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NORWAY: NATIONAL INFLUENZA CENTRE:

Influenza Virological and Epidemiological Information prepared for the WHO Consultation on the Composition of Influenza Virus Vaccines for the Northern Hemisphere 2020–2021

Geneva, February 2020

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Division of Infection Control and Environmental Health;

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Content

The 2019-2020 influenza season, Norway

Summary

- Seroepidemiology data from August 2019 indicate that immunity in Norway against circulating influenza A(H1N1) was quite strong, with considerable immunity also against clade 3C.2a A(H3N2) viruses but with much poorer antibody levels against clade 3C.3a viruses. There was also some immunity against currently circulating B/Yamagata lineage viruses, but much less against B/Victoria-lineage viruses.
- Added to this comes the immunity due to the subsequent influenza vaccination campaign in the autumn. Vaccination rates were raised compared to the 2018/19 season.
- The influenza activity crossed the outbreak threshold during Christmas (week 52/2019). After a small peak in week 1, the influenza activity increased again in week 4/2020 and was at that point on a low level intensity.
- In week 4, the number of hospitalisations was increasing and at a medium level comparable to the preceding season. Overall, the highest hospitalisation rates were found in the elderly (60 years or older), followed by young children. The same pattern was seen for influenza A, but for influenza B the highest hospitalisation rates were found in children (0-4 and 5-14 years).
- Excess all-cause mortality has mainly been within expected levels.
- There is no clearly predominant virus. Influenza A(H3N2) virus is the most numerous, constituting approximately 50% of detections. Second-most numerous is influenza B of the Victoria lineage, making up 28%, followed by influenza A(H1N1) (19%) and with only 4% being B/Yamagata lineage.
- The majority of the H3N2 viruses belong to the 3C.2a1b subgroup of viruses with the T131K substitution.
- All the characterised influenza B-Victoria viruses have been triple-deletion variants like B/Washington/02/2019.

A look back at the previous season

The 2018/19 influenza outbreak began in week 52. It reached medium intensity in week 6, a level at which it remained for three weeks. The outbreak peaked in week 7, lasted 13 weeks and ended by week 13. Measured by consultations for ILI, the outbreak of 2018/19 was of lesser magnitude than average.

Influenza A(H1N1) virus predominated, constituting approximately 60% of detections. The remainder was mainly A(H3N2) virus, with unusually few (1%) influenza B viruses. Nevertheless, among the elderly, A(H3N2) infection was more likely than A(H1N1). Among the few influenza B viruses, the B/Victoria-lineage was slightly more frequent than the B/Yamagata-lineage. Only B/Victoria-lineage viruses were observed from week 23 and onwards. The majority of the H1N1 viruses were characterised as subclade 6B.1A5 viruses, but during the summer months a new subgroup under 6B.1A5 emerged possessing a number of substitutions in HA (K130N;K160M;T216K;E235D;H296N and V321I).

A number of different subgroups of H3N2 viruses circulated, but the main group was subclade 3C.2a1b. During the summer, viruses in this group carrying the Q197R together with K207R became more prominent.

All influenza B/Yamagata-lineage viruses were HA clade 3, and most of them closely resembled B/Phuket/3073/2013. Two of them, however, carried a large number of amino acid substitutions in both HA and NA.

Among the B/Victoria-lineage viruses, the “African” triple deletion variant (clade 1A(Δ3)B) was the most prevalent.

In 2018/19, there was a lower level of hospitalisations and less influenza patients requiring intensive care unit (ICU) admission when compared to the two preceding seasons. There were also few weeks with excess all-cause mortality in the population. The highest influenza-associated hospitalisation rates were found in the elderly (60 years or older) and in young children (0-4 years). Fewer elderly people were hospitalised. However, in young children, the hospitalisation rate was relatively high.

The 2019/20 season thus far

The components of the surveillance system are briefly described in Appendices.

