Influenza in Sweden

Season 2010-2011
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Preface

Each winter, influenza epidemics of different magnitudes occur. Depending on the characteristics of the circulating viruses and the immunity towards them in different age groups, people and society are affected in different ways. If the elderly are affected, many get severely ill, leading to a great strain on hospitals and excess mortality. Small children may also need hospital care but deaths are rare. Slightly older children handle influenza infection fairly well but extensive care of a sick child may lead to substantial absence from the work place for the parents. If a new strain of influenza was to emerge and create a pandemic it could lead to such an extensive absence of the working population that it would constitute a threat to important public functions. Some influenza strains can be very aggressive and cause severe illness, leading to great strain on intensive care units as well as deaths in all age groups. None of these consequences are detectable through a single reporting system. In order to get an overall picture of on-going influenza activity, Smittskyddsinstitutet (SMI) has established a number of different epidemiological reporting systems for influenza, from direct reporting by people who are ill to the collection of data from different healthcare providers and the web. In order to assess immunity to an expected virus in different age groups, SMI conducts yearly studies of influenza-specific antibodies in blood samples.

Virological surveillance is at least as important as epidemiological surveillance. When new strains of virus emerge, reference methods for diagnostics are established at SMI. Viruses from around the country are characterized with regard to vaccine resemblance, sensitivity to antivirals and other factors that may affect the severity of the infection they cause.

This report describes the monitoring systems in use during the winter season 2010-2011 and the results of both epidemiological and virological surveillance. Data are analyzed in relation to data from earlier influenza seasons and the measures taken to limit the consequences of the epidemic. Some international data are also included.

Annual influenza reports in English have been available since 2000, and may be found on SMI’s website.¹ For the first time, this report is also available in Swedish.

¹ http://www.smittskyddsinstitutet.se/publikationer/arsrapporter-och-verksamhetsberättelser/smis-arsrapporter-om-influenzasasonen/
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Summary

The first post-pandemic season 2010-11 was intense and protracted, with three circulating influenza viruses. The two dominating types of viruses, influenza A(H1N1)pdm09 and influenza B, mainly affected children and young people, and there was no obvious excess mortality among the elderly population. The extensive influenza B epidemic, which also struck the rest of Europe, was unexpected and unusual. A few young patients with influenza B suffered severe pneumonia, requiring intensive care, and one death occurred.

A total of 3689 laboratory-confirmed diagnoses of influenza were reported during the season. Of these, 1,129 cases were influenza A(H1N1)09, 1,866 were influenza B and 694 were seasonal influenza A. The highest incidence of A(H1N1)pdm09 was, as in 2009, found in children between the ages of 0 and 4. However, unlike 2009, the incidence among school children was low. Some of the youngest children were either not yet born or too young to be vaccinated during the pandemic in 2009, and therefore completely lacked protection for the 2010-11 season. Otherwise, the 2009 pandemic vaccination had a surprisingly good protective effect of between 70 and 80% during 2010-11.

In total, 401 (35%) of the reported cases received health care and 63 (5.5%) required intensive care. These were higher percentages than those recorded during the pandemic. At least 63 persons were taken into intensive care due to influenza A(H1N1)pdm09, and at least 10 deaths occurred. This constituted a significantly lower incidence of severe illness than in other countries (such as England and Denmark) that did not vaccinate as many persons as Sweden did during the pandemic year. However, as feared, there was still a relatively severe second “pandemic wave” during the 2010-11 season.

Most strains of influenza that were characterised at SMI bore resemblance to vaccine and no extensive resistance to the type of antiviral recommended in Sweden was found.

Vaccination of medical risk-groups for severe influenza was reported to be lower than during the pre-pandemic seasons, but there are no exact national figures.
Monitoring and reporting systems

The influenza pyramid (Diagram 1) below illustrates the different ways that influenza affects those who are infected. A portion of infected people do not get any symptoms, while others get sick but simply stay home or continue with their daily activities. Of these, a portion actively seek healthcare, and a portion of these are so ill that they are hospitalised. Finally, some of the ill require intensive care, and a small portion die as a result of influenza infection.

