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Modified surveillance of influenza A(H1N1)v virus infections in France

Influenza A(H1N1)v investigation teams[1,2]
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Up to early July 2009, surveillance of H1N1 cases in France was based on the identification of all possible cases in order to implement, around each of them, control measures aimed at delaying the spread of the virus. The global dissemination of the virus and the starting community transmission in France led us to shift to a population-based surveillance relying mainly on the identification and investigation of clusters of influenza-like illness, on the identification and individual follow-up of confirmed hospitalised cases as well as on the monitoring, through various sentinel systems, of the use of ambulatory and hospital care for influenza-like symptoms.

Introduction

As soon as the first human cases due to infection with the novel influenza A(H1N1)v virus had been reported to the international community at the end of April, the influenza surveillance in France was adapted in order to actively detect cases. The main objectives of this strengthened surveillance and of the accompanying control measures were to delay the spread of the virus in the country. The first cases were identified in France on 1 May in two travellers returning from Mexico. As of 6 July, 358 cases have been notified. This article describes the clinical and epidemiological characteristics of those cases and the recent changes in the surveillance system made on the basis of this analysis.

Methods

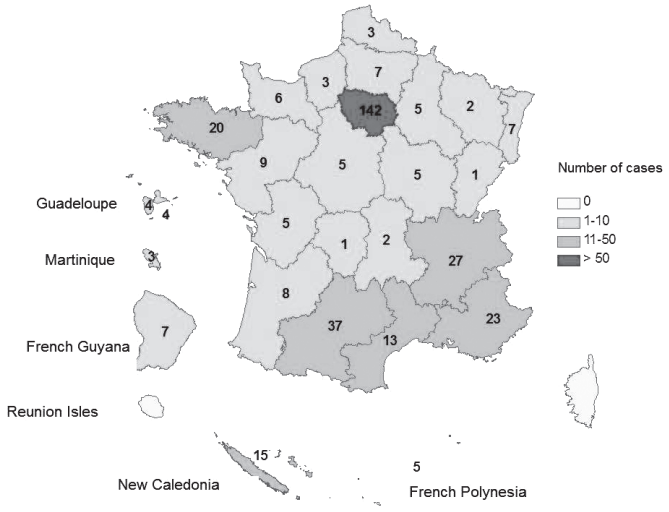
In the initial phase, the surveillance aimed at identifying cases in travellers returning from affected areas in order to promptly implement control measures around each case and to contain the virus spread. A case definition and recommendations for management of the cases and their close contacts were released as early as 26 April and described in a previous paper [1]. Briefly, a possible case was defined as a person with an acute respiratory illness and a history, in the seven days preceding the onset of symptoms, of either travel in an affected area or contact with a possible, probable or confirmed case. In order to capture cases from previously undetected chains of transmission, clusters of acute respiratory illnesses defined as at least three cases in less than a week in close communities were also to be notified.

All symptomatic persons returning from affected areas were advised to call the local hospital-based emergency unit (Centre 15). If the patient was assessed as fulfilling the case definition, the Centre 15 had to call the National Institute for Public Health Surveillance (Institut de veille sanitaire, InVS) for case validation, which triggered the implementation of the specific A(H1N1)v case management protocol (nasal sampling of the case, systematic hospital-based isolation, antiviral treatment by a neuraminidase inhibitor). Antiviral prophylaxis was recommended for close contacts of probable or confirmed cases, which were asked to observe a home quarantine. Nasal samples had to be sent to one of the 24 and then 31 laboratories which had been authorised by the Ministry of Health to run, in a bio safety level 3 environment, the A(H1N1)v RT-PCR developed by the two National Influenza Reference Centres (CNR). Positive samples were sent to the CNR for confirmation and further investigations.

This case management protocol has evolved over time. Since 26 June, only severe cases, based on the judgment of the treating physician, have to be hospitalised. The antiviral indications have been restricted to severe cases or to cases with an underlying condition that could increase their risk of complication and, as prophylaxis, recommended for their household contacts with an underlying condition. The indications for sampling of possible cases have also been restricted to severe cases, to patients under antiviral

Figure 1

Geographical distribution of confirmed cases of influenza A(H1N1)v, France, 26 April – 6 July 2009 (n=358)



treatment whose condition is not improving, to contacts under antiviral prophylaxis developing an influenza-like illness, to cases returning from the southern hemisphere and to at least three cases in each suspected A(H1N1)v cluster.

Case-based epidemiological and virological data have been collected by InVS and its regional epidemiological units (CIRE) through an interactive application (adapted from Voozano®, Epiconcept®), allowing real time exchange of information between InVS, the 16 CIRE, the CNR and the local public health offices in charge of the case management [2]. A clinical follow-up of the confirmed cases has been set up in collaboration with the clinicians in charge of the cases. Daily feedbacks have been posted on the InVS website (http://www.invs.sante.fr) since the 26 April. Several syntheses of the influenza A(H1N1)v epidemiological situation in France have already been published [3,4].

Results

As of 6 July, InVS received 4,867 notifications of possible cases, of whom 4,744 were from mainland France, 66 from the French Caribbean islands, 13 from French Guiana, 22 from the Reunion Island, one from Mayotte, 16 from New Caledonia and five from French Polynesia. All these possible cases were tested and 358 cases were confirmed as due to the A(H1N1)v virus. Twenty six cases were diagnosed as infected by a seasonal influenza virus (12 with H1N1, 14 with H3N2), one as co-infected with (H1N1) and (H1N1)v.

Figure 2

Distribution of confirmed cases of influenza A(H1N1)v, by date of onset of symptoms and travel history, France, 26 April – 6 July 2009 (data available for 315 cases)

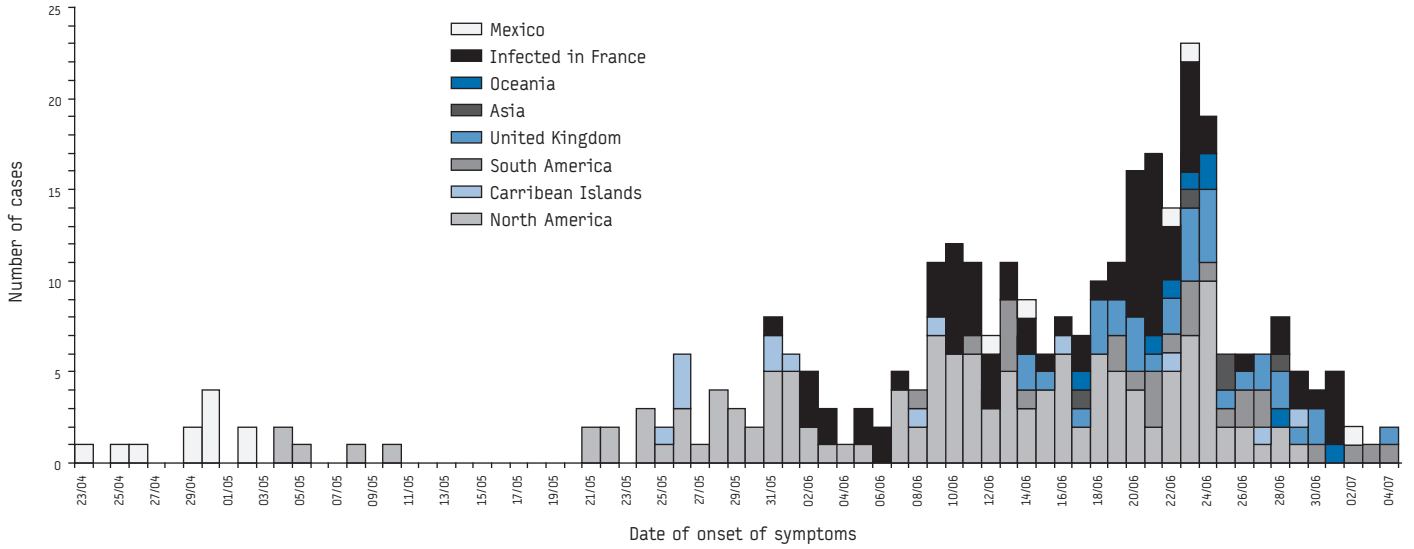
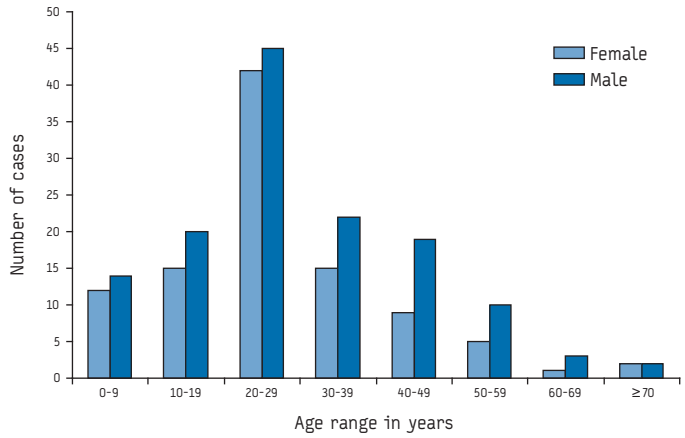


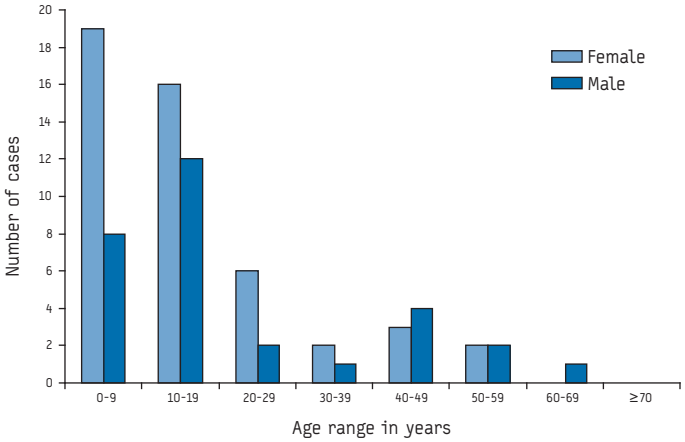
Figure 3

Distribution of confirmed cases of influenza A(H1N1)v, by age, sex and travel history, France, 26 April – 6 July 2009 (data available for 335 cases)

3a. Imported cases (n=245)



3b. Indigenous cases (n=90)



Geographical distribution

Of the 358 confirmed cases, 40% came from the Ile-de-France region which includes Paris. Twenty seven cases were from the French overseas territories (Figure 1).

