

Impact of the influenza A(H1N1) 2009 pandemic to the 17-25 year age group and to the students of the Medical School, Aristotle University of Thessaloniki.

Angeliki Melidou, Maria Broufa, Konstantinos Dakis, Athina Dimosiari,
Christina Menexi, Nikolaos Nakos, Aggelos Simopoulos,
Antonella Tsika, Nikolaos Malisiovas

2nd Department of Microbiology, Medical School, Aristotle University of Thessaloniki

ABSTRACT: *Introduction:* In 2009 a novel A(H1N1) influenza virus emerged and caused a pandemic. The scope of this study was to identify the impact of the pandemic to the 17-25 year age group and to normal University function.

Methods: a) Epidemiological data was obtained from the National Influenza Center for northern Greece, regarding the 17-25 age group. b) Absence records from the first semester of 2008-2009 and 2009-2010 were obtained from the School of Medicine, Aristotle University of Thessaloniki and a questionnaire was given to 100 medical students.

Results and discussion: a) Two pandemic waves were identified; the first was during weeks 27-35 and the second during weeks 43-52.

Of the 4949 examined samples, 1632 were confirmed pandemic H1N1 2009 infections (33%), and 362 (22%) belonged to the 17-25 age group. Of the latest, 53% were male and 47% were female. Most infections belonging to this group were mild, and developed influenza like illness (ILI) symptoms. Only 19% developed pneumonia or other complications and 2 were fatal. 4% was vaccinated against influenza and 2% against *S. pneumoniae*. Only 7% received Tamiflu treatment. 9% noted a travel history related to their infection.

b) The second wave was synchronous with the 1st University Semester. However, no statistical difference between absence levels during 2008-2009 and 2009-2010 was identified and no students had reported ILI symptoms.

Conclusively, whereas the 17-25 age group was indeed of the mostly affected from the pandemic, it seems that unexpectedly there was no impact to normal University function.

Key Words: Pandemic, Influenza, Students, University, Greece.

INTRODUCTION

During April 2009 a novel A(H1N1) influenza virus emerged in Mexico and since then has spread worldwide. The virus was found to be an A(H1N1) virus that was antigenically and genetically unrelated to human seasonal influenza viruses and genetically related to viruses known to circulate in swine¹.

Immediately, Greece enhanced the surveillance system. A telephone hotline was used to provide information and guidance to the public, advise health

professionals, and guide cases under investigation for pandemic H1N1 2009 to designated reference hospitals for clinical evaluation and nasopharyngeal swab collection. Specimens were sent to one of the two reference laboratories, in Athens (Hellenic Pasteur Institute) covering southern Greece and in Thessaloniki (Aristotle University of Thessaloniki, Medical School, 2nd Department of Microbiology) covering northern Greece. Instructions were posted on the walls of every public building, including universities and hospitals.

Corresponding author: Dr Angeliki Melidou, National Influenza Centre for northern Greece, 2nd Department of Microbiology, Medical School, Aristotle University of Thessaloniki, 541 24, Thessaloniki, Greece, Tel. 2310 999103, Fax: 2310 999140, email: amelidou@med.auth.gr

Guidelines for case and contact management and for infection control were prepared by the Hellenic Centre for Disease Control and Prevention (KEELPNO)². These were sent to hospitals and published on the KEELPNO website (<http://www.keelpno.gr/articles/topic/?id=994>). At the Aristotle University of Thessaloniki, a University Pandemic Committee was immediately established and measures were taken to inform students how to react in case they experience a respiratory infection. Specifically, they were advised not to attend lectures and to report the infection to the Departmental and the School secretary.

Two pandemic waves were eventually identified. The first wave which was shorter occurred during the summer months, weeks 27-35, following the initial introduction of the novel virus in Greece. During the second longer and more severe wave, weeks 43-52, most of the secondary schools were occluded, either as a precautionary measure or for quarantine purposes. A similar impact to the university function was indeed expected. From studies conducted in Greece, in other countries of Europe and America, but also in WHO, it was determined that children and young adults were the groups that were mostly affected by the H1N1 2009 pandemic.

The scope of this study was to identify the actual impact of the pandemic to the 17-25 year age group and to the normal University operation, using epidemiological data obtained from the National Influenza Center for northern Greece, which is hosted at the 2nd Department of Microbiology, Medical School, Aristotle University of Thessaloniki, as well as from the separate University departments.