Diagram 1. Influenza pyramid

Diagram 1 describes the data collection systems we have used to monitor the activity from the base of the pyramid to the top.
<table>
<thead>
<tr>
<th>Reporting system/method</th>
<th>Implementation</th>
<th>What does the system/method show?</th>
<th>Number/percentage reported during the season</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Statutory Laboratory Reporting of Cases of Influenza A(H1N1)pdm09</td>
<td>All laboratories have to report influenza diagnoses along with identity in the web-based reporting system, SmiNet, as soon as possible, in accordance with the Communicable Diseases Act</td>
<td>The number of laboratory-confirmed cases of influenza A(H1N1)pdm09</td>
<td>1,129 cases</td>
</tr>
<tr>
<td>2. Statutory Clinical Reporting, all Hospitalised Cases of A(H1N1)pdm09</td>
<td>Cases treated in hospital have to be clinically reported. Risk group, vaccination status and level of care are requested but the information is voluntary.</td>
<td>All cases that are treated in hospital (along with symptoms, risk group, vaccination status and level of care, though information is incomplete)</td>
<td>401/1,129 (35%) of all laboratory-confirmed cases were reported clinically</td>
</tr>
<tr>
<td>3. Intensive Care Data for A(H1N1)pdm09 week 40/2010 - week 20/2011</td>
<td>Voluntary supplement to the statutory reporting form</td>
<td>Severity of the disease based on level of care (intensive care, respirator, ECMO).</td>
<td>63 out of the 401 patients (16%) treated in hospital were reported in intensive care</td>
</tr>
<tr>
<td>4. Aggregate laboratory reporting and denominator data week 40/2010 - week 20/2011</td>
<td>Weekly reports from the laboratories to SMI on the number of samples that have been analyzed for influenza and the proportion of positive samples.</td>
<td>Number of positive samples and denominator data for calculating the proportion of influenza-like illness caused by influenza virus.</td>
<td>18,442 analyzed samples of which 3,689 (20%) tested positive; 1,129 for A(H1N1)pdm09, for 694 seasonal influenza A and 1866 for influenza B.</td>
</tr>
<tr>
<td>5. Deaths. Duty to Report /Record Search, A(H1N1)pdm09</td>
<td>Duty to report for pathologists – coordination of cases reported in accordance with the Communicable Diseases Act with influenza and death records. Local analysis of influenza as the cause of death</td>
<td>The number of deceased</td>
<td>10 deceased identified (A(H1N1)pdm09)</td>
</tr>
<tr>
<td>6. Sentinel Surveillance week 40/2010 - week 20/2011</td>
<td>Selected general practitioners and primary care offices report the number of patients each week and the proportion of these experiencing influenza-like symptoms. Approximate catchment population is reported in the beginning of the season.</td>
<td>The proportion of patients in outpatient care that have influenza-like symptoms and the proportion of the catchment population with influenza-like symptoms. The latter shall be reported weekly to the ECDC</td>
<td>762/197 650 (0.4%) persons seeking care from a GP at a sentinel unit and 762/396 161 (0.1%) of persons listed with the reporting physician gave influenza-like symptoms (ILS).</td>
</tr>
<tr>
<td>7. Sentinel Sampling week 40/2010 - week 20/2011</td>
<td>Samples are taken from some of the ILS patients seen through the sentinel surveillance system and analyzed by SMI for influenza</td>
<td>The proportion of sentinel patients with influenza</td>
<td>1161 samples analyzed of which 299 (25.8%) tested positive for influenza</td>
</tr>
</tbody>
</table>
8. Virus Characterization
Continual collection and characterization of samples positive for influenza from various laboratories and positive sentinel samples. Characterization through genotypic assays
Viruses’ vaccine resemblance and possible resistance to antivirals
114 strains were characterized with respect to vaccine resemblance and 106 with respect to antiviral resistance. All strains resembled the vaccine and no strain was resistant to the approved antivirals

A population-based, cohort study in Stockholm where the participants report via telephone or web should they contract a respiratory infection. Their symptoms determine whether they have influenza-like illness (ILI) or other type of acute respiratory infection (ARI). Approximately 2,700 participants 2010-11. The number of participants with ILI, corrected with the proportion of sentinel samples positive for influenza in the sentinel sampling each week, gives a rough estimate of how many have been ill with influenza.
Provides an estimated number of people ill with ARI and ILI as well as a rough estimate of how many of these have influenza.
Number with ARI: 1,859.
Number with ILI: 658
Average number of ill/week 38-20: 1.98 %
ARI, 0.70 % ILI

10. "Webbsök" (Web Search)
An automated system that uses search data from the medical site Vårdguiden.se. The number of searches on influenza and influenza symptoms are entered into a statistical model which estimates the proportion of patients with ILI
Works as a complement to sentinel reporting.
Between week 27/2010 and week 26/2011, almost 17,000 searches including the word influenza were conducted.

11. Sero-epidemiology
Serologic analysis regarding influenza A(H1N1)pdm2009 using haemagglutination inhibition was performed on a representative sample of the population from 2007, October 2009 and May 2010.
Proportion by age group with antibodies that bind to receptor structure H of the pandemic influenza virus as a result of infection or vaccination, as well as the change in this proportion since 2007.
Over 50% of the population sampled in June 2010 had antibodies. – The proportion was highest (76%) among children (3-14 years old) and lowest (26%) among those aged >65.

12. Vaccination Coverage
Report from the County Medical Officers of Communicable Disease Control (Smittskyddsläkarna) – on the proportion of seasonally vaccinated persons over the age of 65 in each county. Different methods of calculation in different counties and the data are not fully comparable or reliable
An estimate of the proportion of those over 65 years of age who were vaccinated with seasonal influenza vaccine
Average vaccine coverage in the age group 65+ was estimated to be 56% 2010-11; 64% 2008-09

13. Telephone Advice Line (1177)
Information on the primary reason for contacting the medical advice line (phone number 1177), as well as the age group, is manually transferred to SMI. 14 county councils are connected to the service.
Primary reason for calling by age group (adults and children)
~302,000 calls regarding one of the following: breathing difficulties, fever, sore throat or coughing.
Statutory reporting of influenza A(H1N1)pdm09

When A(H1N1)pdm09 was identified in 2009, statutory reporting in accordance with the Communicable Diseases Act was approved by the Swedish Parliament. During the 2010-11 season the obligation remained for the microbiological laboratories to report all verified cases. A clinical report was obligatory for patients who had been admitted to hospital. The reporting was done through SmiNet. In addition to identity, age, date of disease onset, and diagnosis, the clinical report form requested information on risk groups, level of care and vaccination status. Unfortunately, these forms were often incompletely filled during the 2010-11 season.

Sentinel surveillance

A selection of Sweden's general practitioners act as sentinels, or informants, within the influenza surveillance system in Swedish outpatient care. Each week, they send information via SmiNet on the number of patients with influenza-like symptoms they have examined during the past week as well as the total number of patients they have examined. At the beginning of the season, they also report how many patients belong to their catchment area.

Sentinel surveillance in Sweden is generally done in accordance with the recommendations developed by the influenza monitoring group of the European Centre of Disease Prevention and Control (ECDC), the European Influenza Surveillance Network (EISN). However, we receive a relatively low number of reports compared with other countries. This may be because influenza patients can be on sick leave for a week without a doctor's certificate in Sweden, or because patients turn to emergency departments rather than their general practitioners when their influenza illness is severe enough to warrant medical care. Despite the low numbers of reported cases, the shape of the sentinel graphs correspond well with the ones we see through other reporting systems.

