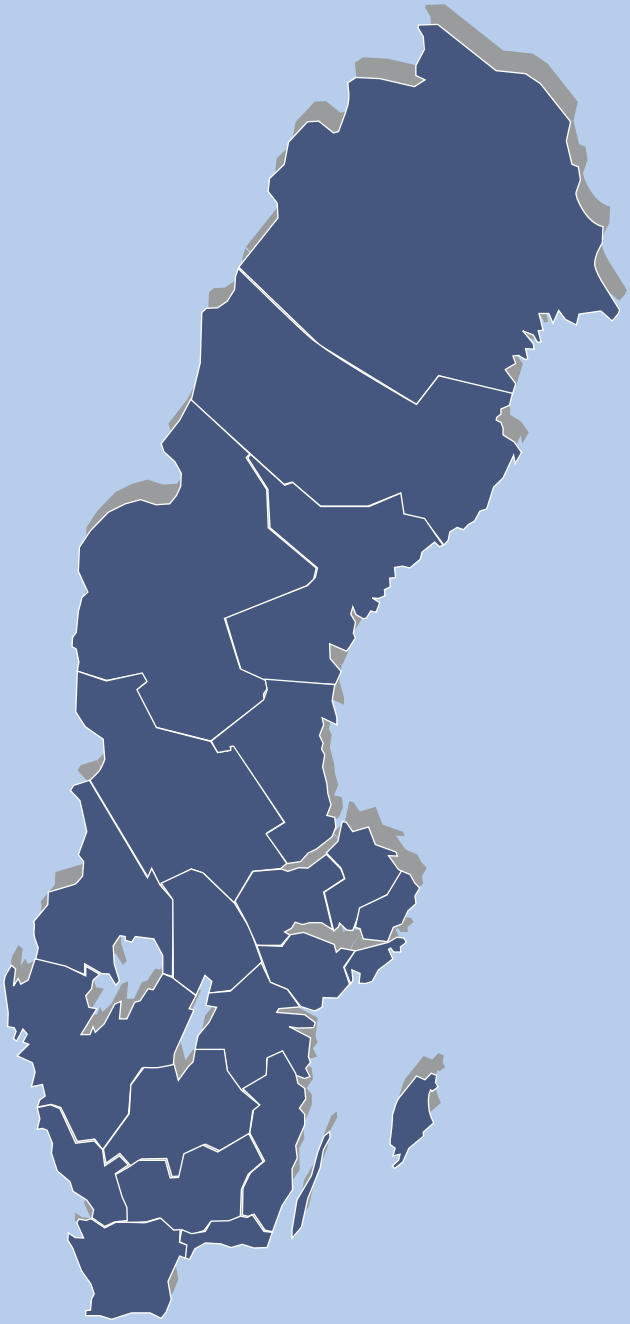
INFLUENZA

Annual Report 2007-2008



SMITTSKYDDSINSTITUTET

The National Influenza Reference Centre
Swedish Institute for Infectious Disease Control
(SMI)

ANNUAL REPORT

JULY 2007- JUNE 2008

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Contents

1. Monitoring of the influenza activity in Sweden
2. Reports from SMI on the influenza activity in Sweden
3. Characterisation of influenza strains
4. Data from the 2007–2008 season
5. Quality control of laboratory diagnosis of influenza
6. Research and method development

1) MONITORING OF THE INFLUENZA ACTIVITY IN SWEDEN

1:1 Sentinel Surveillance

The Swedish influenza sentinel reporting system 2007–2008 consisted of 149 sentinel units recruited by the County Medical Officers of Communicable Disease Control, including both individual GPs and larger health care centres. All twenty one counties participated in the surveillance. Date of visit, age and sex of the patients were reported, and the reports were sent to the County Medical Officers and to the National Influenza Centre at the Swedish Institute for Infectious Disease Control (SMI), either by fax or by the web-based reporting system SentiNet. Each week, reports were received from between 28 and 70 of the sentinel units. The total weekly number of out-patient visits at the reporting units ranged from 2321 to13355. The total number of persons listed by the involved units can't be given exactly due to the structure of the Swedish health care system, but ranges between 142160 and 470029.

1:2 The Sentinel Sampling System

Sentinel sampling was introduced during season 2006-07. During the 2007-2008 season, a total of 36 units consisting of sentinel units, infectious disease clinics, paediatric clinics have participated. Geographically, the units were evenly distributed throughout Sweden. Nineteen out of 21 Swedish counties were included. During 32 weeks, 712 samples were received and analysed at SMI. One to 41 samples were received per week. The weekly number declined towards the end of the season.

The primary diagnostic tool was real-time PCR for influenza type and influenza A subtypes. A swabbing protocol for each sample, according to the minimum requirements from EISS, was completed by the clinician. Approximately 20 % of the samples analysed were positive for influenza.

1:3 Reports of laboratory verified influenza diagnoses

During the influenza season the 25 laboratories sent weekly reports on the number of influenza cases, diagnosed by antigen detection, nucleic acid amplifications (NAA) and/or virus isolation. Influenza isolation was performed at four virus laboratories, placed at University Hospitals and at SMI. The laboratories that did not perform virus isolation sent representative patient samples to SMI for isolation. Influenza strains were isolated from all regions in Sweden.

1:4 Death rates

Information on the weekly death rate in Sweden was purchased from Statistics Sweden. Mean weekly death rate for each influenza-free set of weeks with the same number between week 40 year 1993 and week 20 year 2008 was calculated, and was used as reference for the evaluation of weekly excess mortality.

2) REPORTS FROM SMI ON THE INFLUENZA ACTIVITY IN SWEDEN

2:1 Weekly reports to the Swedish Collaborators

Each Wednesday, national and international influenza information collected during the week, including the WHO country reports, were summarised and made available at the SMI homepage Thursday (www.smittskyddsinstitutet.se). An electronic Newsletter was also sent to all interested parties, including the County Medical Officers of Communicable Disease Control, Departments of Infectious Diseases in Sweden, Microbiological Laboratories and to the National Board of Health and Welfare. A summary of the activity during the entire season was distributed at the end of the summer, when all definitive data were available.

2:2 Other spread of information in Sweden

Media is constantly interested in influenza, and usually contacts SMI to get information. In most instances those contacts resulted in correct and informative articles. The institute has a journal ”Smittskydd” and an electronic newspaper “EpiAktuellt”, where reports of the season on the influenza situation are published when appropriate. An information day for influenza collaborators was arranged in September, and attended by about 100 persons. A short film on influenza vaccination of risk groups was produced and broadcasted repeatedly during the vaccination period in the Swedish State Television.

2:3) Reports to WHO and other National Influenza centres

Sweden reports to WHO via Flunet, and starts reporting when the first laboratory verified case occurs. Since year 2000 we participate in the European Influenza Surveillance Scheme (EISS), and provide weekly information to the EISS homepage.

3) CHARACTERISATION OF INFLUENZA STRAINS

3:1 Genotypic and phenotypic characterisation

Virus strains isolated by SMI or sent to SMI from other laboratories were examined for type and subtype of virus by IF with monoclonal antibodies (WHO, Chemicon). HA, NA and M2-sequencing were also performed. For further characterisation with ferret sera, the strains were also sent to Mill Hill in London. All the influenza strains were also investigated genotypically or phenotypically for antiviral resistance to amantadine and neuraminidase inhibitors.

4) DATA FROM SEASON 2007-2008

4:1 Summary of influenza activity in Sweden

The first laboratory verified influenza cases and the first six ILI cases reported by sentinel physicians were reported in week 40 2008, but they were isolated cases. More consistent infuenza activity started around Christmas, and initially A/H1 dominated among the laboratory verified cases. A peak was observed around week 7. Sporadic influenza B cases were identified throughout the season, and the activity increased successively. From week 8 to week 16 around 50 cases were reported weekly. The total influenza activity, as reported by the laboratories, culminated the week 10 with 101 diagnoses (Fig 4:1:2), which is less than the preceding season when 236 cases were reported during the peak week. The sentinel reports followed a similar pattern, and the magnitude of the activity was similar to that of 2005-2006 for ILI (Fig 4:1:3*).* Overall, the activity was widespread and of medium intensity. The total number of laboratory diagnoses was 1246 (466 A and 780 B) compared to 1372 (1351 A and 21 B) the previous season. The proportion of influenza B (62%) exceeded the number of the preceding season.

All samples collected in the sentinel sampling system were analysed with molecular methods. A total of 712 samples collected during the season were typed and subtyped for influenza. 141/712 (19,8%) became positive (Fig 4:1:4). During this season, the majority were influenza B (67%) followed by influenza A H1 29% and H3 4%.

Fig 4:1:1 Laboratory verified cases of influenza A and B during the 2007-2008 influenza season.

