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SHORT REPORT
The role of the intensive care unit in real-time surveillance of emerging pandemics: the Italian GiViTI experience

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SUMMARY

The prompt availability of reliable epidemiological information on emerging pandemics is crucial for public health policy-makers. Early in 2013, a possible new H1N1 epidemic notified by an intensive care unit (ICU) to GiViTI, the Italian ICU network, prompted the re-activation of the real-time monitoring system developed during the 2009–2010 pandemic. Based on data from 216 ICUs, we were able to detect and monitor an outbreak of severe H1N1 infection, and to compare the situation with previous years. The timely and correct assessment of the severity of an epidemic can be obtained by investigating ICU admissions, especially when historical comparisons can be made.

Key words: Infectious disease epidemiology, influenza, pandemic, surveillance system.

Ever since humans began to live in organized societies, epidemic infectious diseases have periodically threatened their health. On many occasions, these epidemics have been sufficiently severe to cause widespread death and illness. Despite substantial improvements in living conditions, epidemics remain a threat to human populations. In recent years, the term *pandemic* has been coined to refer to these situations, although the precise dependency of its definition from spread and severity of disease is still unclear and has been the object of controversy [1].

The 21st century has experienced two significant pandemic infectious disease threats: SARS in 2003 and H1N1 influenza in 2009. In the case of H1N1, the degree of spread and the potential for severe pneumonia were correctly recognized, but only when several countries had already been hit by the pandemic [2].

The World Health Organization (WHO) recognizes six pandemic phases to tailor the response actions, which are exclusively based on the amount of spread. Nonetheless, severity is at least as important as spread in defining the most appropriate countermeasures [3].

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† GiViTI, Gruppo Italiano per la Valutazione degli Interventi in Terapia Intensiva (Italian Group for the Evaluation of Interventions in Intensive Care Medicine) is an independent collaboration network of Italian intensive care units. Members of GiViTI are given in the Supplementary online Appendix.

Hence, the prompt availability of reliable epidemiological information on both these aspects is crucial to inform public authorities and enable early targeted actions.

The experience of H1N1 demonstrated how unreliable the estimates coming from prevalent influenza surveillance programmes can be. These programmes are based on patients who consult a physician on their own initiative, a phenomenon influenced by many factors, such as the level of population alarm. Estimated case-fatality ratios published during the emergency differed by more than 50-fold [4], leading to much confusion about how to respond to the pandemic.

Because intensive care unit (ICU) admission criteria are not subject to significant changes over time, and the number of cases and deaths are clearly identifiable, the question of pandemic spread and severity can be approached from the ICU perspective [4, 5]. The creation of an early warning system based on ICU admissions monitoring was one of the objectives of the International Forum for Acute Care Trialists (InFACT) [6], whose members include GiViTI, the Italian ICU network.

GiViTI is one of the first and largest ICU networks in the world. In 2013, 350 (63·6%) of the ~550 Italian units were adhering to the Margherita-PROSAFE project on continuous quality of care assessment [7]. Two hundred and thirty-six (67·4%) of these ICUs collected high-quality records on all admitted patients (about 87 000) that met the strict criteria adopted in the study [7]. Since data are immediately synchronized with the server at the coordinating centre, we were able to identify the ICUs registering patients in real time. They were arbitrarily defined as those that, at the time of analysis, were entering the patients into the software system with a maximum delay of 5 days from admission. Notably, as many centres do not see patients with epidemic disease, it is crucial to restrict the analysis to those registering data in real time in order to reliably estimate the population at risk.

Early in February 2013, a GiViTI ICU informed the coordinating centre about five new cases of severe H1N1 pneumonia. We therefore re-activated the real-time monitoring system for H1N1 infection which was developed during the 2009–2010 pandemic [4] and closed after almost no cases had been reported in the 2011–2012 season.

Patients with a suspected or proven H1N1 infection were eligible for inclusion in the registry. Those transferred from one ICU to another were identified and counted only once. Hospital mortality of transferred patients was assessed at the discharge from the last hospital in which they stayed.

The kernel density estimation approach was used to represent the evolution of the epidemic for the seasons 2009–2010, 2010–2011 and 2011–2012. This method allows the *a posteriori* estimation of the density of new cases over time, which corresponds to the number of H1N1 infections admitted to an ICU bed per day. A different approach was followed for the 2012–2013 season. Since the epidemic was still spreading at the time of the first analysis, a method that allowed prediction of future dynamics was used. In the case of single peak epidemics, such as H1N1 influenza, the natural sigmoid shape of the cumulative distribution can be well represented by the logistic function. We then plotted the cumulative frequency of H1N1 infected patients over time and fitted a logistic function, using the least-square method. Since the derivative of a cumulative function represents the density of the phenomenon under scrutiny, we derived the logistic function to obtain the disease density function. Notably, the logistic-based method and the kernel approach estimate the same density function, their results can consequently be compared to each other, once standardized to represent the number of patients with H1N1 influenza per 1000 ICU beds.