Imported and indigenous cases

The first cases were detected in travellers returning from Mexico, then the United States (US) and Canada (Figure 2). Among the 261 cases in travellers, 16 were from Mexico, 121 from the US, 21 from Canada, 27 from South America, 13 from the non-French Caribbean islands, five from Asia, 24 from Oceania and 33 from the United Kingdom (UK). Data on country of travel was unavailable for one case.

For 92 cases, there was no history of recent travel. For 30 among these, belonging to six clusters, no link, even indirect, to any person travelling abroad was found.

For five cases, the information about a recent travel history was missing.

Clusters

In total, 18 clusters were identified. Eight occurred in schools and eight in households. One episode of domestic transmission occurred in the working environment and one in a rugby team. The size of the clusters includes both confirmed cases and probable cases, defined as cases with an epidemiological link with a confirm case. Within the eight household clusters, two, initiated by travellers, extended to the work place. They involved respectively seven and eight cases. The number of cases in the school clusters varied from three to 67, with an average of 14 cases per cluster. Three large clusters of respectively 17, 32 and 67 cases occurred in one secondary and two primary schools. For only one of these three clusters, a link with travel abroad has been identified. In the rugby team cluster, seven out of 38 persons who had travelled from an affected area were affected.

Table

Clinical characteristics of the confirmed cases of influenza A(H1N1)v in France, 26 April – 6 July 2009

Symptoms	Number of cases with the symptom / number of cases with this data available	Proportion of cases (%)
Cough	294 / 336	88%
Fever (≥ 38°C)	286 / 333	86%
Myalgia	158 / 330	48%
Asthenia	131 / 326	40%
Headache	86 / 223	27%
Runing nose	83 / 325	26%
Sore throat	72 / 323	22%
Shiver	57 / 319	18%
Joint pain	23 / 324	7%
Conjunctivitis	18 / 326	6%
Shortness of breath	20 / 332	6%
Vomiting	18 / 328	5%
Diarrhoea	14 / 324	4%
Nausea	11 / 326	4%

Demographic characteristics

There were 183 male and 155 female cases (data on sex was not available for 20 cases). The sex ratio male to female was 1.2. Age of the cases ranged from 7 months to 77 years, with a mean of 25 years and a median of 23 years. Domestic cases were younger (mean 17 years) than imported ones (mean 28 years) ($p<0.0001$) (Figure 3).

Clinical characteristics

The clinical characteristics of the cases are shown in the Table. They appear to be similar to those observed in seasonal flu cases.

Two patients were admitted to hospital with bacterial pneumonia, one of them had asthma and required ventilation, but both recovered. No death due to this virus has been identified in France.

Case management

For imported cases who were not symptomatic on their return, the onset of disease occurred on average 1.4 days after their return (range 0 to 6 days). On average, these and the domestic cases notified the relevant healthcare units 1.8 days after the onset of symptoms. The length of stay in hospital for the 96 cases admitted for isolation purpose and for whom this information was available varied between 0 and 7 days (mean and median of 3 days). The two patients hospitalised for pneumonia stayed in hospital 6 and 10 days respectively.

Discussion

The intensive mobilisation of multiple public health stakeholders and health professionals made it possible to set up in a very reactive way a system of surveillance of the first influenza A(H1N1)v cases at the national level. This surveillance allowed the collection of clinical and epidemiological information on cases and the implementation, around each case, of control measures in order to slow down the spread of the virus.

It is not possible to estimate the exhaustiveness of this surveillance. It is likely that mild cases have not been systematically identified. However, the absence of large clusters, up to early July, suggests that the system was capable of preventing sustained chains of transmission from the initial imported cases.

The follow-up of imported and secondary cases and the results of the cluster investigations were essential indicators of the level of indigenous transmission, allowing the adaptation of the control measures to the evolving epidemiological situation. Similarly, the decreasing average age over time reflects the change over time of the main pattern of transmission from sporadic cases in travelling young adults to secondary transmission in families and schools

The identification, at the beginning of July, of several clusters of significant size, some of them without any identified link with a travel abroad, indicated the occurrence, at least in some French regions, of a, though still limited, transmission in the population. This, together with the global spread of the virus, which made it superfluous to update the list of affected countries, led to the decision, released on 8 July, to modify the definition of a possible case by removing any reference to a return from an affected area. At the same time the case-based surveillance was replaced by a population-based surveillance relying mainly on the identification and investigation of clusters of influenza-like illness, on the identification and individual follow-up of confirmed hospitalised

cases as well as on the monitoring, through various sentinel systems, of the use of ambulatory and hospital care for influenza-like symptoms.

Regarding the overall response to the pandemic, these important changes in surveillance methods signed the transition from a delaying to a mitigation strategy. Indeed, between 7 and 23 July, 22 new clusters were identified, including 193 cases of whom 59 were confirmed. For 16 of these 22 episodes, no link with a travel abroad has been identified.

Our data show that the spread of the virus in the community occurred later than in neighbouring countries such as Spain or the UK [4,5]. Comparative analysis of surveillance data between countries, in connection with the respective methods of case management, could help to investigate this difference.

The new surveillance procedures, which include the detection and investigation of clusters, will contribute to further characterisation of the dynamic of the virus spread in France and will be used to better describe mechanisms and parameters of transmission.

*The InVS investigating team is composed of more than 90 members of staff of the Institut de Veille Sanitaire and its regional units (Cellules Interrégionales d'Epidémiologie [CIRE]), and it was constituted to manage the response to the epidemic, to assess suspected cases and to regularly update international information.

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Enhanced surveillance of influenza A(H1N1)v in Greece during the containment phase

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Following the emergence of a novel influenza virus (influenza A(H1N1)v) with pandemic potential in late April 2009, public health measures were put in place in an effort to contain disease spread in Greece. These included enhanced surveillance of infections due to influenza A(H1N1)v virus, in order to continuously ascertain the situation and guide further public health action. On 15 July, Greece moved to mitigation phase. This report summarises surveillance findings in Greece during the delaying (or "containment") phase, from 30 April to 14 July 2009.

Introduction

In late April, a number of human cases of influenza due to a novel swine-origin virus strain were identified in Mexico and the United States. This prompted the World Health Organization to declare a "public health emergency of international concern" [1], advising national public health authorities to enhance surveillance activities for influenza. As community transmission of influenza A(H1N1)v virus began to be established around the world, a phase 6 pandemic was declared on 11 June 2009 [2]. As of 19 July the number of confirmed cases worldwide was 137,232 with 779 deaths [3]. On 15 July, Greece moved to mitigation phase. We herein report surveillance findings for cases reported until 14 July.

Public health measures

In Greece, an enhanced surveillance system for influenza A(H1N1)v was set up by 30 April 2009. The main target was travellers coming back from affected areas and their contacts. Information was disseminated to the public through the media, the internet, and by posters and leaflets distributed at international points of entry. Thermal imaging cameras were installed at airports in order to screen incoming travellers for fever. A telephone hotline was used to provide information and guidance to the public, advise health professionals, and guide cases under investigation for influenza A(H1N1)v to designated reference hospitals for clinical evaluation and nasopharyngeal swab collection. Specimens were sent to one of two reference laboratories, one in Athens (Hellenic Pasteur Institute) covering southern Greece and one in Thessaloniki (Aristotle University of Thessaloniki, Second Microbiology Laboratory) covering northern Greece. The diagnosis was confirmed with real-time PCR. In early July a third laboratory was introduced into the system (University of Athens School of Medicine, Department of Microbiology).

All cases under investigation for influenza A(H1N1)v were managed in the reference hospitals; they were referred there by primary care physicians, from non-reference hospitals, from other healthcare facilities such as airport medical offices, or they could present to the emergency department of a reference hospital on their own. This applied to both Greek and foreign citizens, regardless of insurance status.

Guidelines for case and contact management and for infection control were prepared by the Hellenic Centre for Disease Control and Prevention (KEELPNO). These were sent to hospitals and published on the KEELPNO website (http://www.keelpno.gr/articles/topic/?id=994).

Methods

A case definition was adopted, which closely matches the case definition that was agreed upon on the European level [4]. A "case under investigation" was defined as a person meeting clinical criteria (fever >38oC plus symptoms of acute respiratory infection such as cough, dyspnoea, sore throat, etc.) and epidemiological criteria (in the week before onset of symptoms: history of travel to an affected area or history of close contact with a confirmed case during his/her infectious period). A "probable case" was defined as a person meeting clinical and epidemiological criteria plus a positive laboratory result for influenza A of an unsubtypable type. A "confirmed case" was defined as a person tested positive for influenza A(H1N1)v.

However, due to the rapidly changing nature of the pandemic, clinicians were allowed at their discretion to submit samples from patients not fitting the case definition, particularly in regard to the affected areas which were no longer easy to define as more and more countries reported community transmission.

All cases investigated for influenza A(H1N1)v were notified directly to KEELPNO on an individual basis, both by hospital clinicians and by the reference laboratories.

