To determine clinical characteristics of patients hospitalized in the United Kingdom with pandemic (H1N1) 2009, we studied 1,520 patients in 75 National Health Service hospitals. We characterized patients who acquired influenza nosocomially during the pandemic (H1N1) 2009 outbreak. Of 30 patients, 12 (80%) of 15 adults and 14 (93%) of 15 children had serious underlying illnesses. Only 12 (57%) of 21 patients who received antiviral therapy did so within 48 hours after symptom onset, but 53% needed escalated care or mechanical ventilation; 8 (27%) of 30 died. Despite national guidelines and standardized infection control procedures, nosocomial transmission remains a problem when influenza is prevalent. Health care workers should be routinely offered influenza vaccine, and vaccination should be prioritized for all patients at high risk. Staff should remain alert to the possibility of influenza in patients with complex clinical problems and be ready to institute antiviral therapy while awaiting diagnosis during influenza outbreaks.

Nosocomial influenza is a well-recognized problem in acute-care hospital settings (1,2). Outbreaks of influenza A have been reported in general wards (3,4), pediatric units (5), neonatal intensive care units (ICUs) (6–8), hemopoietic and solid organ transplantation units (9–11),
oncology and neurology units (12,13), and facilities for the elderly and for long-term care (14–17). Associated illness and death rates are particularly high in immunocompromised patients (18–20).

On June 11, 2009, the World Health Organization reported the first influenza pandemic of the 21st century (21,22). Although most cases of pandemic (H1N1) 2009 have been mild or subclinical, patients with severe disease have considerably affected hospital systems (23). Three nosocomial outbreaks of pandemic (H1N1) 2009 were reported in hemopoietic transplantation units and oncology wards. One outbreak was reportedly mild (24), and the other 2 involved aggressive illness, severe complications, and deaths (25,26).

In addition to outbreaks of nosocomial influenza, sporadic nosocomial influenza infections also occur but generally are not reported in the literature. We describe the clinical and epidemiologic characteristics of nosocomial pandemic (H1N1) 2009 infections during 2009–2010 in the United Kingdom that were identified during surveillance rather than through outbreak control activity.

**Methods**

During the pandemic (H1N1) 2009 outbreak in the United Kingdom, the Influenza Clinical Information Network (FLU-CIN) collected clinical and epidemiologic data for patients with virologically confirmed pandemic (H1N1) 2009 virus infection admitted to hospitals (27). Data included demography, symptoms, medical history, influenza vaccination history, relevant timelines, investigations and results, treatment (e.g., antiviral and antibacterial drugs), outcome, and cause of death when available. Trained health care workers abstracted data from case notes. During May 11, 2009–January 31, 2010, data were accrued from 75 National Health Service hospitals in 31 cities or towns in England, Scotland, Wales, and Northern Ireland.

From this source cohort, we defined patients with nosocomial pandemic (H1N1) 2009 as those admitted to a hospital for a reason other than acute respiratory infection in whom respiratory symptoms developed ≥72 hours (3 days) after admission. In addition, we included infants who had not left the hospital since birth in whom pandemic (H1N1) 2009 had developed. We included transfers from other hospitals when a transfer was for a reason other than influenza and when the history of influenza clearly indicated that it had been acquired at another hospital.
Results

Of 1,520 patients in the FLU-CIN cohort, illnesses in 30 (2.0%) (15 children) met the criteria for nosocomial influenza (Tables 1, 2 [adults] and Tables 3, 4 [children]). Patient ages ranged from 41 days to 76 years at onset of influenza symptoms (median age 44 years for adults and 1 year for children).

Concurrent Conditions and Reasons for Admission

Twelve (80%) adults and 14 (93%) children had serious underlying illnesses. The most common illnesses were hematologic malignancy for adults (5), and congenital abnormality or prematurity (7) or malignancy (4) for children.

Of the 15 adults, 2 had been admitted for elective surgical procedures; 1 for emergency surgery; and 8 for deterioration of chronic conditions, including complications caused by chemotherapy, malignancy, or transplantation. Two patients were admitted for pancreatitis (1 of whom had underlying myeloma); 1 patient was admitted for obstetric complications, and another patient was admitted for psoriasis. Of 15 children, 3 were admitted for elective procedures, 6 had been in the hospital since birth (because of prematurity or congenital abnormality), 1 was transferred from another hospital, and 5 had acute conditions (Table 2).