Influenza-like illness (ILI) in primary health care

The proportion influenza-like illness (ILI) exceeded the epidemic threshold (as defined by national, present-season MEM-levels) in week 52. There was a small peak in the proportion of ILI in week 1. After a trough in week 3, the activity increased again the following week (Figure 1). We expect further increase during coming weeks. Earlier seasons with a similar development have reached the peak in late February or March (Figure 2).

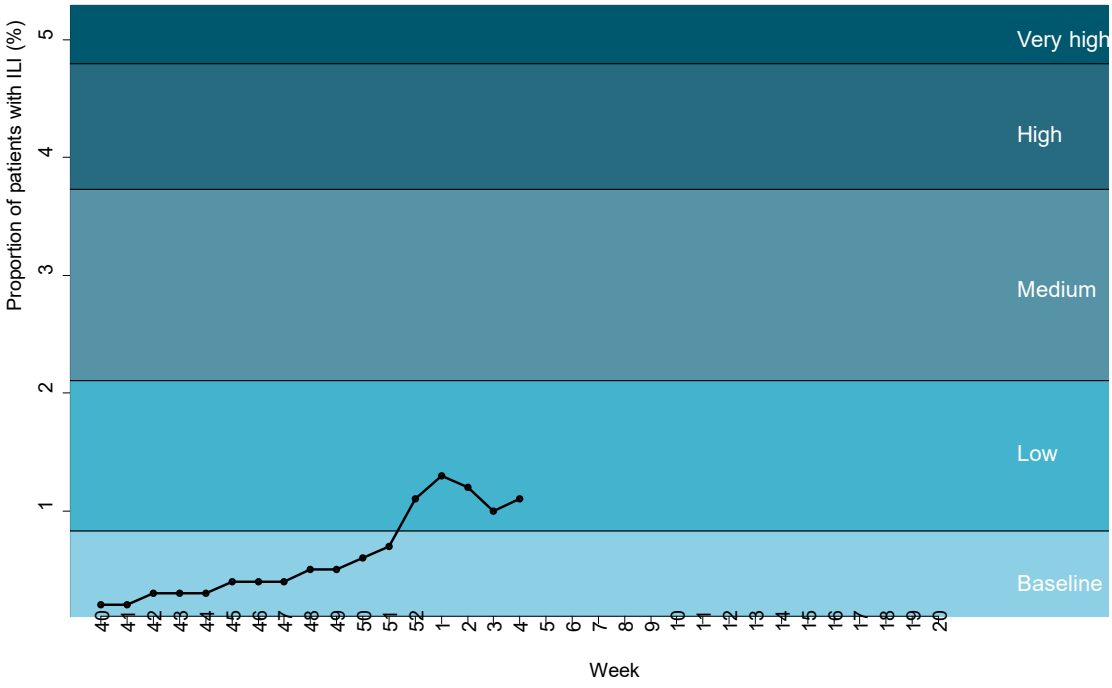


Figure 1: Level of influenza intensity depicted as weekly proportion of patients in general practice and emergency clinics presenting with ILI, Norway 2019-2020 season

