

and second-round PCR were 94°C for 3 min, followed by 40 cycles of 94°C for 30 s, 55°C for 30 s, and 72°C for 2 min. Expected amplification products were 458 bp (PCR-1) and 304 bp (PCR-2). Using dilutions of a synthetic template corresponding to the target sequence, we estimated the sensitivity of the amplification assay to be <5 copies of target sequence by limiting-dilution assay.

Negative (sterile water) and positive controls (synthetic template dilutions) were added systematically to each amplification run. A PCR control intended to check the quality of the nucleic acids extraction procedure was also performed systematically on 4 randomly selected samples of each batch (n = 32); this control was based on the detection of an extremely prevalent DNA virus (Torque Teno virus and related viruses, family *Anelloviridae*) by using a highly conserved amplification system (3).

Among the 576 plasma samples tested, no positive signal was identified for KIs-V DNA after agarose gel electrophoresis of PCR-1 and PCR-2. Amplification controls (negative, positive, anellovirus DNA) confirmed the validity of these results.

Using the PCR detection system adopted by Satoh et al., combined with the extraction of large plasma volumes, we were not able to detect KIs-V DNA in the blood of donors tested, suggesting an uncommon frequency in healthy persons in France. Information related to HEV status or ALT levels were not available here because both parameters are not evaluated for routine blood donor screening in France; HEV seroprevalence studies involving blood donors from northern and southwestern France indicate discrepant results ($\approx 3\%$ – $\approx 52\%$, IgG), possibly related to serologic assay performances and/or geographic differences (4). The precise identity of KIs-V remains uncertain, but according to its extensive initial

characterization, complementary studies probably will confirm its viral origin. Molecular characterization of new full-length sequences will be needed to investigate the real genetic diversity of KIs-V and to help design optimized molecular detection systems.

The implication of KIs-V in human health remains under debate. The original publication highlighted the fact that HEV antibody-positive persons in Japan who had moderately elevated ALT levels at a prevalence of KIs-V infection that is non-negligible; such findings could suggest a link between the virus and liver dysfunctions. HEV and KIs-V also could share the same route of contamination, i.e., foods (5). Further investigations involving diverse human cohorts need to be undertaken to better understand the natural history of KIs-V in humans.

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Usefulness of School Absenteeism Data for Predicting Influenza Outbreaks, United States

To the Editor: School closure has been proposed as a strategy for slowing transmission of pandemic influenza (1). Studies of influenza A(H1N1)pdm2009 (pH1N1) suggested that early and sustained school closure might effectively reduce communitywide influenza transmission (2,3). However, empirical evidence identifying the optimal timing of school closures to effectively reduce disease transmission after an outbreak occurs is limited.

That school absenteeism data improve school-based disease surveillance and response has been suggested (4–6). In 2009, Sasaki et al. demonstrated that the pattern of influenza-associated school absenteeism in the days before an influenza outbreak predicted the outbreak course with high sensitivity and specificity (7). However, that study used absenteeism data from Japan, which are generally not applicable to the United States, because most US absenteeism data

collected at the local level do not specify cause. Furthermore, few US jurisdictions collect electronic health data for students.

In New York City (NYC; New York, New York, USA), electronic health data are collected daily on $\approx 70\%$ – 80% of the total nurse visits in the city's public schools, kindergarten through grade 8, and on all-cause school absenteeism. Using these data, we adapted the algorithm developed by Sasaki et al. for use with all-cause absenteeism data from NYC schools and validated our findings by using the daily count of school nurse visits for fever/influenza over the same period (7). To reduce variance, we aggregated absenteeism data for September 6, 2005, through June 26, 2009, for 1,206 public schools in NYC at the school day and school district levels. A negative binomial regression model was then fit to these data, adjusting for day of week, whether the preceding day was a holiday, school type (elementary, middle), school

day (linear term), and sine and cosine terms to account for seasonality. This modeling approach was used to standardize the outcomes across school districts and to further reduce variance caused by factors unassociated with influenza transmission.

A similar regression model was also fit to the daily school district-level count of school nurse visits for fever/influenza syndrome over the same period. However, for this model, seasonal influenza periods, determined by virus isolate data, were censored before modeling.