Pandemic Vaccination Status and Use of Antiviral and Antibacterial Drugs

None of the patients had received pandemic influenza vaccine. Although 14 adults were eligible because of concurrent conditions, influenza symptoms developed in 11 either before vaccine became available or before they would have seroconverted if vaccinated at the earliest opportunity (vaccine became available in the United Kingdom at the end of October 2009). Four children were eligible because of age and concurrent conditions, and symptoms developed in 3 before vaccine became available or before they would have seroconverted Only 2 patients (both adults) had received seasonal influenza vaccine.

Twenty-one (72%) of 29 patients (10 children) received antiviral medication as inpatients (data were unknown for 1 patient); all initially received oseltamivir as monotherapy. Therapy for
1 patient (no. 18) was switched to zanamivir after 10 days of oseltamivir therapy because drug-resistant virus carrying the H275Y mutation was identified. Administration of antiviral drugs ranged from 0 to 8 days after symptom onset; 12 (57%) of 21 patients who received therapy did so within 48 hours. Sixteen patients were already receiving antibacterial drugs when influenza symptoms began. Two of these patients had a bacterial co-infection: coagulase-negative staphylococci in a blood culture for 1 patient and *Pseudomonas aeruginosa* in an unspecified intravenous line in 1 patient. Twelve patients received antibacterial drugs during their respiratory illness, 2 of whom had *Haemophilus influenzae* in sputum samples and 1 (co-infected with rhinovirus) who had had a blood culture positive for *Klebsiella* sp.

**Signs and Symptoms**

The most common signs were fever (8 [53%] adults and 12 [80%] children), cough (10, mostly adults), coryza (8, mostly children), and dyspnea (7). Fewer patients had malaise (4); myalgia (3); anorexia, nausea, diarrhea (2 each); and arthralgia, sore throat, headache, vomiting, altered consciousness, sneezing, and rash (a child) (1 each).

**Course of Illness**

Median length of hospitalization before onset of influenza symptoms was 11 days for adults (range 4–78 days) and 13 days (range 6–54 days) for children, excluding infants in a hospital since birth. For infants in a hospital since birth, the interval from birth to onset of influenza signs ranged from 41 to 123 days (median = 78 days).

Results of chest radiography ≤3 days after onset of influenza symptoms were documented for 8 adults and 5 children (43%). Of these patients, 4 adults and 1 child (38%) had radiologically confirmed pneumonia.

Level 0 is care given to patients whose care needs can be met through normal ward care. Level 1 care is given to patients at risk for a deteriorating condition or recently relocated from higher levels of care whose needs can be met in an acute-care ward with additional advice and support from the critical-care team. Level 2 care is given to patients requiring more detailed observation or intervention, including support for a single failing organ system and those changing from higher levels of care (high dependency unit). Level 3 care is given to patients requiring advanced respiratory support alone or basic respiratory support and support for ≥2
organ systems. This level includes all patients with complex conditions requiring support for multiorgan failure (ICU).

Seven adults and 8 children (50%) required level 3 care (ICU, pediatric ICU, or neonatal ICU). One (3%) adult required level 2 care. Six adults required mechanical ventilation and 1 required noninvasive ventilation (data for ventilatory support were unknown for 1 adult). Three children required mechanical ventilation and 1 required noninvasive ventilation. The remaining 4 children who received level 3 care were 3 infants and 1 child, each of whom required a period of close monitoring, but did not ultimately require ventilation. The remaining 7 adults and 7 children required level 0 or 1 care.

Outcomes and Mortality Rates

Five (33%) of 15 adults died in the acute-care hospital that provided treatment, 2 within 30 days of symptom onset. Of adults who died, 3 had underlying malignancy (1 noted to be terminal) or were immunocompromised and 2 had diabetes (type I and type II respectively). Pandemic (H1N1) 2009 was included in the recorded causes of death for all 5 adults. Although some patients had a prolonged hospital stay of $\leq7$ months, all remaining adults recovered from influenza and were discharged from the hospital.

