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EPIDEMIOLOGY AND CONTROL OF INFLUENZA A(H1N1)v IN THE NETHERLANDS: THE FIRST 115 CASES

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Introductions of the new influenza A(H1N1) variant virus in the Netherlands led to enhanced surveillance and infection control. By 24 June 2009, 115 cases were reported, of whom 44% were indigenously acquired. Severity of disease is similar to reports elsewhere. Our point estimate of the effective reproductive number (R_e) for the initial phase of the influenza A(H1N1)v epidemic in the Netherlands was below one. Given that the R_e estimate is based on a small number of indigenous cases and a limited time period, it needs to be interpreted cautiously.

Introduction

The first human infections with the new influenza A(H1N1) variant virus [A(H1N1)v], a novel triple reassortant swine influenza virus, were diagnosed in two patients in the United States on 14 and 17 April 2009 [1]. Subsequently, this virus was identified as the cause of a large, ongoing epidemic of respiratory disease in Mexico [2]. Following the report of community transmission in more than two regions, the World Health Organization (WHO) declared on 11 June 2009 the outbreak of influenza A(H1N1)v to be a pandemic [3]. In this short report we summarise the infection control and surveillance activities undertaken in the Netherlands in response to the emergence of influenza A(H1N1)v, as well as the epidemiological characteristics of the first 115 laboratory confirmed cases.

Infection control and case finding

In response to the emergence of the new, potentially pandemic, A(H1N1)v strain of influenza virus, the Centre for Infectious Disease Control of the National Institute for Public Health and the Environment (RIVM) in the Netherlands advised on 25 April that individuals who developed fever within seven days after returning from Mexico should consult their general practitioner (GP) by telephone. On 29 April, new influenza A(H1N1)v virus infection was upgraded to a Category A notifiable disease, requiring doctors and laboratories to report the name of the patient to the Municipal Health Service when the disease was suspected or identified. Notifications are entered by Municipal Health Services into a national anonymous web-based database, including information on travel history, contact with symptomatic cases and clinical symptoms. Enhanced surveillance was carried out for clusters and for suspected patient-to-healthcare worker transmissions.

The case definitions (Table) were based on the European Union case definitions [4].

Indigenous cases were defined as cases with no history of travel abroad during the incubation period. In this report we only include laboratory-confirmed cases. Case finding was carried out by Municipal Health Services, who set out to offer laboratory testing to all reported possible cases of A(H1N1)v from 29 April onwards. Case finding was enhanced by testing all household and other close contacts of confirmed cases. From 28 May travellers with fever within seven days of arriving from the United States were also advised to consult their GP. As of 23 June, contacts (even if symptomatic) are no longer required to be tested for A(H1N1)v, unless this is indicated for their clinical management.

To control the spread of infection and attenuate disease in those infected, oseltamivir treatment was recommended from 30 April onwards for all possible, probable and confirmed cases, and for their contacts, irrespective of symptoms. This included airplane passengers seated in the same row as the index case as well as those in the two rows in front and behind. Infected individuals were advised to stay indoors for at least 10 days after the date of onset or shorter if laboratory testing turned negative after day five. The national pandemic influenza preparedness plan includes detailed instructions for protective equipment for health care workers [5]. Entry screening at airports, school closure and hospitalisation for infection control purposes have not been employed.

As of 23 June, asymptomatic contacts of confirmed cases are no longer recommended to receive oseltamivir. However, symptomatic contacts of laboratory-confirmed cases are still recommended to be treated with oseltamivir, and they continue to be notifiable.

Laboratory methods

Laboratory testing is carried out by the National Influenza Centre in the Netherlands (represented by Erasmus Medical Centre, Rotterdam and RIVM, Bilthoven) using general influenza A and A(H1N1)v specific real-time RT-PCR, initially with confirmation by sequence analysis [6]. Results of laboratory testing have been available within 32 hours after sampling to allow timely oseltamivir treatment and prophylaxis.

Methods to estimate key epidemiological parameters

For all indigenous cases we tried to identify a most probable source by examining the patients' contact history reported by Municipal Health Services who interviewed cases. For all epidemiologically linked cases, we subsequently estimated the generation interval as the average number of days between the

dates of symptom onset in the source case and in the secondary case.

To estimate the effective reproduction number (R_e), we divided the epidemiological curve in windows of duration equal to the estimated generation interval. For each pair of successive windows in the period from 30 May to 18 June we calculated the ratio

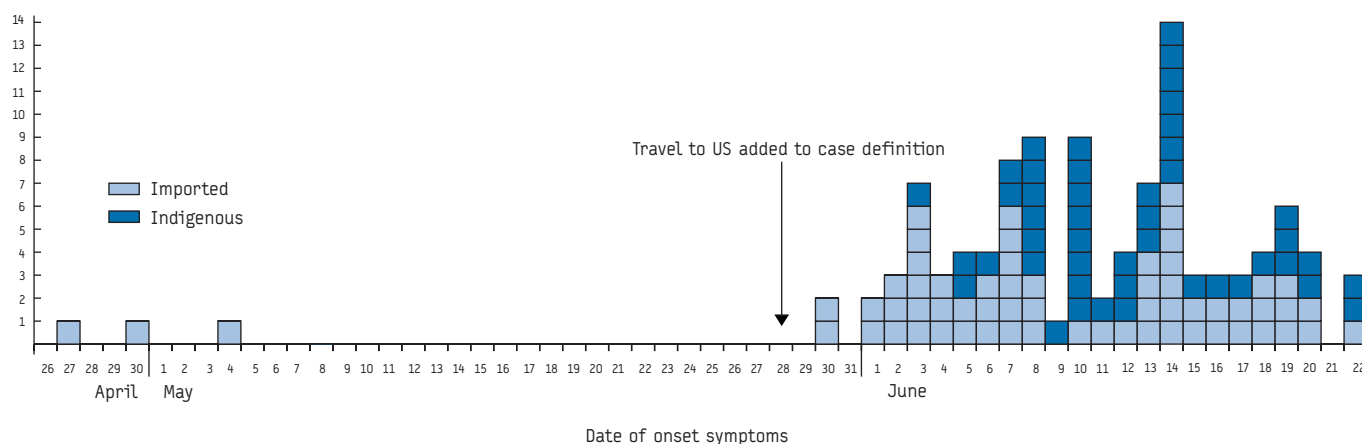
TABLE

Case definitions for new influenza A(H1N1)v [4]

Clinical criteria
Any person with one of the following three:
• fever $> 38^{\circ}\text{C}$ AND signs and symptoms of acute respiratory infection,
• pneumonia (severe respiratory illness),
• death from an unexplained acute respiratory illness.
Laboratory criteria
At least one of the following tests:
• RT-PCR,
• viral culture (requiring BSL 3 facilities),
• four-fold rise in novel influenza virus A(H1N1) specific neutralising antibodies (implies the need for paired sera, from acute phase illness and then at convalescent stage 10-14 days later minimum).
Epidemiological criteria
At least one of the following three in the seven days before disease onset:
• a person who was a close contact to a confirmed case of novel influenza A(H1N1) virus infection while the case was ill,
• a person who has travelled to an area where sustained human-to-human transmission of novel influenza A(H1N1) is documented,
• a person working in a laboratory where samples of the novel influenza A(H1N1) virus are tested.
Case classification
A. Case under investigation
Any person meeting the clinical and epidemiological criteria.
B. Probable case
Any person meeting the clinical AND epidemiological criteria AND with a laboratory result showing positive influenza A infection of an unsubtypable type.
C. Confirmed case
Any person meeting the laboratory criteria for confirmation.

FIGURE 1

Cases of laboratory-confirmed influenza A(H1N1)v virus infection by day of symptom onset and import status, the Netherlands, reported between 29 April and 24 June 2009 (n=108, further seven asymptomatic cases, of which one was imported, are not included)



between the number of indigenous cases in one window and the total number of cases in the previous window. Re was then estimated by the average of this ratio.

Results

Incidence and travel history

On 30 April the first laboratory-confirmed case of A(H1N1)v in the Netherlands was reported in a three-year-old girl who on 27 April returned with her parents from a family visit in Mexico. By 24 June, 115 confirmed cases were reported, of whom 64 (56%) were most likely imported and 51 (44%) were indigenously acquired (Figure 1). Three of the indigenous cases were in individuals who

had not been in contact with any known case or cluster. These sporadic cases were tested for the new influenza A(H1N1)v virus because they presented with influenza-like illness (n=2) or viral pneumonia (n=1). So far, no cases of influenza A(H1N1)v have been detected in the sentinel influenza surveillance.

Clinical picture and vaccination status

None of the 115 reported confirmed cases has died. Two (2%) have been admitted to hospital, including a previously physically fit man who required admission to an intensive care department with severe viral pneumonia. He was tested for influenza A(H1N1)v after presenting with respiratory failure. He had not been in contact with any known cases, and had not travelled during the incubation period. The other hospital admission concerned a tourist with asthma visiting the Netherlands. She presented with influenza-like symptoms, and did not have pneumonia. She was admitted for social indications, and was discharged after less than 24 hours. One further case had clinically diagnosed pneumonia but was not admitted to hospital. Of all cases for whom information was available (n=46), three (7%) had underlying chronic illnesses. No cases in pregnant women have been reported.

Of the 48 indigenous, non-sporadic cases, six (13%) were asymptomatic at the time of sampling. It is yet unknown, however, whether they became symptomatic after sampling. Symptoms reported by laboratory-confirmed, symptomatic cases for whom this information was available included: sore throat, cough and/or coryza (93 cases, 90%), fever $\geq 38^{\circ}\text{C}$ (76 cases, 88%), myalgia (54 cases, 52%) and diarrhoea (9 cases, 9%).

Of 111 cases for whom the seasonal influenza vaccination status for 2008-9 was known, 17 (15%, 95% CI 9-23%) reported to have been vaccinated. In 2007, an estimated 10% of the practice populations of less than 65 years of age of GPs participating to a research network (LINH, the National Information Network of General Practice) were vaccinated, whilst 15% were targeted for vaccination [7]. In our case-series, 7% of cases below 65 years of age were in the target group for seasonal influenza vaccination due to underlying illnesses (see above), and only two cases were 65 years or older. The relatively high vaccine coverage among cases compared to the coverage among the general population is consistent with a lack of effectiveness of the 2008-9 seasonal influenza vaccine against the new influenza A(H1N1)v [8].

Epidemiological characteristics

Indigenous cases were younger than imported cases, with a median age of 18 and 31 years, respectively ($p < 0.05$, Figure 2). Cases occurred in most Municipal Health Service regions, with three main clusters of indigenous transmission (Figure 3).

Of the 51 indigenous cases, 36 cases could be epidemiologically linked to an index case, 12 cases could be linked to a cluster and three cases were sporadic. Of four indigenous cases in healthcare workers who did not report contact with a case outside of work, one was considered as resulting from patient to healthcare worker transmission.