METHODS

The study was conducted in two parts:

a) Epidemiological data was obtained from this Center, regarding the 17-25 year age group. In total 4949 suspected pharyngeal swabs were examined. All clinical specimens were accompanied by a Standard Form with information on age, sex, date of onset, date of specimen collection, place of residence, clinical features and complications of each patient, travel history, vaccination history and administration of antiviral treatment.

RNA was extracted from the clinical specimen

using Qiagen Viral RNA mini kit, according to the manufacturer's instructions and pandemic H1N1 2009 infections were confirmed using the CDC swine influenza real-time RT-PCR kit, following WHO recommendations. A "confirmed case" was defined as a person tested positive for pandemic H1N1 2009 virus. Results were reported to KEELPNO, WHO (World Health Organization) and ECDC (European Centre for Disease Control)³.

b) Absence records from the 3rd year of study, first semesters of 2008-2009 and 2009-2010, were obtained from 6 departments of the School of Medicine, Aristotle University of Thessaloniki, in order to observe the department's function and compare it with the previous year. Information was also collected from the appropriate departments and from the school secretary regarding student reports of absence, as well as reports of respiratory infections during the first semester, 15th of October 2009-15th of January 2010, a period which coincides with the second pandemic wave.

A questionnaire was also given to 100 medicine students, studying at various semesters, between 17-25 years of age, in order to gather information regarding their nationality, travel history and most importantly respiratory infection history at the period of interest, laboratory confirmation of infection, vaccination status and antiviral drug treatment.

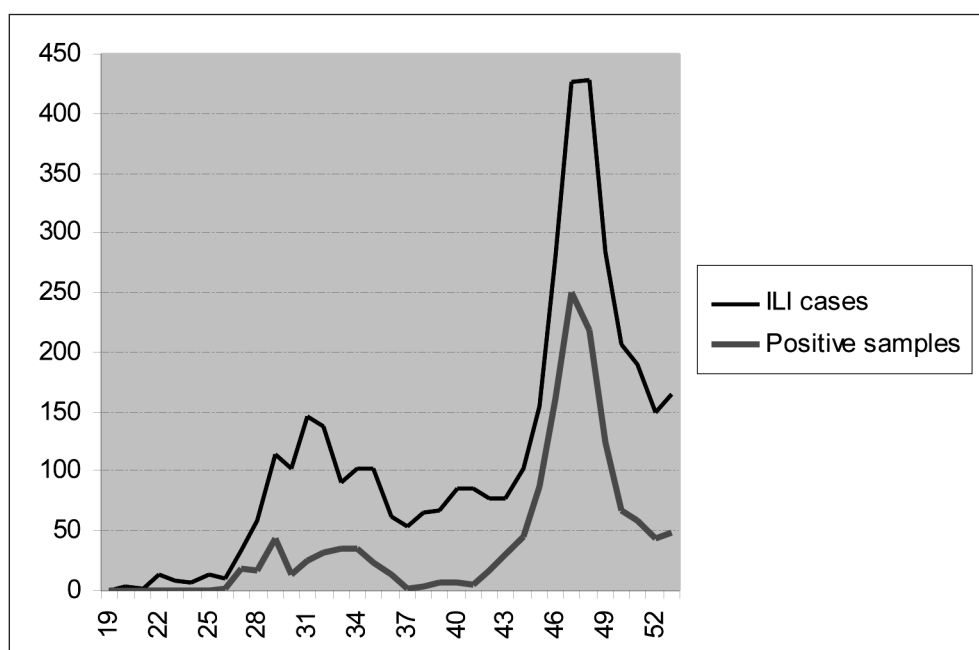
RESULTS

a) On 27th of May 2009, the first pandemic influenza H1N1 2009 virus was detected in northern Greece at a 20-year old student returning from the United Kingdom⁴. Between April 2009 and March 2010, 1632 specimens were confirmed infections (33%). The first wave which was shorter occurred during the summer months, weeks 27-35, following the initial introduction of the novel virus in Greece. During the second longer and more severe wave, weeks 43-52, most of the secondary schools were occluded, either as a precautionary measure or for quarantine purposes.