Of 15 children, 3 (20%) were known to have died, although only 1 (a neonate with multiple congenital problems) died at the hospital where surveillance was conducted; acute respiratory distress syndrome/lower respiratory tract infection was stated as a cause of death. Another child, with malignancy, whose death was expected, died at home shortly after discharge. The third child was transferred to another hospital, and cause of death is unknown. All other children recovered from pandemic (H1N1) 2009. Two children remained in the hospital for treatment of their underlying malignancy, and the other children were discharged.

Discussion

Although pandemic (H1N1) 2009 produced a generally mild illness, in the United Kingdom, as elsewhere, severe illness developed in a small proportion of relatively young patients who required hospitalization (28). Although nosocomial outbreaks of pandemic (H1N1) 2009 have been described, (24–26) sporadic nosocomial cases of pandemic (H1N1) 2009 identified during surveillance activities have not been described. The present case series has the
advantage of being derived from a larger cohort of hospital inpatients in whom confirmation of pandemic (H1N1) 2009 was obtained by using nationally standardized PCR criteria, from settings where clinical management and infection control precautions were driven by national guidelines (29,30), and with data abstracted by trained nurses (27).

We based our definition of nosocomial influenza on a recent study of health care–associated influenza in children (31). A recent systematic review of incubation periods of acute respiratory viral infections found that the median incubation period for influenza was 1.4 days for influenza A, and symptoms developed in 95% of patients in ≤2.8 days (32). These findings suggest that our cutoff point, 3 days after admission, make inclusion of community cases unlikely. In addition, in no patients did onset of respiratory illness occur <4 days after hospital admission; median length of hospitalization before symptom onset was 11 days for adults and 13 days for infants. Therefore, inadvertent inclusion of community-acquired cases is highly unlikely.

On the basis of information obtained in the study, we cannot determine where and from whom patients acquired influenza. However, 3 routes are possible. First, infection could have been acquired from other patients; 1 patient shared a bay with a patient who was presymptomatic at the time but for whom influenza was diagnosed 1 day later. Second, transmission from visitors of patients cannot be ruled out. Although national guidelines strongly discourage persons with influenza-like symptoms from visiting patients (29), this recommendation may have been difficult to implement, particularly for parents of sick children who often provide most hands-on care in a hospital. Third, transmission may have occurred from an infectious health care worker (because staff continue to work when infected with influenza [33]) or from contaminated hands of a health care worker. Transmission from asymptomatic persons might occur in all 3 instances (34).

Nosocomial cases in this study occurred equally in adults and children. Consistent with previous findings (3), most patients had ≥1 serious underlying illnesses, notably hematologic malignancies, congenital disorders, or prematurity. Staff and caregivers of patients with hematologic malignancy and prematurity are often particularly vigilant for symptoms suggestive of infectious disease. Although we detected nosocomial influenza in patients admitted to nonmedical areas (for emergency or elective surgery), many cases of nosocomial infection in
other patient groups probably have been overlooked, particularly because influenza in these
groups is likely to have been milder. Additionally, some patients are likely to have been
discharged from a hospital during the incubation period of nosocomially acquired pandemic
influenza. Thus, in this case series, detecting such patients would not have been possible.

More than half of patients required level 2 or level 3 care, which is higher than that
required by the source cohort (12%) (27). Approximately one fifth of children and one third of
adults died. Although the deaths of 2 patients were expected because of the stage of their
underlying malignancy, this case-fatality rate is far higher than that for patients with pandemic
(H1N1) 2009 and concurrent conditions in the source cohort (5%) (27). The combined factors of
increased host susceptibility (18–20), prolonged virus shedding in immunocompromised children
(35), and increased likelihood of development of drug resistance (36) raise questions about the
need for enhanced infection control procedures in special-care infant units, pediatric wards, and
hemopoietic transplant units and a requirement that staff working in these areas be vaccinated
(37–39). Precautions should include restricting unnecessary movement of patients to units with
particularly vulnerable patients and postponement of semi-elective (nonurgent) procedures for
hematology patients during peak pandemic activity.