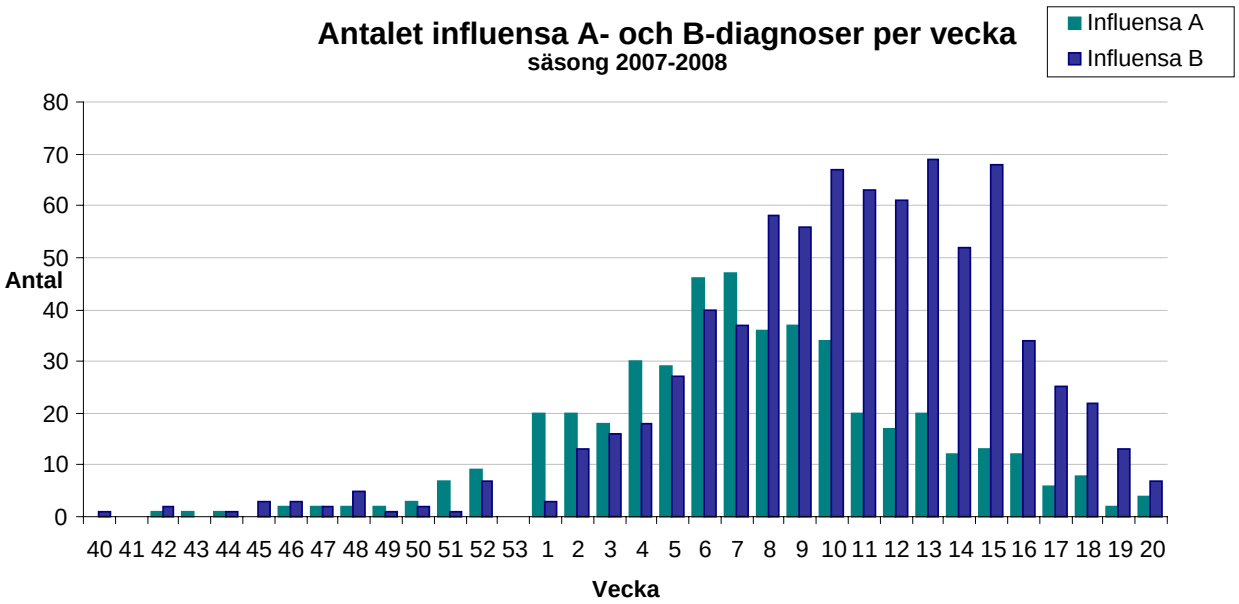


Fig 4:1:2 Number of laboratory verified influenza cases

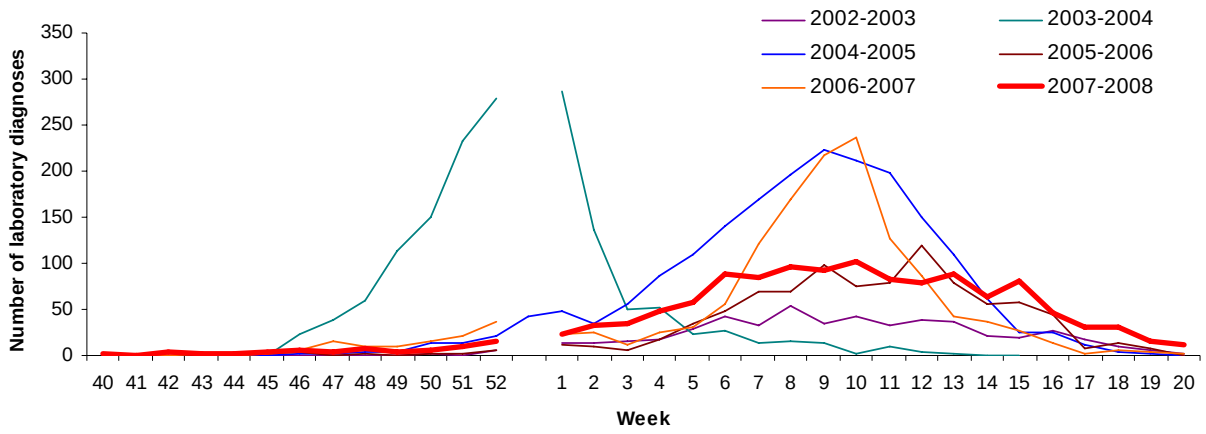


Fig 4:1:3 Proportion (%) cases with influenza-like illness (ILI) out of total number of patient visits in the sentinel system

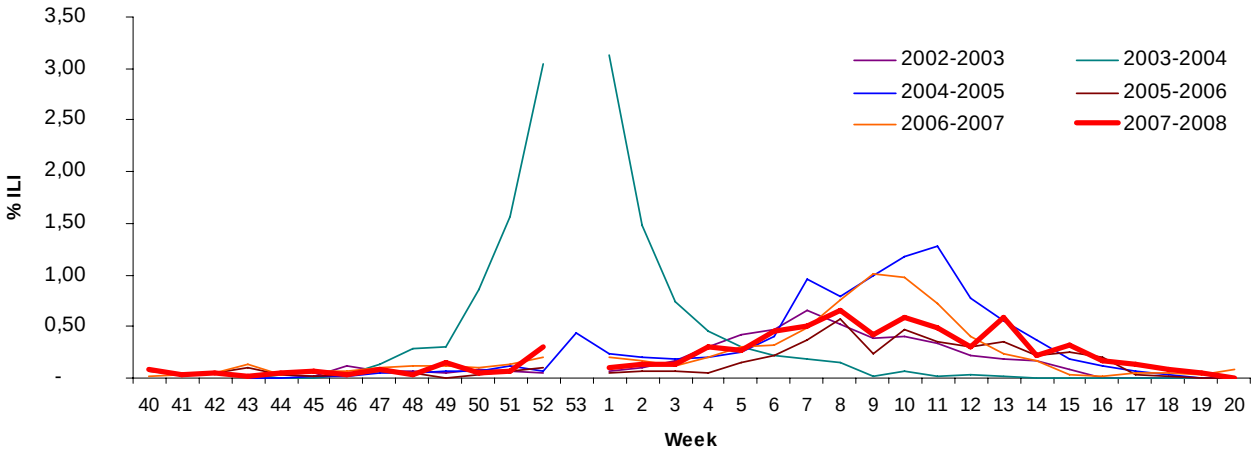
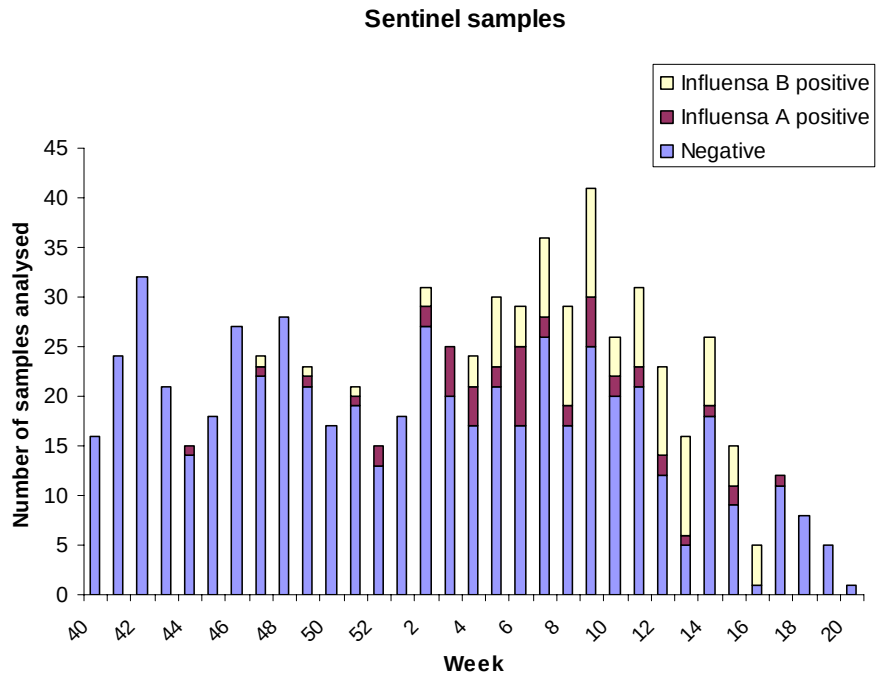


Fig 4:1:4 Number of samples and verified influenza cases in the sentinel sampling system.



4:2 Age distribution in the laboratory and sentinel systems

The age distribution in the two systems reflects that GPs practices mostly cover only otherwise healthy adults. The young children and elderly often get more severely ill and seek hospital care directly if they need medical attention. Usually the specimens are drawn from these more seriously ill patients. However, the observed distribution of the laboratory cases this for the season was closer to the expected, if the cases had been evenly distributed in relation to the population. The previous season, 527 persons above 65 were diagnosed with influenza, compared to 231 expected. This probably reflects that the dominant strains, A/H1 and B do not affect the elderly as severely as A/H3 In the sentinel system, the majority of reported cases were between 15 and 65 years old as usually in Sweden (Table 4:1 and 4:2).
The weekly incidences in the two systems analysed in relation to the expected number of cases with regard to the size of respective populations is shown (Fig 4:2:3 and 4:2:4). An early appearance of children in the sentinel reporting and dominance of the elderly late in the laboratory reports can be discerned.