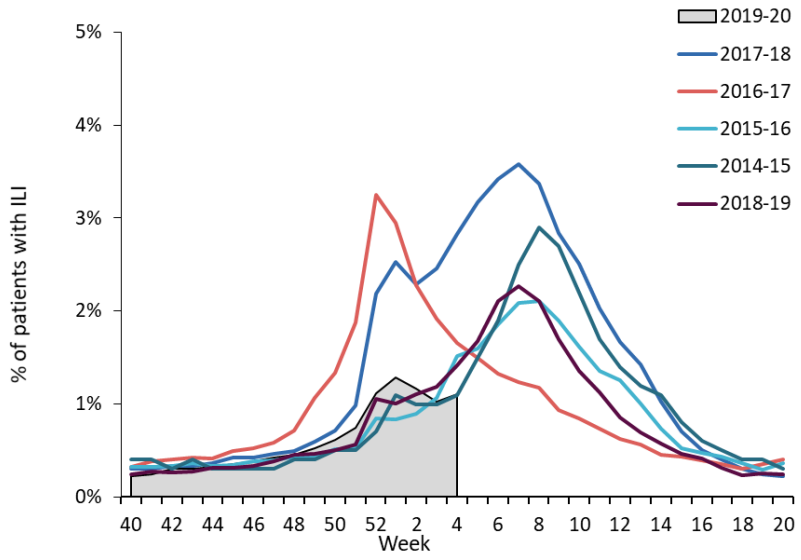


Figure 2: Weekly incidence of ILI, Norway 2019-2020 season (grey). The graph shows the proportion of patients in general practice and emergency clinics presenting with ILI, by calendar week. The five previous seasons are also shown.

Severe influenza: laboratory confirmed hospitalised cases

The number of laboratory confirmed influenza cases among hospitalised patients began to increase in week 46, reached a temporary peak in week 1 and started to increase again from week 4 (Figure 3). In week 4, the cumulative number of hospitalised patients per 100 000 population was at the same level as in the preceding 2018-19 season (Figure 4). So far this season, 83% of the detections have been Influenza A and 17% influenza B. The highest weekly and cumulative incidence rates were found in the elderly (60 years or older) and in young children (0-4 years) (Figure 5). For influenza A, the hospitalisation rate was highest among the elderly and young children. Whereas for influenza B, the hospitalisation rate was highest among children (age groups 0-4 and 5-14 years).

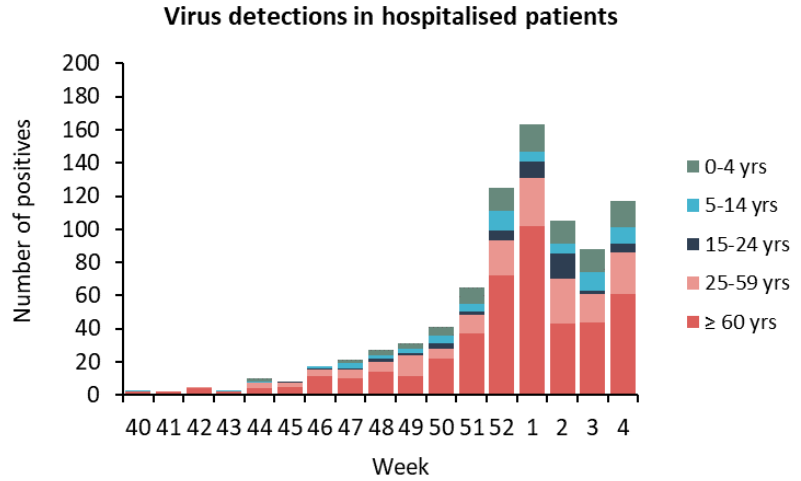


Figure 3: Virus detections in hospitalised patients until week 4 of the 2019/2020 influenza season, stratified on age groups, based on reports from nine sentinel medical microbiology laboratories.

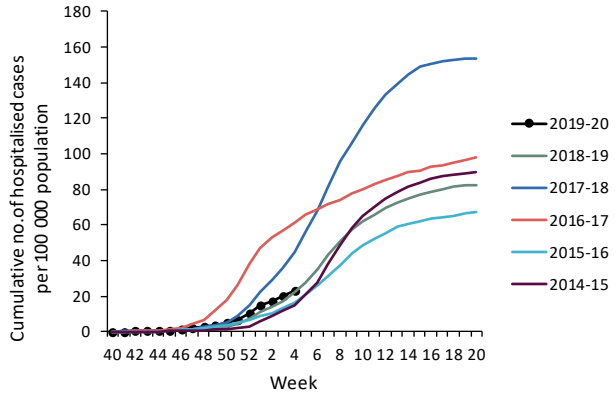


Figure 4: Estimated cumulative incidence of hospitalised patients with confirmed influenza per week compared to the previous five influenza seasons.

