Folkhälsomyndigheten
PUBLIC HEALTH AGENCY OF SWEDEN

Influenza in Sweden

2015–2016 Season

Influenza in Sweden

2015–2016 Season

Commitments and conflicts of interest

In the case of the Public Health Agency of Sweden's own experts and specialists who have contributed to reports, any conflicts of interest and commitments are assessed within the framework of their conditions of employment.

Regarding external experts and specialists who participate in the Public Health Agency of Sweden's work on drawing up reports, the agency requires that they submit written declarations of potential conflicts of interest or commitments. Such circumstances may exist if an expert, for example, has received or receives financial remuneration from an organization with interests in the outcome of the matter with which the agency is dealing or if there exists an earlier or current standpoint on or involvement in the matter in question such that it may be surmised that impartiality cannot be maintained.

The Public Health Agency of Sweden then decides whether circumstances exist that would impede an objective appraisal of the material drawn up and thus affect the agency's ability to act objectively and impartially. The assessment may result in the expert being able to be engaged for the assignment or that the agency proposes measures concerning the expert's engagement or that the expert is not judged to be able to participate in the work in question.

Those external experts who have contributed to the present report have submitted a declaration of any conflicts of interest or commitments in accordance with the Public Health Agency of Sweden's requirements before beginning their work. In the judgment of the Public Health Agency of Sweden, there exist no circumstances that might jeopardize the agency's credibility. The declarations and any complementary documents are public documents and may be accessed at the Public Health Agency of Sweden.

Article number: 16028
ISBN 978-91-7603-662-4 (pdf)

Preface

This report describes the monitoring systems for influenza in use during the winter season of 2015–2016 and the results of both epidemiological and virological surveillance. Data are also compared to previous influenza seasons.

The report is prepared for the World Health Organization (WHO) as part of the Public Health Agency of Sweden's function as a National Influenza Centre (NIC).

Annual reports in English about the influenza seasons in Sweden have been available since 2000 and can be found on the Public Health Agency's website.[1]

The report has been prepared by Helena Dahl, Åsa Wiman, Tove Samuelsson Hagey, and Mia Brytting of the Unit for Laboratory Surveillance of Vaccine Preventable Diseases and by AnnaSara Carnahan, Emma Byström, and Sarah Axelsson of the Unit for Vaccination Programs.

Public Health Agency of Sweden

Ann Lindstrand
Head of Unit
Unit for Vaccination Programs

Mia Brytting
Head of Unit
Unit for Laboratory Surveillance of Viral Pathogens and Vaccine Preventable Diseases

[1] Folkhälsomyndigheten. http://www.folkhalsomyndigheten.se/publicerat-material/publikationer/. Suggested search query: "Influenza in Sweden".

Table of contents

Summary

The influenza season of 2015–2016 was dominated by influenza A(H1N1)pdm09, with a small wave of influenza B/Victoria towards the end of the season. Overall, the season had high activity but slightly fewer laboratory-confirmed cases compared to the previous, intense season. The season had a high number of severe cases and significant excess mortality was observed in the 15-64 age group.

Overall, 74 of cases during the 2015–2016 season were influenza A. A subset of these were subtyped, and 95 % were A(H1N1)pdm09. Of the influenza B cases, the lineage was determined for 71 samples, of which 92.8% were B/Victoria. Laboratory reports, web searches, and telephone calls to 1177 (regarding fever in children) indicated that the epidemic started at week 49, 2015, which was slightly earlier than usual. All surveillance systems showed a plateau over the Christmas and New Year holidays. The peak of laboratory cases was week 6, 2016, and by week 17, the epidemic had ended. Based on the percentage of positive samples, the season peaked in week 52 in northern Sweden, week 4 in the middle of Sweden, and week 6 in southern Sweden.

This season, 43 % more patients have required intensive care due to influenza compared to last season. Of patients requiring intensive care, nearly half were aged 40–64 years and approximately a third were ≥65 years old. Of the intensive care cases, two thirds belonged to a medical risk group or were ≥65 years old. However, over half of patients aged 40–64 years did not belong to a medical risk group, and for those 15–39 years old, 40 % did not belong to a medical risk group.

No excess mortality was seen in the population as a whole for the 2015–2016 season. However, significant influenza-related excess mortality was seen during weeks 4–6 in the 15–64-year-old age group. In the analysis of the 261 deaths that occurred within 30 days of a laboratory-confirmed influenza diagnosis, 79 % of the deaths were in the age group ≥65 years, followed by 40–64 years at 18 %. Approximately 9.2 % of those ≥65 years of age diagnosed with influenza A had died within 30 days of diagnosis, which is comparable with data for influenza A(H1N1)pdm09 from previous seasons. The mortality rate for influenza A cases aged 40–64 years was also comparable to previous data at 2 %.

Vaccination coverage among those 65 years and older remained at just under 50 % – approximately the same level as that of the 2014–2015 season. Because the number of people in this age group has increased, a greater number of people were vaccinated this season than last. There are great variations within Sweden, with vaccination coverage having increased in 6 out of 21 counties/regions. Among those under 65 years of age, it is estimated that 5–10 % belong to a risk group that is recommended to be vaccinated in Sweden, but vaccination coverage was only 2 % in this age group. Of those who belonged to a risk group and who required intensive care due to influenza during this season, only 11.5 % had been vaccinated.

The median age of laboratory-confirmed influenza A cases was 48 years, which was similar to influenza A(H1N1)pdm09 cases in the previous three seasons (range: 39–50 years). The median for influenza B cases was 33 years, which was lower than the previous three seasons (range: 46–60 years). Approximately 73 % of influenza cases this season were under 65 years of age, compared to 47 % in 2014–2015, for example, which was dominated by A(H3N2). Since neither influenza A(H1N1)pdm09 or influenza B/Victoria have circulated to any great extent in recent seasons, children under 5 years had a high incidence because many had not yet been infected with either virus.

The age profile of influenza A(H1N1)pdm09 has changed from having infected primarily children and adults under 65 years of age during the 2009 pandemic to also causing significant morbidity among those 65 years and older. Despite this trend, the overall incidence in the elderly is lower compared to an intense influenza A(H3N2) season, indicating that they still have some protection against A(H1N1)pdm09. In addition, no significant excess mortality among elderly was seen during the 2015–2016 season.

Viral characterization of samples collected through sentinel sampling and from Swedish laboratories showed that most of the circulating A(H1N1)pdm09, A(H3N2), and B/Yamagata strains were similar to the strains included in the trivalent seasonal influenza vaccine. In addition, B/Victoria strains were similar to the vaccine strain contained in the quadrivalent vaccine. Because B/Yamagata was included in the trivalent vaccine, it gave no protection against the circulating B/Victoria strain. Vaccination breakthrough was detected in 11 percent of the 369 positive sentinel samples, with a median age of 67.5 years.

Only two of the 136 A(H1N1)pdm09-samples collected from regional laboratories were resistant to oseltamivir, and both samples were taken from patients treated with oseltamivir. None of the other samples analyzed (41 A(H3N2), 53 B/Victoria, and 12 B/Yamagata) were resistant to either of the two neuraminidase inhibitors, oseltamivir and zanamivir.

Sammanfattning

Säsongen 2015–2016 dominerades av influensa A(H1N1)pdm09 med en mindre våg av influensa B/Victoria mot slutet av säsongen. Under säsongen sågs en hög aktivitet, men något färre laboratorieverifierade fall jämfört med den föregående, intensiva säsong. Under säsongen rapporterades många svårt influensasjuka och en signifikant överdödlighet i åldersgruppen 15–64 år.

Totalt sett var 74 procent av fallen influensa A. Av de prover som subtypades var 95 procent A(H1N1)pdm09. Bland de influensa B-positiva prover som analyserades för linjelikhet visade sig 92 procent höra till linjetypen B/Victoria. Data från laboratorieövervakningen, Webbsök och telefonsamtal till 1177 Vårdguiden (gällande feber bland barn) visade att epidemin startade vecka 49, vilket var något tidigare än vanligt. I alla övervakningssystem stannade aktiviteten av under jul- och nyårshelgerna. Toppen bland laboratoriefallen kom vecka 6 och vecka 17 hade epidemin avslutats. Utifrån andelen positiva prover kom influensatoppen vecka 52 i norra Sverige, vecka 4 i mitten av landet och vecka 6 i södra Sverige.

Jämfört med föregående säsong var det 43 procent fler patienter som behövde intensivvård. Av dessa hörde knappt hälften till åldersgruppen 40–64 år och cirka en tredjedel var personer ≥ 65 år. Av de intensivvårdade tillhörde två tredjedelar en medicinsk riskgrupp eller var ≥ 65 år. Bland patienter i åldrarna 40–64 år var det över hälften som inte tillhörde en medicinsk riskgrupp för svår influensasjukdom, och bland patienter 15–39 år var andelen 40 procent.

Sett till hela befolkningen uppmättes ingen överdödlighet för säsongen 2015–2016, men en signifikant överdödlighet sågs under veckorna 4–6 i åldersgruppen 15–64 år. Totalt 261 dödsfall inträffade inom 30 dagar av en laboratorieverifierad influensadiagnos, varav 79 procent gällde personer i åldersgruppen ≥ 65 år, följt av gruppen 40–64 år (18 procent). Av de ≥ 65 år med diagnosen influensa A avled cirka 9,2 procent inom 30 dagar av sin diagnos, vilket är jämförbart med tidigare säsongers data för influensa A(H1N1)pdm09. Även dödligheten i gruppen 40–64 år är jämförbar med tidigare data, och denna säsong var det 2 procent av influensa A-fallen som avled inom 30 dagar.

Vaccinationstäckningen bland personer ≥ 65 år låg kvar på samma nivå som säsongen 2014–2015, knappt 50 procent. Eftersom antalet personer i åldersgruppen har ökat var det fler som vaccinerades denna säsong. Det var dock stora variationer i landet och vaccinationstäckningen ökade i 6 av 21 landsting och regioner. I gruppen < 65 år uppskattas att 5–10 procent tillhör en riskgrupp, men vaccinationstäckningen bland dem var endast 2 procent. Av de som tillhörde en riskgrupp och behövde intensivvård under säsongen var endast 11,5 procent vaccinerade.

Medianåldern för de laboratorieverifierade influensa A-fallen var 48 år, vilket liknar den för influensa A(H1N1)pdm09-fallen under de senaste tre säsongerna (spann: 39–50 år). Medianåldern för influensa B var 33 år, vilket är lägre än de

föregående tre säsongerna (spann: 46–60 år). Cirka 73 procent av influensafallen denna säsong var personer under 65 år, jämfört med till exempel 47 procent säsongen 2014–2015 som dominerades av A(H3N2). Varken influensa A(H1N1)pdm09 eller influensa B/Victoria har cirkulerat i någon större omfattning under de senaste säsongerna så barn 0–4 år hade en hög incidens av influensa eftersom många inte smittats av dessa virus tidigare.

Åldersprofilen för influensa A(H1N1)pdm09 har ändrats, från att drabba barn och vuxna under 65 år under pandemin 2009 till att också orsaka betydande sjuklighet bland de som är 65 år och äldre. Trots detta är incidensen lägre bland äldre jämfört med en intensiv influensa A(H3N2)-säsong, vilket tyder på att de fortsatt har ett visst skydd mot A(H1N1)pdm09. I denna åldersgrupp sågs inte heller någon signifikant överdödlighet under säsongen.

Viruskarakteriseringen av prov från sentinelprovtagningen och från laboratorier i landet visade att de flesta cirkulerande stammar av A(H1N1)pdm09, A(H3N2) och B/Yamagata liknade de stammar som ingick i det trivalenta säsongsinfluensavaccinet, och att B/Victoria-stammarna liknade vaccinstammen som ingick i det fyrvalenta vaccinet. Eftersom B/Yamagata ingick i det trivalenta vaccinet gav det inget skydd mot den cirkulerande B/Victoria-stammen. Inom sentinelprovtagning påvisades vaccinationsgenombrott i 11 procent med en medianålder på 67,5 år.

Inom laboratorierapporteringen var endast 2 av 136 fall med A(H1N1)pdm09 resistenta mot antiviralen oseltamivir, och båda de proverna var tagna från patienter som behandlats med oseltamivir. Inga av de andra analyserade proverna (41 st. A(H3N2), 53 st. B/Victoria och 12 st. B/Yamagata) visade resistens mot de två neuraminidashämmarna, oseltamivir och zanamivir.

Background

Each winter, influenza epidemics of varying magnitude occur in Sweden. People and society are affected in different ways depending on the characteristics of the circulating viruses and the immunity towards them in different age groups.

New influenza strains, particularly those different enough to cause a pandemic, can be very aggressive and cause severe illness, and these can cause great strain on intensive care units and can lead to deaths in all age groups. None of these effects are detectable through a single reporting system. In order to get an overall picture of ongoing influenza activity and to remain prepared in case of a pandemic, the Public Health Agency of Sweden (*Folkhälsomyndigheten*) has a number of different epidemiological reporting systems for influenza ranging from the collection of data from different healthcare providers to the analysis of web searches.

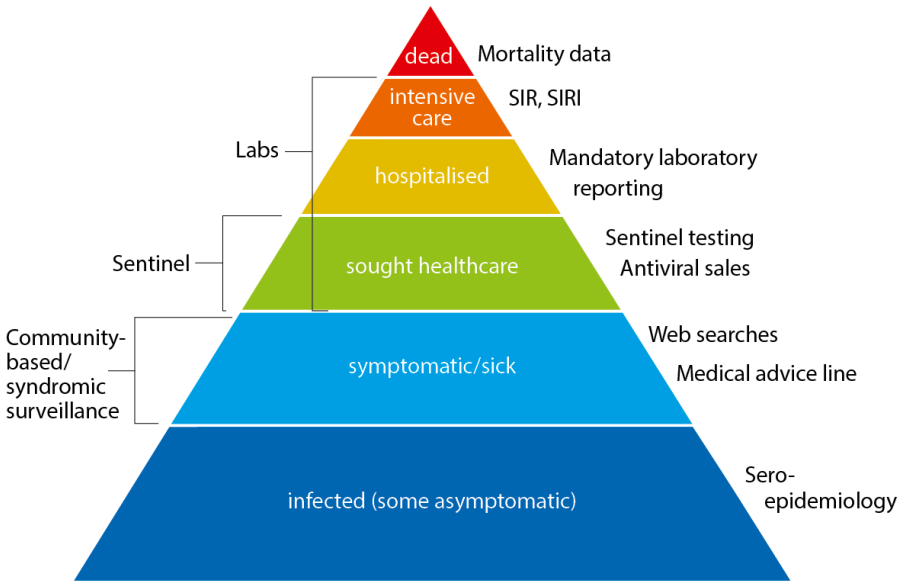
Virological surveillance is as important as epidemiological reporting systems. Viruses are typed as influenza A or B by regional laboratories in real time during the influenza season, and some laboratories also determine the subtype for influenza A. Throughout the season, viruses from around the country are characterized by the Public Health Agency with regard to subtype and lineage, vaccine similarity, sensitivity to antiviral drugs, and other factors that might affect the severity of the infections they cause. Viruses are also isolated and sent to the WHO Collaborating Centre (WHO CC) in Mill Hill, London, for further characterisation and to provide a basis for vaccine strain selection. When new strains of influenza virus emerge, reference methods for diagnostics are established at the Public Health Agency and shared with all microbiological laboratories in Sweden.

Surveillance systems

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

Table 1 describes the data collection systems that were used to monitor influenza activity at the various levels of the influenza pyramid in Sweden during the 2015–2016 season. Each system is described in detail below the table.

Figure 1. The "influenza pyramid" showing possible outcomes of an influenza infection.