Table 4:1 Laboratory verified cases by gender and age group during season 2007-08.
"Expected cases" is the number of cases that would have occurred if they had been evenly distributed in relation to the population of the respective age groups.

Age group	Observed cases	Expected cases
0-4	95	70
5-14	82	142
15-64	793	818
65+	275	216
Total	**1246**	**1246**

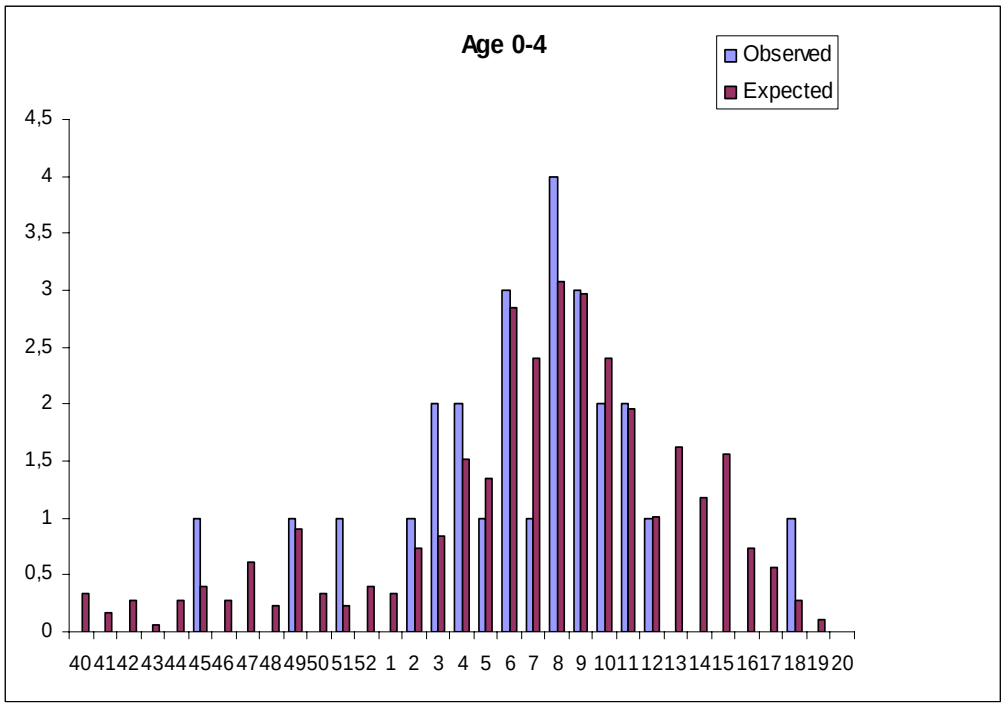
Gender group	Observed cases
Female	605
Male	610
Unknown	26
Total	**1246**

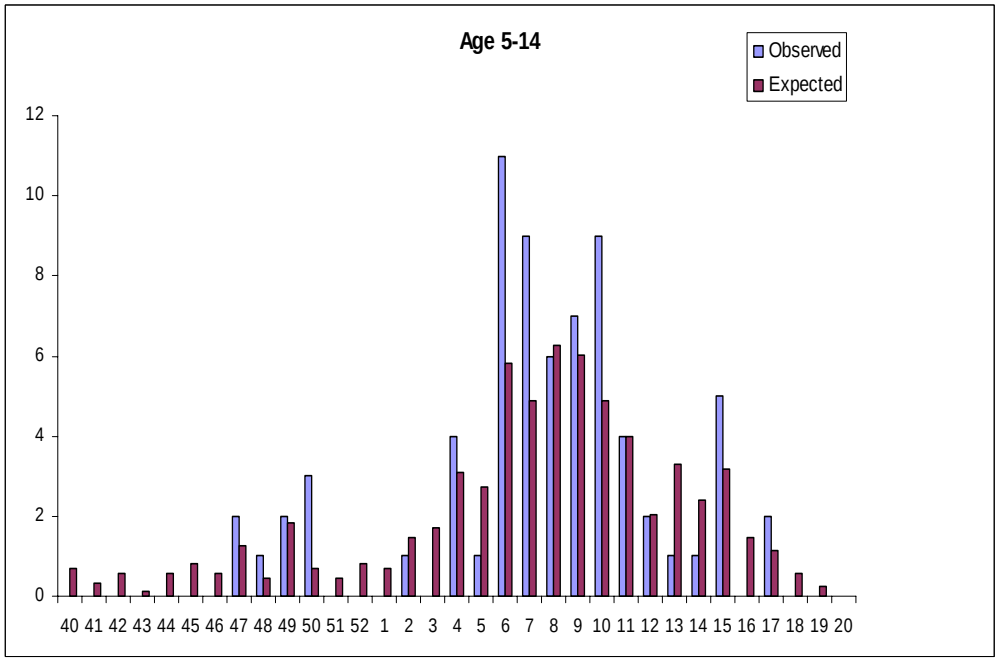
Table 4:2 ILI cases by gender and age group.
"Expected cases" is the number of cases that would have occurred if they had been evenly distributed in relation to the population of the respective age groups.

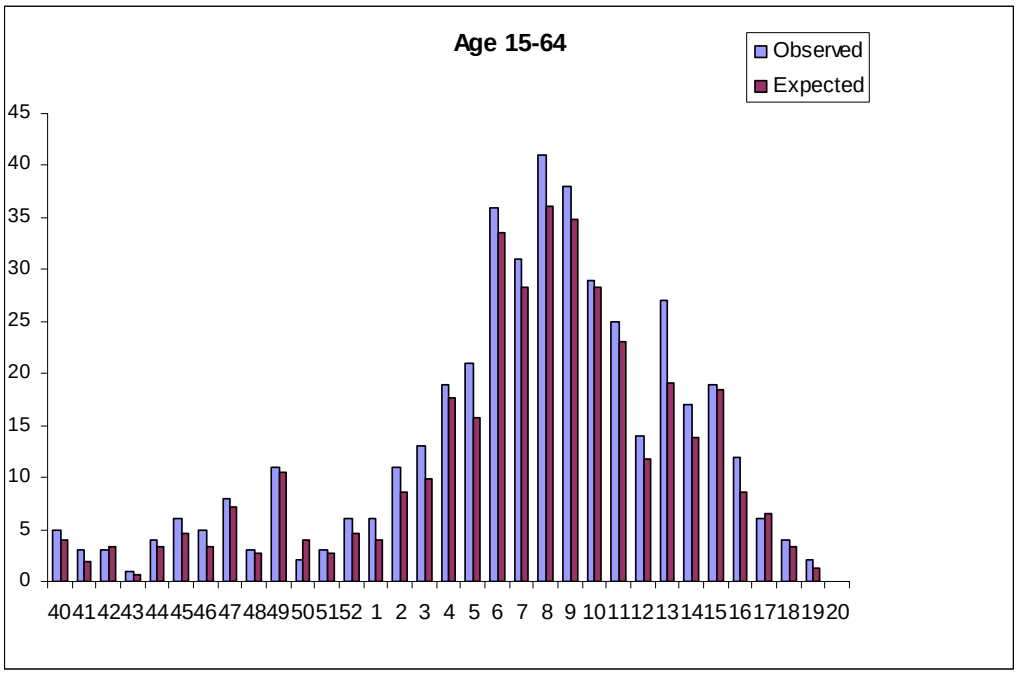
Age group	Observed cases	Expected cases
0-4	26	32
5-14	71	65
15-64	431	375
65+	43	99
Total	**571**	**571**

Gender group	Observed cases
Female	321
Male	250
Total	**571**

Fig 4:2:3 Age distribution of ILI cases during season 2007-08
"Expected" is the number of cases that would have occurred if the cases were evenly distributed in relation to the population of the respective age groups.