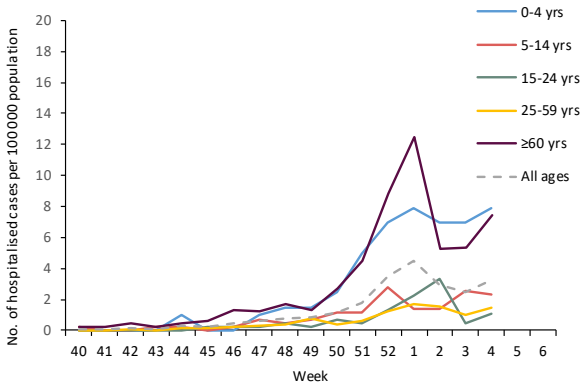


Figure 5: The estimated incidence rate of hospitalised patients per week stratified on age groups, until week 4 of the 2019/2020 influenza season. The estimation is based on reports from nine sentinel medical microbiology laboratories.

Influenza patients in intensive care units

In week 4 2020, the number of patients with laboratory confirmed influenza admitted to ICUs (n =22) was lower than in the previous three seasons (Figure 6).

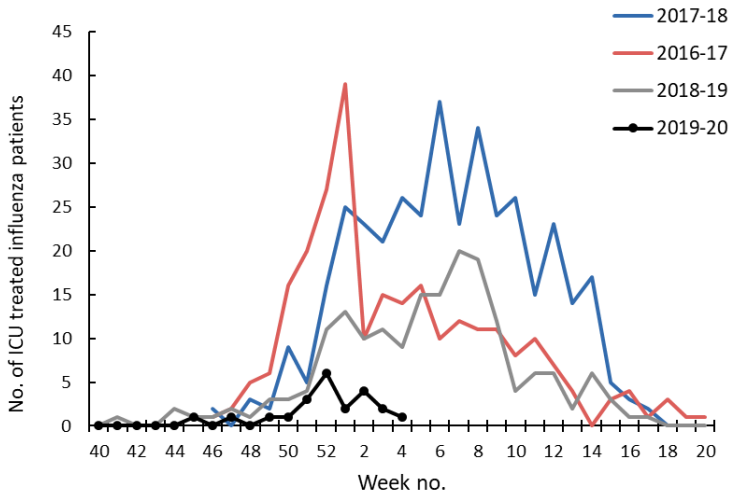


Figure 6. The number of patients admitted to ICUs during the current and previous three influenza seasons. Data source: The Norwegian Intensive Care Registry (NICR). The number for week 4 is likely to be incomplete.

Excess all-cause mortality

From week 40 2019 to week 4 2020, the all-cause mortality was mainly within expected levels. However, excess all-cause mortality was estimated for week 2, in total for Norway, and for older adults (65 years and older), and children (5 to 14 years).

Laboratory confirmed influenza: Virological surveillance

Altogether, 87636 patients in Norway have been tested for influenza during weeks 40/2019-4/2020, resulting in 4060 detections of influenza A and 1889 detections of influenza B. There was a gradual increase in the detections of influenza viruses since the beginning of October, with a more marked increase in weeks 50 – 52/2019. After this, there was some stagnation during the first weeks of January, after which the increase appears to have resumed in week 4/2019. Weekly totals and proportions of influenza positives are now at an intermediate level (Figure 7). Historically, seasons with a corresponding development of proportion positives have had outbreaks peaking in late February or March.