SIR: Swedish Intensive Care Registry
SIRI: Swedish Intensive Care Registry – Influenza module

Table 1. Description of all systems used to monitor influenza activity during the 2015–2016 season. *The data are from the period of week 40, 2015, to week 20, 2016, if no other dates are given.*

Reporting system/ method	**Implementation**	**What does the system/ method show?**	**Results (2015–2016)**
Vaccination coverage	Periodic collection of coverage data from county councils.	Vaccination coverage per age group.	49.1 % coverage among those 65 years or older ~2 % coverage among risk groups under 65 years
"Webbsök" (Web Search)	An automated system that uses search data from the national medical advice site 1177.se. The numbers of searches on influenza and influenza symptoms are entered into a statistical model that estimates the proportion of patients visiting general practitioners (GPs) with influenza-like illness (ILI).	Estimates the proportion of patients with ILI.	Between week 27, 2015, and week 26, 2016, 126,304 queries related to influenza were entered, which was 1.1 % of the total number of queries on the webpage 1177.se. Webbsök's influenza season lasted for 18 weeks (week 49, 2015–week 13, 2016), with weeks 5–7 being at a high level.
Telephone Advice Line (1177 Vårdguiden)	Weekly aggregated data on the primary reason for contacting the medical advice line (phone number 1177) and the age group of the person concerned are manually reported to the Public Health Agency through the system Hälsoläge. Data are collected from 20 of Sweden's 21 county councils.	Primary reason for calling by age group (adults and children).	Approximately 536,000 calls regarding one of the following symptoms: breathing difficulties, fever, sore throat, or coughing. Fever in children accounted for 4.5 % of all calls to 1177 during the year. The epidemic started week 49, 2015, and the peak was week 6, 2016, with 9.1 % of calls due to fever in children. The end of epidemic was week 17.
Antiviral sales	Weekly data from the Swedish eHealth Agency	Number of packages sold by type of sale, including prescriptions and health care requisitions.	8,647 packages
Statutory laboratory reporting of influenza, voluntary reporting of denominator data	Legal obligation for all laboratories to report influenza diagnoses along with full patient identity in the web-based reporting system, SmiNet, in accordance with the Communicable Diseases Act.	Number of laboratory-confirmed cases of influenza A and B together with age, gender, and geographical distribution. Proportion of samples tested that are positive for an influenza virus and sub-/lineage type	6,727 laboratory-confirmed cases of influenza A and 2,423 cases of influenza B. 48,135 samples, 19.0% positive: - 14.0 % influenza A - 5.0 % influenza B Of influenza A-cases subtyped: - 94.8 % A(H1N1)pdm09 - 5.2 % A(H3N2) Of influenza B-cases with determined lineage: - 75.6 % B/Victoria - 24.4 % B/Yamagata

Reporting system/ method	Implementation	What does the system/ method show?	Results (2015–2016)
Voluntary clinical reporting of laboratory-confirmed influenza cases (all types) in intensive care (SIRI)	Collaboration with the Swedish Intensive Care Registry (SIR). Treating physicians in intensive care units are asked to report clinical information about patients with laboratory-confirmed influenza.	Severity of infections with different influenza subtypes and impact on the intensive care units.	363 laboratory-confirmed cases of influenza were reported from SIR. Of those, 157 were reported as influenza A (unknown subtype), 154 were A(H1N1)pdm09, 4 were A(H3N2), and 48 were influenza B.
Excess mortality	Weekly data on the aggregated number of deaths in Sweden, by age group, is sent from the Swedish Tax Agency to the Public Health Agency and analysed with statistical models.	Influenza-attributable excess mortality (FluMoMo model) All-cause mortality (EuroMoMo model)	Significant influenza-attributable excess mortality was seen among persons 15–64 years old between weeks 4 and 6, 2016, but no excess mortality was seen in the population as whole.
Deaths within 30 days	Weekly data on date of death is sent from the Swedish Tax Agency to the Public Health Agency and analysed intermittently.	Death within 30 days of influenza diagnosis	261 of 8,652 persons with an influenza diagnosis had died within 30 days of diagnosis, of which 83 % were influenza A and 17 % were influenza B. Most (79%) were ≥65 years old.
Sentinel sampling	Samples from some patients who present with ILI, as well as some patients with acute respiratory illness (ARI), are analysed by the Public Health Agency for influenza.	The proportion of sentinel patients with ILI or ARI who have an influenza infection (see also virus characterisation below).	1,341 samples were analysed, of which 369 (27.5 %) tested positive for influenza: - 70.5 % A(H1N1)pdm09 - 24.4 % B/Victoria-like - 3.0 % A(H3N2) - 2.1 % B/Yamagata-like

Reporting system/ method	Implementation	What does the system/ method show?	Results (2015–2016)
Virus characterisation	Continual genotypic and phenotypic assays of laboratory and sentinel samples that tested positive for influenza.	Viruses' vaccine similarity and possible resistance to antiviral drugs and sub-/lineage typing of influenza A and B.	Genetic characterisation - 27 of 42 A(H3N2) viruses belonged to clade 3C.2a, a clade where strains cross-react with the vaccine strain (a clade 3C.3a virus) - 15 of 42 A(H3N2) strains belonged to clade 3C.3a (the same clade as the vaccine strain) - 99 of 99 A(H1N1)pdm09 viruses belonged to clades or subclades that have antigenic properties similar to the vaccine strain - 13 of 13 B/Yamagata viruses belonged to genetic clade 3, where strains react well with the vaccine strain in the trivalent vaccine - 56 of 56 B/Victoria viruses belonged to the same genetic clade as the vaccine strain in the quadrivalent vaccine Analysis for mutations associated with resistance to neuraminidase inhibitors: - 241 viruses analysed - Two oseltamivir-resistant A(H1N1)pdm09 viruses detected Phenotypical analysis for resistance to oseltamivir and zanamivir: - 34 viruses analysed - All tested viruses were sensitive to both oseltamivir and zanamivir

Epidemiological surveillance

Vaccination coverage

Since 2003, data on vaccination coverage among persons 65 years old and older have been gathered by Sweden's 21 county medical officers for their respective county councils.[2] Various methods for estimation have been used in different counties, including the use of vaccination registries, the number of vaccine doses given or distributed, sentinel reports on vaccination coverage, surveys among GPs, or patient record data. Although the methods vary between counties, the methods have been roughly the same within the counties for the last five years. The data from the 21 county councils have been collated yearly after the influenza season to monitor changes in vaccine acceptance and the progress toward the WHO and EU target of 75% vaccination coverage in this age group. The analysis provides a rough estimate of the proportion of those over 65 years old who were vaccinated against influenza each season.

Since the 2014–2015 season, an estimate of the vaccination coverage in medical risk groups under the age of 65 years has also been included, using data from 12 county councils[3] where data on vaccines by age group are available.

Webbsök

Webbsök ("Web search") is an automated system established in 2008 that uses a statistical model and completely anonymous data from a medical advice website to estimate the development of sentinel influenza-like illness (ILI) incidence. Data are received daily and collated weekly. The results are published on the web every Monday morning during the influenza season in the form of a graph, which is three days ahead of the publication of the weekly influenza bulletin.

Telephone advice line

In collaboration with the telephone advice service 1177 Vårdguiden, the Public Health Agency receives aggregated weekly data on calls from a system called Hälsoläge. The age group (child or adult) and reason for calling are registered for all callers. Only one reason for contact can be stated per call; if a caller describes multiple symptoms, the most important one is registered as the reason for contact. Anonymised data on reasons for calling that might indicate an upper respiratory infection are analysed by the Public Health Agency each week. The reported data include the number of calls related to cough (adults, children separately), fever (adults, children separately), and sore throat (all ages combined). The proportion of

[2] Between 2003 and 2014, one of the county medical officers or their staff collated the vaccination coverage data. In 2014, this task was transferred to the Public Health Agency.

[3] Gävleborg, Halland, Jämtland, Jönköping, Kalmar, Kronoberg, Norrbotten, Stockholm, Värmland, Västernorrland, Västra Götaland, and Östergötland.

calls related to fever among children has been found to be a good indicator of influenza activity in the community.

Antiviral Sales

Every Monday, the Public Health Agency receives data from the Swedish eHealth Agency (eHälsomyndigheten) on the previous week's sales of the antivirals zanamivir and oseltamivir. Data include all sales categories, i.e. prescriptions and health care requisitions.

Hälsorapport

Hälsorapport ("Health report") is a web-based reporting system that builds on the experience and knowledge gained from the Sjukrapport and Influensakoll systems (see previous annual reports). Approximately 35,000 persons aged 0 to 85 years were randomly selected and invited to participate in Hälsorapport from November 2015 to November 2016. About 5,000 of the invited persons or parents of the invited children agreed to participate and have been sent a monthly survey during the year, including one on influenza vaccination and medical risk for severe influenza. Weekly symptom reporting is not currently in progress; however, the system is being tested and updated to ensure that such reporting can easily be added should the need arise.

Because Hälsorapport is a pilot study and data analysis was still on-going at the time of this report's publication, its results will not be presented here.

Laboratory reporting of influenza

Between May 2009 and November 2015, all laboratory-confirmed influenza A(H1N1)pdm09 cases were reported in accordance with the Communicable Diseases Act. As of December 1, 2015, statutory reporting was removed for influenza A(H1N1)pdm09, and instead statutory reporting was introduced for influenza A and B. The additional clinical report that had been mandatory for hospitalised patients with laboratory-confirmed influenza A(H1N1)pdm09 was also removed. All microbiological laboratories are now required to report all laboratory-confirmed cases of influenza. There is no requirement, however, for the laboratories to subtype positive cases and as such cases are primarily reported as influenza A or B. The reporting is done through the SmiNet system. Denominator data (the total number of samples analysed) is reported voluntarily via e-mail.

Voluntary reporting of influenza cases in intensive care

The Public Health Agency receives daily, anonymized data on influenza patients in intensive care through a collaboration with the Swedish Intensive Care Registry (SIR). A special influenza module in the registry, known as SIRI, allows the treating physician at an intensive care unit to report age, sex, underlying medical

conditions, complications, antiviral treatment, vaccination status, and influenza type for patients under treatment.

In addition to the data available through SIRI, the Public Health Agency can also create aggregated reports at SIR's public web portal.[4] Aggregated reports show all completed periods of intensive care for patients diagnosed with influenza, either as primary or secondary/other diagnosis, for patients whose intensive care has ended.

Excess mortality

In order to identify crude and influenza-related excess mortality during the influenza season, the aggregate number of deaths is transferred from the Swedish Tax Agency each week and analysed by the Public Health Agency as part of the European monitoring of excess mortality for public health action (Euro-MOMO) collaboration. The EuroMoMo model estimates the crude excess mortality for the whole country, by age group, and regionally for the northern, eastern, and southern parts of Sweden. As of the 2015–2016 season, the FluMoMo model has provided weekly estimates of excess mortality due to either influenza activity or extreme temperatures. The model uses data on the number of deaths regardless of cause, the average temperature, and the percentage of samples analyzed found to be positive for influenza each week. Analyses are performed for the whole country and by age group.

Deaths within 30 days after influenza infection

The Public Health Agency has access to data on individual deceased persons through the Swedish Tax Agency. A search in this registry is performed intermittently to identify which influenza patients are deceased and to retrieve their dates of death. As of December 1, 2015, it is possible to include all reported influenza cases in the analysis. However, comparisons to previous seasons are not easily done because only influenza A(H1N1)pdm09 cases were previously reportable (May 2009–Nov 2015).

The number of influenza-related deaths is estimated by calculating the time between diagnosis of influenza and death. If 30 days or fewer have elapsed, the death is considered to be influenza-related. This measurement is imprecise because the death might have been caused by something else entirely, and the timing is just a coincidence, but this measure is nonetheless frequently used in influenza surveillance. Importantly, this measure excludes anyone who might have died from influenza without getting a laboratory-confirmed diagnosis, meaning that there is most likely a large number of unrecorded deaths from influenza.

[4] SIR's web portal is open for anyone to use: http://portal.icuregswe.org/ver2/

Virological surveillance

Sentinel sampling

Only a minority of cases of ILI is caused by influenza. As such, other epidemics that lead to ILI are sometimes misconstrued as influenza epidemics. In order to estimate what proportion of the patients seeking care for ILI actually has influenza, sentinel physicians, infectious disease clinics, and paediatric clinics are encouraged to collect nasal samples from patients with ILI. The Public Health Agency carries out laboratory analyses for influenza free of charge for these samples. Representative positive samples are also used to characterize the circulating strains of influenza.

Virological analysis of sentinel samples contributes to national and international surveillance of circulating influenza viruses. Patient characteristics, including age, sex, risk factors, syndrome (ILI vs. acute respiratory illness (ARI)), and vaccination status, are analysed with respect to the types of influenza that are circulating.

Subtyping and lineage typing

All diagnostic laboratories perform typing by real-time PCR for influenza A and B. Three of these laboratories (Göteborg, Lund, and Umeå) also perform subtyping for A(H3N2) and A(H1N1)pdm09, but none perform influenza B lineage typing. The Public Health Agency of Sweden performs subtyping and lineage typing by real-time PCR for all samples sent in to the agency from the diagnostic laboratories and on all positive samples analysed within sentinel surveillance.

Virus characterisation

Selection of samples for further characterisation

Influenza-positive samples are collected from laboratories and from the sentinel surveillance program. Samples representing different geographical locations, collection time periods, and types/subtypes are selected for further characterisation. In addition, laboratories are asked to send influenza-positive samples from severely ill or deceased patients, patients with vaccine failure, and patients who do not respond to antiviral treatment. Because isolation of influenza virus on cell cultures in Sweden is only performed by the Public Health Agency of Sweden, and because phenotypic analyses such as the neuraminidase inhibition (NAI) and hemagglutinin inhibition (HAI) assays need isolated virus, Swedish laboratories are continuously asked to provide a representative selection of specimens that can be isolated on cell culture.

Characterisation methods

Characterisation of influenza viruses at the Public Health Agency of Sweden is mainly performed by sequence analysis. This season, the majority of the

sequencing for both influenza A and B was full-genome sequencing performed with NGS (Next Generation Sequencing) on an Ion Torrent platform using direct material (i.e. not virus isolates). This method allows for subtyping of all known influenza A subtypes.

Through NGS, the hemagglutinin (HA) gene is characterised with respect to vaccine similarity and changes in receptor affinity (lung receptors versus upper respiratory tract receptors). In addition, the HA target sequences for the subtype/lineage-specific real-time PCR systems used for detection of influenza in clinical samples are analysed for sequence mismatches compared to the real-time PCR primers and probes. The neuraminidase (NA) gene is analysed with respect to amino acid substitutions known to result in reduced or highly reduced inhibition by NA inhibitors according to guidelines from the WHO. Two aspects of the matrix protein (M) gene are analysed by sequencing, and the M2 gene of influenza A is analysed for amino acid substitutions resulting in resistance to amantadine, and the M target sequences of both influenza A and B of the real-time PCR systems are analysed for sequence mismatches. The genes for non-structural protein 1 (NS1) and polymerase basic protein 2 (PB2) are analysed for mutations known to be associated with changes in virulence.

Some genetic characterisations are also performed by real-time PCR, including influenza B lineage typing and H275Y mutation analysis of influenza A(H1N1)pdm09 viruses. Phenotypic analysis of sensitivity to NA inhibitors is performed with the NAI assay, which requires viruses isolated on cell culture. This analysis generates IC_{50} values (half maximal inhibitory concentration) for oseltamivir (Tamiflu®) and zanamivir (Relenza®) from which the sensitivity of the influenza virus to these inhibitors is calculated and interpreted according to criteria given by the WHO.

A representative selection of the isolated virus samples is sent to the WHO CC in London for antigenic characterization of HA by HAI assay and for phenotypic analysis of sensitivity to NA inhibitors by NAI assay.

Additional monitoring activities

Ad hoc reporting

The county medical officers report anything noteworthy regarding influenza that has come to their attention within their counties, primarily by means of a weekly telephone conference. Informal information regarding outbreaks from the health care sector and the public is also followed up during these conferences.

International events

Foreign epidemiology and virology is monitored through the websites of the WHO and the European Centre for Disease Prevention and Control (ECDC) as well as other national and regional websites and media sources. International reporting on influenza-related research, outbreaks, and other events in the media is also monitored.