Sentinel sampling

It is difficult to make a diagnosis of influenza based solely on the patient's symptoms. An influenza-like illness is not always caused by influenza, and other epidemics that lead to influenza-like symptoms are sometimes misconstrued as influenza epidemics. In order to estimate how large a proportion of the patients seeking care for influenza-like illness that actually have influenza, nasal samples for influenza diagnostics are taken from some of the patients reported in the sentinel system. The diagnostics are carried out free of charge at SMI and the material is also used to characterize the circulating strains of influenza.

Sjukrapport

A minority of the patients that are infected with influenza have such severe symptoms that they need to see a physician, and therefore not caught in surveillance systems that rely on reports from the health care system. In an attempt to map illness in the general population, SMI has been operating the population-
based surveillance system, Sjukrapport (roughly, sick or illness report), since the 2007-08 season. Each year, between 12,000 and 15,000 residents of Stockholm County are invited to report when they fall ill with acute respiratory infection, providing their full identity. The reporting is done via automated telephone service or the web. When reporting, the patient answers questions regarding symptoms, such as coughing, fever and muscular pain that could be signs of influenza. The system classifies the reported symptoms as ILI (influenza like illness) or acute respiratory illness (ARI), according to the case definitions that have been set by the European Commission.

The results of the reports are presented weekly on the web as graphs showing the proportion of the patients reporting ILI or ARI. By comparing this data with the proportion of ILI patients with a positive result in the sentinel sampling (see below) for each week, we also produce an estimate of the proportion of people fallen ill with influenza in the community. As the participants register their full identity and accept the conditions of the study at the initial registration, the representation of the participants with regard to age and gender distribution can be controlled, and any imbalance corrected at the recruitment for the next season.

**Webbsök (web search)**

Webbsök is an automated system using completely anonymous data from the medical advice website, Vårdguiden (www.vardguiden.se), to estimate the development of the sentinel graph in a statistical model. The system was established by SMI in 2008. Data is received daily and Webbsök thus provides an estimate of the influenza activity as much as a week earlier than the sentinel surveillance system. The results from Webbsök are published on the web every Monday in the form of a graph which is created to predict the sentinel surveillance data to be published on Thursday.

**Data on death rates**

In order to identify excess mortality, the aggregate number of deaths is transferred from Statistics Sweden each week and analysed against a standard graph of the expected mortality when influenza is not present. Excess mortality is also calculated within the framework of a European cooperation project run from Denmark, Monitoring of Mortality (MOMO), with the National Board of Health and Welfare as the contacting authority. From the 2011-12 season and on, the National Board of Health and Welfare will be responsible for the analysis of excess mortality in Sweden.

**Seroepidemiological studies**

Serum samples representative of the population by gender and age and covering the whole of Sweden are taken from surplus samples at chemical laboratories across the country. The samples are analyzed for antibodies that would prevent influenza A(H1N1)pdm2009 from agglutinating red blood cells (haemagglutination inhibition, HI). The proportion of samples for different age groups with noticeable
antibodies and a level signifying protection has been compared with the equivalent data from 2007 and 2009. Unfortunately, it is not possible to distinguish antibodies that have been induced by vaccination from those resulting from illness.

**Telephone advice line (1177)**

Through a partnership with 1177, SMI analyses data from calls to the medical advice line 1177 each week. Data on the age and reason for calling are registered for all caller. Anonymised data on complaints that indicate upper respiratory infection or gastroenteritis in children and adults respectively is manually transferred to SMI each week.

The data are based on the reasons for contact that the nurses on the medical advice line report. If a caller describes multiple symptoms, the most important one is registered as the reason for contact. Only one reason for contact can be stated per call. Seven reasons for contact that can be related to influenza are analysed by SMI each week.

By comparing this data to the spread of influenza, we see indications of which symptoms are most characteristic for the currently circulating influenza virus(es). We may also identify peaks of symptoms outside the influenza season that may relate to other diseases and for which the microbiological reason may be identifiable.

**Other information sources**

The County Medical Officers of Communicable Disease Control report on anything noteworthy that has come to their attention in their counties. Foreign epidemiology is monitored through the websites of WHO and ECDC, and often through national websites. Informal information regarding outbreaks from the health care sector and the public is followed up on, as is national and international reporting on influenza in the media.

**Reports to Swedish collaborators/authorities**

During the influenza season, SMI condenses national and international data into a detailed weekly report, which is published on SMI’s website. A preliminary summary of the season is included in the final weekly report (week 20). A detailed annual report is sent to WHO and ECDC the following autumn. Starting in 2011, the annual report will also be published in Swedish.

SMI arranges regular information days ("SMI day") on influenza in preparation for the upcoming influenza season and the start of vaccination. Where necessary, the County Medical Officers of Communicable Disease Control, microbiological laboratories, the National Board of Health and Welfare and other affected authorities are informed of exceptional events. Different groups such as the National Pandemic Group handle issues of common interest.
Reports to international collaborators/authorities

SMI is the WHO National Influenza Centre for Sweden and part of ECDC's network dedicated to the monitoring of influenza, the European Influenza Surveillance Network (EISN). As such, SMI has an important commitment to report weekly influenza data to the ECDC database TESSy, which then forwards the data to the WHO database "Flunet". A representative selection of the samples positive for influenza collected by SMI are sent to WHO Collaborating Centre (WHO CC) for further characterization.

Swedish media

The media has access to the influenza data on SMI's website. During seasonal epidemics, SMI is normally contacted by the national media. Time permitting, we try to answer the questions we receive, and in most cases the media reports are accurate.
Epidemiological data

Laboratory-confirmed cases

A total of 3,689 laboratory-confirmed diagnoses of influenza were reported during the season (Diagram 2). This constituted approximately one third of the number of diagnoses during the 2009 pandemic but was otherwise the highest number since 1993, when registration of laboratory-confirmed cases first began. The season was unusual and lengthy (approx. 20 weeks) since three viruses – A(H1N1)pdm09, influenza B and A(H3N2) – were circulating (Diagram 3).

