Epidemiology of 2009 Pandemic Influenza A Virus Subtype H1N1 Among Kenyans Aged 2 Months to 18 Years, 2009–2010

Karen K. Wong,[1,a] **Wallace D. Bulimo,**[4] **Japhet Magana,**[5] **Rachel A. Achilla,**[4] **Sandra K. Schwarcz,**[2,3] **Maylor Simwa,**[5] **Janet M. Majanja,**[4] **Meshack O. Wadegu,**[4] **Finley A. Osuna,**[4,5] **Silvanos O. Mukunzi,**[4] **Josephat K. Mwangi,**[4] **Julia M. Wangui,**[4] **Janet N. Muthoni,**[4] **James O. Njiri,**[4] **Beryl D. Obura,**[4] **Benjamin H. Opot,**[4] **Keneth K. Mitei,**[4] **Jane Barani,**[5] **Samwel Lifumo,**[5] **and David C. Schnabel**[4]

[1]Department of Medicine and [2]Division of Preventive Medicine and Public Health, Department of Epidemiology and Biostatistics, University of California–San Francisco and [3]San Francisco Department of Public Health; and [4]US Army Medical Research Unit–Kenya and [5]Kenya Medical Research Institute, Nairobi

Background. The US Army Medical Research Unit–Kenya (USAMRU-K) conducts surveillance for influenza-like illness (ILI) in Kenya. We describe the temporal and geographic progression of A(H1N1)pdm09 as it emerged in Kenya and characterize the outpatient population with A(H1N1)pdm09 infection.

Methods. We included patients with ILI aged 2 months to 18 years enrolled during June 2009–August 2010. Respiratory specimens were tested by real-time reverse-transcription polymerase chain reaction for influenza virus. Patients with A(H1N1)pdm09 infection were compared to those with seasonal influenza A virus infection and those with ILI who had no virus or a virus other than influenza virus identified (hereafter, "noninfluenza ILI").

Results. Of 4251 patients with ILI, 193 had laboratory-confirmed A(H1N1)pdm09 infection. The first pandemic influenza case detected by USAMRU-K surveillance was in August 2009; peak activity nationwide occurred during October–November 2009. Patients with A(H1N1)pdm09 infection were more likely to be school-aged, compared with patients with seasonal influenza A virus infection (prevalence ratio [PR], 2.0; 95% confidence interval [CI], 1.3–3.1) or noninfluenza ILI (PR, 3.2; 95% CI, 2.4–4.3).

Conclusions. USAMRU-K ILI surveillance detected the geographic and temporal distribution of pandemic influenza in Kenya. The age distribution of A(H1N1)pdm09 infections included more school-aged children, compared with seasonal influenza A virus infection and noninfluenza ILI.

In March and April 2009, 2009 pandemic influenza A virus subtype H1N1 (A[H1N1]pdm09) emerged in Mexico and the United States [1, 2]. The strain spread rapidly worldwide, and on 11 June 2009, the World Health Organization declared the start of the pandemic phase [3]. In Kenya, A(H1N1)pdm09 was first identified on 29 June 2009 and was traced to 4 parallel introductions of the virus to Nairobi from the United Kingdom [4].

Little has been published about the epidemiology of A(H1N1)pdm09 in Africa [5]. Understanding the emergence and spread of the pandemic across the geographically diverse regions of Kenya is important for future pandemic preparedness. We describe the emergence of A(H1N1)pdm09 in Kenya among children, as detected by the US Army Medical Research Unit–Kenya (USAMRU-K) outpatient ILI surveillance network, and compare the characteristics of patients with A(H1N1)pdm09 infection to those of patients with seasonal influenza A virus infection and those with ILI who had no virus or a virus other than influenza virus identified (hereafter, noninfluenza ILI).

MATERIALS AND METHOD

ILI Sentinel Surveillance

USAMRU-K is part of the Department of Defense Global Emerging Infections Surveillance and Response System (GEIS), a laboratory-based global surveillance network for civilian and military populations [6]. The goal of the surveillance network is to identify virus strains worldwide that may affect military populations, their families, and the local populations and to collaborate with other health organizations to develop public health interventions, including vaccines.