Vaccine against pandemic (H1N1) 2009 became available at the end of October 2009. Assuming a 2-week period for vaccine administration, case-patients in groups at risk with
influenza onset dates after November 30, 2009, could have been vaccinated and would have had
time to seroconvert (14 days). Using these criteria, we determined that 4 cases (in 3 adults and 1
child) (13%) were potentially preventable by vaccination; 2 of these patients required escalated
care and 1 patient died. Although 72% of patients received antiviral therapy, similar to 75% in
the source cohort (27), we observed avoidable delays between recording of respiratory symptoms
and start of specific antiviral therapy in some adults and all children. Although under ordinary
circumstances, the complex clinical picture of such patients might result in delayed or incidental
finding of influenza, in a pandemic situation or during a seasonal epidemic, clinicians should be
alert to the possibility of influenza. Delays encountered in this series most likely reflect a failure
to consider such a diagnosis early. Other reasons are caution or uncertainty in using oseltamivir
in patients younger than the drug licensing permits (12 months) in nonpandemic situations,
reluctance to empirically instigate antiviral treatment in advance of a confirmed diagnosis of
pandemic (H1N1) 2009, lack of confidence about absorption of oseltamivir by nasogastric tube
insertion in patients already receiving mechanical ventilation or concerns about potential gastrointestinal side effects.

Nosocomial infections with pandemic (H1N1) 2009 in this case series were associated with high rates of illness and death. This finding highlights the need for adherence to infection control guidelines for staff and visitors (including the need to urge visitors not to visit when they are ill, particularly when providing hands-on care for vulnerable children), staff vaccination, maintenance of clinical suspicion for influenza in areas of high risk, prompt (empirical) antiviral treatment for vulnerable patients in whom influenza is possible or likely, and consideration of postponing nonurgent procedures for hematology patients during periods of known high influenza activity. This report demonstrates that nosocomial transmission is a recurrent problem when the prevalence of influenza is high and the total effect of nosocomial influenza is underestimated by outbreak reports alone.

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References

1. Salgado CD, Farr BM, Hall KK, Hayden FG. Influenza in the acute hospital setting. Lancet Infect Dis. 2002;2: 145–55. PubMed DOI: 10.1016/S1473-3099(02)00221-9

2. Maltezou HC, Drancourt M. Nosocomial influenza in children. J Hosp Infect. 2003;55:83–91. PubMed DOI: 10.1016/S0195-6701(03)00262-7

3. Kapila R, Lintz DI, Tescon FT, Ziskin L, Louria DB. A nosocomial outbreak of influenza A. Chest. 1977;71:576–9. PubMed DOI: 10.1378/chest.71.5.576

4. Sartor C, Zandotti C, Romain F, Jacomo V, Simon S, Atlan-Gepner C, et al. Nosocomial influenza outbreak: disruption of services in an internal medicine unit. Infect Control Hosp Epidemiol. 2002;23:615–9. PubMed DOI: 10.1086/501981

5. Hall CB, Douglas RG Jr. Nosocomial influenza infection as a cause of recurrent fever in infants. Pediatrics. 1975;55:673–7. PubMed

6. Munoz FM, Campbell JR, Atmar RL, Garcia-Prats J, Baxter BD, Johnson LE, et al. Influenza A outbreak in a neonatal intensive care unit. Pediatr Infect Dis J. 1999;18:811–5. PubMed DOI: 10.1097/00006454-199909000-00013

7. Sagrera X, Ginovart G, Raspall F, Rabella N, Sala P, Sierra M, et al. Outbreaks of influenza A virus infection in neonatal intensive care units. Pediatr Infect Dis J. 2002;21:196–200. PubMed DOI: 10.1097/00006454-200203000-00007

8. Meibalane R, Sedmak G, Sasidharan P, Garg P, Grausz J. Outbreak of influenza in a neonatal care unit. J Pediatr. 1977;91:974–6. PubMed DOI: 10.1016/S0022-3476(77)80907-4

9. Weinstock DM, Eagan J, Malak SA, Rogers M, Wallace H, Keihm TE, et al. Control of influenza A on a bone marrow transplant unit. Infect Control Hosp Epidemiol. 2000;21:730–32. PubMed DOI: 10.1086/501726

10. Vu D, Peck AJ, Nichols WG, Varley C, Englund JA, Corey L, et al. Safety and tolerability of oseltamivir prophylaxis in haematopoietic stem cell transplant recipients: a retrospective case–control study. Clin Infect Dis. 2007;45:187–93. PubMed DOI: 10.1086/518985
11. Malavaud S, Malavaud B, Sandres K, Durand D, Marty N, Icart J, et al. Nosocomial outbreak of influenza virus A(H3N2) infection in a solid organ transplant department. Transplantation. 2001;72:535–7. PubMed DOI: 10.1097/00007890-200108150-00032