In total, nine clusters of more than one case were identified, including three larger clusters with 19, 12 and 9 cases, respectively. The mean generation (or serial) interval for these clusters was 2.5 days (standard deviation (SD) 0.9 days, cluster of 19 cases, n=13), 3.1 days (SD 1.1 days, cluster of 12 cases, n=8) and 2.8 days (SD

FIGURE 2

Cases of laboratory-confirmed influenza A(H1N1)v by age group and import status, the Netherlands, 29 April – 24 June 2009 (n=115)

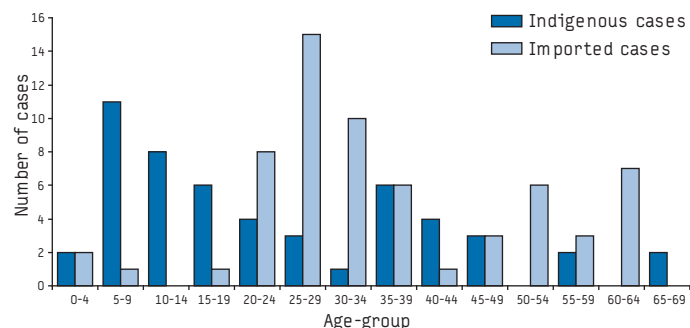
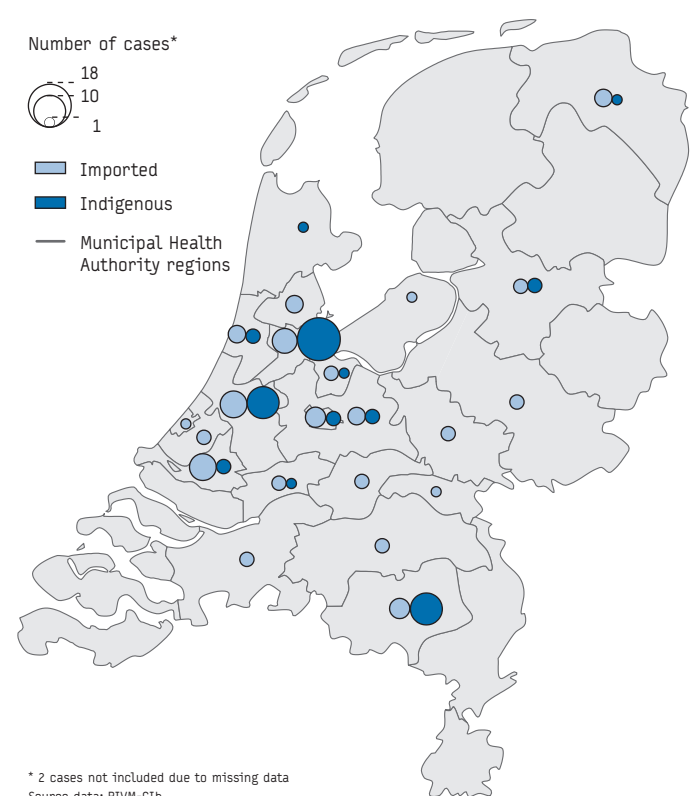


FIGURE 3

Cases of laboratory-confirmed influenza A(H1N1)v by Municipal Health Service region, the Netherlands, 29 April – 24 June 2009 (n=115)



1.7 days, cluster of 9 cases, n=5). Overall, the generation interval was 2.7 days (SD 1.1, N=32).

Based on this, we applied a generation interval of three days as moving average window to the epidemic curve. The mean ratio of the number of indigenous cases in one window to the total number of cases in the previous window (the effective reproductive number R_e) was 0.5 between 30 May and 18 June. We did not include cases with a date of onset after 18 June and due to the reporting delay we may have missed cases in this period, which would have resulted in an underestimation of R_e . We observed that no epidemiological links could be traced back to the seven asymptomatic cases, suggesting a very low R_e for asymptomatic cases. However, due to the small number of indigenous cases, the confidence bounds on these estimates of R_e can be considered to be very wide. The implicitly assumed delta distribution gives an upward bias in the point estimate of R_e . However, as the SD of the generation interval was small relative to the doubling time of the epidemic, this bias is negligible [9].

Conclusions

Despite repeated introductions of the new influenza A(H1N1)v into the Netherlands, our enhanced surveillance results suggest that indigenous transmission of this virus has remained relatively limited. A large proportion of cases were imported, and only 15% of these caused secondary cases. Moreover, only three clusters of more than four cases were detected, all relatively limited in size. This suggests that the R_e was below one, consistent with our estimate of R_e based on the epidemiological curve. Our point estimate of R_e for the influenza A(H1N1)v epidemic in the Netherlands was lower than the R_0 estimated for Mexico or the US [10]. However, as the number of indigenous cases was low, this point estimate needs to be considered cautiously. The estimated R_e was based on observations in the period 30 May and 18 June, and is likely to change in future months. Explanations for the relatively low R_e estimate may include the rigorous case-finding and infection control implemented in the Netherlands following the introductions of the influenza A(H1N1)v virus. However, our data do not allow drawing conclusions on the effectiveness of this policy. Our observations are consistent with an absence of effectiveness of the 2008-9 seasonal influenza vaccine against the current pandemic strain.

The incidence of reported cases of influenza A(H1N1)v in the Netherlands is much lower than in the United Kingdom [11]. This may reflect the phase of epidemic; the epidemic in the UK could be more advanced due to earlier and more frequent introductions, especially from the US. It may also reflect chance effects early on in the epidemic, where introductions into schools are likely to lead to intense transmission.

The clinical picture and severity of disease among our cases is similar to what was reported elsewhere [12]. However, due to the limited time of follow-up, we may have somewhat underestimated the severity in our report.

The occurrence of a new strain of influenza virus coupled with intense efforts to control it offer a unique opportunity to document its key epidemiological, virological and pathogenetic properties. This information is crucial for modeling aiming to predict the future burden of disease and to design strategies for most effective control of this pandemic. However, changes to the strain's properties, including emergence of resistance, would render these predictions invalid. Continued surveillance is therefore of key importance.

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Rapid communications

ENHANCED EPIDEMIOLOGICAL SURVEILLANCE OF INFLUENZA A(H1N1)v IN ITALY

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As of 7 July 2009, a total of 158 laboratory-confirmed cases of influenza A(H1N1)v were reported in Italy, from half of the 21 Italian regions. To date all cases have had symptoms consistent with seasonal influenza and no severe or fatal cases have been reported. An active surveillance of cases has been set up in Italy in order to undertake appropriate measures to slow down the spread of the new virus. This report describes the routine and enhanced surveillance currently ongoing in Italy.

Background

Following the recent emergence in late April of a new influenza A(H1N1)v virus in the United States and Mexico [1], the same strain has been detected in an increasing number of countries [2,3], and on 11 June the World Health Organization (WHO) officially declared the influenza pandemic. In response to this situation the WHO has recommended enhancing the collection of information on the chain of transmission of the first identified cases in order to timely identify groups of population at higher risk and to guide preventive actions. The information to be gathered is also crucial for validation and refinement of the parameters used in mathematical models to estimate the potential impact of the pandemic. In Italy,

the health authorities have developed specific recommendations for epidemiological and virological surveillance [4] based on the WHO and the European Centre for Disease Prevention and Control recommendations [5,6].

The first confirmed cases of influenza A(H1N1)v in Italy were reported in travellers. The preliminary virological findings have previously been described [7]. This report provides the first description of Italian response and main epidemiological findings of the new influenza A (H1N1)v virus infections in Italy.

Methods

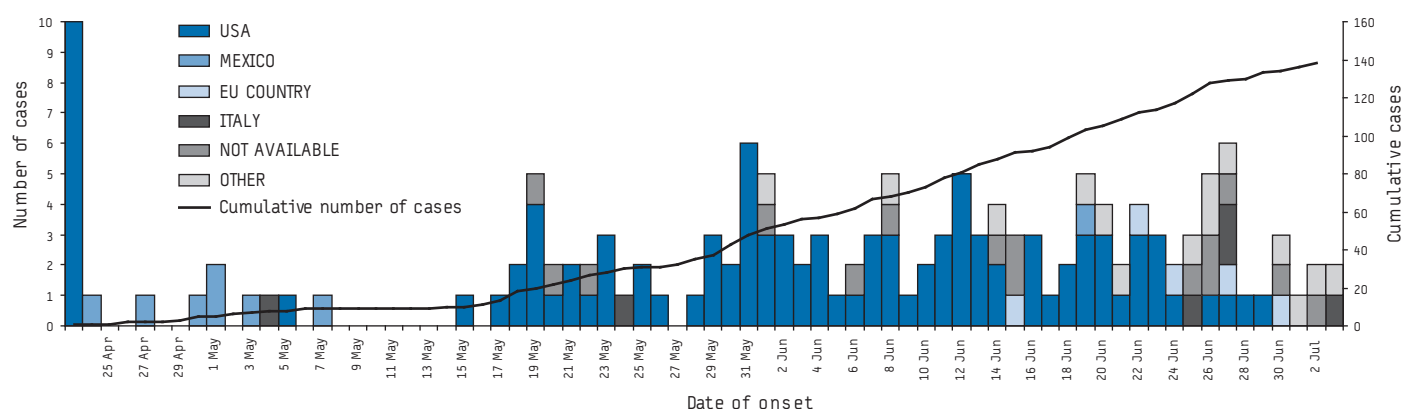
A(H1N1)v surveillance

Since 26 April, suspected, probable and confirmed cases of influenza A(H1N1)v virus are to be reported to the Italian Ministry of Health according to the specific European Union case definition [8].

A suspected case is any person meeting the clinical and epidemiological criteria, a probable case is any person meeting the clinical and epidemiological criteria and with a positive laboratory

FIGURE 1

Distribution of travel-related and locally transmitted confirmed cases of influenza A(H1N1)v virus infection in Italy, by date of onset and place of travel, and cumulative number of cases, as of 7 July 2009 (n=138*)



Note: Of the total number of 158 confirmed cases reported by 6 July 2009, 20 cases are excluded from this Figure because of missing information on the date of onset.

result showing influenza A infection of an unsubtypable type, a confirmed case is any person meeting the laboratory criteria for confirmation [4].

In order to control the spread of the disease, an active surveillance system of individuals presenting with influenza-like illness and recent history of travel to the affected areas has been set up. All individuals coming from affected areas receive specific medical advice through the health authorities at the airports and seaports, in order to refer to the hospital in case of symptoms. Information about demographic data, illness (e.g. date of onset), and type of travel (e.g. flight number or type of cruise ship) has to be collected. Moreover, specific distancing measures (early isolation of cases and precautionary school closure) and antiviral prophylaxis of close contacts of cases have been set up, in order to contain the spread of A(H1N1)v virus in the country. Any person who has been in close contact with a confirmed case is asked to remain at home for 7-10 days avoiding contacts with others.

Local health authorities should notify any suspected, probable or confirmed cases within 12 hours of symptoms onset, to the Ministry of Health (MoH) and to the National Centre for Epidemiology and Health Promotion (CNESPS) at the Italian National Institute of Health (Istituto Superiore di Sanità, ISS) [4].

In Italy, influenza surveillance is routinely based on a nationwide sentinel surveillance network together with a structured virological surveillance (INFLUNET). The system is based on general practitioners and paediatricians with the aim of monitoring the incidence of influenza-like illness, identifying the extent of the seasonal epidemics and collecting information on circulating strains. Web-based electronic forms are used for data reporting.

Epidemiological investigation of confirmed cases and close contacts

In order to facilitate standardised and timely reporting and updating, the CNESPS in collaboration with the MoH, has developed specific forms for epidemiological investigation of confirmed cases [4] to be recorded on-line. These forms are available at a secure website (<https://www.iss.it/Site/FLUFF100/login.aspx>). This tool is based on the United Kingdom Avian Influenza Management System (AIMS), which was designed to record, organise and

analyse the epidemiological, clinical and personal data for human cases of avian influenza [9], and to facilitate the fulfilment of the International Health Regulations (IHR) requirements.

The information must be collected and entered into the website by the local health authorities within 12 hours after case confirmation. This includes demographic data and details of clinical illness (e.g. date of onset, signs and symptoms, severity, outcome). Data on contacts include exposure data (e.g. relationship to case, type/date of contact, household information) and subsequent development of illness and/or asymptomatic infection. Follow-up information is requested after 15 days from the first epidemiological investigation.

Results

Data from A(H1N1)v surveillance

As of 7 July 2009, a total of 995 suspected cases have been reported to the Italian surveillance system of influenza A(H1N1)v. Of those, 439 (44%) cases were laboratory-tested as negative (excluded), 158 (16%) cases were confirmed and 398 (40%) cases are still under investigation. Of the cases still under investigation 347 had symptoms onset more than one week before 7 July. This indicates that probably only 51 cases can be defined as being still under investigation.