Reporting

National reporting

During the influenza season, the Public Health Agency condenses national and international data into a detailed weekly bulletin that is published on the agency's website.[5] A preliminary summary of the 2015–2016 season was included in the week 21 bulletin.[6] The bulletin provides timely analysis of the current situation in Sweden and abroad and has a wide readership. In fact, the influenza bulletin webpage was the second-most visited page (excluding the entrance pages) of the agency's website during the season, with 90,545 unique viewings.

Where necessary, the county medical officers, microbiological laboratories, the National Board of Health and Welfare, and other concerned authorities are informed of exceptional events.

The media have access to updated influenza data through the bulletins on the Public Health Agency's website, as well as new items published as needed. During seasonal epidemics, the Public Health Agency is normally contacted by the national media and participates in TV and radio interviews and answers questions for online and print media.

International reporting

The Public Health Agency is the WHO National Influenza Centre for Sweden and is part of the European Influenza Surveillance Network (EISN), the ECDC's network dedicated to the monitoring of influenza. As such, the Public Health Agency has an important commitment to report epidemiological influenza data weekly to the ECDC database TESSy, which then forwards the data to the WHO database FluNet.

A representative selection of the influenza-positive samples collected through the sentinel surveillance system and directly from regional laboratories is isolated and sent to the WHO CC in London for further characterisation, as mentioned above.

Characterisation data, including NAI results from the WHO CC, are reported to TESSy and to the Global Initiative on Sharing All Influenza Data (GISAID).

Following the end of the season, a detailed annual report (which you are reading) is sent to the WHO and the ECDC and is published on the Public Health Agency's webpage.

---

[5] https://www.folkhalsomyndigheten.se/folkhalsorapportering-statistik/statistikdatabaser-och-visualisering/sjukdomsstatistik/influensa-veckorapporter/aktuell-influensarapport/

[6] https://www.folkhalsomyndigheten.se/pagefiles/21772/Influensarapport_2016v19-20_finalversion%20v1.pdf

Epidemiological data

Vaccination coverage

Coverage among those 65 years of age and older

The national vaccination rate among those ≥65 years of age was approximately the same as the previous season, although most counties vaccinated fewer people. In total, an estimated 925,000 people were vaccinated, corresponding to 49.1% of the population ≥65 years of age, compared with 49.7% last season (see Table 2). Thus, vaccination coverage has remained constant at just under 50% for the past two years. Coverage increased in several counties, including Dalarna, Kalmar, Stockholm, and Västra Götaland (see Figure 2).

In Dalarna, where vaccination coverage is measured by a questionnaire among the elderly, the proportion who responded that they were vaccinated increased from 36% to 45% in the past year. In Västra Götaland, coverage increased by about 4 percentage points, in Kalmar by about 2 percentage points, and in Stockholm by about 2 percentage points. Coverage also increased slightly in Östergötland and Gävleborg.

The highest coverage rate was again achieved in Jönköping, where more than 60% of the elderly were vaccinated. In addition, Värmland, Kronoberg, Halland, and Blekinge attained a vaccination coverage of at least 55% (see Table 3 for vaccination coverage per county).

The statistics from Västernorrland and Jämtland do not include doses given at institutionalized care facilities, meaning that vaccination coverage is underestimated. Comparisons between years are possible, however, and in both counties, coverage fell compared to the previous season. Several other counties also saw decreased vaccination coverage, including Jönköping, Värmland, Kronoberg, Halland, Blekinge, Skåne, Västmanland, Norrbotten, Gotland, and Västerbotten.

Sörmland, where only data on the number of delivered doses of vaccine are available, saw a decrease from 40,000 the previous season to about 37,600 this season. According to data from primary care, approximately 24,000 persons aged ≥65 years were vaccinated in Sörmland. Using these two measures, vaccination coverage is estimated to lie between 39% and 61% in Sörmland.

This season, Uppsala was able to estimate vaccination coverage among those ≥65 years using financial data and data on vaccination in institutionalized care facilities for the first time. According to this method, vaccination coverage in this age group was 40%.

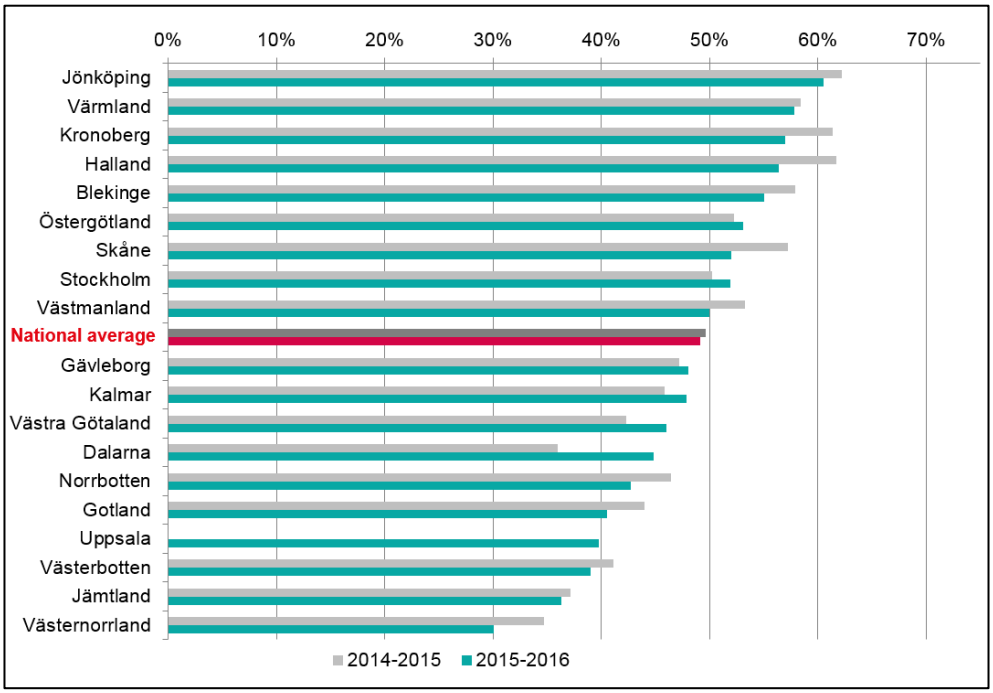
The estimates for Västra Götaland and Skåne that were used in this report were based on a vaccination registry and debited doses, respectively, but survey results are also available for both counties. For both counties, survey results showed a higher vaccination coverage (Skåne: 58%, Västra Götaland: 5%).

Table 2. Mean yearly proportion of vaccinated persons older than 65 years in Sweden, as estimated by the 21 county medical officers.

Season for vaccination	Estimated proportion of the population above 65 years old vaccinated with seasonal vaccine (%) *
2015–2016	49.1
2014–2015	49.7
2013–2014	45.8
2012–2013	44.2
2011–2012	46.1
2010–2011*	55.2
2009–2010**	44
2008-2009	65.8
2007-2008	60
2006-2007	56
2005-2006	61
2004-2005	55
2003-2004	51

* Please note that the number has been adjusted for the 2010–2011 season compared to previous annual reports in light of new information.
** Very few counties reported seasonal vaccination coverage in 2009 because the focus was on the pandemic vaccination. Sixty per cent of the Swedish population was vaccinated with an adjuvanted monovalent vaccine in 2009.

Figure 2. Estimated proportion of vaccinated persons above 65 years old per county council in Sweden, seasons 2014–2015 and 2015–2016



Note: Data from Jämtland and Västernorrland do not include doses given in long-term care facilities, etc., which will underestimate the coverage rate. In Sörmland, coverage is measured using the number of delivered doses, which cannot reliably be used to estimate doses given to elderly persons. In Uppsala, only delivered dose data were available in 2014–2015, so no value is shown. Data from Örebro for the 2015–2016 season are not yet available.

Table 3. Estimated proportion of vaccinated persons above 65 years old per county council in Sweden

County Council	2014–2015 (%)	2015–2016 (%)
Blekinge	58	55
Dalarna	36	45
Gotland	44	41
Gävleborg	47	48
Halland	62	56
Jämtland *	37	36
Jönköping	62	61
Kalmar	46	48
Kronoberg	61	57
Norrbotten	46	43
Skåne*	57	52
Stockholm	50	52
Sörmland *	-	-
Uppsala *	-	40
Värmland	58	58
Västerbotten	41	39
Västernorrland *	35	30
Västmanland	51	50
Västra Götaland*	42	46
Örebro	50	*
Östergötland	52	53
Average	**50 (49.7)**	**49 (49.1)**

Different estimation methods were used in each county, which makes comparison difficult. Percentages are based on the population of the county on December 31, 2014 and 2015, respectively. (Source: Statistics Sweden.) *See notes above under Table 2.

Vaccination coverage in medical risk groups

It is difficult to estimate vaccination coverage among the medical risk groups because these groups are hard to define and because data are often missing. The Swedish Board of Health and Social Welfare (*Socialstyrelsen*) has estimated that 5–10% of the population under 65 years of age belong to a medical risk group. Twelve county councils (see above) have data on the number of persons vaccinated under 65 years of age, although risk group status is often unknown. An analysis of these data show that, once again, only about 2% of those under 65 years of age were vaccinated during the 2015–2016 season (see Table 4 for breakdown by age group). The coverage is similar to that seen in the two previous seasons and indicates that many of those who could benefit the most from vaccination are not reached.

Table 4. Percentage vaccinated per age group
Data from County Councils in Gävleborg, Jönköping, Kalmar, Kronoberg, Norrbotten, Värmland, Västernorrland, and Västra Götaland.

Age Group	Percentage Vaccinated
0–17 years	0.5%
18–39 years	1.1%
40–64 years	3.9%
65–74 years	46.6%
75–84 years	54.2%
85+ years	57.1%
Average	
<65 years	50.3%
≥65 years	2.1%

Webbsök

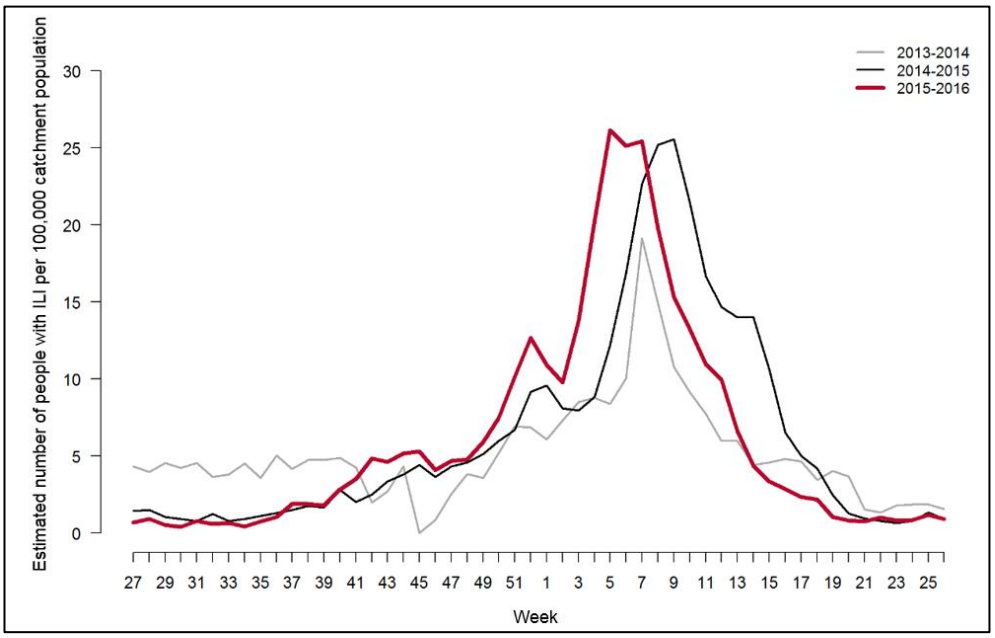
From week 27, 2015, to week 26, 2016, over 126,000 queries related to influenza were submitted to the 1177.se search engine. This is 14,000 fewer searches than during the previous season. In the 2013–2014 season, which was rather mild, 64,000 searches were made to the 1177.se search engine.

According to Webbsök, the 2015–2016 influenza season lasted for 18 weeks, from week 49, 2015, to week 13, 2016 (Figure 3). During three of these weeks (weeks 5–7), Webbsök showed a high level of influenza activity[7]. During the previous season (2014–2015), influenza activity lasted for 19 weeks and was at a high level for four weeks. The seasonal pattern corresponds largely to that seen in laboratory-based surveillance.

Webbsök again proved to be a reliable indicator of epidemic development (Figure 4). By providing data on Monday mornings, it provides an early signal of the activity in the previous week.

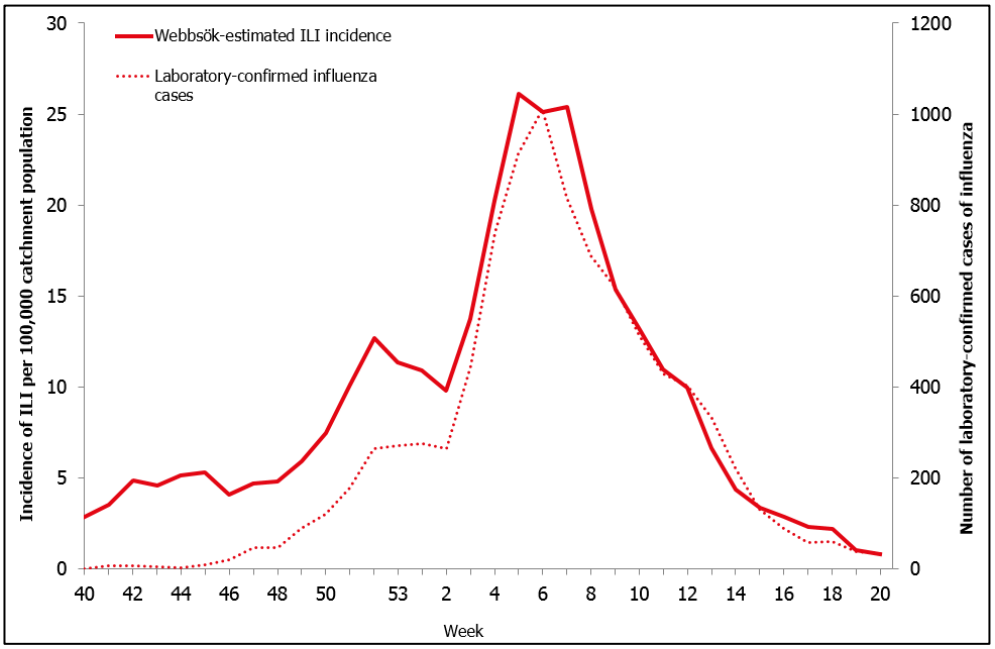
[7] The Webbsök threshold for a high level was 22 ILI patients per 100,000 population for the 2015–2016 season.

Figure 3. Webbsök's estimated proportion of the population with ILI per week, 2013–2016.



Webbsök's ILI estimate was above the epidemic threshold during weeks 51–13 of the 2013–2014 season, during weeks 50–16 of the 2014–2015 season, and during weeks 49–13 of the 2015–2016.