The age distribution showed a trend towards children and young adults, with 362 (22%) of the confirmed cases being at the 17-25 age group. During the first university semester period (15th October 2009-15th January 2010) 202 (54%) of the examined 17-25 year old cases were found positive for the novel

Table 1. Percentage of examined and confirmed 17-25 year old cases during the whole pandemic and the first university semester periods.

	Total examined	Confirmed cases (%)	Confirmed 17-25 cases (% of the total confirmed)	Confirmed 17-25 cases (% of the total examined)
Apr. 2009 - Jan. 2010	4949	1632 (33%)	362 (22%)	362 (7,3%)
Oct. 2009 - Jan. 2010	2771	1216 (44%)	202 (17%)	202 (7,3%)

Table 2. Two pandemic influenza waves. Notified cases of influenza-like illnesses (ILI) and laboratory confirmed pandemic H1N1 2009 infections by week (19-53).

virus. Sex distribution showed similar infection rates at both sexes (53% male and 47% female). (Table 1) ($P < 0.05$).

The analysis of these cases showed that after some sporadic cases and a slow increase in June 2009, a significant increase of newly reported cases was observed at mid July. During this first wave, the majority of the infected individuals (70%) were travellers. 9% of the infected 17-25 individuals reported a travel history mostly during the summer period. A second peak initiated at week 43 and lasted until the end of 2009. (Table 2).

83% of confirmed cases were presented with mild ILI (Influenza-Like-Illness), with fever ranging from 38- 40,5°C, acute onset of symptoms, cough, catarrh, sore throat, fatigue, headache, muscle pain and in

some cases conjunctivitis, diarrhoea and/or vomiting.

Among the 17-25 age group cases, 17% were hospitalized. The majority of them were during months November and December. The medical complications related to hospitalisation were acute respiratory failure, pneumonia, hypoxia, acute tracheitis, and tracheobronchitis. A wide age range distribution was observed in hospitalised patients, but more severe outcomes were generally associated with older patients (median age 52 years old). At the age group of interest, of the 362 confirmed cases, 19% developed more severe symptoms. Specifically, 35 patients developed pneumonia, 17 had difficulty in breathing, 8 developed ARDS, 2 cardiac disorder, 1 neurological disorders, 1 polyorganic failure, 3 conjunctivitis.

In total, 45 (2.7%) confirmed cases of pandemic

H1N1 2009 infection were fatal. Most of them were between 50-81 years of age, while 2 (0.1%) belonged to the 17-25 year age group. Obesity has been considered as a possible risk factor of the fatal cases. However, there were also a small number of asymptomatic cases, mostly detected during the summer period. The number of asymptomatic cases was possibly higher, but this could not be determined, as at the progress of the pandemic only severe cases were laboratory examined.

Regarding the antiviral treatment, at the onset of the pandemic, all patients received oseltamivir (Tamiflu) after the laboratory confirmation of pandemic H1N1 2009 infection, but only 21% of the cases were treated from the onset of the symptoms. After widespread transmission within the country, patients no longer received treatment unless necessary. During the period September to December, only 75 confirmed cases received antiviral treatment (5,2%), 27 of them were at the 17-25 age group.

Regarding the vaccination status of the age group of study, 11 patients (3%) were vaccinated against seasonal influenza (2009-2010 season), the majority of the vaccinations occurred during November. It is worth mentioning that 5 of the confirmed pandemic H1N1 2009 cases have been vaccinated with the vaccine that contained the pandemic strain. 2% was vaccinated against *S. pneumoniae*.

b) Data that was obtained the files of the Medical School, Aristotle University of Thessaloniki for a total of 6 departmental units, showed that the number of 3rd year registered students was 373 at the 2008-2009 academic year and 313 at the 2009-2010 academic year. The number of absentees were 815 and 852 respectively, whereas students that replenished the 3rd year/1st semester obligatory laboratories were 297 and 343 respectively. No statistical significance was found ($P < 0,05$). Only 7 students notified the department secretary for absence because of influenza illness, whereas none informed the University Pandemic Committee or the School Secretary regarding their illness, as they were specifically advised.

Results from the questionnaire showed that 71%, out of 100 individuals, reported that they indeed experienced an upper respiratory infection during the period of study. Regarding vaccination, 3% were vac-

inated against pandemic influenza, 3% against common flu and 6% against *S. pneumoniae*. One student confirmed the influenza infection by PCR and none was admitted to a hospital or received Tamiflu treatment. No relevance was found between travel history or nationality with the history of respiratory infections.