Diagram 2. Total number of laboratory-confirmed cases per week of influenza A (H1N1)pdm09, 2009-11(from statutory reporting), and seasonal influenza A and B, 2005-11 (from voluntary laboratory reporting)
Diagram 3. Number of laboratory-confirmed cases per week by influenza type

Diagram 4. Laboratory-confirmed cases per week of A(H1N1)pdm09, seasons 2009-10 and 2010-11. The 2009-10 season has been truncated.

Influenza A(H1N1)pdm09
The first peak of laboratory-confirmed influenza (Diagrams 2 and 3) was seen in week 1 of 2011 and coincided with the peak of the "second pandemic wave" of A(H1N1)pdm09 (Diagram 4). In total, 1,129 cases of A(H1N1)pdm09 were reported, compared to 11,009 during the first wave in 2009. The highest weekly value (2,431 cases) during the past two seasons was seen in week 46 of 2009 (truncated in Diagram 4).
The first cases of laboratory-confirmed influenza A(H1N1)pdm09 were reported from Jämtland and Värmland (Diagram 5) but, in total, the incidence was the highest in Skåne (Diagram 6, Table 2).

Diagram 5. Incidence each week of laboratory-confirmed A(H1N1)pdm09 per 100,000 population, by county, in the 2010-11 season

Diagram 6. Incidence of laboratory-confirmed A(H1N1)pdm09 per 100,000 population in the 2010-11 season
Table 2. Number and incidence of laboratory-confirmed influenza A(H1N1)pdm09 per county, sorted by incidence

<table>
<thead>
<tr>
<th>County</th>
<th>Number of cases</th>
<th>Incidence (per 100,000 population)</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skåne</td>
<td>280</td>
<td>23.1</td>
<td>1,212,896</td>
</tr>
<tr>
<td>Dalarna</td>
<td>60</td>
<td>21.8</td>
<td>275,709</td>
</tr>
<tr>
<td>Stockholm</td>
<td>293</td>
<td>14.8</td>
<td>1,977,874</td>
</tr>
<tr>
<td>Kronoberg</td>
<td>25</td>
<td>13.7</td>
<td>182,108</td>
</tr>
<tr>
<td>Västra Götaland</td>
<td>207</td>
<td>13.3</td>
<td>1,557,241</td>
</tr>
<tr>
<td>Kalmar</td>
<td>28</td>
<td>12.0</td>
<td>233,448</td>
</tr>
<tr>
<td>Värmland</td>
<td>30</td>
<td>11.0</td>
<td>273,726</td>
</tr>
<tr>
<td>Halland</td>
<td>32</td>
<td>10.9</td>
<td>293,399</td>
</tr>
<tr>
<td>Gotland</td>
<td>6</td>
<td>10.5</td>
<td>57,012</td>
</tr>
<tr>
<td>Uppsala</td>
<td>34</td>
<td>10.4</td>
<td>326,831</td>
</tr>
<tr>
<td>Östergötland</td>
<td>34</td>
<td>8.0</td>
<td>422,895</td>
</tr>
<tr>
<td>Örebro</td>
<td>19</td>
<td>6.8</td>
<td>277,515</td>
</tr>
<tr>
<td>Blekinge</td>
<td>9</td>
<td>5.9</td>
<td>152,286</td>
</tr>
<tr>
<td>Västmanland</td>
<td>14</td>
<td>5.6</td>
<td>249,886</td>
</tr>
<tr>
<td>Jönköping</td>
<td>16</td>
<td>4.8</td>
<td>335,120</td>
</tr>
<tr>
<td>Södermanland</td>
<td>12</td>
<td>4.5</td>
<td>267,275</td>
</tr>
<tr>
<td>Västernorrland</td>
<td>10</td>
<td>4.1</td>
<td>243,411</td>
</tr>
<tr>
<td>Gävleborg</td>
<td>10</td>
<td>3.6</td>
<td>275,954</td>
</tr>
<tr>
<td>Västerbotten</td>
<td>7</td>
<td>2.7</td>
<td>257,728</td>
</tr>
<tr>
<td>Jämtland</td>
<td>3</td>
<td>2.4</td>
<td>126,733</td>
</tr>
<tr>
<td>Norrbotten</td>
<td>0</td>
<td>0.0</td>
<td>249,811</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1,129</strong></td>
<td><strong>12.2</strong></td>
<td><strong>9,248,858</strong></td>
</tr>
</tbody>
</table>
Of the laboratory-confirmed cases of influenza A(H1N1)pdm09, 401 cases were hospitalised and 63 required intensive care (Table 3). The proportion of the cases of laboratory-confirmed influenza A(H1N1)pdm09 requiring hospital or intensive care was higher than during 2009-10 (Diagram 7). The same was reported in other countries. In total, 10 deaths caused by influenza A(H1N1)pdm09 were identified during the season. Nine of these came from a group with increased risk of severe influenza illness.

Table 3. Number of cases and incidence (per 100,000 population) of diagnosis, hospitalisation, intensive care, and death, by age group for laboratory-confirmed cases of A(H1N1)pdm09

<table>
<thead>
<tr>
<th>Age group</th>
<th>Laboratory-confirmed</th>
<th>Hospital care</th>
<th>Intensive care</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Incidence</td>
<td>Number</td>
<td>Incidence</td>
</tr>
<tr>
<td>0-4</td>
<td>143</td>
<td>26.6</td>
<td>72</td>
<td>13.4</td>
</tr>
<tr>
<td>5-14</td>
<td>58</td>
<td>5.8</td>
<td>14</td>
<td>1.4</td>
</tr>
<tr>
<td>15-39</td>
<td>526</td>
<td>17.6</td>
<td>141</td>
<td>4.7</td>
</tr>
<tr>
<td>40-64</td>
<td>346</td>
<td>11.3</td>
<td>137</td>
<td>4.5</td>
</tr>
<tr>
<td>&gt;65</td>
<td>56</td>
<td>3.4</td>
<td>37</td>
<td>2.2</td>
</tr>
<tr>
<td>Total</td>
<td>1129</td>
<td>12.2</td>
<td>401</td>
<td>4.3</td>
</tr>
</tbody>
</table>

There is no legal obligation to supplement a previously reported case with information on intensive care or death. The data in Table 3 may therefore be incomplete.