Almost all confirmed cases (n=152) were travel-related, the remaining six cases who acquired the infection in Italy were close contacts of a confirmed travel-associated case. Among the 152 A(H1N1)v cases who had travelled out of the country, 137 (87%) had available data regarding the travel during the week before the date of onset. Of these, 100 (73%) had returned from the United States (US), 8 (6%) had travelled from Mexico, 9 (7%) had been in another European Union Member State, and 14 (10%) had travelled to other countries (Argentina, Canada, Peru, Philippines, and Singapore) (Figure 1). All cases returning from Mexico were reported in the first two weeks of surveillance (24 April - 8 May), and to date, the majority of confirmed cases were travellers to the US.

For the 148 (94%) influenza A(H1N1)v cases with available information on age, the median age was 28 years (range 0-69 years) and 83 (56%) were male. Cases younger than 19 years of age constituted 34% of the cases, 59% were aged between 20 and 49 years, and only 7% of cases were 50 years or older (Figure 2).

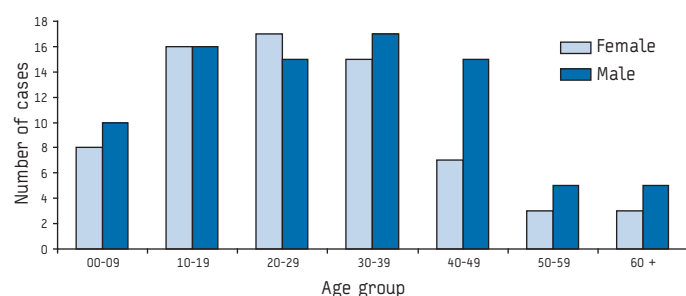
To date, there have not been significant signals of increased influenza activity through the INFLUNET system. Outputs from this system are published on a weekly basis (available in Italian at the website: <http://www.iss.it/iflu/>).

Data from epidemiological investigation of confirmed cases

Results of the epidemiological investigations of confirmed cases are available for 86 cases. Among these cases, 22 (26%) have been admitted to hospital. It is important to note that some hospitalisations were due to isolation purposes, and therefore the proportion of patients admitted to hospital is not an indicator of the severity of disease. The mean length of stay in hospital was 3.4 days (range 0-7 days). Time elapsed from disease onset to laboratory confirmation was 3.1 day (range 0-12 days). The list of symptoms and the proportion of confirmed cases reporting specific symptoms are given in the Table. Most of the symptoms were reported at disease onset. The most frequent symptoms reported were fever and/or respiratory symptoms, and the least frequent were the gastrointestinal symptoms.

FIGURE 2

Distribution by age group and sex of cases of influenza A(H1N1)v virus infection reported in Italy, as of 7 July 2009 (n=148*)



Note: Of the total number of 158 confirmed cases reported by 6 July 2009, 10 cases are excluded from this Figure because of unavailable data on age.

Of the 86 confirmed cases investigated two were healthcare workers. One had travelled abroad, the other one had acquired the infection in Italy due to contact with a confirmed case in hospital setting. Further five confirmed cases were tourists (not Italian residents) travelling on a cruise ship.

Of the 86 confirmed cases investigated, all received antiviral treatment, once diagnosed, and 90% were treated within 48 hours of symptom onset. Overall 371 close contacts have been identified and put under surveillance, and the average number of contacts for every confirmed case was 5.2 (range 1-39 contacts). Information on prophylaxis of close contacts was available for 319 individuals, 125 of these (39%) received antiviral drugs (114 took oseltamivir, six got zanamivir, and five did not specify the drug taken). Of reported close contacts, 14 (4%) were infected and confirmed as cases, including four who had not received prophylaxis (one because of underlying medical conditions). In 39% of close contacts, antiviral prophylaxis was administered more than 48 hours after symptoms onset of the confirmed case they had been in contact with.

The information on the vaccination status for seasonal influenza in the previous season was available for 73 confirmed cases. The number of persons reported to have been vaccinated during the 2007-8 and 2008-9 seasons was 9 and 2, respectively.

Among 80 confirmed cases for whom information on pre-existing conditions was available, nine persons reported chronic pre-existing conditions (such as cancer, diabetes, heart disease, immunodeficiency conditions). In addition, one case of otitis media in a seven-month-old child and pneumonia in two adults (30 years of age) were reported after the 15 days requested follow-up of cases.

Discussion

The results presented provide some general information on demographic characteristics (age, sex), travel history, clinical

presentation, treatment and prophylaxis of patients infected by influenza A(H1N1)v in Italy.

To date, no local sustained transmission has been reported in Italy. Our results should nevertheless be cautiously interpreted, as approximately all confirmed cases were imported from affected areas. Moreover, since 14 May 2009 the number of confirmed cases has been increasing most probably due to the application of specific RRT-PCR test from the US CDC [7] and due to the increasing number of cases worldwide. In particular, in the last week (30 June - 7 July) the number of reported confirmed cases increased from 100 to 158 and the number of close contacts that had been infected and confirmed as cases increased from 4 to 14.

This preliminary description of the current Italian situation highlights that surveillance activities in Italy are effective at this stage of the outbreak for containment purposes. In fact, 90% of confirmed cases received treatment within 48 hours after symptoms onset. However, it should be noted that only 39% of close contacts received prophylaxis. This is probably due to heterogeneity of the use of antiviral prophylaxis because no specific national guidelines are available. No sustained local transmission has been reported to date in Italy (7 July 2009), except for 14 secondary cases.

Epidemiological investigation with the web-based reporting system is crucial in order to gain specific information on pre-existing chronic conditions and complications among hospitalised cases. This data will help to build a comprehensive database in order to better monitor the epidemic in Italy, in particular to identify risk groups and factors contributing to the development of the epidemic. Moreover, this could represent an important opportunity to share data within EU countries using similar approaches [9].

It is clear that this kind of epidemiological investigation cannot be maintained during the epidemic peak when the number of cases

TABLE

Number and proportion of confirmed cases of influenza A(H1N1)v in Italy reporting specific symptoms, in general and at disease onset, (n=86 cases for whom this information was available)

Symptoms	Number (%) of cases reporting the symptom	Number of cases reporting the symptom at disease onset
Fever non specified	3 (3%)	2
Fever $\geq 38^{\circ}\text{C}$	58 (67%)	42
Fever $< 38^{\circ}\text{C}$	11 (13%)	7
Headache	36 (42%)	24
Muscle pain	37 (43%)	28
Joint pain	22 (26%)	15
Dry cough	35 (41%)	26
Productive cough	7 (8%)	4
Cough not specified	18 (21%)	12
Sore throat	35 (41%)	26
Runny nose	39 (45%)	25
Shortness of breath	8 (9%)	5
Diarrhoea	8 (9%)	2
Vomiting	6 (7%)	4
Nausea	6 (7%)	3
Conjunctivitis	10 (12%)	8
Asthenia	38 (44%)	31
Other (various)	2 (2%)	1

becomes too high. However, collecting information on the first few cases, especially those locally transmitted, could be crucial in order to describe the mechanisms of transmission and biological parameters to fill the existing epidemiological gaps.

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Rapid communications

AN OUTBREAK OF INFLUENZA A(H1N1)v IN A BOARDING SCHOOL IN SOUTH EAST ENGLAND, MAY-JUNE 2009

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An outbreak of influenza A(H1N1)v was confirmed in May and June 2009 in a boarding school in South East England involving 102 symptomatic cases with influenza-like illness. Influenza A(H1N1)v infection was laboratory-confirmed by PCR in 62 pupils and one member of staff. Control measures were implemented as soon as a case was confirmed and included school closure, active case finding and treatment as well as post-exposure prophylaxis offered to the entire school population. Had the outbreak had been detected earlier, the school closed earlier and prophylaxis commenced after the initial cases were detected, we may have seen lower levels of transmission.

Background

The first case of influenza A(H1N1)v in the United Kingdom (UK) was reported by the Health Protection Agency (HPA) on 27 April 2009 [1]. Following this initial report, the number of confirmed cases has risen steadily.

On 27 May 2009, a case of influenza A(H1N1)v was confirmed in a 14 year-old pupil at a boarding school in South East England. The case did not meet the HPA's algorithm for testing at the time. The algorithm for testing of influenza A(H1N1)v at the time included travel to the United States or Mexico or contact with a probable or confirmed case. While this patient had influenza-like symptoms, there was no history of travel to an affected area or relevant contact. Swabs were taken from this pupil under the auspices of a private medical care service for independent schools. It subsequently became obvious that a significant outbreak was in progress in the school.

This paper describes the epidemiology and public health response to this outbreak. This is the first published report of an outbreak of influenza A(H1N1)v in a boarding school.

The index case and initial investigation

The index case became symptomatic on 24 May 2009, swabs were taken on 26 May and a positive result by PCR with primers specific for influenza A(H1N1)v [2] was received on 27 May. The positive result was notified to the local Health Protection Unit (HPU) on the evening of the same day, 27 May. The school was scheduled to close on the next day, 28 May, for a planned break during term time.

The initial risk assessment suggested that the index case had very limited contact with other pupils while symptomatic. His close

contacts were identified as 15 other pupils who were also boarders at the school. All 15 close contacts were assessed for influenza-like illness (ILI), and offered post-exposure prophylaxis with oseltamivir, in accordance with HPA guidance at the time.

Following the identification of the first positive case, further enquiries were undertaken at the school by the HPA. It became apparent that there had been an ongoing outbreak of ILI at the school which preceded the confirmed diagnosis of influenza A(H1N1)v in the index case. A total of 39 cases had reported to the school's health services with ILI prior to the identification of the index case on 27 May 2009. Following this finding, a decision was taken to extend the response beyond the initial 15 cases, to include the entire school population. Active case finding was initiated by asking all students and staff with ILI to telephone one of the nine "flu response centres" around the country for assessment. If appropriate, they were recommended testing and treatment. This was necessary as staff and students were dispersed across the country following the closure of the school for a short break. This led to the identification of further possible and probable cases associated with the school.

The HPA case definition was used: A possible case was any person meeting the clinical and epidemiological criteria; a probable case was any person meeting the clinical and epidemiological criteria and with a positive test for influenza A infection that was untypable at the local laboratories.

Descriptive epidemiology

Setting

The outbreak occurred in a boarding school in South East England with a total population of 2,132 made up of 1,307 pupils and 825 members of staff.

Case definition

Since it was obvious that there was a rise in the number of ILI cases before the index case, we considered these as "clinical" cases and included them in our description of the outbreak. We therefore categorised our cases into confirmed cases and clinical cases.

Confirmed cases were cases of influenza A(H1N1)v confirmed by laboratory testing of swabs taken while the patient is symptomatic with ILI.

Clinical cases were among pupils documented as attending a healthcare facility at the school with ILI from 1 May 2009 to the confirmation of the first case on 27 May 2009.

Outbreak description

In total, there were 102 symptomatic cases with ILI. Nose and throat swabs were taken from all cases symptomatic at the time the outbreak was detected. Influenza A(H1N1)v infection was laboratory-confirmed by PCR with primers specific for influenza A(H1N1)v in 63 of the 102 cases, 62 pupils and one member of staff. The remaining 39 cases were no longer symptomatic at the time the outbreak was recognised, and it was too late to take throat swabs. These 39 were classified as cases of ILI, epidemiologically linked in time and space to the confirmed cases.

The onset of the outbreak was estimated to have been on 1 May 2009 and the end on 3 June 2009. The school was closed from 28 May to 7 June 2009, extending the scheduled break by four days. The incubation period for influenza A(H1N1)v is unknown but estimated to be between one and seven days [3], therefore cases presenting with symptoms after 3 June 2009 were considered to have resulted from secondary transmission outside the school setting.

Potential source of exposure

There were two potential points of contact between pupils from this boarding school and other schools (schools A and B in Figure 1) that had already had confirmed cases of influenza A(H1N1)v. No confirmed cases of influenza A(H1N1)v or clinical ILI cases were seen in the specific students who reported contact with students from school A during a social function. The second point of contact was with a group of students who visited school B for a tennis match on May 9. One of the students in contact with school B developed symptoms on 24 May 2009 and tested positive for influenza A(H1N1)v. Contact during this event may represent the source of the outbreak assuming that the ILI cases that occurred before this

event may not have been due to influenza A(H1N1)v. School B had been closed due to an outbreak of influenza A(H1N1)v between 11 and 18 May 2009 in six members of staff and students.