DISCUSSION

The results provide an overview of the epidemiological characteristics of 362 confirmed infections from pandemic influenza H1N1 2009, in northern Greece, between April 2009 to March 2010. 22% of infected individuals belonged to the 17-25 age group.

The age distribution of the infections clearly indicates that the rate of infection is greater in the age group of 6-16 years old (40%), followed by the 17-25 age group (22%). (Table 1) It is interesting that 54% of the examined 17-25 year old cases were positive for the novel virus during the first university semester period. (Table 1). The very low incidence of infections at individuals over 60 years of age is consistent with studies from other countries^{5,6}. It is still unclear if the low incidence is due to partial immunity of older individuals from former infections with H1N1 influenza viruses or because the virus was not sufficiently introduced in this subpopulation. Sex distribution, on the other hand, showed similar infection rates at both sexes, which seems to be similar to reports from other countries⁷.

Additionally, the analysis of these cases showed that the first significant increase of newly reported cases was observed at mid July, a trend which was also reported from other countries in Europe⁸. During this first wave, the majority of infected individuals were travellers (70%). The age group under investigation, 17-25, represent the group that was mostly travelling at during this period. A second pandemic wave initiated at week 44 and lasted until the end of 2009. Since the beginning of January, there is a downward trend in Greece. (Table 2).

The data show that most common symptoms include fever, cough, catarrh, sore throat, fatigue, headache and muscle pain, and most infections with pandemic influenza had mild, uncomplicated clinical features. This agrees with reports from other countries^{9,10}. 81% of 17-25 year old individuals de-

veloped mild infection from influenza. Asymptomatic patients were mostly detected during the summer period, during which all contacts of laboratory confirmed cases were investigated.

After widespread transmission of the virus within the country, clinicians had to laboratory-confirm the infection only in more severe cases. It is also remarkable that the hospitalisation rate changed considerably over the weeks. During the first weeks, the majority of cases were hospitalised only due to infection control measures. As the pandemic progressed, hospitalisation was considered as a proxy for the severity of the disease in patients. The hospitalisation rate increased dramatically during November and December, as almost 90% of hospitalisations occurred this period. A closer look at those cases shows that patients with underlying conditions had two times higher hospitalisation rate than in cases without underlying conditions, while more severe outcomes during hospitalisation were generally associated with older patients. This is similar to findings from other countries as well⁷. At the age group of interest, hospitalisation occurred at the 17% of cases. This percentage corresponds to the number of 17-25 year old cases that developed severest symptoms (19%). It is also important to note that some hospitalisations were due to isolation purposes or due to underlying medical conditions and therefore the proportion to patients admitted to a hospital is not an indicator of the severity of the disease.

According to our results the death rate was 2.7%, somewhat higher than the percentage worldwide (1,2-1,3%), though the mortality in Europe had not been reported higher than 0,44% (<http://www.who.int/csr/disease/swineflu/en/>). Regarding this relatively high case-fatality ratio, it should be considered that only the laboratory-confirmed cases were accounted and that during the second and more severe wave, only cases with severe symptoms were examined. In fact, only 2 confirmed cases in the 17-25 age group were fatal. Obesity has been generally considered as a possible risk factor of the fatal cases¹¹.

In the beginning of the pandemic in Greece, antiviral treatment was administered to all patients after laboratory confirmation of the infection. This policy was reported by other countries as well¹², and was soon abandoned due to the high risk of development

of resistant pandemic H1N1 2009 strains. After widespread transmission within the country, antiviral treatment was limited to complicated or high-risk cases. 17-25 year old confirmed cases rarely received antiviral treatment (7%).

Additionally, according to the epidemiological analysis, 3% of the confirmed 17-25 year old cases were vaccinated for seasonal influenza (2009-2010 season), while the majority of the vaccination occurred during November. It is notable that 1% of the 17-25 year old patients with confirmed pandemic H1N1 2009 infection had been vaccinated with the vaccine that contained the pandemic strain. However, the fact that they developed the symptoms only 2-3 days after the vaccination indicates that they had not any vaccine coverage at the time of the infection.