Age 15-64
Observed
Expected
45
40
35
30
25
20
15
10
5
0
40 41 42 43 44 45 46 47 48 49 50 51 52 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20

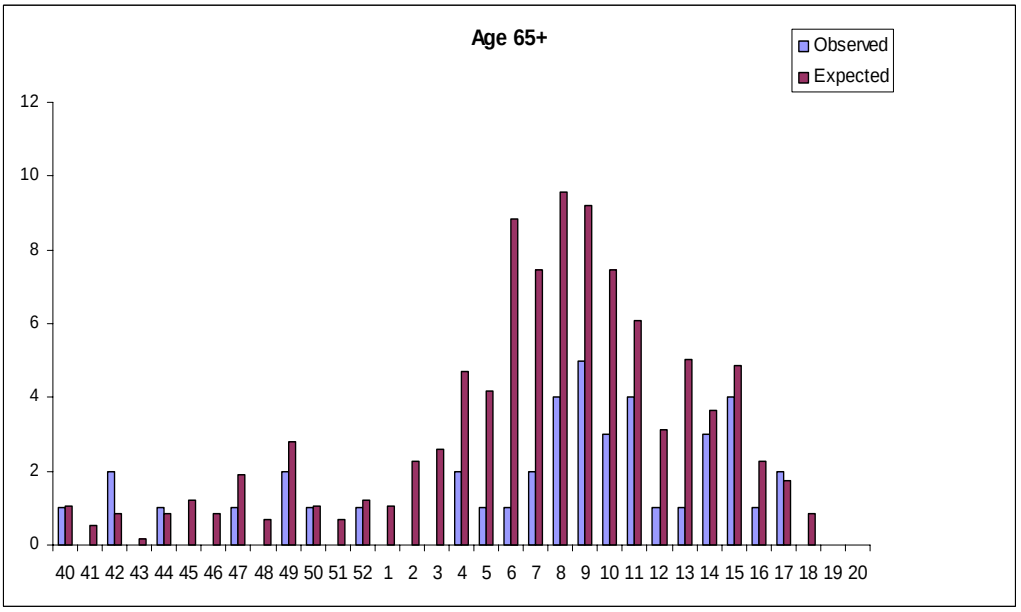
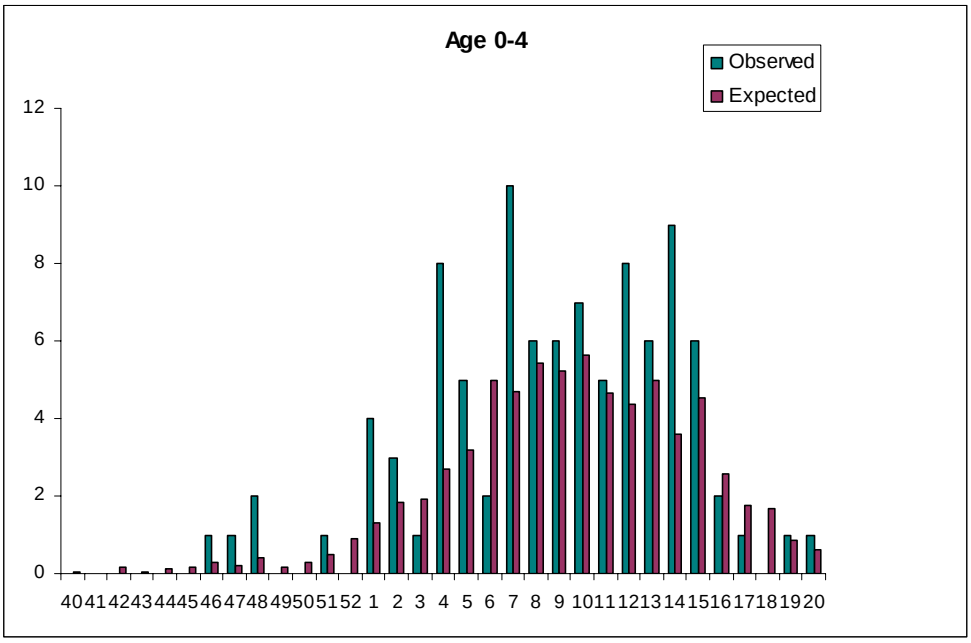
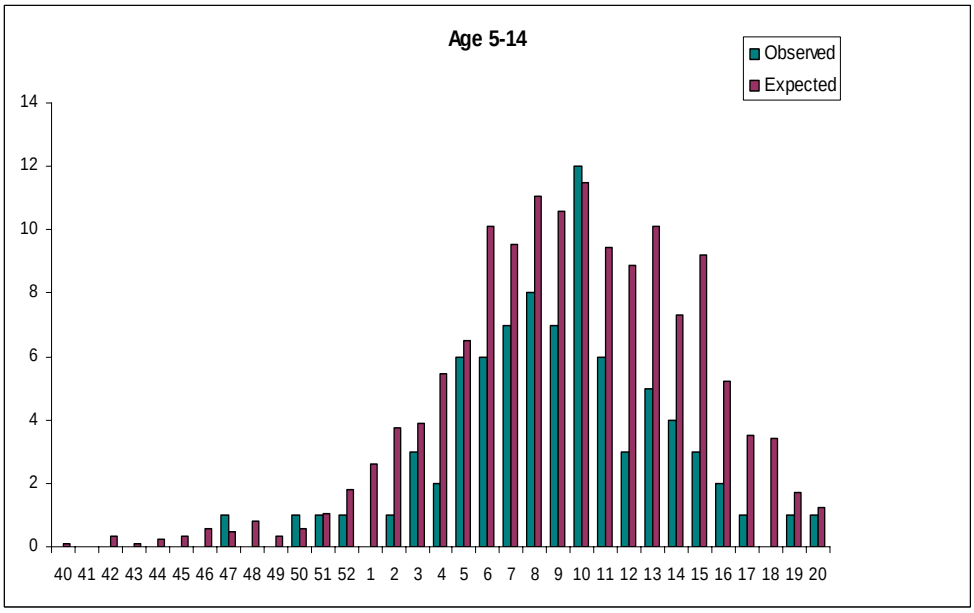
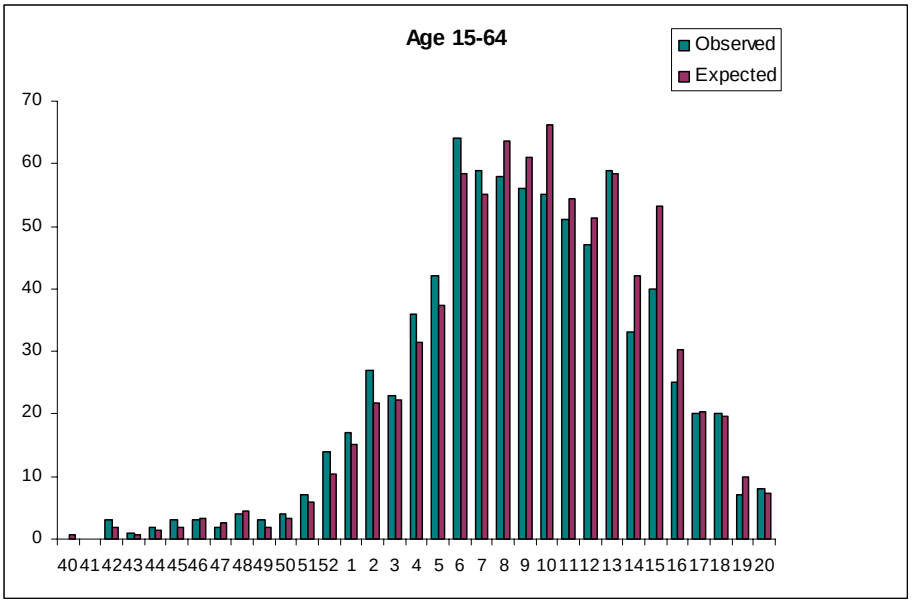

Age 65+
Observed
Expected
12
10
8
6
4
2
0
40 41 42 43 44 45 46 47 48 49 50 51 52 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20

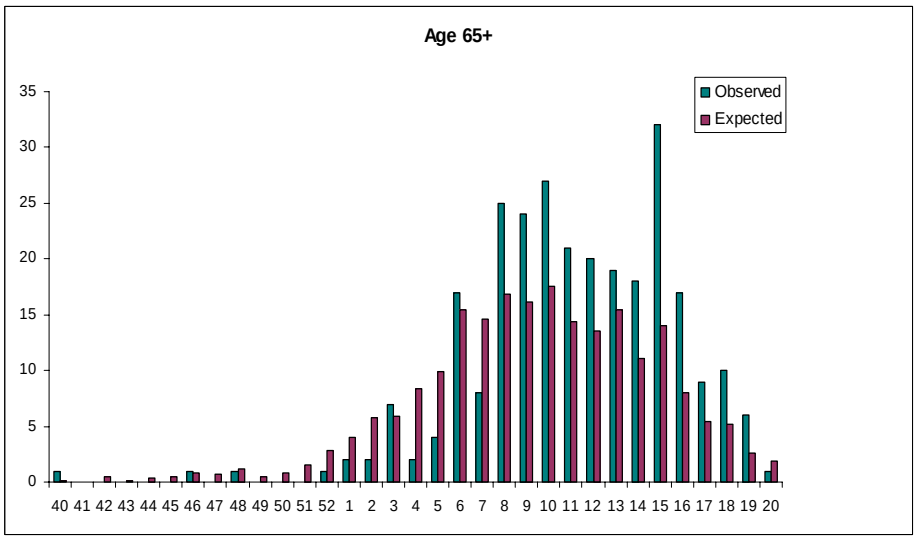
Fig 4:2:4 Age distribution of laboratory verified cases during season 2007-08

"Expected" means the number of expected cases in relation to the whole population.