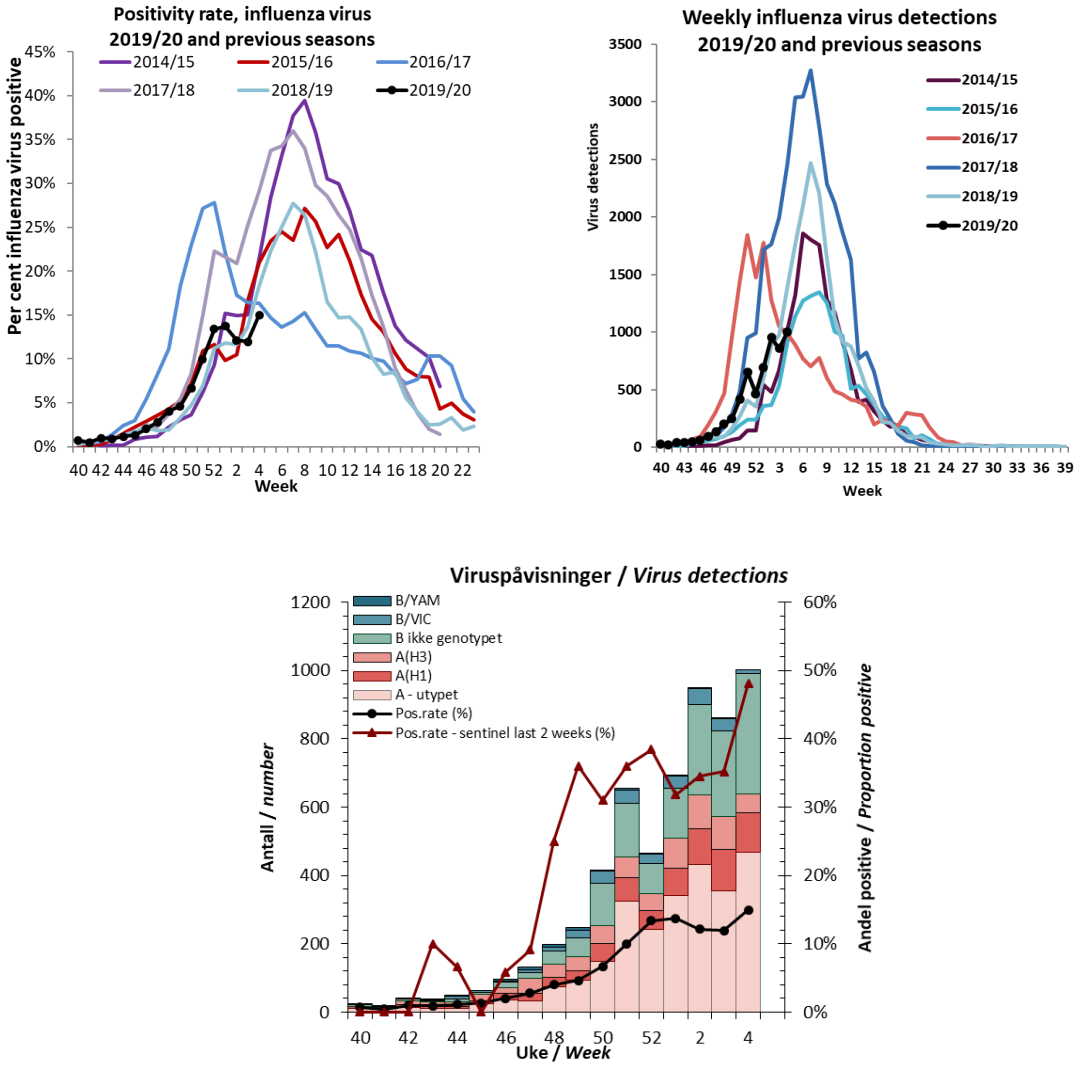


Figure 7: Laboratory detections, Norway 2019-2020. Upper left-hand panel: Weekly proportion of influenza virus positive specimens, with previous season proportions shown for comparison. Upper right-hand panel: Weekly number of influenza virus detections, with previous season numbers shown for comparison. Lower panel: Weekly number of the different influenza viruses is displayed as stacked bars, while influenza virus positivity rates of sentinel specimens (2-wk average) and all lab testing, respectively, are shown as line graphs.

The proportions of the different influenza viruses in the all-laboratories data and from the sentinel specimens are in good agreement (Figure 8).

