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### Surveillance and outbreak reports

#### **SURVEILLANCE OF HOSPITALISATIONS FOR 2009 PANDEMIC INFLUENZA A(H1N1) IN THE NETHERLANDS, 5 JUNE – 31 DECEMBER 2009**

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**We analysed and reported on a weekly basis clinical and epidemiological characteristics of patients hospitalised in the Netherlands for the 2009 pandemic influenza A(H1N1) using information from the national mandatory notification system. The notification criteria changed on 15 August 2009 from all possible, probable and confirmed cases to only laboratory-confirmed pandemic influenza hospitalisations and deaths. In the period of comprehensive case-based surveillance (until 15 August), 2% (35/1,622) of the patients with pandemic influenza were hospitalised. From 5 June to 31 December 2009, a total of 2,181 patients were hospitalised. Of these, 10% (219/2,181) were admitted to an intensive care unit (ICU) and 53 died. Among non-ICU hospitalised patients, 56% (961/1,722) had an underlying medical condition compared with 70% (147/211) of the patients in ICU and 46 of the 51 fatal cases for whom this information was reported. Most common complications were dehydration among non-ICU hospitalised patients and acute respiratory distress syndrome among patients in ICU and patients who died. Children under the age of five years had the highest age-specific hospitalisation rate (62.7/100,000), but relatively few were admitted to an ICU (1.7/100,000). Characteristics and admission rates of hospitalised patients were comparable with reports from other countries and previous influenza seasons. The national notification system was well suited to provide weekly updates of relevant monitoring information on the severity of the pandemic for professionals, decision makers, the media and the public, and could be rapidly adapted to changing information requirements.**

### Introduction

On 30 April 2009, the first case of human infection with the 2009 pandemic influenza A(H1N1) was reported in the Netherlands, and on 5 June 2009 the first patient was hospitalised [1]. From 15 August 2009, only patients with a laboratory-confirmed pandemic influenza infection who were hospitalised and/or died because of the severity of their illness were notifiable. This was in line with international consensus that registration of all cases of pandemic influenza A (H1N1) is not efficient anymore when there is widespread community transmission and that surveillance efforts should focus on severe disease to enable mitigating the impact of the pandemic [2-3]. The World Health Organization (WHO) suggested surveillance of severe acute respiratory illness (SARI) in a number of sentinel hospitals, with a case definition of sudden onset of fever (>38°C) and cough or sore throat in the absence of other diagnoses, shortness of breath or breathing difficulty, and requiring hospital admission [4]. As it was not a realistic option to establish and validate such a novel surveillance system in the Netherlands in a very short time, it was decided to modify the nationwide mandatory notification system and limit this system to hospital admissions and/or deaths due to laboratory-confirmed pandemic

notification system and limit the system to hospital admissions and/or deaths due to laboratory-confirmed pandemic influenza virus infection. Reports from the southern hemisphere give important information on the impact of the first wave of the pandemic. However, such data cannot be transferred directly to Europe because of the differences in population composition, health systems, notification systems, climate and the prevalence of other infectious diseases that can all affect the spread and impact of an epidemic.

In this report, we analyse the clinical and epidemiological characteristics of the first patients hospitalised and deceased in the Netherlands with a confirmed 2009 pandemic influenza A(H1N1) virus infection and we discuss the mandatory notification system for all hospital admissions.

## Methods

### **Notification system**

From 30 April to 14 August 2009 all possible, probable and confirmed cases of 2009 pandemic influenza A(H1N1) were notifiable. On 15 August, the notification criteria changed, and from that date only cases who were admitted to hospital or died because of the severity of a laboratory-confirmed pandemic influenza virus infection had to be notified. Within a few days a new questionnaire was developed, which had to be as short as possible in order not to overburden the municipal health services and physicians. In the Netherlands, the attending medical doctor and the head of the involved microbiology laboratory both have to report the name and clinical characteristics of the hospitalised patient to the municipal health service. Notifications are entered by the municipal health services into a national anonymous and password-protected web-based database, including information on underlying medical conditions (co-morbidity), vaccination status, treatments, complications such as pneumonia, and admission to an intensive care unit (ICU).

### **Laboratory confirmation**

In the Netherlands, initially the National Influenza Centre (NIC, consisting of the National Institute for Public Health and the Environment (RIVM), Bilthoven and the Erasmus Medical Centre, Rotterdam) and later the 11 laboratories of the Outbreak Assistance Laboratories Network tested nose and throat samples for pandemic influenza A(H1N1) virus [5]. When the pandemic was evolving, additional peripheral and hospital laboratories also performed diagnosis of pandemic influenza using molecular diagnostic tests made available by the NIC in conjunction with an external quality assurance programme. The Centre for Infectious Disease Control at RIVM acted as central confirmation laboratory.