Conclusively, it seems that the student age group (17-25 years) was of the most affected group from the H1N1 2009 pandemic. The second most severe pandemic wave coincided with the 1st University Semester and it was expected that the pandemic would have a huge impact on the function of the university, as it did with secondary schools at this period. However, data that was gathered from the Medical School of the Aristotle University of Thessaloniki showed that the various departments were fully operational and functioned normally during the pandemic period. There was no significant difference at the absence levels compared to the previous year and only 7 out of 313 students reported an influenza infection, though they failed to report it to the School Secretary as they were specifically advised from the University Pandemic Committee. These facts raise a question as to whether the medical students did not get infected at all, or maybe a mild infection was not sufficient to keep them away from the classroom. Interestingly, accounting the questionnaire answers, 71% did report an influenza like illness during the period of study. The high proportion of reported infections coincides with the fact that the student age group 17-25 years, was proven to be of the higher affected groups. It was evident however, that all students failed to report their respiratory infection to the Medical School secretary, despite being specifically advised to do so. Only 1 student confirmed the respiratory infection at the laboratory. Medicine students also failed to vac-

ciate, despite the fact that they are constantly located in hospitals and health care units. The conflict of the data could be attributed to the fact that their infections were mild. It is probable that they have also developed a cross-immunity level, due to their constant presence in hospitals.

Clearly, the young adults were mostly affected by the influenza pandemic. Constant epidemiological

surveillance is considered essential, to monitor the effect of the novel virus to this population. It would be useful if efforts were focused in persuading students to follow the instructions and report their possible infections to the Pandemic Committee.

Επιπτώσεις της πανδημίας γρίπης A(H1N1) 2009 στην ηλικιακή ομάδα 17-25 και στους φοιτητές της Ιατρικής Σχολής του Αριστοτελείου Πανεπιστημίου Θεσσαλονίκης.

Αγγελική Μελίδου, Μαρία Μπρούφα, Κωνσταντίνος Δάκης, Αθηνά Δημοσιάρη,
Χριστίνα Μενέξη, Νικόλαος Νάκος, Άγγελος Σιμόπουλος,
Αντωνέλλα Τσίκα, Νικόλαος Μαλισιόβας

Β' Εργαστήριο Μικροβιολογίας, Ιατρική Σχολή, Αριστοτέλειο Πανεπιστήμιο Θεσσαλονίκης

ΠΕΡΙΛΗΨΗ: *Εισαγωγή:* Το 2009 ένας νέος A(H1N1) ιός γρίπης εμφανίσθηκε και προκάλεσε πανδημία. Ο σκοπός αυτής της μελέτης ήταν να προσδιοριστεί η επίπτωση της πανδημίας στην ηλικιακή ομάδα 17-25 ετών και στην ομαλή λειτουργία του πανεπιστημίου.

Μέθοδοι: α) Λήφθηκαν επιδημιολογικά δεδομένα από το Εθνικό Κέντρο Γρίπης της Βόρειας Ελλάδας. Συνολικά 4949 ύποπτα φαργγικά επιχρίσματα εξετάστηκαν στο Εθνικό Κέντρο Γρίπης για τη Βόρεια Ελλάδα. β) Λήφθηκαν τα αρχεία απουσιών του πρώτου εξαμήνου του 2008-2009 και 2009-2010 και δόθηκε ερωτηματολόγιο σε 100 φοιτητές της Ιατρικής Σχολής του Αριστοτελείου Πανεπιστημίου Θεσσαλονίκης.

Αποτελέσματα και Συζήτηση: Δύο πανδημικά κύματα προσδιορίστηκαν, το πρώτο τις εβδομάδες 27-35 και το δεύτερο τις εβδομάδες 43-52.

Από τα 4949 εξετασθέντα δείγματα, 1632 επιβεβαιώθηκαν πανδημικές H1N1 2009 λοιμώξεις (33%), και 362 (22%) ανήκε στην ηλικιακή ομάδα 17-25. 53% ήταν άρρενες και 47% ήταν θήλυς. Οι περισσότερες λοιμώξεις αυτής της ομάδας ήταν ήπιες, και εμφάνισαν συμπτώματα γρίπης. 19% εμφάνισε πνευμονία ή άλλες επιπλοκές και 2 ήταν θανατηφόρες. Μόνο 4% εμβολιάσθηκε κατά της γρίπης και 2% κατά του *S. pneumoniae*. Μόνο 7% έλαβε θεραπεία με Tamiflu. 9% σημείωσε ιστορικό ταξιδιού σχετιζόμενο με τη μόλυνσή τους.

