Folkhälsomyndigheten
PUBLIC HEALTH AGENCY OF SWEDEN

Influenza in Sweden

2016–2017 Season

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Preface

This report describes the monitoring systems for influenza in use during the winter season of 2016–2017 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 Marie Rapp 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 2016–2017 season was dominated by influenza A(H3N2) that came in two waves. Overall, 95% of cases were influenza A, and of those subtyped more than 99% were A(H3N2). The season was intensive with more laboratory-confirmed cases compared with previous seasons. At first, the season came to an intense peak in the northern part of the country, followed by a second peak in the south. The median age of influenza A cases was 73 years, reflecting the dominance of A(H3N2). Like the 2014–2015 season, which was also dominated by A(H3N2), the majority (65%) of the influenza cases this season were among people 65 years and older.

The web-search based system Webbsök signalled the start of this early season in week 45, which coincided with the start of the vaccination campaign in Sweden. The epidemic threshold was crossed in other surveillance systems in week 47 or 48. The highest incidences were seen in the north (Norrland) and middle parts (Svealand) of the country at the beginning of the season and at the peak (week 52), whereas the highest incidences during the second peak (week 8) were seen in the southern parts of the country (Götaland). The number of laboratory-confirmed influenza A cases was at a low level from week 10 onwards. Influenza B dominated from week 17 to the end of the epidemic in week 20, but at a very low level.

The average vaccination coverage among people 65 years and older was 49% and has been between 49% and 50% during the last three seasons. Data on vaccination coverage is collected in different ways, and small differences from year to year can occur due to methodological differences. The coverage rate is highest among people 75 years and older (55%). This is encouraging because increasing age raises the risk of severe influenza infections. There is great variation among county councils/regions, moreover vaccination coverage increased in 9 out of 21 county councils. It is estimated that 5–10% of people under the age of 65 belong to a risk group, but the vaccination coverage in this age group is only 2%. Only 32% of those with known vaccination status who belonged to a risk group and needed intensive care during this season were vaccinated.

The sales pattern for antiviral medications, used for the treatment of severe influenza disease and as prophylaxis, in Sweden follows laboratory data and shows the same two peaks (week 52 in 2016 and week 8 in 2017). The number of packages sold increased significantly this season, mainly through increased requisitions in healthcare. This is probably due in part to communication efforts regarding low vaccine effectiveness and the intensity of the season in the older age group, leading to an increased use of antivirals. No resistance to neuraminidase inhibitors was detected among the 266 virus strains characterized.

Compared with the previous season, fewer patients (259 vs. 362) required intensive care this season, and the vast majority (69%) were aged 65 years or older. The age distribution among intensive care patients is different compared with the previous

season, which was dominated by influenza A(H1N1)pdm09, as older individuals are more affected by influenza A(H3N2).

Influenza infection is often a contributing factor to deaths among elderly individuals during seasons dominated by influenza A(H3N2). An analysis of the 734 deaths that occurred within 30 days of a laboratory-confirmed influenza diagnosis, showed that 95% of deaths were among those aged 65 years and over, followed by those aged 40-64 years (4.8%). Of those aged 65 years and over who had been diagnosed with influenza A, 8.5% had died within 30 days. The proportion of deceased cases increased with increasing age and varied between 0.05% for individuals under age 40 years and 18% for those between 90 and 94 years. Excess mortality modelling also showed a high mortality rate among those aged 65 years and over.

A selection of 240 strains collected through sentinel sampling and from laboratories in Sweden were genetically characterized. Characterization showed that all influenza A(H1N1)pdm09, A(H3N2), and B strains belonged to genetic groups where most strains have been found to be antigenically similar to the vaccine strains in the trivalent (for A and B/Victoria strain) and quadrivalent vaccines (for all strains including B/Yamagata lineage). Vaccination breakthrough infections were detected in 24% of patients sampled within the sentinel sampling system, with a median age of 74 years. Vaccination effectiveness depends on various factors, such as age, immune system function, and time between vaccination and disease. In addition, vaccine effectiveness varies due to the degree of matching between circulating and vaccine strains. The proportion of A(H3N2) vaccination breakthroughs reported within the sentinel system rose at the same time as the Stockholm County Council reported decreasing vaccination effectiveness (28%). The Public Health Agency’s analysis of circulating influenza strains found that the proportion of vaccine breakthroughs rose as the proportion of circulating A(H3N2) strains with the T135K mutation increased.

Sammanfattning

Säsongen 2016–2017 dominerades av influensa A(H3N2) som kom i två vågor. Totalt sett var 95 procent av fallen influensa A och av de som subtypats var mer är 99 procent A(H3N2). Säsongen var intensiv med fler laboratorieverifierade fall jämfört med föregående säsonger med en första intensiv topp i norra delen av landet och en andra topp i söder. Medianåldern för influensa A fallen var 73 år, vilket reflekterar att influensa A(H3N2) cirkulerat. Såsom säsongen 2014–2015, som också dominerades av A(H3N2), var majoriteten (65 %) av influensafallen denna säsong bland personer 65 år och äldre.

Webbsök indikerade att säsongen startade redan vecka 45 vilket sammanföll med vaccinationsstarten. Övriga övervakningssystem indikerade epidemistart vecka 47 eller 48. Den första, högre toppen i de laboratorieverifierade fallen inföll redan vecka 52 främst i Norrland och delar av Svealand (främst Värmland, Dalarna och Stockholm). Den andra toppen kom vecka 8, främst i Götaland och övriga delar av Svealand. Från vecka 10 och framåt var antalet laboratorieverifierade fall på låg nivå och vecka 17 skiftade dominansen till influensa B. Vecka 20 var epidemins sista vecka enligt laboratorieövervakningen.

Medelvärdet för vaccinationstäckningen bland personer 65 år och äldre var 49 procent och har varit mellan 49 och 50 procent under de senaste tre säsongerna. Vaccinationstäckningen samlas in på olika sätt och små skillnader från år till år kan uppstå. Täckningsgraden är som högst bland personer 75 år och äldre (55 %). Detta är positivt eftersom stigande ålder ökar risken för svår sjukdom vid influensainfektion. Det är stora variationer mellan landstingen/regionerna. Vaccinationstäckningen har ökat i nio landsting denna säsong. Bland personer under 65 år uppskattas att 5-10 procent tillhör en riskgrupp, men vaccinationstäckningen i denna åldersgrupp är endast 2 procent. Av de som tillhörde en riskgrupp och behövde intensivvård under denna säsong var endast 32 procent med känd vaccinationsstatus vaccinerade.

Försäljningsmönstret för antivirala läkemedel för behandling av svår influensasjukdom samt profylax i Sverige följer laboratoriefallen och även här sågs två toppar (v 52 och 8). Denna säsong har antalet sålda förpackningar ökat markant, främst rekvisitioner inom vården. Detta beror sannolikt till viss del på kommunikationen kring låg vaccineffekt och den svåra säsongen i den äldre åldersgruppen, vilket lett till en ökad användning av antiviraler. Ingen resistens mot neuraminidashämmarna har påvisats bland de 266 virusstammarna som analyserats.

Jämfört med föregående säsong har färre patienter (259 jämfört med 362) behövt intensivvård denna säsong och de allra flesta (69 %) var 65 år och äldre. Jämförelsevis ses en annan åldersfördelning bland intensivvårdade denna säsong då äldre drabbas i större utsträckning av influensa A(H3N2) jämfört med A(H1N1)pdm09 som dominerade föregående säsong.

Bland äldre individer är influensainfektion ofta en bidragande faktor till dödsfall under säsonger som domineras av influensa A(H3N2). I analysen av de 734 dödsfall som skett inom 30 dagar av en laboratorieverifierad influensadiagnos var 95 procent av dödsfallen i åldersgruppen 65 år och äldre, följt av 40-64 år (4,8 procent). Av de personer 65 år och äldre som fått diagnosen influensa A hade 8,5 procent avlidit inom 30 dagar. Andelen fall som avlidit ökade med stigande ålder och varierade mellan 0.05 % för personer under 40 år och 18 % för personer mellan 90 och 94 år. Även genom överdödlighetsövervakningen sågs en hög dödlighet ibland personer 65 år och äldre.

Viruskarakteriseringen av 240 av de stammar som samlats in genom sentinelprovtagningen och från laboratorier i landet visar A(H1N1)pdm09-A(H3N2)- och B/Victoria-stammarna tillhör genetiska grupper där majoriteten har visat sig var antigentiskt lika de stammar som ingick i det trivalenta säsongsinfluensavaccinet, eller det fyrvalenta vaccinet (B/Yamagata). Inom sentinelprovtagning påvisades vaccinationsgenombrott i 24 procent av patienterna med en medianålder på 74 år. Vaccinationseffektiviteten beror på olika faktorer såsom ålder, immunförsvar samt tid mellan vaccination och insjuknande. Dessutom varierar vaccineffektiviteten på grund av matchningen mellan vaccinet och cirkulerande stammar. Andel vaccinationsgenombott av A(H3N2) ökade inom sentinelprovtagningen samtidigt som Stockholms landsting rapporterade sjunkande vaccinationseffekt för personer över 65 år (28 %). Vid analys av cirkulerande influensastammar fann Folkhälsomyndigheten att andelen vaccinationsgenombrott ökade inom sentinelprovtagningen när andelen cirkulerande A(H3N2)-stammar med mutation T135K ökade.

Influenza surveillance in Sweden

Influenza epidemics recur in Sweden each winter, with a range of effects depending on the characteristics of the circulating viruses and the immunity 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 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.

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.[2] A preliminary summary of the 2016–2017 season was published June 12, 2017.[3] The bulletin provides timely analysis of the current situation in Sweden and abroad and has a wide readership.

Vaccine strains 2016–2017

In the end of February 2016, the WHO recommended[4] that the trivalent vaccine for use in the northern hemisphere contain the following viruses for the 2016–2017 season:

- A/California/7/2009-like virus (influenza A(H1N1)pdm09)

[2] Public Health Agency of Sweden, Current Influenza Report, https://www.folkhalsomyndigheten.se/folkhalsorapportering-statistik/statistikdatabaser-och-visualisering/sjukdomsstatistik/influensa-veckorapporter/aktuell-influensarapport/

[3] Public Health Agency of Sweden, Influenza Weekly Report Archive, 2016–2017, https://www.folkhalsomyndigheten.se/folkhalsorapportering-statistik/statistikdatabaser-och-visualisering/sjukdomsstatistik/influensa-veckorapporter/arkiv-20162017/

[4] WHO, Recommended composition of influenza virus vaccines for use in the 2016–2017 northern hemisphere influenza season http://www.who.int/influenza/vaccines/virus/recommendations/2016_17_north/en/

- A/Hong Kong/4801/2014-like virus (influenza A(H3N2))
- B/Brisbane/60/2008-like virus (influenza B/Victoria lineage)

The WHO recommended that the quadrivalent vaccines contain, in addition to the viruses listed above, a B/Phuket/3073/2013-like virus (B/Yamagata lineage).

Vaccine strains 2017–2018

In the end of February 2017, the WHO recommended[5] a change in the influenza A(H1N1)pmd09 component of the vaccine. Thus, the recommended composition of the trivalent vaccine for use in the northern hemisphere for the 2017–2018 season is:

- A/Michigan/45/2015-like virus (influenza (H1N1)pdm09)
- A/Hong Kong/4801/2014-like virus (influenza A(H3N2))
- B/Brisbane/60/2008-like virus (B/Victoria lineage).

The WHO recommended that the quadrivalent vaccines contain, in addition to the viruses listed above, a B/Phuket/3073/2013-like virus (B/Yamagata lineage).

Updates to National policies and recommendations

Prior to and during the 2016–2017 season, the following policies and recommendations were updated:

- Updated vaccination recommendations, September 2016[6]
- Updated web-based information about vaccination and influenza[7]
- Information to pregnant women about seasonal influenza vaccination in Swedish and English.[8] Also available in several other languages.
- Vaccination against influenza in the Swedish National Immunization Program – support for a governmental decision – April 2016[9]

Pandemic planning documents were last updated 2015 and work is ongoing to harmonize these with new WHO guidelines.

The Public Health Agency has signed contracts for pandemic vaccine supply during 2016–2020.

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[5] WHO, Recommended composition of influenza virus vaccines for use in the 2017-2018 northern hemisphere influenza season, http://www.who.int/influenza/vaccines/virus/recommendations/201703_recommendation.pdf?ua=1

[6] Public Health Agency of Sweden, September 2016, Rekommendationer om influensavaccination till riskgrupper. https://www.folkhalsomyndigheten.se/publicerat-material/publikationsarkiv/r/rekommendationer-om-influensavaccination-till-riskgrupper/

[7] Search for "influensa" at https://www.folkhalsomyndigheten.se".