The first confirmed case of influenza A(H1N1)v at the boarding school developed symptoms on 20 May 2009, pre-dating the onset of symptoms in the index case (27 May) by seven days (Figure 1). The incubation period for influenza A(H1N1)v is estimated to be between one and seven days indicating that there may have been ongoing transmission in the school from as early as 13 May 2009.

Attack rates by house of residence and school year group

All school years and all houses of residence were affected by the outbreak. Taking the entire school population (pupils and staff), there was a clinical attack rate of 5% (102/2,132). However, given that the living circumstances of the students were significantly distinct from those of members of staff, the student population was considered as the affected cohort. Among the students, the clinical attack rate was 8% (101/1,307). The attack rates among the pupils were also calculated by house of residence as well as by school year (Figure 2). These attack rates varied by house, ranging from 1.8% (1/55) to 18.9% (10/53), as well as by school year, ranging from 5.4% (14/258) to 11.9% (32/268). The school year with pupils aged between 16 and 17 years had the highest attack rate of 11.9%.

Clinical epidemiology

The distribution of symptoms among the cases is illustrated in Figure 3. These were typical of influenza-like illnesses. There were no hospitalised cases. Information on the duration of symptoms was not available.

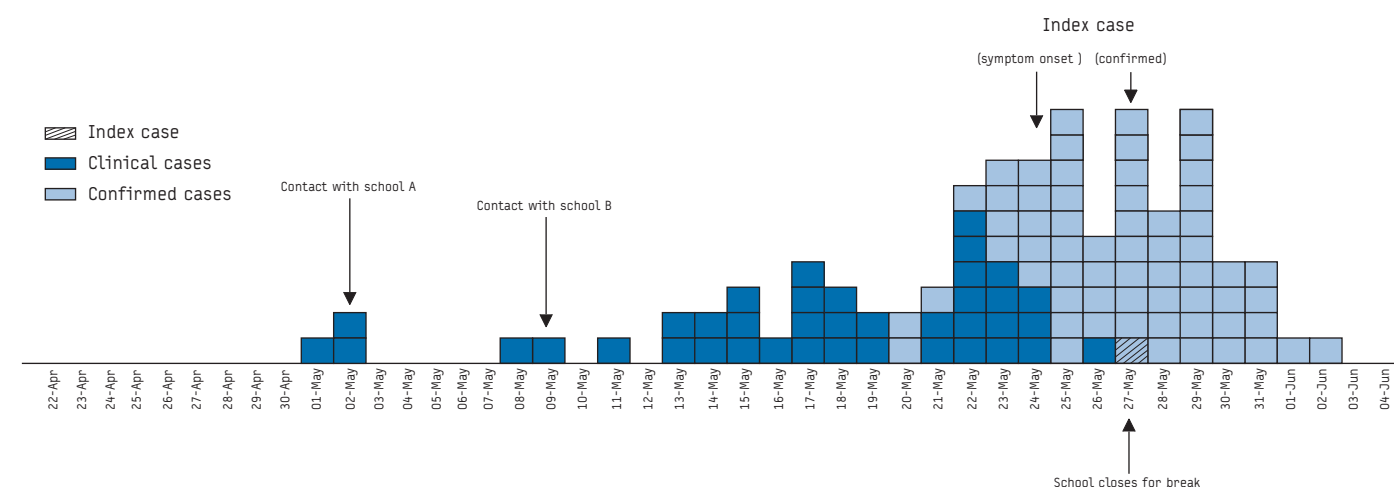
The public health response

School closure

The school closed to all pupils from 27 May until 7 June 2009. The advice to close for seven days according to HPA guidance at

FIGURE 1

Confirmed influenza A(H1N1)v and clinical ILI in pupils, boarding school South East England, May-June 2009 (n=102)



ILI: influenza-like illness

Date of onset is shown for confirmed cases. For clinical cases, the date that medical treatment was sought was used as a proxy measure for date of onset.

the time became redundant as the school was already closed for a scheduled break for four days, and this break was extended by a further seven days as the school preferred to open on a Sunday. Those without symptoms of ILI who had their state exams scheduled for Monday, 1 June 2009, were permitted to return on 31 May, while the rest of the school remained closed. These pupils were assessed for symptoms, and if symptomatic, were offered anti-viral medicines and testing. They were permitted to take their exams under special conditions to minimise the risk of transmission.

Antiviral prophylaxis

Following the identification of additional probable and possible cases associated with the school, the HPA's advice of prophylaxis was extended beyond the initial group of close contacts to all staff (n=825) and students (n=1,307) attending the affected school. Despite the HPA's advice, the estimated uptake of antiviral prophylaxis among those for whom it was recommended was only 48%. We do not know whether cases occurred in those who took the oseltamivir and do not have information on why the uptake

of prophylaxis was not higher. These issues will be explored in a subsequent study.

Information to parents

Parents were informed by letter that the school had a confirmed case of influenza A(H1N1)v and that the school would close until 7 June 2009. A second letter was subsequently issued detailing advice to offer antiviral prophylaxis to all the pupils and staff at the school.

Clinic at school

An assessment and collection point was established at the college to offer assessment and treatment to returning students, staff members and families of resident staff.

Discussion and conclusion

This outbreak represents the first in a boarding school. The index case had no associated travel history or clear contact with a confirmed or probable case. The other school outbreak described in the literature [4], in New York, United States, involved 45 confirmed cases.

The initial risk assessment following the identification of the index case indicated there were few close contacts, and therefore post-exposure prophylaxis was limited to this group. It became evident during the investigation that the school had had an ongoing outbreak of ILI in the weeks prior to the identification of the index case. It is likely that many of these cases of ILI were due to influenza A(H1N1)v. Swabs taken from some of these cases who were still symptomatic identified a further three confirmed cases. Influenza A(H1N1)v could not be confirmed in most of the earlier cases of ILI as they were no longer symptomatic at the time the outbreak was detected. The source of the outbreak in this school was probably contact with pupils in another school with confirmed cases. This outbreak will add evidence to the hypothesis that the number of confirmed cases of influenza A(H1N1)v underestimates the burden of disease as has been reported previously [5].

It has been evident from previous reports (including unpublished data) that schools represent an important location for transmission [1]. The reported symptoms suggest an illness of no worse severity than seasonal influenza. None of the cases were hospitalised. While all school years and houses were affected, there was considerable variation in the attack rates between boarding houses. Further insight into this variation will depend largely on gaining some understanding of the transmission dynamics following the first case in the school and the extracurricular and social activities the pupils participated in while exposed to symptomatic cases.

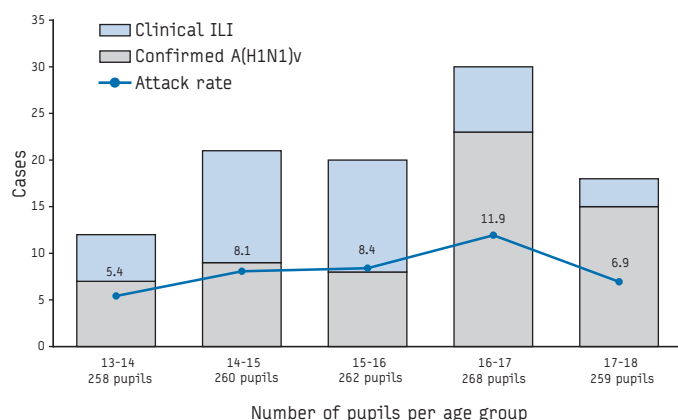
Control measures were implemented as soon as the index case was confirmed. The school closed on 27 May 2009 and post-exposure prophylaxis was offered to the whole school from 31 May 2009. Had the outbreak had been detected earlier, the school closed earlier and prophylaxis commenced after the initial cases were detected according to the HPA's guidance at the time, we may have seen lower levels of transmission within the school.

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FIGURE 2

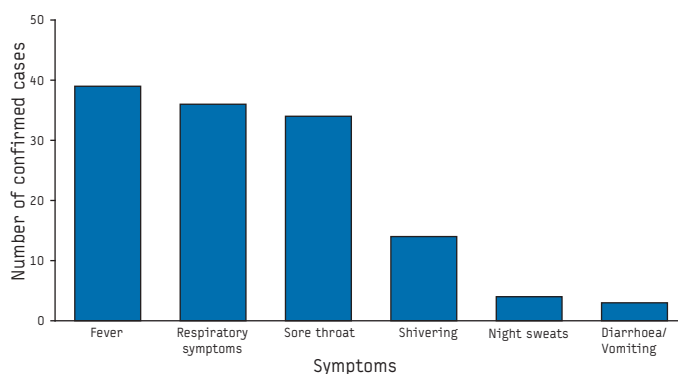
Cases of clinical ILI and influenza A(H1N1)v by age group, boarding school South East England, 1 May-3 June 2009 (n=102)



ILI: influenza-like illness

FIGURE 3

Symptoms reported by confirmed cases of influenza A(H1N1)v by age group, boarding school South East England, May-June 2009 (n=63)



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Rapid communications

PRELIMINARY DESCRIPTIVE EPIDEMIOLOGY OF A LARGE SCHOOL OUTBREAK OF INFLUENZA A(H1N1)v IN THE WEST MIDLANDS, UNITED KINGDOM, MAY 2009

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2. The members of the team are listed at the end of the article

This report describes the preliminary results from the investigation of a large school outbreak of influenza A(H1N1)v in Birmingham, United Kingdom in May 2009, when influenza A(H1N1)v was confirmed in 64 of 175 (36%) symptomatic pupils and members of staff. Initial findings in this study suggest that the symptoms were mild and similar to those of seasonal influenza, with an illness attack rate of nearly one third.

Introduction

On 27 April 2009, the first two confirmed cases of the pandemic influenza A(H1N1)v in the United Kingdom (UK) were reported in Scotland. As of 2 July 2009 there have been 7,447 cases reported in the UK [1]. During the early phase of the outbreak, the majority of the cases were amongst travellers, initially those returning from Mexico and then also those returning from the United States (US). The first indigenously acquired case was reported on 1 May 2009 and since then an increasing number of indigenous cases have been reported [2].

Since the outbreak in the UK began, transmission has occurred in a number of school settings [3]. We present the results of a preliminary epidemiological investigation on an influenza A(H1N1)v outbreak that began in mid May in a primary school in Birmingham, West Midlands, England.

Epidemiological description of the outbreak

On 18 May 2009, the Health Protection Agency (HPA) was informed of an increased rate of absenteeism in a primary school in Birmingham, West Midlands. The school has 419 pupils in the primary school and 60 in a nursery and is located in inner city Birmingham, in the West Midlands region, England. Symptoms reported included fever, respiratory and gastrointestinal symptoms. None of the symptomatic pupils had a history of school absence for holiday travel in the seven days before onset of symptoms. On 19 May 2009, given that some symptoms described were influenza-like, nose and throat swabs were arranged for a small number of symptomatic pupils. One specimen was confirmed on 21 May by real-time PCR specific for influenza A(H1N1)v.

On 21 May, the school closed for seven days; this period coincided with a scheduled school holiday of one week. Between Saturday, 23 May and Monday, 25 May, the investigation team attempted to contact, by telephone, parents of pupils as well

as members of staff on lists provided by the school in order to administer a brief questionnaire. Information collected included: demographic details, symptoms, recent travel history and details of out-of-school activities. Information about household and close social contacts was also recorded.

