). This suggests that 2009 H1N1 influenza was not efficiently transmitted in the home, perhaps because of

the reduced susceptibility among people over the age of 60 years or because of differential social-mixing patterns. It is also possible that the reporting of cases in the household was incomplete or that many of the infections were asymptomatic. It is unclear whether transmission may have been less efficient owing to seasonal effects. Other schools in New York City and elsewhere with confirmed or suspected cases have not reported attack rates as high as those reported here. Differences between schools in the timing and size of the initial outbreak, patterns of student interaction, holiday scheduling, and the physical facilities could lead to variations in the rates of transmission.

Although the disease characteristics estimated from this outbreak are similar to those for seasonal influenza strains, this should not make us complacent about the potential impact of 2009 H1N1 influenza. The reproductive number, incubation period, and generation time that were seen in the influenza pandemic of 1918 were also similar to those seen in inter pandemic periods,¹⁹ and the fact that a large number of persons are probably susceptible to the 2009 H1N1 virus could mean that there will be substantially more cases than are seen in a seasonal epidemic. Even modest increases in the rate of transmission or the severity of disease over the levels seen with inter pandemic influenza strains could have a substantial impact on public health.

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APPENDIX

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