Online monitoring of flu in Belgium

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Background The diagnosis and treatment of patients with the A(H1N1) pandemic flu caused some serious burden for general practitioners (GPs) in the summer and autumn of 2009.

Objective The aim of this study was to track the incidence of influenza and influenza-like illness (ILI) in Belgium and to describe the characteristics of the affected patients.

Methods In July 2009, the Belgian online influenza surveillance system (BOISS) was set up to monitor the spread of influenza and ILI. Registrations were made by 93 GPs from all 10 Belgian provinces who participated at least 1 week during the first 12 months of the registration. Only patients who met the WHO criteria for flu were recorded.

Results In total, 1254 patients (53% men) with influenza or ILI were included. Mainly younger persons were affected: 43% was

under the age of 20 years. A risk factor for influenza-related complications was determined in 19% of cases, mainly patients with chronic respiratory problems. A treatment with oseltamivir or zanamivir was prescribed in 13%, and 3% of the patients was admitted to a hospital. The time of the peak incidence (44th week) and the magnitude (623 cases per week per 100 000 inhabitants) corresponded with the figures of the existing paper-based registration network. The small sample size and possible reporting biases may have influenced the findings of the study.

Conclusions The BOISS provides a good alternative to conduct surveillance activities for influenza and ILI in Belgium. It provides complementary information regarding ILI compared to the existing data capturing.

Keywords A(H1N1), influenza, influenza-like illness, surveillance.

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Introduction

During spring 2009, influenza A(H1N1) was associated with a high morbidity and mortality rate in Mexico and the United States. During the summer, the virus spread to Europe.

Before the 14th of July, all cases of influenza A(H1N1) in Belgium were systematically recorded through mandatory reporting by all physicians. From the 14th of July, the incidence of A(H1N1) flu was no longer systematically reported for every case, but it was estimated from the recordings of a sentinel network consisting of almost 200 general practitioners (GPs) distributed evenly over the Belgian territory.¹ The evolution of the incidence of flu was monitored for the entire country by ways of estimations of the sentinel network, but the network did not permit to monitor the evolution on a regional basis or in local municipalities. Hence, the figures from the network were only available with a delay of 1 week.

The diagnosis and treatment of patients with the A(H1N1) pandemic flu caused some serious burden for

GPs because they are the first-line health care providers in the Belgian health care system. The government installed Local Health Hotline Centers (LHHC) to facilitate and coordinate care for patients with flu. However, these LHHC were established to be activated only if the local associations of GPs decided that they could no longer cope with the increased number of patients. Neither local associations of GPs nor the LHHC had an instrument to monitor the incidence of flu on a local basis. With this in mind, the Dutch- and French-speaking universities of Brussels (Vrije Universiteit Brussel and Université Libre de Bruxelles, respectively) developed an online registration system, permitting the GPs and LHHC to register all patients who sought help for influenza or influenza-like illness (ILI). In addition, the registration system offered the possibility to make analysis per practice, per municipality, per province, per region and for the entire country. The aim of this study was to track the incidence of ILI in Belgium in real time and to describe the characteristics of the affected patients.

Methods

In July 2009, the Belgian Online Influenza Surveillance System (BOISS) was set up to monitor the incidence of influenza and ILI in real time. Registrations were made by GPs or LHC as soon as possible through the online registration system. The GPs were recruited through an e-mail sent to the 200 GP-trainers from the Dutch- and French-speaking Universities of Brussels. These GP-trainers work in the teaching practices where medical students are being trained in family medicine. They are distributed over all provinces of the country, but are more concentrated in Brussels and its surrounding provinces. The e-mail provided a link to the website where they could enrol in the surveillance system by activating an account. The LHC were recruited with a similar e-mail sent to the local authorities. Only GPs or LHC who activated their account could register patients. A reminder email was sent after 2 weeks. In total, 93 GPs from all 10 Belgian provinces, whether coordinated from a LHC, reported data for at least 1 week between 15 July 2009 and 14 July 2010.