β) Το δεύτερο κύμα συνέπεσε με το 1^ο Ακαδημαϊκό εξάμηνο. Ωστόσο, καμία στατιστικά σημαντική διαφορά μεταξύ των απουσιών κατά το 2008-2009 και 2009-2010 εντοπίστηκε και κανένας φοιτητής δεν δήλωσε νόσο.

Συμπερασματικά, ενώ η ηλικιακή ομάδα 17-25 ήταν από τις περισσότερο προσβεβλημένες από τον νέο ιό, φαίνεται πως δεν υπήρξε καμία επίπτωση στη φυσιολογική λειτουργία του Πανεπιστημίου.

Λέξεις Κλειδιά: Πανδημία, Γρίπη, Φοιτητές, Πανεπιστήμιο, Ελλάδα.

REFERENCES

1. World Health Organization (WHO). New influenza A(H1N1) virus infections: global surveillance summary, May 2009. *Wkly Epidemiol Rec* 2009; 84(20):173-9.
2. Lytras T, Theocharopoulos G, Tsiodras S, Mentis A, Panagiotopoulos T, Bonovas S., influenza surveillance report group. Enhanced surveillance of Influenza A(H1N1)v in Greece during the containment phase. *Euro Surveill*. 2009 Jul 23;14(29).
3. Commission Decision of 30 April 2009 amending Decision 2002/253/EC laying down case definitions for reporting communicable diseases to the Community network under Decision n° 21/19/98/EC. 2009/363/EC. *Official Journal L* 110/58. 01.05.2009. Available from: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:110:0058:0059:EN:PDF>
4. Panagiotopoulos T, Bonovas S, Danis K, Iliopoulos D, Dedoukou X, Pavli A, et al. Cluster of new influenza A(H1N1) cases in travellers returning from Scotland to Greece - community transmission within the European Union?. *EuroSurveill*. 2009; 14(21):pii=19226.
5. Centers for Disease Control and Prevention (CDC). Novel H1N1 Flu: Facts and Figures. Available from: <http://www.cdc.gov/h1n1flu/surveillance.htm>.
6. Hahne S, Donker T, Meijer A, Timen A, van Steenbergen J, Osterhaus A, et al. Epidemiology and control of influenza A(H1N1)v in the Netherlands: the first 115 cases. *Euro Surveill*. 2009; 14(27):pii=19627.
7. Gilsdorf A, Poggensee G, on behalf of the working group pandemic influenza A(H1N1)v. Influenza A(H1N1)v in Germany: the first 10,000 cases. *Euro Surveill*. 2009; 14(34):pii=19318.
8. ECDC working group on influenza A(H1N1)v. Preliminary analysis of influenza A(H1N1)v individual and aggregated cases reports from EU and EFTA countries. *Euro Surveill*. 2009; 14(23):pii=19238.
9. Ciblak MA, Albayrak N, Odabas Y, Basak Atlas A, Kanturvardar M, Hasoksuz M, et al. Cases of influenza A(H1N1)v reported in Turkey, May-July 2009. *Euro Surveill*. 2009; 14(32):pii-19304.
10. European Centre for Disease Prevention and Control (ECDC). Surveillance Report. Pandemic (h1n1) 2009: Analysis of individual case reports in EU and EEA countries. Available from: [http://ecdc.europa.eu/en/health-topics/Documents/090810_Influenza_A\(H1N1\)_Analysis_of_individual_data_EU_EEA-EFTA.PDF](http://ecdc.europa.eu/en/health-topics/Documents/090810_Influenza_A(H1N1)_Analysis_of_individual_data_EU_EEA-EFTA.PDF).
11. Centers for Disease Control and Prevention (CDC). Intensive - care patients with severe novel influenza A(H1N1) virus infection, Michigan, June 2009. *MMWR Morb Mortal Wkly Rep*. 2009;58.
12. Rizzo C, Declich S, Bella A, Caporali MG, Lana S, Pompa MG, Vellucci L, Salmaso S. Enhanced Epidemiological Surveillance of Influenza A(H1N1)n in Italy. *Euro Surveill*.2009; 14(27):pii=19266.