For diagnostics, real-time RT-PCR assays for general detection of influenza virus type A and specific detection of pandemic influenza A(H1N1) virus were used with a confirmation by sequencing [5].

### **Dissemination**

Weekly reports summarising new and cumulative numbers of hospitalisations by age and by underlying conditions were prepared for discussion by the multidisciplinary response team of RIVM. In these reports, notification data were linked to data from the sentinel surveillance of influenza-like illness (ILI), crude mortality registers, and virological surveillance. Implications were discussed with decision makers at the Ministry of Health following these weekly meetings. Results were disseminated online every week, followed by a press briefing.

### **Data analysis**

We calculated descriptive statistics for all study variables. For categorical variables percentages were reported and for continuous variables the median (with range). Only laboratory-confirmed cases were included in the analysis. We categorised patients according to age groups. All descriptive statistics were calculated for non-ICU hospitalised patients, patients admitted to an ICU and deceased patients. All statistical analyses were conducted using SAS version 9.1 (SAS Institute).

## Results

### **Clinical characteristics**

From 5 June to 14 August 2009, the period before the notification criteria changed, 2.2% (35/1,622) of the notified patients with a confirmed pandemic influenza infection were admitted to a hospital [1]. From 5 June to 31 December 2009, a total of 2,181 patients were hospitalised for severe laboratory-confirmed infection with pandemic influenza. Of these, 10.0% (219/2,181) were admitted to an ICU. In the same period, a total of 53 patients died due to laboratory-confirmed infection with pandemic influenza, five of whom died without hospital admission.

### **Epidemiological characteristics**

The median age of non-ICU hospitalised patients was 17 years (range 0-89 years). For patients admitted to an ICU the median age was 42 years (range 0-82 years), and for patients who died the median age was 52 years (range 0-85 years)

(Table 1). Incidence of non-ICU hospitalisations peaked in the group of 0-4 year-olds and thereafter declined with age. Incidence of ICU admissions and deaths, however, showed a second peak in the group of 55-64 year-olds (Table 2). The highest incidence for ICU admission overall was observed in patients aged between 55 and 64 years (2.06 per 100,000 population), whereas the highest incidence for non-ICU hospitalisation was among children under the age of five years (62.7 per 100,000 population).

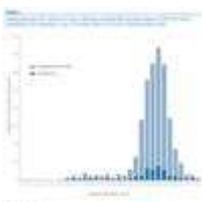
Of the non-ICU hospitalised patients 29.5% (508/1,722) had pneumonia, while among the patients who were admitted to an ICU, 74.3% (153/206) had pneumonia and 63.3% (126/199) needed mechanical ventilation. Pneumonia was reported for 31 of 46 fatal cases for whom this information was available and 21 of 49 patients who died had received mechanical ventilation.

**Table 1.** Characteristics of patients hospitalised for 2009 pandemic influenza A(H1N1), the Netherlands, 5 June–31 December 2009 (n=2,186)

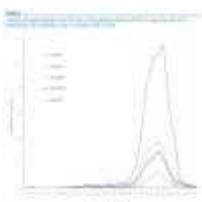
**Table 2.** Cumulative incidence for hospitalisation, admission to an ICU and deaths due to 2009 pandemic influenza A (H1N1) per 100,000 population by age group, the Netherlands, 5 June–31 December 2009 (n=2,186)

From week 40 to week 46 2009, we observed an exponential rise in the number and incidence of hospital admissions (non-ICU) and ICU admissions due to pandemic influenza (Figures 1-3), but this did not give rise to changes in the distribution of age groups among hospitalised patients. After week 46, the number and incidence of non-ICU hospitalisations and ICU admissions for pandemic influenza by week decreased. There was only limited geographical variation in the incidence of hospital admissions (ICU and non-ICU) due to pandemic influenza by municipal health service region in the Netherlands (Figure 4).

**Figure 1.** Hospital admissions (ICU and non-ICU) due to laboratory confirmed 2009 pandemic influenza A(H1N1) by week of hospitalisation, the Netherlands, 5 June–31 December 2009 (n=2,034 with a reported admission date)



**Figure 2.** Incidence of hospital admissions (non-ICU) due to 2009 pandemic influenza A(H1N1) by age group and week of hospitalisation, the Netherlands, 5 June–31 December 2009 (n=1,962)





The data reported in this paper are based entirely on the routine national infectious disease notification system. This system made it possible to provide weekly updates of relevant pandemic monitoring information on severe pandemic influenza for dissemination to professionals, decision makers, the media, and the public. Changes in the web-based notification system were communicated by the Centre for Infectious Disease Control and implemented rapidly by municipal health services, physicians and heads of medical microbiology laboratories. Nevertheless, a nation-wide mandatory notification system puts restrictions on the amount of information that can be requested from hospital and public health physicians. Therefore, it was not possible to provide information on the reason for hospital admission, other than that it was for laboratory-confirmed pandemic influenza. Also, follow-up of patients by the municipal health service, for example to obtain information on date of discharge from the hospital, was not considered feasible.

