NIPH
Norwegian Institute of Public Health

REPORT

2018

NORWAY: NATIONAL INFLUENZA CENTRE:

Influenza Epidemiological Information prepared for the WHO Informal Meeting on Strain Composition for Inactivated Influenza Vaccines for use in the Season 2018-19

Geneva, February 2018

NORWAY:
National Influenza Centre

Influenza Epidemiological Information prepared for the

WHO Informal Meeting on Strain Composition for

Inactivated Influenza Vaccines for use in the Season 2018-19

Geneva, February 2018

Published by

National Influenza Centre, Oslo
Department of Influenza
Norwegian Institute of Public Health
P.O. Box 4404 Nydalen
N-0403 Oslo, NORWAY
Tel: (+47) 21 07 65 20
Fax: (+47) 21 07 64 47
e-mail: NIC-Norway@fhi.no
www.fhi.no/influensa

Title:
NORWAY:
National Influenza Centre

Influenza Epidemiological Information prepared for the
WHO Informal Meeting on Strain Composition for
Inactivated Influenza Vaccines for use in the Season 2018-19
Geneva, February 2018

Publication type:
Report

Order:
The report can be downloaded as pdf
at www.fhi.no/en/publ/

ISBN: 978-82-8082-907-8 (electronic)

Contents

1: The 2017-2018 influenza season, Norway

Summary

- Extensive influenza activity at medium intensity has been taking place in Norway since late December
- All-country ILI incidence indicates medium intensity
- Influenza B viruses of the B/Yamagata lineage are in clear majority, around 67%
- Among influenza A viruses, subtype H3N2 is more frequent than H1N1pdm09. Influenza B/Victoria lineage viruses are occurring only sporadically.
- The B/Yamagata (clade 3) and H3N2 viruses are similar to the viruses circulating during the previous season in Norway.
- Genetic clade 3C.2a makes up the majority of the H3N2 viruses; however most recent H3 viruses belong to subgroup 3C.2a1.
- Only one out of nine genetically characterised B/Victoria viruses this far is the double deletion variant.
- The H1N1 viruses circulating are similar to the H1 viruses circulating during the summer months in Norway 2017.
- Both the B/Yamagata-lineage and A(H3N2) viruses are frequently infecting the elderly
- The incidence of laboratory-confirmed influenza hospitalisations is highest in the elderly.
- Excess mortality has been observed in the elderly in week 51/2017 to week 3/2018. Fatal influenza cases have also been reported from intensive care units.
- The prevalence of protective antibody against the circulating antigenic variant of influenza A(H3N2) virus increased considerably after last winter's H3N2-dominated outbreak. The strengthened pre-season population immunity probably has restricted the impact of this virus this winter, perhaps in contrast to other countries that are harder hit by H3N2.
- Also seroprevalence against the circulating variant of A(H1N1)pdm09 virus was high this autumn.
- A decrease in population immunity against B/Phuket/3073/13-like B/Yamagata-lineage viruses has been observed over the last two years.

A look back at preceding seasons

The preceding 2016/17 season main outbreak peaked unusually early and was strongly dominated by influenza A(H3N2) viruses, belonging to different subclades under the 3C.2a clade. The outbreak, which was of medium intensity, was associated with higher than usual excess mortality, primarily among the elderly. Influenza B viruses, mostly of the Yamagata lineage, predominated toward the end of the season.

Influenza A(H1N1)pdm09 viruses predominated in the 2015/16 season. Last time there was a major countrywide influenza B/Yamagata lineage outbreak was during the 2012/13 season. B/Yamagata lineage viruses also predominated in Northern Norway in the 2014/15 season.

Incidence of influenza-like illness

The incidence of influenza-like illness (ILI) in Norway is monitored through The Norwegian Syndromic Surveillance System (NorSSS). NorSSS is a population-based automated electronic system that daily provides data from all GPs and emergency clinics in primary health care in Norway. The Department of Influenza at the Norwegian Institute of Public Health (NIPH) receives data from the Norwegian Health Economics Administration (HELFO). NorSSS has been in operation since 2014 and is supported by retrospective data from the 2006-07 season and onwards.

The ILI consultation rate began to rise gradually from week 47/2017 and crossed the epidemic threshold in week 51 (Fig.2, right). Influenza activity of medium intensity has been present from week 52/2017 through week 5/2018 (Fig. 2, left). A temporary peak in ILI activity was observed in week 1/2018, but after a slight decline in ILI activity in week 2, the increase has resumed. Ten outbreaks in health care institutions, 4 caused by influenza B and 6 by influenza A, have been reported since the start of the season.

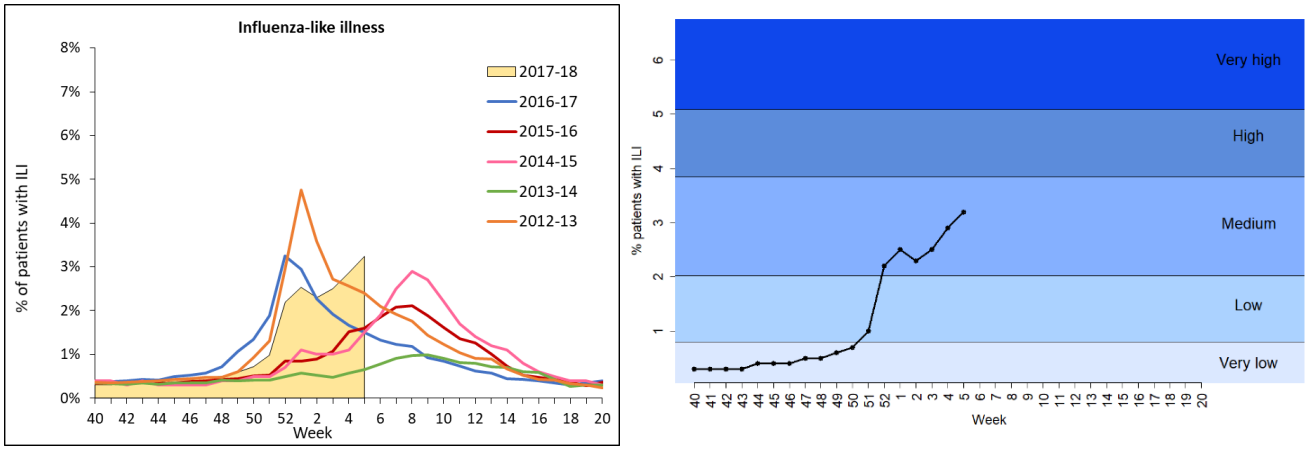


Figure 2: Weekly incidence of ILI, Norway 2017-2018.
Proportion of patients in general practice and emergency clinics presenting with ILI, by calendar week. In the left-hand panel a selection of previous seasons is also shown. In the right-hand panel, the ILI incidence is shown against the present-season MEM intensity thresholds.

Virological surveillance.

A network of volunteer sentinel physicians throughout the country collects specimens from patients with ILI for analysis at the National Influenza Centre. In addition, medical microbiology laboratories that perform influenza diagnostics weekly report the number of positives and the number of specimens tested. These laboratories also contribute influenza positive specimens to the NIC for further characterisation. Even though most of these laboratories are affiliated to hospitals, the majority of specimens tested for influenza virus tend to be from outpatients attending general practitioners.

Sporadic cases of laboratory verified influenza were recorded weekly throughout the summer and early autumn 2017 (cf. our report for the September 2017 VCM). A clear increase in the numbers was noticed from late November onwards (Figure 3, table 1). Initially, influenza A(H3N2) were in majority, but the rise from late November was primarily driven by influenza B viruses of the Yamagata lineage. The latter viruses have been in majority since week 49/2017. The all-laboratories positivity rate exceeded the 10 per cent mark in the week before Christmas (wk 51) and passed 20 per cent the subsequent week. Following a levelling off in early January, the rise resumed in mid-January and by week 5 it had reached 34%.