Inclusion criteria for patients

All patients with fever ($>38^{\circ}\text{C}$), and cough or shortness of breath, and general malaise were registered. Patients with seasonal influenza as well as those with A(H1N1) influenza were recorded. In view to help GPs to plan their workload, it was not important to differentiate between seasonal influenza and A(H1N1) influenza. The LHC were asked to avoid double registrations by double checking every registration with the participating GPs.

The registration included gender, age group, zip code, date of the first consultation, high-risk conditions for developing influenza-related clinical complications (Table 1), certainty of diagnosis (on a scale of 0–5), treat-

ment with oseltamivir or zanamivir, hospitalization and mortality. The certainty of the diagnosis was based on the symptoms and the clinical signs but the physicians were able to change the certainty of the diagnosis according to the evolution of the disease and the results of eventual diagnostic procedures.

Data capturing software and statistical methods

We opted for an online questionnaire in Dutch (<http://huis.vub.ac.be/griep>) and French (<http://huis.vub.ac.be/grippe>). Processing was carried out using the digital platform of the Faculty of Medicine and Pharmacy (MINF) of the Dutch-speaking University of Brussels. The data were gathered by means of a Personal home page Hypertext Pre-processor (PHP) program and immediately stored in a Structured Query Language (SQL) database. Several control measures ensured data quality and limited missing data. Every 2 weeks, participating GPs and LHC received a reminder e-mail up till the end of March 2010. Data cleaning and data analyses were performed using spss17.0 (SPSS Inc., Chicago, IL, USA).

Weekly incidences were calculated per 100 000 inhabitants. Belgian primary health care has no patient census list. As people are not registered with a particular GP or practice, it is difficult to determine the patient population of a particular GP. Weekly a nominator was calculated according to the number of participating GPs during that week. The nominator per participating GP was estimated by dividing the Belgian population (10 666 866) by the total number of GPs in Belgium (9259) resulting in 1152 patients per GP.

Privacy and ethical approval

Both the anonymous patient data and personal information of the participating GPs were treated with the utmost

	All patients (<i>n</i> = 1254) (%)	Treated with oseltamivir or zanamivir (<i>n</i> = 148) (%)	Hospitalized (<i>n</i> = 41) (%)
Chronic respiratory disease, including patients using drugs for asthma over the last 3 years	8.3	33.6	14.6
Chronic heart disease	1.7	8.6	2.4
Moderate to severe renal or hepatic insufficiency	0.3	1.3	0.0
Immunosuppression because of illness or treatment	1.0	6.6	7.3
Diabetes	1.7	9.9	4.9
Pregnancy	0.9	5.3	0.0
Elderly, aged > 65 years of age	3.1	12.5	9.8
Children younger than 5 years of age	4.8	13.8	22.0
Hospitalized with a other severe clinical picture	0.2	1.3	4.9
No risk factors	81.1	23.0	51.2

Table 1. Risk factors for influenza-related complications in patients with influenza or influenza-like illnesses

discretion. The online registration system did not permit to analyse data from individual patients or GPs. The GPs only had access to the data of their own patients. The study protocol was approved by the ethics committee of the University Hospital of Brussels.

Results

Incidence

In total, 1254 patients (53% men) with influenza or ILI were included. Mainly younger persons were affected: 43% was under the age of 20 years and only 6.2% was over 60 years (Figure 1).

The weekly incidence of influenza or ILI ranged between 116 and 221 cases per 100 000 inhabitants between the 29th week (mid July) and the 41st week (beginning of October) (Figure 2). From the 42nd week (mid October), the weekly incidence increased, and in the 44th week (end October), a peak incidence of 623 cases per 100 000 inhab-

Figure 1. Age distribution of patients with influenza or influenza-like illnesses ($n = 1254$).

itants was measured. From the 47th week (mid November), the weekly incidence decreased to about 150 cases per 100 000 inhabitants. During spring 2010, the online registration recorded several small peaks.