Figure 4. Webbsök's estimated proportion of persons with ILI and the number of laboratory-confirmed cases, 2015–2016. *The axes have been adjusted to highlight the matching trends reported through the two systems.*



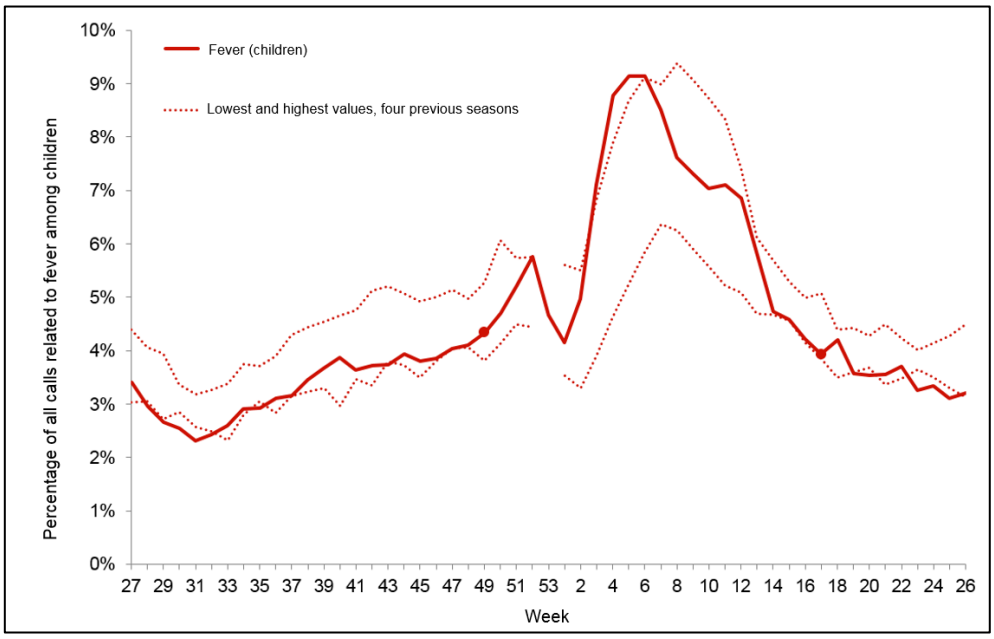
Telephone advice line

As previously noted, telephone calls to the medical telephone advice line 1177 Vårdguiden regarding fever among children has been found to be the best indicator from this source of influenza activity in the community.

The number of calls regarding fever among children exceeded the epidemic threshold in week 49, 2015. An average of 4.5% of the calls throughout the season were regarding children with fever (Figure 5). The highest number (7,286) and percentage of calls (9.1%) was registered during week 6, 2016. The total number of calls regarding fever among children was similar to the previous season (2014–2015). The peak weeks corresponded to the peak of laboratory-based surveillance.

A noticeable peak in calls is seen around the Christmas holidays every year, followed by a drop. The reason for this pattern might be decreased access to face-to-face health care services during the holidays leading to an increase in telephone consultations.

Figure 5. Percentage of telephone calls regarding fever in children received by the medical advice line 1177 Vårdguiden, 2015–2016.

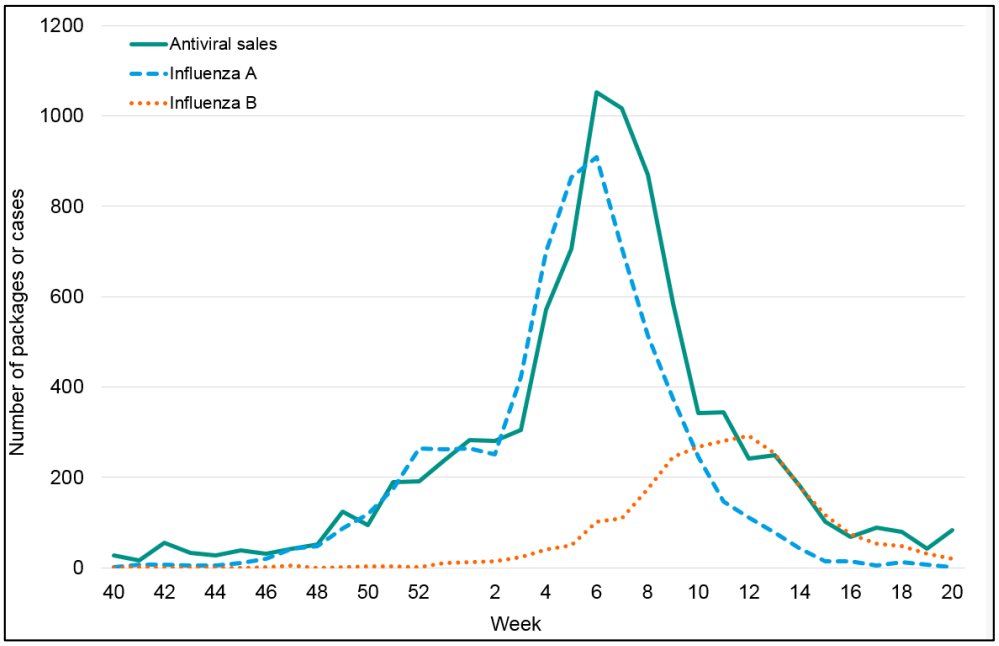


*The dots indicate the start and end points of the epidemic.

Antiviral sales

Figure 6 shows total sales of antivirals and the number of laboratory-confirmed cases of influenza A and B during the 2015–2016 season. The highest peak of both series was reached in week 6, 2016.

Figure 6. Antiviral sales and number of laboratory-confirmed cases of influenza A and B per week, 2015–2016



Over the past four seasons, total antiviral sales varied from just over 3,250 packages in the 2013–2014 season to just under 9,000 packages in the 2014–2015 season, with 8,647 packages sold during the 2015–2016 season (see Table 5). The total volume of sales and of laboratory-confirmed cases follow each other over time.

Table 5. Total antiviral sales and laboratory-confirmed influenza cases in the past four seasons

	Antiviral sales	**Influenza cases (A and B)**
2012–2013	6,788	8,197
2013–2014	3,271	2,607
2014–2015	8,998	10,389
2015–2016	8,647	9,134

Hälsorapport

During January 2016, participants in Hälsorapport received a questionnaire about influenza vaccination and risk group status. Overall, 4,220 participants responded to the survey (approximately 91%). Of the respondents, just under 11% said they had one or more of the diseases/conditions that were listed or were pregnant during the autumn/winter. An additional 25% of the adult participants were 65 years of age or older, but did not otherwise belong to a risk group.

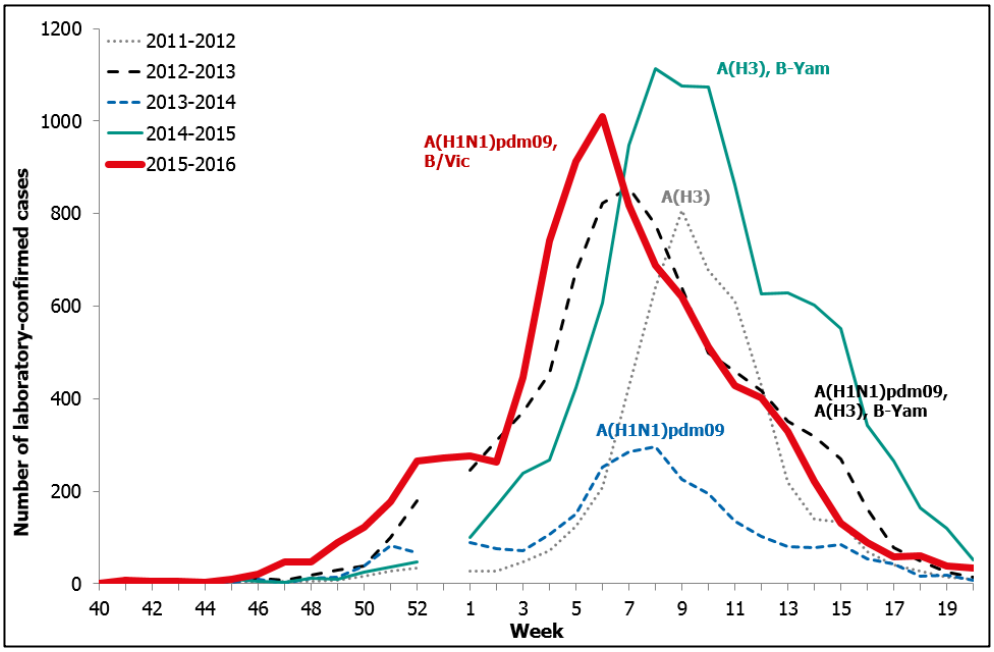
About half of all those who were characterized as belonging to a risk group had been vaccinated this season. The most common risk disease/condition among participants was asthma at 40%, which means that the percentage of participants

belonging to a medical risk group is likely overestimated. In reality, only those with severe asthma would likely be recommended vaccination by the treating physician or nurse.

Laboratory-based surveillance

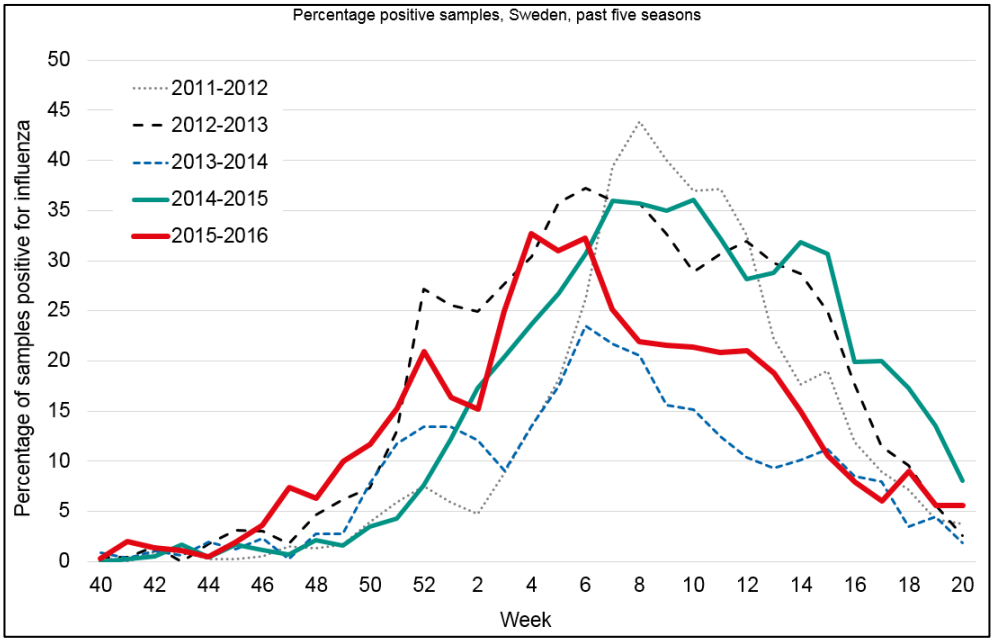
The influenza season was dominated by influenza A(H1N1)pdm09 followed by a smaller wave of influenza B/Victoria towards the end of the season. The influenza epidemic started in week 49 and peaked in week 6, 2016, with 1,010 laboratory-confirmed cases nationally (see Figure 7). In total, 9,155 cases were reported during the season, which was fewer compared to the previous, intense season of 2014–2015, for which over 10,000 cases were reported.

Figure 7. Total number of laboratory-confirmed cases of influenza (all types) per week and the dominating influenza type(s) per season from 2011 to 2016.



More than 48,000 people were tested for influenza during the season, which was higher compared to the 2014–2015 season. Overall, 19% of samples taken were positive for influenza A or B (Table 6). The percentage of positive samples was the highest during weeks 4–6 at 31–33%, which was lower compared to previous, intense seasons when peaks have reached 35% or higher (see Figure 8).

Figure 8. Percentage of samples testing positive for influenza, per week, in the past five seasons.



Viral distribution

The 2015–2016 season was dominated by influenza A with 6,727 confirmed cases (74% of all cases), followed by influenza B with 2,423 confirmed cases (26% of all cases) (Figure 9 and Table 6). The majority (90%) of the cases during the peak of the season were influenza A, and of those samples subtyped, influenza A(H1N1)pdm09 was by far (95%) the most common subtype. After the peak of influenza A(H1N1)pdm09 activity, the season shifted towards influenza B in week 9.

Influenza B activity peaked weeks 9-13 and continued to dominate until the end of the season. The Public Health Agency determined the lineage of 136 samples that were positive for influenza B, of which the majority (76%) were influenza B/Victoria. The wave of influenza B had weekly case counts similar to previous high-activity influenza B-dominant or co-dominant seasons, although the wave was significantly smaller than that of the previous season (Figure 10).

Figure 9. Number of laboratory-confirmed cases by influenza type and week, 2015–2016.

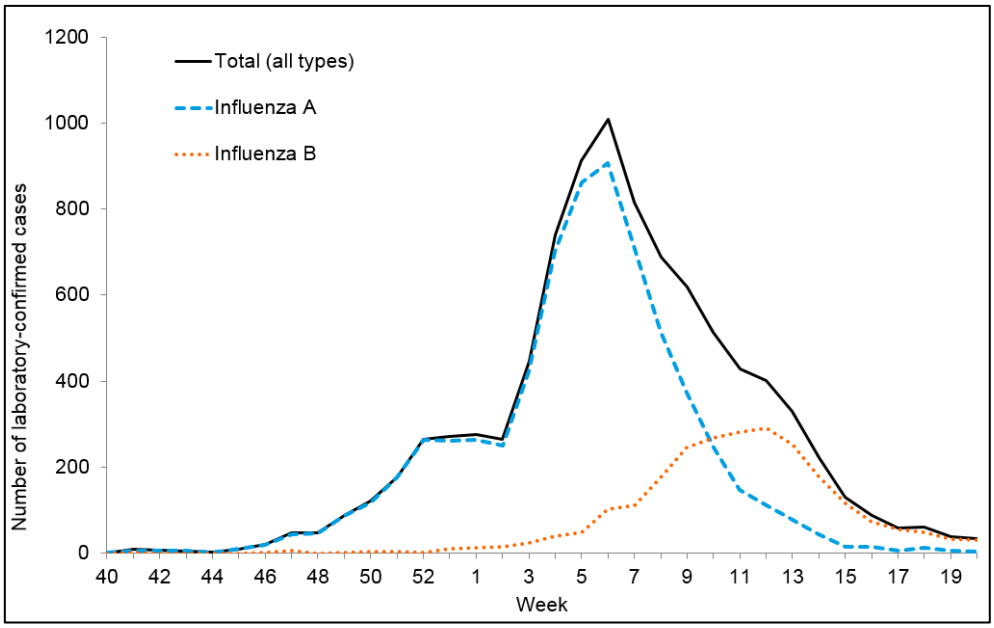
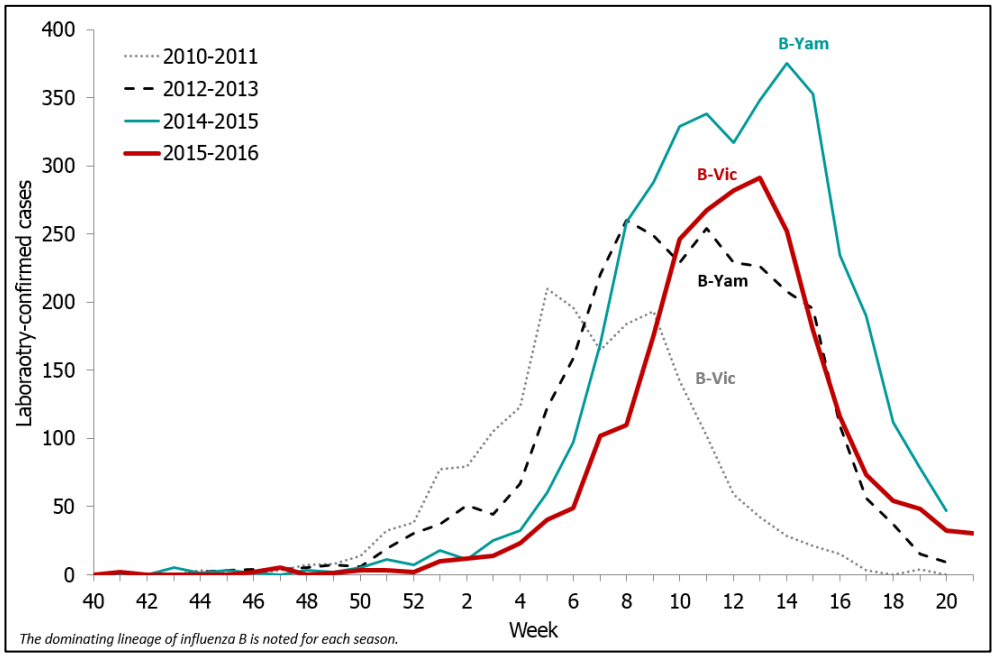


Figure 10. Number of laboratory-confirmed cases of influenza B per week during recent B-dominant seasons.