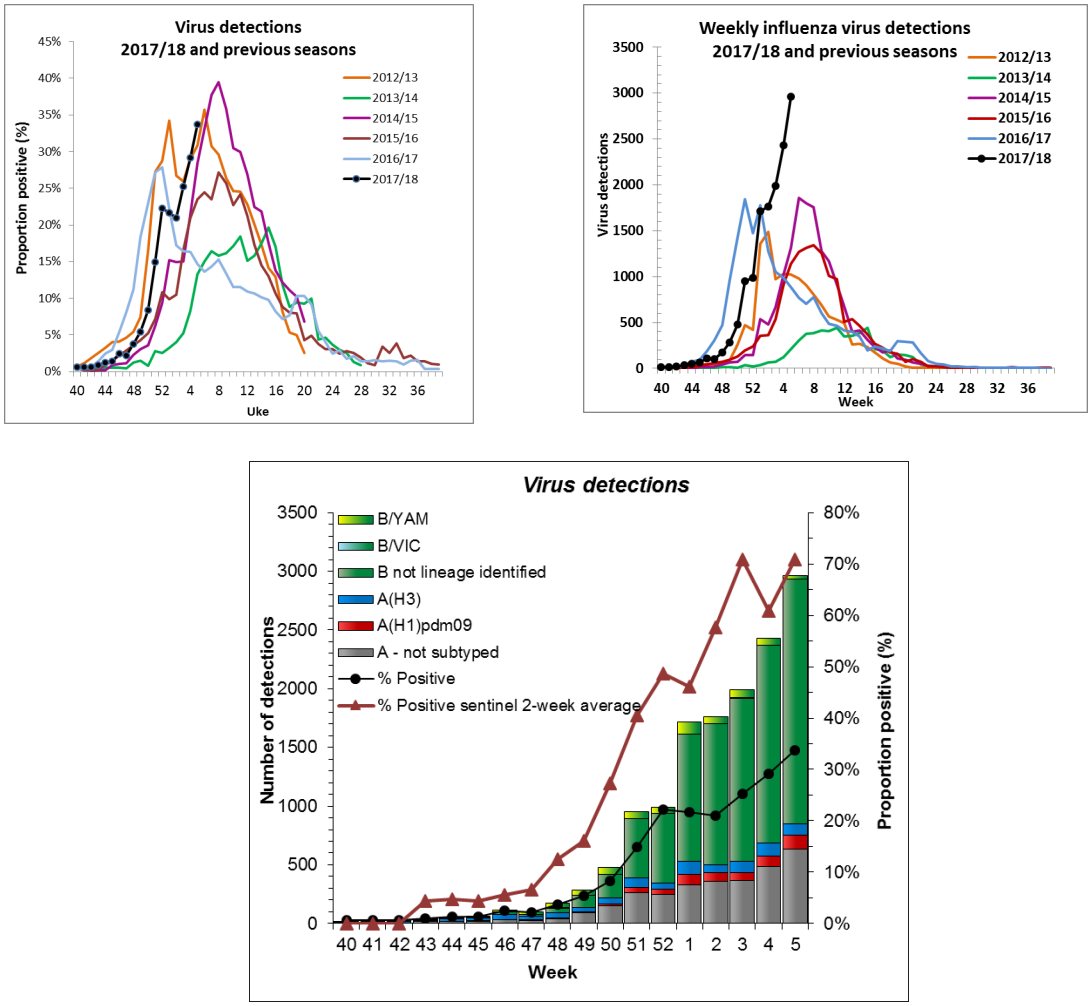


Figure 3: Laboratory detections, Norway 2017-2018. Upper left-hand panel: Weekly proportion of influenza virus positive specimens, with previous season proportions shown for comparison. Upper right-hand panel: Weekly number of influenza virus detections, with previous season numbers shown for comparison. Lower panel: Weekly number of the different influenza viruses is displayed as stacked bars, and influenza virus positivity rates of sentinel specimens and all lab testing, respectively, are shown as line graphs.

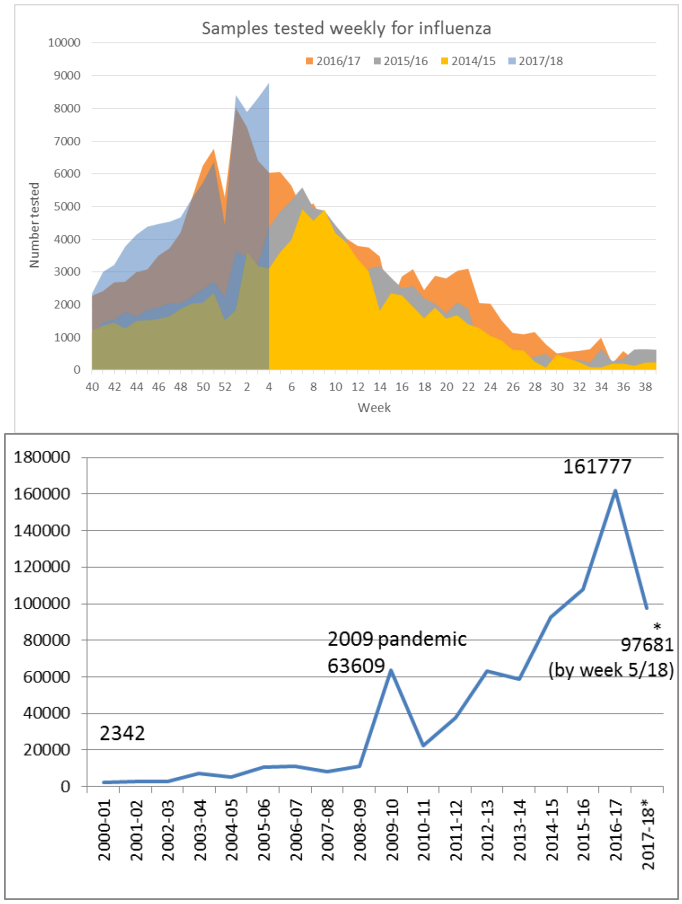


Figure 4. Number of tests for influenza virus carried out in Norwegian medical microbiology laboratories, as recorded in weekly reports to the NIC. Upper panel: Number of tests per week, comparison of current season and three preceding seasons. Lower panel: Number of tests per season, since reporting of this parameter began in year 2000 (*current-season total is incomplete).

By week 5 more than 97 000 specimens had been analysed for influenza virus in Norwegian medical microbiology laboratories this season (Figure 4). Among all reported influenza virus infections, two thirds have been type B and one third type A (figure 5). A(H3N2) constitutes the majority of the subtyped type A viruses, making up nearly 80 % of the sentinel type A specimens. Among genotyped type B viruses, Yamagata/16/88-lineage viruses are strongly predominant (98 %).

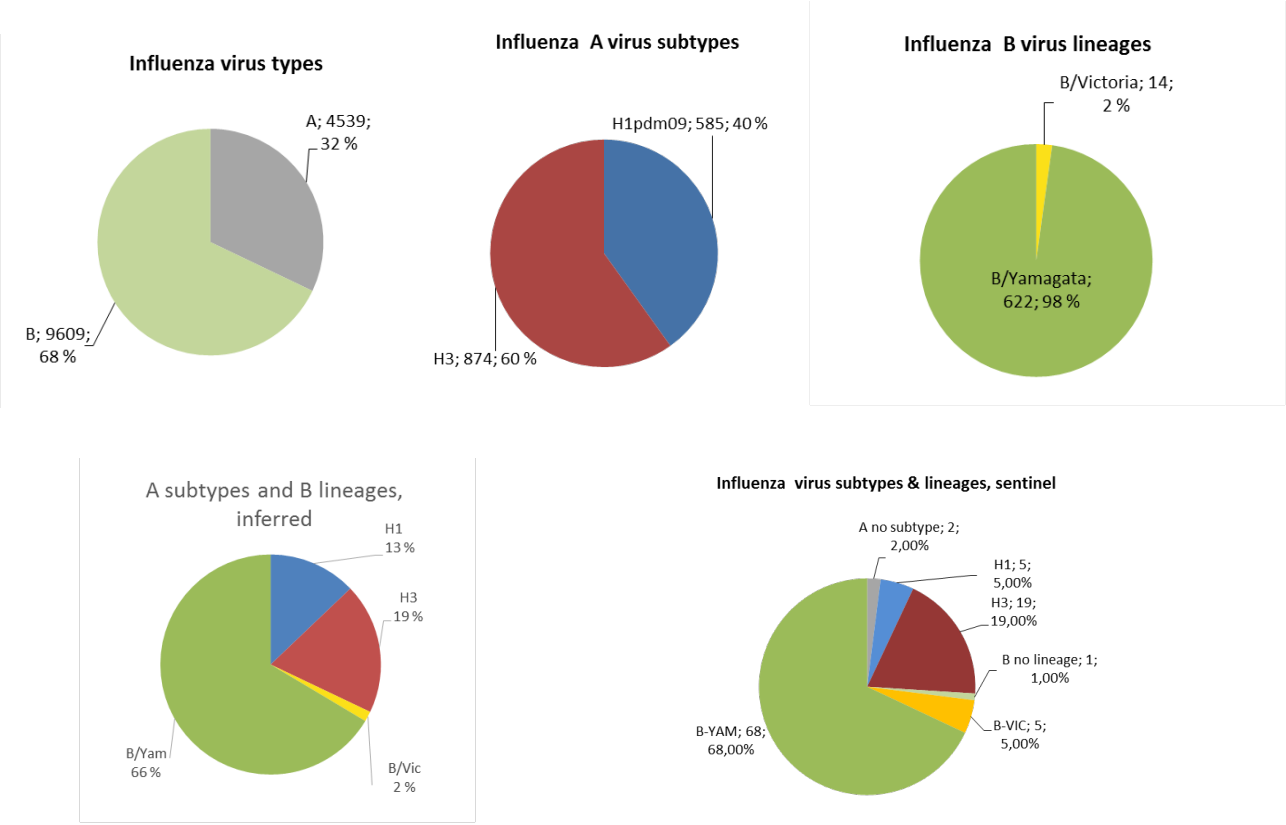


Figure 5. Proportions of 2017/18 season influenza virus subtypes and lineages among viruses analysed in Norway, by 8th of February 2018. For comparison, all-laboratories proportions of A/B type, A subtypes and B lineages are shown in the upper row. The subtype and lineage frequencies are superimposed on type distributions in the lower left panel, for comparison with the distribution among sentinel specimen data. The relative frequencies are generally consistent. The proportion of the H1 subtype is exaggerated in the all-laboratories data because more than three times more viruses have been tested for H1 than for H3. Sentinel data are not biased in this way but the numbers are more limited.

Table 1: Weekly incidence of influenza-like illness (ILI), number of specimens tested for influenza, proportion of specimens positive for influenza virus, and influenza virus detections per type/subtype/lineage (sentinel plus non-sentinel), in Norway from week 40/2017 through week 5/2018.

		Viruspåvisninger/*Virus detections*							
UKE/ *week*	% ILI	Prøver/ *Specimens*	% positive	A(utypet) *not subtyped*	A(H1) pdm09	A(H3)	B ikke genotypet *not lineage typed*	B/ Victoria lineage	B/ Yamagata lineage
40	0,3 %	2349	0,6 %	3	1	5	4	0	2
41	0,3 %	3007	0,6 %	5	1	4	6	0	2
42	0,3 %	3219	0,7 %	2	3	9	5	0	2
43	0,3 %	3782	0,9 %	14	2	9	9	0	1
44	0,4 %	4140	1,3 %	19	1	18	6	0	8
45	0,4 %	4387	1,4 %	16	10	20	10	0	6
46	0,4 %	4472	2,5 %	31	3	40	25	0	12
47	0,5 %	4539	2,2 %	26	4	32	13	1	24
48	0,5 %	4671	3,7 %	41	5	48	38	1	41
49	0,6 %	5235	5,4 %	95	6	33	107	0	43
50	0,7 %	5722	8,4 %	148	15	54	201	2	59
51	1,0 %	6367	14,9 %	260	45	82	504	2	57
52	2,2 %	4438	22,3 %	246	48	47	600	0	47
1	2,5 %	7933	21,6 %	331	88	111	1083	1	102
2	2,3 %	8412	20,9 %	357	74	67	1206	1	56
3	2,5 %	7894	25,2 %	363	71	95	1388	4	69
4	2,9 %	8324	29,2 %	488	89	107	1682	0	64
5	3,2 %	8790	33,7 %	635	119	93	2086	2	27
Total	Total	97681		3080	585	874	8974	14	622
UKE/ *week*	UKE/ *week*	Prøver/ *Specimens*	% positive	A(utypet) *not subtyped*	A(H1) pdm09	A(H3)	B ikke genotypet *not lineage typed*	B/ Victoria lineage	B/ Yamagata lineage
			Type A:	4539		Type B:	9610		

Pre-season seroprevalence and age-distribution of viruses detected in 2017-18 season.