Risk factors and treatment

A risk factor for developing influenza-related complications was present in 19% of the cases with influenza or ILI, concerning mainly patients with chronic respiratory problems (8.3%), children under the age of 5 years (4.8%), elderly persons (3.1%), cardiac patients (1.7%), and patients with diabetes (1.7%) (Table 1).

A treatment with oseltamivir or zanamivir was prescribed in 13% of the patients. The treated patients had no risk factors in 23% of cases, and the most common risk factors among treated patients were chronic respiratory problems (34%), children under the age of 5 years (14%), elderly persons (13%), patients with diabetes (10%), and cardiac patients (9%).

Hospitalizations and mortality

Three percent of the patients were admitted to a hospital, and 51% of them had no risk factors for developing complications of influenza. The most common risk factors among hospitalized patients were age under 5 years (22%), chronic respiratory problems (15%), and age over 65 years (10%).

Two patients died, resulting in a case-fatality ratio of 0.16%. Both died in the 44th week of the year. The first patient was aged between 30 and 39 years and had a chronic respiratory problem and diabetes. The second patient was aged between 70 and 79 years and also suffered from a chronic respiratory illness.

Figure 2. Weekly incidence of flu and influenza-like illness per 100 000 inhabitants in Belgium for the Belgian online influenza surveillance system online registration and the registration by the National Institute of Public Health (IPH).¹

Discussion

BOISS is an online influenza surveillance network that was developed to provide health care professionals and consumers with the most up-to-date information on the incidence of the pandemic flu. The cases were recruited by a network of GPs covering all Belgian provinces. The diagnosis of flu was mainly based on symptoms and clinical signs. A regional as well as a national overview on influenza activity was generated. The study demonstrates the utility of Information and Communication Technologies and indicates certain possibilities for their application in epidemiological surveillance. It shows that it is possible, in a simple way, to generate information about the response of the health care system to a new problem, in this case, the incidence of pandemic flu, the prescription of antiviral agents, and hospital admission.

Our study showed that A(H1N1) flu was predominantly present in older children and young adults, with almost no cases reported in patients older than 60 years. These findings are in line with a previous report of Rothberg and Hassler.² Most complications occurred among previously healthy individuals. Respiratory disease was the most frequent risk factor resulting in flu-complications. It has been shown that data from deputizing medical services can provide low cost and timely ILI surveillance.

Representativeness of the data

Only 93 GPs returned data from a total of over 9000 GPs working in Belgium. This low participation rate may rise some questions about the representativeness of the data. On the other hand, almost 50% of the 200 invited GPs participated in the research. Not all GPs recorded cases in all weeks. For that reason, a weekly nominator was calculated according to the number of participating GPs during that week. With this technique, representativeness of the data was guaranteed.

The reliability of our results for the Belgian territory can be derived from the similarity with the results of the existing sentinel network (Figure 2).¹ Based on visual comparison of both data series, the time of the peak incidence and the magnitude of the BOISS correspond with the figures of the sentinel registration network (797 cases per 100 000 inhabitants in the 44th week). The incidence of ILI before and after the flu peak was estimated slightly lower by the paper-based registration of the sentinel network compared to the BOISS. During the flu peak, the incidence was estimated slightly lower by the BOISS. During spring 2010, the BOISS recorded several small peaks which were not detected by the paper-based sentinel network. These non-significant differences can be explained by the fact that the GPs participating in the BOISS were not taken into account for the weekly incidence when they

did not record patients. In the paper-based registrations, the GPs were included in the weekly incidence, even if they did not record any patients. This inaccuracy of the BOISS should be resolved in future implementations of the system.

Because no cases were reported since mid March 2010, the reminder e-mails were no longer sent from April on. This is probably the reason why the incidence of ILI as detected by BOISS has decreased to zero since April.