Diagram 7. Number of patients that received hospital and intensive care of the total number of reported laboratory-confirmed cases in 2009-10 (blue) and 2010-11 (red)
The pandemic vaccination 2009 continued to show a very good protective effect during the 2010-11 season, according to calculations of protection against hospitalisation due to A(H1N1)pdm. The calculated protective effect using the screening method was 77% in people between 18 months and 65 years of age (95% confidence interval 68-84%).

The second wave of A(H1N1)pdm09 seems to have been significantly milder in Sweden than in countries with less vaccination coverage in 2009, leading to fewer deaths and patients in intensive care in relation to the population. However, the analysis of the effectiveness of the vaccine is very complex, owing to a lack of precise data for vaccine coverage, and is still on-going.

Seasonal influenza

In total, there were 2,560 cases of seasonal influenza A and B during the 2010-11 season. The incidence was the highest in Skåne. For 85 cases the patient's age was not reported.

Influenza B

The 2010-11 season was unique due to the vast number of diagnoses of influenza B in Sweden, as well as in the rest of Europe and some other parts of the world. In total, 1,866 laboratory-confirmed cases were reported, which constitutes a record for influenza B. The peak point was reached in week 5. After this, there was a small dip, most likely due to the school holidays, and finally there was a second, lower peak, in week 9 (Diagram 8). Just as for influenza A(H1N1)pdm09, the highest incidence was reported from Skåne (Diagram 9).

Diagram 8. Number of laboratory-confirmed cases of influenza B by week between 2005 and 2011 (from voluntary laboratory reporting)
Diagram 9. Incidence of laboratory-reported influenza B per 100,000 population, by county, in the 2010-11 season

In terms of age, the highest incidence was in the age group 5-14. The fact that older children and young adults are affected is typical for influenza B. There have been reports from several countries of intensive care and deaths due to influenza B and in Sweden there was one patient who died despite extracorporeal membrane oxygenation (ECMO) treatment.

Influenza A

A total of 694 cases of seasonal influenza A were reported (Diagram 10). This is a relatively low number and yet the incidence of laboratory-confirmed influenza A was higher than in most other European countries. The strains characterised were of the subtype H3. As usual, the highest incidence was found among the very young and the very old (Table 4). The most laboratory-confirmed cases were reported, just as in the case of influenza B, during week 5 (Diagram 10) and the incidence was the highest in Uppsala County (Diagram 11).
Diagram 10. Laboratory-confirmed cases of seasonal influenza A reported by week between 2005 and 2011 (from voluntary laboratory reporting)

Diagram 11. Incidence of laboratory-confirmed influenza A per 100,000 population, by county, 2010-11 season

The highest incidence of laboratory-confirmed illness was seen, as in 2009, in children between the ages of 0 and 4, but unlike in 2009, the incidence was very low in school children (Table 4). For voluntary reporting, the age and gender of the patients is missing from the information from some counties, and as a result, this table covers 3,604 patients.
### Table 4. Number of laboratory-confirmed cases of A(H1N1)pdm09, seasonal influenza A and B, and incidence per 100,000 population by age group, 2010-11 season

<table>
<thead>
<tr>
<th>Age group</th>
<th>A(H1N1)pdm09</th>
<th>Seasonal influenza A and B</th>
<th>A(H1N1), A and B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number Incidence</td>
<td>Number Incidence</td>
<td>Number Incidence</td>
</tr>
<tr>
<td>0-4 years of age</td>
<td>143 26.1</td>
<td>69 12.6</td>
<td>135 24.6</td>
</tr>
<tr>
<td>5-14 years of age</td>
<td>58 5.8</td>
<td>29 2.9</td>
<td>335 33.5</td>
</tr>
<tr>
<td>15-64 years of age</td>
<td>872 14.3</td>
<td>364 6.0</td>
<td>1078 17.7</td>
</tr>
<tr>
<td>&gt;65 years of age</td>
<td>56 3.3</td>
<td>201 11.9</td>
<td>264 15.6</td>
</tr>
<tr>
<td>Total</td>
<td>1129 12.1</td>
<td>663 7.1</td>
<td>1812 19.4</td>
</tr>
</tbody>
</table>

*For 85 cases, no information on age or gender was provided. These data are not included in Table 4. The total number of influenza diagnoses was 3,689.

### Sentinel surveillance

The sentinel surveillance system is used for reporting influenza-like illness (ILI). Type and subtype of influenza is shown by analysis of samples received through the sentinel surveillance system.

### Sentinel reporting

In total, 64 units participated in the surveillance system, having a catchment area of 197,650 patients. However, not all units reported during all weeks. Each week, an average of 39 units reported. All in all there were 762 reports of patients with ILI. Diagram 12 shows the percentage of patients with ILI reported through the sentinel surveillance system.

There was a great discrepancy between the number of laboratory-confirmed cases and the number of sentinel surveillance reports of ILI during the pandemic year 2009-10 and the 2010-11 season. In 2009, there were 11,435 reported laboratory-confirmed cases and 1,253 patients with ILI reported. In the 2010-11 season, there were 3,689 laboratory-confirmed cases and 762 ILI patients reported. Our conclusion is that there were considerably more samples taken in outpatient care during 2009-10 and that the sentinel surveillance system produces a better comparative image of total influenza activity during the pandemic year than that of the laboratory reports.
The highest incidence of reported ILI from the sentinel surveillance system was seen in children between the ages of 5 and 14 (Table 5).