[8] Public Health Agency of Sweden, September 2016, Influenza Vaccination. https://www.folkhalsomyndigheten.se/publicerat-material/publikationsarkiv/v/vaccination-mot-influensa-information-for-dig-som-ar-gravid-engelska/

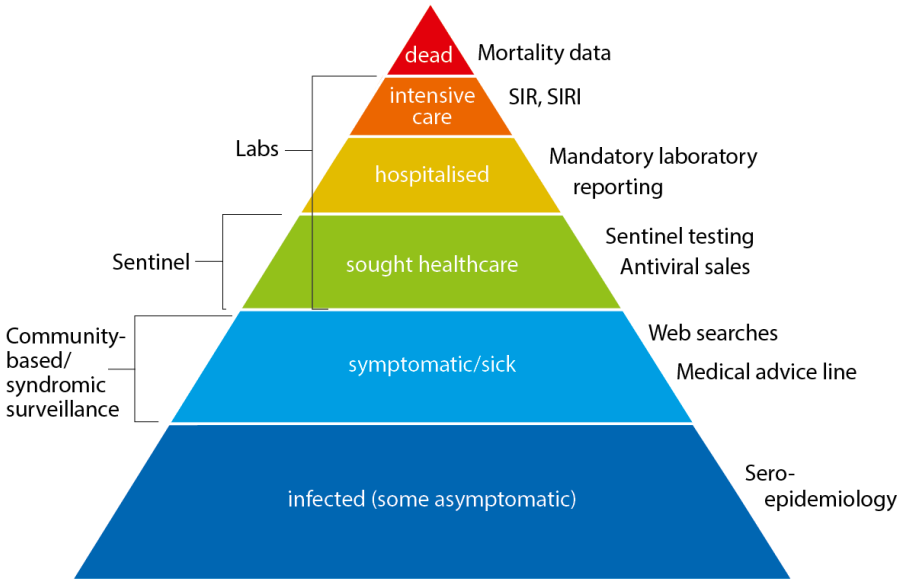
[9] https://www.folkhalsomyndigheten.se/smittskydd-beredskap/vaccinationer/vaccinationsprogram/sarskilda-program/

Surveillance 2016–2017

The pyramid below illustrates the different ways that influenza affects those who are infected (Figure 1), from those infected without any symptoms to the small portion who 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 2016–2017 season and summarises the results of each system. Each system is described further at the start of each section below showing the season's results.

Table 2 shows which week each system, as applicable, crossed the threshold for epidemic start, reached its peak notation (for this season, we have included two peaks for each system), and crossed the threshold for the end of the epidemic, as well as the maximum intensity level measured by the system during the season.

Figure 1. The "influenza pyramid" showing possible outcomes of an influenza infection and the surveillance systems at each level.



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 2016–2017 season. *The data are from the period of week 40, 2016, to week 20, 2017, if no other dates are given.*

Reporting system/ method	**Implementation**	**What does the system/ method show?**	**Results (2016–2017)**
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 with influenza-like illness (ILI).	Estimates the proportion of patients with ILI.	Between week 27, 2016, and week 26, 2017, a total of 123,874 queries related to influenza were entered, which was 1.2% of the total number of queries on the website 1177.se. Webbsök's influenza season lasted for 19 weeks (week 45, 2016–week 11, 2017), with weeks 50–1 being at medium 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 348,500 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 48, 2016, and the peaks were week 51, 2016 and week 4–5, 2017, with 6.3% of calls due to fever in children. The epidemic ended week 15.
Statutory laboratory reporting of influenza Voluntary reporting of denominator data and sub-/lineage typing results	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	13,069 laboratory-confirmed cases of influenza A and 708 cases of influenza B. 68,241 samples, 19.2% positive: - 95% influenza A - 5% influenza B Of influenza A-cases subtyped: < 1% A(H1N1)pdm09 >99% A(H3N2) Of influenza B-cases with determined lineage: - 27% B/Victoria - 73% B/Yamagata

Reporting system/ method	Implementation	What does the system/ method show?	Results (2016–2017)
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).	- 1,120 samples were analysed, of which 233 (21%) tested positive for influenza: 91% A(H3N2) - 5% A not subtyped (low viral load) - 1% A(H1N1)pdm09 - 1% B/Victoria-like - 1% B/Yamagata-like - 85% of the patients had clinical symptoms of ILI
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 - 139 of 198 A(H3N2) viruses belonged to genetic group 3C.2a1, a subgroup in which the majority of the strains are antigenically similar to the vaccine strain (a 3C.2a virus). - 69 of 198 A(H3N2) strains belonged to subgroup 3C.a (i.e. the same group as the vaccine strain). - All 10 A(H1N1)pdm09 viruses belonged to group 6B, a subgroup in which the majority of the viruses have antigenic properties similar to the vaccine strain. - The 29 analysed B/Yamagata viruses belonged to genetic clade 3, a group where strains react well with the vaccine strain in the quadrivalent vaccine. - All 12 B/Victoria viruses belonged to the same genetic clade (1A) as the vaccine strain in the vaccine. Analysis for mutations associated with resistance to neuraminidase inhibitors: - 266 viruses analysed - All were sensitive to both oseltamivir and zanamivir. Phenotypical analysis for resistance to oseltamivir and zanamivir: - 21 viruses analysed - All tested viruses were sensitive to both oseltamivir and zanamivir.
Antiviral sales	Weekly data from the Swedish eHealth Agency	Number of packages sold by type of sale, including prescriptions and health care requisitions.	15,068 packages
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.	259 laboratory-confirmed cases of influenza were reported from SIRI. Of those, 197 were reported as influenza A (unknown subtype), 3 were A(H1N1)pdm09, 50 were A(H3N2), and 9 were influenza B.

Reporting system/ method	Implementation	What does the system/ method show?	Results (2016–2017)
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 (FluMoMo) among persons aged 65 years and over and the entire population between week 51, 2016, and week 11, 2017.
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	734 of 13,087 persons with an influenza diagnosis had died within 30 days of diagnosis, of which 97% were influenza A. Most (95%) were aged 65 years and over.

Table 2. Week of epidemic start, peak, and end, as well as maximum intensity level by surveillance systems, 2016–2017 season.

System	Start	Peak	End	Max intensity
"Webbsök" (Web Search)	45	52, 7	11	medium
Telephone Advice Line (1177 Vårdguiden)	48	51, 4–5	15	medium
Laboratory-based surveillance (number of cases)	47	52, 8	20	high
Laboratory-based surveillance (% positive)	46	52, 7	**	Medium
Sentinel sampling	48	52, 7	13	*
Antiviral sales	*	52, 8	*	*
Laboratory-confirmed influenza cases in intensive care (SIRI)	*	52, 7	*	*
Excess mortality	51	1, 9	11	*

* Epidemic thresholds/intensity levels not assigned.
** The percentage positive with laboratory-based surveillance remained above baseline levels until the end of the surveillance period in week 20.

Vaccination coverage

Data on vaccination coverage among persons 65 years of age and older have been gathered by Sweden's 21 county medical officers for their respective county councils since 2003.[10] 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 general practitioners, or patient record data. These methodological differences result in coverage estimates of varying quality and precision. Although the methods vary between counties, the methods within most counties have been roughly the same for the past several years. Since the 2014–2015 season, an estimate of the vaccination coverage in other age groups has also been included, using data from 13 county councils[11] *where registry data by age group are available throughout the season as well as annually.*

Coverage among those 65 years of age and older

The national vaccination rate among those aged 65 and over was the same as the previous season at 49% (see Figure 2 and Table 3). Vaccination coverage has remained steady at just under 50% for the past three years. In total, approximately 945,000 people aged 65 and over were vaccinated. Coverage is highest among people aged 75 and over (55%, see Table 5)[5], which is encouraging because the risk of severe influenza increases with age. However, none of the age groups' coverage rates approached the WHO target of 75%.

Comparisons among counties/regions are difficult because estimates are based on different methods (see above). There is uncertainty around each value, but Table 4 and Figure 3 below still give a picture of present vaccination coverage rates throughout Sweden. Comparisons within the same county over time can be useful; in fact, we see that most county councils increased their vaccination coverage while Stockholm and Västra Götaland decreased slightly. At the top are the regions of Jönköping and Värmland, where around 60% of those aged 65 and over were vaccinated. The county councils in Kronoberg, Halland, and Blekinge again reached a vaccination coverage of at least 55%.

[10] 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.

[11] Data collected from vaccine registries in Gävleborg, Jämtland, Jönköping, Kalmar, Kronoberg, Norrbotten, Skåne, Stockholm, Värmland, Västernorrland, Västra Götaland, and Östergötland. Data from Stockholm include only vaccinated risk groups. Data from Västernorrland do not include doses given at county residential facilities, which means coverage is underestimated. Skåne reports a higher coverage via survey (56%) and billing data (54.4%) than via the registry (45.5%).

Figure 2. Vaccination coverage among those aged 65 and over in Sweden, 2011–2012 to 2016–2017.

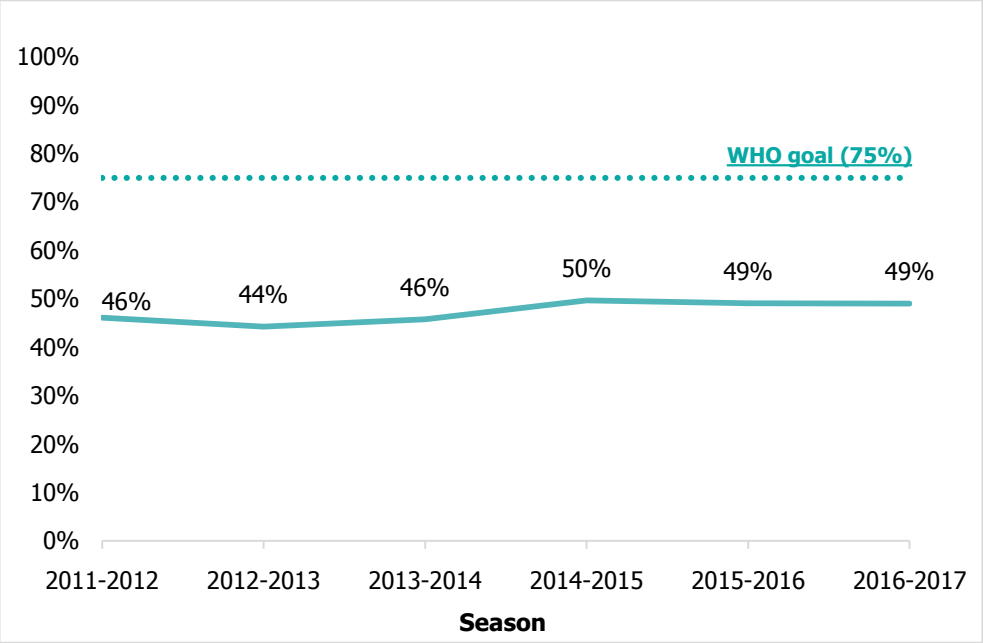


Table 3. Mean yearly proportion of vaccinated persons older than 65 years in Sweden, as estimated using data from the 21 county medical officers, 2003–2004 to 2016–2017.

Season for vaccination	Estimated proportion of the population aged 65 and over vaccinated with seasonal vaccine (%) *
2016–2017	49.1
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

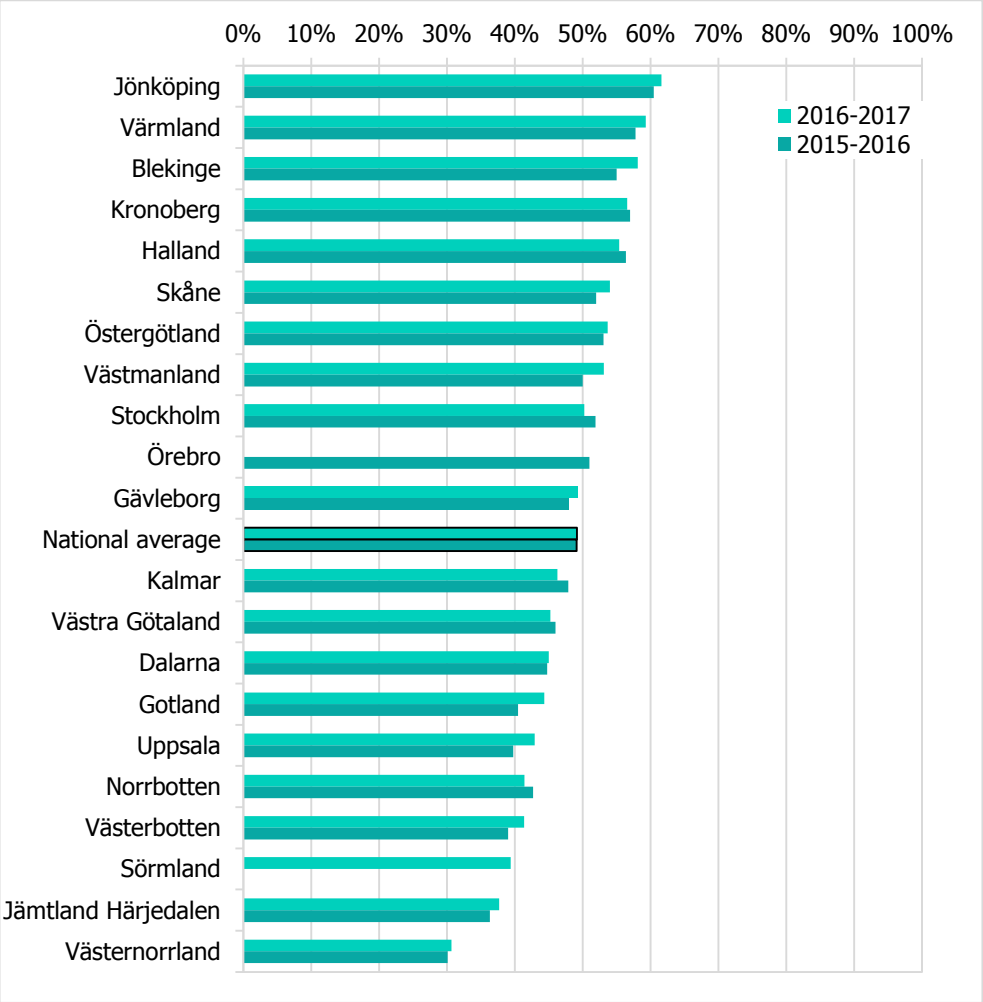
* Very few counties reported seasonal vaccination coverage in 2009 because the focus was on the pandemic vaccination. Sixty per cent of the Swedish population was vaccinated with an adjuvanted monovalent vaccine in 2009.