Residuals of both models were then used to calculate school district-specific z-scores for each day from September 25, 2006, through June 26, 2009, by dividing the model residual by the school district-specific standard deviation of the outcome. To determine the threshold and pattern in lagged days that best predicts an outbreak of absenteeism and fever/influenza syndrome, we applied the Sasaki et al. algorithm to the absenteeism z-score

time series. We calculated receiver operating characteristic (ROC) curves by observing whether z-score thresholds of 1, 1.5, 2, or 2.5 reached either 1, 2, or 3 days in a row, were followed by an influenza outbreak in the same school district in the next 7 days. An influenza outbreak was indicated by a z-score of at least 3 (online Technical Appendix, wwwnc.cdc.gov/EID/pdfs/11-1538-Techapp.pdf).

Results revealed a moderately positive in-phase correlation between absenteeism and fever/influenza syndrome by school district during the pH1N1 period ($r = 0.264$) but a weak correlation over the entire study period (September 6, 2005–June 26, 2009) ($r = 0.086$). When data were aggregated across the city, the correlation between absenteeism and fever/influenza z-scores during the pH1N1 period and the entire study period increased to 0.304 and 0.210, respectively. When estimating a cross-correlation function to the citywide

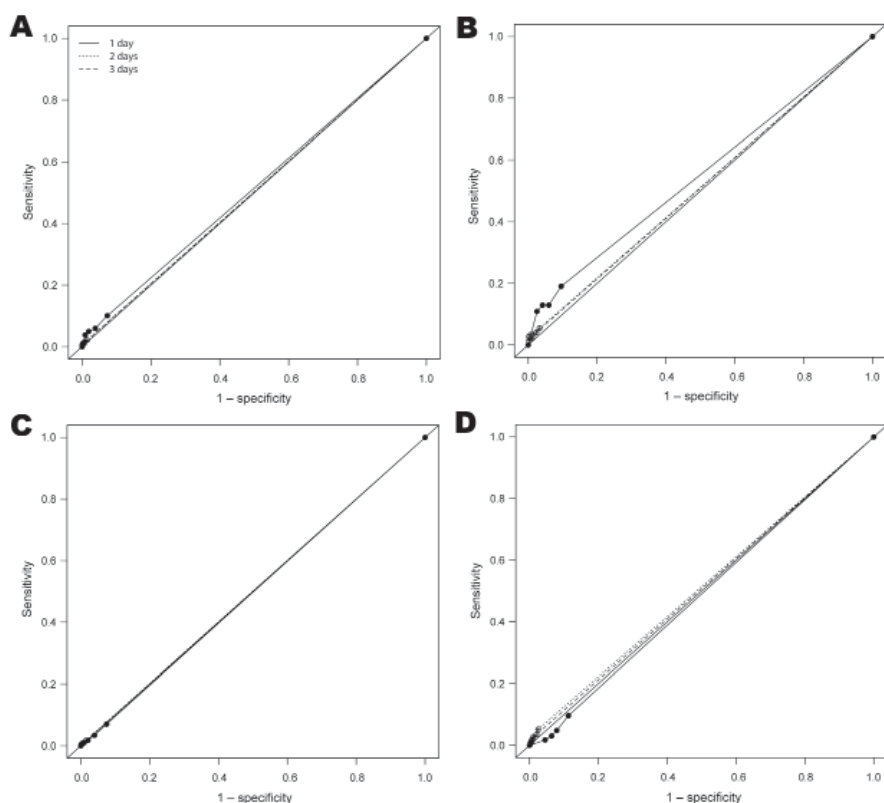


Figure. Receiver operating characteristic (ROC) curves showing A) predictive ability of school absenteeism to detect an outbreak (z-score ≥ 3) of fever/influenza for the entire study period; B) fever/influenza for the pandemic (H1N1) 2009 period; C) absenteeism for the entire study period; and D) absenteeism for the pandemic (H1N1) 2009 period. ROC curves were based on observations of whether 4 absentee threshold z-score levels—1, 1.5, 2, or 2.5—were reached or exceeded for either 1 day, 2 consecutive days, or 3 consecutive days as a predictor of the school district outbreak status during the next 7 days. In the ROC curves, sensitivity on the y-axis indicates the true-positive rate, and 1–specificity on the x-axis indicates the false-positive rate. The study was conducted September 6, 2005–June 26, 2009, in New York City, New York, USA.

data, the absenteeism time series correlated most strongly with the fever/influenza syndrome time series at a 2-day lag (pH1N1 period, $r = 0.550$; entire study period, $r = 0.213$), indicating that changes in absenteeism were most strongly correlated with changes in fever/influenza syndrome visits 2 days earlier.