Table 5. Number of reported ILI cases and incidence per age group from the sentinel surveillance system

<table>
<thead>
<tr>
<th>Age group</th>
<th>Number of ILI cases</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4 years of age</td>
<td>41</td>
<td>7.5</td>
</tr>
<tr>
<td>5-14 years of age</td>
<td>125</td>
<td>12.5</td>
</tr>
<tr>
<td>15-64 years of age</td>
<td>533</td>
<td>8.7</td>
</tr>
<tr>
<td>&gt;65 years of age</td>
<td>63</td>
<td>3.7</td>
</tr>
<tr>
<td>Total</td>
<td>762</td>
<td>8.2</td>
</tr>
</tbody>
</table>

Sentinel sampling

During the season, 1,161 sentinel samples were submitted. A total of 299 samples (25.8%) tested positive for influenza: 113 for influenza A and 186 for influenza B. Diagram 13 shows the number of sentinel samples submitted each week and number and percentage of those positive during the season.
Of the positive samples, 26.8% tested positive for A(H1N1)pdm09, 7.4% for A/H3 and 62.2% for influenza B. Diagram 14 shows the number of sentinel samples positive for influenza B, influenza A(H1N1)pdm09, and influenza A(H3).

Two samples tested positive for the pandemic influenza as well as A/H3. Out of the samples that tested positive for influenza B, 86.7% resembled the B/Victoria/2/87 lineage and 8.1% the B/Yamagata/16/88 lineage.

Approximately 4% of the positive samples could not be subtyped/typed in terms of resemblance to a lineage due to a low viral load in the original sample.

Diagram 13. Number of sentinel samples submitted each week and number and percentage of those positive, 2010-11
Excess mortality

Despite of the high level of influenza activity, there were few signs of influenza-related excess mortality during the season (Diagram 15). The peak around Christmas was likely due mostly to the cold. The low rate of excess mortality despite a high level of influenza activity was likely due to the small proportion of influenza A(H3) during the season. Other types of influenza have less of an effect on the elderly and therefore have a lesser effect on the total number of deaths.
Population-based surveillance

Sjukrapport

Through Sjukrapport, participants report symptoms of cold and fever. The reporting of symptoms is divided into acute respiratory illness and influenza-like illness, which is defined as a display of influenza-like symptoms.

There were a total of 1,859 reports of acute respiratory illness (ARI) among the estimated 2,700 Sjukrapport participants (Diagram 16). This was a slight increase in the compared to the proportion among participants during 2009-10. The proportion of ILI (a total of 658 reports) in Sjukrapport was also somewhat higher in 2010-11 than in the previous season (Diagram 17).

Laboratory reports showed that influenza A(H1N1)pdm09 was the dominant type around the turn of the year. For the same period, there was a hint of an increase in influenza-like illness amongst the Sjukrapport participants. In week 4, an increase of influenza B started to show in the laboratory reporting. A while later, there was an increase of influenza-like illness among the participants in Sjukrapport, the highest recorded incidence of which was for the age group 0-14.
Estimate of the number of people ill with influenza

Because the data from we have used the proportion of positive sentinel samples in Stockholm to estimate how large a proportion of the people reporting influenza-like illness actually were infected by an influenza virus.

A rough estimate of the number of people in the community that are ill with influenza can thus be made using the data from Sjukrapport and a number of assumptions. It is important to emphasize that this is an estimate and is based on the following assumptions:

- That the population in Sjukrapport is representative of Stockholm.
That those reporting to Sjukrapport are representative of the people that seek care from a physician in the sentinel sampling system.

That those sampled in the sentinel sampling have had ILI that matches the Sjukrapport definition.

Using the proportion of influenza-like illness reported to Sjukrapport each week since week 48 and the proportion of sentinel samples in Stockholm testing positive for influenza during the same period, we have estimated the proportion of Stockholm's population that have been ill with influenza. For each week, this proportion is then multiplied by the total population of Stockholm County in 2010 (source Statistics Sweden).

The numbers have been added and the total number of people ill in Stockholm during the weeks 48-11 has been calculated. In order to avoid misleading figures, we have also chosen to only report an estimate for the weeks 48 to 11, when sentinel samples were taken from 5 or more people in Stockholm.

If the sentinel sampling units instead sample all those who have sought care for acute respiratory illness and if in addition all of the above-mentioned assumptions regarding reports on such illness are taken into account, a higher number will be produced (the upper limit of the estimate).

Furthermore, if we assume that the infection is spread throughout the country in the same way as in Stockholm, an estimate can be made for Sweden's entire population.

This process gives us an estimate of the number of people ill with influenza during the weeks 48-11 of between 80,000 to 210,000 for Stockholm and between 380,000 and 980,000 for all of Sweden. This is 50% higher than the estimate for the pandemic. As the seasonal influenza viruses circulated for a longer period of time than the pandemic period and affected older people, it is likely that the total number of people who fell ill was higher during the 2010-11 season. Based on what are now relatively old studies, a normal estimate is that between 5 and 15% of the population will fall ill with seasonal influenza, which matches our estimate for 2010-11.