12. Schepetiuk S, Papananoum K, Qiao M. Spread of influenza A virus in hospitalised patients with cancer. Aust N Z J Med. 1998;28:475–6. PubMed DOI: 10.1111/j.1445-5994.1998.tb02089.x

13. Muchmore HG, Felton FG, Scott LV. A confirmed hospital epidemic of Asian influenza. J Okla State Med Assoc. 1960;53:142–5. PubMed

14. Van Voris LP, Belshe RB, Shaffer JL. Nosocomial influenza B virus in the elderly. Ann Intern Med. 1982;96:153–8. PubMed

15. Read CA, Mohsun A, Nguyen-Van-Tam JS, McKendrick M, Kudesa G. Outbreaks of influenza A in nursing homes in Sheffield during the 1997/98 season: implications for diagnosis and control. J Public Health Med. 2000;22:116–20. PubMed DOI: 10.1093/pubmed/22.1.116

16. Chang YM, Li WC, Huang CT, Huang CG, Tsao KC, Cheng YH, et al. Use of oseltamivir during an outbreak of influenza A in a long-term care facility in Taiwan. J Hosp Infect. 2008;68:83–7. PubMed DOI: 10.1016/j.jhin.2007.08.022

17. Lee C, Loeb M, Phillips A, Nesbitt J, Smith K, Fearon M, et al. Zanamivir use during transmission of amantadine-resistant influenza A in a nursing home. Infect Control Hosp Epidemiol. 2000;21:700–4. PubMed DOI: 10.1086/501727

18. Whimbey E, Elting LS, Couch RB, Lo W, Williams L, Champlin RE, et al. Influenza A virus infections among hospitalized adult bone marrow recipients. Bone Marrow Transplant. 1994;13:437–40. PubMed

19. Hirschhorn LR, McIntosh K, Anderson KG, Dermody TS. Influenzal pneumonia as a complication of autologous bone marrow transplantation. Clin Infect Dis. 1992;14:786–7. PubMed

20. Yousuf HM, Englund J, Couch R, Rolston K, Luna M, Goodrich J, et al. Influenza among hospitalized adults with leukaemia. Clin Infect Dis. 1997;24:1095–9. PubMed DOI: 10.1086/513648

21. Perez-Padilla R, de la Rosa-Zamboni D, Ponce de Leon S, Hernandez M, Quiñones-Falconi F, Bautista E, et al. Pneumonia and respiratory failure from swine-origin influenza A (H1N1) in Mexico. N Engl J Med. 2009;361:680–9. PubMed DOI: 10.1056/NEJMoa0904252
22. Novel Swine-origin Influenza A (H1N1) Virus Investigation Team, Dawood FS, Jain S, Finelli L, Shaw MW, Lindstrom S, et al. Emergence of a novel swine-origin influenza A (H1N1) virus in humans. N Engl J Med. 2009;360:2605–15. PubMed DOI: 10.1056/NEJMoat0903810

23. Writing Committee of the WHO Consultation on Clinical Aspects of Pandemic (H1N1) 2009 Influenza, Bautista E, Chotpitayasunondh T, Gao Z, Harper SA, Shaw M, et al. Clinical aspects of pandemic 2009 influenza A (H1N1) virus infection. N Engl J Med. 2010;362:1708–19. PubMed DOI: 10.1056/NEJMra1000449

24. Chironna M, Tafuri S, Santoro N, Prato R, Quart M, Germinario CA. A nosocomial outbreak of 2009 pandemic influenza A (H1N1) in a paediatric oncology ward in Italy, October–November 2009. Euro Surveill. 2010;15:19454. PubMed

25. Lalayanni C, Sirigou A, Iskas M, Smias C, Sakellari J, Anagnostopoulos A. Outbreak of novel influenza A (H1N1) in an adult haematology department and haematopoietic cell transplantation unit: clinical presentation and outcome. J Infect. 2010;61:270–2. PubMed DOI: 10.1016/j.jinf.2010.06.013

26. Kharfan-Dabaja MA, Velez A, Richards K, Greene JN, Field T, Sandin R. Influenza A/pandemic 2009/H1N1 in the setting of allogeneic hematopoietic stem cell transplantation: a potentially catastrophic problem in a vulnerable population. Int J Hematol. 2010;91:124–7. PubMed DOI: 10.1007/s12185-009-0464-5