Upon conclusion of the telephone interview parents of all asymptomatic children were advised that their children should start a prophylactic course of antiviral medicine being distributed at the school on 23 and 24 May. A total of 304 asymptomatic children were prescribed prophylaxis. Parents of children who were symptomatic at the time of interview or who had been symptomatic in the previous seven days were asked to stay at home so that specimens (nose and throat swabs) could be collected from their child(ren). At the time of swabbing, all symptomatic children were provided with a treatment course of oseltamivir. Contact tracing was carried out to identify household contacts and close social contacts. The contacts were then followed up by an out-of-hours general practitioner (GP) service and provided with antiviral prophylaxis.

All pupils and staff attending the primary school were contacted. Of 563 pupils/members of staff, 175 (31%) were symptomatic and required testing. Of those 175, 64 (37%) were found to be positive for influenza A(H1N1)v. A further 139 symptomatic household contacts were tested out of 664 identified. Household contacts are

FIGURE 1

Confirmed cases of influenza A(H1N1)v among pupils and staff by date of illness onset, school outbreak West Midlands, May 2009 (n=64)

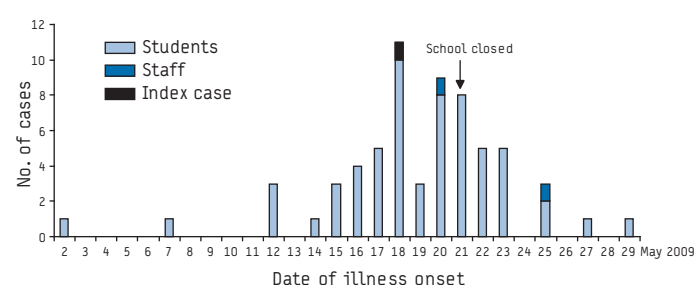


TABLE 1

Symptoms reported by influenza A(H1N1)v cases among pupils and staff, school outbreak West Midlands, May 2009 (n=64 confirmed cases*)

Symptoms	Cases (percentage)
Fever	54 (84%)
Nasal congestion	45 (70%)
Sore throat	38 (59%)
Nausea/vomiting	26 (41%)
Muscle/joint pain	23 (36%)
Diarrhoea	14 (22%)
Headache	21 (33%)
Respiratory symptoms	20 (31%)
Additional free text reports**	
Cough	12 (19%)
Eye problems	1 (1.6%)
Dizziness	1 (1.6%)

* A person could report more than one symptom.

** These symptoms were not included in the questionnaire but were reported by respondents.

excluded from the data analysis, and analysis is restricted to only laboratory confirmed cases.

Figure 1 shows the date of symptom onset for cases of influenza A(H1N1)v in the school. Of the 64 cases, 31 (48%) reported symptom onset between 18 and 21 May. At the time of interview and before treatment had started, symptoms reported by the 64 confirmed cases included: subjective fever (54, [84%]); nasal congestion (45 [70%]) and sore throat (38 [59%]) (Table 1). No cases were hospitalised and the duration of illness was not recorded.

Table 2 shows the attack rate by school year group. The index case was confirmed on 21 May, but the earliest reported date of onset was 2 May (see Figure 2) in a year 4 pupil (aged nine years). The next date of onset was 7 May in a year 5 pupil (aged 11 years). Neither of these early cases had a travel history or history of contact with a confirmed case. Fifty-three percent of cases were female and the highest attack rate was seen in pupils in year group 5 (23%). Excluding two members of staff, cases ranged in age from 4 to 12 years, with a mean of 8.5 years and a median of 9 years. None of the cases had a recent history of travel outside the UK.

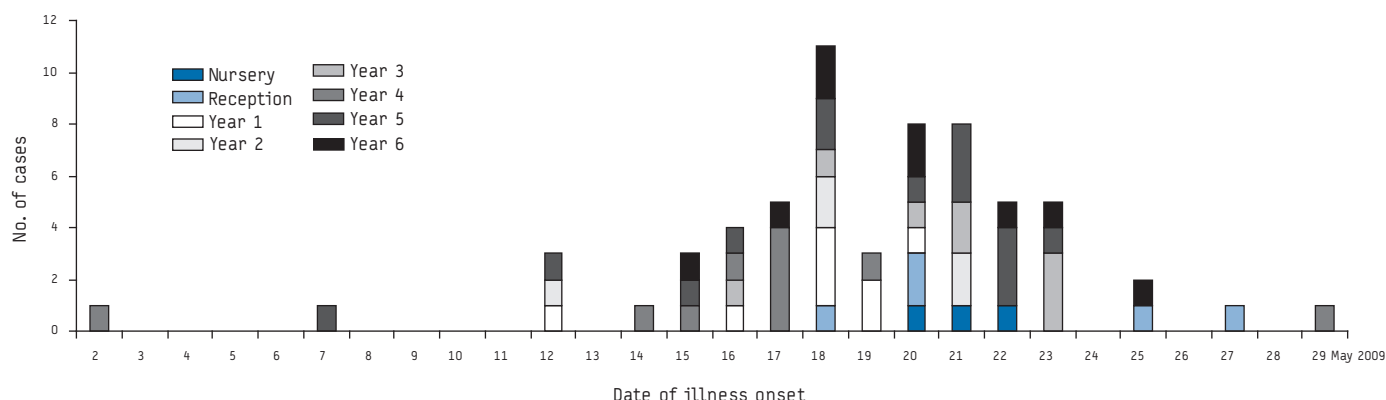
TABLE 2

Proportion of influenza A(H1N1)v cases among pupils in each school year and attack rate by year group school outbreak West Midlands, May 2009 (n=62 confirmed cases)

Class (age-range in years)	Number of pupils in class	Laboratory-confirmed cases	Attack rate for pupils
Nursery (4)	58	3	(3/58) 5.2%
Reception (5-6)	61	5	(5/61) 8.2%
Year 1 (6-7)	60	8	(8/60) 13%
Year 2 (7-8)	59	5	(5/59) 8.5%
Year 3 (8-9)	59	8	(8/59) 14%
Year 4 (9-10)	62	10	(10/62) 16%
Year 5 (10-11)	60	14	(14/60) 23%
Year 6 (11-12)	60	9	(9/60) 15%
Total	479	62	(62/479) 13%

FIGURE 2

Date of illness onset for confirmed cases of influenza A(H1N1)v among pupils, by school year, school outbreak West Midlands, May 2009 (n=62)



Discussion and conclusion

A total of 64 confirmed cases of influenza A(H1N1)v have been identified in pupils and members of staff in a school in the Midlands, UK. This large primary school outbreak resulted in an overall clinical attack rate of 30% and a microbiologically confirmed attack rate of nearly 13%. The clinical attack rate in this single school is higher than the average attack rate of 24% reported for outbreaks of seasonal influenza in UK schools during the 2005-6 influenza season [4].

Feedback from interviewers and the GP out-of-hours service suggested that symptoms were generally mild in children, predominantly fever, nasal congestion and sore throat consistent with other case series from the UK reported thus far [3]. No children were hospitalised and no data were available on the duration of illness or on underlying disease in the cases. Most cases reported date of onset of symptoms between 18 and 21 May, suggesting that the rate of transmission may have been highest during the period immediately prior to the school closing, when high absenteeism had been reported. The latest date of onset was 29th May, and most cases were asymptomatic by the time the school re-opened after the holidays on 1 June.

Subsequent to this incident, there have been no further cases in the school. However, cases continue to be identified in the local area with an increasing number of local schools reporting high absenteeism and confirmed cases. Cases occurring outside schools suggest ongoing and widespread community transmission in the area.

Further investigation of this school incident includes sequential swabbing of a subset of families with confirmed cases and presentation of data on those pupils who were symptomatic but were not laboratory-confirmed cases. These analyses will be presented at a later date.

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Rapid communications

OUTBREAK OF INFLUENZA A(H1N1)v WITHOUT TRAVEL HISTORY IN A SCHOOL IN THE TOULOUSE DISTRICT, FRANCE, JUNE 2009

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In June 2009, for the first time in France, a confirmed outbreak of influenza A(H1N1)v without history of travel occurred in a secondary school in Toulouse district. A total of 15 cases were confirmed among students of which three were asymptomatic. This report describes the outbreak and its public health implications.

Background

In France, in order to detect early influenza A(H1N1)v virus circulation [1], reporting of clusters of at least three cases of respiratory tract infections occurring within one week in a small community without other identified aetiology has been set up [2]. In the early phase of the pandemic, this surveillance was complementary to the national active surveillance of recent travellers from affected areas [3].

On 12 June 2009, the headmaster of a secondary school in the suburb of Toulouse, South Western France, notified 11 absentees among sixth-grade students in the same class that had reported fever and respiratory symptoms. The regional unit of the Institut de Veille Sanitaire and the local health authority requested nasal and throat specimens for viral testing of the three most recent and severe cases among the 11 sick children. On 13 June, two cases were confirmed with influenza A(H1N1)v virus infection.

An investigation was conducted to describe the outbreak and to identify the source of transmission.

Methods

A retrospective cohort study was conducted among all students and staff members of the class in which the first cases were reported. The following case definitions of suspected and confirmed cases were used:

- A **possible case** of influenza A(H1N1)v virus infection was defined as a person with high fever ($\geq 38^{\circ}\text{C}$) or asthenia or myalgia and at least one acute respiratory symptom (cough or dyspnoea);
- A **probable case** was defined as a possible case with a history of close contact to a probable or confirmed case during 24h and until the seven days after the onset of those cases' symptoms;
- A **confirmed case** was defined as a person confirmed by real-time PCR specific for influenza A(H1N1)v virus.

Subsequently, active case finding was initiated among contacts (close family members and social contacts) of all cases (possible, probable or confirmed) of sick pupils of the class. Passive case-finding was also conducted in the whole school by means of posters.

Nasal and throat swabs were taken from all children and staff members of the class: at the school infirmary for asymptomatic children and at the Toulouse regional hospital for symptomatic children. All possible or probable cases identified through subsequent case finding were also investigated at the hospital.

Staff and school children were interviewed face-to-face using a standardised questionnaire. Information on demographics (sex, age), potential exposure to influenza A(H1N1)v virus since 1 June 2009 (personal or close family, travel history, infection in a relative, social gathering) and medical data for symptomatic cases (fever, cough, asthenia, dyspnoea etc.) were collected. The outbreak was described by time and person, and exposure factors were analysed.

Results

The class included 30 students at the age of 11 to 12 years, and 18 staff members had been in contact with the pupils. All students and eight staff members were investigated. We found 20 cases (18 students and two staff members) corresponding to the case definition (five probable cases and 15 confirmed cases). The attack rate was 60% among children and 25% among staff members. Three cases were asymptomatic.

The reported symptoms were headache (94%), cough (88%), fever (76%), asthenia (53%), sore throat (41%) and rhinorrhoea (35%). No complications were reported and no death occurred.

The onset of the outbreak (Figure) among the 17 symptomatic cases was abrupt (10 and 11 June) which could indicate a common exposure to an unrecognised case and secondary transmission from person to person in the following days (12 to 14 June).

12 out of 17 (71%) cases corresponded to the definition of a possible case (Table).

Assuming that a positive real-time PCR was the gold standard, we estimated the sensitivity of the definition of a possible case at 47%, its specificity at 78%, its positive predictive value at 58%

and its negative predictive value at 69% among all students and staff members of the class.

In the course of subsequent case finding, nine symptomatic contacts were investigated and only one of them, a student of another class of the school, was confirmed. No case was found among about 120 close family contacts that were traced and among social contacts reported to have had extracurricular activities together with the cases.

None of the students or staff had a history of travelling after 1 June to countries affected by influenza A(H1N1)v or had been in contact with someone symptomatic. However, several children's relatives worked in sectors related to travel (international firms, airplane construction or air travel staff).

Actions taken

All symptomatic cases were admitted to hospital, examined and treated with antiviral curative treatment (oseltamivir). All close contacts were quarantined and received prophylactic treatment (120 relatives and other social contacts). Each family of a student of the class was interviewed and followed up. The family was asked to call the emergency mobile medical service (Centre 15) if a family member became symptomatic.