Table 4. Estimated proportion of vaccinated persons above 65 years old per county council in Sweden

County Council	2015–2016 (%)	2016–2017 (%)
Blekinge	55	58
Dalarna	45	45
Gotland	41	44
Gävleborg	48	49
Halland	56	55
Jämtland Härjedalen *	36	38
Jönköping	61	62
Kalmar	48	46
Kronoberg	57	57
Norrbotten	43	41
Skåne*	52	54
Stockholm	52	50
Sörmland *	-	39
Uppsala *	40	43
Värmland	58	59
Västerbotten	39	41
Västernorrland *	30	31
Västmanland	50	53
Västra Götaland*	46	45
Örebro	51	***
Östergötland	53	54
Average	**49 (49.1)**	**49 (49.1)**

*Notes: Different estimation methods were used in each county, which makes comparison difficult. Percentages are based on the population of the county on December 31, 2015 and 2016, respectively. (Source: Statistics Sweden.) Data from Jämtland Härjedalen and Västernorrland do not include doses given in long-term care facilities, etc., which underestimates the coverage rate. Sörmland has data from a new vaccine registry for the first season, and no coverage was calculated for 2015–2016 because only data on the number of delivered doses was available, which cannot reliably be used to estimate doses given to elderly persons. Data from Örebro for the 2016–2017 season were not yet available. Three coverage estimates for 2016–2017 were available for Skåne Region using data from a survey (56%), billing data (54.4%), and the vaccine registry (45.5%). In this report, we use the coverage rate based on billing data. For 2015–2016, two coverage rates were available for Västra Götaland and Skåne, one based on survey responses and one based on registry or billing data, respectively. This report uses the latter estimates rather than the survey estimates. For both regions, survey responses showed a higher coverage rate (Skåne: 58%, Västra Götaland, 54%).

Figure 3. Estimated proportion of vaccinated persons aged 65 and over per county council in Sweden for seasons 2015–2016 and 2016–2017.*



*See notes above under Table 4.

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. Approximately 5–10% of the population under 65 years of age belong to a medical risk group.

Thirteen 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 shows that, once again, only about 2% of those under 65 years of age were vaccinated during the season (see Table 5 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 5. Percentage vaccinated per age group[12]

Age group	0–17 years	18–39 years	40–64 years	65–74 years	75–84 years	85+ years	Average <65 years	Average ≥65 years
Percentage vaccinated	0.3%	1.3%	4.1%	42%	55%	55%	**2.2%**	**47%**

Syndromic surveillance of community disease burden

Two systems of syndromic surveillance are being used this season, Webbsök ("Web search") and telephone calls to medical advice line 1177 Vårdguiden. Webbsök 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.

In collaboration with the medical telephone advice line 1177 Vårdguiden, the Public Health Agency receives aggregated weekly data on calls from a system called Hälsoläge. The age group (child or adult) and main reason for calling are registered for all callers. The reported data include the number of calls related to cough, fever, and sore throat. The proportion of calls related to fever among children has been found to be a good indicator of influenza activity in the community.

Web search data (Webbsök)

Webbsök was the first system to cross the epidemic threshold during the season and indicated that the 2016–2017 influenza season started week 45, 2016, and was at a medium level during weeks 50, 2016, to week 1, 2017.

From week 27, 2016, to week 26, 2017, a total of 123,874 queries related to influenza were submitted to the 1177.se search engine. This is similar to the previous season.

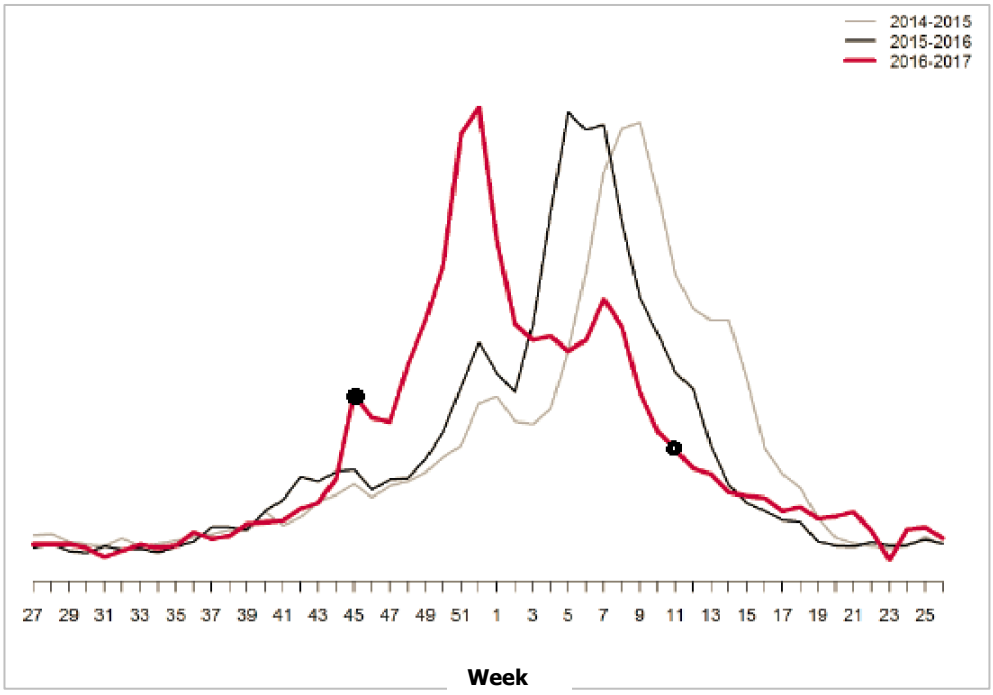
According to Webbsök, the 2016–2017 influenza season lasted for 19 weeks, from week 45, 2016, to week 11, 2017 (Figure 4). During four of these weeks (weeks 50, 2016–1, 2017), Webbsök showed a medium level of influenza activity[13]. During the previous season (2015–2016), the influenza activity lasted for 18 weeks and showed a medium level for six weeks and a high level for three weeks. The seasonal pattern corresponds largely to that seen in laboratory-based surveillance,

[12] As above, these calculations are based on data collected from vaccine registries in the 13 counties/regions with vaccine registries (see footnote 5) – except Östergötland, where data are not available in these age groupings.

[13] The Webbsök threshold for a high level was 28 ILI patients per 100,000 population for the 2016–2017 season.

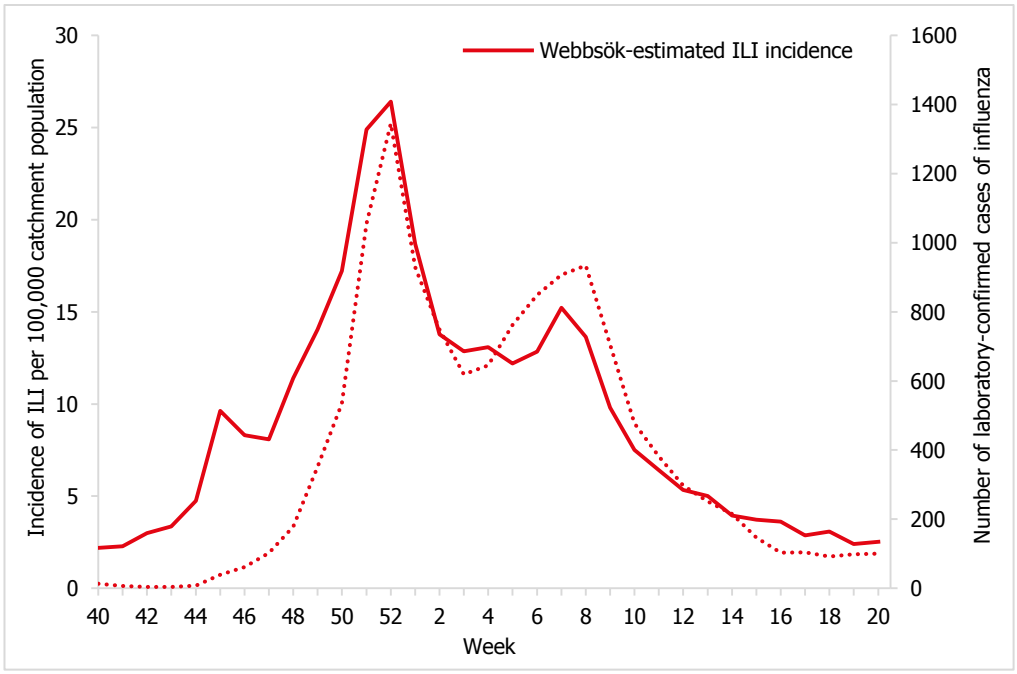
but the intensity levels differ (Figure 5). By providing data on Monday mornings, it provides an early signal of the activity in the previous week.

Figure 4. Webbsök's estimated proportion of the population with ILI per week, 2014–2017, with start and end points of the epidemic marked.



Note: Webbsök's ILI estimate was above the epidemic threshold during weeks 50–16 in 2014–2015, during weeks 49–13 in 2015–2016, and during weeks 45–11 in 2016–2017. The dots indicate the start and end points of the epidemic.

Figure 5. Webbsök's estimated proportion of persons with ILI and the number of laboratory-confirmed cases, 2016–2017.



Note: The axes have been adjusted to highlight the matching trends reported through the two systems.

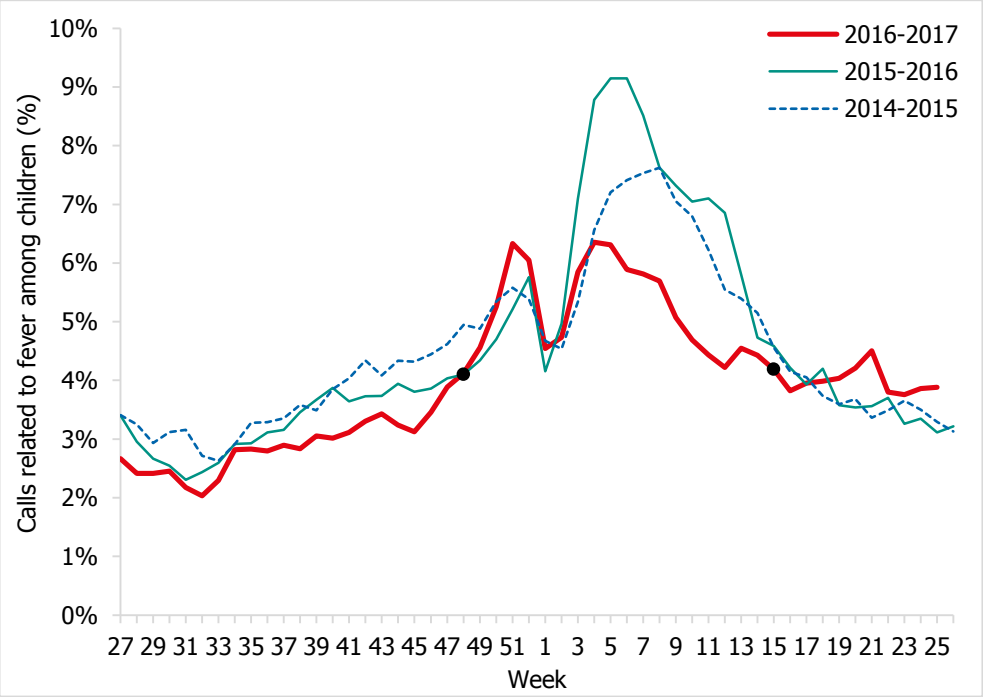
Telephone advice line data (1177 Vårdguiden)

The number of calls to 1177 Vårdguiden regarding fever among children exceeded the epidemic threshold in week 48, 2016, and ended week 15, 2017. The number of calls was at a low level for most of the season, but there were two peaks of medium intensity during week 52, 2016, and during weeks 1–3, 2017.

An average of 4.5% of the calls throughout the season were regarding children with fever (Figure 6). The highest number (4,311) and percentage of calls (6.4%) was registered during week 4, 2017. The total number of calls regarding fever among children was similar to the two previous seasons, but with a lower second peak. The peak weeks corresponded to the peaks 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 6. Percentage of telephone calls regarding fever in children received by the medical advice line 1177 Vårdguiden for the past three seasons.



Note: The dots indicate the start and end points of the epidemic.

Laboratory-based surveillance

All laboratory-confirmed cases of influenza fall under statutory reporting requirements (as of Dec 1, 2015), but subtyping is not required. Denominator data (the total number of samples analysed) is reported voluntarily via e-mail. Sampling for influenza in Sweden is primarily done in hospital settings.

The influenza season 2016–2017 was dominated by influenza A(H3N2). In contrast to the previous seasons, there was no wave of influenza B at the end of the season (see Figure 7).

The epidemic started in week 47, 2016, and continued for 25 weeks (to week 20, 2017). After the start of the epidemic, the number of laboratory-confirmed influenza cases increased during the subsequent weeks until a high peak in week 52, 2016, when 1 345 cases were reported. This is unusual compared to previous seasons because influenza activity usually decreases during the Christmas and New Year holidays. At the beginning of 2017, the number of laboratory-confirmed influenza cases decreased at first but then increased again to a second peak in week 8, at the end of February (see Figure 8).

The vast majority of the cases during both peaks were influenza A, and of the samples subtyped, influenza A(H3N2) was the dominating subtype throughout the season. Of the cases reported for weeks 40–20, 95% of the cases were influenza A and 5% were influenza B. At week 17, 2017, the dominance shifted to influenza B, but there was no real epidemic wave as has been seen during the two previous seasons. Influenza B/Victoria was most prevalent of the samples that were assigned a lineage.

The number of laboratory-confirmed influenza cases in total (13,068 cases) and during the peak week (1,345 cases) were the highest numbers ever reported. Meanwhile, the number of individuals sampled also increased, so the percentage of positive samples was in fact similar to the previous season (2015–2016, see Table 6 and Figure 9).

Figure 7. Number of laboratory-confirmed cases by influenza type and week, 2015–2016 and 2016–2017.