27. Nguyen-Van-Tam JS, Openshaw PJM, Hashim A, Gadd EM, Lim WS, Semple MG, et al. Risk factors for hospitalisation and poor outcome with pandemic A/H1N1 influenza: United Kingdom first wave (May–September 2009). Thorax. 2010;65:645–51. PubMed DOI: 10.1136/thx.2010.135210

28. Simpson CR, Ritchie LD, Robertson C, Sheikh A, McMenamin J. Vaccine effectiveness in pandemic influenza–primary care reporting (VIPER): an observational study to assess the effectiveness of the pandemic influenza A (H1N1)v vaccine. Health Technol Assess. 2010;14:313–46. PubMed

29. Department of Health. Pandemic (H1N1) influenza: a summary of guidance for infection control in healthcare settings [cited 2010 Aug 9]. http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_110902

30. British Infection Society, British Thoracic Society, Health Protection Agency. Pandemic flu: clinical management of patients with an influenza-like illness during an influenza pandemic. Provisional
guidelines from the British Infection Society, British Thoracic Society and Health Protection Agency in collaboration with the Department of Health. Thorax. 2007;62(Suppl 1):1–46. PubMed

31. Leckerman KH, Sherman E, Knorr J, Zaoutis TE, Coffin SE. Risk factors for healthcare-associated, laboratory-confirmed influenza in hospitalized pediatric patients: a case–control study. Infect Control Hosp Epidemiol. 2010;31:421–4. PubMed DOI: 10.1086/651311

32. Lessler J, Reich NG, Brookmeyer R, Perl TM, Nelson KE, Cummings DA. Incubation periods of acute respiratory viral infections: a systematic review. Lancet Infect Dis. 2009;9:291–300. PubMed DOI: 10.1016/S1473-3099(09)70069-6

33. Elder AG, O'Donnell B, McCruden EA, Symington IS, Carman WF. Incidence and recall of influenza in a cohort of Glasgow healthcare workers during the 1993–4 epidemic: results of serum testing and questionnaire. BMJ. 1996;313:1241–2. PubMed

34. Patrozou E, Mermel LA. Does influenza transmission occur from asymptomatic infection or prior to symptom onset? Public Health Rep. 2009;124:193–6. PubMed

35. Klimov AI, Rocha E, Hayden FG, Shult PA, Roumillat LF, Cox NJ. Prolonged shedding of amantadine-resistant influenza A viruses by immunodeficient patients: detection by polymerase chain reaction–restriction analysis. J Infect Dis. 1995;172:1352–5. PubMed

36. Harvala H, Gunson R, Simmonds P, Hardie A, Bennett S, Scott F, et al. The emergence of oseltamivir-resistant pandemic influenza A (H1N1) 2009 virus amongst hospitalised immunocompromised patients in Scotland, November–December 2009. Euro Surveill. 2010;15:1pii:19536.

37. Rakita RM, Hagar BA, Crome P, Lammert JK. Mandatory influenza vaccination of healthcare workers: a 5-year study. Infect Control Hosp Epidemiol. 2010;31:881–8. PubMed DOI: 10.1086/656210

38. van Delden JJ, Ashcroft R, Dawson A, Marckmann G, Upshur R, Verweij MF. The ethics of mandatory vaccination against influenza for health care workers. Vaccine. 2008;26:5562–6. PubMed DOI: 10.1016/j.vaccine.2008.08.002

39. Tilburt JC, Mueller PS, Ottenberg AL, Poland GA, Koenig BA. Facing the challenges of influenza in healthcare settings: the ethical rationale for mandatory seasonal influenza vaccination and its implications for future pandemics. Vaccine. 2008;26(Suppl 4):D27–30. PubMed DOI: 10.1016/j.vaccine.2008.07.068
Table 1. Characteristics of 15 hospitalized adults with nosocomial pandemic (H1N1) 2009, United Kingdom, 2009–2010