Note: During the 2010–2011 season, influenza B/Victoria and A(H1N1)pdm09 co-dominated with 50% and 31% of the positive cases, respectively. In the 2012–2013 season, dominance was split three ways by influenza B/Yamagata, A(H1N1)pdm09, and A(H3N2), with approximately one third of the positive cases each. In the 2014–2015 season, influenza A(H3N2) accounted for 69% of cases, and B/Yamagata accounted for 23%.

Table 6. Laboratory results of samples analysed and reported through the laboratory reporting system over the last four seasons.

	2012–2013	2013–2014	2014–2015	2015–2016
Analysed samples	**31,750**	**22,330**	**42,668**	**48,135**
Proportion positive samples	*25.8%*	*11.6%*	*24.30%*	*19.0%*
Total positive for influenza A	**5,340**	**2,372**	**6,671**	**6,727**
A(H1N1)pdm09 *	2,435	1,737	663	2,049
A(H3N2)	548	169	2,052	112
A, not subtyped**	2,357	466	3,956	4,566
Total positive for influenza B	**2,857**	**213**	**3,718**	**2,423**
B/Victoria lineage***	8	2	2	59
B/Yamagata lineage***	148	24	63	19
B, not typed to any lineage	2,701	187	3,653	2,345

* Not typed as N1, but classified as A(H1N1)pdm09 based on H1 typing.
** For the period 2012–2015, influenza A cases not subtyped but A(H1N1)pdm09-negative were considered to be influenza A(H3N2) cases. Data on subtype for the 2015–2016 season come from the Public Health Agency and the three regional laboratories that regularly perform subtyping.
*** All typing for lineage was performed at the Public Health Agency laboratory.

Age and sex distribution

The dominance of influenza A(H1N1)pdm09 is reflected in the age distribution of the influenza A cases (see Table 7 and Figures 11A-B). Children aged 0–4 years old had the highest incidence for both influenza A and B, with 130 and 41 cases per 100,000 populations, respectively. The highest proportion of influenza A cases (33%) was seen among individuals aged 40–64 years, followed by individuals aged 65 years or older (27%).

The highest proportion of influenza B cases (37%) was seen among individuals aged 15–39 years. The proportion of influenza B per age group was similar to the 2010–2011 season in, which was the last season B/Victoria circulated in Sweden.

The median age of the cases of the respective influenza types is presented in Table 8. There was no significant difference in sex distribution.

Table 7. Number (No.) and incidence (Inc.) per 100,000 population and age group of laboratory-confirmed cases of influenza A and influenza B in Sweden, 2015–2016.

Age group	Influenza A		Influenza B		Total influenza	
	No.	Inc.	No.	Inc.	Total No.	Total Inc.
0-4 years	764	130.3	238	40.6	1,002	170.9
5–14 years	296	26.2	263	23.3	559	49.4
15–39 years	1,647	53.3	904	29.3	2,551	82.6
40–64 years	2,205	71.2	346	11.2	2,551	82.4
>65 years	1,809	92.9	669	34.4	2,478	127.3
Total	6,721	68.2	2,420	24.6	9,141	92.8

Table 8. Median age (years) of patients reported through the statutory and voluntary laboratory reporting systems combined during the last three seasons.

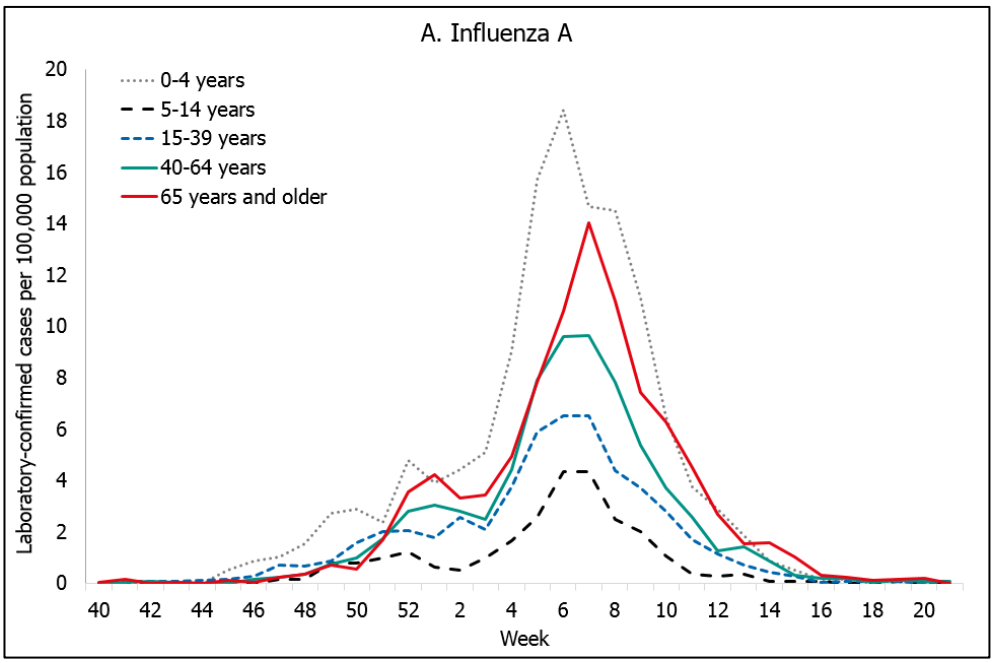
	2012–2013	2013–2014	2014–2015	2015–2016^
Influenza A	-	-	-	48
Influenza A(H1N1)pdm09	39	45	50	-
Influenza A(H3N2)*	64	58	72	-
Seasonal influenza B**	46	49	60	33

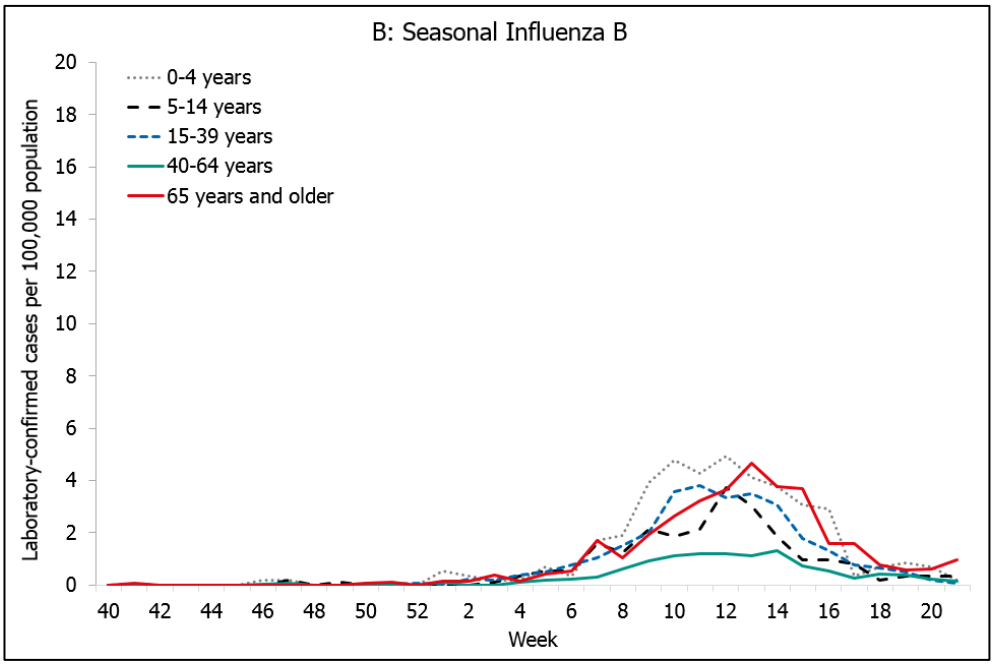
* For the period 2012–2015, all influenza A-positive samples that were negative for A(H1N1)pdm09 were classified as influenza A(H3N2).

** The median age for influenza B-positive samples was calculated for all types combined because only a small portion of the samples were analysed for lineage.

^ For the 2015–2016 season, the mandatory reporting of influenza only includes influenza A and B and no subtyping.

Figure 11. Weekly incidence of influenza A and B per age group in Sweden, 2015–2016 season (see panels A and B).



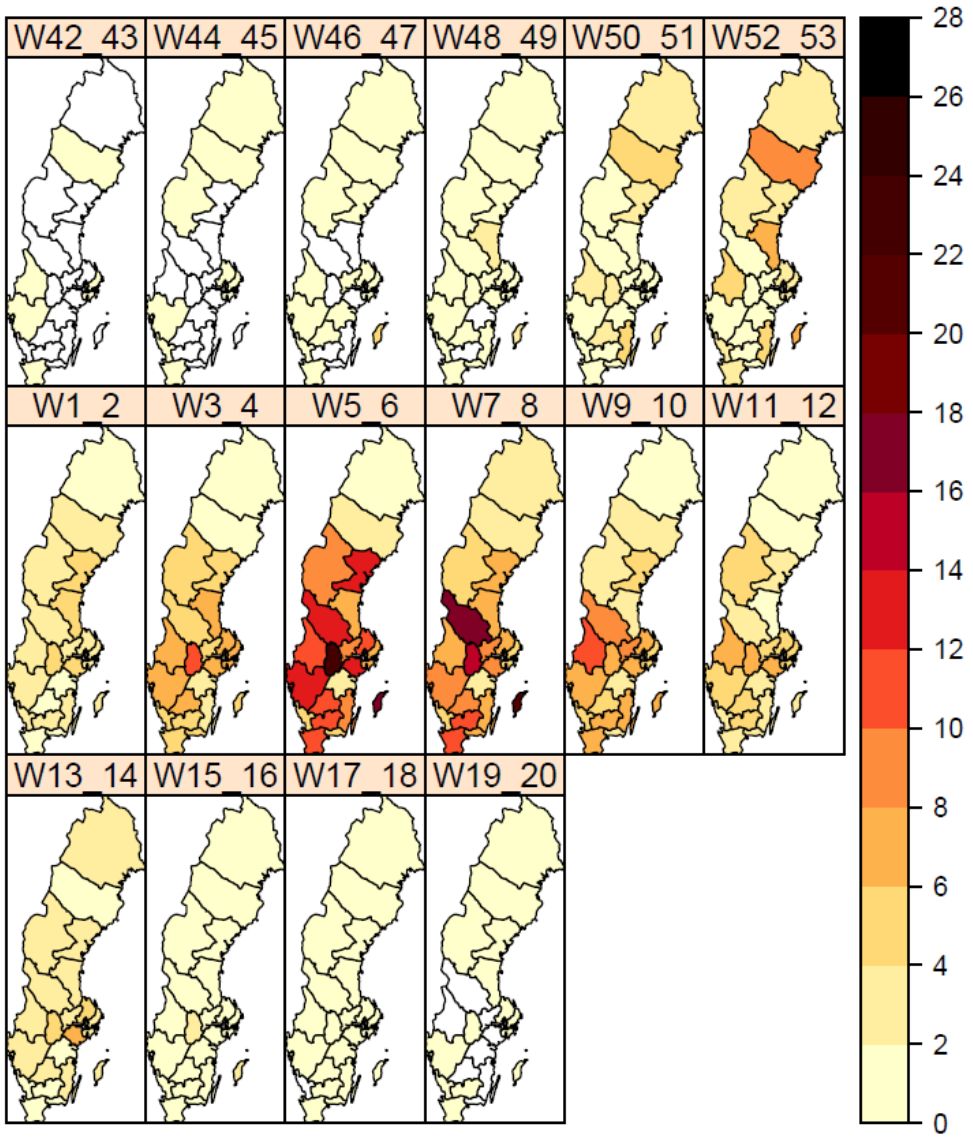


Geographic distribution

The influenza epidemic spread throughout Sweden. The northern parts (Norrland) of Sweden had a more intense start of the season compared to the rest of the country. The percentage of positive samples peaked in Norrland in week 52, while the middle parts of Sweden (Svealand) saw a peak in week 4, and lastly the southern parts (Götaland) in week 6 (see Figure 12). The incidence was also higher in the northern parts of Sweden in the beginning of the season compared to the rest of the country.

The cumulative incidence for the season was the highest in Svealand (middle of Sweden), with a cumulative incidence of 101 cases per 100,000 population. Incidence in Götaland (southern Sweden) was 90 cases per 100,000 population, and in Norrland (northern Sweden) it was 74 cases per 100,000 population. The largest numbers of cases were reported from the large urban regions of Stockholm, Västra Götaland (Gothenburg) and Skåne (Malmö). When looking at the number of reported cases in relation to the population, Örebro, Gotland, Sörmland, Värmland, Dalarna, and Västra Götaland had the highest cumulative incidence, with 100 cases per 100,000 population or higher. It is difficult to draw any conclusions regarding differences in intensity of the epidemic based on differences in incidence of laboratory-confirmed cases due to the large variations in sampling frequency among counties.

Figure 12. Bi-weekly incidence of laboratory-confirmed influenza per 100,000 population and county from week 42, 2015, to week 20, 2016. *The colour scale indicates the incidence; white indicates an incidence of 0 or (for the period of week 42–47) that no report was received from the county laboratory.*



Influenza cases in intensive care

Data reported through SIRI

A total of 363 patients in intensive care with laboratory-confirmed influenza infection were reported through SIRI during the season, excluding duplicates.

The majority, 315 cases (87%), were infected with influenza A, while 48 cases (13%) were infected with influenza B (Table 9). The median age of the patients for all influenza types was 56 years. The majority of the cases, 156 cases, were 40–64 years old. A significant difference was seen in the sex distribution, with more men (60%) than women (40%) reported.

Of the patients in intensive care, 245 cases (67%) belonged to a medical risk group or were ≥65 years of age. However, among cases aged 40–64 years, more than 50% did not belong to a medical risk group. Similarly, 40% of patients aged 15–39 years did not belong to a medical risk group. Chronic heart-lung disease (n = 108), immunosuppression (n = 54), and extreme obesity (n = 27) were the most common risk factors, just as in previous seasons. Eight of the cases reported were pregnant.

Overall, 245 cases were recommended for seasonal influenza vaccination either due to having a medical risk group or due to age. Of these, vaccination status was known for 148 patients (41%), of whom 17 cases were vaccinated (12%).

Of the 363 cases treated in intensive care for influenza during the season, 89 cases died. Of those who died, 74 cases belonged to a medical risk group or were 65 years or older and at greater risk for severe influenza. Conversely, 15 of the fatal cases did not belong to a risk group.

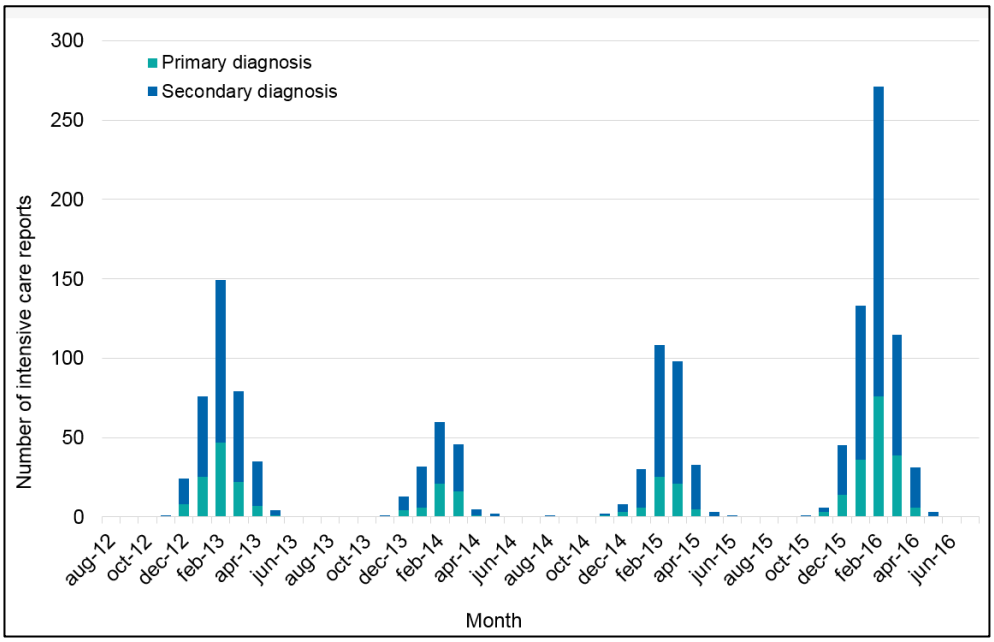
Table 9. Age distribution of laboratory-confirmed influenza patients in intensive care by influenza type.