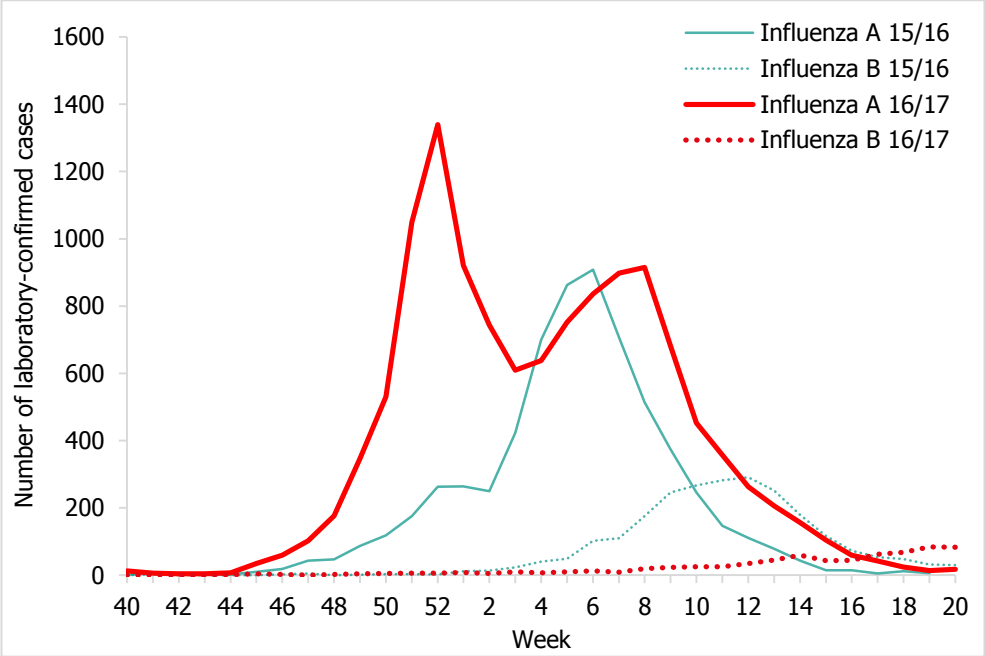


Figure 8. Total number of laboratory-confirmed cases of influenza (all types) per week and the dominating influenza type(s) per season, 2012–2017.

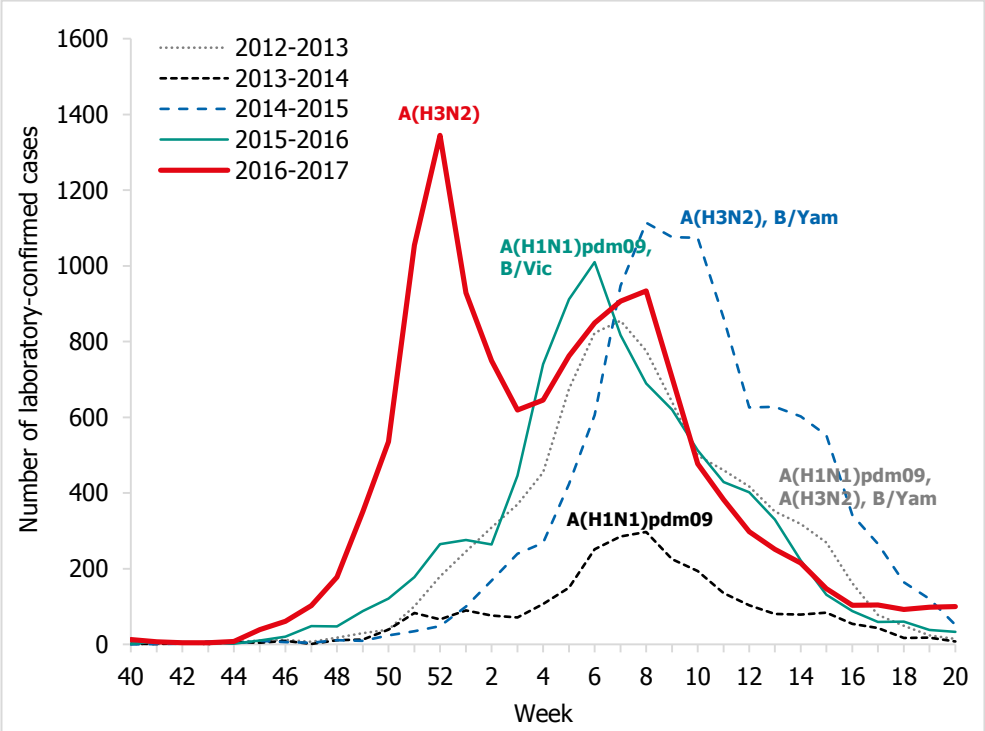
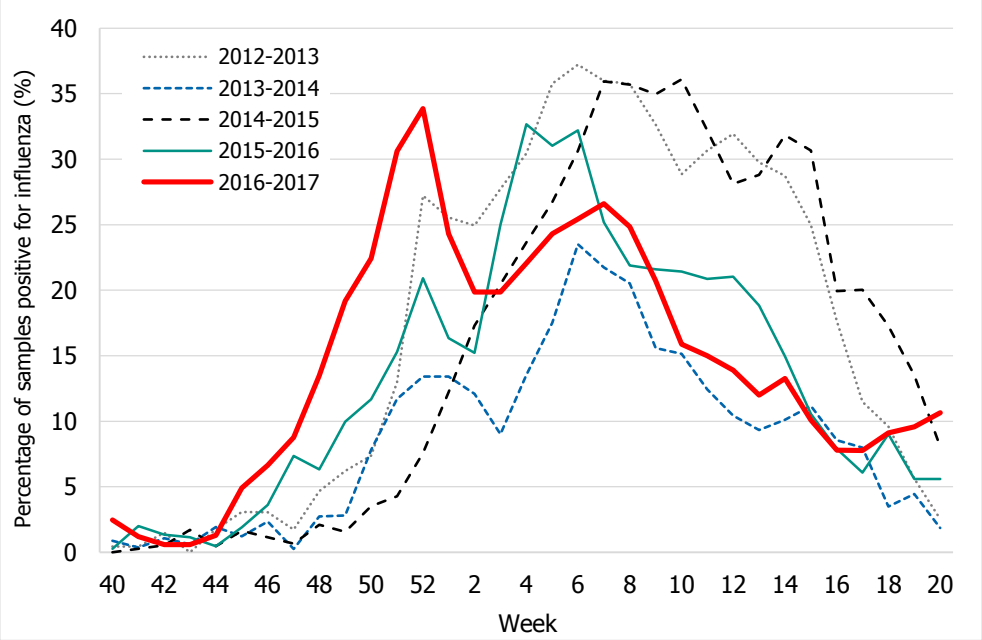


Table 6. Number of laboratory-confirmed influenza cases (all types), total samples analysed, and percentage of samples positive for influenza by season, 2012–2017.

	Number of laboratory-confirmed cases	Number of analysed samples	Percentage of samples positive for influenza
2012–2013	8,196	31,754	26%
2013–2014	2,607	22,330	12%
2014–2015	10,389	42,688	24%
2015–2016	9,150	48,135	19%
2016–2017	13,069	68,241	19%

Figure 9. Percentage of samples testing positive for influenza, per week, 2012–2017.



Viral distribution

The 2016–2017 season was dominated by influenza A, with 12,360 laboratory-confirmed cases (95% of all cases). Only 708 cases of influenza B were reported (5% of all cases). Subtyped influenza A-positive samples were almost exclusively influenza A(H3N2) (99%) (see also the *Subtyping and lineage determination* section). Table 7 summarises the laboratory reporting results over the last five seasons, including the number of analysed samples and the proportion of positive samples as well as the total samples positive by type, subtype, and lineage.

Table 7. Laboratory results of samples analysed and reported through the laboratory reporting system over the last five seasons.

	2012–2013	2013–2014	2014–2015	2015–2016	2016–2017
Analysed samples	**31,750**	**22,330**	**42,668**	**48,135**	**68,241**
Proportion positive samples	*26%*	*12%*	*24%*	*19%*	*19%*
Total positive for influenza A	**5,340**	**2,372**	**6,671**	**6,727**	**12,361**
A(H1N1)pdm09 *	2,435	1,737	663	2,049	14
A(H3N2)	548	169	2 052	112	2,061
A, not subtyped**	2,357	466	3,956	4,566	10,286
Total positive for influenza B	**2,857**	**213**	**3,718**	**2,423**	**708**
B/Victoria lineage***	8	2	2	59	11
B/Yamagata lineage***	148	24	63	19	30
B, not typed to any lineage	2,701	187	3,653	2,345	667

* 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 and 2016–2017 seasons are 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 2016–2017 season mostly affected individuals aged 65 years and over (Figure 10). It is well established that influenza A(H3N2) affects older age groups most severely, which is reflected in the median age of cases (see Table 8) and in the age distribution of cases (see Table 9 and 10). This is in contrast to the previous season (2015–2016) where influenza A(H1N1)pdm09 dominated and more so affected individuals aged 40–64 years. Compared with previous seasons dominated by influenza A(H3N2), the distribution of cases by age group this season is similar, but the incidence has more than doubled, likely in part due to increased sampling. The incidence of laboratory-confirmed influenza among those aged 65 years and over was 411 cases per 100,000 individuals (see Table 9) compared with 192 in the last season dominated by influenza A(H3N2), 2014–2015. Among the elderly, individuals aged 90–94 years had the highest incidence, with 1,231 cases per 100,000 individuals (see Table 10).

The median age for individuals with laboratory-confirmed influenza A was 73 years and 58 years for individuals with influenza B. More women (52%) than men (48%) had influenza, which was a significant difference ($p < 0.0001$).

Children 0–4 years of age have not been affected to the same extent as in the previous season, although this age group had the second highest incidence in relation to the other age groups with 74 cases per 100,000 individuals (Table 10).

Figure 10. Weekly incidence of influenza A per age group in Sweden, 2016–2017 season.

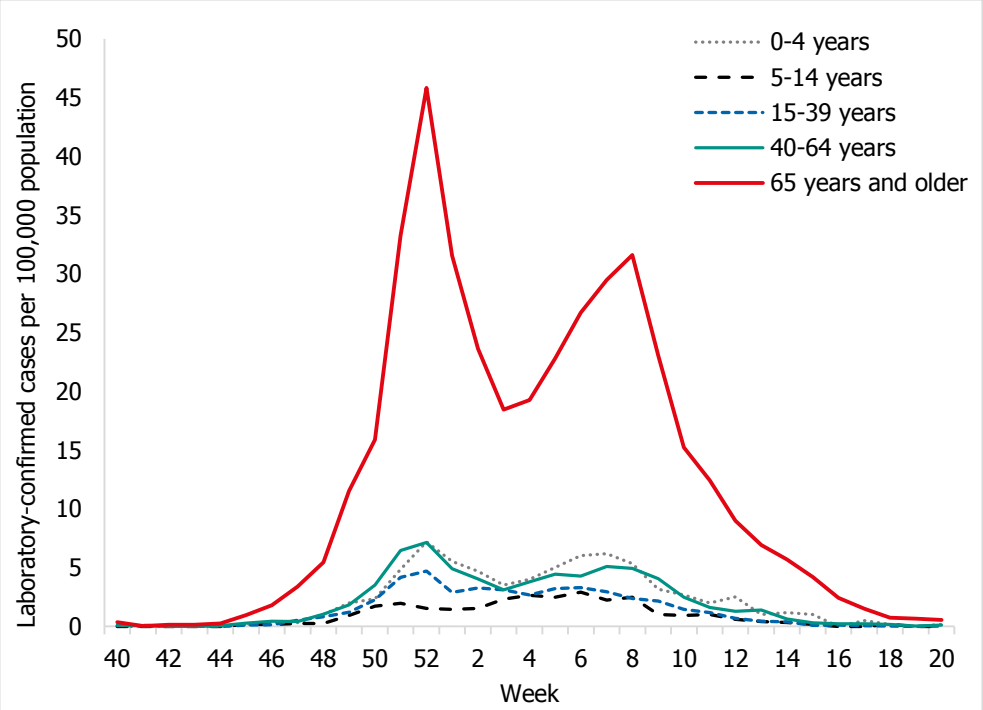


Table 8. Median age (in years) of laboratory-confirmed influenza cases by subtype* and season, 2012–2017.

	2012–2013	2013–2014	2014–2015	2015–2016	2016–2017
Influenza A	-	-	-	48	74
Influenza A(H1N1)pdm09	39	45	50	-	-
Influenza A(H3N2)*	64	58	72	-	-
Seasonal influenza B**	46	49	60	33	58

* For the period 2012–2015, all influenza A-positive samples that were negative for A(H1N1)pdm09 were classified as influenza A(H3N2). From 2015–2016 onward, median age is shown by type rather than subtype.
** 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.

Table 9. Incidence and percentage of cases, by age group, of laboratory-confirmed influenza A(H3N2) cases (2011–2012 and 2014–2015) or all influenza A cases (2016–2017) for seasons dominated by influenza A(H3N2)

	2011–2012 (94% H3N2)		2014–2015 (58% H3N2)		2016–2017 (95% H3N2*)	
Age group	**Incidence**	**Percentage**	**Incidence**	**Percentage**	**Incidence**	**Percentage**
0–4	53	7%	33	3%	74	4%
5–14	18	4%	16	3%	31	3%
15–39	25	17%	25	13%	46	11%
40–64	33	22%	37	19%	69	17%
65+	126	50%	192	62%	411	65%
Total	**48**	**100%**	**61**	**100%**	**125**	**100%**

Note: Data does not include sentinel cases or cases where the age is unknown.
*Based on the small proportion of influenza A samples that were subtyped during the 2016–2017 season, see Subtyping and lineage determination below.

Table 10. Number and incidence (per 100,000 population) of laboratory-confirmed influenza per age group and influenza type, Sweden, 2016–2017.