In figure 6, the pre-season population immunity within age groups against the different influenza viruses, described in section 3, is shown together with the in-season occurrence of infections for the corresponding viruses and age groups, displayed as incidence of laboratory verified cases.

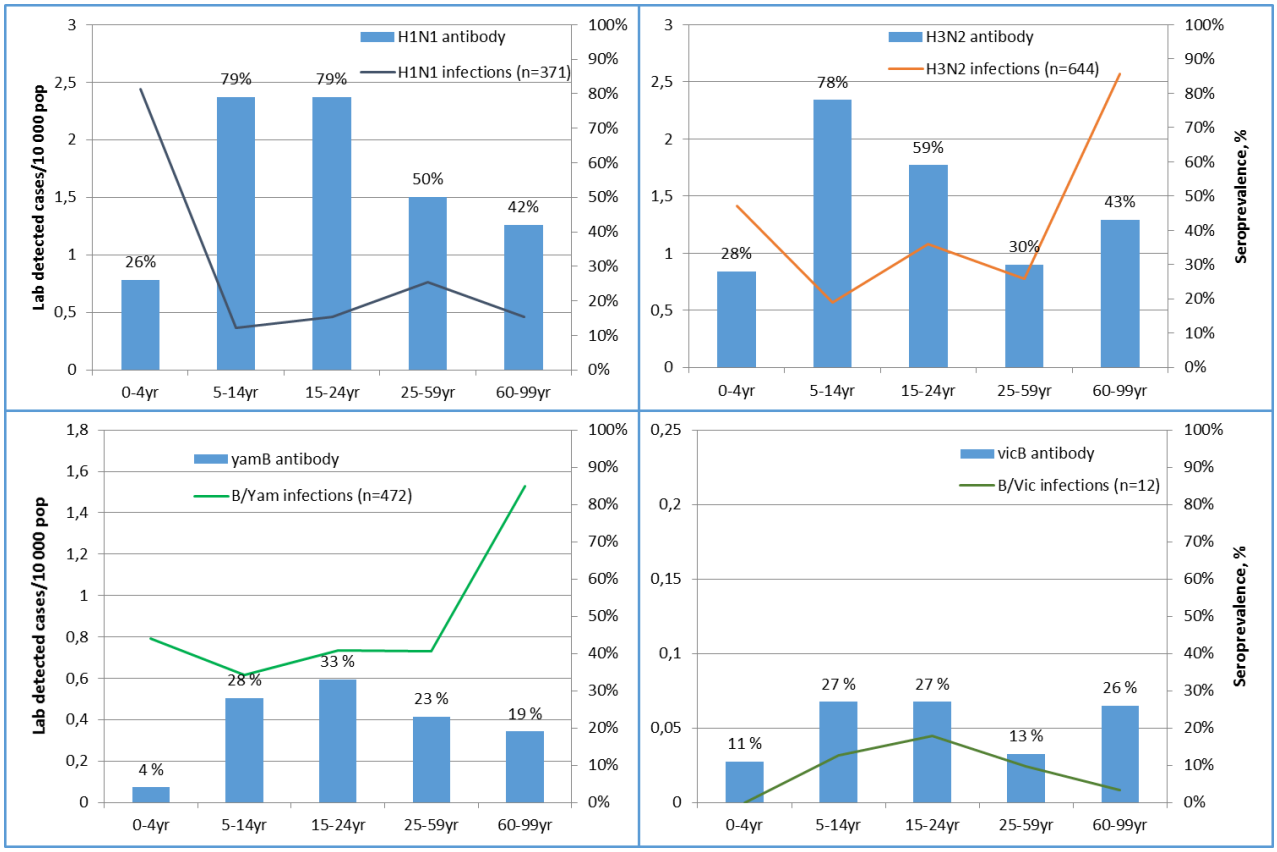


Figure 6. Prevalence of protective antibody to various influenza viruses in August 2017 (% seropositive, bars) and the age distribution of the different influenza viruses in the 2017/2018 influenza season (up to week 5/2018, incidence per 10^4 population, line plot).

Since the number of viruses subjected to type, subtype and variant testing differs widely, the incidences are comparable between age groups in the same panel, but incidences are not comparable between the panels.
The age profiles of immunity, as well as of infection, are very different between the different subtypes and lineages.
In the school-age children and young adults, there is a good correspondence between high pre-season seroprevalence and suppressed incidence of infection for A(H1N1). The recorded incidence of A(H3N2) infections is also lowest in the school-age children which had the highest pre-season seroprevalence. However, the HI seroprevalence data do not appear to explain why the H1N1pdm09 virus preferentially affects the infants and A(H3N2), but not A(H1N1)pdm09, preferentially affects the elderly.
For the B/Phuket/3433/2013-like B/Yamagata-lineage viruses, the pre-season seroprevalence was relatively low in the elderly where the incidence is the highest. However, the seroprevalence is considerably lower in the infants, which do not seem to be selectively targeted by the virus.
B/Victoria-lineage viruses circulate only sporadically and too few have been identified to make any meaningful age profiling for these viruses.

Surveillance of laboratory-confirmed influenza in hospitalised patients

In the laboratory-based surveillance system of influenza-confirmed hospitalisation, eight microbiological hospital laboratories participate. These laboratories cover approximately 60% of the Norwegian population, and report each week the number of influenza virus detections in hospitalised patients (all wards) according to influenza type (A, B) and age group. From week 40/2017 through week 5/2018 influenza virus has been detected in 1768 hospitalised patients. The number hospitalisations increased from week 50/2017 to week 1/2018, and after a slight decrease in week 2 and 3/2018 it has again increased until week 5/2018 (Figure 7). Most patients hospitalised with influenza have been 60 years or older. Influenza B virus has been the most frequently detected influenza type among the hospitalised patients (60%). This is the fourth year this surveillance system has been in operation.

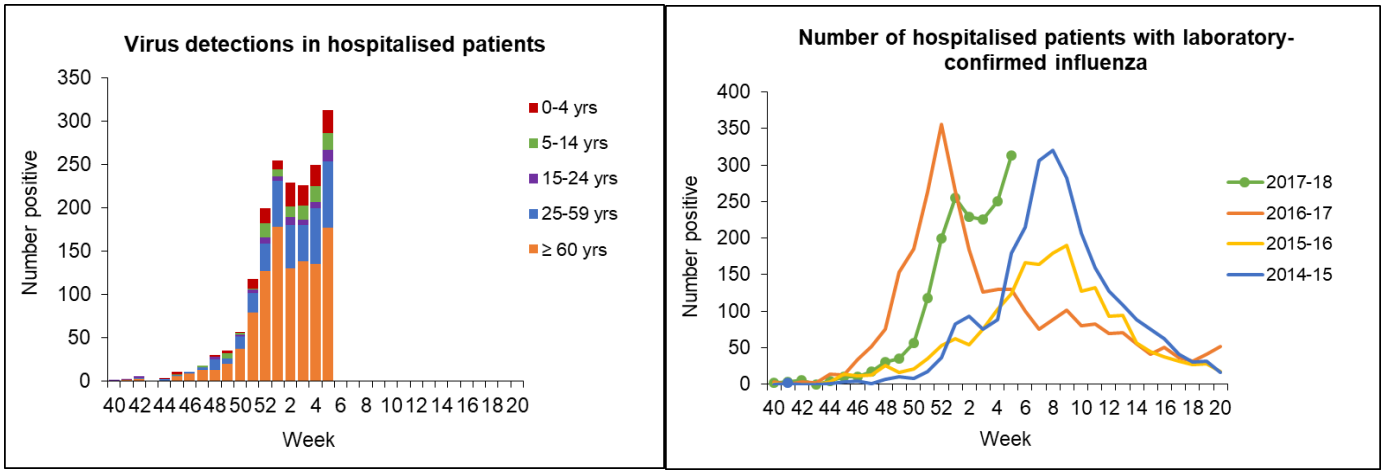


Figure 7. Left hand panel: The number of influenza virus detections in hospitalised patients per week during influenza season 2017/2018, age-distributed. Right hand panel: The number of hospitalised patients with confirmed influenza per week the four last influenza seasons. To be able to compare the seasons, week 1/2016 is the average of the number of patients hospitalised with influenza in week 53/2015 and week 1/2016.

Influenza patients in intensive care units

From the 2016/17 season it has been piloted whether the Norwegian Intensive Care Registry (NICR) can be used as a data source for a national surveillance of influenza patients in intensive care units. Almost all ICUs in Norway report data to NICR. As part of the pilot, NICR has asked all ICUs from week 46/2017 weekly to report the number of patients in ICUs with laboratory-confirmed influenza, the number of patients in ICUs with clinically suspected influenza and the number of deaths among patients with confirmed or suspected influenza admitted to ICUs (Table 2). Anonymised data are reported from NICR to the NIPH.

Table 2. The number of confirmed or suspected influenza ICU admissions and deaths from week 46/2017 until week 5/2017.

Number of patients admitted in ICUs with laboratory-confirmed influenza	151
Number of patients admitted to ICUs with clinically suspected influenza	102
Number of deaths among patients with laboratory-confirmed or clinically suspected influenza admitted to ICUs	11

Excess all-cause mortality

The NIPH has been conducting weekly all-cause mortality surveillance since the 2015/2016 season, using the EuroMOMO algorithm. Historical data are available from 2008. This season, significant excess mortality, has been observed in the elderly (≥65 years) in Norway in five consecutive weeks (week 51/2017 to week 3/2018). So far, the level of all-cause excess mortality this winter has been lower compared to last winter, but the numbers may still increase. The numbers for the last 2-3 weeks are uncertain due to delay in reporting and may therefore be adjusted.