Reported influenza type	Number of patients	Median age in years (min, max)
A(H1N1)pdm09	154	57 (0, 88)
A(H3N2)	4	56 (9, 84)
A, no subtype stated	157	56 (2, 88)
B	48	45.5 (0, 89)
Total	**363**	**56 (0, 89)**

Data from SIR

In addition to the data available through SIRI, the Public Health Agency can also create aggregated reports at SIR's public web portal. Aggregated reports show all completed periods of intensive care for patients diagnosed with influenza, either as primary or as secondary/other diagnosis for patients whose intensive care has ended. An analysis of these data also shows that a higher number of patients with influenza received intense care during the 2015–2016 season than in other recent seasons (see Figure 13).

Figure 13. Number of patients with laboratory-confirmed influenza who received intensive care per season, 2012–2016



Most intensive care units are connected to SIR (89 units), and as such are able to report to SIRI – however, it must be noted that such reporting is voluntary. The number of units registered for reporting with SIR has remained relatively constant during the period 2012–2016. A preliminary evaluation of SIRI regarding coverage shows that the system is improving, and the number of units reporting to SIRI has more than doubled since its inception in the 2012–2013 season (from 22 units to 53 units). A large part of this increase took place this season, when 22 new units began reporting to SIRI.

The increase in the number of reporting units makes it difficult to compare the crude number of reported patients in intensive care over time. However, if a comparison is made using only the units reporting in all seasons (n = 16), 22% more cases were reported this season than in 2012–2013, and 35% more than in 2014–2015 – both of which were intense seasons. Using only data from units reporting in the previous and current season (n = 31), the number of cases was 43% higher this season.

In terms of the reporting of influenza-positive cases in intensive care, coverage has also improved. Looking only at comparable reports, a total of 431 cases with an influenza diagnosis were reported through SIR for the 2015–2016 season[8], and 321 were reported through SIRI. A comparison of these totals gives an indication of the coverage rate of SIRI and suggests that about 75% of the SIR cases were also reported in SIRI this season compared with about 50% in the 2012–2013 and 2013–2014 seasons (see Table 10).

[8] As of July 28, 2015.

Table 10. The number of intensive care patients with laboratory-confirmed influenza, per season, reported to SIR and SIRI

	Total in SIR	Total in SIRI	Percentage reported in SIRI
2012–2013	258	135	52 %
2013–2014	111	54	49 %
2014–2015	223	176	79 %
2015–2016	431	321*	75 %

** Although a total of 363 patients have been reported through SIRI, 42 of these patients have not ended their care and are thus excluded from this comparison (SIR data only include patients whose intensive care has ended).*

Influenza-related excess mortality

During the 2015–2016 season, there was significant excess mortality seen in the age group 15–64 years of age, but not in the population as a whole or among the elderly (see Figure 14).[9] The excess mortality among individuals 15–64 years of age was seen weeks 4–6, which is the period leading up to and including the peak of influenza A(H1N1)pdm09 activity in the country. The Euro-MOMO project also estimated a statistically significant influenza-related excess mortality in the age group of 15–64 years on the European level (http://www.euromomo.eu/).

Data from the previous five seasons have also been used in the FluMoMo model. Table 11 below shows which weeks each season (if any) had a significant influenza-related excess mortality overall or for a specific age group.

Table 11. Weeks with significant influenza-related excess mortality per age group (only significant age groups shown), 2010–2011 season to 2015–2016 season.

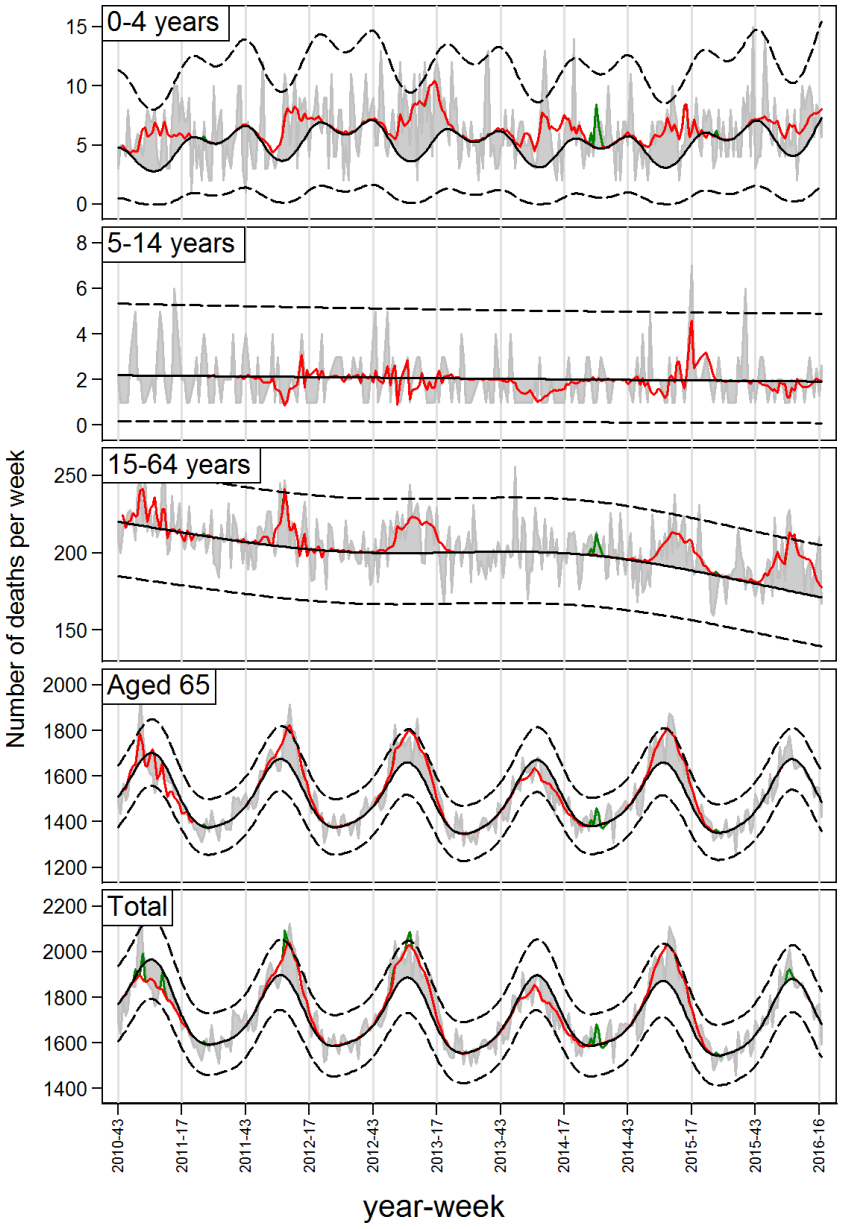
Season*	Week	Age Group
2011–2012	Week 7, 2012	15-64 years
	Week 8, 2012	≥65 years
	Week 9, 2012	total population, ≥65 years
	Week 10, 2012	≥65 years
2014–2015	Week 7, 2015	total population, ≥65 years
	Week 8, 2015	total population, ≥65 years
	Week 10, 2015	total population, ≥65 years
2015–2016	Week 4, 2016	15–64 years
	Week 5, 2016	15–64 years
	Week 6, 2016	15–64 years

**No significant excess mortality was seen in any age group or in the total population during the 2010–2011, 2012–2013, or 2013–2014 seasons.*

[9] Figure 13 shows the expected number of deaths in black, the actual number of deaths in grey, influenza-related excess mortality in red, and temperature-related excess mortality in green, as estimated by the FluMoMo model. Some variation in the number of deaths is expected week to week, which is illustrated with the dashed lines marking the 95% confidence intervals for the estimates. That is, if the estimated excess mortality is within these bounds, it is not statistically significant. However, if it touches or exceeds these boundaries, it is considered a significant excess mortality.

In the previous season (2014–2015), a significant influenza-related excess mortality was seen in the age group ≥65 years during peak weeks 7, 8, and 10 (see Figure 14). This is the group where influenza-related excess mortality is most often seen, particularly during seasons dominated by A(H3N2), as was the case in the 2014–2015 season. Previous seasons of intense influenza A(H3N2) activity, such as 2012–2013 and 2011–2012, highlight how common influenza-related excess mortality is in the elderly.

Figure 14. Number of deaths per week (grey), influenza-related excess mortality (red), and temperature-related excess mortality (green) in each age group and in total, in Sweden 2010–2016.



Deaths 30 days after influenza diagnosis

In total, 261 of 8,652 persons who received an influenza diagnosis during the 2015–2016 season and whose personal identification number was included in the case report, had died within 30 days of diagnosis. Of these, 217 had influenza A and 44 had influenza B. Of the influenza A cases who died, 24 were subtyped as A(H1N1)pdm09, while the remaining 193 were not subtyped. During this season, it is reasonable to assume that most of these had influenza A(H1N1)pdm09.

The vast majority of deaths within 30 days occurred among the elderly (79%), followed by adults aged 40–64 years (18%, see Table 12). Five children died, aged 2, 4, 5 (two children), and 8 years. All but one had an un-subtyped influenza A-infection, and the fifth had confirmed influenza A(H1N1)pdm09.

Approximately 9.2% of persons 65 years of age and older with laboratory-confirmed influenza A had died within 30 days. This percentage is within the normal range when compared to data from previous seasons on deaths within 30 days of influenza A(H1N1)pdm09 diagnosis in this age group (in past seasons, this was 7–13%). Two percent of those in the age group 40–64 years with influenza A died within 30 days, which also matches data from the past few seasons.

Of those persons 65 years of age and older with laboratory-confirmed influenza B, 5.8% had died within 30 days. Because this is the first season of data for influenza B, no comparisons with previous seasons can be made.

Table 12. The number and incidence of laboratory-confirmed cases and deaths within 30 days per age group for influenza A and influenza B

Influenza A	Cases	Incidence of influenza	Deaths within 30 days	Incidence of death	Percentage of cases who died (%)
0–4 years	764	130.3	2	0.34	0.3
5–14 years	296	26.2	3	0.27	1.0
15–39 years	1,647	53.3	2	0.06	0.1
40–64 years	2,205	71.2	43	1.55	2.0
65+ years	1,809	92.9	167	10.58	9.2
Total	**6,721**	**68.2**	**217**	**2.65**	**3.2**
Influenza B					
0–4 years	238	40.6	0	0.00	0.0
5–14 years	263	23.3	0	0.00	0.0
15–39 years	904	29.2	0	0.00	0.0
40–64 years	346	11.2	5	0.16	1.4
65+ years	669	34.4	39	2.00	5.8
Total	**2,420**	**24.6**	**44**	**0.45**	**1.8**

Virological data

Sentinel sampling

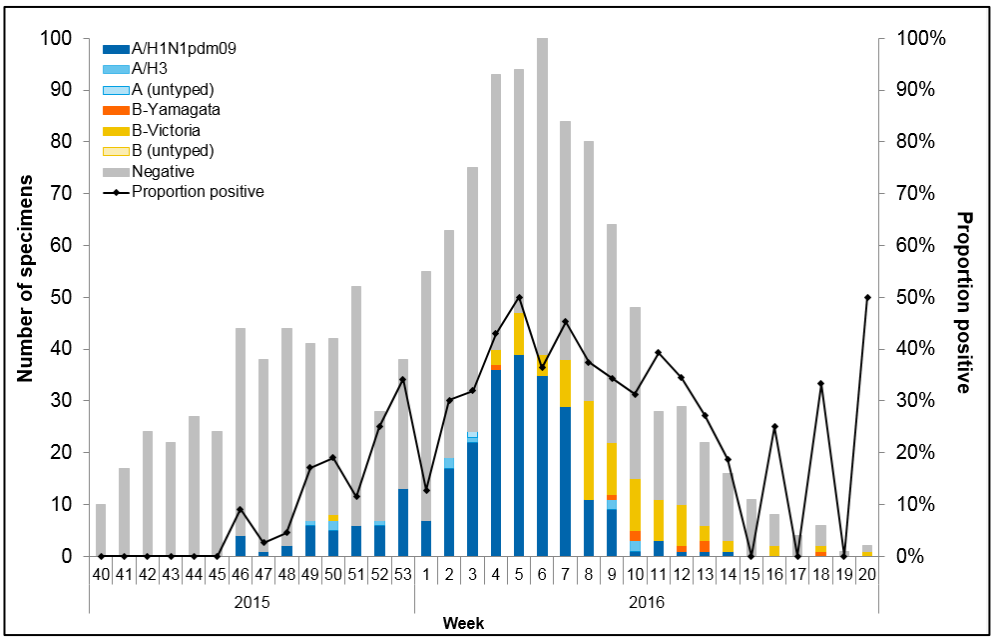
During the 2015–2016 season, 1,341 sentinel samples were submitted from 90 participants, including 80 GPs, 8 pediatric clinics, and 2 infectious disease clinics. Eighty-three percent of the samples were collected by GPs. In total, 369 samples (27.5%) tested positive for influenza, which was about the same as during the preceding season (26.7%).

In the first part of the season, influenza A(H1N1)pdm09 dominated with high intensity during weeks 2–9 (>30% positive samples). Influenza B, this season predominately of the B/Victoria lineage, started a little later and occurred mainly during weeks 5–12 (Figure 15).

Of the positive samples, 271 (73.4%) were positive for influenza A and 97 (26.3%) were positive for influenza B. One sample showed a co-infection of B/Victoria and A(H1N1)pdm09. Of the influenza A positives, 259 (95.6%) were influenza A(H1N1)pdm09 and 11 (4.4%) were influenza A(H3N2). One influenza A sample could not be subtyped due to low virus concentration.

In total, 89 (91.8%) of the influenza B-positive samples belonged to the B/Victoria/2/87 lineage and 8 (8.2%) to the influenza B/Yamagata/16/88 lineage.

Figure 15. Number of sentinel samples submitted each week and the number and percentage of the positive samples by subtype/lineage, 2015–2016.



Clinical features

Of the patients sampled through the sentinel system, 89.5% had ILI (Table 13), and only a few had ARI. In total, 57.6% of the samples came from women. The median age for influenza A(H1N1)pdm09 cases was lower compared to the two previous seasons.

Table 13. Summary of laboratory results, median age, and proportion of patients with ILI from the sentinel sampling system for the last three seasons.

	Season 2013–2014			**Season 2014–2015**			**Season 2015–2016**		
	Analyses	**Median age (years)**	**ILI**	**Analyses**	**Median age (years)**	**ILI**	**Analyses**	**Median age (years)**	**ILI**
Analysed	**1,302**			**1,399**			**1,341**		
Negative	1,082	41	84%	1,026	42	75%	972	43.5	82%
Proportion positive	*16.9%*			*26.7%*			*27.5%*		
Positive for influenza A	**193**			**232**			**271**		
A(H1N1)pdm09	154	37	94%	32	37.5	84%	259	28.5	86%
A(H3N2)	31	35	100%	187	40	88%	11	40	100%
A, not subtyped	8	49.5	100%	13	40	100%	1	59	100%
Positive for influenza B	**28**			**141**			**97**		
B/Victoria	3	15	100%	2	31	50%	89	18	84%
B/Yamagata	23	51	100%	139	45	90%	8	47	75%
B, not typed to any lineage	2	65	86%	0	0	0%	0	0	0%

Influenza infection among vaccinated patients

Vaccination status was reported for 1,324 of the 1,341 patients sampled during the season. Of these, 107 (8.1%) were vaccinated. Influenza infections were detected in 12 vaccinated patients (11%), including 7 patients with influenza A(H1N1)pdm09 (median age 67 years) and 1 patient with influenza A(H3N2). Four patients were positive for influenza B/Yamagata (median age 65 years). Influenza B/Victoria was not included in the trivalent vaccine this season; therefore, the six vaccinated patients who tested positive for influenza B/Victoria are not included as vaccine failures. Ten of the twelve infections occurred in immunocompromised patients.