On 15 June, the school was closed for one week. The school was reopened on 22 June, since no secondary case had been observed seven days after the last reported case (14 June).

Discussion

This is the first confirmed outbreak of pandemic influenza A(H1N1)v infection reported in France without a well identified chain of transmission. Our investigation could not find any history

of travel nor any contact with a previously identified imported case among the children and staff members of this class.

The high attack rate in a single school class, as well as the abrupt onset of the epidemic curve suggests that the children could have shared a strong common exposure. Cases that occurred from 12 to 14 June were probably due to secondary transmission from earlier cases. The fact that no secondary case was observed outside the school after its closure, isolation of cases and prophylaxis of contacts, suggests that these complementary measures were effective to limit transmission to the community.

The source of the outbreak remains unknown. A contact with a previously undiagnosed case could have occurred without being reported. This contact may have occurred within a family, since many parents had occupations related with international travels. Contact with Spanish residents in the area is also possible, related or unrelated with the parents' occupation. Trade and travels to Spain are frequent in this area of France and the incidence of A(H1N1)v influenza was higher in Spain than in France at the time of the outbreak.

The investigation of the whole school class identified three asymptomatic cases with confirmed influenza A(H1N1)v virus infection. Underreporting of symptoms is unlikely in the context of this intense investigation. Asymptomatic influenza infection is known to occur among about 33% of cases in the seasonal influenza [4]. In a population of 20 cases, we could expect between 12% and 54% of asymptomatic cases, which correspond to our observation (3 of 20 cases).

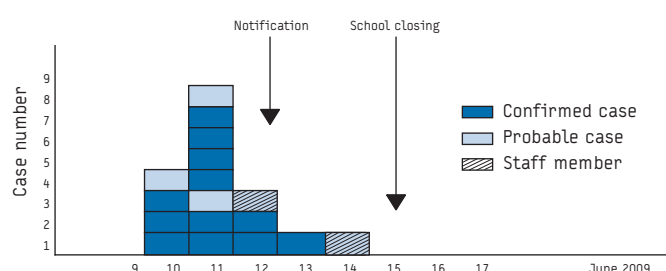
The low sensitivity (47%) of the French definition of a possible case means that many children had indeed several other symptoms (headache, sore throat, rhinorrhoea, vomiting etc.) than those included in the influenza-like syndrome. This may be due to the high variability of symptoms in children and suggests that this definition was not appropriate for children. In addition, this definition could also be inadequate for adults because the clinical presentation of this new virus was not well-known at the beginning of the outbreak.

Several public health implications arise from this outbreak. After the experience of this cluster, systematic hospitalisation of cases was stopped. Many people in the general population of Toulouse attended newly opened dedicated influenza A(H1N1) consultations, even if they didn't fulfil the case definition. They were evaluated and none of them was laboratory-confirmed.

This outbreak was an important event that allowed adjusting the surveillance of influenza A(H1N1)v in the early phase that focussed mainly on imported cases. Surveillance is now moving to wide community surveillance through sentinel networks, surveillance of hospitalised severe cases and reporting of clusters.

FIGURE

Epidemic curve for influenza A(H1N1)v school outbreak, Toulouse district, France, June 2009 (n=17)*



* For three additional asymptomatic confirmed cases the date of onset was not known.

TABLE

Distribution of possible influenza A(H1N1)v cases among students and staff members according to laboratory results, Toulouse district, France, June 2009 (n=38)

		Confirmed cases of influenza A(H1N1)v		Total
		Yes	No	
Possible case of influenza A(H1N1)v	Yes	7	5	12
	No	8	18	26
Total		15	23	38

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Research articles

FORESIGHT INFECTIOUS DISEASES CHINA PROJECT - A NOVEL APPROACH TO ANTICIPATING FUTURE TRENDS IN RISK OF INFECTIOUS DISEASES IN CHINA: METHODOLOGY AND RESULTS FROM AN INITIAL APPLICATION

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The project devised a simple but novel methodology for identifying possible future trends in infectious diseases in animals and humans in China, of priority concern to the Chinese authorities. It used a model of disease drivers (social, economic, biological or environmental factors that affect disease outcomes, by changing the behaviour of diseases, sources or pathways) devised for the Foresight Programme in the United Kingdom. Nine families of drivers were adapted to Chinese circumstances and matrices were constructed to identify the likely relationship of single infectious diseases or families of diseases to the drivers. The likely future trends in those drivers in China were determined by interviews with 36 independent Chinese experts. These trends included not only potentially adverse animal and human movements but also opportunities for innovative surveillance methods, more use of hospitals, antimicrobials and vaccines. Some human behaviours and social trends were expected to increase the risk of infections (in particular sexually transmitted and healthcare-associated infections) while at the same time the experts thought the awareness of risk in the Chinese population would increase. The results suggested a number of areas where the Chinese authorities may experience difficulties in the future, such as rising numbers of healthcare-associated infections, zoonoses and other emerging diseases and sexually transmitted infections (including HIV). Not making firm predictions, this work identifies priority disease groups requiring surveillance and consideration of countermeasures as well as recommending strengthening basic surveillance and response mechanisms for unanticipatable zoonoses and other emerging disease threats.

Introduction

In 2006 the United Kingdom (UK) government published the final results of the *Foresight Project on the Detection and Identification of Infectious Diseases* (September 2004 - April 2006). This produced a vision on risks from infectious diseases in plants, animals and humans over the next 10 to 25 years [1-5]. Particular emphasis was placed on how external factors or *drivers* (defined as social, economic, biological or environmental factors, see Table 1) could lead to changes in patterns of disease [6]. The project was international in scope with an intention to inform

practical policies by showing how health threats can be anticipated, detected, prevented and controlled or at least how their effects can be mitigated in any country.

Based on this experience, a Project Group, including the authors, applied this future risks approach to China where there was both a recent history of emerging and changing infectious diseases and an especially rapid social change and therefore there was particular relevance for such an application [7]. These preliminary results were used to predict the more likely changes in infectious diseases and thus inform surveillance priorities, while at the same time refining and improving the Foresight methodologies for a later and larger application. The objective of this paper is to describe the methodology that was developed for the Foresight Infectious Diseases China sub-Project (hereafter referred to as *the China Project*) and the results of its initial application in China.

Methods

A workshop was held at the Health Protection Agency in the UK where objectives for the China Project work were agreed. The overall goals reflecting the policy priorities of the Government of China were to improve human health, to sustain economic development and to promote social stability as stated by the Chinese authors [8]. The specific objective was then to identify groups of human and animal infections that would be most likely to pose problems and challenges to these policy priorities in the next two decades. The rationale was that this would allow authorities to prioritise these groups for purposes of surveillance, prevention and control or mitigation.

The approach developed by the Future Risks component of the main Foresight Infectious Diseases Project was to have a simple model of drivers, sources, pathways and outcomes (Figure) [5]. *Drivers* would be a range of factors, social and otherwise (Table 1) that directly or indirectly can influence the incidence of infectious diseases. Sources were defined as phenomena or biological events that give rise to potential new diseases, enable existing diseases to become more harmful, enable existing diseases to infect new hosts, or enable existing diseases to spread to new areas, *pathways* were

TABLE 1

Nine groups of societal drivers (total = 96). Foresight Infectious Diseases China Project.

A. Governance and social cohesion
• Biosecurity governance of technology (drugs and pesticides)
• Social cohesion as an enabler or constraint on identification and control of infectious diseases
• Illegal practices and consequent spread of diseases of 'pest' species such as myxomatosis
• International/national/regional interactions affecting governance
• Lack of interaction between policy and regulatory agencies leading to delays in detection and identification
• Inter-ministerial agencies
• Openness with the public
• Marginalisation of some groups
• Political leadership on health issues
B. Demography and population change
• Immigration
• Urbanisation
• Migrant labour
• Overall population
• Ageing population
• Dietary and occupation changes (affecting exposure and susceptibility of population to disease risks)
• Population movements (e.g. from rural to urban or from developing to developed world)
• Animal immigration
• Overall animal populations
• Urbanisation of animals
• Animal population movements
• Movement of animals around the country
C. Conflict
• Difficulties in maintaining administrative systems and so loss of effective identification and surveillance systems
• Movement of refugees spreading diseases
• Internal conflict
• Loss of effective identification and surveillance systems for animals
• Unrestricted movements of animals around the country
D. Technology and innovation and their governance
• Impact of innovation on disease identification and treatments
• Ability to control infections; control strategies, e.g. for diseases that are easier (SARS, smallpox) or more difficult ('flu, AIDS) to control
• Impact of GM crops on agriculture and development of plant diseases
• Emergence of drug or pesticide resistant strains of infectious organisms; half lives of existing drugs and pesticides
• Role of technology in disease surveillance systems (detecting new, emerging diseases or monitoring movements of existing pathogens)
• Dissemination of information
• New, faster identification of organisms
• Development of new antivirals and vaccines
• Improved diagnostics, leading to more accurate, less costly and more rapid detection of diseases
• Transplant surgery
• Other high technology medicine
• More use of antimicrobials for humans
• Longer survival of patients with chronic diseases
• Longer survival of patients with chronic diseases
• Ability to control infections and improved control strategies in animals
• Drug or pesticide resistant strains in animals
• New surveillance systems for animal diseases
• Greater information dissemination (web-based information for disease diagnosis, for alerting experts to existence of new diseases, for providing faster and better public dissemination of disease-related information)
• Faster identification of infections in animals
• Use of antimicrobials in animals
• Improved diagnostics for animal infections

E. Changes in agriculture and land use

- Changes in animal husbandry methods, e.g. intensive rearing methods or closer mixing of animal and human populations as part of urbanisation
- Greater genetic uniformity in animal and plant populations; less 'biodiversity', less varied crop mosaics
- More intensive farming systems
- Development of new crops
- New developments in production economics involving greater movement of animals and hence more exposure to diseases such as foot and mouth disease
- More frequent proximity of different farming systems
- Changing patterns of land use

F. Economic factors (income, prosperity, employment)

- Overall wealth
- Income disparity
- Education levels in the general population
- Future oil and other energy supplies
- Quality of sanitation and water supplies
- Background pollution levels affecting the natural immunity of animals and humans
- Poverty and malnutrition
- Waste disposal as a source of disease spread (humans)
- The availability of a pool of experts to detect and identify infectious diseases
- Unemployment
- Waste production and disposal in animals
- Pool of experts in animal health

G. Trade and market related factors

- Changing patterns of trade in crops and animals
- Behaviour and structure of markets
- Future diets and demands for exotic products
- Illegal trading in human foods
- Food preservation technology
- The misuse of disease surveillance systems as trade barriers
- Changing patterns of trade in animals
- Illegal trade in animals
- Trade barriers to trade in animals

H. Transport and tourism

- International movement of drug or vaccine resistant strains of organisms
- Changes in the rates of internal movements of people, food, animals etc
- Future levels of tourism to and from China
- Levels of internal tourism
- Changes in patterns of stock-keeping and so movement of diseases; compressed time scales
- Internal migration

I. Human activity and social pressures

- Demands for more healthy food
- Demands for more 'sustainable' production systems
- Changes in sexual practices
- Changing life styles – consumerist, individualist, communitarian
- Public perceptions of risk and willingness to change behaviours
- Public demands for greater levels of safety
- Demands for lower levels of pollution
- Ecological awareness in the public
- Public willingness to accept change
- Media reporting as a driver of how governments react to disease
- Crowding in hospitals
- Farmers and producers perception of risk and biosecurity
- Willingness to change farming practices
- Media reporting on animal health issues

mechanisms or routes by which a disease-causing organism can be transferred from one host to another, within or between species and outcomes were the infectious diseases themselves [5]. For example, changes in the way animals are reared for food production favouring intensive farming and the keeping of animals in close proximity in large numbers would lead to the spread of zoonoses that by definition affect humans.