Monthly reported respiratory viruses

The national monthly reporting scheme for laboratory diagnoses of viruses is based on a voluntary partnership arrangement between medical microbiology laboratories in Norway. The scheme has been running since 1969. The purpose of these reports has been to contribute to the monitoring of communicable infections in the population, especially since many types of infections are not notifiable. Reports from the various microbiology laboratories of positive findings in the current month are collected at the Norwegian Institute of Public Health and then compiled into a summation form for the current year.

Figure 8 shows the monthly reported detections of respiratory infections that were laboratory confirmed during the previous months in Norway. During the autumn of 2017 through November, rhinoviruses were a major cause of respiratory illness. Respiratory syncytial virus (RSV) has played a much lesser role during the last few months after causing a larger outbreak last winter. Human metapneumovirus, on the other hand, are more frequently detected this winter.
The number of patients tested for the different viruses varies, thus the proportions displayed do not accurately portray the actual proportions of infections.

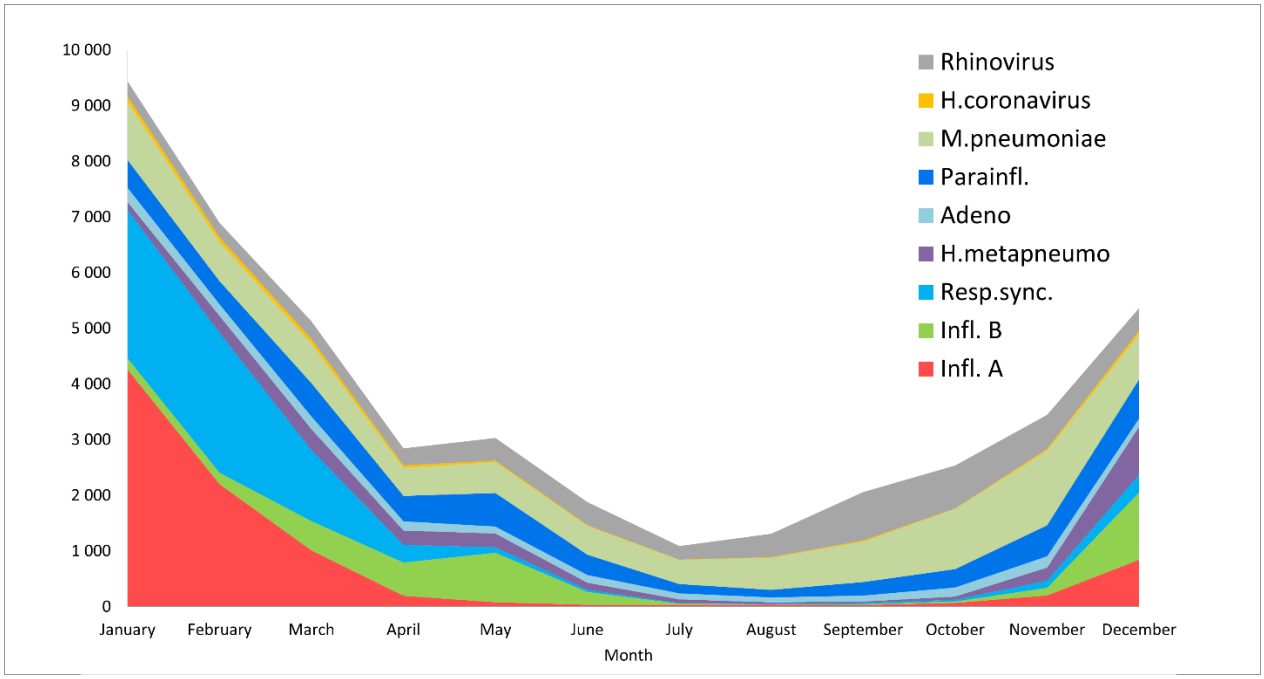


Figure 8: Number of respiratory virus detections in Norway reported monthly, from January through December 2017. Data for January 2018 are not yet available.

2: Characterisation of influenza viruses circulating in Norway, 2017-18 season

B/Yamagata/16/1988 lineage

Out of 619 samples PCR positive for B/Yamagata in NIC Norway, 9.7% have so far been sequence analysed and HA sequences of 5% of all PCR-positive influenza B viruses have been submitted to GISAID. All B/Yamagata viruses from this season in Norway belonged to the genetic clade 3 and resemble the B/Yamagata viruses from the previous season in Norway. A small group of viruses in the beginning of the season possessed the HA amino acid substitutions Q122K and T181A, otherwise all viruses have had few or none substitutions compared to the vaccine strain (Figure: Section 4: Phylogeny). The majority of the NA genes possessed the amino acid substitutions I51M, R67H and I173M.

From week 40 to week 5, 24 influenza B/Yamagata viruses (4% of B/Yamagata viruses received in NIC Norway), both virus isolates and clinical samples, have been shipped to the WHO Collaborating Centre for Reference and Research on Influenza, Crick Worldwide Influenza Centre. About 3 % have been propagated in cells in the NIC.

Influenza A(H3N2)

By week 5, 542 samples have been PCR-positive for H3 in NIC Norway, 18% of those have been sequence analysed and HA sequences of 9% of all PCR-positive H3 viruses have been submitted to GISAID. Strain-based reporting of virus characterisation data has been done routinely through TESSy. Both H3 viruses of genetic clades 3C.2a and its sub-clade 3C.2a1 have been circulating as during the previous season and the summer months of 2017. The 3C.2a clade has predominated the H3N2 viruses in Norway also this season. However, most of the most recent viruses sequenced (week 4) belonged the 3C2.a1 group of viruses (Figure 9). Several sub-clusters of H3N2 viruses was circulating.

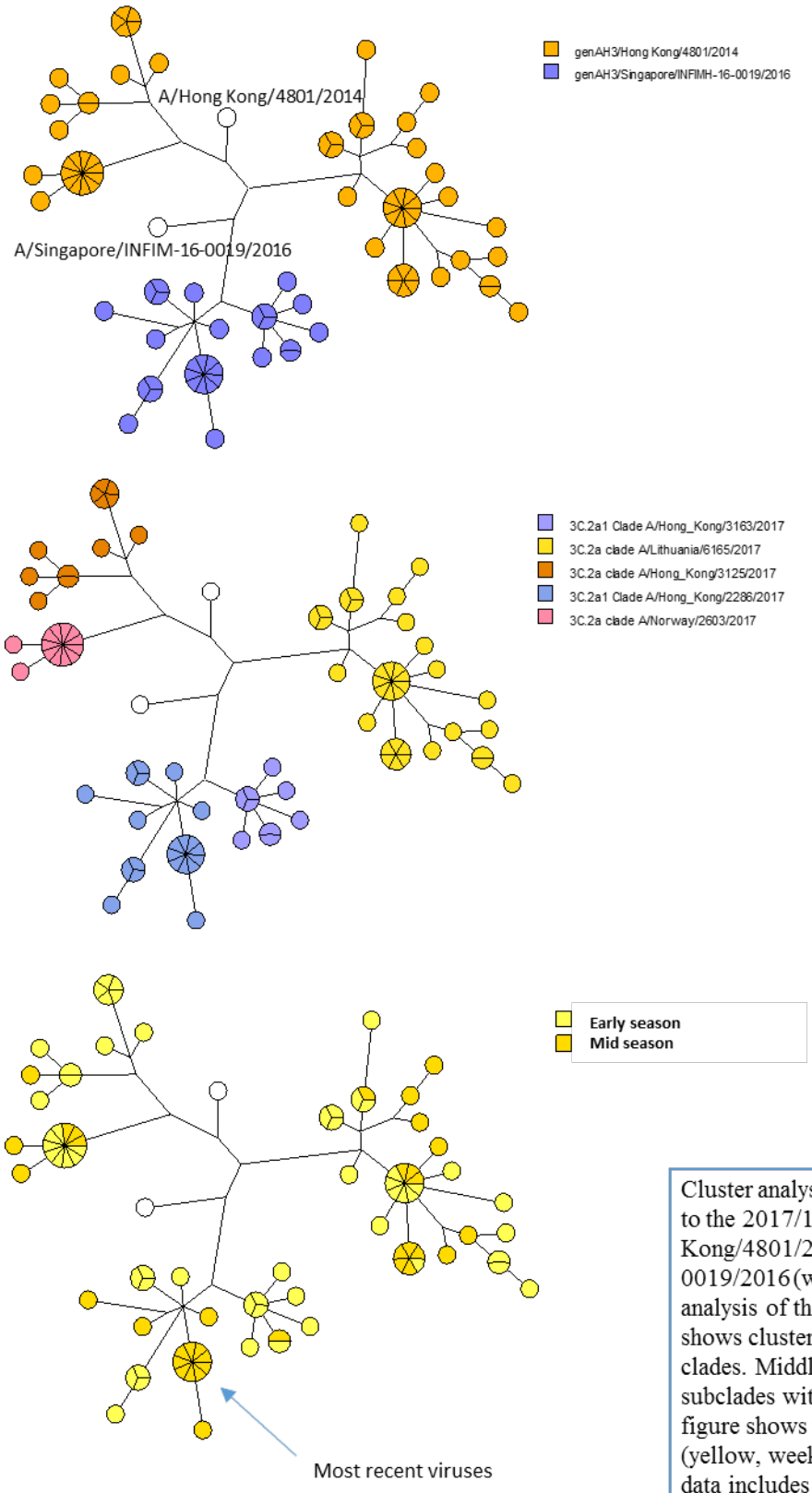
The main group of viruses within the genetic 3C.2a clade are most closely related to the reference virus A/Lithuania/6165/2017 possessing the T131K, R142K and R261Q substitutions in HA (in reference to A/Texas/50/2012, see phylogeny section). Both T131K and R142K are in antigenic site A and have been related to antigenic drift. These viruses caused the rapid increase in cases in Norway previous season. Based on genetic cluster analysis and phylogeny this subclade could be considered for a new sub-clade name. Some recent viruses also possessed S91N or the N144R substitution.