The highest age-specific rates of hospital admission were seen in the age group of 0-25 year-olds. In absolute numbers and in incidence, most admissions occurred in the age group of the 0-4 year-olds, but only 3% (16/581) of them were admitted to an ICU. Of the admitted patients older than 45 years, 18% (105/580) were admitted to an ICU. Infants might have been admitted to hospital for observation even in the absence of signs of respiratory distress or other complications, or for supervised oseltamivir therapy, although personal communications from a number of paediatricians suggested that the majority of small children admitted with laboratory-confirmed pandemic influenza were admitted because of serious illness.

The observed hospitalisation, ICU and mortality rates are compatible with data reported from other countries [6-10]. Hospitalisation rates from countries in the southern hemisphere ranged (by country) from 2.0 to 31.8 per 100,000 population, and mortality rates ranged from 0 to 3.6 per 100,000 population [8]. In the Netherlands, hospitalisation rates due to pandemic influenza by age group ranged from 2.8 to 62.7 (overall 13.1) per 100,000 population and mortality rates ranged from 0.05 to 0.61 (overall 0.32) per 100,000 population. High rates of hospitalisation in the age group of 0-4 year-olds were also reported for Queensland and New South Wales (Australia), Ireland and other European countries [6-7,10-11]. While in seasonal influenza epidemics, the highest incidence of severe morbidity and deaths is expected in the oldest age groups, we observed the declining incidence in ICU admissions and deaths in patients older than 65 years following a peak in the age group of 55-64 year-olds, which could be compatible with a reported protection of those exposed to influenza A(H1N1) before 1957.

The majority of severe cases were people with pre-existing underlying medical conditions: 55.8% (961/1,722) of the hospitalised patients, 69.7% (147/211) of the cases admitted to ICU, and 46 of the 51 deceased patients. Asthma was the most common underlying condition, followed by other chronic lung disease and cardiovascular disease. This is in line with reports from other countries [6-7,11]. However, compared with other countries, obesity was reported for very few hospitalised patients and was not a risk factor in the Netherlands. However, no systematic data was collected on length and weight of the hospitalised patients not reported to be obese, which may have resulted in underreporting as obesity is likely to have been a subjective assessment of the attending physician.

A further limitation of this study is the fact that the Dutch notification system does not provide specific data on SARI. The reported cases include patients admitted for severe influenza illness with other complications than respiratory distress. Therefore, the Dutch SARI cases that are reported to the WHO and the European Centre for Disease Prevention and Control (ECDC) are laboratory-confirmed pandemic influenza cases, in contrast to some other countries that report all clinical SARI cases. Also, we could not determine why no complications were reported for 65 of 188 patients who were admitted to an ICU. It is possible that the attending physicians did not consider ARDS as a specific complication or that patients with respiratory distress did not fulfil all the diagnostic criteria for ARDS.

Comparison of the severity of the current epidemic with previous influenza seasons can not be based on direct analyses of hospital-based surveillance data, as there are no reliable historical records of hospital admissions and deaths related to laboratory-confirmed influenza, but will need to rely on the ongoing ILI sentinel surveillance among general practitioners (GPs). We recently related this GP ILI surveillance to retrospective respiratory hospitalisation rates over the years 1999 to 2005 [12-14]. So far, the admission rates in 2009 seem similar to the estimates over the period 1999-2005, although the admission rates for children and adults seem among the highest rates compared with the 1999-2005 influenza seasons, whereas the admission rates for the elderly ( $\geq 65$  years of age) seem among the moderate or lowest rates compared with 1999-2005. Analyses as in [13] on trends in ILI GP consultations by age or in [14] on hospitalisations and mortality for respiratory diseases versus ILI GP consultations including 2009, could allow comparing the severity of the current epidemic with previous influenza seasons. A surveillance system with real-time availability of SARI cases would have made such analyses possible during the ongoing epidemic, but only if data on SARI cases (or similar clinical diagnosis) had also been available for earlier seasons, which is not the case in the Netherlands.

In conclusion, the national notification system was well suited and could rapidly be adapted to changing information requirements, although a national notification system puts restrictions on the amount of information that can be requested. While we could not confirm an association with obesity, other reported characteristics of hospitalised patients with confirmed pandemic influenza in the Netherlands were in line with those reported by other countries, including countries in the southern hemisphere. This report is based on the 2009 phase of the pandemic in the Netherlands. Numbers, distribution by age group and characteristics could still change when the pandemic develops further, thus continued surveillance and vigilance is essential.

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