USAMRU-K has conducted surveillance for ILI at 8 outpatient health facilities in Kenya since July 2006. All surveillance sites are at public hospitals in geographically diverse regions of Kenya (Supplementary Figure 1). Mbagathi District Hospital, located in Nairobi, serves an urban population and is located in Kenya's Rift Valley region. New Nyanza General Hospital, located in Kisumu in the tropical Lake Victoria basin region, serves an urban population. Kisii District Hospital and Kericho District Hospital, periurban sites, are located in the western highlands region, which is characterized by high altitude and frequent rainfall. Alupe Subdistrict Hospital is located on the Kenya-Uganda border in the rural town of Busia. Isiolo District Hospital is located north of the central highlands, in the arid northern plains. Malindi District Hospital, a periurban site, and Port Reitz District Hospital, an urban site, are located in the coastal region characterized by a tropical climate.

At all sites, from Monday through Friday during normal working hours, trained clinical officers identified patients who met the World Health Organization case definition of ILI (fever [temperature >38.0°C] and cough or sore throat) and who presented within 72 hours of symptom onset [7]. Clinical officers administered a standardized questionnaire to eligible patients to collect demographic, exposure, and symptom data, and they collected nasopharyngeal swab specimens. Exclusion criteria for this study were age <2 months or >18 years, presence of obvious exudative pharyngitis or tonsillitis, and absence of a consenting parent or legal guardian. Infants aged <2 months were not enrolled in the surveillance system because of the nonspecific clinical presentation of influenza in very young infants. Adults aged >18 years were enrolled in USAMRU-K ILI surveillance; however, they compose only 2% of all patients enrolled in the surveillance because of the general infrequent healthcare utilization patterns of adult Kenyans for mild health conditions, and therefore they were excluded from this analysis. We collected samples from a maximum of 2 members of the same household who presented on the same day. Each site enrolled a maximum of 5 patients per day (25 samples per week). The selection of patients was decided by the clinical officers; however, generally the first 5 patients meeting case criteria and willing to participate were recruited. Study patients were not selected based on any known likelihood of exposure to the A(H1N1)pdm09 strain.

Study Period

Patients with ILI presenting to surveillance sites between 1 June 2009 (the month in which the first A(H1N1)pdm09 case was identified) and 31 August 2010 were included.

Laboratory Testing of ILI Cases

Patients had duplicate nasopharyngeal swab specimens taken to ensure that enough of the respiratory sample was available for testing of multiple respiratory pathogens, for sharing of samples with collaborating laboratories, and for storing a portion of the sample for potential future research. Swabs were placed in viral transport medium, stored at −80°C, then transported to the National Influenza Center at the Kenya Medical Research Institute (KEMRI) in Nairobi for testing. Typing and subtyping of influenza viruses was performed by real-time reverse-transcription polymerase chain reaction (RT-PCR), using the Applied Biosystems 7500 Real-Time PCR System in accordance with the Centers for Disease Control and Prevention (CDC) real-time RT-PCR protocol for the detection and characterization of influenza viruses [8].

Identification of Patients Infected With A(H1N1)pdm09 or Seasonal Influenza A Virus

Patients with pandemic influenza cases were those who had laboratory-confirmed A(H1N1)pdm09 detected by real-time RT-PCR. Cases of seasonal influenza A virus infection included all patients with laboratory-confirmed seasonal influenza A virus subtype H1N1 (A[H1N1]) and influenza A virus subtype H3N2 (A[H3N2]) infections. Cases of influenza A virus infection that did not have subtyping information available were not counted as either A(H1N1)pdm09 or seasonal influenza A virus infection.

Statistical Analysis

Bivariate analysis was performed to identify features associated with A(H1N1)pdm09 versus seasonal influenza A virus infection, A(H1N1)pdm09 infection versus noninfluenza ILI, and seasonal influenza A virus infection versus noninfluenza ILI. We report prevalence ratios (PRs) with 95% confidence intervals (CIs). Analysis was performed with EpiInfo 3.5.1.

Ethical Considerations

The study was approved by KEMRI, the Walter Reed Army Institute of Research (WRAIR) Ethical Review Boards, and the CDC (KEMRI SSC protocol 981, WRAIR protocol 1267, and CDC protocol 4716). Written informed consent was obtained from the parent or guardian by a clinical officer or laboratory technician trained by the study team. Information was given in English, Kiswahili, or the local language, if indicated. Patients 7 years and older were able to refuse participation.