For the China Project the Future Risks model was developed to make predictions relevant to the Chinese situation. The Project Group identified drivers, considered what was known of their relationship to important groups of animal and human infections (plant infections were outside their expertise). It then determined through consultation with Chinese experts what was thought to be likely to happen to the drivers in the next two decades in China and hence assessed qualitatively what might be expected to occur in regards to the spread and prevalence/incidence of these infections in China over that time.

FIGURE
Basic Foresight risk model for infectious disease risks

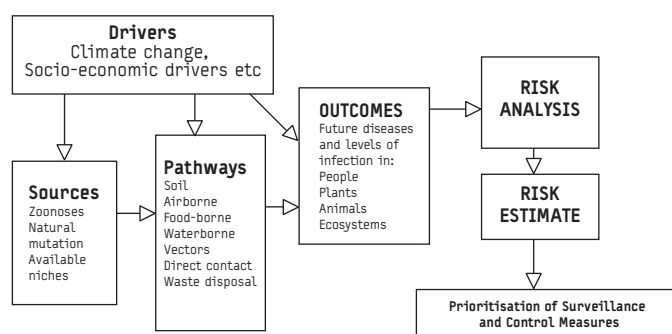


TABLE 2
Selected animal and human diseases. Foresight Infectious Diseases China Project

Exemplar animal infections
Foot and mouth disease
Avian influenza
Classical swine fever
Bovine spongiform encephalopathy
Selected groups of human infections
Gastrointestinal infections
HIV and other sexually transmitted infections
Malaria and other vector-borne infections
Influenza
Severe acute respiratory syndrome (SARS)
Parasitic infections
Vaccine preventable diseases
Antimicrobial resistant organisms
Zoonoses (taken to include novel infections and novel variants of previous infections)
Healthcare-associated infections
Bloodborne infections

In detail, the Project Group used the drivers established for the main Foresight Project, and adapted these to reflect changes known to be underway in China focusing only on animal and human diseases. As a result a list of 96 drivers grouped into nine families was obtained (Table 1). These included:

- Factors that affect the sources of the infectious disease (e.g. changes in patterns of animal husbandry)
- Factors affecting how infectious diseases are spreading (e.g. changes in the movement of people and changes in institutional structures)
- Factors affecting the assets at risk (businesses, people, animals)
- Factors that are likely to influence vulnerabilities to infectious diseases (e.g. increasing numbers of elderly people and people living with chronic diseases)
- Changing priorities and requirements for surveillance to detect anticipated risks and changes in risks (e.g. detection of healthcare-associated infections)
- Priorities and opportunities for control of risks and diseases (e.g. appreciation of the need for biosecurity around the controlled use of dangerous pathogens in laboratories and industry)

For animal diseases, four exemplar infections were chosen by the veterinary experts in the Project Group to represent both known infections (foot and mouth disease and classical swine fever) and emerging or novel infections (avian influenza and bovine spongiform encephalopathy). While the approach taken for human diseases was to identify 11 important families of infectious diseases or single diseases (Table 2).

The Project Group then used their expert knowledge to populate the two-dimensional matrices establishing the causative relationships or associations between the drivers and the infectious diseases (examples in the Appendix). For instance, recognised drivers increasing the risk of human immunodeficiency virus (HIV) infection and other sexually transmitted infections included adverse changes in sexual behaviours, increasing migrant labour, decline in educational levels and falls in the earning capacity of women. Conversely, the opposite trends in these drivers might be expected to lead to decreases in sexually transmitted infections, including HIV. These relations are shown in Table 3 for HIV and other sexually transmitted infections as an example [9]. The Group recognised that the relationships between some of the drivers and the animal and human infections were uncertain and therefore these cells were not populated in the matrices.

The main data gathering consisted in obtaining expert opinion from Chinese scientists on the likely future trends in the drivers in their country. A detailed structured questionnaire was developed and piloted within the Project Group itself. Some questions were asked more than once in different forms in order to check on the consistency of answers. Following approval from the Ethics Committee of the Chinese Academy of Medical Sciences, Peking Union Medical College (PUMC), 36 Chinese experts (four per each family of drivers) were identified by the Chinese collaborators in the Project Group from the Chinese academic community (personal details of the experts are not disclosed in this paper but are available from the authors upon request). The selection was based on relevant expertise in the families of drivers in China rather than knowledge about infectious diseases.

The expert opinions were then derived from face-to-face interviews undertaken by a team of postgraduate students from PUMC using the questionnaire. The experts were asked whether

in their opinion the drivers were going to worsen, improve or stay the same in the next two decades. For example, a question from the section on Transport and Tourism (Family H of the drivers) was phrased as follows: *Concerning internal migration in the next 15 to 20 years do you expect this to increase, decrease or stay the same?* Experts could also say that the future situation was genuinely uncertain, or that they had no opinion. Notes were kept of additional remarks and comments made by the experts. The students who performed the interviews were trained so as to achieve consistency in the process and this was checked by repeating 10% of interviews with a different student.

The results of the 36 interviews were analysed in China to arrive at consensus expert views on the likely future trends in the drivers. Consensus was considered to have been achieved where three out of four or all four of the experts agreed.

These consensus trends were then applied back to the matrices (Tables 3 and 4) to identify which of the animal and human diseases would be more likely to increase or decrease in the future in China.

After the work the authors held a meeting in Beijing and reviewed the experience to indicate lessons that should be taken into account in the future use of this methodology ('lessons learnt') planned in China.

Results

Expected trends in the drivers

Of the 96 drivers, consensus was achieved for 51 while for further three drivers the experts agreed the future was uncertain. For 23 of the 51 there was complete consensus between the four experts while for 28 there was only consensus between three out of four experts. These detailed results are shown in Table 5. The drivers for which there was consensus are listed in Table 3.

TABLE 3

Example of the relationship between drivers and infections – Human Immunodeficiency Virus (HIV). Foresight Infectious Diseases China Project.

Factors likely to be associated with...	... increased HIV transmission	... reduced HIV transmission
Governance and social cohesion	Decreasing social cohesion Increasing illegal practices Marginalisation of some groups	Increasing political leadership on health issues Increasing openness with the public
Demography and population change	Increasing urbanisation and use of migrant labour Increasing population movements (e.g. from rural to urban or from developing countries to China)	Ageing population
Conflict	Movement of refugees spreading diseases Internal conflict	
Technology and innovation and their governance	Emergence of drug resistant strains Longer survival of patients with chronic diseases	Impact of innovation on disease identification and treatments Dissemination of information New, faster identification of organisms Development of new antivirals and vaccines Improved diagnostics, Greater information dissemination
Economic factors	Greater income disparity Increased poverty Unemployment	Increased overall wealth Improved education levels
Transport and tourism	International movement of drug-resistant strains Increases in the rates of internal movements of people More tourism to and from China	
Human activity and social pressures	Changes in sexual practices to more unsafe sex More injecting drug use	Public demands for greater levels of safety Public perceptions of risk and willingness to change behaviours (if unsafe sex) Media reporting as a driver of how governments react to disease

TABLE 4

Areas of expert consensus on future trends in drivers. Foresight Infectious Diseases China Project.

A. Governance and social cohesion
• Social cohesion will increase
• International/national/regional interactions will increase
• Government openness with the public will increase
• Political leadership on health issues will increase
B. Demography and population change
• Use of migrant labour will increase
• Human population movements will increase
• Animal immigration into the country will increase

• Urbanisation of animals will increase
• Internal animal population movements will increase
• Movement of animals around the country will increase
C. Conflict
• Stress on administrative systems will increase and with it there will be loss of effective identification and surveillance systems
• There will be some loss of effective identification and surveillance systems for animals
D. Technology and innovation and their governance
• There will be more innovation in disease identification and treatments for humans
• The potential to control human infections will generally increase
• The emergence of drug or pesticide resistant strains of infectious organisms will increase
• There will be more opportunities for innovative disease surveillance systems (detecting new, emerging diseases or monitoring movements of existing pathogens)
• The ability to disseminate information will increase
• The ability to identify organisms will increase as will the speed of identification
• Numbers of new antivirals and vaccines will become available
• Diagnostic ability will improve, leading to more accurate, less costly and more rapid detection of diseases
• High technology medicine will increase
• Use of antimicrobials for human infections will increase
• Identification and treatment of human diseases will increase
• Ability to control infections in animals will increase
• Drug or pesticide resistant strains appear more often in animals
• There will be more opportunities for developing surveillance systems for animal diseases
• Information dissemination about animal disease will increase
• Infections in animals will be identified more rapidly and easily
• There will be more use of antimicrobials in animals
• There will be improved diagnostics for animal infections
E. Changes in agriculture and land use
• The genetic uniformity in animal and plant populations will increase
• There will be developments in production economics involving greater movement of animals and hence more exposure to diseases such as foot and mouth disease
F. Economic factors (income, prosperity, employment)
• Overall wealth will increase
• Education levels in the general population will improve
• The availability of oil and other energy supplies will worsen
• Quality of sanitation and water supplies will improve for humans
• Poverty and malnutrition will decline
• Waste disposal as a source of human disease spread will improve
• The availability of a pool of experts to detect and identify human infectious diseases will improve
• The available pool of experts in animal health will enlarge
G. Trade and market related factors
• The behaviour and structure of markets as affecting infections will improve
H. Transport and tourism
• More internal movement of people, food, other goods live animals and microorganisms
• Future levels of tourism to and from China will increase
• Levels of internal tourism will increase
I. Human activity and social pressures
• Sexual practices will become more risky
• There will be other changes in lifestyle increasing risk of infection
• Public tolerance of infection risk will decline and the willingness to change behaviours to reduce such risk will increase
• Public demands for greater levels of safety will increase
• Ecological awareness in the public will increase
• Media reporting as a driver of how governments react to infectious disease will increase
• Crowding in hospitals will increase
• Farmers and producers will become more aware of infection risk and biosecurity
• Media reporting on animal health issues will increase

Notable areas of consensus on expected trends in the drivers were as follows: There would probably be greater social cohesion and more transparency in Chinese governance with greater leadership shown by government on human health issues. Movements of animals around the country and internationally (meaning into and out of China) would be likely to increase and there would probably be more animals in urban areas. Similarly, there would most likely be more and larger scale internal human migrations and movements of people and more use of migrant labour within China. Tourism within, and to and from China was also considered likely to increase.

It was expected that because of growth and urbanisation additional stress would be placed on administrative systems which could threaten some surveillance for animal and human diseases. Conversely technological developments would provide more opportunities for surveillance, better detection of organisms and there would probably be more dissemination and sharing of information.

The production of waste from animals was considered likely to increase substantially and, with it, problems of waste disposal but there was no consensus that the same would happen for human waste. Genetic uniformity was expected to increase in crops and animals. In human healthcare, high technology medicine, the development of new medicines and vaccines would all increase. In the additional remarks the experts in the relevant areas said that in their opinion, this would take place because of

technological change, growing number of older people and people with chronic conditions and increasing healthcare expectations in the population. However the experts were not sure whether or not China's population would age overall. It was felt that the use of hospitals and overcrowding in hospitals would probably increase, as would the use of antimicrobials in humans and in animals.

Overall individual wealth and levels of education were expected to rise, though there was no consensus on what would happen concerning income disparities. It was felt that sexual behaviour would change in ways that overall would increase the risk of acquiring and passing on sexually transmitted infections including HIV and other blood-borne viruses. However, it was also expected that the population would become less accepting of risks from infection and that there would be greater demands for safety, more ecological awareness of the importance of the environment and greater media reporting of health and environmental issues. Human sanitation was expected to improve but the availability of energy sources would probably worsen. The intellectual capacity of China was expected to rise with more experts in animal and human health.