Age group	Population ‡	Influenza A		Influenza B	
		Cases	Incidence	Cases	Incidence
0–4	597,041	436	74	32	5.5
5–14	1,163,953	348	31	56	5.0
15–39	3,139,971	1,407	46	118	3.8
40–64	3,117,331	2,141	69	199	6.4
65–69	573,266	851	148	59	10
70–74	539,911	1,296	235	51	9.4
75–79	356,786	1,494	419	58	16
80–84	247,030	1,648	667	56	23
85–89	162,745	1,546	950	47	29
90–94	75,564	931	1,232	21	28
≥95	21,555	245	1,132	10	46
Total	**9,995,153**	**12,343**	**405**	**707**	**15**

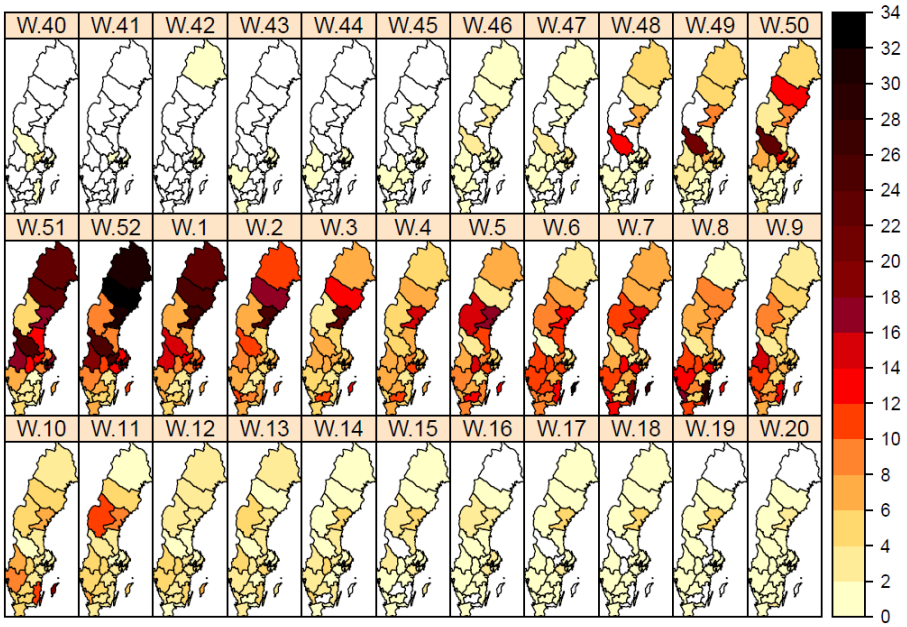
**The table does not include sentinel cases or cases where the age is unknown.*
‡ Population on December 31st, 2016. Source: Statistics Sweden, Statistikdatabasen.

Geographic distribution

The northern parts of Sweden (Norrland) as well as some middle parts of the country (Svealand) had an earlier and more intense start of the influenza epidemic compared to other parts of the country. As shown in Figure 11, the highest incidences were seen in the north and middle parts of the county at the beginning of the season and at the peak (week 52), whereas the highest incidences during the second peak were seen in the southern parts of the country (Götaland). The percentage of samples positive for influenza showed a similar geographic trend with peaks in week 52, 2016, and week 7, 2017.

Altogether, the North had the highest overall incidence per 100,000 individuals this season, with 170 cases, followed by the middle parts (Svealand), with 143 cases, and the southern parts (Götaland), with 110 cases. The greatest numbers of cases were reported from the largest urban areas (Stockholm, Gothenburg and Malmö). However, in relation to population size, Västernorrland had the highest overall incidence, with 275 cases per 100,000, followed by Gotland, Västerbotten, Dalarna, and Värmland, with 150–185 cases per 100,000 individuals. The number of laboratory-confirmed cases might be affected by health care seeking behaviour as well as differences in sampling in the various regions; hence, no direct conclusions should be drawn regarding actual influenza activity using the measured incidence.

Figure 11. Weekly incidence of laboratory-confirmed influenza per 100,000 population and county from week 40, 2016, to week 20, 2017.



Note: The colour scale indicates the incidence.

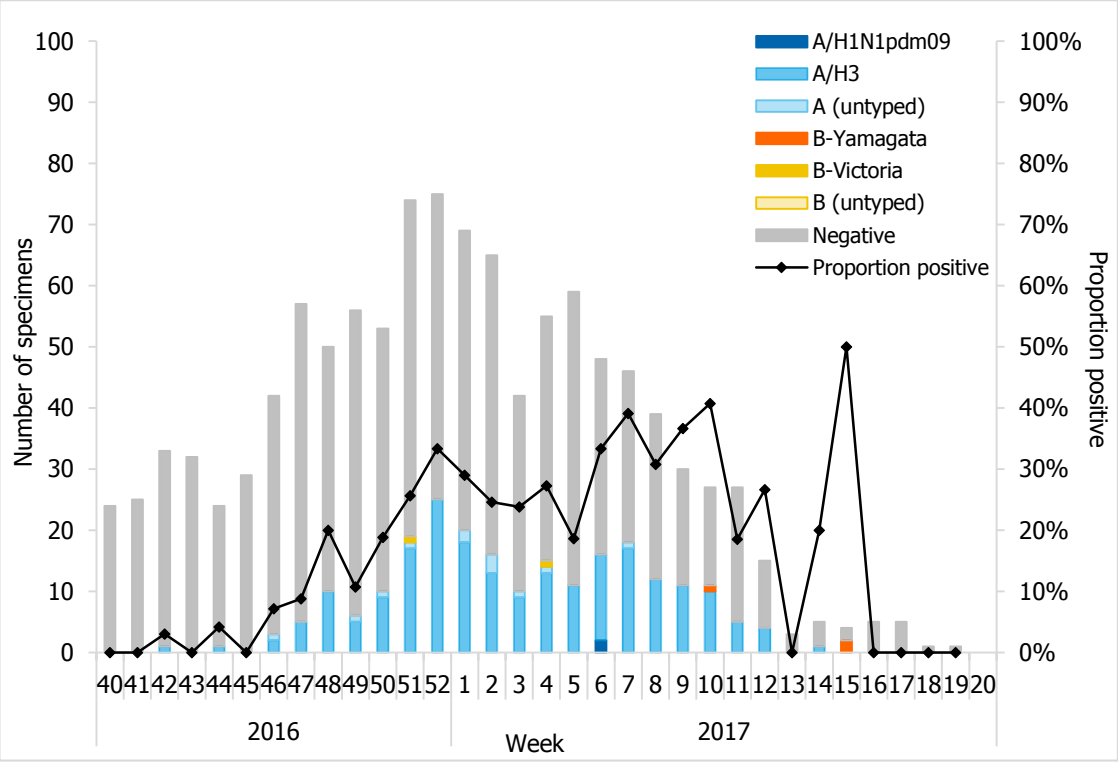
Sentinel sampling

Virological analysis of sentinel samples from sentinel general practitioners, infectious disease clinics, and paediatric clinics contributes to national and international surveillance of circulating influenza viruses. In order to estimate what proportion of the patients seeking care for ILI actually has influenza, the different clinics are encouraged to collect nasal samples from patients with ILI. 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. 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.

During the season 2016–2017, 1,120 sentinel samples were submitted from 85 participants, including 74 general practitioners, 9 paediatric clinics, and 2 infectious disease clinics. Seventy-four per cent of the samples were collected by general practitioners. In total, 233 samples (21%) tested positive for influenza. Figure 12 shows the distribution of samples taken, positive samples by subtype, and percentage positive by week.

Of the positive samples, 227 (97%) were positive for influenza A and 6 (3%) were positive for influenza B. Of the subtyped influenza A-positives samples, 213 (99%) were influenza A(H3N2) and 2 (1%) were influenza A(H1N1)pdm09. Twelve influenza A samples could not be subtyped due to low virus concentration. Six samples were positive for influenza B. Of these, three samples belonged to the B/Yamagata/16/88 lineage, two to the B/Victoria/2/87 lineage, and one sample came from a child vaccinated a few days earlier and positive for both lineages.

Figure 12. Number of sentinel samples submitted each week and the number and percentage of the positive samples by subtype/lineage, 2016–2017.



Clinical features

Of the 1,119 patients sampled through the sentinel system where the symptoms were known, 85% had ILI (Table 11) and 15% had ARI. In total, 56% of the samples came from women. A quarter (24%) of the samples were collected from patients belonging to a risk group (due to age and/or medical risk). In total, 63% of the samples were from patients aged 65 years and over. The most common reported risk groups were heart disease (n = 45), lung disease (n = 38), and diabetes (n = 37).

Table 11. Summary of laboratory results from the sentinel sampling system, including median age and proportion of patients with ILI, for the last three seasons.

	Season 2014–2015			Season 2015–2016			Season 2016–2017		
	Number	**Median age**	**ILI %**	**Number**	**Median age**	**ILI %**	**Number**	**Median age**	**ILI %**
Total analysed	**1,399**	42	75%	**1,341**	43.5	82%	**1,120**	36	85%
Negative	1,026			972			887		
Proportion positive	27%			28%			21%		
Influenza A	**232**			**271**			**227**		
A(H1N1)pdm09	32	37.5	84%	259	28.5	86%	2	27	100%
A(H3N2)	187	40	88%	11	40	100%	213	34	90%
A, not subtyped	13	40	100%	1	59	100%	12	35	93%
Influenza B	**141**			**97**			**6**		
B/Victoria	2	31	50%	89	18	84%	2	4	100%
B/Yamagata	139	45	90%	8	47	75%	3	44	100%
B, both lineages	0	0	0%	0	0		1	3	0%

Influenza infection among vaccinated patients

Vaccination status was reported for 1,075 (96%) of the 1,119 patients sampled during the season. Of these, 122 (11%) were vaccinated. Among the patients belonging to a risk group, 40% were vaccinated.

Influenza was detected among 36 vaccinated patients. Six patients had onset of influenza disease less than two weeks after their flu vaccination, but because full immunity is not obtained in that time period, they were excluded from the analysis of vaccine failures. Both influenza B vaccine strains (B/Victoria and B/Yamagata) were detected from a child vaccinated with the live attenuated vaccine.

Influenza virus A(H3N2) was detected in 29 vaccinated persons (vaccine failures). Twenty-one of the vaccinated patients were aged 65 years and over, and the median age for all 29 cases was 74 years. For the eight patients below 65 years of age, three patients belonged to a medical risk group and four did not, and data concerning risk group was missing for one patient.

Subtyping and lineage determination

All diagnostic laboratories perform influenza typing using molecular assays for influenza A and B. With the end of statutory laboratory reporting for A(H1N1)pdm09 (1 Dec 2015) and the introduction of statutory laboratory reporting for all influenza A- and B-positive samples, subtyping is not mandatory. During the 2016–2017 season, subtyping was performed at three regional laboratories (Lund, Göteborg, and Umeå). The Public Health Agency performs subtyping and lineage typing by real-time PCR for all samples sent in from the diagnostic laboratories and on all positive samples from sentinel surveillance.

In total, 2,075 influenza A-positive samples were subtyped during the season, of which 2,061 (99%) were A(H3N2) and 14 (<1%) were A(H1N1)pdm09.

The lineage was determined for 41 influenza B-positive samples. Eleven (27%) belonged to the B/Victoria lineage, and 30 (73%) belonged to the B/Yamagata lineage. Subtyping results for sentinel reporting are presented in Table 12.

Table 12. Proportion of positive samples within the sentinel sampling system (*Sentinel*) and laboratory reporting systems (*Lab*) by subtype/lineage, 2014–2017.

	2014–2015		2015–2016		2016–2017	
Influenza type	**Sentinel**	**Lab**	**Sentinel**	**Lab**	**Sentinel**	**Lab**
A(H1N1)pdm09	9%	6%	70%	64%	1%	<1%
A(H3N2)	52%	58%	3%	13%	96%	>99%
B/Victoria lineage	1%	1%	24%	18%	1%	<1%
B/Yamagata lineage	38%	35%	2%	6%	2%	<1%

Virological analyses

A representative selection (geographical locations, collection time periods, and types/subtypes) of the influenza-positive samples from laboratories and from the sentinel surveillance program are further analysed by sequencing, and some of these are isolated and sent to WHO CC in London for further analysis. Swedish laboratories are also 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.

The sequencing technology used is NGS (Next Generation Sequencing), which allows sequencing of all known influenza A subtypes and both B lineage types. Through NGS, the haemagglutinin (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 reduced or highly reduced inhibition by NA inhibitors. Two aspects of the matrix protein (M) gene are analysed by sequencing, and the M2 gene of influenza A is analysed with respect to 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.

Phenotypic analysis of sensitivity to the NA inhibitors oseltamivir (Tamiflu®) and zanamivir (Relenza®), is performed with the NAI assay, which requires viruses isolated on cell culture. 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.

All characterisation data are reported to TESSy and to the Global Initiative on Sharing All Influenza Data (GISAID).

Virus isolation on cell culture

The majority of the samples selected for isolation are collected from other laboratories. The quality of the sample differs depending on, for example, the type of specimen, time since sampling, and storage and shipping temperatures. Fifty-five of the collected samples with Ct ≤ 30 were cultured on MDCK cells. Ten samples were excluded due to contamination with bacteria or fungi. Fifty-three per cent of the remaining samples tested positive for influenza.

During the 2016–2017 season, 23 virus isolates and 16 clinical samples were shipped to the WHO CC for further characterisation (one shipment in January and one in June).

Characterisation of viruses

Table 13 summarises the sequenced genes per subtype/lineage for the 2016–2017 season.

Table 13. Number of sequenced gene segments for each subtype/lineage for the 2016–2017 season.