Results

On 18 May, the first case of influenza A(H1N1)v was detected in a 19-year-old male, who had returned from New York city two days earlier. On 26 and 27 May the second and third cases were

detected in two students returning from the United Kingdom. These were the first cases imported from another European Union country [5].

By Tuesday 14 July 2009, 1,258 cases had been investigated and a total of 312 (25%) laboratory-confirmed cases had been reported, of whom 208 (66.6%) described a history of recent travel abroad. Of the remaining, i.e. domestically-acquired cases, 23 (7.4%) had been in direct contact with a traveller, 53 (17.0%) had no well-defined epidemiological link to another case, 25 (8.0%) were linked to other non-traveller cases, and for three (1.0%) the mode of transmission could not be ascertained. Figure 1 shows the epidemic curve. A definite increase in the numbers of reported cases with symptom onset from 30 June onwards was observed. Before this date 23% of cases (25 out of 107) were domestic; from 30 June onwards 37% (73 out of 196) were domestic including 23% (46 out of 196) for whom no epidemiological link to another case could be identified.

The mean time from symptom onset to diagnosis of influenza A(H1N1)v infection was 2.8 days (SD 1.6 days). The most frequent countries of travel for travel-associated cases were the United States, the United Kingdom and Australia (in descending order). This probably reflects the high number of people travelling to and from these countries, mainly foreign tourists and Greeks living abroad.

The age distribution was not significantly different between travel-associated and domestically-acquired cases. The mean age was 23.6 years (SD 14.0) and 26.4 years (SD 13.6) respectively. No significant differences were identified between sexes; of the total 312 cases reported, 170 were male (54.5%) and 142 were female (45.5%).

The clinical features of the described influenza A(H1N1)v cases were very similar to those observed in seasonal influenza patients. In the vast majority of cases the illness was mild, and the most prevalent symptoms were fever and a dry cough reported by more than 80% of cases. Sore throat, rhinorroea, muscle pain and headache were each reported by about half of the cases. The frequency of diarrhoea and vomiting was low, under 10% of cases, contrary to some reports [6], but consistent with the epidemiological picture across Europe [7]. Hospitalisation is not representative of disease severity, because initially it was used as a means of isolation. No deaths were reported.

Of those reporting fever, 30% had a temperature lower than or equal to 38oC. Thus we estimate that only about 60% of our cases initially fulfilled the clinical criterion of fever >38oC specified in the case definition.

A number of clusters were identified. These included a cluster of five Americans and an Italian guide from a group of tourists visiting Athens in mid-June, and a cluster of 14 American students who fell ill while on a visit in Thessaloniki in early July. There were also clusters of domestic transmission, for example a woman returning from the US who transmitted the virus to her family (four cases) and a hospital employee with no known exposure to an infectious case who transmitted the virus to his family and one colleague (five cases). Also, a complex cluster of seven cases was detected, starting from an 18-year-old male who had returned from London (Figure 4). One case highly publicised by the media was that of

Figure 1

Cases of laboratory-confirmed influenza A(H1N1)v reported in Greece until 14 July 2009, by day of symptom onset and type of transmission, (n=300, missing data for 12 cases)

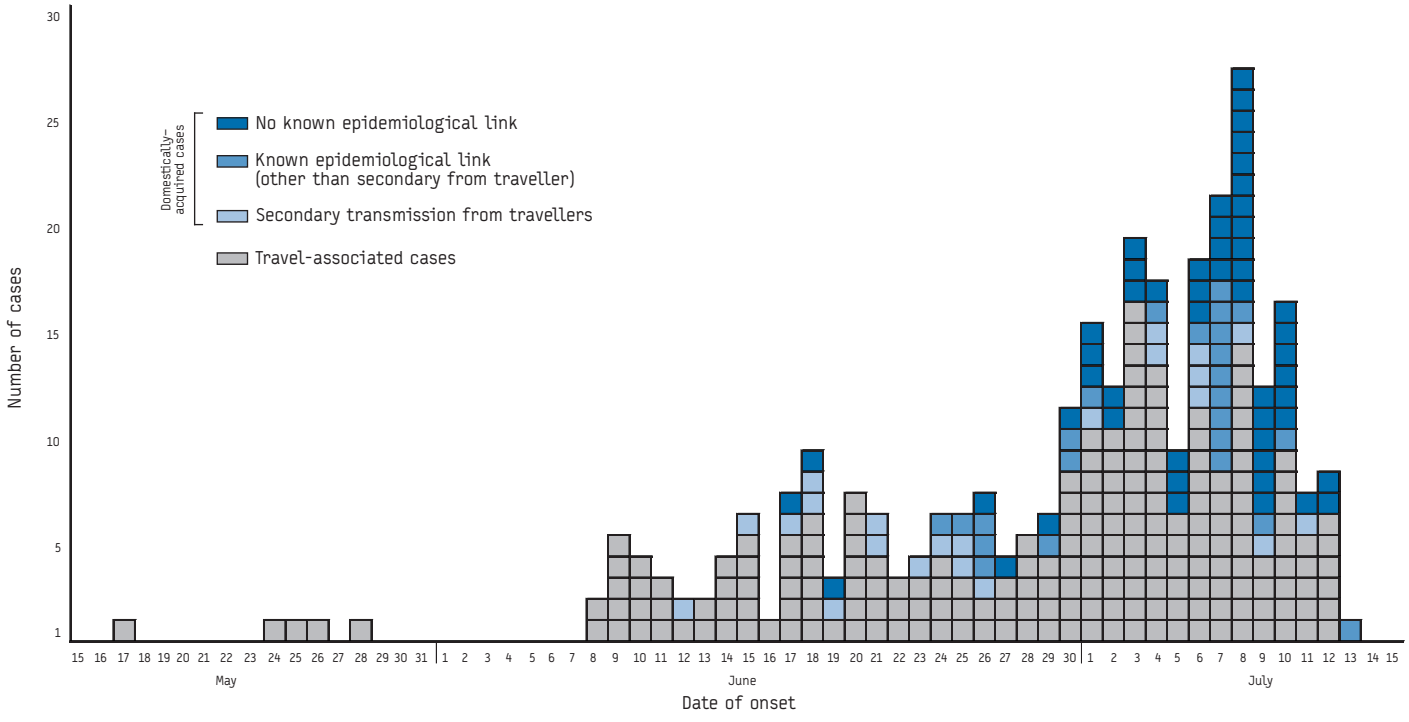


Figure 2

Travel-associated influenza A(H1N1)v cases reported in Greece until 14 July 2009, by country of travel (n=206)

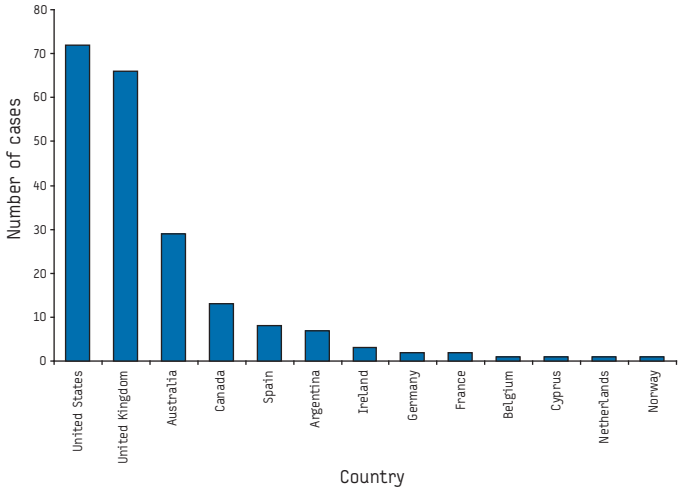
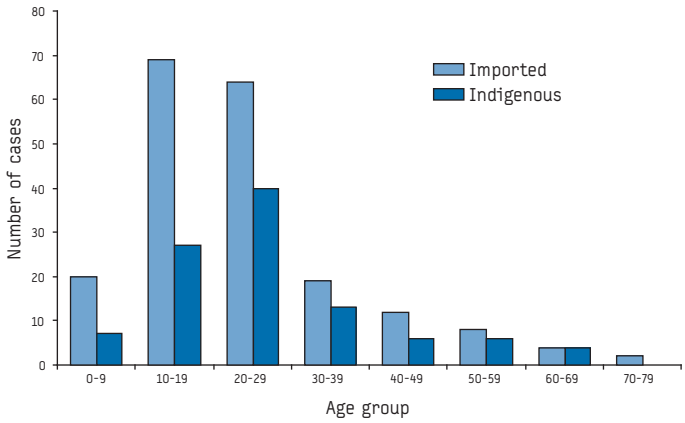


Figure 3

Age distribution of influenza A(H1N1)v cases reported in Greece until 14 July 2009, by type of transmission (n=301)



Table

Clinical features of laboratory-confirmed influenza A(H1N1)v cases in Greece, reported by 14 July 2009

Symptom	Cases with symptom / Cases for whom information was available	Percentage
Fever	235 / 277	85%
Cough	224 / 274	82%
Myalgia	137 / 262	52%
Headache	136 / 266	51%
Rhinorroea	134 / 270	50%
Sore throat	110 / 269	41%
Diarrohea	20 / 266	8%
Vomiting	14 / 263	5%
Dyspnoea	8 / 267	3%
Pneumonia	2 / 269	1%

a South American footballer, who plays for a Greek superleague team. He and his family (four cases) fell ill shortly after returning to Greece.

As already mentioned, of the 101 domestically-acquired cases of influenza A(H1N1)v, 53 had no well-defined epidemiological link to another probable or confirmed case. Of these, 13 were airport employees, two were hospital employees, seven worked in bars or restaurants in tourist areas, three worked in tourist-related occupations (a travel agent, a bus driver and a tour guide) and one was a taxi driver. This highlights the rapid spread of the virus and points to occupational exposure by specific risk groups.