The findings from the BOISS are consistent with previous reports: in New Zealand, data from existing surveillance systems were compared with other surveillance systems such as the online Google Flu Trends.³ The patterns of the online surveillance were closely aligned with the national surveillance systems for ILI. The real-time surveillance systems provided useful information complementary to existing surveillance systems. Similar findings were reported in Australia, where data captured by the three separate surveillance systems provided complementary information regarding influenza.⁴ In addition, a study by Coory *et al.* showed that ILI reported from sentinel general practices were in accordance with corresponding weekly percentages reported from a deputizing medical service. The latter did not use a standardized definition of ILI and no laboratory confirmation of suspected cases.⁵

Outside Mexico, A(H1N1) flu presented as a mild disease in most cases. However, it is crucial that a rapid, effective surveillance can monitor the disease, while the severity of the A(H1N1) virus remains unknown.⁶

The representativeness of the results per municipalities depends mainly on the participation of the local GPs. Accurate figures for a municipality can be obtained only if a majority of the local GPs participate in the registration. The LHHC were set up to coordinate the registration and care for influenza patients. However, the LHHC were activated in only a few cities and municipalities.

GPs play an important role in the management of seasonal flu. Unfortunately, the role of GPs has been made very difficult by time-consuming administrative burdens and a lack of clear communication about policy changes as the situation progressed. The same management problems occurred in other countries.⁷

There might be some discussion about the representativeness of our hospitalizations and case-fatality data. Because of the small sample of participating GPs, the case-fatality figures might not be accurate. The two fatal cases were reported in an attempt to provide the most complete information rather than to give the most accurate case-fatality figures. On the other hand, our incidence figures were not hampered by patients attending the hospital emergency services without first attending their GP. Patients were informed by the Interministerial Influenza Coordination Committee to attend their GP and not an

emergency service with flu symptoms. In this context, the rates of hospital admissions are likely to be reliable.

Comparison with the paper-based network

Participation by GPs is voluntary in both networks, based on their age, sex, and geographical distribution. The 200 GPs in the paper-based network can be considered to be representative for the profile of GPs in Belgium. The GPs participating in the BOISS network are distributed over all ten Belgian provinces. Unfortunately, no other detailed information about their representativeness is available.

The paper-based network covers about 2% of the Belgian population. The BOISS covers only 1%, but this is still a fair number. For both networks, the registration is continuous: for the paper-based network by means of weekly forms and for the BOISS by means of an internet-based registration. On the forms of the paper-based network age and sex of the patients, complaints and clinical signs are recorded. The forms are sent to the central study manager, together with four secretion samples from nose and throat.

Compared to the existing Belgian paper-based sentinel registration network, the BOISS network has the advantage that it provides data in real time, whereas the paper-based sentinel registration provides data with 1 or 2 weeks delay. The availability of influenza data in real time offers the policy makers the possibility for a timely adaptation of their influenza strategy. The only delay for the BOISS network is caused by the interval between the contact with the patient and the online registration by the GP. Delays in the paper-based registration are caused by untimely posting and packaging by the GPs, slow despatching by postal services and time needed for virologic testing. Thereupon, the reports are only released once a week. This delay in reporting could be improved by direct data extraction from the Electronic Patient Records, but even with these advanced surveillance systems, some delay can occur, for example when patient records are not updated timely or even worse not completed, leading to missing data. However, this could be solved by a software-assisted data introduction in patient records obliging physicians to complete a minimum data set, defined for a specific surveillance program.

For both networks, not all GPs participate every week. Therefore, the incidence of flu is calculated on a weekly basis, taking into account the denominator of the particular week. This denominator is based on the number of participating GPs in the particular week.

Anonymity of the patients is always preserved in both networks. The paper-based network records several other infectious and non-infectious health problems. The paper-based network represents Belgium in the European Influenza surveillance system (EuroFlu) which is coordinated by

the European Centre for Disease Prevention and Control influenza program. The BOISS is designed for the data capture of flu and ILI data exclusively.