Age 15-64
Observed
Expected
70
60
50
40
30
20
10
0
40 41 42 43 44 45 46 47 48 49 50 51 52 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20


Age 65+
Observed
Expected
35
30
25
20
15
10
5
0
40 41 42 43 44 45 46 47 48 49 50 51 52 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20

4:3 Estimated excess mortality

There was excess mortality related to the influenza B activity, and the area above the mortality curve that has been normalised for absence of influenza activity (red – black in fig 4:3:1) was around 1000 persons. The correlation between the mortality and influenza B activity is shown in Fig 4:3.2, and in this curve it can be seen that the RSV-peak does not correlate to peak mortality.

Fig 4:3:1 The weekly number of deaths in Sweden from week 40, 1993 to week 20, 2008, and the number of laboratory verified influenza cases during the same period. (The peak of mortality in September 1994 reflects the Estonia ferry catastrophe). Adjusted means for corresponding influenza-free weeks are also included.

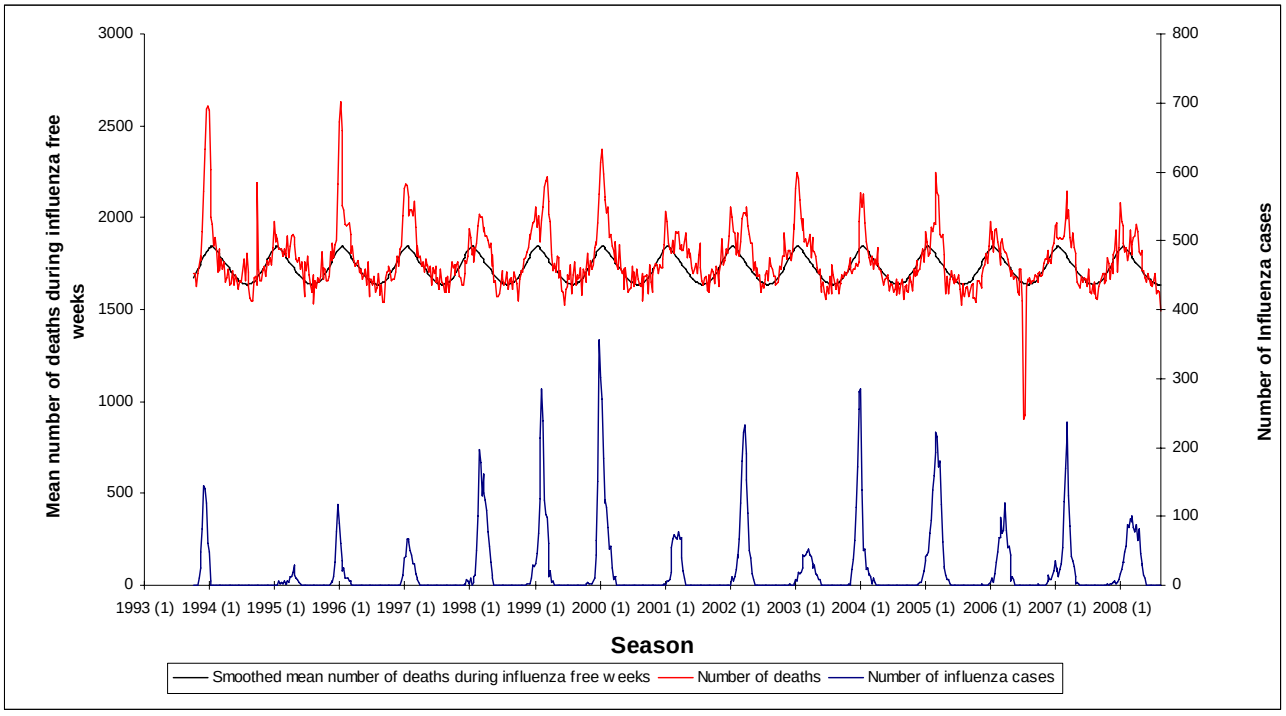
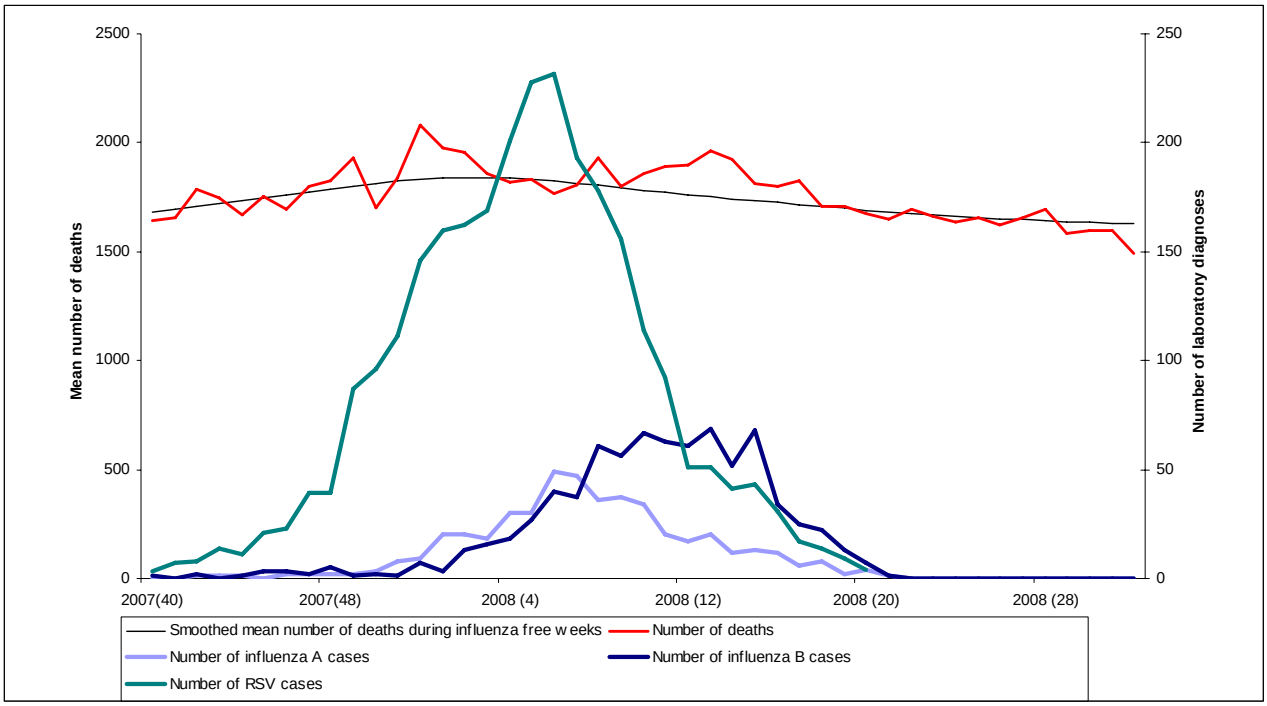


Fig 4:3:2 Weekly number of laboratory reports of influenza A, B and RSV and to total number of deaths and adjusted means for influenza-free weeks for the 2007-08 season.



4:4 Characterisation of influenza strains

All samples collected in the sentinel sampling surveillance were analysed with molecular methods. A total of 712 samples collected during the season were typed and subtyped for influenza A. 141/712 (19.8%) samples became positive. Out of these, 47/141 (33.3%) were influenza A and the remaining 66.7% influenza B (fig 4:1:1). H1 was detected in 32/37 (86.5%) and influenza A H3 in 5/37 (13.5%) of influenza A positive samples. For 10/47 (21.3%) of the influenza A positive samples, the subtype could not be analysed, a higher proportion this season than last season (9%). All the non-typable influenza A samples contained low copy numbers according to the first analysis. The high proportion of non-typable influenza A samples might reflect that patients with influenza A H1N1 shed lower amount of virus, compared to H3N2 or a less sensitive H1 PCR, despite that the tests perform equally well in the validation of the systems. Further, from nine of the positive samples with high copy numbers, virus was isolated and characterised by genotypic and phenotypic methods (table 4:4).