Possible consequent trends in the infections

The application of the changes in the drivers (Table 1) against the matrices (Appendix) indicated that if the predicted trends materialised, and no countermeasures were applied, adverse changes (rises) in the rates of the following groups of infections would be expected:

TABLE 5

Analysis of expert opinions as to whether the selected drivers would improve or worsen in the coming two decades

Drivers	Expert 1	Expert 2	Expert 3	Expert 4	Consensus (or not)
A. GOVERNANCE AND SOCIAL COHESION					
1. Biosecurity governance (currently there is little biosecurity governance or regulation in China)	A	A	C	C	no consensus
2. Social cohesion	C	C	C	C	Social cohesion will increase
3. Illegal practices	D	C+	C	A	no consensus
4. International/Regional interactions	C	A&C	C+	C	International and regional interactions will increase
5. Lack of interaction between policy and regulatory agencies	D	C	A	A	no consensus
6. Inter-ministerial agencies: will these become more common?	C	D	C	D	no consensus
7. Problems across international agencies (sharing of information with international agencies)	C	D	D	C	no consensus
8. Openness with the public (government transparency)	C+	C+	C	C	Government transparency will increase
9. Marginalisation of some groups	D	C	A	A	no consensus
10. Political leadership	C+	C+	C	C	More political leadership relating to health issues
B. DEMOGRAPHY AND POPULATION CHANGE					
11. Immigration	D	D	A	D	no consensus
12. Urbanisation	D	A	A	D	no consensus
13. Migrant labour	D	A	A	A	More use of migrant labour
14. Overall population (specify detailed changes if possible)	B	D	D	D	no consensus
15. Elderly population	B	A	C	D	no consensus
16. Dietary and occupational changes	B	A	C	C&D	no consensus
17. Population movements	A	A	A	D	More population movement
18. Animal immigration	A	A+	D	A	More animal movements
19. Animal populations (increase or reduce)	B	A	A	D	no consensus

20. Urbanisation of animals	A	A+	A	A	More animals in urban areas
21. Animal population movements	A	A	A	A	More movements of animals
22. Movement of animals around the country	A	A	B	A	More movements of animals
C. CONFLICT					
23. Difficulties in maintaining administrative systems so loss of effective identification and surveillance systems	A	A	A+	D	Stress on administrative systems
24. Movement of refugees	C	B	B	D	no consensus
25. Internal conflict	A+	D	B	D	no consensus
26. Loss of effective identification and surveillance systems (for animals)	A or B	A	A	A	More stress on animal surveillance systems
27. Unrestricted movement of animals around the country	B or C	A	B	A	no consensus
D. TECHNOLOGY AND INNOVATION AND THEIR GOVERNANCE					
28. Impact of innovation on human disease identification and treatments	C+	C	C	C	More innovation in human disease diagnosis and treatment
29. Ability to control human infections and control strategies	C	C	C	C	Improved infection control strategies
30. Use of genetically modified crops	D	B	D	D	no consensus
31. Drug- and pesticide-resistant organisms	A	A	A+	C	More drug- or pesticide-resistant organisms
32. New surveillance opportunities (e.g. web-based and remote systems)	C	C	C	C	Increased opportunities for surveillance in animals
33. Information dissemination	C	C+	C	C	Better information dissemination
34. Faster identification of organisms	C	C+	C	C	Faster organism identification
35. Antiviral, antimicrobial and vaccine development	C	C	D	C	More antimicrobials and vaccines becoming available
36. Improved diagnostics	C	C	C	C	Improved diagnostics
37. Transplant surgery	B	D	D	B	no consensus
38. Other high technology medicine	C	C	C	C	More high technology medicine
39. Use of antimicrobials for humans	C	C	C	A	More use of antimicrobials in humans
40. Longer survival of patients with chronic diseases	D	B	A	B	no consensus
41. Impact of innovation on human disease, (identification and treatments)	C	C	C	C	More identification of human disease and more treatment
42. Ability to control infections, control strategies in animals	C	C	C	C	Greater ability to control animal infections
43. Drug- or pesticide-resistant strains in animals	A	A	A	A	More drug resistant strains in animals
44. New surveillance systems for animal diseases	C	C	A	C	More surveillance systems for animal diseases
45. Information dissemination concerning animals	C	C+	C	C	Better information dissemination concerning animals
46. Faster identification of infections in animals	C	C+	B	C	Faster identification of infection in animals
47. Use of antimicrobials in animals	A	C	C	C	More use of antimicrobials in animals
48. Improved diagnostics for diseases in animals	C	C	C	C	Better identification of infection in animals
E. AGRICULTURE AND LAND USE CHANGE					
49. Changes in animal husbandry methods	D	D	A	D	Future unclear
50. Greater genetic uniformity in crops and animals	A	A	A	D	Greater genetic uniformity in crops and animals
51. Intensive farming	D	A	D	B	no consensus
52. New crops	D	B	A	D	no consensus
53. More attention to economics	C+	C	A	C	More movements of animals for economic reasons
54. Proximity of different farming systems	D	D	A	D	Future unclear
55. Changing patterns of land use	A+ or D	C	A	D	no consensus
F. ECONOMIC FACTORS (INCOME PROSPERITY AND EMPLOYMENT)					
56. Overall wealth	C	D	C	C	Wealth increasing overall
57. Income disparity	C	A	D	C	no consensus

58. Education levels in the general population	B	C	C	C	Education levels will improve
59. Future oil and other energy supplies	A+	D	A	A	Availability of energy sources will worsen
60. Quality of sanitation and water supplies	C	C	C	A	Sanitation will improve
61. Background pollution levels	B	C	A+	A	no consensus
62. Poverty and malnutrition	C	C	C	C	Poverty will decline
63. Waste disposal	C	A	C	C	Waste disposal will improve
64. Pool of experts in human disease	A	C+	C	C	Numbers of experts in human health will increase
65. Unemployment	A	C	C	A	no consensus
66. Waste production and disposal (from animals)	A	A	D	C	no consensus
67. Pool of experts in animal health	C	C	C	C	Numbers of experts in animal health will increase
G. TRADE AND MARKET RELATED FACTORS					
68. Changing pattern of trade	C	D	A	C	no consensus
69. Behavior and structure of markets	C	C	A	C	Behaviour of markets will improve
70. Future diets and demands for exotic products	D	D	A	D	no consensus
71. Illegal trade	D	A	A	D	no consensus
72. Food preservation technology (please specify changes)	C	C	A	D	
73. Trade barriers	A	D	D	D	Future unclear
74. Changing patterns of trade in animals	C	A	D	A	no consensus
75. Illegal trade in animals	C	A	A	C	no consensus
76. Trade barriers for trade in animals	B	C	C	D	no consensus
H. TRANSPORT AND TOURISM					
77. International movement of people, foods, other goods, live animals, microorganisms	A	A	C	D	no consensus
78. Changes in the rates of internal movement of people, food, other goods, live animals, microorganisms	A	A	A	D or A	More movement of all
79. Future levels of international tourism a) from China, b) to China	A	A	A	D	Increased tourism to and from China
80. Internal tourism (inside China)	A	A	A	D or A	Increased internal tourism
81. Emergence of 'just in time' stockkeeping (shops and industry having low levels of stock and relying on new supplies arriving at the right time)	A	D	B	D	no consensus
82. Internal migration	A	A	A	D or A	no consensus
I. HUMAN ACTIVITY AND SOCIAL PRESSURES					
83. Demands for more healthy food	B	B	C	C	no consensus
84. Demands for more sustainable production	D	D	D	C	no consensus
85. Changes in sexual practices	A	A	A+	A	More risky sexual behaviours
86. Changing lifestyles	A	A	D	A	Changes in lifestyles making more liable to risk of infections
87. Public perceptions of and acceptance of risk	C	C+	C	C	Less public tolerance of risk
88. Demands for greater levels of safety	C	C	C	C	More public demands for more safety
89. Demands for lower levels of pollution	A	C	C	D	no consensus
90. Ecological awareness	D	C	C	C	More awareness of ecological factors
91. Willingness to change	C	D	D	C	no consensus
92. Media reporting on human diseases	C	D	C	C	Greater media reporting
93. Overcrowding in hospitals	A	A	A	A	More overcrowding in hospitals
94. Farmers and producers perception of risk and biosecurity	C or D	C	C	C	Farmers more aware of risk and biosecurity issues
95. Willingness to change farming practices	D	D	D	C	no consensus
96. Media reporting on animal health issues	C	C	D	C	More media reporting on animal health issues

Legend

A = Intensify (getting worse) B = Stay the same C = Become less intensive (getting better) D = Future unclear
A+ or C+ were used if the expert said that large change was anticipated.
Consensus was reached if at least three of the four experts agreed.

- Animal infections (e.g. foot and mouth disease, avian influenza and classical swine fever) as a result of animal movements;
- Infections acquired as a result of receiving healthcare (nosocomial or healthcare-associated infections);
- Infections caused by drug-resistant organisms in animals and humans;
- Human sexually transmitted infections, including HIV;
- Human blood-borne viral infections associated with high-technology care (such as hepatitis B and C);
- Food-borne infections affecting humans and zoonoses in humans and animals including emerging infections;
- Imported and exotic infections.

Discussion and lessons learnt

Historically China has been a potent source of infections that have come to affect or threaten Europe. The influenza pandemics of 1957 and 1968, the avian influenza A(H5N1) ('bird flu') and severe acute respiratory syndrome (SARS) all appeared first in China [6-7]. The Foresight China Project has identified a number of likely future trends for drivers of infectious diseases in China that could potentially lead to increases in rates of healthcare-associated infections, drug-resistant organisms, sexually transmitted infections and zoonoses as well as other novel infections and variants of previously identified infections. The results identifying the probable changes in drivers in China can be compared to those obtained in the main Foresight project for the UK and Africa even if only limited predictions can be made as to their impact on actual diseases. These comparisons reveal some broad similarities in the trends in the drivers thus recognising the universality of some international changes [5].

Lessons from this application

The China Project also revealed a number of methodological issues that need addressing. The selection of drivers used in this study and the relationship between the drivers and infections were probably not sufficiently evidence-based and need to be supported by a literature review. The questions put to the experts were probably too open-ended and there were difficulties in the analysis of their additional comments. Because the subject of the project was known, there were difficulties in getting the experts to focus on the trends in the drivers without considering the trends in the infections that might result from these changes. Also, it was notable how the recent Chinese experience with SARS in 2003 influenced some of the expert opinions which tended to hark back to that event. The number of experts (only four per family of drivers) was perhaps too limited and for some of the areas it was felt that if the experts could have met together rather than individually, a more useful consensus would have been achieved.

It is important not to over-interpret the suggested trends indicated here. Aside from this being a limited initial application, there are difficulties in drawing any conclusions from this form of qualitative predictions. What should be concluded when two drivers are running contrary to each other? For example, it was suggested that sexual behaviours will become more risky while at the same time the public will generally become more aware of risks. An additional point is whether such a unitary approach can be undertaken for countries that are as large and diverse as China. Trends that might apply in the richer east and semi-tropical south of China might be quite different in the less well resourced western provinces and the temperate and continental north of China. In a way these considerations do not matter as long as the predictions are not seen as what will certainly happen. What are

being suggested are the more likely changes in disease risks and possible threats that the authorities should be aware of and prepare for. These changes are not inevitable as future trends also depend on countermeasures deployed either against the infections or to offset the underlying drivers. The real conclusion is to suggest priorities for surveillance and development of countermeasures. The results suggest these priorities should include animal infections associated with animal movements, and, in humans, zoonoses, sexually transmitted infections, healthcare-associated infections and antimicrobial resistance. Equally, the authorities could consider whether to take a precautionary approach and implementation of countermeasures at an early stage, for example by giving more priority to hygiene in hospitals and rational approaches to antimicrobial prescribing. However, historical events including developments like SARS and highly pathogenic avian influenza in China indicate that to some extent future events in infectious diseases can never be entirely anticipated [7,10]. Hence it is crucial to establish basic surveillance and response mechanisms in a strong modern public health framework that can detect and respond to whatever threats should appear in the future.

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Appendix. Examples from the two matrices with the presumed relationship between animal and human infections and the drivers (full matrices are available on application to the corresponding author).

Available in pdf:

http://www.eurosurveillance.org/public/public_pdf/Foresight_China_Appendix.pdf

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