However, no influenza A(H1N1)v cases have been identified from sentinel surveillance to date, indicating that overall the circulation of the A(H1N1)v virus in Greece is still limited.

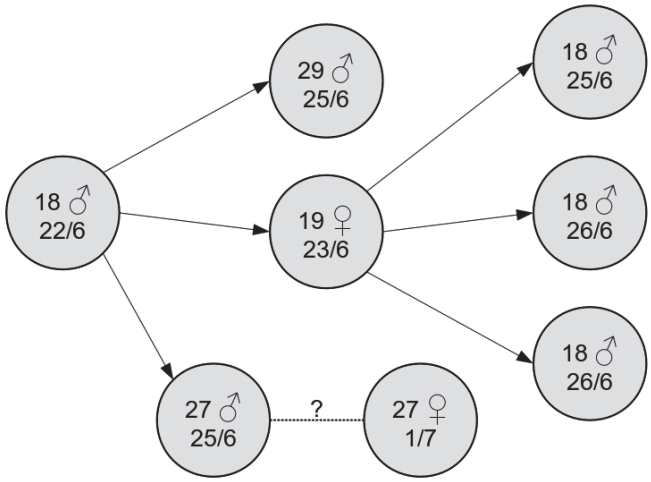
Discussion

These results support the importance of surveillance activities in order to monitor the epidemic and guide public health action by collecting data on epidemiological parameters and mechanisms of transmission in the community.

Several cases were identified during the first two and a half months of enhanced surveillance of A(H1N1)v influenza in Greece. Most of the identified cases concerned travellers from affected countries, especially those with community-wide sustained transmission, and about one in ten cases were secondary cases directly related to travellers. Furthermore, half of the cases without well-identified epidemiological link to another probable or confirmed case were persons related to the tourist industry in Greece. As the number of cases increased, we noticed a gradual increase in secondary and tertiary cases and eventually we identified domestic confirmed cases where no traceable link to a confirmed case was established. The increase in the number of reported cases observed from 30 June onwards might in part reflect the increased frequency of tourist visits to Greece in this period. This was accompanied by a high number of cases infected in the community during the same period.

Figure 4

Example cluster of in-country transmission (n=7). The age, sex and date of symptom onset are shown



A number of conclusions can be drawn from the surveillance results in Greece:

1. Many of the samples collected from clinicians did not fit the definition for "cases under investigation", either in terms of clinical parameters or in terms of epidemiological criteria. Particularly the "affected areas" proved to be a fast-moving target, as cases were becoming identified from an ever increasing number of countries not previously declared as affected, and cases were tested and identified on the basis of clinical judgement exercised by astute clinicians. Ironically, the fact that clinicians did not abide by the case definition agreed at European and national level allowed us to have a better picture of the evolving epidemic, enabling the detection of the first cases imported from an EU country [5], as well as community-acquired cases.

2. Given the above mentioned shortcomings of the case definition, which tends to systematically ignore patients with local transmission unless contact with a probable or confirmed case can be documented, the actual proportion of domestic cases might be underestimated in our findings.

3. During the summer, a peak influx of tourists is anticipated from countries with higher prevalence of influenza A(H1N1)v to Greece and other southern European countries. Greece is expected to host 13-14 million tourists this year, which is more than the national population of 11 million. This is expected to introduce a large number of infected subjects, and might account for an earlier start of the next influenza season. Furthermore, the advice against travel when a person is ill is apparently not adhered to by the general public. For example, media reported of several tourists who having spent a significant amount on travel expenses were unwilling to delay or postpone their trip and travelled while symptomatic.

4. The continuation of enhanced surveillance of influenza A(H1N1)v, including contact tracing around cases, would be inadvisable as case counts increase. Under such circumstances it is exceedingly difficult to maintain this practice, and its public health benefit is doubtful [8].

In conclusion, we report the cases of influenza A(H1N1)v recorded in Greece during the containment phase, from 30 April to 14 July. In an effort to contain disease spread and in order to continuously ascertain the situation and guide further public health action several measures were taken. However, our results illustrate that the spread of this disease is rapid, transmission in the community could not be prevented, and we anticipate there may be evidence of wider community transmission in our country soon and out of season. In this evolving situation, healthcare and public health resources need to be managed efficiently and sparingly.

As a result, a decision was announced on 15 July to move public health measures in Greece to a mitigation phase, which was communicated as "patient protection phase". In this phase, contact tracing was discontinued and the recommendation for chemoprophylaxis of all close contacts was withdrawn; chemoprophylaxis is now recommended for particularly vulnerable contacts, at the physician's discretion. Criteria for testing mainly include severe cases requiring hospitalisation, and selected cases from clusters of influenza-like illness; testing can be also carried out in special situations according to clinical judgment. Treatment with antivirals is now recommended for cases with severe symptoms or belonging to high-risk groups. Surveillance shifted to: a) notification of laboratory-confirmed severe cases who are hospitalised, b) laboratory reporting of influenza A(H1N1)v cases, c) sentinel surveillance of influenza-like illness, including a clinical and a laboratory component. Surveillance can contribute in an important way to public health decisions.

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Members of the influenza surveillance report group:

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Clinical features of cases of influenza A (H1N1)v in Osaka prefecture, Japan, May 2009

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This report describes the clinical characteristics of influenza A(H1N1)v virus infection in Osaka. By the end of May, 171 cases had been reported in Osaka. Most patients were from one school. No patient had a serious underlying medical condition.Clinical symptoms were mild and resembled those of seasonal influenza. The sensitivity of the rapid antigen test was 77%. Antivirals were given to the majority of the cases. Early antiviral treatment may have shortened the duration of fever.

Background

In Japan, the first case of influenza A (H1N1)v was found at Narita International Airport quarantine station on 9 May. The patient was a high school student who had traveled to Canada [1]. The first non-travel case was detected on 16 May in Kobe. On the same day, subsequent cases were found in Osaka prefecture, about 30 km from Kobe [2]. In the beginning, the authorities decided to hospitalise all patients for the purpose of isolation, based on the infection control law [3,4]; consequently 18 patients were hospitalised in Osaka. On 18 May, Osaka prefecture revised its hospitalisation policy based on clinical severity because of the rapid increase of the number of cases. Patients with mild symptoms were treated as outpatients and placed under medical observation at home. By 20 July, 847 cases had been reported in Osaka. Among them, 171 cases had been reported by the end of May. Most patients were adolescents. Of the 171 cases (including 13 who resided in other prefectures) 105 were from one school. This paper summarises the clinical characteristics of influenza A(H1N1)v cases reported in Osaka by the end of May.

Investigation in Osaka

The National Institute of Infectious Diseases (NIID) in Japan started an investigation on 17 May. By then, two clusters had been found in Osaka. One was the previously mentioned school and the other was a nearby elementary school. Although the numbers of cases were increasing day by day, most cases were linked to these two clusters. We focused the NIID investigation on these clusters; the remaining cases were investigated by the local health center.

Case definition

A case of influenza A (H1N1)v is defined as a person with influenza A(H1N1)v virus infection confirmed by real-time RT-PCR.

Cluster 1

- Secondary school: 1,934 students and 143 employees.
- Study population: 105 cases (103 students, 2 teachers), male: 83, female: 22
- Median age: 16 years (range: 13 to 53 years)
- One patient had mild asthma. No patient had a serious underlying medical condition.

Data collection

Direct face-to-face interviews were carried out by the NIID with 17 hospitalised patients, and telephone interviews were performed with 88 home-quarantined patients by school teachers with our technical assistance.

Cluster 2

- Elementary school: 624 pupils (no information on employees).
- Study population: 7 cases (pupils only), male: 2 , female: 5
- Median age: 11 years. (range: 9 to 12 years)
- One patient had asthma. No patient had a serious underlying medical condition.

Data collection

Direct face-to-face interviews with the patients and their parents were conducted by the NIID or the local health center.

Other cases

- Study population: 59 cases (31 secondary school students, 7 elementary school pupils, 21 other), male: 33, female: 33
- Median age: 15 years (range: 6 to 48 years)
- No patient had a serious underlying medical condition.

Data collection

Direct face-to-face interviews with the patients (or their parents) were conducted by the NIID or the local health center.

Clinical findings

Symptoms and laboratory data

Fever, cough and sore throat were most frequently observed (Table 1, 2). Most of the cases had clinical features similar to seasonal influenza [5]. 19.8% of cluster 1 and 14% of cluster 2 cases had diarrhoea, while usually fewer (approximately 10%) patients have diarrhoea with seasonal influenza in Japan [6]. Standard blood test results of 12 hospitalised patients showed no results specific to this virus. Cluster 2 included the first cases of the outbreak of influenza A (H1N1)v in children in Japan. No

significant differences were found between age groups in symptoms or severity of illness.

Rapid antigen test

Rapid antigen tests were conducted in the majority of cases. However, information on when this was performed was available for 35 cases only. The sensitivity of the rapid antigen test depended on when the kit was used; it was highest on day 1 (82.4%) and was relatively low on days 0 (75%) and 2 (60%) (Table 3). It is difficult to determine the accuracy of the rapid antigen test kit from the data presented here because of insufficient information (e.g. type of kit used). However, we conclude that the rapid antigen test cannot be used to rule out the possibility of influenza A(H1N1)v virus infections.