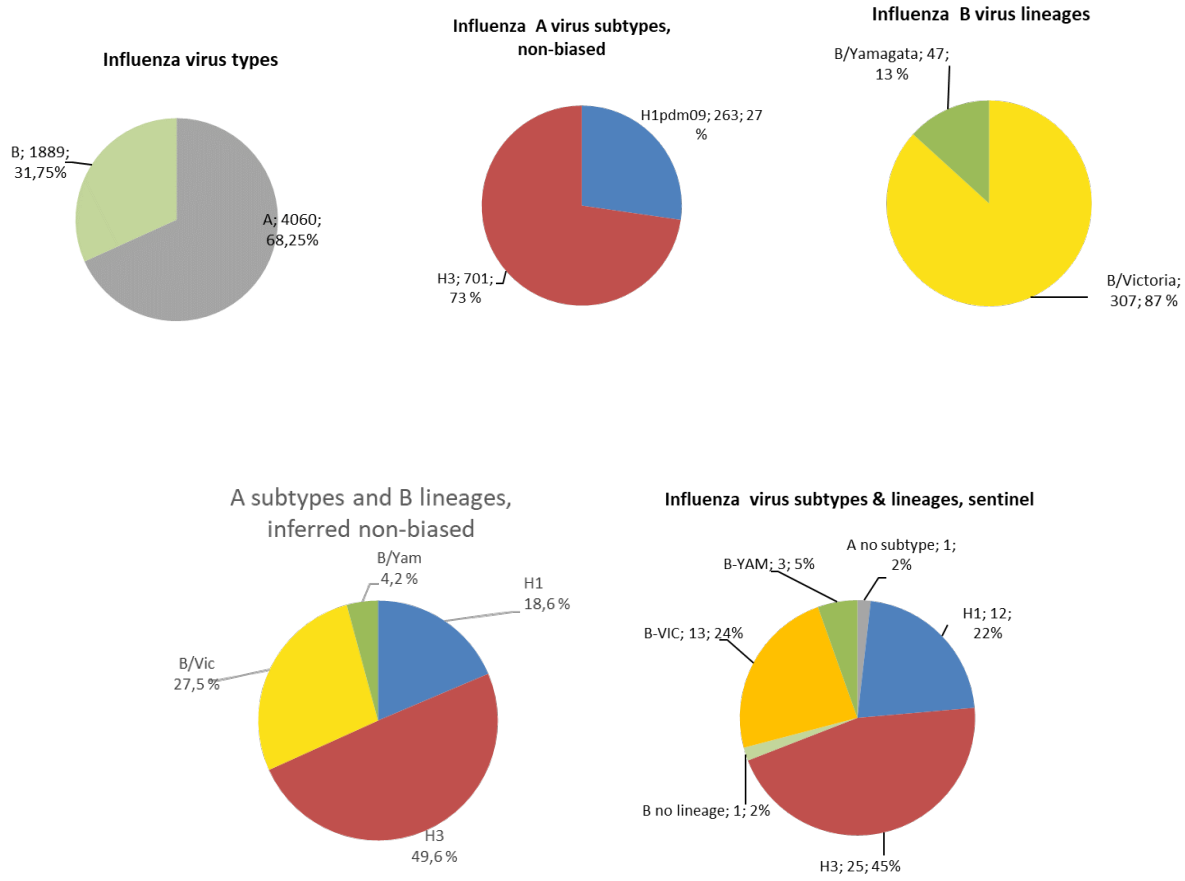


Figure 8. Proportions of 2019/20 season influenza virus subtypes and lineages among viruses analysed in Norway, by week 4, 2020. All-laboratories proportions of A/B type, A subtypes and B lineages are shown in the first three upper diagrams. The subtype and lineage frequencies are superimposed on type distributions in the lower left panel, for comparison with the distribution among sentinel specimen data (lower right panel).

To limit the subtype testing bias in the all-laboratories data (nearly three times more viruses have been tested for H1 than for H3), only H1 positives that have also been tested for H3 are counted in the top-middle diagram. The sentinel data are not subtype biased in this way but the numbers are more limited at this point.