The minority of the H3 3C.2a1 viruses from last season possessing the K92R and H311Q HA substitutions are the ones dominating the sub-clade this season. All Norwegian 3C.2a1 viruses now possess K92R and H311Q, and the most recent viruses possess E62G, T135K and R142G in addition

The Norwegian viruses in the 3C.2a clade share NA genes with the 3C.2a1 viruses. One could speculate that the 3C.2a1 neuraminidase together with the 3C.2a HA improves viral fitness. One sequenced virus from the beginning of the season (A/Norway/3396/2017) possessed several NA amino acid substitutions L140I, V145M, G248E, V303I and S315R (Section 4: Phylogeny).

From week 40 to week 5, 46 influenza H3 viruses (8.5% of H3 viruses received in NIC Norway), both virus isolates and clinical samples, have been shipped to the WHO Collaborating Centre for Reference and Research on Influenza, Crick Worldwide Influenza Centre. 8.5% have been cell-propagated in the NIC.

Figure 9: Cluster analysis of H3 viruses circulating in Norway



Cluster analysis of HA H3 viruses in Norway compared to the 2017/18 H3 vaccine components A/Hong Kong/4801/2014 and A/Singapore/INFIMH-16-0019/2016 (white circle). Maximum parsimony analysis of the first 920b of the HA genes. Upper figure shows clustering in regard to the defined genetic clades. Middle figure shows clustering in regard to subclades within the defined genetic clades. Lower figure shows viruses from the beginning of the season (yellow, week40-50) and mid season (orange, week 51-data includes up to week 5) in different clades..

Influenza A(H1N1)pdm09

Also this season few H1 viruses have circulated in Norway, 133 have been PCR positive for H1N1 at the NIC Norway and 35 of these have been sequence analysed (26 %) and HA sequences of 16.5 % of all PCR-positive H1 viruses have been submitted to GISAID. Strain based reporting of virus characterisation data was done routinely through TESSy. These H1 samples belonged to the A/Slovenia/2903/2015 6B.1 group of viruses and grouped phylogenetically with the A/Paris/1289/2017 reference virus, but with the amino acid substitutions S74R, S164T and I295V in addition. Some of the recent viruses also possessed T120A (see phylogeny section). Most of the genetic sequenced NA genes possessed the G77R, V81A, I188T and I314M substitutions.

From week 40 to week 5, 16 influenza H1N1 viruses (12% of H1N1 viruses received in NIC Norway), both virus isolates and clinical samples, have been shipped to the WHO Collaborating Centre for Reference and Research on Influenza, Crick Worldwide Influenza Centre. 12% have been propagated in cells in NIC Norway.

B/Victoria/2/1987 lineage

Out of 15 samples PCR positive for B/Victoria at the NIC Norway by week 5, 60% have so far been sequence analysed. All belong to the clade 1A viruses. Most Norwegian B/Victoria viruses possess the I261L substitution in HA. One single virus, B/Norway/347-2/2018, had the double deletion of HA amino acids 162 and 163 and possessed the D129G and I179V substitutions in addition (see phylogeny section).
The NA gene of most B/Victoria viruses possessed the substitutions A62T, I120V and S295R, while the NA of the double-deletion variant possessed F12L, I120V, T211I and S295R

From week 40 to week 5, four influenza B/Victoria viruses (27% of B/Victoria viruses received in NIC Norway), both virus isolates and clinical samples, have been shipped to the WHO Collaborating Centre for Reference and Research on Influenza, Crick Worldwide Influenza Centre. 7% have been propagated in cells in NIC Norway.

Proportions vaccinated and infected with influenza

Samples from persons vaccinated for the 2017/1 season made up 2.8% of all samples received to the NIC Norway. Most people vaccinated in Norway are elderly and this and last season the elderly were overrepresented with H3 influenza. Table 3 summarises the percentage of patients vaccinated with lab confirmed influenza.

Table 3: Percentage vaccinated with lab-confirmed influenza

Season	Dominating virus	Vaccinated and infected (%)	Vaccinated infected (n)	Infl. Positives (n)	Samples from vaccinated (%)
2014-15	H3/B	0,9	22	2511	1,4
2015-16	H1/B	0,4	16	3917	1,2
2016-17	H3	1,7	40	2386	2,9
2017-18 to week 5	Byam	1,1	15	1327	2,8

Antiviral resistance monitoring

Monitoring of antiviral susceptibility has not revealed any neuraminidase inhibitor resistance in Norwegian viruses this season. The NIC at FHI has analysed 5% of viruses received so far for phenotypical resistance. In total 7.6 % of the H3 viruses, 42 % of the H1 viruses, 2,6 % of the Yamagata viruses and 6.7 % of the Victoria viruses have been analysed for antiviral drug resistance either phenotypically or genetically.

Table 4. Norwegian influenza viruses resistant to M2 blockers (adamantanes) and the neuramidase inhibitors oseltamivir and zanamivir, during the period from week 40/2017 through week 5/2018.

per. 11/02-18	Oseltamivir (Tamiflu®)		Zanamivir (Relenza®)		Adamantanes (Amantadin, Rimantadin)	
virus	Number tested	Number Oseltamivir-resistant virus	Number tested	Number Zanamivir-resistant virus	Antall testet	Antall Adamantan-resistant virus
H3	40	0 / (0 %)	40	0 / (0 %)	1	1 / (100 %)
B	17	0 / (0 %)	17	0 / (0 %)		
H1	56	0 / (0 %)	14	0 / (0 %)	1	1 / (100 %)

Two screening tools were used to determine oseltamivir/zanamivir susceptibility: sequence analysis of viral genes or a fluorescence-based neuraminidase inhibition assay.
* we do not test routinely for adamantane resistance, since almost no circulating viruses are susceptible to this class of drug.

3: Seroepidemiology Data, August 2017

The National Seroepidemiological Influenza Programme for the year 2017 analysed a total of 2093 serum samples collected during the weeks 31-35 from clinical/microbiological laboratories covering the 19 counties of Norway. The anonymised convenience sera are aiming to be representative of the Norwegian population geographically and by age composition.
The 2017 serum panel was tested by haemagglutination-inhibition (HI) against the 2017/18 seasonal influenza vaccine strains (trivalent/quadrivalent) (Table 1), i.e. A/Michigan/45/15 (a H1N1pdm09 B.1-like virus), A/Hong Kong/5738/14 (a H3N2/Hong Kong/4801/2014 3C.2a-like virus), B/Brisbane/60/08 (a B/Victoria-lineage 1A-like virus), and B/Phuket/3073/13 (a B/Yamagata-lineage 3-like virus). Two additional viruses were also included in the analyses: H1N1pdm09/California/07/09 (the previous H1N1 vaccine virus X-179A), and A/Norway/3806/2016 (a recent H3N2isolate representing the genetic clade 3C.2a1-like viruses). HI titres ≥ 40 against the influenza A strains and ≥80 against ether-treated influenza B strains were considered as protective levels and recorded as seropositive in this analysis. The results are shown in Table 5 and Figure 10.

The 2017 HI assay: For the year 2017 the HI assay antigens were used with 4 HAU, in agreement with the CONSISE HI assay consensus recommendation. The previous years 8 HAU have been used. The 4 HAU gave a somewhat higher HI titres as compared to 8 HAU. The HI results presented for August 2017 have not been corrected for this difference. Studies are in progress to clarify the differences in various age groups for each antigen used.

Summary of outcomes

The population seroprevalence to current influenza A vaccine viruses in August 2017 was relatively high, indicating good protective immunity against the two influenza A vaccine viruses in most age groups. The seroprevalence to A/H1N1pdm09 viruses, including the new H1N1 vaccine strain A/Michigan/45/15, was high (57 %, 'All ages'), an increase of 11 percentage points from the previous year, even though very few H1pdm09 viruses were detected the preceding season. The seroprevalence to the H1pdm09 the last two years are the highest observed since the pandemic in 2009. A/H3N2, the dominant virus the preceding season, constituted about 95 % of circulating viruses in the 2016-2017 season. Thus, high seroprevalence (45 %, 'All ages') was seen in August 2017 to the H3N2 vaccine strain (A/Hong Kong/4801/14-like viruses, a 3C.2a genetic clade virus, represented by A/Hong Kong/5738/14), as well as to genetic subclade 3C.2a1 viruses (represented by the reference strain A/Norway/3806/2016). The seroprevalence to H3N2 ('All ages') is a two-fold increase (21 percentage points) compared to the previous year. However, seroprevalence against the two influenza B vaccine viruses B/Victoria/Brisbane/60/08 and B/Yamagata/Phuket/3073/13 was low to moderate (20 % and 23 %, respectively), and were mainly unchanged for 'All ages' and for most age groups as well, from last year.

Influenza A(H1N1)pdm09

In August 2017 the prevalence of protective antibodies against A(H1N1)pdm09 was 57 % ('All ages'), an increase of 11 percentage points from August 2016. A similar increase was also seen in all age groups (between 10 to 15 percentage points) except for those below 5 years of age with a reduction of 5 percentage points in seroprevalence against H1pdm09 from the previous year. The seroprevalence to the new H1 vaccine strain A/Michigan/45/15 is very similar to the previous vaccine strain X179A (A/California/07/09) both for 'All ages' and in the various age groups.