Treatment

A systematic review revealed that oseltamivir and zanamivir were effective in reducing symptom duration in patients with laboratory-confirmed influenza.⁸ However, the effect sizes were small and often unlikely to be clinically significant. Only for the patients at-risk, oseltamivir and zanamivir were generally more clinically efficient than in healthy adults. Anyhow, the efficacy of antiviral drug in ILI remains doubtful.⁹

In Belgium, GPs provided free oseltamivir and zanamivir for patients with one or more of the risk factors in Table 1. In the United Kingdom, the management of the A(H1N1) flu was rather controversial. The UK government advised to issue anti-virals to persons of all ages with ILI symptoms. This advice is contrary to the World Health Organisation advice.¹⁰

Although clear recommendations about the treatment with oseltamivir and zanamivir were available, the GPs often did not treat their at-risk patients: only 13% of all cases were treated, whereas 19% was at-risk and 23% of the treated cases had no risk factor.

Hospitalization and mortality

The case-fatality ratio from our study is within the figures of previous studies. A Mexican study showed an overall fatality of 2.2% (0.3% for the 10- to 19-year-old group and 6.3% for the 50- to 59-year-old group).¹¹ Forty-three percent of deaths were concentrated in only two of the 32 Mexican states, and 51% received medical attention in social security institutions. Only 17% of the deaths received hospital attention within 72 hours, and 42% died within 72 hours of hospital attention. Luckily, the pandemic flu was less severe in other countries. A study in Milwaukee among symptomatic patients estimated a case-fatality ratio of 0.048%, while 0.24% of the symptomatic patients required admission in an intensive care unit (ICU), and 1.4% required hospitalization. Hospitalization rate appeared to be lowest in persons aged 5–17 years.¹² Another study estimated that among patients with laboratory-confirmed A(H1N1), the risk of hospital admission was 4.5% and the case-fatality rate was 0.3%.¹³ The case-fatality ratio from our study is within the figures of the previous studies. In comparison with these studies, however, we should emphasize that our results are based on only two fatal cases.

The hospitalization rate in our study also ranges within the limits of most international studies. In Canada, the risk of hospital admission was highest among patients <1 year old and those 65 years or older. Adults more than 50 years

old accounted for 7% of all cases, but for 70% of deaths.¹³ In Saudi Arabia, the mean age of patients hospitalized with flu was 25 years with a predominance of male patients (71%).¹⁴ In Ireland, hospitalization rates for confirmed A(H1N1) influenza were highest in the age group of 15–19 year olds and lowest in those aged 65 years and over.¹⁵ Nine percent of the hospitalized cases were admitted to ICUs and 2% died. Fifty-one percent of hospitalized cases and 42% of ICU cases were not in a recognized risk group. Asthma was the most common risk factor among these cases.

Limitations of the study

The small sample size and possible reporting biases may have influenced the findings of the study. Although the feasibility of the registration to provide nationwide data has been proved, the present study did not allow local analysis of cases and trends. The small number of registrations would have lead to serious difficulties with confidence limits on any local data.

Conclusion

The BOISS provides a good alternative to conduct surveillance activities for influenza and ILI in Belgium. The fast availability of information about flu incidence could offer an added value to assist national policy makers in treatment decisions and provide information for preventive immunization programs. The BOISS provides complementary information regarding ILI compared to the existing data capturing. The complementary information includes risk factors, treatment, and hospitalization. Based on the data captured by the BOISS system, the pandemic A(H1N1) flu peaked around the 44th week (end October) to return within a few weeks to a normal, non-epidemic level.

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Conflict of Interest

None of the authors have a conflict of interest, including ownership of shares, consultancy, speaker's honoraria, or research grants from commercial companies or professional or governmental organizations with an interest in the topic of the paper.

Ethical approval

The study protocol was approved by the ethical committee of the University Hospital of Brussels.

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