	H	N	M	NS	PB2	PB1	NP	PA
A(H3N2)	198	213	232	225	186	178	211	191
A(H1N1)pdm09	10	12	13	13	7	8	12	10
B/Yamagata	29	29	29	29	26	26	23	23
B/Victoria	12	12	12	12	11	12	10	11

HA - Haemagglutinin. 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(H3N2)

The HA gene of 198 A(H3N2) viruses (including 12 collected between week 29 and 39, 2016) were analysed further. Of these, 69 viruses belonged to subgroup 3C.2a, characterised by the substitutions L3I, N144S, F159Y, K160T, N1225D, and Q311H. The majority (138 viruses) belonged to subgroup 3C.2a1, characterised by the additional substitution N171K and often with N121K (see phylogenetic tree in Appendix 1). A similar distribution between these two subgroups was also seen among the viruses circulating in Europe.[14] Viruses in these subgroups are considered antigenically similar, but evolution is seen in both subgroups.[15]

Early monitoring of vaccine effectiveness in Sweden and Finland suggested levels of effectiveness of 28% and 32% in persons aged 65 years or over, respectively.[16] In Sweden, 34 viruses from vaccinated individuals were further analysed. The majority (29/34) of the vaccinated individuals were aged 65 years or over, and the remaining five were 63, 62, 52, 51, and 12 years old. Of the 34 viruses, 24 belonged to clade 3C.2a1, with 22 containing the T135K (thirteen viruses), I140M (six viruses), or K92R+H311Q (three viruses) substitutions. The remaining 10 viruses from vaccinated individuals were 3C.2a viruses containing the N121K+N122D+S144K+S262N (six viruses), N121K+S144K (two viruses), or T131K+R142K+R261Q (two viruses) substitutions. The antigenic analyses performed on circulating strains so far have not revealed any specific amino acid substitutions or combination of substitutions that seem to cause any mismatch to the vaccine strain A/Hong Kong/4801/2014 in subgroup 3C.2a. However, some of the substitutions mentioned above could potentially affect antigenicity. For

[14] Flu News Europe, week 20, 2017, http://flunewseurope.org/Archives

[15] WHO, Recommended composition of influenza virus vaccines for use in the 2017-2018 northern hemisphere influenza season, http://www.who.int/influenza/vaccines/virus/recommendations/201703_recommendation.pdf?ua=1

[16] Hergens, M. P., U. Baum, M. Brytting, N. Ikonen, A. Haveri, A. Wiman, H. Nohynek and A. Ortqvist (2017). "Mid-season real-time estimates of seasonal influenza vaccine effectiveness in persons 65 years and older in register-based surveillance, Stockholm County, Sweden, and Finland, January 2017." Euro Surveill 22(8).

example, amino acid T135 is located in antigenic epitope A, and the substitution T135K results in loss of glycosylation A.[17] A total of 36 Swedish A(H3N2) virus isolates have been sent to WHO CC in London for further antigenic analyses.

The NA gene of 213 viruses were analysed, and none of them harboured any mutations known to be associated with reduced or highly reduced inhibition to oseltamivir or zanamivir. A total of 21 A(H3N2) viruses were also analysed phenotypically with respect to sensitivity to NA inhibitors. Twelve of these were analysed at the Public Health Agency of Sweden, while 16 (including seven of those analysed by the Public Health Agency of Sweden) were analysed by WHO CC. All 21 viruses were sensitive to both inhibitors. Of 3,082 analysed European viruses, all but seven were sensitive to both oseltamivir and zanamivir.[18] All 232 Swedish viruses for which the M2 gene was sequenced were resistant to amantadine, one due to the substitution S31D and the remaining due to S31N. The NS gene of the 225 analysed viruses and the PB2 gene of the 186 analysed viruses did not contain any mutations known to be associated with increased virulence. Nine of these viruses were collected from severe cases (requiring intensive or ECMO–treatment), and both NS and PB2 could be analysed in seven of the cases, and NS only could be analysed in two of the cases.

Characterisation of influenza A(H1N1)pdm09

All ten A(H1N1)pdm09 viruses (of which eight were collected between week 36 and 39, 2016) for which the HA gene was sequenced belonged to subclade 6B.1, which is defined by amino acid substitutions S162N and I216T. In addition, seven of the viruses also had the S183P and R205K substitutions (see phylogenetic tree for influenza A(H1N1)pdm09 in Appendix 2). Reports from antigenic analyses showed that the 6B.1 viruses were similar to the vaccine strain A/California/09/2009.[18]

None of the 12 viruses for which the NA gene was sequenced had any mutations known to be associated with reduced or highly reduced inhibition to oseltamivir or zanamivir. Among the 53 analysed viruses in Europe, all but one (which showed reduced inhibition to zanamivir but normal inhibition to oseltamivir) were sensitive to both inhibitors. All 13 analysed Swedish viruses were resistant to amantadine due to the S31N substitution in the M2 gene. No amino acid substitutions known to be associated with increased virulence were seen in the NS1 gene (13 analysed viruses, including one virus from a deceased patient) or PB2 gene (7 analysed viruses).

[17] Long, J., R. V. Bushnell, J. K. Tobin, K. Pan, M. W. Deem, P. L. Nara and G. J. Tobin (2011). "Evolution of H3N2 influenza virus in a guinea pig model." PLoS One 6(7): e20130

[18] Flu News Europe, week 20, 2017, http://flunewseurope.org/Archives

Characterisation of influenza B/Yamagata

Further analysis of 29 B/Yamagata-like viruses (including two viruses collected during week 39, 2016) by sequencing of the HA gene showed that these belonged to genetic clade 3, which is characterised by amino acid substitutions S150I, N165Y, and G229D (see phylogenetic tree in Appendix 3). This clade also dominated (341/356) among the European viruses this season.[20] Circulating B/Yamagata strains have reacted well against the 2016–2017 vaccine strain (B/Phuket/3073/2013) used in the quadrivalent vaccine.[19] Three Swedish strains were sent to WHO CC in London for further antigenic analysis.

None of the 29 viruses for which the NA gene was sequenced had any mutations known to be associated with reduced or highly reduced inhibition to oseltamivir or zanamivir. In addition, two B/Yamagata viruses were analysed phenotypically with respect to sensitivity to NA inhibitors, and both were sensitive to both inhibitors. Among the European viruses, no B/Yamagata viruses with reduced or highly reduced inhibition to NA inhibitors was identified.[20]

Characterisation of influenza B/Victoria

Analysis of 12 B/Victoria-like viruses (including one collected during week 38, 2016) by sequencing of the HA gene showed that these belonged to clade 1A, characterised by amino acid substitutions N75K, N165K, and S172P (see phylogenetic tree in Appendix 3). All 152 characterised European viruses[20] also belonged to this clade, as does the Influenza B/Victoria virus included in the trivalent vaccine, B/Brisbane/60/2008. The majority of circulating B/Victoria-viruses that were analysed were antigenically similar to this vaccine strain.[21] Two Swedish B/Victoria strains was sent to WHO CC in London for further antigenic analysis.

None of the 12 B/Victoria-like viruses for which the NA gene was sequenced had any mutations known to be associated with reduced or highly reduced inhibition to oseltamivir or zanamivir. In addition, one B/Victoria virus was also analysed phenotypically with respect to sensitivity for NA inhibitors, and it was sensitive to both inhibitors. Of the analysed European influenza B/Victoria viruses, all but three were sensitive to both inhibitors.[20]

[19] WHO, Recommended composition of influenza virus vaccines for use in the 2017-2018 northern hemisphere influenza season, http://www.who.int/influenza/vaccines/virus/recommendations/201703_recommendation.pdf?ua=1

[20] Flu News Europe, week 20, 2017, http://flunewseurope.org/Archives

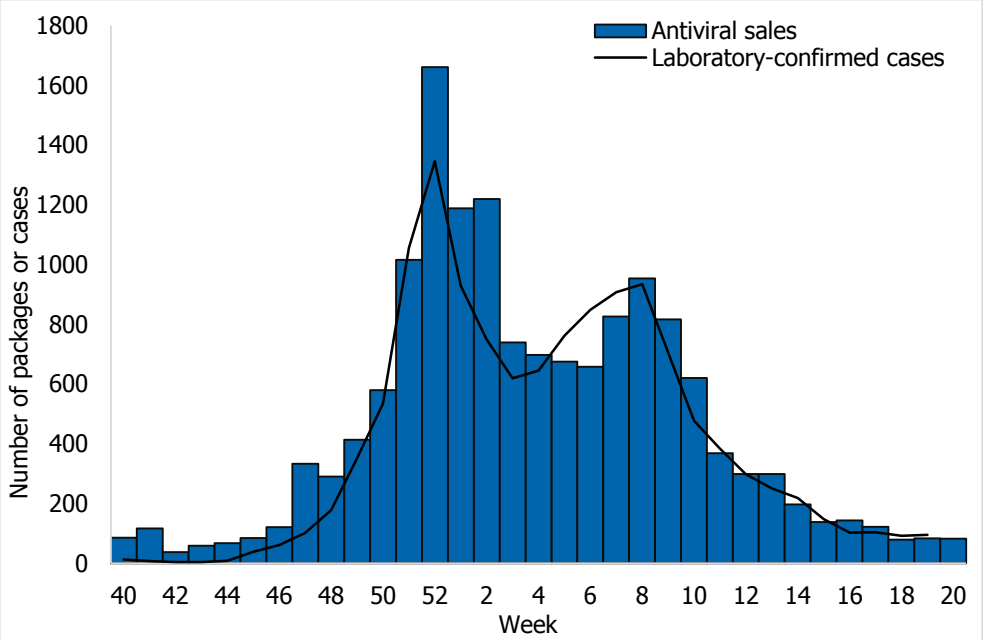
[21] WHO, Recommended composition of influenza virus vaccines for use in the 2017-2018 northern hemisphere influenza season, http://www.who.int/influenza/vaccines/virus/recommendations/201703_recommendation.pdf?ua=1

Antiviral sales

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

Figure 13 shows the total number of antiviral packages sold per week and the number of laboratory-confirmed cases of influenza (A and B) during the 2016–2017 season. The two peaks in laboratory-confirmed cases are clearly visible, with the highest level of antiviral sales in week 52 and a second peak during week 8.

Figure 13. Antiviral sales and the number of laboratory-confirmed cases of influenza A and B per week, 2016–2017.



Until the previous season, the volume of antiviral sales followed the number of laboratory-confirmed influenza cases over time, with the number of packages sold being slightly lower than the number of influenza cases (see Table 14 below). This season, the number of packages sold increased significantly, mainly due to increased requisitions from health care providers. This is likely due in part to the age group affected and reports of low vaccine effectiveness. Antivirals were used for treatment of ill patients in risk groups and severely ill patients and as post-exposure prophylaxis in, for example, elder care facilities and hospital wards.

Table 14. Total antiviral sales and laboratory-confirmed influenza cases in the past five seasons.

	2012–2013	2013–2014	2014–2015	2015–2016	2016–2017
Prescriptions	3,258	1,445	3,610	3,720	4,806
Health care requisitions	3,504	1,819	5,389	4,930	10,262
Total sales	**6,762**	**3,264**	**8,999**	**8,650**	**15,068**
Total influenza cases	**8,197**	**2,607**	**10,389**	**9,150**	**13,069**

Influenza cases in intensive care

The Public Health Agency receives daily, anonymised 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 underlying medical conditions, complications, antiviral treatment, vaccination status, influenza type, and other data for patients under treatment. In addition to the data available through SIRI, aggregated reports are also available at SIR's public web portal. Aggregated reports show all patients in intensive care who were diagnosed with influenza, either as primary or as secondary/other diagnosis, for patients whose intensive care has ended.

Data from SIRI

During the season, 259 patients with influenza were reported as having received intensive care. The majority of the cases had influenza A, 250 cases, while 9 cases had influenza B (see Table 15 and Figure 14). Of patients with reported influenza subtyping results, 3 patients had influenza A(H1N1)pdm09 and 50 patients had influenza A(H3N2). Most of the patients were admitted to intensive care during weeks 51 and 52, 2016, as well as weeks 5 and 7, 2017, which corresponds to the weeks in which most cases of laboratory-confirmed influenza were reported.

Individuals aged 65 years and over were the most affected age group (179 patients), followed by the age group 40–64 years (60 patients). The median age for patients with influenza A(not subtyped) and influenza A(H3N2) was 72 years, whereas it was 82 years for patients with influenza A(H1N1)pdm09 and 66 years for influenza B, although not many patients received the latter two diagnoses. More men (55%) than women (45%) with influenza were treated in intensive care, which was not a significant difference.

Of all reported cases, 216 were risk group patients, either due to age (65 years and older) or one or more medical risk factor. Among patients under the age of 65 years, more than half (60%) did not have a medical risk factor for severe influenza, similar to the previous A(H1N1)pdm09-dominated season, although the number of cases of younger individuals was smaller. Chronic heart-lung disease (n = 112), immunosuppression (n = 39), and chronic liver/kidney disease (n = 25) were the most commonly reported risk factors in the 2016–2017 season. One of the patients with influenza was pregnant.

Altogether, 216 patients were recommended seasonal influenza vaccination due to age or medical risk factor. Vaccination status was known for 111 patients, of whom 90 were recommended vaccination – and of these 90 patients, 38% were vaccinated. All vaccination failures occurred in patients with influenza A. No vaccination failure is known among the patients diagnosed with influenza B. The median age for vaccination failures was 76 years. Vaccine effectiveness decreases with age, and the majority of the patients with vaccine failure for influenza A were aged 65 years and over (30 patients). Vaccine effectiveness may vary at an

individual level depending on factor such as age, immunity, and time from vaccination to time of infection. Moreover, vaccine effectiveness also depends on the level of matching between circulating and vaccine strains. Thus, cases are seen among vaccinated individuals each season.

Information regarding primary diagnosis in intensive care was reported for 245 patients. Influenza with pneumonia (n = 42), viral influenza (n = 38), and septic shock (n = 28) were the most common primary diagnoses.

Of the patients requiring intensive care, 62 individuals died. The majority (76%) of the deceased had a medical risk factor or were aged 65 year or above and therefore were at increased risk of severe influenza infection. Among patients aged 40–64 years who died, 6 of 17 did not have a medical risk factor for severe influenza infection. The median age of those who died was 74.5 years.

Figure 14. Number of patients with influenza in intensive care by influenza type and number of laboratory-confirmed cases, 2016–2017 season.