Table 1. Demographic and Exposure Characteristics of Children With Influenza-Like Illness (ILI), Overall and by Causes, Kenya, June 2009–August 2010

| Characteristic | Patients With ILI, by Cause | | | |
	Overall[a] (n = 4251)	A(H1N1)pdm09 (n = 193)	Seasonal Influenza A Virus[b] (n = 255)	Noninfluenza[c] (n = 3127)
Age, y				
0–1	2264 (53)	66 (34)	100 (39)	1774 (57)
2–4	1706 (40)	91 (47)	132 (52)	1188 (38)
5–11	275 (7)	35 (18)	23 (9)	160 (5)
12–18	6 (<1)	1 (1)	0	5 (<1)
Sex				
Male	2218 (52)	100 (52)	126 (49)	1643 (53)
Female	2033 (48)	93 (48)	129 (51)	1484 (48)
Hospital				
Alupe	423 (10)	4 (2)	10 (4)	367 (12)
Isiolo	233 (6)	21 (11)	7 (3)	165 (5)
Kericho	465 (11)	12 (6)	29 (11)	351 (11)
Kisii	738 (17)	42 (22)	50 (20)	496 (16)
Malindi	325 (8)	8 (4)	19 (8)	224 (7)
Mbagathi	723 (17)	38 (20)	53 (21)	533 (17)
New Nyanza	753 (18)	40 (21)	54 (21)	545 (17)
Port Reitz	591 (14)	28 (15)	33 (13)	446 (14)
Exposure[d]				
Household contact	1296/4250 (30)	73/193 (38)	94/255 (37)	904/3126 (29)
Attends school	924/4247 (22)	82/193 (43)	79/255 (31)	591/3123 (19)

Data are no. (%) of patients, unless otherwise indicated.

Abbreviation: A(H1N1)pdm09, 2009 pandemic influenza A virus subtype H1N1.

[a] Percentages may not add up to 100, because of rounding.

[b] A total of 183 were infected with influenza A virus subtype H3N2, and 72 were infected with seasonal influenza A virus subtype H1N1.

[c] No virus or a virus other than influenza virus was identified.

[d] Data are no. of patients with the exposure/no. with data available (%).

Separate assent forms were provided for children 7–11 and 12–17 years of age. Parents or guardians were allowed to provide consent for children who were unable to give assent because of their medical status. If the patient or guardian was illiterate, the healthcare worker read the consent form to them.

RESULTS

Study Population

During the period of pandemic activity in Kenya, from 1 June 2009 to 31 August 2010, 4251 patients with ILI were identified, of whom 1124 (26%) had influenza virus and 3127 (74%) did not have influenza virus (Table 1). Of 447 patients with influenza A virus subtyping results, 193 had A(H1N1)pdm09 infection, 183 had A(H3N2) infection, and 72 had A(H1N1) infection; 1 patient was coinfected with A(H1N1)pdm09 and A(H3N2). Of patients with ILI, 2264 (53%) were aged <2 years, and 3970 (93%) were aged <5 years. Patients with A(H1N1)pdm09

infection were similar in terms of sex and reporting of ill household contacts, compared with all patients with ILI. Of 193 patients with A(H1N1)pdm09 infection, 157 (81%) were aged <5 years, and 82 (43%) reported attending school.