Of strains sent from other laboratories to SMI for further subtyping, 49 % were influenza A H1N1, 15% H3N2, and 36% influenza B. Due to the report of oseltamivir resistant H1N1, such samples were requested from SMI, resulting in the somewhat skewed numbers in relation to the epidemic situation , (table 4:4).
All the influenza strains further characterised were similar to the strains prevalent in Europe (Fig 4:4:1-4:4:4). The vaccine used in the northern hemisphere contained A/Salomon Islands/3/2006 (H1N1), A/Wisconsin/67/2005 (H3N2) and B/Malaysia/2506/2004 (B/Victoria/2/87-like). All the 36 H1N1 strains were similar to A/Brisbane/59/2007 (clade 2B, St Petersburg/96/07). All the 11 H3N2 strains

were similar to the A/Brisbane/10/2007 (clade A), the used vaccine strain in the southern hemisphere during 2008. More diversity was found among the 27 influenza B strains. The majority (96%) of the characterised influenza B strains belonged to the B/Yamagata/16/88-like lineage (78% were similar to B/Chelyabinsk/306/07, 11% were similar to B/Hong Kong/864/06 and 8% were similar to B/Florida/4/2006, the used vaccine strain in the southern hemisphere during 2008)). Only one sample (4%) was similar to the year vaccine strain for the season B/Malaysia/2506/2004. The vaccine strains for season 2008-09 are A/Brisbane/59/2007 (H1N1), A/Brisbane/10/2007 (H3N2) and B/Florida/4/2006.

During the last seasons an increased frequency of A/H3N2 strains resistant to amantadine due to mutations in the M2-gene has been noted. All the eleven characterised A/H3N2 strains from the 2007-08 season were resistant (fig 4:4:2). None of the 36 A/H1N1 strains were amantadine resistant.

At the end of January, Norway reported an increased incidence of oseltamivir resistant A/H1N1 due to H274Y alteration in the N1 gene. We found this alteration in 4 out of 36 (11%) characterised strains. They were collected from all parts of Sweden, one during December and three during February. (Fig 4:4:3) No mutation known to induce resistance against neuraminidase inhibitors in the genes encoding the neuraminidases for influenza A/N2 and B was identified.

Table 4:4) Table of isolates for which extended pheno- and genotyping were performed.

Strain	Sample collection day (dd/mm/YYYY)	Subtype	Information	Origin
A/Stockholm/11/07	21/08/2007	H3		Växjö
A/Stockholm/12/07	21/08/2007	H3		Växjö
B/Stockholm/2/07	30/09/2007	B(Yamagata/16/88)		Skövde
A/Stockholm/13/07	24/10/2007	H1		Göteborg
B/Stockholm/3/07	04/11/2007	B(Yamagata/16/88)		Stockholm
B/Stockholm/4/07	07/11/2007	B(Yamagata/16/88)		Stockholm
A/Stockholm/14/07	20/11/2007	H1		Uppsala
B/Stockholm/5/07	22/11/2007	B(Yamagata/16/88)		Stockholm
A/Stockholm/15/07	30/11/2007	H1		Stockholm
B/Stockholm/6/07	11/12/2007	B(Yamagata/16/88)		Stockholm
A/Stockholm/16/07	11/12/2007	H1		Stockholm
A/Stockholm/17/07	13/12/2007	H1		Stockholm
A/Umeå/2/07	15/12/2007	H1		Umeå
A/Stockholm/18/07	11/12/2007	H1		Stockholm
A/Stockholm/19/07	21/12/2007	H1		Uddevalla
A/Stockholm/1/08	?	H1		Stockholm
A/Stockholm/2/08	?	H3		Stockholm

A/Stockholm/3/08	02/01/2007	H1		Stockholm
A/Stockholm/4/08	02/01/2007	H1		Stockholm
A/Stockholm/5/08	?	H1		Stockholm
A/Stockholm/8/08	30/01/2008	H1		Sundsvall
A/Stockholm/9/08	02/02/2008	H1		Karlstad
A/Stockholm/10/08	04/02/2008	H1		Uppsala
A/Stockholm/6/2008	12/24/2007	H1		Stockholm
A/Stockholm/7/2008	08/01/2008	H3		Falun
B/Stockholm/1/2008	17/01/2008	B (Yamagata/16/88 lineage)		Stockholm
B/Stockholm/2/2008	10/02/2008	B (Yamagata/16/88 lineage)		Stockholm
B/Stockholm/3/2008	14/02/2008	B (Yamagata/16/88 lineage)		Stockholm
B/Stockholm/4/2008	20/02/2008	B (Yamagata/16/88 lineage)		Stockholm
B/Stockholm/5/2008	05/03/2008	B (Yamagata/16/88 lineage)		Karlstad
A/Stockholm/11/2008	23/11/2007	H3		Stockholm
A/Stockholm/12/2008	30/10/2007	H3		Stockholm
A/Stockholm/13/2008	18/02/2008	H1		Göteborg
A/Stockholm/14/2008	?/02/2008	H1		Göteborg
A/Stockholm/15/2008	14/04/2008	H3		Stockholm
A/Umeå/1/2008	05/01/2008	H1		Umeå
B/Umeå/1/2008	16/01/2008	B (Yamagata/16/88 lineage)		Umeå
A/Umeå/2/2008	28/01/2008	H1		Umeå
A/Umeå/3/2008	01/02/2008	H1		Umeå
A/Umeå/4/2008	02/02/2008	H1		Umeå
A/Umeå/5/2008	04/02/2008	H1		Umeå
A/Umeå/6/2008	04/02/2008	H1		Umeå
A/Umeå/7/2008	05/02/2008	H1		Umeå
B/Umeå/2/2008	07/02/2008	B (Yamagata/16/88 lineage)		Umeå
A/Umeå/8/2008	07/02/2008	H3		Umeå
A/Umeå/9/2008	10/02/2008	H1		Umeå
B/Umeå/3/2008	13/02/2008	B (Victoria/2/87 lineage)		Umeå
A/Umeå/10/2008	13/02/2008	H1		Umeå
A/Umeå/11/2008	14/02/2008	H1		Umeå
B/Umeå/4/2008	14/02/2008	B (Yamagata/16/88 lineage)		Umeå
A/Umeå/12/2008	15/02/2008	H1		Umeå
A/Umeå/17/2008	17/02/2008	H1		Umeå
A/Umeå/13/2008	21/02/2008	H1		Umeå
B/Umeå/5/2008	26/02/2008	B (Yamagata/16/88 lineage)		Umeå
A/Umeå/14/2008	04/03/2008	H1		Umeå

A/Umeå/15/2008	05/03/2008	H1		Umeå
A/Umeå/16/2008	20/03/2008	H1		Umeå
B/Umeå/6/2008	18/04/2008	B (Yamagata/16/88 lineage)		Umeå
B/Umeå/7/2008	22/04/2008	B (Yamagata/16/88 lineage)		Umeå
B/Stockholm/6/2008	29/04/2008	B (Yamagata/16/88 lineage)		Stockholm
A/Stockholm/16/2008	28/04/2008	H3		Stockholm
A/Stockholm/17/2008	26/04/2008	H3		Stockholm
B/Stockholm/7/2008	12/05/2008	B (Yamagata/16/88 lineage)		Stockholm
B/Stockholm/8/2008	05/05/2008	B (Yamagata/16/88 lineage)		Stockholm
A/Stockholm/18/2008	27/04/2008	H3		Stockholm
A/Sweden/1/2008	21/01/2008	H1	Sentinel doctor	Stockholm
A/Sweden/2/2008	05/02/2008	H1	Sentinel doctor	Kristianstad
B/Sweden/1/2008	26/02/2008	B (Yamagata/16/88 lineage)	Sentinel doctor	Halmstad
B/Sweden/2/2008	27/02/2008	B (Yamagata/16/88 lineage)	Sentinel doctor	Jönköping
B/Sweden/3/2008	25/02/2008	B (Yamagata/16/88 lineage)	Sentinel doctor	Sundsvall
B/Sweden/4/2008	07/03/2008	B (Yamagata/16/88 lineage)	Sentinel doctor	Skelefteå
B/Sweden/5/2008	17/03/2008	B (Yamagata/16/88 lineage)	Sentinel doctor	Umeå
B/Sweden/6/2008	19/03/2008	B (Yamagata/16/88 lineage)	Sentinel doctor	Falun
B/Sweden/7/2008	01/04/2008	B (Yamagata/16/88 lineage)	Sentinel doctor	Malmö

Figure 4:4:1) The phylogenetic tree of the amino acid sequences of the HA of influenza A/H3 strains isolated in Sweden 1996-2008 compared to the vaccine

Figure 4:4:2) The phylogenetic tree of the amino acid sequences of the HA of influenza A/H3 strains isolated in Sweden 2004-2008 compared to the vaccine strains. Amantadine resistant strains are indicated in bold. The prevalence of amantadine resistance are presented in the bracket.