| Patient no. | Age, y/sex | Reason for admission | Main underlying illnesses | Signs and symptoms |
|-------------|------------|----------------------|--------------------------|--------------------|
| 1           | 51/F       | Pancreatitis         | None recorded            | Fever, unknown data in other fields |
| 2           | 44/M       | Transplant complications | Lymphoma              | Productive cough, headache, coryza, myalgia |
| 3           | 34/M       | Emergency surgery    | Diabetes                 | Unknown              |
| 4           | 18/F       | Elective surgery     | Neurodegenerative disease | Dyspnea, malaise    |
| 5           | 48/M       | Chemotherapy         | Hematologic malignancy   | Fever, sore throat  |
| 6           | 43/M       | Pancreatitis         | Chronic liver disease    | Fever, malaise, myalgia |
| 7           | 51/M       | Not recorded          | Lymphoma                | Fever, dry cough, diarrhea, myalgia, arthralgia |
| 8           | 39/F       | Metastatic soft tissue | Malignancy             | Dry cough, dyspnea  |
| 9           | 76/M       | Elective surgery     | Diabetes, heart disease  | Productive cough, diarrhea, dyspnea |
| 10          | 45/F       | Not stated            | Myeloma                 | Fever, productive cough, nausea, anorexia, malaise |
| 11          | 44/F       | Psoriasis             | Psoriasis               | Fever, unknown data in other fields |
| 12          | 22/M       | Posttransplant complications | Renal transplant, congenital abnormalities | Fever, cough, anorexia, malaise |
| 13          | 52/M       | Elective procedure   | Lymphocytic leukemia     | Dyspnea, altered consciousness |
| 14          | 33/F       | Obstetric complications | None recorded          | Fever, productive cough |
| 15          | 60/M       | Cerebrovascular disease | Diabetes, obesity      | Unknown              |

Table 2. Timelines and outcomes for 15 hospitalized adults with nosocomial pandemic (H1N1) 2009, United Kingdom, 2009–2010

| Patient no. | Age, y/sex | Hospital admission to symptom onset, d | Symptom onset to receipt of antiviral therapy, d | Maximum level of care* | Outcome† |
|-------------|------------|-----------------------------------------|-----------------------------------------------|------------------------|----------|
| 1           | 51/F       | 26                                      | 0                                             | 0/1                    | Unknown data |
| 2           | 44/M       | 14                                      | 0                                             | 0/1                    | Recovered |
| 3           | 34/M       | 8                                       | 0                                             | 3                      | Died     |
| 4           | 18/F       | 4                                       | Not given                                    | 2                      | Transferred to other hospital |
| 5           | 48/M       | 9                                       | 4                                             | 0/1                    | Recovered |
| 6           | 43/M       | 5                                       | 0                                             | 0/1                    | Recovered |
| 7           | 51/M       | 29                                      | 0                                             | 3                      | Died     |
| 8           | 39/F       | 5                                       | 3                                             | 0/1                    | Died     |
| 9           | 76/M       | 11                                      | Not given                                    | 3                      | Died     |
| 10          | 45/F       | 24                                      | 2                                             | 0/1                    | Recovered |
| 11          | 44/F       | 14                                      | Not given                                    | 3                      | Transferred, improved |
| 12          | 22/M       | 5                                       | 0                                             | 3                      | Died     |
| 13          | 52/M       | 78                                      | 1†                                           | 3                      | Recovered |
| 14          | 33/F       | 7                                       | 3                                             | 0/1                    | Recovered |
| 15          | 60/M       | 13                                      | Not given                                    | 3                      | Recovered |

*Level 0 care is given to patients whose care needs can be met through normal ward care. Level 1 care is given to patients at risk for a deteriorating condition or recently relocated from higher levels of care whose needs can be met in an acute-care ward with additional advice and support from the critical-care team. Level 3 care is given to patients requiring advanced respiratory support alone or basic respiratory support and support for 2 or more organ systems; this level includes all patients with complex conditions that required support for multiorgan failure (intensive care unit). Level 2 care is given to patients requiring more detailed observation or intervention, including support for a single failing organ system and those changing from higher levels of care (high dependency unit).

†Deaths were attributed to pandemic (H1N1) 2009.