**Symptoms in connection with the influenza peak**

As described earlier, SMI receives information each week from the medical advice line 1177 concerning the main reasons for contact. Data on the seven contact reasons related to influenza are presented in the diagram for the past two seasons (Diagram 18); from week 27, 2009 to week 26, 2010 as dotted lines and from week 27, 2010 until week 20, 2011 as solid lines. Just as in 2009-10, fever in children was the most common cause for contact in connection to the influenza peak.
Diagram 18. Statistics for telephone calls regarding influenza-related symptoms received by the medical advice line 1177

Through Websök, SMI models ILI reported through the sentinel surveillance system (Diagram 19) based on searches at Vårdguiden.se. In the diagram, data from week 27, 2010 until week 26, 2011 (season 2010-11) are shown in red; week 16 to week 26, 2009 (parts of season 2008/2009) are shown in yellow; and week 27, 2009 to week 26, 2010 (season 2009/2010) are shown in blue. Sentinel reports for 2010/11 are shown in black.
Diagram 19. Webbsök's model of the estimated proportion of patients with influenza-like illness (ILI)
Virological data

Voluntary laboratory reporting

With the exception of the pandemic season 2009-10, the highest number of influenza diagnoses since the beginning of registration in 1993 was in 2010-11. Swedish laboratories conducted 18,442 influenza analyses during the season, of which 3,689 (20%) tested positive for influenza A or B. Of the positive samples 1,866 (50.5%) were positive for influenza B, 1,129 (31%) for A(H1N1)pdm09 and 694 (18.5%) for seasonal influenza A. SMI received 94 out of the 694 samples, positive for influenza A which were not positive for A(H1N1)pdm09 and they were all subtyped as A/H3. Out of the 1,866 samples positive for influenza B, 75 were sent to SMI for further characterisation. Out of the samples analyzed, 90.3% resembled the B/Victoria/2/87 lineage and 9.7% the B/Yamagata/16/88 lineage. B/Victoria was included in the seasonal vaccine for the 2010-11 season.

Characterization methods and selection of samples

The majority of the characterizations done at SMI consist of sequence analyses. The influenza A genome consists of eight gene segments which encode for ten proteins. SMI is continuously characterizing three of these segments that encode four proteins. For influenza B two gene segments are analyzed.

Haemagglutinin (HA) from influenza A and B is characterized in terms of vaccine resemblance and changes in receptor affinity. In addition, certain mutations in the HA gene also make the virus bind to receptors in the lungs instead of receptors in the upper respiratory tract. The subtype-specific PCR analysis for influenza A and the PCR analysis for lineage-typing of influenza B also target the HA gene. A representative selection of samples that have been characterized at SMI are sent to the WHO Collaboration Centre (WHO CC) laboratory in London for further phenotypic analysis using haemagglutination inhibition (HI).

The neuraminidase (NA) gene is characterized for resistance to the neuraminidase inhibitors Oseltamivir and Zanamivir (Tamiflu® and Relenza®). A phenotypic characterisation, NAI, for determination of antiviral sensitivity is also carried out at SMI. This measures the activity of NA in the virus isolate when subjected to Oseltamivir or Zanamivir, whereby the strain's sensitivity to each respective neuraminidase inhibitor can be calculated. The above-mentioned analyses are carried out for both influenza A and B.

The matrix gene (MA) in influenza A encodes two proteins, M1 and M2. This gene is often targeted in the PCR methods used to detect influenza A in clinical samples. M1 is needed in viral assembly while M2 encodes for an ion channel and is genetically characterized to determine resistance to amantadine.

Phenotypic analysis is based on cultivated viruses. At present, only the virus laboratories at Umeå University and SMI isolate influenza from tissue cultures.
This means that SMI is in constant contact with the laboratories around Sweden to obtain representative sample material that can be grown in tissue cultures.

SMI requests that the Swedish laboratories submit positive samples from patients who are severely ill, who have fallen ill despite being vaccinated, who are unresponsive to antiviral treatment or who have died as a result of influenza illness.

All sequences that have been obtained during the season have been entered into the public database, Global Initiative on Sharing All Influenza Data (GISAID).

**Characterization of influenza**

Diagram 20 shows the results from subtyping and lineage typing of positive sentinel samples during the 2010-11 season.

**Diagram 20. Results from subtyping and lineage typing of positive sentinel samples.**

Influenza A(H1N1)pdm09

During the 2010-11 season, SMI sequenced 49 HA genes and 47 NA genes from samples positive for A/H1N1)pdm09 (refer to the phylogenetic tree for HA, appendix 1). The table shows the grouping of the samples into subgroups (Table 6).

**Table 6. Characterisation of influenza A(H1N1)pdm09, 2010-11**

<table>
<thead>
<tr>
<th>Number</th>
<th>Subgroup</th>
<th>Key mutations</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>AH1/California/7/2009</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>A/California/7/2009/(A/Christchurch/16/2010)</td>
<td>D94N, N125D, V250A</td>
</tr>
<tr>
<td>24</td>
<td>AH1/California/7/2009; A/England/142/2010</td>
<td>S185T</td>
</tr>
</tbody>
</table>
Two strains cultivated in MDCK cells carried the mutation E119K in NA, one of them in mix with wild type strain. Mutation E119V is a well characterised mutation resulting in Oseltamivir-resistance in H3N2 strains. The E119K strains were analysed phenotypically along with 9 additional strains using NAI. All proved sensitive to Oseltamivir and Zanamivir indicating that E119K does not influence susceptibility to Oseltamivir or Zanamivir. Two of the ten strains were also analyzed phenotypically using NAI by the WHO CC in London, with the same results as SMI regarding sensitivity to Oseltamivir and Zanamivir.

In Spring 2011, influenza A(H1N1)pdm09 strains with mutations in the region of the probe used in the diagnostic real time PCR specific to A(H1N1)pdm09 were identified. This information was immediately transmitted to the Swedish laboratories together with a request that they submit strains displaying deviating amplification curves in real time PCR. A total of seven samples displaying mutations in the probe region were collected. The mutations led to a lower sensitivity in the analysis and a new PCR system has now been evaluated at SMI.

**Influenza A/H3N2**

SMI sequenced 34 HA genes, 27 NA genes and 28 MA genes from the samples positive for A/H3 that were submitted during the season (refer to the phylogenetic tree for HA, Appendix 2). The samples were grouped into the following subgroups (Table 7).