Comparison of laboratory and sentinel surveillance data

A comparison of the proportion of positive samples detected through sentinel sampling and those reported through the statutory laboratory reporting systems combined showed that a lower proportion of samples were positive for A(H3N2) within the sentinel system compared to the laboratory reporting system. The opposite was seen for the A(H1N1)pdm09 positive samples (Table 14). This season was dominated by A(H1N1)pdm09 and B/Victoria, which mainly affected younger persons (Tables 4 and 6).

Table 14. Proportion of samples positive for different influenza types within the sentinel sampling system (*Sentinel*) and laboratory reporting systems (*Lab*).

	2013–2014 (%)		2014–2015 (%)		2015–2016 (%)	
Influenza type	**Sentinel**	**Lab**	**Sentinel**	**Lab**	**Sentinel**	**Lab**
A(H1N1)pdm09	73.1	67.2	9.4	6.4	70.5	63.5
A(H3N2)	14.4	24.6	52.3	57.8	3	13.0
B/Victoria lineage	1.3	0.6	0.5	1.1	24.4	17.9
B/Yamagata lineage	11.2	7.6	37.8	34.7	2.1	5.6

Subtyping and lineage determination

With the end of statutory laboratory reporting for A(H1N1)pdm09 and the introduction of statutory laboratory reporting for all influenza A- and B-positive samples, subtyping has only been performed at three regional laboratories (Lund, Göteborg, and Umeå) and at the Public Health Agency of Sweden during the 2015–2016 season. In total, 2,161 influenza A-positive samples were subtyped, of which 2,049 were A(H1N1)pdm09 and 112 were A(H3N2). Subtyping results for the laboratory reporting are presented in Table 6.

In total, the lineage was determined for 78 influenza B-positive samples. Fifty-nine were B/Victoria like, and 19 belonged to the B/Yamagata lineage. In addition, all 369 influenza-positive samples in the sentinel reporting were either sub- or lineage-like typed. Subtyping results for sentinel reporting are presented in Table 13. The proportions of samples positive for different subtypes for the three last seasons are presented in Table 14.

Characterisation of viruses

A representative selection of the influenza-positive samples were further analysed by sequencing (see Table 15 for number of sequenced genes per subtype), real-time PCR, isolation an NAI assay. A selection of samples were also sent to the WHO CC in London for analysis with hemagglutination inhibition and NAI assay.

Table 15. Number of sequenced gene segments for each subtype/lineage for the 2015–2016 season.

Subtype/Lineage	Gene Segment	Number of sequenced viruses
A(H1N1)pdm09	H	99
	N	105
	M	110
	NS	108
	PB2	89
	PB1	89
	NP	101
	PA	92
A(H3N2)	H	42
	N	41
	M	43
	NS	42
	PB2	38
	PB1	29
	NP	41
	PA	40
B/Yamagata	H	13
	N	12
	M	7
	NS	11
	PB2	13
	PB1	11
	NP	11
	PA	11
B/Victoria	H	56
	N	53
	M	52
	NS	53
	PB2	52
	PB1	52
	NP	51
	PA	51

HA - Hemagglutinin. NA - Neuraminidase. M - Matrix protein. NS - Non-structural protein. PB2 - Polymerase basic protein 2. PB1 - polymerase basic protein 1. NP - Nucleoprotein. PA - Polymerase acidic protein.

Characterisation of influenza A(H1N1)pdm09

Of the 99 A(H1N1)pdm09 viruses for which the HA gene was sequenced, 94 belonged to the subclade 6B.1 (defined by the amino acid substitutions S84N, S162N and I216T), four belonged to subclade 6B.2 (defined by the amino acid substitutions V152T and V173I), and one belonged to clade 6B (defined by the amino acid substitutions K163Q, K283E, and A256T), see the phylogenetic tree in Appendix 1. A clear dominance of viruses in subclade 6B.1 has also been seen among the characterized viruses circulating in Europe during the 2015–2016 season (European Centre for Disease Prevention and Control. Influenza virus characterization, May 2016). Six viruses from vaccinated individuals were sequenced, and they all belonged to subclade 6B.1. Five of these cases (aged 37, 63, 67, 78, and 81 years) had no known immunosuppression, and the immune

status was unknown in the sixth case (age 68 years). Age might be playing a role in the vaccine failure in most of these cases. The majority of the characterized European viruses in clade 6B and the subclades 6B.1 and 6B.2 have been shown to be antigenically similar to the vaccine virus A/California/07/2009 according to antigenic analyses performed by the WHO CC in London (European Centre for Disease Prevention and Control. Influenza virus characterization, November 2015-May 2016). A total of 19 Swedish influenza viruses have been sent to the WHO CC in London for antigenic analyses as a contribution to the overall evaluation of antigenicity of circulating European A(H1N1)pdm09 viruses.

Of the 105 viruses for which the NA gene was sequenced, a total of eight viruses originated from patients that had received oseltamivir (Tamiflu®), one of them prophylactically. The H275Y substitution, which confers resistance to oseltamivir but not to zanamivir (Relenza®), was present in two of the viruses both originating from oseltamivir-treated patients for a proportion of 100% in the prophylactically treated patient and 80% in the other case. In addition, 31 samples, including one from an oseltamivir-treated case where sequencing was not possible due to low virus concentration, were analysed exclusively for the H275Y substitution with real-time PCR, and none of them contained the substitution. A total of 14 viruses were also analysed phenotypically with NAI assay for sensitivity to oseltamivir and zanamivir, and all were sensitive to both inhibitors. Seven of these viruses and two additional viruses were also analysed by the WHO CC in London. All nine viruses were sensitive to both NA inhibitors. In Europe, 2,700 A(H1N1)pdm09 viruses were tested for susceptibility to NA inhibitors. Of these, 26 showed reduced susceptibility to oseltamivir due to the H275Y substitution. All but one of the 110 analysed A(H1N1)pdm09 viruses carried the S31N amantadine-resistance substitution in M2. The sample that was sensitive to amantadine was collected in week 49 in the northern part of Sweden.

No amino acid substitutions known to be associated with increased virulence were detected in the NS1 or PB2 genes that were analysed. This included viruses from 23 severe cases (intensive care, patients treated with extracorporeal membrane oxygenation (ECMO), or deceased patients). For 17 of these cases both NS and PB2 could be sequenced, while in six cases only the NS gene could be sequenced. None of the 99 viruses for which HA was sequenced, including eight specimens from the lower respiratory tract, contained any substitution at position 222 in HA, which can harbour mutations associated with an increased affinity for receptors in the lower respiratory tract. A total of 19 of the 99 analysed samples, including five from the lower respiratory tract, originated from severe cases.

Characterisation of influenza A(H3N2)

Of the 42 A(H3N2) viruses for which the HA gene was sequenced, 27 belonged to subclade 3C.2a (characterized by the substitutions L3I, N144S, F159Y, K160T, and N1225D), and 15 belonged to subclade 3C.3a (characterised by the substitutions A138S, F159S, and N225D), see the phylogenetic tree in Appendix 2. This clade distribution was also seen among the viruses circulating in Europe (Flu News Europe, week 20, 2016). The vaccine strain for the 2015–2016 season –

A/Switzerland/9715293/2013 – belongs to subclade 3C.3a, but cross-reactivity has been shown to subclade 3C.2a viruses (WHO Recommended composition of influenza virus vaccines for use in the 2015–2016 northern hemisphere influenza season, Weekly epidemiological record 90, 97-108). Thirteen of the Swedish A(H3N2) influenza viruses have been sent to the WHO CC in London for antigenic analyses as a contribution to the overall evaluation of antigenicity of circulating European A(H3N2) viruses. Of the 42 viruses for which the HA gene was sequenced, one originated from a vaccinated individual aged 68 years.

None of the 41 A(H3N2) viruses, including one virus from an oseltamivir-treated immunocompromised patient for which the NA gene was sequenced, contained any of the substitutions known to result in reduced or highly reduced inhibition by oseltamivir and/or zanamivir. Eleven viruses were also analysed phenotypically by NAI assay, and all were sensitive to oseltamivir and zanamivir. Nine of these viruses and one additional virus were also analysed by the WHO CC in London and were all found to be sensitive to both inhibitors.

In Europe, 172 A(H3N2) viruses were tested for susceptibility to NA inhibitors during the season. One showed reduced susceptibility to oseltamivir due to the E119V substitution in NA (Flu News Europe week 20, 2016). Like the previous season, all analysed influenza A(H3N2) viruses carried the S31N amantadine-resistance substitution in M2. No amino acid substitutions known to be associated with increased virulence were detected in the NS1 or PB2 genes that were analyzed.

Characterisation of influenza B

B/Yamagata

Further analysis of 13 B/Yamagata-like viruses by sequencing of the HA gene showed that these belonged to clade 3 (which is characterised by amino acid substitutions S150I, N165Y, and G229D, with a great majority of viruses also carrying N116K, N202S, K298E, and E312K). One of the characterised viruses originated from a vaccinated patient, aged 71 years, with no known immunosuppression. All characterized European viruses this season also belonged to clade 3 (Flu News Europe, week 20, 2016), and the majority of the analysed viruses have been shown to be antigenically similar to the vaccine virus for the 2015–2016 season – B/Phuket3073/2013 (also a clade 3 virus) – according to antigenic analyses performed by the WHO CC in London (European Centre for Disease Prevention and Control. Influenza virus characterization, December 2015-May 2016). Three of the Swedish B/Yamagata viruses have been sent to the WHO CC in London for antigenic analyses as a contribution to the overall evaluation of antigenicity of circulating European B/Yamagata viruses.

None of the NA substitutions known to result in reduced or highly reduced inhibition to oseltamivir and/or zanamivir were identified in any of the 12 analysed viruses. Two viruses were also analysed phenotypically by NAI assay, and all were sensitive to oseltamivir and zanamivir. One of these viruses was also analysed by the WHO CC in London and was sensitive to both inhibitors.

In Europe, all of the B/Yamagata viruses screened were sensitive to both oseltamivir and zanamivir (Flu News Europe, week 20, 2016).

B/Victoria

The 56 B/Victoria viruses for which the HA gene was sequenced all belonged to genetic clade 1A, which is characterised by amino acid substitutions N75K, N165K, and S172P (see phylogenetic tree in Appendix 3). All characterized European viruses this season also belong to clade 1A (Flu News Europe, week 20, 2016), and the analysed viruses have been shown to be antigenically similar to the vaccine virus included in the quadrivalent vaccine (but not the trivalent) for the 2015–2016 season (B/Brisbane/6072008 in clade 1A), according to antigenic analyses performed by the WHO CC in London (European Centre for Disease Prevention and Control. Influenza virus characterization, November 2015-May 2016). Five of the Swedish B/Yamagata viruses have been sent to the WHO CC in London for antigenic analyses as a contribution to the overall evaluation of antigenicity of circulating European B/Yamagata viruses.

The NA gene of 53 B/Victoria viruses was sequenced and did not contain any of the mutations known to result in reduced or highly reduced inhibition by oseltamivir and/or zanamivir. Two viruses were also analysed phenotypically by NAI assay, and all were sensitive to oseltamivir and zanamivir. Two of these viruses and two additional viruses were also analysed by the WHO CC in London and were found to be sensitive to both inhibitors.

In Europe, all of the B/Victoria viruses screened were sensitive to both oseltamivir and zanamivir (Flu News Europe, week 20, 2016)

Virus isolation on cell culture

Isolation of influenza viruses on cell culture in Sweden is only performed at the Public Health Agency of Sweden. We continuously ask Swedish laboratories to provide a representative selection of specimens that can be isolated on cell culture. One problem with only using samples collected from other laboratories is that the quality differs depending on, for example, the kind of specimen, time since sampling, and storage and shipping temperatures. Fifty-four of the collected samples with Ct ≤ 30 were cultured on MDCK cells. Ten samples were excluded due to contamination with bacteria or fungi. Sixty-nine per cent of the remaining samples tested positive for influenza.

The cultures are used for phenotypic analyses at the Public Health Agency of Sweden and for further characterization at the WHO CC in London. During the 2015–2016 season, 37 virus isolates and 16 clinical samples were shipped to the WHO CC (one shipment in January and one in June).

Quality assurance

Seasonal influenza

One-step real-time RT-PCR assays are used to identify circulating influenza viruses. These assays are used to detect influenza A and B, to subtype the influenza A-positive samples, and to discriminate between the two influenza B lineages. These assays have also been evaluated and implemented for avian influenza diagnostics. They are sensitive, rapid, and can easily be scaled up if necessary. Several of these PCR assays have been developed to be performed as duplex PCR assays. This is true for the detection of influenza A and B, subtyping of influenza A(H1N1)pdm09 and A(H3N2), and for typing of B/Yamagata and B/Victoria lineages. The Public Health Agency continuously monitors the genomic sequences of circulating influenza strains to which the PCR assays are directed in order to detect mutations that could affect their sensitivity. The Public Health Agency also performs regular validation of each assay twice a year, both ahead of the influenza season and during the peak.

During the 2015–2016 season, the probes for the influenza A(H1N1)pdm09 PCR assay were validated and updated due to changes in the circulating strains. The assay was updated to include only one probe. After validation, this information was shared with the Swedish laboratories. The laboratories that use the PCR systems established by the Public Health Agency are encouraged to send all samples with deviating results to the agency for sequence analysis. Furthermore, the Public Health Agency assists Swedish laboratories that have developed their own PCR systems by validating their methods through sequencing of representative samples. The Public Health Agency also provides positive control material to Swedish laboratories upon request.

Control of sensitivity in commercial rapid PCR-kits

During the 2015–2016 season, an increasing number of laboratories included a commercial "rapid PCR" assay among their diagnostic tools. In order to ensure that circulating influenza strains were detected with these assays, the Public Health Agency of Sweden agreed to send supernatants from cell cultures to three laboratories using three different kits used in Sweden. The kits tested were Simplexa Flu A_B & RSV Direct.5, GeneXperts Xpert Flu, and GeneXperts Xpert® Flu/RSV XC. The three laboratories received a number of samples on two occasions – in the beginning and at the end of the season. A total of 10 positive samples were tested with the three different kits, and all gave 100% correct results. The results were shown on our homepage so that other laboratories using the same kits had knowledge of the results.

External quality assurance programmes

The Public Health Agency participates in the following three external quality assurance (EQA) programmes:

1) The annual WHO EQA for influenza. The PCR result for 2015 was 10/10 correct. The results from the phenotypic (MUNANA) and genotypic (H275Y allelic discrimination by Real-time PCR) NAI susceptibility testing was 2/2 correct.
2) The INFRNA panel from Quality Control for Molecular Diagnostics (QCMD). The result for 2015 was 12/12 samples correctly typed and subtyped.
3) The ERLI-Net influenza virus EQA program, which is arranged every other year, was sent to the participating laboratories in June 2015. The samples included in the panel for rapid detection and culture of influenza virus were analyzed with real-time PCR (eight samples), virus isolation on cell culture (eight samples), and sequencing of the HA gene for determination of genetic clade (seven samples, i.e. those that were positive in real-time PCR). Our laboratory analyzed all samples with 100% correct results.

   Two of the samples (i.e. those that were already in high enough concentration for direct analysis) included in the panel for antiviral susceptibility testing were tested for phenotypic NAI susceptibility using MUNANA. The results were 2/2 correct results. These two samples and the seven additional samples were also analysed by sequencing for mutations in NA associated with reduced or highly reduced inhibition by NAI. The results were 8/9 correctly reported. The result that was incorrectly reported was a result obtained by sequencing of a sample that contained a mix of 275H/Y. The mix was actually detected, but it was reported in a format that was not accepted by the system, so only H275Y was registered.