Treatment

Among 171 cases in Osaka, antivirals were given to 165 (96%); oseltamivir to 95 (56%) and zanamivir to 68 (40%) of the cases. Further two cases took zanamivir at first, and then switched to oseltamivir. Information on the duration of symptoms under treatment was available for 90 cases. Of these 90 cases, 44 received oseltamivir, 45 zanamivir and one switched from zanamivir to oseltamivir in the middle of clinical course. There was no significant difference in the duration of fever between two medications (oseltamivir 2.32 days, zanamivir 2.36 days, P=0.88, t test). Nevertheless, the results indicated that earlier administration of antivirals contributed to a reduction in the duration of fever (Table 4). However, this result is not enough to completely evaluate the effectiveness of antivirals, because we could not compare these groups to a group without prescriptions. Also, we could not assess whether antivirals reduced severity of illness, since the symptoms of all cases were mild.

Outcome

A few patients had underlying medical conditions, such as asthma. All these cases had a relatively quick and uneventful recovery. Because of the infection control law, 18 patients were hospitalised but all had mild symptoms and had no clinical indication for admission.

Conclusions

In Osaka, the majority of influenza A (H1N1)v cases occurred among healthy children and adolescents. The proportion of patients who had diarrhoea was slightly higher compared to that observed in seasonal influenza patients, but other clinical symptoms resembled those of seasonal influenza. No severe cases occurred. The results of the rapid antigen test were not sufficient to diagnose influenza A (H1N1)v virus infections. Antivirals were given to the majority of the cases. The analysis showed that early antiviral treatment shortened the duration of fever. One limitation of our study was that the methods of collection of clinical information were not standardised. Further studies are necessary to determine the accuracy of rapid antigen tests and the effectiveness of antivirals.

Table 1

Clinical symptoms of cases of influenza A(H1N1)v in cluster 1 (secondary school n=105), Osaka, Japan, May 2009

Symptom	Number of cases	Proportion of cases (%)
High fever of or above 38˚C	94/105	89.5%
Cough	86/104	82.7%
Low grade fever below 38˚C, feverish, chills	66/99	66.7%
Sore throat	68/104	65.4%
Nasal discharge, nasal congestion	62/104	59.6%
General fatigue	56/97	57.7%
Headache	50/96	52.1%
Joint pain	32/94	34.0%
Muscle pain	19/96	19.8%
Diarrhoea	19/96	19.8%
Conjunctivitis	6/94	6.4%
Vomiting	5/94	5.3%

Table 2

Clinical symptoms of cases of influenza A(H1N1)v in cluster 2 (elementary school, all ≤12 years old, n=7), Osaka, Japan, May 2009

Symptom	Number of cases	Proportion of cases (%)
High fever of or above 38˚C	7/7	100%
Cough	7/7	100%
Nasal discharge, nasal congestion	6/7	86%
General fatigue	5/6	83%
Headache	5/6	83%
Sore throat	5/7	71%
Low grade fever below 38˚C, feverish, chills	5/7	71%
Joint pain	3/5	60%
Muscle pain	3/5	60%
Diarrhoea	1/7	14%
Conjunctivitis	0/5	0%
Vomiting	0/5	0%

Table 3

Rapid kit test results of RT-PCR positive cases of influenza A(H1N1)v in Osaka, Japan, May 2009 (n=35)

Result of rapid test	Number of days from onset				Total
	Day 0	Day 1	Day 2	Day 3	
Positive	9	14	3	1	27
Negative	3	3	2	0	8
Positive rate (%)	75.0	82.4	60.0	100	77.0

Table 4

Prescription day and duration of fever in confirmed cases of influenza A(H1N1)v in Osaka, Japan, May 2009 (n=90)

Prescription day from onset of fever*	Number of cases	Average duration of fever	Standard deviation (SD)	P-value**
Day 0	39	1.90 days	0.821	P < 0.001
Day 1	39	2.51 days	0.970	
Day 2-5	12	3.42 days	1.379	

* Fever ≥ 38˚C
** One-way ANOVA

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A case of verocytotoxin-producing Escherichia coli O157 from a private barbecue in South East England

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The following case report describes a cluster of *Escherichia coli* O157 cases in the United Kingdom related to undercooked beef at a barbecue, resulting in an intensive care admission in France with haemolytic uraemic syndrome and highlighting the need to cook beef properly.

Introduction

A 32-year-old British woman became ill with diarrhoea on 1 June 2009 and travelled to France on 2 June. She was subsequently hospitalised in France on 7 June and was transferred to an intensive care unit with haemolytic uraemic syndrome (HUS). Her sister-in-law notified the Health Protection Agency about the case on 12 June. From the information she provided it was suspected that the infection occurred at a barbecue held by the case and her husband on 30 May at their home in Oxfordshire in which two other couples participated.

Methods

Case finding and epidemiological investigation

Information was gathered primarily from the sister-in-law who did not participate in the barbecue. On 15 June the other diners at the barbecue were contacted and food history was obtained from all participants. Faecal samples were sought first from another symptomatic guest, on 15 June, and subsequently, on 18 June, from others who ate at the barbecue but did not have any symptoms.

Environmental investigation

The local Environmental Health Officers were informed and went to the house of the case. They sampled a packet of unopened frozen minced beef bought at the same time as that used at the barbecue and, from the bin, the empty mince packet used for the barbecue with some residual meat and blotting paper in which the meat was wrapped. These samples were sent to the Food, Water and Environmental Microbiology Laboratory in Southampton for testing.

Laboratory confirmation and typing

For testing the empty beef mince packet the entire interior was swabbed and the swab, together with the small piece of raw meat and the blotting paper from the bottom, were placed in enrichment medium. Faecal and environmental isolates were confirmed, phage typed and tested for the presence of verocytotoxin (VT) – encoding genes by the Laboratory of Gastrointestinal Pathogens at the Centre for Infections, Colindale. The isolates were compared by pulsed-field gel electrophoresis (PFGE).

Results

Of the six people who ate at the barbecue only two were symptomatic: the index case hospitalised in France with HUS and an adult male with diarrhoea. He reported having eaten part of an undercooked beef burger at the barbecue. Other guests were well and reported eating similar foods to the two cases at the barbecue, which also included sausages, chicken kebabs and fish but none of them reported having undercooked beef burgers.

Stool specimens from the two cases were positive for *E. coli* O157. Three specimens from guests without illness were negative. The index case was tested in France and the isolate was not available for comparison. The other case in the UK was confirmed as *E. coli* O157 phage type 2, VT2 gene positive. The frozen beef did not grow any presumptive *E. coli* O157 but *E. coli* O157 was identified from the empty beef mince packet (which had contained the meat used to make the beef burgers at the barbecue). The empty meat packet was noticed to be very smelly and contained a bloody sheet of blotting paper at the bottom. The isolate from the meat packet was also phage type 2, VT2 gene positive. PFGE was performed on the PT2 isolates and their profiles were indistinguishable from each other.

Of 290 cases of *E. coli* O157 tested in the first half of 2009 by the Laboratory of Gastrointestinal Pathogens at the HPA 18 were PT2. These 18 PT2 cases were from six regions in England but none from the region in which this cluster occurred. None of the 18 PT2 isolates had the same VNTR type as the case in this cluster. PFGE is not routinely performed on all cases, only on those from suspected clusters.

Conclusions

There was a cluster of verocytotoxin-producing *E. coli* O157 cases related to homemade beef burgers at a private barbecue. Phenotypic and genotypic typing showed that the strain isolated from one case was indistinguishable from that from the investigated food source.

VTEC O157 is a potentially life threatening infection and it has not yet been eliminated from meat products. The public health message of the importance of cooking meat properly, particularly beefmeat products, therefore continues to be an important one. HUS is a rare sequela of VTEC O157 infections, particularly unusual in adults. The only risk factor identified in the case described here was that the patient was epileptic and was taking anti-epileptic medication.

Diagnosis of a British traveller in another European Union member state led to the identification of a cluster in the UK, thanks to the information provided to the Health Protection Agency by the family of the patient. Although identified late, when the second case was discovered, laboratory testing and typing of samples taken from this person and from residual food wrapping allowed identification of the source of infection. No other *E. coli* O157 cases were identified in the Thames Valley region during this time.

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An outbreak of viral gastroenteritis linked to municipal water supply, Lombardy, Italy, June 2009

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We report an outbreak of viral gastroenteritis linked to municipal drinking water in a town in northern Italy in June 2009. Over one month we identified 299 probable cases of whom 30 were confirmed for at least one of the following viruses: norovirus, rotavirus, enterovirus or astrovirus. Water samples and filters from the water system also tested positive for norovirus and enterovirus. Control measures included treating the water system with chlorine dioxide and filters with peracetic acid, while providing temporary alternative sources of drinking water to the population.

Introduction

On 9 June 2009, a general practitioner from the municipality of San Felice del Benaco notified to the local health authority of Brescia (Lombardy region, north Italy) 21 cases of gastroenteritis among guests of a hotel. Patients presented with vomiting, diarrhoea and fever. In the following days, there were also reports of cases among local residents. Located near the lake of Garda, San Felice del Benaco has 3,360 residents but is very touristic during the summer months. We investigated the outbreak in order to identify the source of infection and implement appropriate control measures.

Methods

We defined a probable outbreak case as a person who fell sick with vomiting or diarrhoea after 7 June 2009 and who stayed prior to disease onset in San Felice del Benaco. A confirmed outbreak case was defined as a person who fulfilled the criteria of a probable case and whose stool sample was laboratory-confirmed for at least one of the following viruses: norovirus, rotavirus, enterovirus or astrovirus. Probable cases who tested negative for the presence of virus in the stools were still considered as probable cases.

Active case finding was performed as follows: a public hotline was set up where people could call the health authority for information regarding the disease and report symptoms, date of onset and basic demographic data. In parallel, the outbreak investigation team collected daily information on case-patients presenting at the emergency unit of the local hospital and collected stool samples when possible.