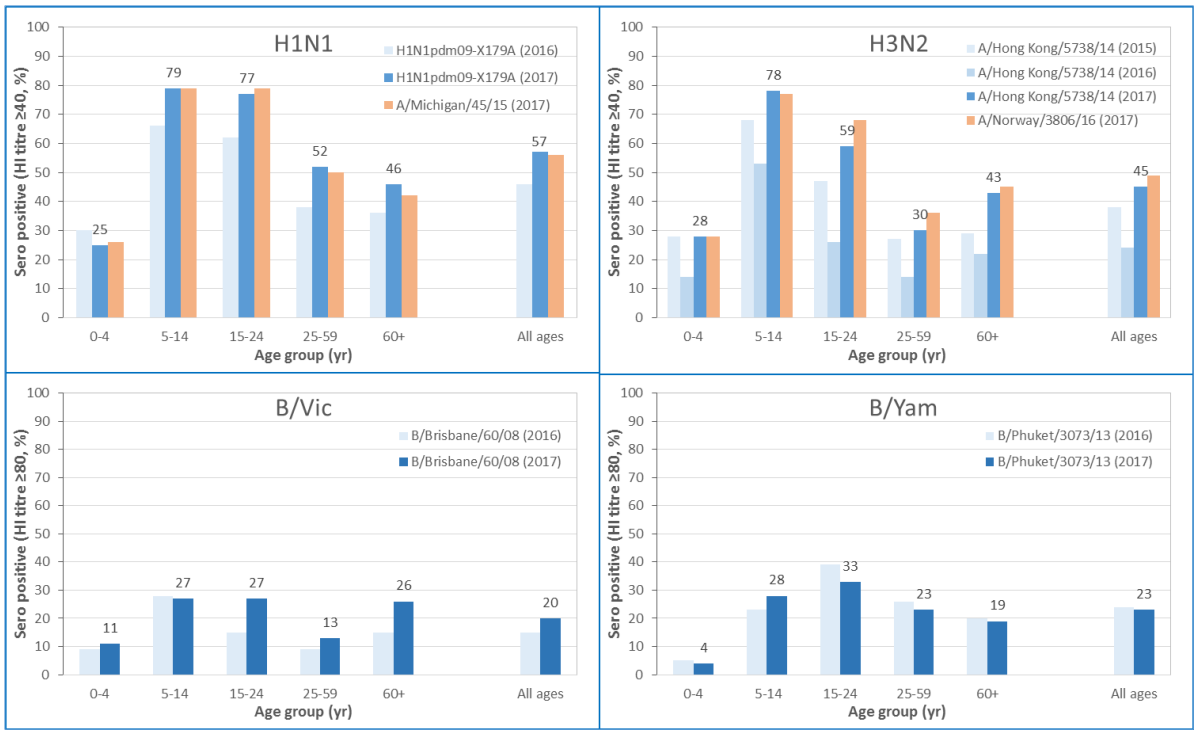


Figure 10. Seroprevalence in August 2017 to current influenza A and B reference and vaccine strains for 'All ages' and in various age groups. For comparison, seroprevalences to some virus strains in August 2015 and 2016 are also shown. Columns in dark colour (blue, red) show the seroprevalence in 2017. Columns in light blue show the corresponding seroprevalences in 2015 and 2016 for some strains. Further details are given in the text.

Influenza A(H3N2)

The seroprevalence in August 2017 to the current H3N2 vaccine strain (A/Hong Kong/4801/14, 3C.2a genetic group, represented by A/Hong Kong/5738/14) had increased significantly compared to the previous year, i.e. from 24 % to 45 % for 'All ages'. This is consistent with the high proportion of H3N2 viruses circulating in the preceding season, about 95 % of detected viruses. Increased seroprevalences were seen in all age groups. The highest increase was in young adults (15-24 year olds) with 33 percentage points, which is a 2.3-fold increase in seroprevalence from last year. A similar increase in seroprevalences (1.5 to 2.1-fold) are also seen in the other age groups to the current H3N2 3C.2a-like vaccine virus. From August 2015 to August 2016 there was a 1.5 to 2 times reduction in seroprevalence to A/Hong Kong (Fig. 10). The reduced pre-season prevalence of protective antibodies in August 2016 might thus have contributed to the dominance of H3N2 viruses circulating the 2016/2017 season. The seroprevalences against genetic clade 3C.2a1 viruses (represented by A/Norway/3806/2016) were nearly the same as for the 3C.2a genetic clade viruses for 'All ages', those below 15 years of age as well as those 60 years and older, while there were somewhat higher seroprevalences (6-9 percentage points) for young adults and adults (25-59 years old).

Influenza B

In August 2017 the prevalence of protective antibodies to influenza B viruses were low to moderate and were mainly unchanged from August 2016 against both B/Victoria- and B/Yamagata-lineage vaccine-like viruses ('All ages'). For most age groups the changes in seroprevalences were less than +/- 5 percentage points. However, for young adults (15-24 year olds) and those 60 years and older an increase of 11 to 12 percentage points in the seroprevalence against the B/Victoria-lineage vaccine-like viruses, represented by B/Brisbane/60/08, were seen (Table 5 and fig 10). Interestingly, relevant to the current flu season with dominance of B/Phuket/3073/13-like B/Yamagata-lineage viruses, the seroprevalence against B/Phuket-like viruses has been decreasing the last two years, after the 2014/2015 season of which B/Phuket-like viruses constituted about 40 % of the circulating viruses. The largest decreases in protective antibodies from August

2015 to August 2017 (8 to 10 percentage points) were seen in those age groups with the highest B/Yamagata virus incidence the current season (Data not shown).

During the preceding 2016/2017 season, a B/Brisbane/60/08 (B/Victoria-lineage) hemagglutinin (HA) double deletion variant was identified in the US and Norway as well as some other countries. Since antigenic characterization using monospecific ferret antisera indicated antigenic drift, there is concern about possible lack of immunity to this variant in the human population. So far in the current season, the deletion variant has been identified in some other countries as well, but still in very low amounts (less than 1 % of circulating influenza viruses, albeit constituting a large proportion of the Victoria-lineage viruses in some countries). Preliminary HI analysis using pre-2017 human sera from our annual serum collection may indicate that sera with antibody against B/Brisbane/60/2008 tended to be reactive also to the deletion variant, suggesting some level of cross-reactive antibodies to the deletion variant virus in the human population (data not shown). However, there are some indications that the immunity in some age groups might be less cross-reactive.

Table 5. Influenza Seroepidemiological results in August 2017 - Comparison between age groups. For comparison data from studies performed for the preceding years 2014-2016 are also included.

Influenza strains (Year[$])	Age groups 0-4	5-14	15-24	0-24	25-59	60+	All ages
H1 X-179A/A(H1N1)pdm09 (2014)	**27**	**52**	**58**	**49**	**31**	**30**	39
H1 X-179A/A(H1N1)pdm09 (2015)	**24**	**53**	**58**	**50**	**30**	36	39
H1 South Africa/3626/13 (2015)[1)]	35	**62**	**57**	**55**	**31**	**22**	40
H1 X-179A/A(H1N1)pdm09 (2016)	30	66	62	56	38	36	46
H1 Slovenia/2903/15 (2016)	34	66	68	60	38	33	47
H1 X-179A/A(H1N1)pdm09 (2017)	***25***	***79***	***77***	***67***	***52***	***46***	*57*
H1 Michigan/45/15 (2017)*	***26***	***79***	***79***	***68***	***50***	***42***	*56*
H3 Switzerland/9715293/13 (2014)[1)]	20	**31**	**24**	26	**12**	27	21
H3 Texas/50/12 (2015)	**35**	**79**	**54**	**60**	**35**	44	47
H3 Switzerland/9715293/13 (2015)	33	**59**	**31**	**42**	**30**	40	37
H3 Hong Kong/5738/14 (2015)[1)]	28	**68**	47	**51**	**27**	**29**	38
H3 Switzerland/9715293/13 (2016)	18	60	29	39	21	33	31
H3 Hong Kong/5738/14 (2016)	14	53	26	34	14	22	24
H3 Hong Kong/5738/14 (2017)*	***28***	***78***	***59***	***60***	***30***	*43*	*45*
H3 Norway/3806/16 (2017)[1)]	***28***	*77*	***68***	***63***	***36***	*45*	*49*
B/Vic Brisbane/60/08 (2014)	**4**	**20**	12	13	**10**	**21**	14
B/Vic Brisbane/60/08 (2015)[2)]	***2***	***32***	*25*	*23*	***17***	***32***	*23*
B/Vic Brisbane/60/08 (2016)	9	28	15	19	9	15	15
B/Vic Brisbane/60/08 (2017)*	***11***	*27*	*27*	***23***	***13***	***26***	*20*
B/Yam Phuket/3073/13 (2014) [1)]	**2**	17	**39**	21	18	16	21
B/Yam Massachusetts/2/12 (2015)[3)]	**12**	**29**	**58**	38	36	33	37
B/Yam Phuket/3073/13 (2015)[3)]	**12**	31	**43**	32	**23**	28	28
B/Yam Phuket/3073/13 (2016)	5	23	39	25	26	20	24
B/Yam Phuket/3073/13 (2017)*	***4***	*28*	***33***	***25***	*23*	***19***	*23*
Sera analysed (n): 2015 Aug	178	353	363	894	788	409	2091
[1)]Sub-panel (n) of 2015 sera (SA+HK)	91	145	130	366	282	156	804
[2)]Sub-panel (n) of 2015 sera (Brisb)	132	279	298	709	654	332	1695
[3)]Sub-panel (n) of 2015 sera (Mass+Phu)	75	183	209	467	462	232	1161
Sera analysed (n): 2016 Aug	188	351	333	874	745	411	2028
Sera analysed (n): 2017 Aug	189	318	353	860	797	436	2093
[1)]Sub-panel (n) of 2017 sera (Norway/3806/16)	162	276	315	713	753	390	1856