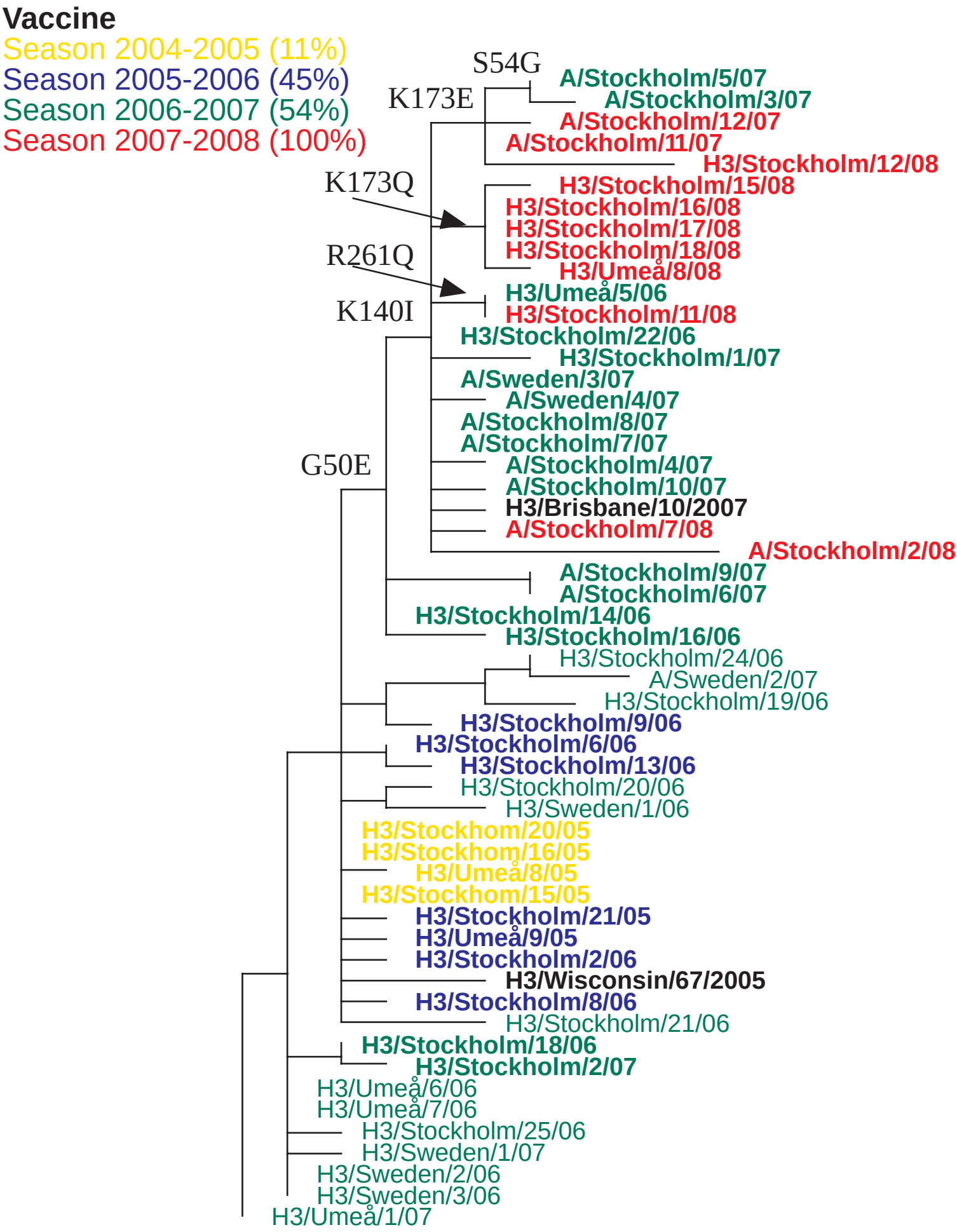


Figure 4:4:3) The phylogenetic tree of the amino acid sequences of the HA of influenza A/H1 strains isolated in Sweden compared to the vaccine strains. Oseltamivir resistant strains are indicated in bold. City and sampling date (yymmdd) are listed behind.

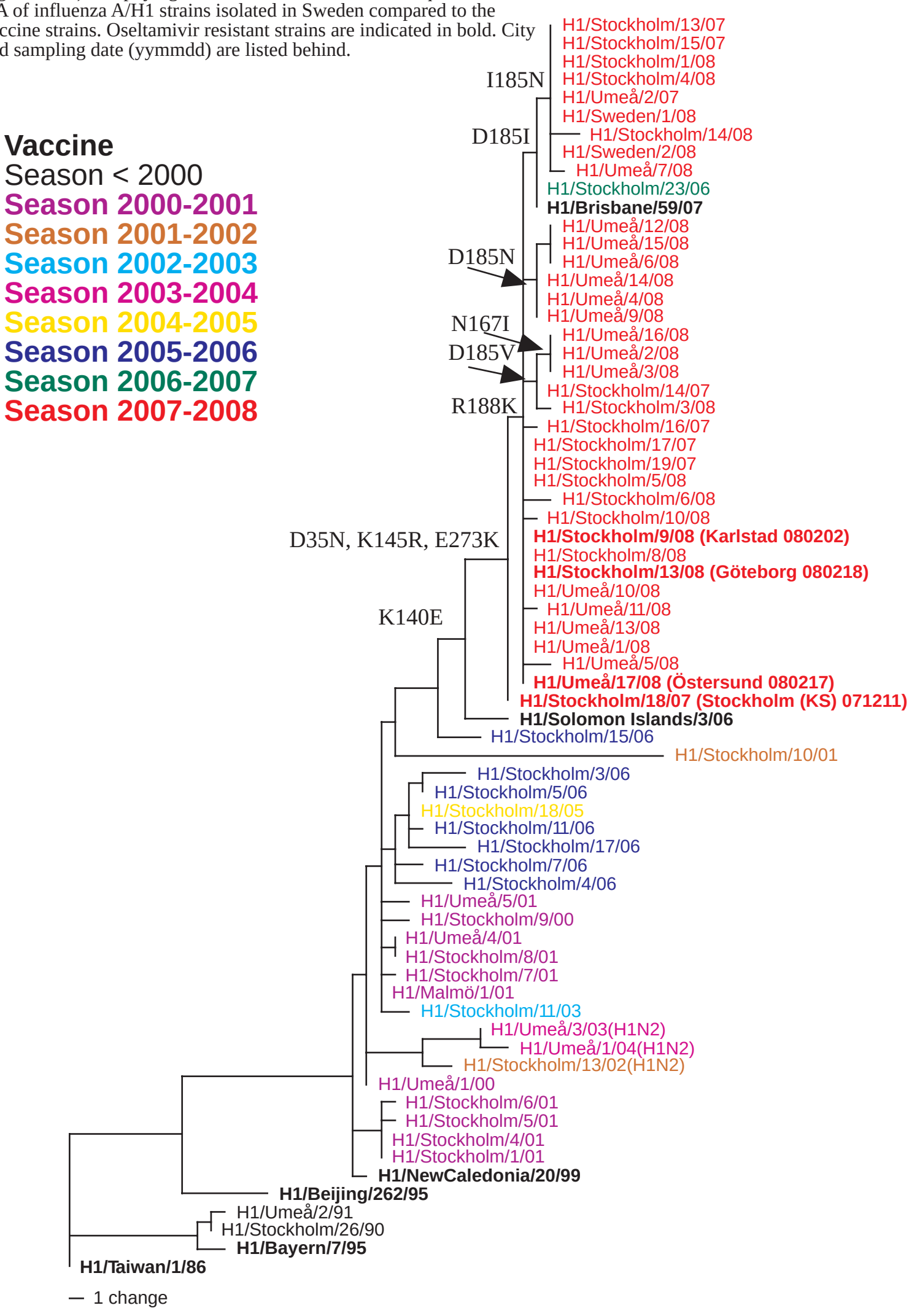
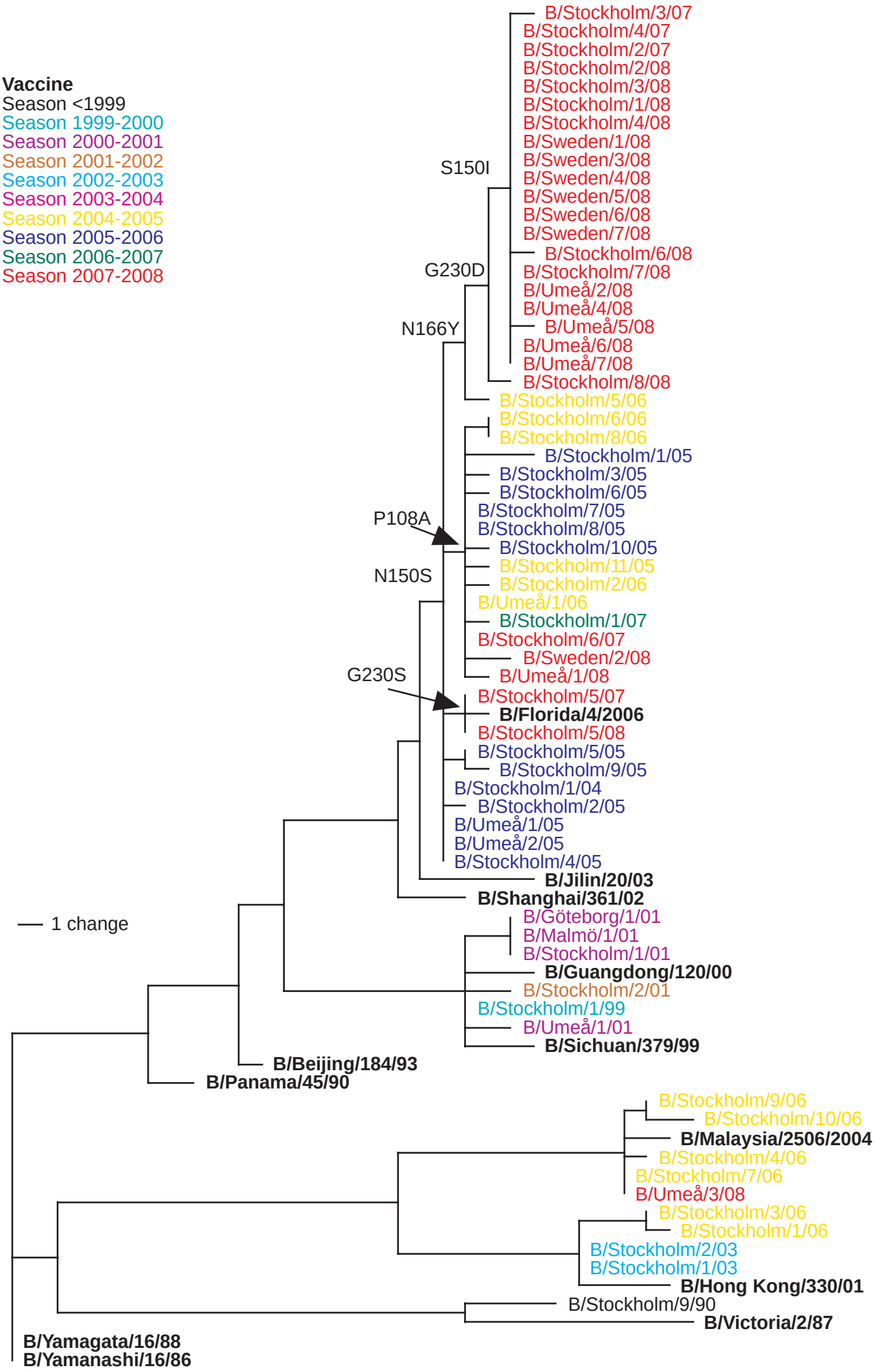