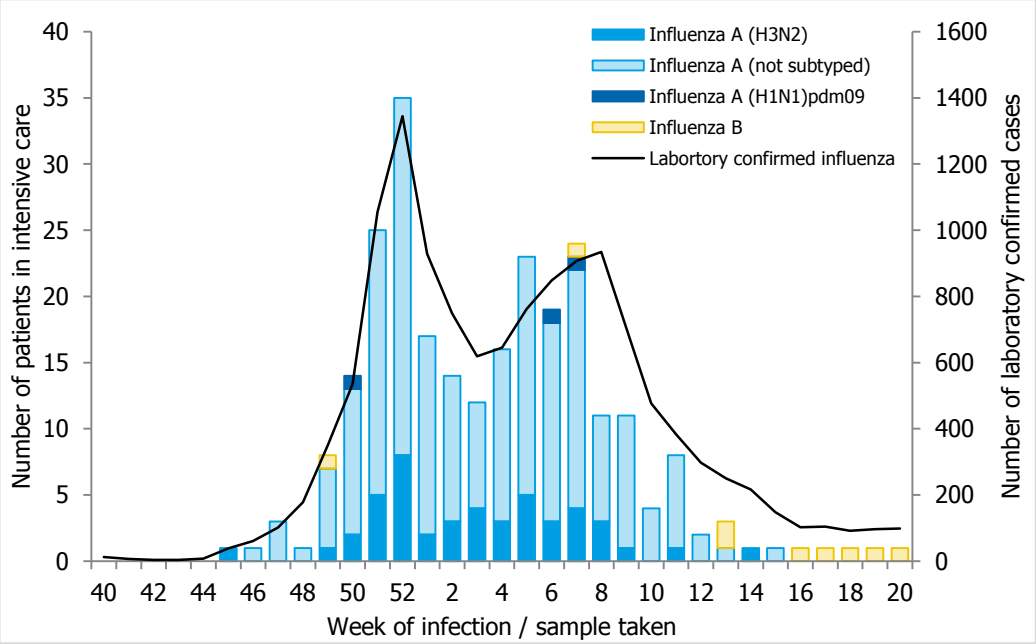


Table 15. Number and median age of patients in intensive care with influenza per influenza subtype, seasons 2012–2013 to 2016–2017, with number of reporting units shown in parentheses for each season.

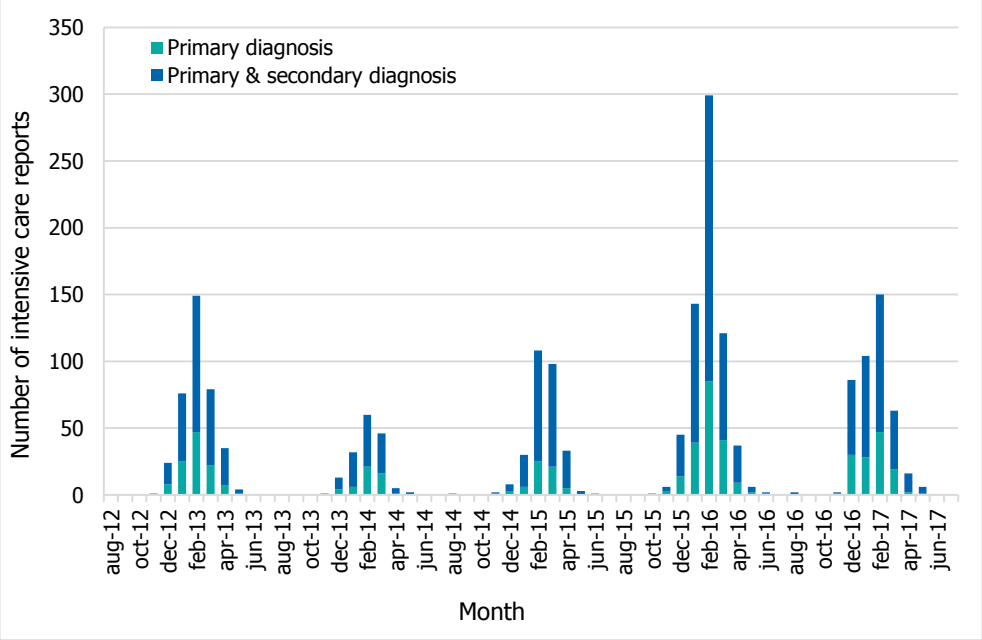
	2012–2013 (n=22)	**2013–2014** (n=24)	**2014–2015** (n=31)	**2015–2016** (n=53)	**2016–2017** (n=49)
			Cases (median age)		
Influenza A (not subtyped)	*	*	*	156 (56)	197 (72)
Influenza A(H1N1)pdm09	67 (56)	50 (58.5)	18 (63)	154 (58)	3 (82)
Influenza A(H3N2)	36 (64)	4 (63)	103 (70)	4 (56)	50 (72)
Influenza B	34 (58.5)	1 (±)	55 (54)	48 (52)	9 (66)
Total	**137**	**55**	**176**	**362**	**259**

***** From season 2012–2013 to 2014–2015, all samples of influenza A were subtyped for influenza A(H1N1)pdm09. Thus, it is assumed that all other influenza A cases were A(H3N2). As of the 2015–2016 season, subtyping is no longer required.
± No median age shown for reasons of patient privacy.

Data from SIR

In addition to the data available through SIRI, aggregated reports are also available at SIR's public web portal. Aggregated reports show all patients in intensive care who were diagnosed with influenza, either as the primary or as the secondary/other diagnosis, and whose intensive care has ended. Data from SIR reveal that fewer patients with influenza received intense care during the 2016–2017 season in comparison to the 2015–2016 season (see Figure 15).

Figure 15. Number of patients with laboratory-confirmed influenza who received intensive care per season, 2012–2017.



Most intensive care units (89 units) are connected to SIR and as such are able to report to SIRI, but this reporting is voluntary. The number of units registered for reporting with SIR has remained relatively constant during the period 2012–2017. The number of reporting units to SIRI more than doubled between its inception in the 2012–2013 season to the 2015–2016 season (from 22 units to 58 units). A preliminary evaluation of SIRI regarding coverage shows that an increase of reporting units in the 2015–2016 season has been sustained this past season, with 63 units having reported.

Table 16 shows the crude number of intensive care patients with laboratory-confirmed influenza reported to SIR and SIRI, respectively, over the past five seasons. The increase in the number of reporting units makes it difficult to compare the crude number of patients in intensive care over time. If a comparison is made, however, using only the units reporting during all seasons (n = 16), the number of cases decreased by 24% in 2016–2017 in comparison to 2015–2016, but no difference was seen compared to the 2014–2015 season, which is the latest previous season dominated by influenza A(H3N2). Using only data from units reporting in the previous and current season (n = 43), the number of cases decreased by 27% (from 323 to 236 cases) this season.

Table 16. The number of intensive care patients with laboratory-confirmed influenza per season reported to SIR and SIRI

	Total in SIR	Total in SIRI
2012–2013	258	135
2013–2014	111	54
2014–2015	223	176
2015–2016	466	363
2016–2017	299	252*

** Although a total of 259 patients were reported through SIRI, 7 of these patients had not ended their care (as of July 25th, 2017) and are thus excluded from this comparison because SIR data only include patients whose intensive care has ended.*

Influenza-related mortality

Influenza-related mortality is often noted during influenza seasons, but it varies depending on the circulating strain and intensity of the season. The Public Health Agency uses different systems to measure influenza-related mortality.

Data on laboratory-confirmed influenza patients are intermittently linked to Swedish Tax Agency data on death to identify deceased individuals and to retrieve their dates of death. If 30 days or fewer have elapsed since the influenza diagnosis, the death is considered to be influenza-related. This measurement is imprecise because the death might have been caused by something else. 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. To identify otherwise unrecorded deaths from influenza, two models are used to identify crude and influenza-related excess mortality during the influenza season using the aggregate number of deaths. The EuroMoMo model estimates the crude excess mortality for the whole country by age group and regionally. The FluMoMo model estimates excess mortality due to either influenza activity or extreme temperatures, both nationally and by age group.

Deaths 30 days after influenza diagnosis

In total, 734 of 13,087 persons who received a laboratory-confirmed influenza diagnosis during the 2016–2017 season died within 30 days of diagnosis. Of these, 713 had influenza A and 21 had influenza B. Of the influenza A cases who died within 30 days, 35 were subtyped as A(H3N2), while the remaining 678 were not subtyped. During this season, it is reasonable to assume that most of these had influenza A(H3N2). Figure 16 shows the number of deaths within 30 days of influenza diagnosis by date of influenza diagnosis.

The vast majority of deaths within 30 days occurred among the elderly aged ≥65 years (95%), while 4.8% occurred among adults aged 40–64 years. Patients who died ranged in age from 33 to 102 years, with a median age of 85 years of age. Patients who had not died within 30 days of diagnosis had a median age of 63

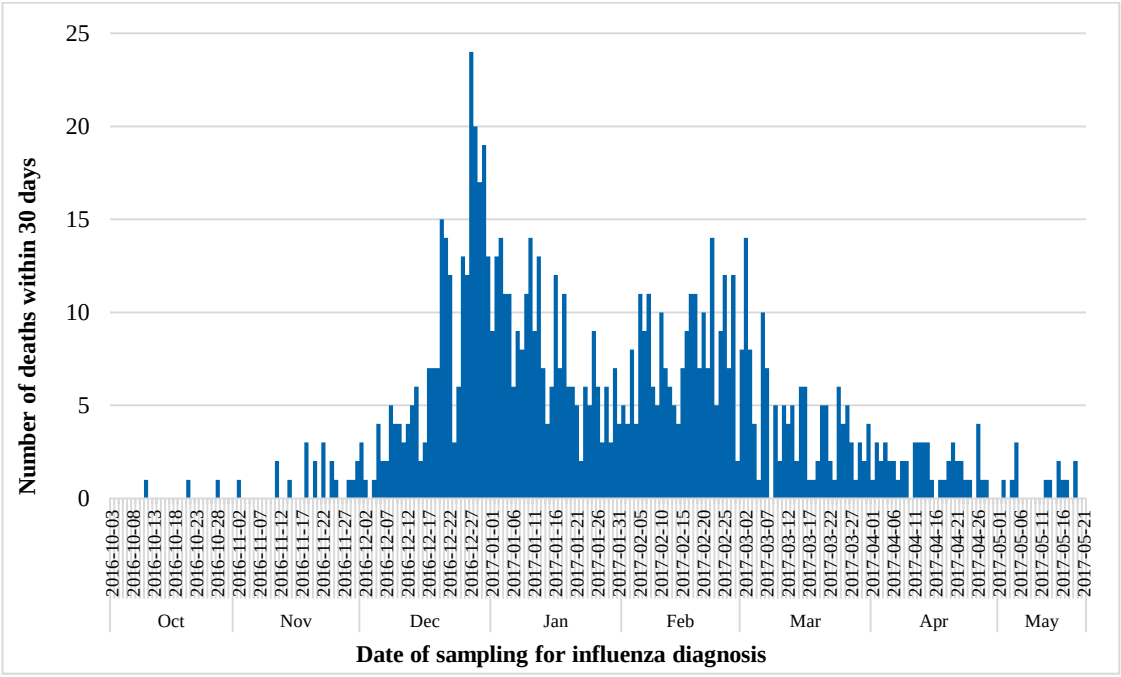
years. More men than women had died within 30 days of diagnosis (52%), although fewer men (48%) had received a laboratory-confirmed diagnosis of influenza.

Overall, 8.5% of those aged 65 years and over who received a laboratory-confirmed influenza A diagnosis died within 30 days. Table 17 shows that the proportion of deaths within 30 days increased with increasing age and varied from 0.05% for persons aged under 40 years to 18.1% for people between 90 and 94 years of age. Seasons dominated by influenza A(H3N2) often result in many deaths among the oldest age groups.

Table 17. Number and incidence of influenza A laboratory-confirmed cases and deaths within 30 days of diagnosis, by age group[22]

	<40 years	40–64 years	65–69 years	70–74 years	75–79 years	80–84 years	85–89 years	90–94 years	≥95 years	Total
Total Cases	2,221	2,166	857	1,295	1,496	1,647	1,553	936	246	12,417
Cases/100,000	46	70	149	239	417	660	937	1,195	1,074	125
Total Deaths	1	34	36	46	80	140	165	169	42	713
Deaths/100,000	0	1	6	8	22	56	100	216	183	7
Deaths among cases (%)	0.05%	1.6%	4.2%	3.6%	5.3%	8.5%	11%	18%	17%	5.7%

Figure 16. Number of deaths within 30 days of influenza diagnosis by date of influenza diagnosis



[22] This analysis includes all laboratory-confirmed influenza cases from week 40, 2016, to week 20, 2017. It excludes 182 patients whose personal identification number was not included in the case report, meaning their status at 30 days could not be ascertained. Because notification of influenza was introduced in December 2015, no comparable data are available from previous A(H3N2)-dominated seasons.

Excess mortality

The FluMoMo model measured significant influenza-related mortality for the entire Swedish population and for the age group 65 years and older for 13 weeks (weeks 51, 2016, through week 11, 2017). As shown in Figure 17, the two peaks of the influenza season can be clearly seen. Excess mortality was more marked in the northern region of Sweden during the first peak of influenza activity, where the highest incidence of influenza was also measured, whereas the southern and eastern regions of Sweden had two more moderate peaks in excess mortality.

The age group of those aged 65 years and over is the group where influenza-related excess mortality is most frequently noted – particularly during seasons dominated by A(H3N2), such as the 2016–2017 season. As shown in the figure, earlier seasons with high levels of A(H3N2) (e.g. 2011–2012, 2012–2013, and 2014–2015) also show similar excess mortality in this age group. However, measured influenza-related excess mortality was higher and lasted longer in 2016–2017 than in other recent seasons (see also Table 18).