Among the influenza A viruses, subtype A(H3N2) predominance over A(H1N1) appears to be quite stable so far into the season (Figure 9). Among influenza B viruses, the B/Victoria/2/87 lineage has been predominating over B/Yamagata/16/88 lineage viruses, except in weeks 46-48 when an early local outbreak with B/Yamagata-lineage viruses lifted the B/Yamagata proportion to even levels with B/Victoria.

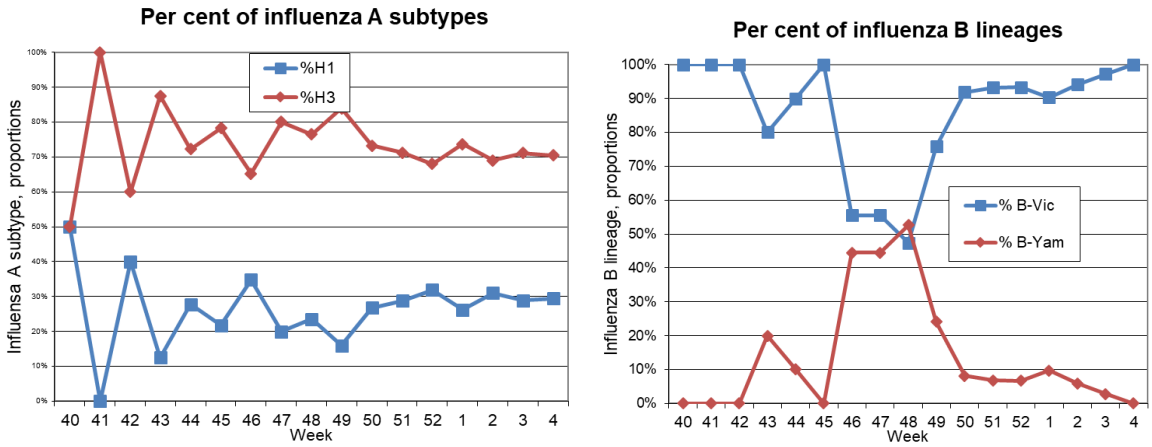


Figure 9. Weekly proportions of influenza A subtypes (left panel), among influenza A viruses that have been tested for both H1 and H3; and influenza B lineages.

Table 1: Weekly incidence of influenza-like illness (ILI), total 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 40/2019 through week 4/2020.

		Virus detections							
week	Clinical surveillance % ILI	*Specimens*	% positive	A *not subtyped*	A(H1)	A(H3)	B *not lineage typed*	B/ Victoria lineage	B/ Yamagata lineage
40	0,2 %	3670	0,7 %	10	6	1	6	3	0
41	0,2 %	3837	0,5 %	10	0	5	2	1	0
42	0,3 %	4154	1,0 %	13	10	9	6	3	0
43	0,3 %	4230	0,9 %	10	6	14	3	4	1
44	0,3 %	4250	1,1 %	11	6	13	8	9	1
45	0,4 %	4659	1,3 %	26	8	18	5	5	0
46	0,4 %	4758	2,0 %	36	20	15	16	5	4
47	0,4 %	4765	2,8 %	34	22	44	15	10	8
48	0,5 %	4950	4,0 %	73	29	39	39	9	10
49	0,5 %	5354	4,6 %	93	27	42	56	22	7
50	0,6 %	6221	6,7 %	148	53	52	125	34	3
51	0,7 %	6553	10,0 %	326	67	62	155	41	3
52	1,1 %	3461	13,4 %	241	57	49	87	28	2
1	1,3 %	5059	13,7 %	340	81	87	146	37	4
2	1,2 %	7838	12,1 %	431	106	100	263	48	3
3	1,0 %	7187	12,0 %	356	120	96	251	35	1
4	1,1 %	6690	15,0 %	469	114	55	352	13	0
Total		87636		2627	732	701	1535	307	47
			Type A: 4060			Type B: 1889			

Age distribution of the different viruses

Preliminary age profiles for the different subtypes and lineages generally indicate that the age patterns this season (Figure 10) do not differ from recent seasons (1). Infants are strongly represented among cases with A(H1N1) infection, and persons 60 years and older are strongly represented among cases with A(H3N2) infection, together with infants. Children below 15 are the ones most affected by B/Victoria-lineage viruses. For B/Yamagata-lineage viruses, there is less data. The pattern from previous seasons indicating that the elderly are the most affected group is less apparent now, but this should be interpreted with caution.