A(H1N1)pdm09: Temporal and Geographic Distribution

The first case of A(H1N1)pdm09 infection detected in our surveillance system was identified on 17 August 2009 in Nairobi, at Mbagathi District Hospital, in a 1-year-old child. In the next 10 days, a 1-year-old child and a 3-year-old child were found to have A(H1N1)pdm09 infection at Malindi District Hospital. A(H1N1)pdm09 was associated with the highest proportion of ILI cases during October and November 2009, when it accounted for 18.7% of all cases (Figure 1). While A(H1N1)pdm09 infection peaked in most hospitals in the surveillance system in late 2009, at Isiolo District Hospital, a second peak of A(H1N1)pdm09 infections occurred in February and March 2010. Although in most sites A(H1N1)pdm09 disappeared by April 2010, sporadic cases of A(H1N1)
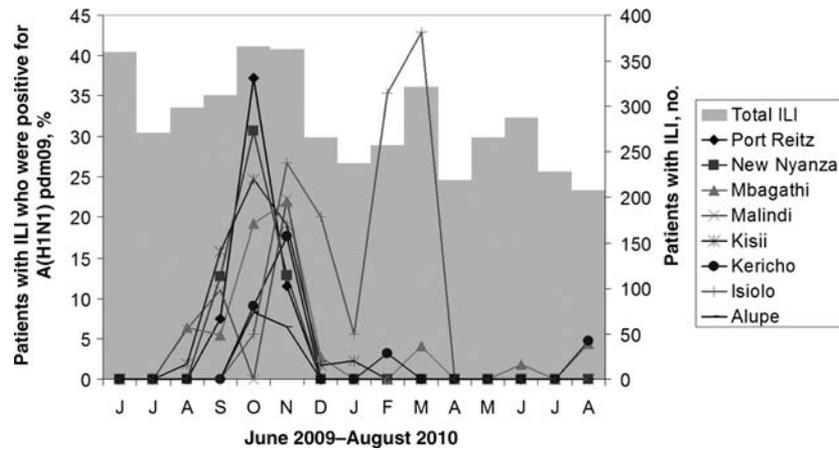
Figure 1. Percentage of patients with influenza-like illness (ILI) who tested positive for 2009 pandemic influenza A virus subtype H1N1 (A[H1N1] pdm09) and number of patients with ILI, by surveillance site, Kenya, June 2009–August 2010.

pdm09 infection continued to be identified at Mbagathi and Kericho District Hospitals into August 2010.

Comparison of Patients With A(H1N1)pdm09 Infection, Seasonal Influenza A Virus Infection, or Noninfluenza ILI

Patients with A(H1N1)pdm09 infection and patients with seasonal influenza A virus infection were more likely to be aged 5–18 years, compared with patients with noninfluenza ILI (PR, 3.2 [95% CI, 2.4–4.3] and 1.6 [95% CI, 1.1–2.3], respectively); however, patients infected with A(H1N1)pdm09 were also more likely to be aged 5–18 years, compared with patients infected with seasonal influenza A virus infection (PR, 2.0; 95% CI, 1.3–3.1) (Table 2). There was no difference in reporting of ill household contacts between patients with A(H1N1)pdm09 infection and those with seasonal influenza A virus infection (PR, 1.0; 95% CI, .8–1.3). School attendance was more common among patients with A(H1N1)pdm09 infection, compared with patients with seasonal influenza A virus

infection (crude PR, 1.4; 95% CI, 1.1–1.8) and those with noninfluenza ILI (crude PR, 2.2; 95% CI, 1.9–2.7). After adjustment for age 5–18 years, prevalence of school attendance was not different between those with A(H1N1)pdm09 infection versus those with seasonal influenza A virus infection (adjusted PR, 1.2; 95% CI, .8–1.5).

DISCUSSION

This study describes the epidemiology of A(H1N1)pdm09 infections in outpatients in Kenya. The surveillance network detected peak pandemic activity nationally in October and November 2010, although there were regional differences in pandemic activity. The age distribution of A(H1N1) pdm09 infections in the outpatient setting included more school-aged children, compared with the age distributions of patients with seasonal influenza A virus infection or noninfluenza ILI.

Table 2. Comparisons of the Prevalence of Select Characteristics Among Patients With Influenza-Like Illness, by Cause, Kenya, June 2009–August 2010

Characteristic	Prevalence Ratio (95% Confidence Interval)		
	A(H1N1)pdm09 vs Seasonal Influenza A Virus[a]	A(H1N1)pdm09 vs Noninfluenza[b]	Seasonal Influenza A Virus vs Noninfluenza[b]
Age 5–18 y	2.0 (1.3–3.1)	3.2 (2.4–4.3)	1.6 (1.1–2.3)
Exposure			
Household contact	1.0 (.8–1.3)	1.3 (1.1–1.6)	1.3 (1.1–1.5)
Attends school	1.4 (1.1–1.8)	2.2 (1.9–2.7)	1.6 (1.3–2.0)
Attends school, adjusted for age 5–18 y	1.2 (.8–1.5)	1.9 (1.5–2.4)	1.6 (1.2–2.1)

Abbreviation: A(H1N1)pdm09, 2009 pandemic influenza A virus subtype H1N1.

[a] One person with A(H1N1)pdm09 and influenza A virus subtype H3N2 coinfection was excluded from analysis.

[b] No virus or a virus other than influenza virus was identified.