The ROC curves illustrate the limited ability of absenteeism and fever/influenza visit patterns to predict absenteeism and fever/influenza outbreaks (Figure). The ROC curves also show that absenteeism in the week before an outbreak has little ability to predict an outbreak of either fever/influenza syndrome or absenteeism during the entire study period or during a period of pandemic influenza.

Thus, non-disease-specific absenteeism data alone are of little use for school-based influenza surveillance. Use of all-cause absenteeism data cannot inform influenza mitigation policies, such as school dismissal, at the school or the school district levels. Not surprisingly, the influenza-specific absenteeism data from Japan were better able to predict an influenza outbreak than were our data because our data were not influenza specific. Other factors specific to the school system in Japan might have also played a role.

In the future, it might be beneficial for schools to collect causes of absenteeism, particularly if it is not feasible to electronically collect data on school nurse visits. Creation of school-based early warning systems for pandemic influenza remains a priority. In NYC, efforts to improve emergency department and primary care electronic medical record systems have been successful (8–10). Similar efforts to improve electronic health data collection and influenza-related absenteeism data in schools might yet demonstrate the usefulness of school-based surveillance systems.

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Letters

Letters commenting on recent articles as well as letters reporting cases, outbreaks, or original research are welcome. Letters commenting on articles should contain no more than 300 words and 5 references; they are more likely to be published if submitted within 4 weeks of the original article's publication. Letters reporting cases, outbreaks, or original research should contain no more than 800 words and 10 references. They may have 1 Figure or Table and should not be divided into sections. All letters should contain material not previously published and include a word count.

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Technical Appendix

Statistical Model Development

Daily counts of absenteeism and fever/influenza syndrome cases for 1,206 public schools in New York City were aggregated by school day and school district for the period September 6th, 2005 to June 26th 2009. This aggregation was performed to reduce the variance in both outcomes. The raw count data varied widely for absenteeism (mean percent absent = 12.7%, SD = 9.3%) and fever/influenza cases (mean count = 0.20, SD = 0.26) by school, by day. As a result, preliminary modeling of the raw case counts produced large residuals.

Separate negative binomial regression models were fit to the daily count of school absenteeism and a daily count of fever/influenza syndrome cases for the period September 6th, 2005 to June 26th, 2009, by school district. For both models, we used an offset term for the total school district enrollment for each day to adjust each count by school population (i.e., larger schools should have a larger number of fever/influenza cases). For the fever/influenza model, daily fever/influenza cases during influenza periods were removed before modeling. At the New York City Department of Health and Mental Hygiene, the start of a influenza period is defined as 2 consecutive weeks of 2 or more influenza isolates confirmed by a World Health Organization collaborating laboratory, and the end of a influenza period is the last week reporting ≥ 1 influenza isolates. Complete censoring of influenza periods from the data enabled us to estimate the expected excess count of fever/influenza cases in these schools. If we had not censored this period, we would have observed an ‘outbreak’ in the data only if the observed count was historically unusual, instead of seasonally unusual, which was the threshold we were seeking.

For both models, terms for day of the week, school type (elementary, middle school), and whether the preceding or proceeding day was a holiday were fit to the data because they were

believed to be independently associated with that day's absentee and fever/influenza syndrome counts. Linear, sine and cosine terms for the school day were also included in these models to account for linear and nonlinear changes in absenteeism and counts of fever/influenza syndrome that were observed upon visual inspection of the data. Inclusion of these covariates in the models to predict counts of absenteeism and fever/influenza helped to further reduce the variance in the data due to factors thought to be unrelated to influenza transmission. Both models resulted in adjusted, predicted counts of all-cause absenteeism and fever/influenza syndrome by school district. A z-score was then calculated by dividing the model residual (observed minus expected) by the school district-specific standard deviation of the outcome for each school district, for each day during the study period. Producing a model-estimated z-score of each outcome enabled us to remove some of the residual variance in the data as well as produce a normalized distribution of the outcomes for each school district to better determine an unexpected rise (i.e., an 'outbreak) for each outcome.