‡Oseltamivir was replaced with zanamivir on day 5 because of identification of the H275Y drug-resistance mutation.
Table 3. Characteristics of 15 hospitalized children with nosocomial pandemic (H1N1) 2009, United Kingdom, 2009–2010

| Patient no. | Age/sex | Reason for admission | Main underlying illnesses | Signs and symptoms |
|-------------|---------|----------------------|--------------------------|--------------------|
| 16          | 12 y/F  | Elective surgery    | Heart disease            | Fever, unknown data in other fields |
| 17          | 2 y/M   | Malignancy           | Malignancy               | Dry cough, coryza   |
| 18          | 4 y/F   | Bone marrow aspirate | Acute myeloid leukemia   | Fever, productive cough |
| 19          | 15 y/M  | Ulcerative colitis   | Ulcerative colitis       | Fever, unknown data in other fields |
| 20          | 123 d/F | Inpatient care from birth | Prematurity             | Fever, dyspnea      |
| 21          | 1 y/F   | Investigation        | Genetic disorder         | Fever, dyspnea      |
| 22          | 1 y/M   | Laryngomalacia, transfer from tertiary care center | Acute lymphoblastic leukemia | Fever, dry cough, coryza |
| 23          | 9 y/M   | Sepsis               | Cerebral palsy, septic pressure sore | Fever, patient sedated and ventilated |
| 24          | 12 y/M  | Anorexia             | Anorexia                 | Fever, coryza, nausea, sneezing |
| 25          | 82 d/M  | Inpatient care from birth | Congenital abnormalities | Coryza, dyspnoea   |
| 26          | 64 d/M  | Inpatient care from birth | Congenital abnormalities | Fever, coryza     |
| 27          | 151 d/M | Prematurity          | Prematurity              | Fever, coryza     |
| 28          | 101 d/F | Inpatient care from birth | Congenital abnormalities | Fever, coryza     |
| 29          | 41 d/F  | Inpatient care from birth | Cystic fibrosis          | Fever, rash       |
| 30          | 9 y/F   | Elective surgery     | Hematologic malignancy   | Fever              |

Table 4. Timelines and outcome for 15 hospitalized children with nosocomial pandemic (H1N1) 2009, United Kingdom, 2009–2010

| Patient no. | Age/sex | Hospital admission to symptom onset | Symptom onset to receipt of antiviral therapy | Maximum level of care* | Outcome |
|-------------|---------|-------------------------------------|-----------------------------------------------|------------------------|---------|
| 16          | 12 y/F  | 10                                  | Not given                                    | 3                      | Recovered |
| 17          | 2 y/M   | 24                                  | Not given                                    | 0/1                    | Died at home |
| 18          | 4 y/F   | 54                                  | 2†                                            | 0/1                    | Recovered |
| 19          | 15 y/M  | 11                                  | 8                                             | 0/1                    | Recovered |
| 20          | 123 d/F | 123‡                               | Unknown data                                 | 3                      | Died after transfer to another hospital |
| 21          | 1 y/F   | 14                                  | 1                                             | 0/1                    | Recovered |
| 22          | 1 y/M   | 6                                   | 5                                             | 3                      | Recovered |
| 23          | 9 y/M   | Unknown (transferred)              | 3                                             | 3                      | Recovered |
| 24          | 12 y/M  | 14                                  | Not given                                    | 0/1                    | Recovered |
| 25          | 82 d/M  | 82‡                                | 1                                             | 3                      | Died§     |
| 26          | 64 d/M  | 64‡                                | Not given                                    | 1                      | Recovered |
| 27          | 151 d/M | 151‡                               | 3                                             | 3                      | Recovered |
| 28          | 101 d/F | 101‡                               | 1                                             | 3                      | Recovered |
| 29          | 41 d/F  | 41‡                                | 1                                             | 3                      | Recovered |
| 30          | 9 y/F   | 12                                  | 1                                             | 0/1                    | Recovered |

*Level 3 care is given to patients requiring advanced respiratory support alone or basic respiratory support and support for ≥2 organ systems; this level includes all patients with complex conditions that required support for multigorgan failure (intensive care unit). Level 0 care is given to patients whose care needs can be met through normal ward care. Level 1 care is given to patients at risk for a deteriorating condition or recently relocated from higher levels of care whose needs met in an acute-care ward with additional advice and support from the critical-care team.

†Oseltamivir was replaced with zanamivir on day 11 because of identification of the H275Y drug-resistant mutation (patient also received acyclovir through hospitalization).

‡Inpatient since birth.

§Attributed to pandemic (H1N1) 2009.