We found temporal differences in pandemic influenza virus circulation in different surveillance sites in Kenya. These differences may have been due to differences in contact rates with infected patients or geographic features, such as climate. Precipitation, humidity, and temperature have been shown to affect influenza virus activity in other parts of the world [9].

Patients infected with A(H1N1)pdm09 were significantly more likely to be aged 5–18 years, compared with those with seasonal influenza A virus infection or noninfluenza ILI. These patients were also more likely to attend school. A(H1N1)pdm09 infection outbreaks have been described in schools in multiple countries, including the United States, Japan, France, and United Kingdom [10–15]. A study comparing the 2009 influenza season to prior seasonal influenza epidemics in the United States, France, and New Zealand found that there was a shift in age distribution toward school-aged children, adolescents, and young adults during the 2009 pandemic season [16]. This difference in age distribution may be due to a higher prevalence of immunity to seasonal influenza virus infection among school-aged children, compared with those aged <5 years. Understanding the age distribution of pandemic versus seasonal influenza virus infection and other causes of ILI may help guide preventive measures, such as targeted vaccination or social distancing. In 2008, a draft pandemic contingency plan in Kenya recommended school closure as a social distancing measure upon declaration of pandemic phase 4 or higher [17]. Mathematical models and some historical data suggest that school closure may mitigate influenza spread; however, without proper timing, the potential effect of school closure on disease spread is undermined [18–22]. The CDC recommends vaccination, hand hygiene, and early identification and isolation of ill students and staff, rather than school closure, as the main methods of reducing transmission in schools [23]. In Kenya, the effect of school closure on influenza transmission is not well studied, and the timing of school closure, the economic and social impact of this intervention, and student behavior outside of school is likely to influence the effectiveness of school closure on disease transmission.

The findings of this study may also inform targeted vaccination strategies in a future influenza pandemic. School-aged children can facilitate community spread of influenza by having a high rate of contact with others and by introducing influenza into their households. Targeting school-aged children for vaccination can provide direct protection to this demographic, as well as indirect protection to the broader population through herd immunity [24]. Surveillance will be the first step in designing and implementing pandemic control measures [25].

The study has several limitations. First, the study is limited to patients <18 years old and does not represent the general Kenyan population. The age distribution of patients with ILI is also affected by patterns of healthcare utilization in Kenya. Our findings of more school-aged children among those with A (H1N1)pdm09 may reflect age differences in symptomatic attack rate of A(H1N1)pdm09, or they may reflect a higher propensity for families to seek health care for older children who have more severe symptoms, if A(H1N1)pdm09 infection causes more severe illness. Information was not collected about nonconsenting patients, and therefore we could not determine whether nonconsenting patients differed from the study population. Second, several of the clinical symptoms on the questionnaire are not applicable to young children, making it difficult to interpret whether patients of different age groups or with different causes of ILI have unique clinical presentations. Third, the proportion of ILI cases due to A(H1N1)pdm09 infection may have been underrepresented during the pandemic season because there was a large number of patients with influenza A virus infection with uninterpretable subtyping results during the pandemic season. It is possible that these nonsubtyped influenza A virus samples were A(H1N1)pdm09, because this strain was predominant from June 2009 through August 2010. However, because of these uncertainties with the nonsubtyped specimens, we were unable to estimate the proportion of ILI cases due to any influenza A virus subtype.

Despite these limitations, the surveillance system was able to describe the epidemiology and geographic evolution of A (H1N1)pdm09 in Kenya. The ability of this surveillance system to detect emerging epidemics could allow for targeting of public health interventions in the future.

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online (http://jid.oxfordjournals.org/). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