Figure 4:4:4) The phylogenetic tree of the amino acid sequences of the HA of influenza B strains isolated in Sweden 1999-2008 compared to the vaccine strains.



5) QUALITY CONTROL OF LABORATORY DIAGNOSIS OF INFLUENZA

In collaboration with the organisation for External Quality Assessment in Sweden (Equalis), panels for quality control of antigen detection with IFA or ELISA and PCR, and for virus isolation, were sent to laboratories performing these types of diagnostic assays in Sweden. The influenza panel for IF consisted of 8 different acetone fixed preparations of the influenza strains expected for the season, grown in MDCK cells, and mixed in different proportions with uninfected cells from a lymphoblastoid cell line. Twenty-eight laboratories reported altogether 37 data sheets. Twenty-three of the participating laboratories reported correct results (283/296 analyses). The results of the External Quality control from 1994-2007 related to methods is presented (Table 5:1).

Table 5:1 External Quality Control Assessment in Sweden (Equalis).
Results of panels for influenza antigen detection from 1994-2007. The number (%) of reported correct results related to total number of examinations performed with the methods is presented.

	Influenza A/H1	**Influenza A/H3**	**Influenza B**
Imagen	254/297 (86%)	240/273 (88%)	202/272 (74%)
Chemicon indirect IF	105/108 (97%)	96/101 (95%)	96/101 (95%)
WHO	43/45 (96%)	42/43 (98%)	38/40 (95%)
Biosoft/Argene (1994-1999)	5/6 (83%)	6/6 (100%)	5/7 (71%)
Biotrin (1994-2007, not 1999)	20/21 (95%)	21/22 (95%)	17/17 (100%)
DPC-PathoDx (2000-2007)	156/178 (88%)	167/176 (95%)	131/143 (92%)
Chemicon direct IF (2000-2006, not 2004, 2007)	21/26 (81%)	20/21 (95%)	14/17 (82%)
Becton-Dickinson (2001-2003)	8/10 (80%)	8/8 (100%)	2/6 (33%)
Real time PCR (2003-2007)	38/38 (100%)	42/42 (100%)	31/31 (100%)
Binax NOW (2004-2007)	32/33 (97%)	37/39 (95%)	20/31 (65%)
QuikVue Influenza (2006-2007)	7/8 (88%)	7/9 (78%)	5/7 (71%)

6) METHOD DEVELOPMENT AND RESEARCH

6.1. In a project funded by Eurocine, a research company focusing on the development of nasal vaccines, SMI is investigating cross protection to influenza A subtypes after nasal immunisation. Studies have been performed in mice and during this winter a study in humans will start.

6:3. Modelling and prediction

In a study funded by the Swedish Emergency Management Agency, detailed modelling for prediction of spread of influenza in the society is performed by PhD Lisa Brouwers and collaborators. The effect of various measures for social distancing and different strategies for vaccination in a pandemic situation are studied.

6:4. Death rates

SMI participates in European monitoring of excess mortality for public health action, Euro-MOMO. (coordinator: Ann Mazick, Statens Seruminstitut, Copenhagen).

6:5. Population-based surveillance

Before the 2007-08 season, around 14 000 persons in the Stockholm area were sent a letter, asking if they were willing to report upper respiratory tract infections and answer some question concerning their symptoms via the webb or by interactive voice response. They were also informed that their data in various population registers would be analysed in an anonymous manner. Around 3500 agreed to report, and the results of the reporting was continuously shown as numbers with ARI and ILI, respectively, at the SMI homepage. The reporting was validated by repeated short questionnaires to part of the 3500 reporters during the season, and by a final questionnaire to all 14000 invited by the end if the season. Evaluation is ongoing, and the main results of the study will be presented late during 2008.

6:6. Webb queries for evaluation of timing and intensity of seasonal influenza activity

A model to estimate the timing and the peak of the influenza season, based on queries related to influenza submitted to a medical web site during two influenza seasons (2005-2007) was developed. The model – which is based on partial least squares regression – consists of two parts: one estimating the number of positive laboratory cases and one estimating the proportion of cases with influenza-like illness as reported by the sentinel GPs. The model was evaluated on previously unseen data during the 2007/2008 season, from which the number of influenza-related web queries (twenty types) for this new season was calculated. The timing of the estimated sentinel peak as well as the estimated laboratory peak coincided with the peaks for the traditional sources. The model over-estimated the intensity, especially so the curve for laboratory verified cases. The dominance of mild influenzas during the season – compared to the two years for which the model was developed – resulting in fewer visits to health care units, could explain the higher intensity found in model.

6:7. Geographic spread of influenza

Based on detailed data of the influenza spread in Sweden obtained at the time for the 1889-90 Russian flu a new Geographic Information System (GIS) method for depiction of temporal spread, and the use of Thiessien polygons for estimation of regional spread was developed-

6:8. Scientific articles and reports:

Bock D. Andersson E. Frisen M. Statistical surveillance of epidemics: peak detection of influenza in Sweden. Biometrical Journal. 50(1):71-85, 2008 Feb.

Andersson E, Kühlman-Berenzon S, Linde A, Schiöler L, Rubinova S, Frisén M: Predictions by early indicators the time and height of the peaks of yearly influenza outbreaks in Sweden. Scand J Publ Health, 2008; 36: 475-482.

Bexelius C, Merk H, Sandin S, Ekman, Nyrén O, Kühlmann-Berenzon PhD S, Linde A, Litton JE: SMS vs. Telephone Interviews for epidemiological data collection – feasibility study estimating influenza vaccination coverage in the Swedish population. Submitted 2008.

Hulth A, Rydevik G, Linde A: Web queries as a source for syndromic surveillance. Submitted

Skog, L, Linde A: the Russian influenza in Sw3en from a Geographic perspective. Submitted

P Petersson, M Hedenskog , D Alves, M Brytting, U Schröder , A Linde, Å Lundkvist. Protective immunity in mice by intranasal influenza vaccination. Submitted.

I Kiss, P Gyarmati, S Zohari, K Wilbe-Ramsay, G Metreveli, E Weiss[3], M Brytting, A Lundkvist, K Nemirov, M Berg, G Czifra, S Belák. Molecular characterization of highly pathogenic H5N1 avian influenza viruses isolated in Sweden in 2006. Submitted.

A Hulth, G Rydevik, A Linde. Web Queries as a Source for Syndromic Surveillance. Submitted

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