National quality assurance programme

As a result of the changes in statutory reporting in place as of December 1, 2015, all laboratories in Sweden are only required to perform detection of influenza A and influenza B and to do so via PCR. Three regional laboratories also perform subtyping for A(H3N2) and A(H1N1)pdm09. In September 2015, The Public Health Agency of Sweden produced a PCR panel for the Swedish laboratories as an EQA on behalf of the External Quality Assessment for Clinical Laboratory Investigations (EQUALIS). Twenty-two laboratories participated in the EQA, and 15 of these reported 10/10 correct answers (Figure 16). This is an improvement compared to last year when only 11 of 21 laboratories reported 10/10 correct answers. A difference from previous years is the increasing use of commercial PCR kits instead of the ordinary real-time PCR assay. In 2014, five laboratories used different kinds of PCR kits, while the number in 2015 was 13.

Figure 16. Results of the Swedish EQA panel 2015

Appendix 1.

Phylogenetic tree influenza A(H1N1)pdm09
Hemagglutinin (HA1)

Season 2015–2016

VACC = Vaccinated

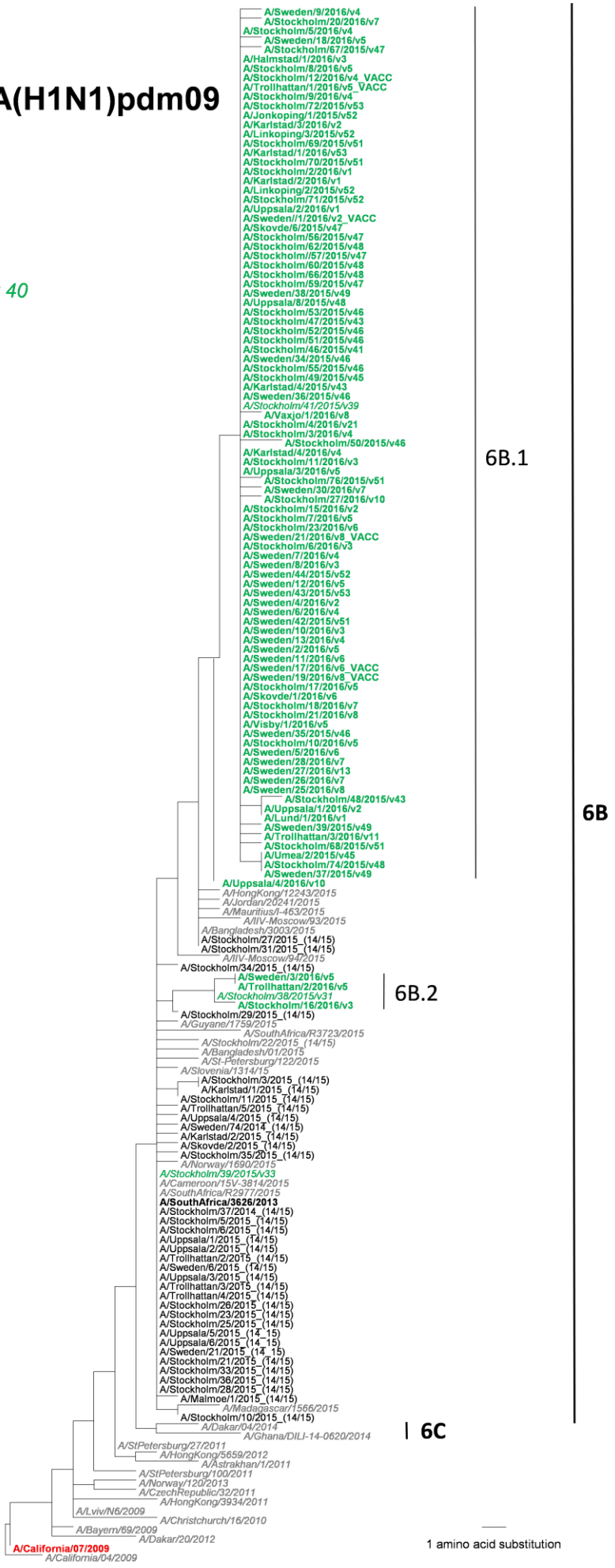
Collection date before week 40

Vaccine strain 2015–2016

Subclade representatives

Reference strains

Previous season: (14_15)



Appendix 2.

Phylogenetic tree, influenza A(H3N2)
hemagglutinin (HA1)

Season 2015–2016

VACC = Vaccinated

Collection date before week 40

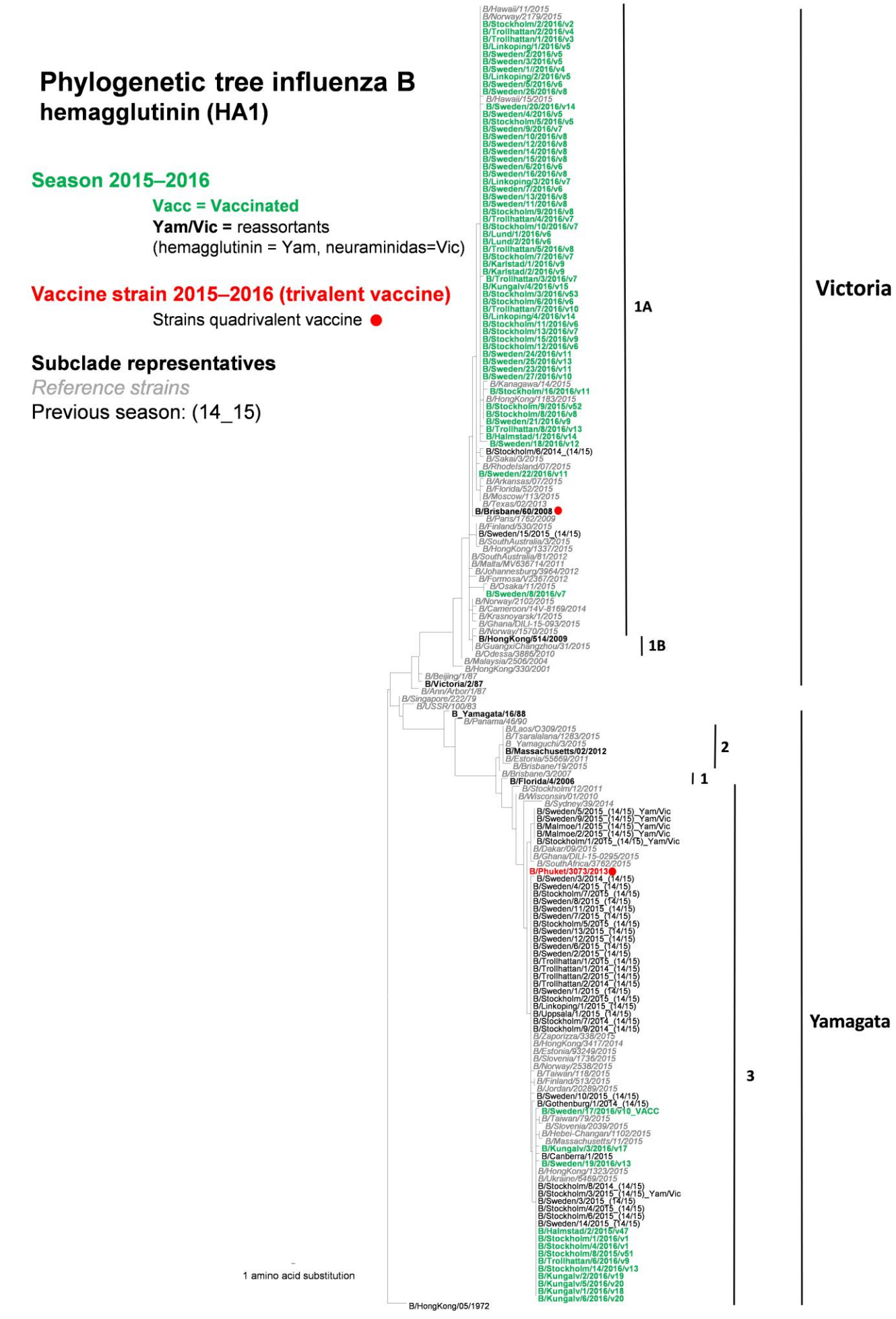
Vaccine strain 2015–2016

Subclade representatives

Reference strains

Previous season: (14_15)

Appendix 3.


Phylogenetic tree influenza B
hemagglutinin (HA1)
Season 2015–2016
Vacc = Vaccinated
Yam/Vic = reassortants
(hemagglutinin = Yam, neuraminidas=Vic)
Vaccine strain 2015–2016 (trivalent vaccine)
Strains quadrivalent vaccine
Subclade representatives
Reference strains
Previous season: (14_15)
B/Hawaii/11/2015
B/Norway/2179/2015
B/Stockholm/2/2016/v2
B/Trollhattan/2/2016/v4
B/Trollhattan/1/2016/v3
B/Linkoping/1/2016/v5
B/Sweden/2/2016/v5
B/Sweden/3/2016/v5
B/Sweden/1/2016/v4
B/Linkoping/2/2016/v5
B/Sweden/5/2016/v6
B/Sweden/26/2016/v8
B/Hawaii/15/2015
B/Sweden/20/2016/v14
B/Sweden/4/2016/v5
B/Stockholm/5/2016/v5
B/Sweden/9/2016/v7
B/Sweden/10/2016/v8
B/Sweden/12/2016/v8
B/Sweden/14/2016/v8
B/Sweden/15/2016/v8
B/Sweden/6/2016/v6
B/Sweden/16/2016/v8
B/Linkoping/3/2016/v7
B/Sweden/7/2016/v6
B/Sweden/13/2016/v8
B/Sweden/11/2016/v8
B/Stockholm/9/2016/v8
B/Trollhattan/4/2016/v7
B/Stockholm/10/2016/v7
B/Lund/1/2016/v6
B/Lund/2/2016/v6
B/Trollhattan/5/2016/v8
B/Stockholm/7/2016/v7
B/Karlstad/1/2016/v9
B/Karlstad/2/2016/v9
B/Trollhattan/3/2016/v7
B/Kungalv/4/2016/v15
B/Stockholm/3/2016/v53
B/Stockholm/6/2016/v6
B/Trollhattan/7/2016/v10
B/Linkoping/4/2016/v14
B/Stockholm/11/2016/v6
B/Stockholm/13/2016/v7
B/Stockholm/15/2016/v9
B/Stockholm/12/2016/v6
B/Sweden/24/2016/v11
B/Sweden/25/2016/v13
B/Sweden/23/2016/v11
B/Sweden/27/2016/v10
B/Kanagawa/14/2015
B/Stockholm/16/2016/v11
B/HongKong/1183/2015
B/Stockholm/9/2015/v52
B/Stockholm/8/2016/v8
B/Sweden/21/2016/v9
B/Trollhattan/8/2016/v13
B/Halmstad/1/2016/v14
B/Sweden/18/2016/v12
B/Stockholm/6/2014_(14/15)
B/Sakai/3/2015
B/RhodeIsland/07/2015
B/Sweden/22/2016/v11
B/Arkansas/07/2015
B/Florida/52/2015
B/Moscow/113/2015
B/Texas/02/2013
B/Brisbane/60/2008
B/Paris/1762/2009
B/Finland/530/2015
B/Sweden/15/2015_(14/15)
B/SouthAustralia/3/2015
B/HongKong/1337/2015
B/SouthAustralia/81/2012
B/Malta/MV636714/2011
B/Johannesburg/3964/2012
B/Formosa/V2367/2012
B/Osaka/11/2015
B/Sweden/8/2016/v7
B/Norway/2102/2015
B/Cameroon/14V-B169/2014
B/Krasnoyarsk/1/2015
B/Ghana/DILI-15-093/2015
B/Norway/1570/2015
B/HongKong/514/2009
B/GuangxiChangzhou/31/2015
B/Odessa/3886/2010
B/Malaysia/2506/2004
B/HongKong/330/2001
B/Beijing/1/87
B/Victoria/2/87
B/Ann/Arbor/1/87
B/Singapore/222/79
B/USSR/100/83
B_Yamagata/16/88
B/Panama/46/90
B/Laos/O309/2015
B/Tsaralalana/1283/2015
B_Yamaguchi/3/2015
B/Massachusetts/02/2012
B/Estonia/55669/2011
B/Brisbane/19/2015
B/Brisbane/3/2007
B/Florida/4/2006
B/Stockholm/12/2011
B/Wisconsin/01/2010
B/Sydney/39/2014
B/Sweden/5/2015_(14/15)_Yam/Vic
B/Sweden/9/2015_(14/15)_Yam/Vic
B/Malmoe/1/2015_(14/15)_Yam/Vic
B/Malmoe/2/2015_(14/15)_Yam/Vic
B/Stockholm/1/2015_(14/15)_Yam/Vic
B/Dakar/09/2015
B/Ghana/DILI-15-0295/2015
B/SouthAfrica/3762/2015
B/Phuket/3073/2013
B/Sweden/3/2014_(14/15)
B/Sweden/4/2015_(14/15)
B/Stockholm/7/2015_(14/15)
B/Sweden/8/2015_(14/15)
B/Sweden/11/2015_(14/15)
B/Sweden/7/2015_(14/15)
B/Stockholm/5/2015_(14/15)
B/Sweden/13/2015_(14/15)
B/Sweden/12/2015_(14/15)
B/Sweden/6/2015_(14/15)
B/Sweden/2/2015_(14/15)
B/Trollhattan/1/2015_(14/15)
B/Trollhattan/1/2014_(14/15)
B/Trollhattan/2/2015_(14/15)
B/Trollhattan/2/2014_(14/15)
B/Sweden/1/2015_(14/15)
B/Stockholm/2/2015_(14/15)
B/Linkoping/1/2015_(14/15)
B/Uppsala/1/2015_(14/15)
B/Stockholm/7/2014_(14/15)
B/Stockholm/9/2014_(14/15)
B/Zaporizza/338/2015
B/HongKong/3417/2014
B/Estonia/93249/2015
B/Slovenia/1736/2015
B/Norway/2538/2015
B/Taiwan/118/2015
B/Finland/513/2015
B/Jordan/20289/2015
B/Sweden/10/2015_(14/15)
B/Gothenburg/1/2014_(14/15)
B/Sweden/17/2016/v10_VACC
B/Taiwan/79/2015
B/Slovenia/2039/2015
B/Hebei-Changan/1102/2015
B/Massachusetts/11/2015
B/Kungalv/3/2016/v17
B/Canberra/1/2015
B/Sweden/19/2016/v13
B/HongKong/1323/2015
B/Ukraine/6469/2015
B/Stockholm/8/2014_(14/15)
B/Stockholm/3/2015_(14/15)_Yam/Vic
B/Sweden/3/2015_(14/15)
B/Stockholm/4/2015_(14/15)
B/Stockholm/6/2015_(14/15)
B/Sweden/14/2015_(14/15)
B/Halmstad/2/2015/v47
B/Stockholm/1/2016/v1
B/Stockholm/4/2016/v1
B/Stockholm/8/2015/v51
B/Trollhattan/6/2016/v9
B/Stockholm/14/2016/v13
B/Kungalv/2/2016/v19
B/Kungalv/5/2016/v20
B/Kungalv/1/2016/v18
B/Kungalv/6/2016/v20
B/HongKong/05/1972
1 amino acid substitution
1A
1B
2
1
3
Victoria
Yamagata

The influenza season of 2015–2016 was was dominated by influenza A(H1N1)pdm09, with a small wave of influenza B/Victoria towards the end of the season. Overall, the season had high activity but slightly fewer laboratory-confirmed cases compared to the previous, intense season. The season had a high number of severe cases and significant excess mortality was observed in the 15-64 age group.

This report describes the monitoring systems for influenza in use during the winter season of 2015–2016 and the results of both epidemiological and virological surveillance. Data are also compared to previous influenza seasons.

The Public Health Agency of Sweden has prepared this report for the World Health Organization (WHO) as part of the agency's function as a National Influenza Centre (NIC).

Rapporten innehåller en svensk sammanfattning.

The Public Health Agency of Sweden is an expert authority with responsibility for public health issues at a national level. The Agency develops and supports activities to promote health, prevent illness and improve preparedness for health threats.

Our vision statement: a public health that strengthens the positive development of society.

Folkhälsomyndigheten

Solna Nobels väg 18, SE-171 82 Solna **Östersund** Forskarens väg 3, SE-831 40 Östersund.

www.folkhalsomyndigheten.se