The local and regional health authorities initiated an environmental investigation at the hotel on 9 June 2009, taking food samples from the kitchen, interviewing and collecting stool samples for microbiological testing from 20 probable cases (both guests and hotel staff). When it was clear that the outbreak was spreading to the larger community (apart from three campsites with their own private water supply, where no cases were reported), the environmental investigation was extended and included collection of water samples from the municipal water supply. Municipal water comes from the nearby lake. Before being distributed to the town as drinking water, it is treated with chlorine dioxide and hypochlorite and passes through sand filters. The investigators collected a total of 94 water samples from the lake at the location where the water is pumped, from filters and from public fountains. Samples were sent to the Lombardy and Emilia Romagna Experimental Zooprophylactic Institute (IZSLER) to test for the presence of bacterial pathogens (*Salmonella* sp., *Shigella* sp., *Campylobacter* sp., *E. coli* O157, *Yersinia enterocolitica, Aeromonas* sp., *Clostridium perfringens* toxins), parasites (*Cryptosporidium* sp.) and viral pathogens (norovirus, rotavirus, enterovirus, astrovirus). Virological methods included negative staining electron microscopy, type A rotavirus ELISA and PCR methods for norovirus, rotavirus, enterovirus and astrovirus.

Results

A total of 299 persons fulfilled the outbreak case definition, including 269 probable and 30 confirmed cases. The epidemic curve in Figure 1 shows the probable and confirmed outbreak cases by date of onset. The outbreak occurred between 8 June and 4 July 2009 and peaked on the 15 and 16 June with 47 outbreak cases per day.

The attack rate for the town of San Felice del Benaco was 8.9% (299/3,360). Age group-specific attack rates ranged from 7% (50/713) in persons aged 65 years and older to 14% (34/242) in the age group 15-24 years (Figure 2). Four cases were hospitalised, all of them children.

There was no fatality. Stool samples obtained from 36 probable cases were examined at the laboratory. Of these, 17 (47.2%) tested

positive for norovirus, 19 (52.8%) for rotavirus, 12 (33.3%) for enterovirus and 4 (11.1%) for astrovirus. Eight cases had both norovirus and rotavirus in the stools and two cases tested positive for norovirus, rotavirus and enterovirus. The laboratory did not find any virus in six cases (but we still included them among probable outbreak cases because of compatible symptoms). *Salmonella* sp., *Clostridium perfringens* and *Campylobacter* sp. were found in samples from two, one and one cases, respectively.

The mean age of confirmed cases of rotavirus was 29 years (range: 0-71) compared to the mean age of 39 years (range: 0-88) for cases of norovirus and 39 years (9-88) for cases of enterovirus. The age distribution of confirmed cases is shown in Figure 3.

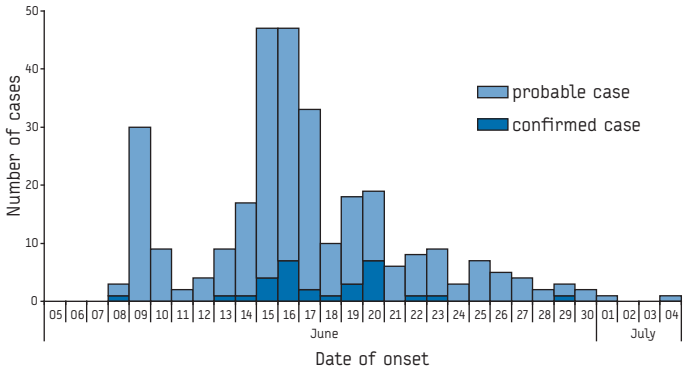
Food samples from the hotel tested negative for the presence of pathogens. On 16 June 2009, preliminary environmental investigation results showed abnormally high levels of *Clostridium perfringens* (4 UFC/100 ml) and *Aeromonas hydrophyla* (16 UFC/100 ml) in water samples from two public fountains. Tests on 44 water samples from from the municipal water system (water from fountains and filers) showed the presence of norovirus and enterovirus. Examination of the municipal water network revealed that: 1) the water company had undertaken work on the collection reservoir which might have limited the effect of chlorination; 2) two filters were 10 years old (cleaned weekly but not disinfected); 3) the chlorine concentration in the water before it passed through the filters was 0.4 mg/l; in filtered water it was only 0.08 mg/l.

Control measures

On 17 June 2009, a special ordinance from the municipality restricted the use of municipal water (inhabitants were told not to use municipal water for drinking and cooking purposes) and provided alternative water supplies to the population via water tankers. Local authorities organised a door-to-door information campaign and distributed leaflets in order to reach as many people as possible. On 19 June 2009, the municipality started disinfecting the water system with chlorine dioxide (0.2 mg/l) and sand filters with peracetic acid. When the presence of norovirus in water and stools of cases was confirmed, the residual concentration of chlorine dioxide in terminal points of the network was increased to 3.4 mg/l for three consecutive days from 23 June 2009. Regular water sampling and testing was performed to monitor the efficiency of control measures. The ordinance on drinking water was maintained until all water quality tests complied with safety norms. Water samples collected after the first treatment with chlorine dioxide and peracetic acid all tested negative for the presence of norovirus.

Figure 1

Probable (n=269) and confirmed (n=30) cases of viral gastroenteritis, by date of onset of symptoms, San Felice del Benaco, Italy, 8 June 2009 - 4 July 2009



Table

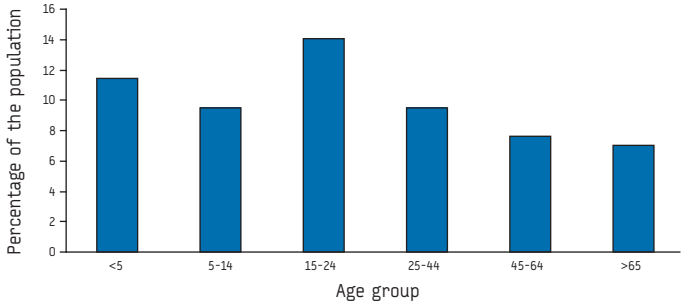
Pathogens found in stools samples of 36 cases of gastroenteritis, San Felice del Benaco, Italy, 8 June 2009 – 4 July 2009

Pathogen	Number of patients with positive results (multiple infection possible)	Percentage (%)
Rotavirus	19	52.8
Norovirus	17	47.2
Enterovirus	12	33.3
Astrovirus	4	11.1
Salmonella sp.	2	5.6
Clostridium perfringens	1	2.8
Campylobacter sp.	1	2.8

Source: Lombardy and Emilia Romagna Experimental Zooprophylactic Institute (IZSLER), Brescia, Italy

Figure 2

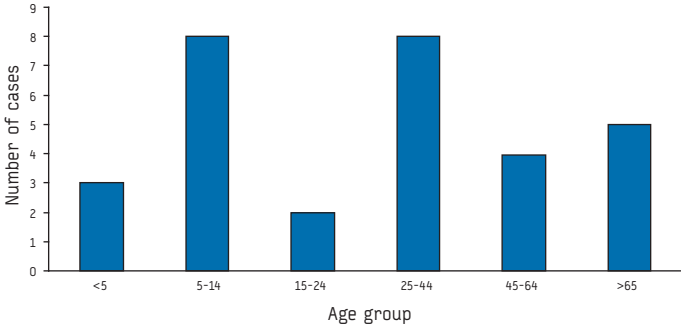
Attack rate of gastroenteritis per age group, outbreak in San Felice del Benaco, Italy, 8 June 2009 - 4 July 2009 ((n=299 cases)



Source: Azienda Sanitaria Locale (ASL) Brescia, Italy

Figure 3

Age distribution of confimed cases of viral gastroenteritis, San Felice del Benaco, Italy, 8 June 2009 - 4 July 2009 (n=30)



Source: Azienda Sanitaria Locale (ASL) Brescia, Italy

Conclusion and discussion

An outbreak of viral gastroenteritis has been microbiologically linked to a contaminated municipal water supply in a small town of Lombardy. Timely control measures and good compliance of the population following the information campaign prevented a much higher attack rate.

The alert came from a cluster of gastroenteritis in a hotel. The direction of the hotel promptly informed a general practitioner who notified the cluster to the public health authorities. An increase of gastroenteritis in the general population was noticed one day after the initial alert. The hotel is located along the lake, near the water reservoir, which could explain why the guests and its staff were among the first to be affected (see the first peak on the epidemic curve on 9 July 2009).

Although the number of residents in San Felice Del Benaco is 3,360, it is important to note that in the summer season many tourists stay in the town and the total population is multiplied by three. Therefore, the attack rates reported above (based on the resident population) are probably overestimates even though the surveillance system did not capture all cases. All age groups were affected. This is consistent with an exposure that is equally distributed across all ages. The relatively high mean age of confirmed rotavirus cases (29 years) is also consistent with an exposure that is not limited to young children.

The municipal water is taken from the lake at a place where the water is stagnant. So far, water samples from the lake tested negative for the presence of norovirus, rotavirus, enterovirus or astrovirus. However, we cannot exclude contamination of the lake due to over-capacity of the sewage system and/or illegal wastage.* In Italy, municipal water systems have been identified as the source of water-borne infections in several norovirus outbreaks (1, 2). It reminds us of the public health importance of well-maintained and monitored water supplies in our towns and cities (3).

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* Authors' correction

Upon the request of authors, one sentence was deleted from the discussion after the publication of the article. The correction was made on 3 August 2009.