**Table 7. Characterisation of influenza A/H3N2, 2010-11**

<table>
<thead>
<tr>
<th>Number</th>
<th>Subgroup</th>
<th>Key mutations</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>A/Perth/16/2009</td>
<td>E62K, N144K, K158N, N189K</td>
</tr>
<tr>
<td>13</td>
<td>A/Hong Kong/2121/2010</td>
<td>D53N, Y94H, I230V, E280A</td>
</tr>
<tr>
<td>12</td>
<td>A/Victoria/208/2009</td>
<td>K158N, N189K, T212A</td>
</tr>
</tbody>
</table>

One isolate that had been cultivated in MDCK cells had a mutation in the NA gene (D151D/N mixed strain), which according to the literature causes reduced sensitivity to Oseltamivir and Zanamivir. Another isolate that had also been cultivated in MDCK cells displayed a mutation D151G in the NA gene. This mutation results in a reduced sensitivity to Zanamivir alone. Ten strains, including the mixed strain with the D151D/N mutation, were phenotypically analyzed using NAI. All proved sensitive to Oseltamivir and Zanamivir. The same ten strains were also analyzed using NAI by the WHO CC in London with the same results regarding sensitivity to Oseltamivir and Zanamivir. The strain with D151G has not yet been phenotypically analyzed. It is however well known that mutations in position 151 of NA often arise upon cultivation in MDCK cells.

The mutation S31N in M2, which induces a resistance to amantadine, was found in 28 of 28 analyzed strains. The matrix sequences were also used in order to validate SMI’s real time PCR system for matrix A.
Influenza B

It was an intense influenza B season, and 75 strains of influenza B were typed for vaccine resemblance through analysis of lineage likeness. A majority (75.9%) resembled B/Victoria/2/1987, the lineage type included in the seasonal vaccine, and 24.1% resembled B/Yamagata/16/88. The vaccine does not protect against the second lineage type.

SMI sequenced the HA gene from 22 Victoria-like strains and 7 Yamagata-like strains (refer to the phylogenetic tree, appendix 3). The strains were grouped into the following subgroups (Table 8).

Table 8. Characterisation of influenza B, 2010-11

<table>
<thead>
<tr>
<th>Number</th>
<th>Subgroup</th>
<th>Key mutations</th>
</tr>
</thead>
<tbody>
<tr>
<td>22</td>
<td>Victoria B/Brisbane/60/2008</td>
<td>N75K, N165K, S172P</td>
</tr>
<tr>
<td>5</td>
<td>Yamagata B/Bangladesh/3333/2007</td>
<td>S150I, N165Y, S229D</td>
</tr>
</tbody>
</table>

The NA gene from 23 Victoria-like strains and seven Yamagata-like strains were sequenced. The mutation I221V/I (mixed strain), which is suspected to cause reduced sensitivity to Oseltamivir, was observed in a B/Victoria-like sample by sequencing of original sample from a patient treated for a short time with Oseltamivir and then with Zanamivir. However, this sample could not be analysed phenotypically since it could not be isolated.

Ten B/Victoria-like strains and 5 B/Yamagata-like strains were phenotypically analyzed using NAI. All proved sensitive to Oseltamivir and Zanamivir. Two of the strains, one B/Victoria-like and one B/Yamagata-like, were also analyzed by WHO CC. The results regarding sensitivity to Oseltamivir and Zanamivir corresponded to those found by SMI.

SMI isolated influenza from 63 samples that were submitted by laboratories in Sweden. All samples were analyzed using sequencing and, on a selected number, a phenotypic analysis using NAI was also carried out. All 63 samples were sent to WHO CC in London for further characterization, with 19 sent at the end of January and 43 at the beginning of June. SMI has received the results from the first submission, which show a good match between the laboratories.

New diagnostic methods and quality assurance

In preparation for the 2010-11 season, a one-step PCR system for the indication of circulating types of influenza had been developed and implemented at SMI. Several other laboratories in Sweden now use that same method. The PCR method is sensitive and quick and can be scaled up to analyse a large number of samples efficiently. This method of analysis can be used for matrix A and B, subtype-specific A(H1N1)pdm09, seasonal A/H3, seasonal A/H1 and the two lineages of
influenza B. The method was also tested for diagnosing suspected cases of avian influenza.

SMI has continuously sequenced the target genes for the PCR systems M1 and M2. The laboratories using the PCR system developed by SMI are asked to submit all samples with deviating results for sequence analysis, as noted above under of influenza A(H1N1)pdm09. SMI has also assisted laboratories in developing their own PCR systems, for example by sequencing submitted samples to validate their methods. SMI also offers checks for positive samples for those who want it.

SMI participates in several external quality programmes. Twice a year, WHO sends out an influenza PCR panel. In recent years, SMI has obtained correct results for all samples. In addition, SMI takes part in panels sent out by QCMD (Quality Control for Molecular Diagnostics) and EISN's Influenza Virus EQA-programme.

In October 2010, SMI produced a PCR panel for quality control of the diagnostics at Swedish laboratories, commissioned by EQUALIS - a provider of external quality assessment for clinical laboratory investigations, based in Sweden. In previous years, the quality panels have contained material for cell cultures and antigen detection (IF and/or quick test), but the introduction of new molecular methods in the country's laboratories means that there is now only a panel for PCR. Twenty laboratories participated in the quality control. Fourteen of these produced 10 out of 10 correct results. Three laboratories could not find a virus in one sample with low virus content. Of the three remaining laboratories, two had two incorrect results and one of them had a contamination in one analysis (Diagram 21).

**Diagram 21. Obtained results from quality control by the panel for PCR-based influenza diagnostics**

![Diagram 21](image-url)

**Summer 2009**
**Season 2009-2010**
**Season 2010-2011**
**Vaccine (season)**
Attachment 2. The phylogenetic tree of the amino acid sequences of HA of A/H3N2.
Attachment 3. The phylogenetic tree of the amino acid sequences of HA of influenza B.
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