Survival curves were produced with the Kaplan–Meier method and regularly updated to monitor the severity and evolution of the outbreak. Informed consent was waived since the study was observational and no information was collected that could identify patients.

Following the notification of a possible new H1N1 epidemic, we were able to re-activate the former surveillance system in only 2 days. This was made possible by the adoption of an electronic case-report form which is centrally controlled by the coordinating centre. We systematically ran the aforementioned analysis on a weekly basis, monitoring the severity of H1N1 cases and their spread across Italian regions. Overall, 216 ICUs participating in the Margherita-PROSAFE project were identified as collecting data in real time and were considered for the analysis. They accounted for 1592 beds, corresponding to 40% of all ICU beds in Italy, and are representative of the 350 ICUs adhering to the GiViTI Margherita-PROSAFE project (see Table 1), which are in turn representative of the Italian situation.

Table 1. *Description of monitored and non-monitored ICUs*

	Margherita-PROSAFE ICUs	Monitored ICUs	Non-monitored ICUs	*P* value
N	350	216	134	–
Type, *n* (%)				0·77
General	263 (75·1)	166 (76·9)	97 (72·4)	
Cardiosurgical	30 (8·6)	18 (8·3)	12 (9·0)	
Surgical	15 (4·3)	9 (4·2)	6 (4·5)	
Neurosurgical	17 (4·9)	10 (4·6)	7 (5·2)	
Paediatric	11 (3·1)	7 (3·2)	4 (3·0)	
Other	14 (4·0)	6 (2·8)	8 (6·0)	
Size of the hospital, *n* (%)				0·19
<300 beds	160 (46·0)	92 (42·8)	68 (51·1)	
300–800 beds	130 (37·4)	82 (38·1)	48 (36·1)	
>800 beds	58 (16·7)	41 (19·1)	17 (12·8)	
Missing	2	1	1	
University affiliation, *n* (%)				0·94
Yes	91 (26·1)	56 (25·9)	35 (26·3)	
No	258 (73·9)	160 (74·1)	98 (73·7)	
Missing	1	0	1	
ICU beds				
Mean (S.D.)	7·4 (3·4)	7·4 (3·0)	7·5 (4·0)	
Median (Q1–Q3)	6·0 (5·0–9·0)	6·5 (5·0–8·3)	6·0 (5·0–9·0)	0·73
Missing	1	0	1	
Beds per nurse				
Mean (S.D.)	2·1 (0·5)	2·1 (0·5)	2·2 (0·6)	
Median (Q1–Q3)	2·0 (1·8–2·3)	2·0 (1·8–2·3)	2·0 (1·8–2·5)	0·40
Missing	4	1	3	
Beds per physician				
Mean (S.D.)	4·3 (1·8)	4·5 (1·9)	4·0 (1·6)	
Median (Q1–Q3)	4·0 (3·0–5·6)	4·4 (3·2–5·6)	4·0 (3·0–5·0)	0·039
Missing	5	0	5	

Based on these units, we detected and monitored in real time an outbreak of severe H1N1 infection. From 4 January to 8 April 2013, 57 cases of H1N1 were admitted to the participating ICUs. Median age was 52 years (interquartile range 42–60); 66·7% were males, while 16·7% of the 18 fertile women were pregnant. All patients but one had at least one organ failure (98·2%), and 61·4% had more than one, with a mean sequential organ failure assessment (SOFA) score [8] of 7·4 (S.D. = 3·5); 56 patients were ventilated, 11 non-invasively, and nine underwent extracorporeal membrane oxygenation. ICU and hospital mortality were 21·1% and 23·6%, respectively, similar to those observed in Italy during the 2009–2010 pandemic (17·1% and 20·2%, respectively) [4]. Demographic, clinical features, and outcome were very similar to those of the previous years. Other relevant studies conducted in different countries reported comparable rates. In Canada, ICU and hospital mortality in 2009–2010 were 16·7% and 17·3%, respectively [9], while in Australia/New Zealand hospital mortality was 16·9% [2].