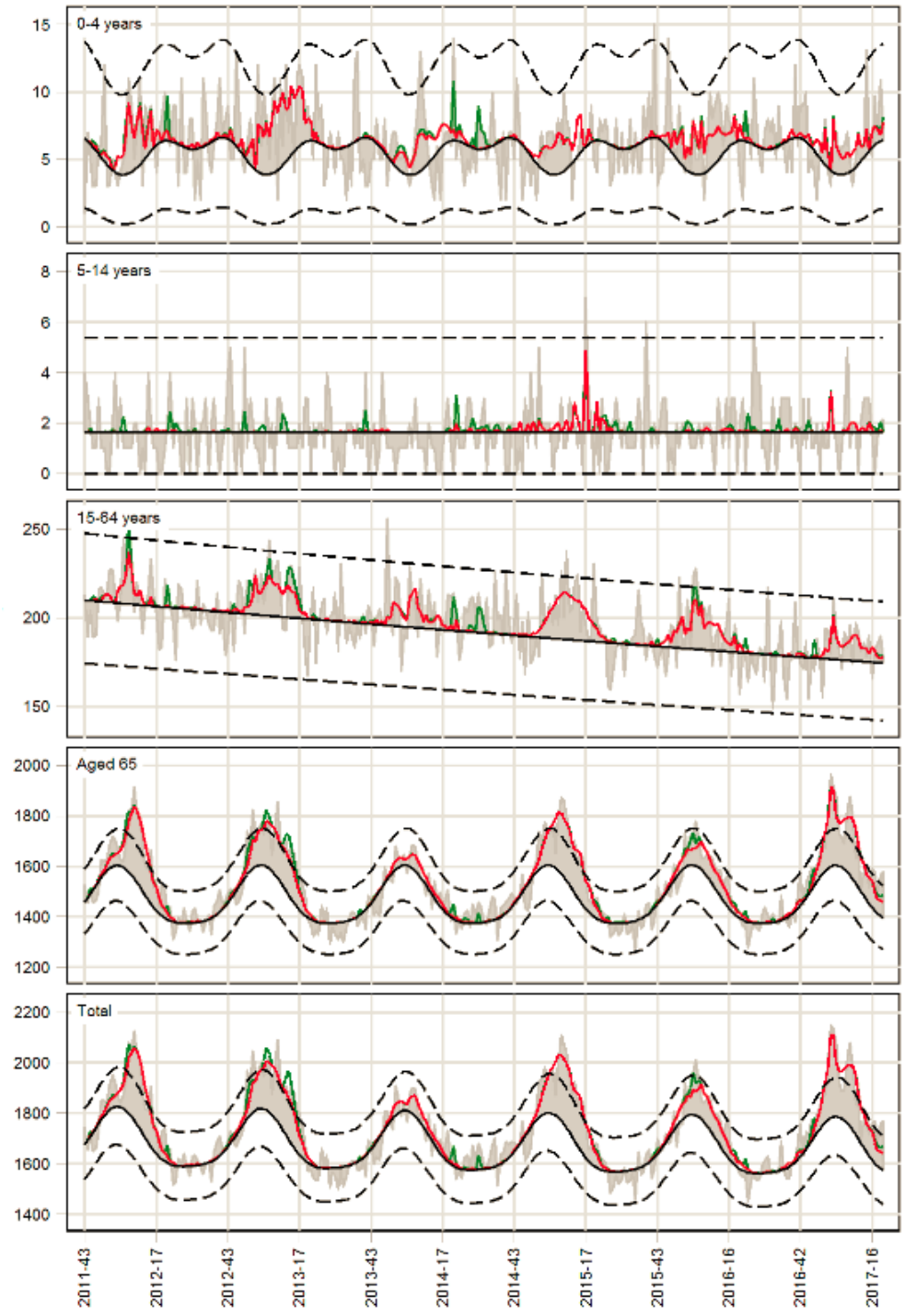
At the European level, excess mortality has been reported among those aged 65 years and over as well as, to a lesser extent, in the age group 15–64 years (see EuroMoMo project: http://www.euromomo.eu/).

Table 18. Weeks with significant influenza-related excess mortality per age group, 2010–2011 season to 2016–2017 season.

Season*	Week	Age Group
2011–2012	Week 7, 2012	15–64 years
	Week 8, 2012	≥65 years
	Week 9, 2012	entire population, ≥65 years
	Week 10, 2012	≥65 years
2014–2015	Week 7, 8 and 10, 2015	entire population, ≥65 years
2015–2016	Week 4–6, 2016	15–64 years
2016–2017	Week 51, 2016 to week 11, 2017	entire population, ≥65 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.*

Figure 17. Number of deaths per week (grey), influenza-related excess mortality (red), and temperature-related excess mortality (green) in each age group and in total, Sweden, 2011–2017. [23]



[23] The expected number of deaths are shown 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.

Quality assurance

Different external quality assurance programmes are used to ensure the quality of the diagnostics done in Sweden and the analysis at the Public Health Agency. The surveillance is dependent on well-standardised virological methods.

At the Public Health Agency, one-step real-time RT-PCR assays are used 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. 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. The PCR protocols are shared with the other laboratories in Sweden. The laboratories that use these PCR systems are encouraged to send all samples with deviating results to the agency for sequence analysis.

Yearly, the Public Health Agency produces a panel PCR for the Swedish laboratories on behalf of the External Quality Assessment for Clinical Laboratory Investigations (EQUALIS). This allows the laboratories to measure the analytic sensitivity and specificity.

The majority of the laboratories performing diagnostics for influenza use commercial rapid PCR kits. In the beginning of the season, a questionnaire is sent to all laboratories with a question concerning methods used. Kits used by two or more laboratories are selected for extra quality controls during the season in order to ensure that circulating influenza strains are detected with these assays.

To ensure that the analyses performed at the Public Health Agency are correct, the agency participates in different external quality assurance programmes.

PCR assays developed and used at the Public Health Agency

During the 2016–2017 season, two additional primers were added to the influenza B PCR assay due to changes in circulating strains. After validation, this information was shared with the Swedish laboratories. Moreover, other improvements were made to the overall assay, such as the validation and upgrade of the real-time PCR instrument, shortened run time, and changes to software analysis.

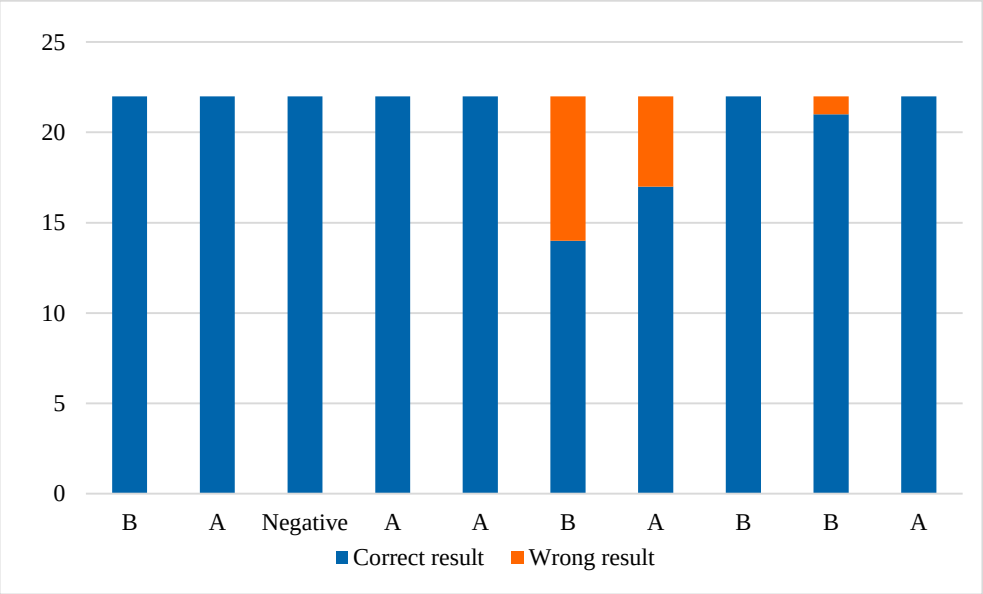
National quality assurance programme for influenza PCR

In September 2016, the Public Health Agency produced a new PCR panel for the Swedish laboratories, which was distributed by EQUALIS. Twenty-two laboratories participated in the panel, and 11 of these reported 10/10 correct answers (Figure 18). This is a decrease compared to last year, when 15 of 22

laboratories reported 10/10 correct answers. The wrong results were all false negatives and were noted in the samples with the lowest viral load.

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 commercial PCR kits, while the number had grown to 13 in 2015 and 14 in 2016, according to EQUALIS results.

Figure 18. Results of the Swedish External Quality Assessment panel 2016



Control of commercial rapid PCR-kits

During the 2016–2017 season, an increasing number of laboratories used commercial "rapid PCR kits" for influenza diagnostics. Results of a questionnaire sent to all 25 microbiological laboratories in Sweden showed that 15 laboratories used a commercial assay, 4 laboratories used an in-house real-time PCR, and 6 laboratories combined both commercial and in-house assays. The use of rapid PCR kits has increased the availability of diagnostics, and this season 10 laboratories offered service around the clock, seven days a week.

Four kits were tested this season (Simplexa Flu A_B & RSV Direct.5, GeneXperts Xpert Flu, GeneXperts Xpert® Flu/RSV XC, and the FilmArray Respiratory panel). The laboratories received a number of samples on two occasions – in the beginning and at the end of the season. A total of 9 positive samples (diluted isolates) were tested with the different kits, and all gave 100% correct results. The results were shown on the Public Health Agency website so that other laboratories using the same kits could have knowledge of the results.

External quality assurance programmes

The Public Health Agency participated in two external quality assurance programmes during 2016.

Annual WHO External Quality Assessment panel for influenza (no 15) 2016

The real-time PCR result was 10/10 correctly typed and 9/10 correctly subtyped (there is no real-time PCR-system for A(H9) in our laboratory).

Phenotypic NAI susceptibility (fluorescence-based assay with MUNANA as the substrate) was correctly reported for the two samples included in the panel.

Genotypic NAI susceptibility testing with NGS was only possible for one of the two samples, and the result for that sample was correct. The other sample was not possible to sequence. As seen with previous panels of this type, the RT-PCR products (used for sequencing) for both samples were weaker than expected compared to the viral titre, indicating degradation of the RNA of inhibition of the RT-PCR.

INFRNA panel from Quality Control for Molecular Diagnostics (QCMD) 2016

The real-time PCR result was 12/12 samples correctly typed and 10/12 correctly subtyped (two B/Victoria curves were below the threshold with our assay).

Appendix 1.

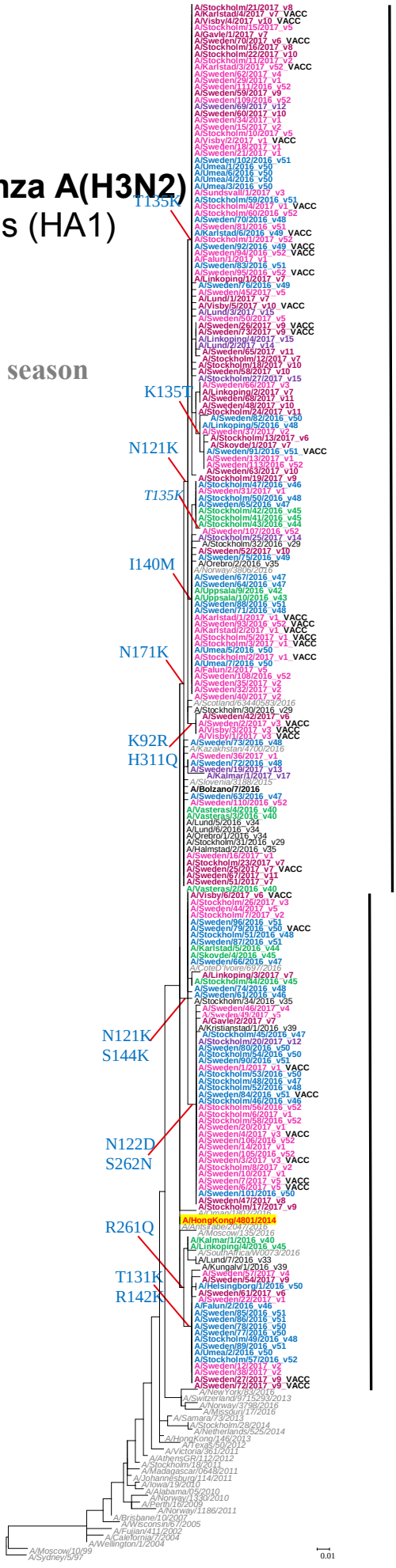
Phylogenetic tree, influenza A(H3N2)
haemagglutinin amino acids (HA1)

weeks 29-39
weeks 40-45
weeks 46-51
weeks 52-5
weeks 6-11
weeks 12-17

2016–2017 season

VACC=Vaccinated
Group representatives
Reference strains

Vaccine strain 2016–2017



Appendix 2.

Phylogenetic tree influenza A(H1N1)pdm09
haemagglutinin amino acids (HA1)

Season 2016–2017
Season 2015–2016
Group representatives
Reference strains

Vaccine strain 2016–2017

Appendix 3.

Phylogenetic tree influenza B
haemagglutinin amino acids (HA1)

Season 2016–2017
Season 2015–2016

Vaccine strain 2016–2017 (quadrivalent vaccine)

Vaccine strain 2016–2017 (trivalent vaccine)

Lineage/clade representatives
Reference strains

This report describes the 2016–2017 influenza season, which was dominated by influenza A(H3N2). The season came to a first, intense peak in the northern part of the country during the Christmas holidays, followed by a second peak in the south in February. The season was intensive and particularly severe for those aged 65 years and over, with high mortality.

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

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
PUBLIC HEALTH AGENCY OF SWEDEN

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

www.folkhalsomyndigheten.se