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Europe's initial experience with pandemic (H1N1) 2009 - mitigation and delaying policies and practices

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Europe has experienced more than two months of the first transmissions and outbreak of the 2009 pandemic of A(H1N1)v. This article summarises some of the experience to date and looks towards the expected autumn increases of influenza activity that will affect every country. To date the distribution of transmission has been highly heterogenous between and within countries, with one country the United Kingdom (UK) experiencing the most cases and the highest transmission rates. Most infections are mild but there are steadily increasing numbers of people needing hospital care and more deaths are being reported. An initial difference in practice between Europe and North America was over case-finding and treatment with some authorities in Europe using active case-finding, contact tracing and treatment/prophylaxis with antivirals to try and delay transmission. This article details the history of this practice in the past two months and explains how and why countries are moving to mitigation, especially treating with antivirals those at higher risk of experiencing severe disease.

The current situation in the United States and Europe

In the three months since its first recognition the pandemic strain of influenza A(H1N1)v virus has spread to all six continents [1]. So many people are being infected that the World Health Organization (WHO) considers counting cases of little value in the more affected countries and hence it has advised to stop testing and reporting individual cases and to move on to other surveillance strategies [2]. In the temperate areas of the southern hemisphere, where it is winter, the first pandemic wave is in progress. In the northern hemisphere most countries are in the initiation phase (Figure).

The United States Centers for Disease Control and Prevention (CDC) broadly estimates that at least a million people have been infected with the pandemic virus in the United States, a large figure, but representing only 0.3% of the US population compared to the 20-30% that is anticipated to be affected in the first wave in the winter season [3]. The picture is also heterogeneous geographically as is often the case with both seasonal and pandemic influenza. Up to 7% of the population may have been infected in New York city in May, while other places are reporting only a few infections [4,5]. CDC expects the virus to keep spreading in the US through the summer and then transmission to accelerate in the autumn [6].

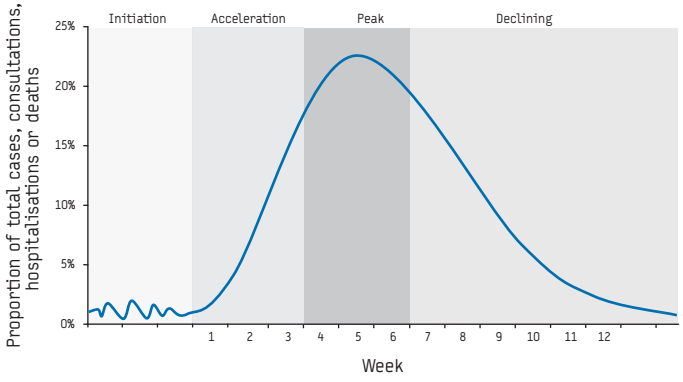
In the European Union all countries have now reported cases and the picture is even more heterogeneous than in the US [1]. Two countries, Spain and the UK account for more than four fifths of the reported cases and France and Germany have recently also reported significant numbers [1,7]. Hospitalisations and deaths are mounting up and the most affected country (UK) has revised its planning assumptions for a major first wave in the light of its particular experience (Table 1) [8].

Reported case numbers will become increasingly meaningless as countries abandon trying to test all cases and stop being able to count cases. However the initial analyses give important information. Initially case reports in Europe were dominated by imported (travel-related) cases [9]. These now represent ever decreasing proportions. In the latest cumulative analysis they accounted for only 13% (1,946 of 14,146) reported cases and the countries that have reported substantial numbers have all observed a strong trend of predominating domestically-acquired infections [7].

The most affected country is the UK and its experience gives useful indications of what is to come. Again the picture is one of heterogeneity with some parts of the UK experiencing intense transmission indicating the start of an acceleration phase with numbers of primary care consultations several times higher that

Figure

Idealised national curve for planning, Europe 2009 (reality is never so smooth and simple)



Single-wave profile showing the proportion of new clinical cases, consultations, hospitalisations or deaths by week. Based on influenza pandemic in London in 1918, second wave.

those experienced at the peak of last winter (when seasonal influenza was the worst in some years) [10]. However other parts are relatively unaffected [10]. The most recent numbers (as of 23 July) are available at the website of the Health Protection Agency: http://www.hpa.org.uk/webw/HPAweb&HPAwebStandard/HPAweb_C/1247816558780?p=1231252394302

Overall the modelled estimated rate of new infections for the week of 23 July of 0.2% (100,000 in the week) in the UK is still someway down the acceleration phase but according to the UK's planning assumptions it might be expected to peak at about 6.5% or around 800,000 clinical infections per week (Table 1) [8].

Severity of the disease and risk groups

It remains the case that most people who are infected in Europe experience a mild illness that does not require treatment. However this in itself is making surveillance more difficult since most people will not need to seek medical attention when infected [11]. For example in a New York city survey very few of the people reporting illness thought it was sufficiently serious to seek medical care (I Weisfuse, personal communication). Certainly many cases are also not coming to the attention of surveillance in Europe.

Table 1

United Kingdom revised planning assumptions for the pandemic – first wave A(H1N1) 2009

Clinical attack rate	30%
Peak clinical attack rate	6.5% (local planning assumption 4.5% to 8%) per week
Complication rate	15% of clinical cases
Hospitalisation rate	2% of clinical cases
Case fatality rate	0.1-0.35% of clinical cases
Peak absence rate	12% of workforce

Source: United Kingdom Department of Health: http://www.dh.gov.uk/en/Publicationsandstatistics/publications/PublicationsPolicyAndGuidance/DH_102892

Table 2

Risk groups for the pandemic (H1N1) 2009

The following groups are considered more at risk of experiencing severe disease than the general population should they become infected with the pandemic A(H1N1)v virus 2009:

People with chronic conditions in the following categories:

- chronic respiratory diseases;
- chronic cardiovascular diseases (though not isolated mild hypertension);
- chronic metabolic disorders (notably diabetes);
- chronic renal and hepatic diseases;
- persons with deficient immunity (congenital or acquired);
- chronic neurological or neuromuscular conditions; and
- any other condition that impairs a person's immunity or prejudices their respiratory (breathing) function, including severe or morbid obesity.

Note: These categories will be subject to amendment and development as more data become available. These are very similar underlying conditions that serve as risk factors for seasonal influenza. What is especially different from seasonal influenza is that the older age groups (over the age of 60 years) without underlying conditions are relatively unaffected by the pandemic strain.

Pregnant women

Young children (especially those under two years)

Crucial information is being published on the *higher risk groups* (those who are more likely to experience severe disease). The conclusions are still preliminary but the initial data from North America and Europe on who is affected by severe symptoms indicate risk groups similar to those for seasonal influenza, though with some important differences, notably the relative absence of cases in older people [12] (Table 2).

Expectations for the autumn in Europe

The European Centre for Disease Prevention and Control (ECDC) expects that in autumn European countries will experience a major first wave well beyond anything that has been experienced to date in this pandemic (Figure) [11]. However it is not possible to predict exactly what percentage of the population will be infected in the autumn wave and when it will come for individual countries. It is unlikely to occur at once and there will be heterogeneity within countries. Even if the experience of the UK is that the first acceleration phase of the pandemic truncates in the summer (perhaps as schools close), ECDC considers it important to prepare for an earlier start in autumn than the time when seasonal influenza usually takes off. Based on the initial surveillance results the UK has revised its planning assumptions for up to 30% of the population to be affected in the first wave [8] (Note: It is important here to distinguish between planning assumptions and predictions. Planning assumptions represent the reasonable worst case scenarion for a first major pandemic wave).

Hence Europe should be prepared to experience a very large number of cases in the coming months with inevitable strain on the health services because of a proportion of cases requiring primary or secondary care [11,13-15] (Table 1). A new approach to surveillance, building on what is already there will be needed and that is being developed by ECDC with Member States and WHO.

Initial differences in practises between North America and Europe

An area of differing practice or even policy between countries has been how to manage the initial cases and transmissions of influenza A(H1N1)v virus. In North America the approach from the start was of mitigation, essentially following WHO's early advice (Table 3) [16]. This includes applying standard guidance on the management of influenza cases and outbreaks similar to those for seasonal influenza, not treating the majority of cases who experience a mild self-limiting illness but offering antivirals to those who are considered at higher risk of experiencing severe disease [17,18]. Prophylaxis is being reserved for these groups when they are thought to have been exposed.

In Europe the initial approach was different from North America with some countries starting by attempting *containment* (trying to stop influenza spread beyond initial outbreaks) with energetic case-finding, treatment, contact-tracing and chemoprophylaxis of contacts (Table 3). Cases were isolated in hospital and quarantine was practised. A country that typified this approach was the UK which practised active finding and treatment of cases and contacts in schools and families, although not isolation in hospital or quarantine [19]. Though the word containment was used this was better described as *delaying* (Table 3). Despite great efforts in May and June daily reports of new laboratory confirmed cases rose to over 500 a day in late June. Hence, the UK found it difficult to sustain the intensive case-finding and contact-tracing strategy and on 2 July announced it was moving to a mitigation strategy which it called a *treatment* approach [20]. The principle is to make

antivirals available for all, but focusing especially on the early treatment of those in risk groups and to limit the use of prophylaxis to protect those at higher risk of severe disease [20]. Some other European countries have also treated all cases and contacts [21] but as their numbers of detected cases are small they were initially able to manage this more readily.

The question therefore was which practise should all European countries follow when they are inevitably affected, either over the summer or sometime in the autumn? Following a request from EU member states for guidance, in June ECDC published the arguments for and against these approaches, which this article will now summarise [22,23].