References

1. Centers for Disease Control and Prevention (CDC). Outbreak of swine-origin influenza A (H1N1) virus infection—Mexico, March–April 2009. MMWR Morb Mortal Wkly Rep 2009; 58:467–70.
2. Centers for Disease Control and Prevention (CDC). Swine influenza A (H1N1) infection in two children–Southern California, March–April 2009. MMWR Morb Mortal Wkly Rep 2009; 58:400–2.
3. World now at the start of 2009 influenza pandemic. http://www.who.int/mediacentre/news/statements/2009/h1n1_pandemic_phase6_20090611/en/index.html. Accessed 25 September 2012.
4. Centers for Disease Control and Prevention (CDC). Introduction and transmission of 2009 pandemic influenza A (H1N1) Virus–Kenya, June-July 2009. MMWR Morb Mortal Wkly Rep 2009; 58:1143–6.
5. Steffen C, Diop OM, Gessner BD, et al. Afriflu–international conference on influenza disease burden in Africa, 1–2 June 2010, Marrakech, Morocco. Vaccine 2011; 29:363–9.
6. Jeremy Sueker J, Blazes DL, Johns MC, et al. Influenza and respiratory disease surveillance: the US military's global laboratory-based network. Influenza Other Respi Viruses 2010; 4:155–61.
7. World Health Organization. Regional office for the Western Pacific. A practical guide for designing and conducting influenza disease burden studies. Manila, Philippines: World Health Organization, Western Pacific Region, 2008.
8. The WHO Collaborating Centre for influenza at CDC. CDC protocol of realtime RTPCR for influenza A (H1N1). Atlanta, USA: World Health Organization, 2009.
9. Soebiyanto RP, Adimi F, Kiang RK. Modeling and predicting seasonal influenza transmission in warm regions using climatological parameters. PLoS One 2010; 5:e9450.
10. Lessler J, Reich NG, Cummings DA, et al. Outbreak of 2009 pandemic influenza A (H1N1) at a New York City school. N Engl J Med 2009; 361:2628–36.
11. Centers for Disease Control and Prevention (CDC). Swine-origin influenza A (H1N1) virus infections in a school - New York City, April 2009. MMWR Morb Mortal Wkly Rep 2009; 58:470–2.
12. Human infection with new influenza A (H1N1) virus: clinical observations from a school-associated outbreak in Kobe, Japan, May 2009. Wkly Epidemiol Rec 2009; 84:237–44.
13. Guinard A, Grout L, Durand C, Schwoebel V. Outbreak of influenza A(H1N1)v without travel history in a school in the Toulouse district, France, June 2009. Euro Surveill 2009; 14:19265.
14. Health Protection Agency West Midlands H1N1v Investigation Team. Preliminary descriptive epidemiology of a large school outbreak of influenza A(H1N1)v in the West Midlands, United Kingdom, May 2009. Euro Surveill 2009; 14:19264.
15. Smith A, Coles S, Johnson S, Saldana L, Ihekweazu C, O'Moore E. An outbreak of influenza A(H1N1)v in a boarding school in South East England, May-June 2009. Euro Surveill 2009; 14:19263.
16. Karageorgopoulos DE, Vouloumanou EK, Korbila IP, Kapaskelis A, Falagas ME. Age distribution of cases of 2009 (H1N1) pandemic influenza in comparison with seasonal influenza. PLoS One 2011; 6: e21690.
17. United Nations Office at Nairobi. Pandemic influenza contingency plan: working draft. Nairobi, Kenya: United Nations Office at Nairobi, 2008.
18. Cauchemez S, Ferguson NM, Wachtel C, et al. Closure of schools during an influenza pandemic. Lancet Infect Dis 2009; 9:473–81.
19. Cauchemez S, Valleron AJ, Boelle PY, Flahault A, Ferguson NM. Estimating the impact of school closure on influenza transmission from Sentinel data. Nature 2008; 452:750–4.
20. Wu JT, Cowling BJ, Lau EH, et al. School closure and mitigation of pandemic (H1N1) 2009, Hong Kong. Emerg Infect Dis 2010; 16:538–41.
21. Heymann AD, Hoch I, Valinsky L, Kokia E, Steinberg DM. School closure may be effective in reducing transmission of respiratory viruses in the community. Epidemiol Infect 2009; 137:1369–76.
22. Cowling BJ, Lau EH, Lam CL, et al. Effects of school closures, 2008 winter influenza season, Hong Kong. Emerg Infect Dis 2008; 14: 1660–2.
23. Guidance for school administrators to help reduce the spread of seasonal influenza in K-12 schools during the 2010–2011 school year. http://www.cdc.gov/flu/school/guidance.htm. Accessed 25 September 2012.
24. Glezen WP, Gaglani MJ, Kozinetz CA, Piedra PA. Direct and indirect effectiveness of influenza vaccination delivered to children at school preceding an epidemic caused by 3 new influenza virus variants. J Infect Dis 2010; 202:1626–33.
25. Heymann DL, Rodier GR. Global surveillance of communicable diseases. Emerg Infect Dis 1998; 4:362–5.