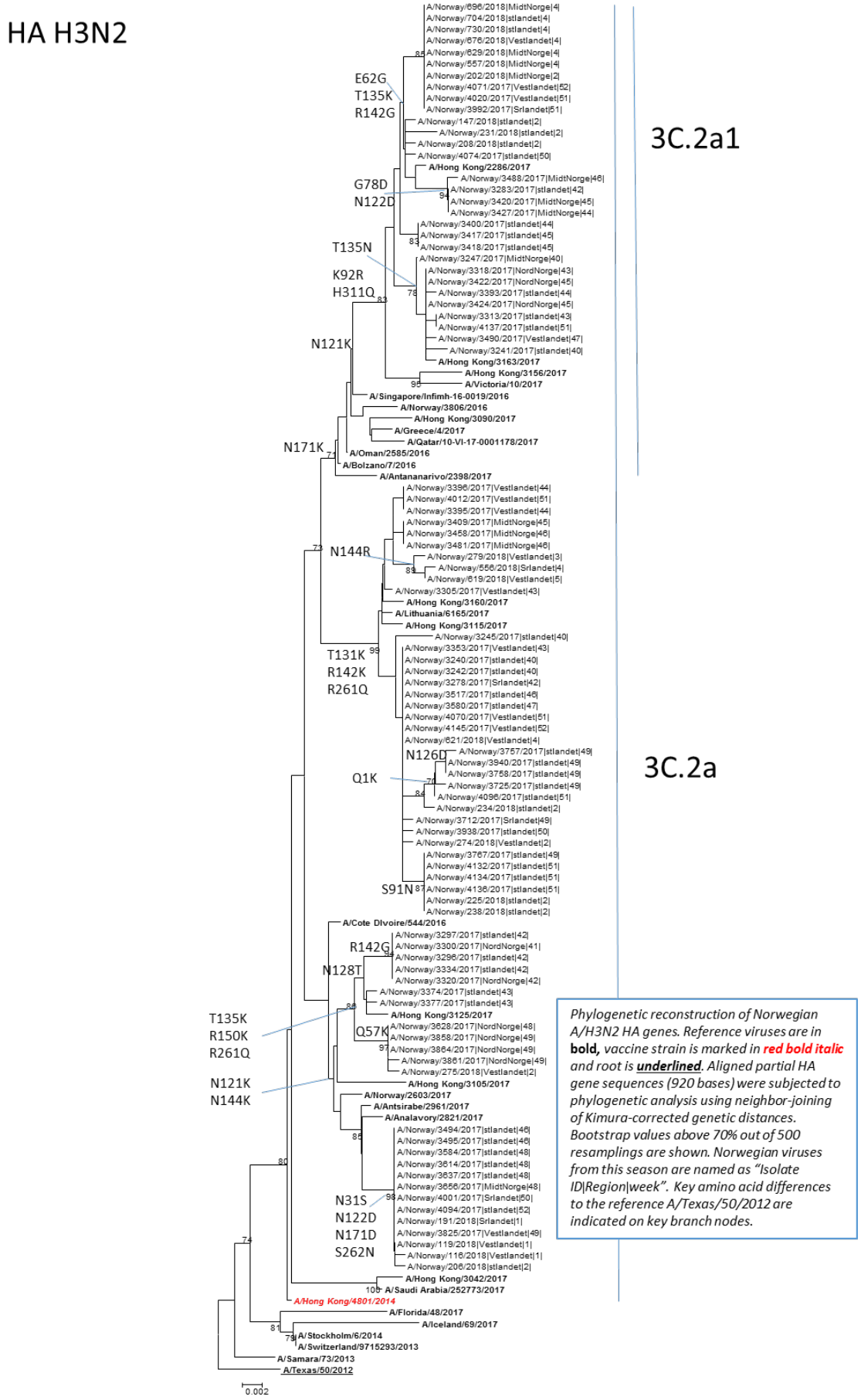
[$]Year of serum collection and HI analysis.

*All entries are per cent of sera having HI titres **≥ 40** for the A strains and **≥ 80** for the ether-treated B strains. The resulting data are weighted according to age group distribution and population density of various counties in Norway.

**Components of the Northern hemisphere influenza vaccine (trivalent/quadrivalent) for the season 2017-2018.

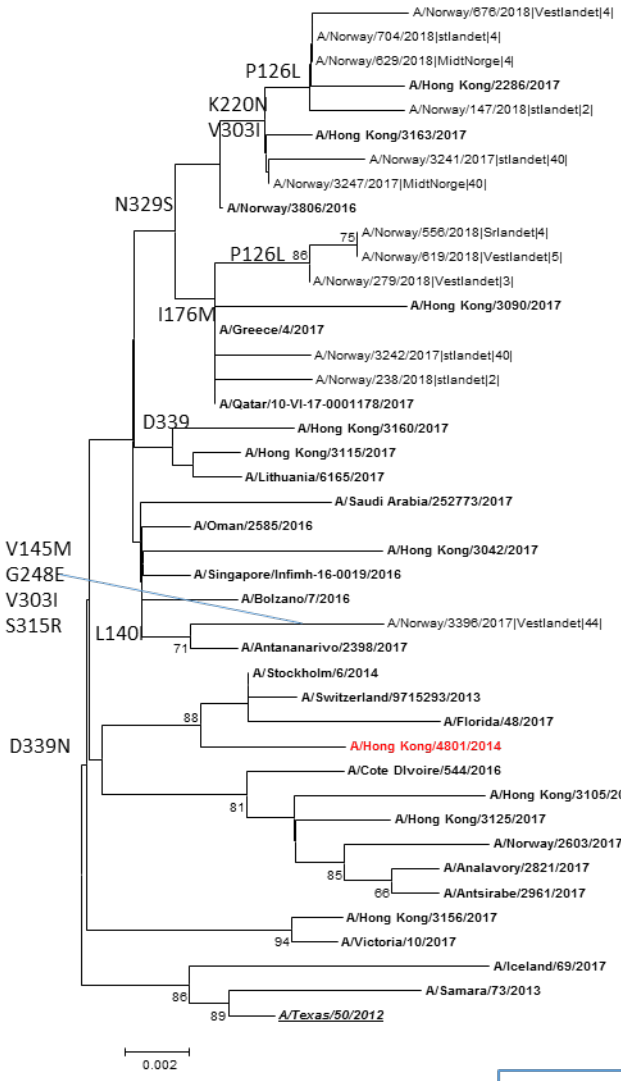
B/Yam: B/Yamagata/16/1988 lineage; **B/Vic**: B/Victoria/2/1987 lineage

4 Phylogeny: Influenza sequences, Norway 2017-18



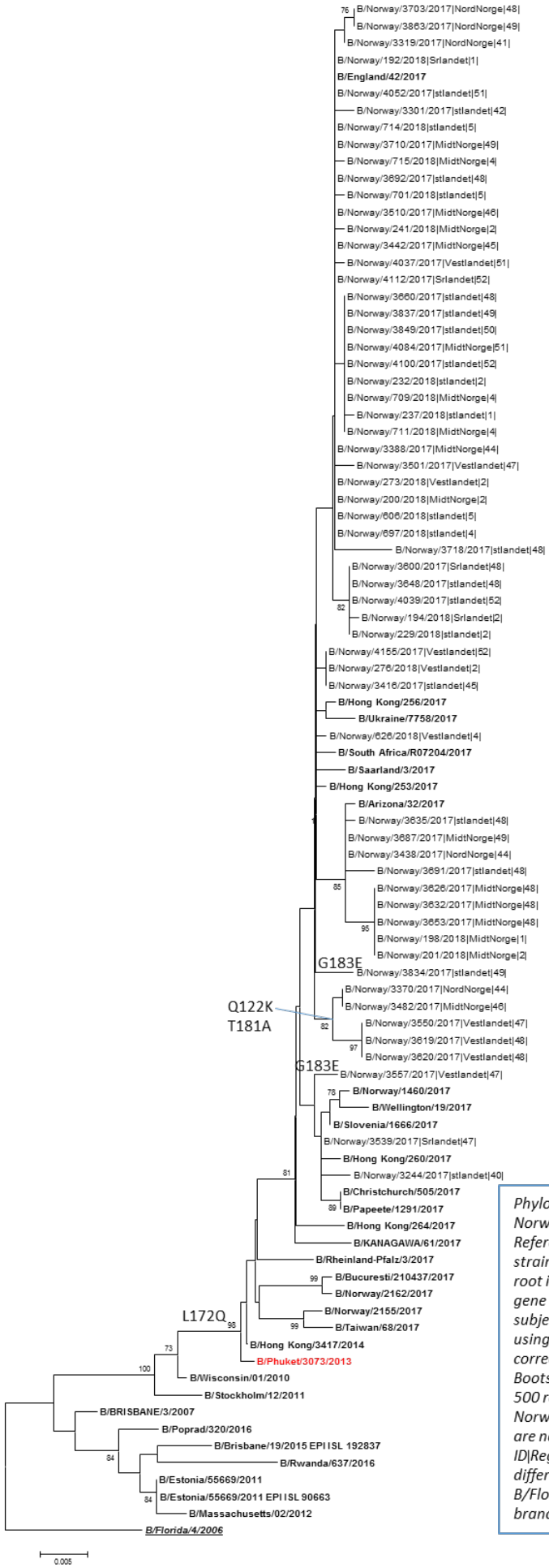
Phylogenetic reconstruction of Norwegian A/H3N2 HA genes. Reference viruses are in **bold,** *vaccine strain is marked in* ***red bold italic*** *and root is* ***underlined****. Aligned partial HA gene sequences (920 bases) were subjected to phylogenetic analysis using neighbor-joining of Kimura-corrected genetic distances. Bootstrap values above 70% out of 500 resamplings are shown. Norwegian viruses from this season are named as "Isolate ID|Region|week". Key amino acid differences to the reference A/Texas/50/2012 are indicated on key branch nodes.*