WHO's position on containment

When announcing pandemic phase 4, WHO indicated that the epidemic had already started to spread beyond a level justifying attempts at containment and a mitigation approach was recommended [16]. Two days later, on 29 April, WHO escalated to phase 5 and then on 11 June to phase 6. According to WHO guidance, under phases 5 and 6, measures differ between affected and not yet affected countries but containment attempts are no longer recommended, the guidance advises member states to implement a mitigation strategy, including considering measures for reducing the spread of infection [16,24]. This includes applying standard guidance on the management of influenza cases and outbreaks similar to those for seasonal influenza (Table 3). This entails not treating the majority of cases who experience a mild self-limiting illness but offering antivirals to those who are considered at higher risk of experiencing severe disease [16-18]. Neither ECDC nor WHO recommend the use of the word 'containment' for influenza outside of the theoretical context of place and time where a pandemic strain first emerges somewhere in the world [25]. Previous modelling work has suggested that containment will be both impractical and unsuccessful once there is extensive community transmission and certainly once the pandemic has entered its acceleration phase [26]. Apart from some very isolated settings, history dictates that European communities will not be able to contain the pandemic strain or isolate themselves from it [27].

The experience with delaying and containment

The 'delaying' strategy was certainly legitimate to attempt, especially in the EU where the initiation phase started at the very end of the seasonal influenza period when influenza transmission would be expected to be low. The delaying strategy is therefore appealing when a pandemic starts in the spring or early summer. The rationale is that an aggressive approach could decrease the effective reproduction number (R) and delay the inevitable acceleration of the pandemic until autumn allowing more time for preparations and for vaccines to be developed and licensed. Besides, identifying the first cases and documenting their clinical presentation has proven to be important at the early stages of a pandemic to gather information needed for the *early assessment* to steer the strategy for response [14,15,28).

Operational aspects

The main issues around the debate on mitigation versus delaying are operational and concern the *opportunity costs* of aggressive case-finding, contact tracing and management (Table 3). The question is whether there are staff available who can deliver the necessary response seven days a week and what else cannot be done because the human and other resources are fully engaged on case-finding, contact-tracing, testing and treating. In the UK delivering the delaying strategy was initially possible because the Health Protection Agency and Health Protection Scotland led the work and combined effectively with local public health and primary care staff to focus massive effort on the initially affected communities. At the same time central authorities concentrated on making final preparations especially readying the health services for the autumn wave. Even so the intense work involving many schools and families was unsustainable. This has demonstrated that where there is active influenza transmission the strain on the work-force from attempting delaying is considerable. Probably only countries with national public health workforces who can be moved around the country could implement such a policy at the population level during initiation. Once into the acceleration phase in the autumn the task will be impossible in any country given what is known now about the effective reproductive number [29]. Australia and New Zealand are unusual in having formal containment phases in their pandemic plans. Their current experience is telling for what Europe could expect in the autumn. Both these countries moved through and beyond containment rapidly into mitigation [30,31].

Communication challenges

Besides burden on staff there are major communication challenges from an initial delaying approach. These arise from starting on a delaying tactic and treating everyone with what may seem a very mild disease, plus their contacts. Then having to move back to mitigation with only offering antivirals to those in the risk

Table 3

Mitigation, containment and delaying – the definitions

Mitigation is a collective term recommended by WHO for actions in affected countries in phases 5 and 6 of pandemic alert, essentially reducing the impact of a pandemic.

In the health sector, the aims of mitigation include:
- reducing the overall number of people affected;
- reducing transmission;
- ensuring healthcare for those who may be infected;
- maximising care for those with disease;
- protecting the most vulnerable; and
- more general interventions.

Containment

Containment means preventing spread of a infection in a defined areas or areas by:
- case-finding: detecting imported infections and first generation transmissions; and
- taking actions to prevent their turning into chains of transmission and outbreaks, notably through vigorous contact tracing, treatment and/or quarantine of contacts.

The objective is to stop as many transmissions as possible and eventually the outbreak 'burns out'.
The term 'containment' is not recommended in this context by WHO or ECDC as it raises expectations that a pandemic virus can be contained once it has got beyond the initial outbreak, as was the case with the 2009 virus because, when it was discovered, transmission was already well beyond a delimited area.

Delaying is a less complete form of containment where the aim is not to contain the pandemic but rather to simply slow down transmission.

Differences

It is important to note that many of the actions and messages being undertaken or promulgated are **the same for delaying and mitigation strategies**.

What is different between the two is that in delaying there is special emphasis put on:
1. Vigorous case-finding and tracing of contact-persons and giving antivirals or alerting them to watch for symptoms;
2. Putting contact-persons or even all travellers from areas with community transmission under quarantine.

groups [8,10]. Explaining this to professionals and the public may not be easy. It is also not clear how it is possible to get patients, especially children to take antivirals and complete course when they are only experiencing mild disease or are contacts of cases [32].

Differences between mitigation and containment

It should be appreciated that looked at overall mitigation and delaying strategies have a lot in common. They only differ in the emphasis in delaying on finding as many infectious cases as possible and treating them and their contacts (Table 3) However that difference is very important as the UK found the work is very demanding on human resources in the field and in the laboratory. This is especially so with using antivirals because of the evidence that to be effective treatment has to be given early, within 48 hours of symptoms starting [33,34].

Exit strategies

If a country decides to adopt delaying it needs to have a very clear exit strategy and triggers for giving up. ECDC does not recommend delaying but if a country does adopt the policy then it could consider the ECDC criteria for being 'affected' as the sign it is time to change to mitigation in all parts of the country [35]. Once policy makers adopt delaying or containment as a formal policy rather than an operational practice it can be especially difficult to change policy in a timely manner and so it is best to keep decisions at the technical level. An additional factor influencing the choice of strategy is that if a number of countries in Europe started on delaying or containment then others might have felt they had to follow. Unlike in the United States and Canada there are no cross-European agreed recommendations on the use of antivirals (although there is an ECDC guidance) [34]. It is therefore difficult to explain why delaying is being done in one country and not in others and this problem will arise again (i.e. in the autumn). Some solution was offered by meetings that took place in early July where experts met to discuss this topic and advised ministers at an informal EU Health Council to allow a degree of coordination. There was also broad agreement based on the UK example that mitigation should be adopted either in the initiation phase or when acceleration starts (Figure) in individual countries [36,37].

Has delaying been effective?

Have attempts at case-finding, contact tracing and treatment of all cases and contacts been effective in Europe so far? The answer depends on whether effectiveness is considered at the individual or population level. For those infected and treated within 24 to 48 hours the answer is almost certainly 'yes'. Trials of both the neuraminidase inhibitors, oseltamivir and zanamivir against seasonal influenza have shown benefit in otherwise healthy adults [33,34] although it must be appreciated that antivirals are not 'magic bullets'. Even if given in time they only shorten the illness by one or two days and do not stop a person being infectious [33,34]. There may be more benefit when antivirals are given to those developing severe illness [34]. There are no such data for the pandemic strain as yet but since only a handful of viruses have shown genetic markers of resistance to either drug (they do have markers of resistance to the adamantenes) a reasonable default assumption is that they should be effective for treatment of infected individual [34,40] The arguments around prophylaxis are more complicated. Certainly many episodes of illnesses will have been prevented but we do not know how successful prophylaxis is in preventing actual infection rather than just preventing the onset of symptoms. A sophisticated view, not supported by ECDC, recalls the accounts of the 1918-19 pandemic, which was also the last A(H1N1)-based pandemic. Then a lower pathogenicity wave in the spring in Europe was followed by a much higher pathogenicity wave in the autumn [41]. So the logic goes it may be better to be infected now by this mild A(H1N1)v virus rather than later by one causing more severe disease.

At a population level it is harder to determine the success of the delaying tactic. Delaying can appear to work by chance alone. Pandemics of influenza, like seasonal influenza each autumn, take an uncertain time to move from initiation to acceleration (contrary to popular belief influenza is only 'infectious' not 'highly infectious' (Table 4)) Considering the United States since April the heterogeneity of transmission has been striking [5]. If relatively pandemic-spared cities like those on the West Coast had attempted delaying they might now be congratulating themselves while cities like Chicago and New York would be wondering what they did wrong. It is highly possible that the efforts made by the UK and other European countries delayed the progression of transmission in May and June. Indeed given the scale of the effort in the UK it seems hard to imagine there has not been some benefit but a final verdict on how much delaying was achieved will have to await the results of considered evaluations which will take some time.

What to do?

In conclusion, what should a European country do when confronted by first cases? It can be difficult when there are only a handful of cases to offer no treatment except to individuals in risk groups. But that may be what national policies dictate, what WHO recommends and what is being done in North America [16-18]. It would also seem to be in line with the ECDC documents [22,23].

When confronted with more cases countries should consider whether to attempt delaying at all, what the advantages are of any time it might buy and the opportunity costs from what else will not be done as a consequence. The conclusion of the Swedish Presidency meeting was that countries should move to mitigation [36,37], and at least two more countries report having taken this decision [38,39].

However that does not mean that the first cases and transmissions in a country do not deserve special attention. There are very legitimate reasons for undertaking enhanced surveillance and working closely with those first affected to determine some of the

Table 4

Infectiousness of some communicable diseases

Infection	Effective (R) or basic reproductive rate (Ro)	Notes
Seasonal influenza	R around 1.1 – 1.2	Higher in crowded communities
Pandemic influenzas	R = 1.5 to 2.5	Higher in crowded communities
Pandemic (H1N1) 2009	R = 1.5 to 2	Presumed higher in crowded communities
Measles	Ro > 10	
Mumps	Ro 4 to 7	

R = effective reproductive rate = the average actual number of people that are observed to be infected by one infected person
Ro = basic reproductive rate = a theoretical concept of the average number of people that one person infects in a wholely susceptible population

known unknowns of the pandemic – for example: what proportions of people in a family are affected, are most older people really immune, how long are people infectious, do those who choose to take antivirals stop excreting virus and do they develop immunity [14,15,40-45] A number of countries are undertaking such work in Europe and ECDC and WHO are working with them to ensure the rapid sharing of protocols and data.

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