The density function plots (Fig. 1) confirmed an outbreak of H1N1 in 2013, but of lesser extent than the first pandemic year (2009) or even the following season (2010–2011). The three final survival curves of the seasons with an epidemic outbreak (2009–2010, 2010–2011, 2012–2013) were very similar and not statistically different, suggesting that the severity of the disease was comparable among the seasons (data not shown).

Pandemics are a recurring threat to human populations and challenge national authorities to organize efficient preparedness plans and responses. Since the scientific community is unable to reliably predict the dynamics of a pandemic, a real-time surveillance programme, capable of providing accurate information about the spread and severity of an emerging outbreak, is vital to inform public health policy [3]. Three criteria are important: (1) data must be

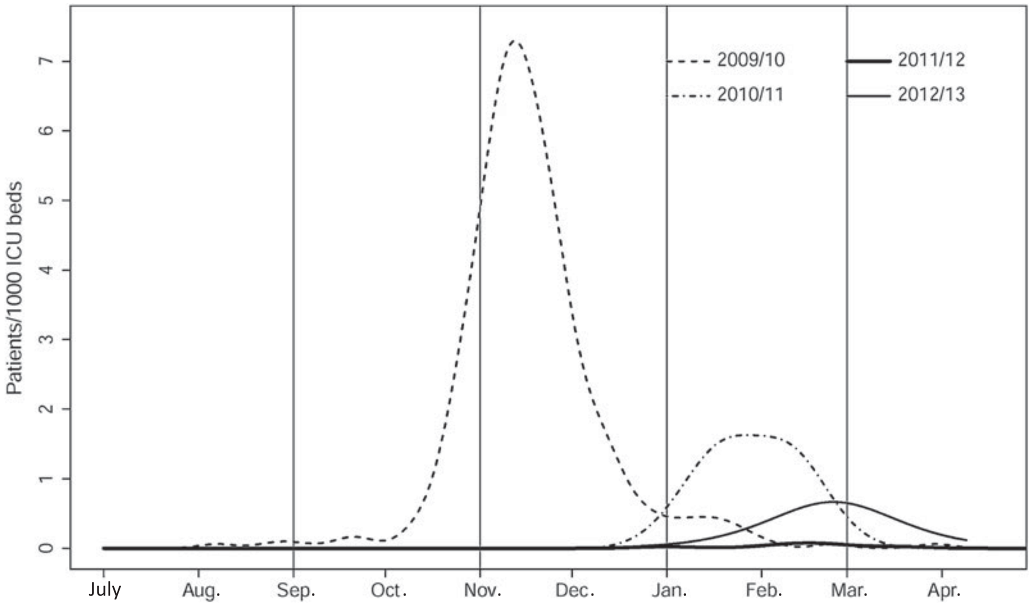

Fig. 1. Density functions plots comparing the incidence of H1N1 cases admitted to the ICU, during seasonal influenza epidemics from 2009 to 2013.

independent from fluctuating context-specific variables, such as the level of population alarm, or the emergency-related change in the healthcare organization; (2) surveillance must be capable of being started rapidly, even for unprecedented diseases; (3) results must be measurable against previous data. All these conditions can be met with the availability of a long-lasting ICU network that can count on a continuous data collection. Similar networks are available in many countries and should be coordinated [10], as strategic assets for pandemic preparedness.

In this framework, the GiViTI research system proved to be fully effective for the purpose of outbreak monitoring. The potential to promptly, and simultaneously, modify the electronic case-report form gives the system the flexibility necessary even for unprecedented epidemics, such as the H1N1 pandemic in 2009, depending on the availability of validated and shared diagnostic tests.

In this case, we were able to detect the outbreak of new severe cases of H1N1 in real time, and to assess the limited impact of the epidemic compared to the 2009–2010 and 2010–2011 seasons. We shared our data early with the Italian Ministry of Health. The Ministry regularly monitors seasonal influenza through a network of general practitioners and paediatricians (InfluNet, website http://www.iss.it/iflu). Their data showed a limited spread compared to 2009, which was in line with our projection based on the density function. Our estimate of mortality rate was also reassuring. Hence, we decided together not to alert the hospitals.

Our study indicates that, under particular circumstances, ICUs play a strategic public health role, being able to support the rapid detection of emerging severe diseases. Such a role should be fully exploited to improve the global preparedness capacity, as the recent Ebola epidemic once again demanded [11].

SUPPLEMENTARY MATERIAL

For supplementary material accompanying this paper visit http://dx.doi.org/10.1017/S0950268815001399.

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DECLARATION OF INTEREST

None.

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