NA H3N2



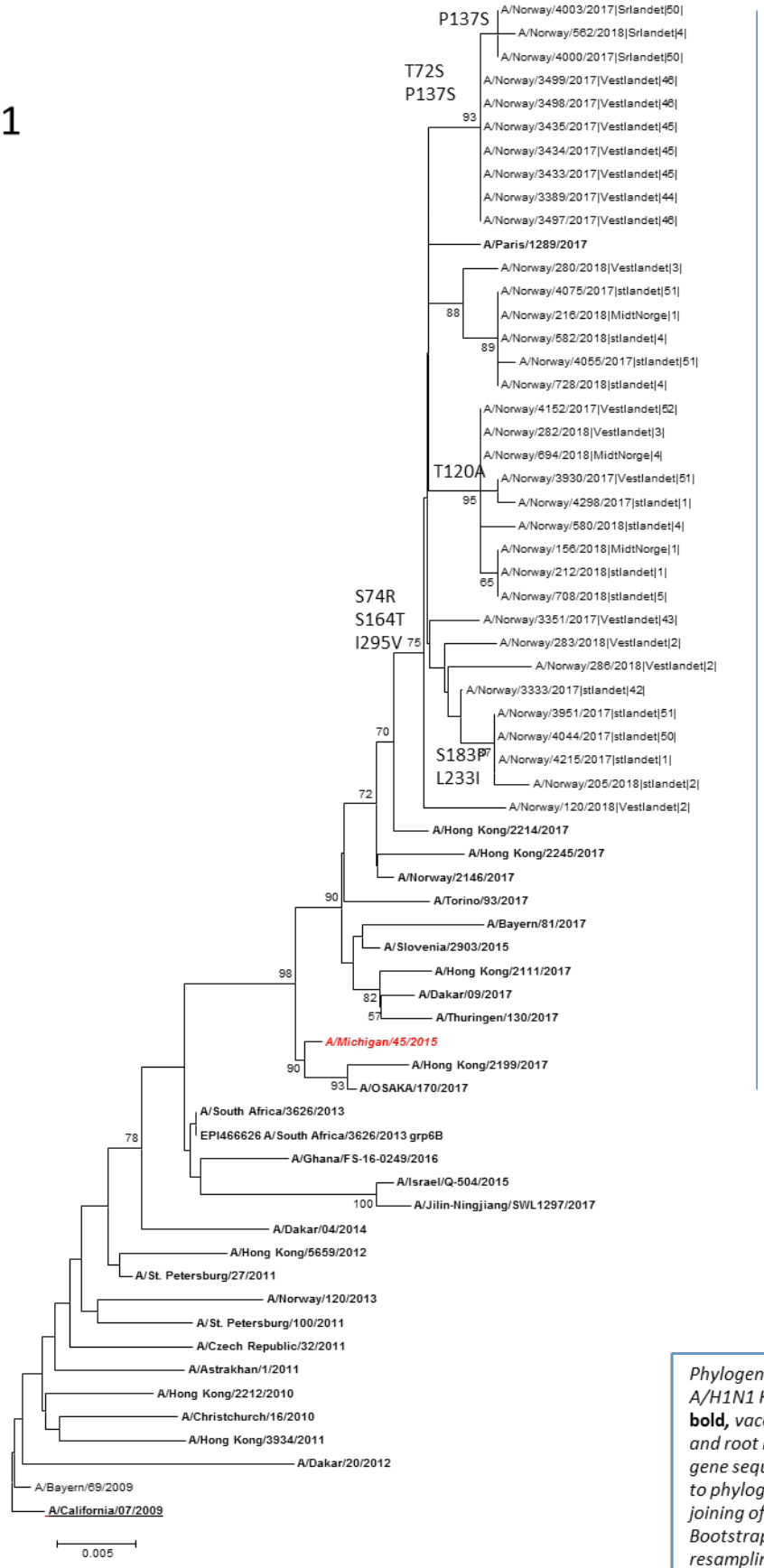
Phylogenetic reconstruction of Norwegian A/H3N2 NA genes. Reference viruses are in **bold,** *and root is* ***underlined****. Aligned partial HA gene sequences (870 bases) were subjected to phylogenetic analysis using neighbor-joining of Kimura-corrected genetic distances. Bootstrap values above 70% out of 500 resamplings are shown. Norwegian viruses from this season are named as "Isolate ID|Region|week". Key amino acid differences to the reference A/Texas/50/2012 are indicated on branch nodes.*

HA B/Yamagata



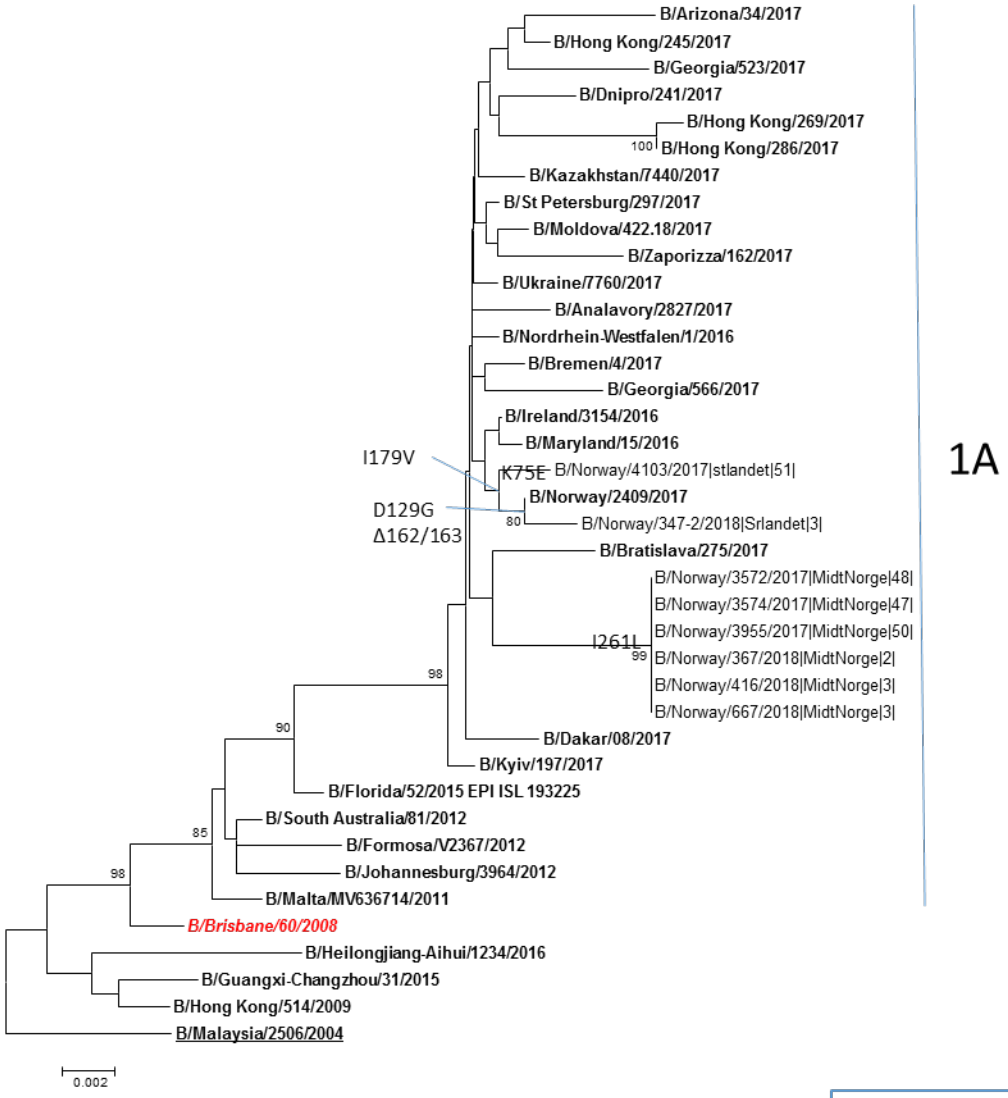
Phylogenetic reconstruction of Norwegian B/Yamagata HA genes. Reference viruses are in **bold,** *vaccine strain is marked in* ***red bold italic*** *and root is* ***underlined****. Aligned partial HA gene sequences (1000 bases) were subjected to phylogenetic analysis using neighbor-joining of Kimura-corrected genetic distances. Bootstrap values above 70% out of 500 resamplings are shown. Norwegian viruses from this season are named as "Isolate ID|Region|week". Key amino acid differences to the reference B/Florida/4/2006 are indicated on branch nodes.*

HA H1N1



Phylogenetic reconstruction of Norwegian A/H1N1 HA genes. Reference viruses are in **bold,** *vaccine strain is marked in* ***red bold italic*** *and root is* ***underlined****. Aligned partial HA gene sequences (1000 bases) were subjected to phylogenetic analysis using neighbor-joining of Kimura-corrected genetic distances. Bootstrap values above 70% out of 500 resamplings are shown. Norwegian viruses from this season are named as "Isolate ID\|Region\|week". Key amino acid differences to the reference A/California/07/2009 are indicated on branch nodes.*

HA B/Victoria



Phylogenetic reconstruction of Norwegian B-Victoria HA genes. Reference viruses are in **bold,** *vaccine strain is marked in* ***red bold italic*** *and root is* ***underlined****. Aligned partial HA gene sequences (1010 bases) were subjected to phylogenetic analysis using neighbor-joining of Kimura-corrected genetic distances. Bootstrap values above 70% out of 500 resamplings are shown. Norwegian viruses from this season are named as "Isolate ID|Region|week". Key amino acid differences to the reference A/Brisbane/60/2008 are indicated on branch nodes.*

Acknowledgements.
This work relies heavily on the essential contributions by the sentinel physicians, Norwegian medical microbiology laboratories, other participants in Norwegian influenza surveillance, as well as the WHO Collaborating Centre for Influenza Reference and Research at the Francis Crick Institute, London, UK and other partners in the WHO Global Influenza Surveillance and Response System and the European Influenza Surveillance Network. Data on the incidence of influenza-like illness are provided by the Department of Infectious Disease Epidemiology and Modelling, Norwegian Institute of Public Health, which also assisted with mortality monitoring, and data on influenza patients in intensive care are provided by the Norwegian Intensive Care Registry.
A number of sequences were accessed in the GISAID database EpiFlu and we gratefully acknowledge the contributions of all the people and institutions that have been developing and maintaining this sharing mechanism, as well as the authors, originating and submitting laboratories of the sequence data that we have used.

We furthermore gratefully acknowledge the excellent technical work performed by Valentina M. Johansen, Anne Maria Lund, Marie Paulsen Madsen, and Marianne Morken.

With best regards,
Karoline Bragstad, Kristian Waalen, Ragnhild Tønnessen, Dagny Haug Dorenberg, Remilyn Ramos-Ocao, Siri Helene Hauge, and Olav Hungnes

National Influenza Centre/Department of Influenza,
Divison for Infection Control and Environmental Health,
Norwegian Institute of Public Health, Oslo, Norway

12 February 2018 (Darwin Day)

Published by the Norwegian Institute of Public Health
February 2018
P.O.B 4404 Nydalen
NO-0403 Oslo
Telefon: + 47-21 07 70 00
The report can be downloaded as pdf
at www.fhi.no/en/publ/