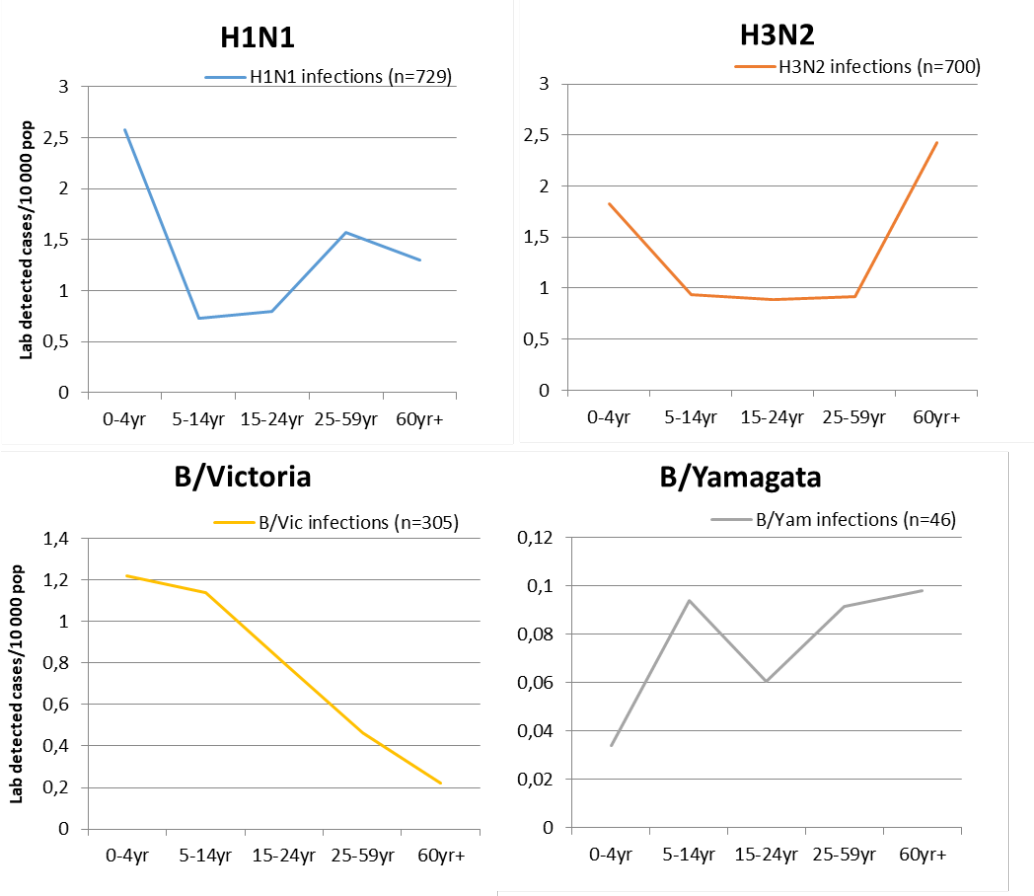


Figure 10. Cumulative incidence per 10 000 population of subtype/lineage detections by age group, based on viruses subtyped in Norwegian laboratories in the 2019/20 influenza season. Since the number of viruses subjected to type, subtype and variant testing differs widely, the incidences are comparable between age groups in the same panel, but incidences are not comparable between the panels.

Genetic characterisation of the viruses in circulation

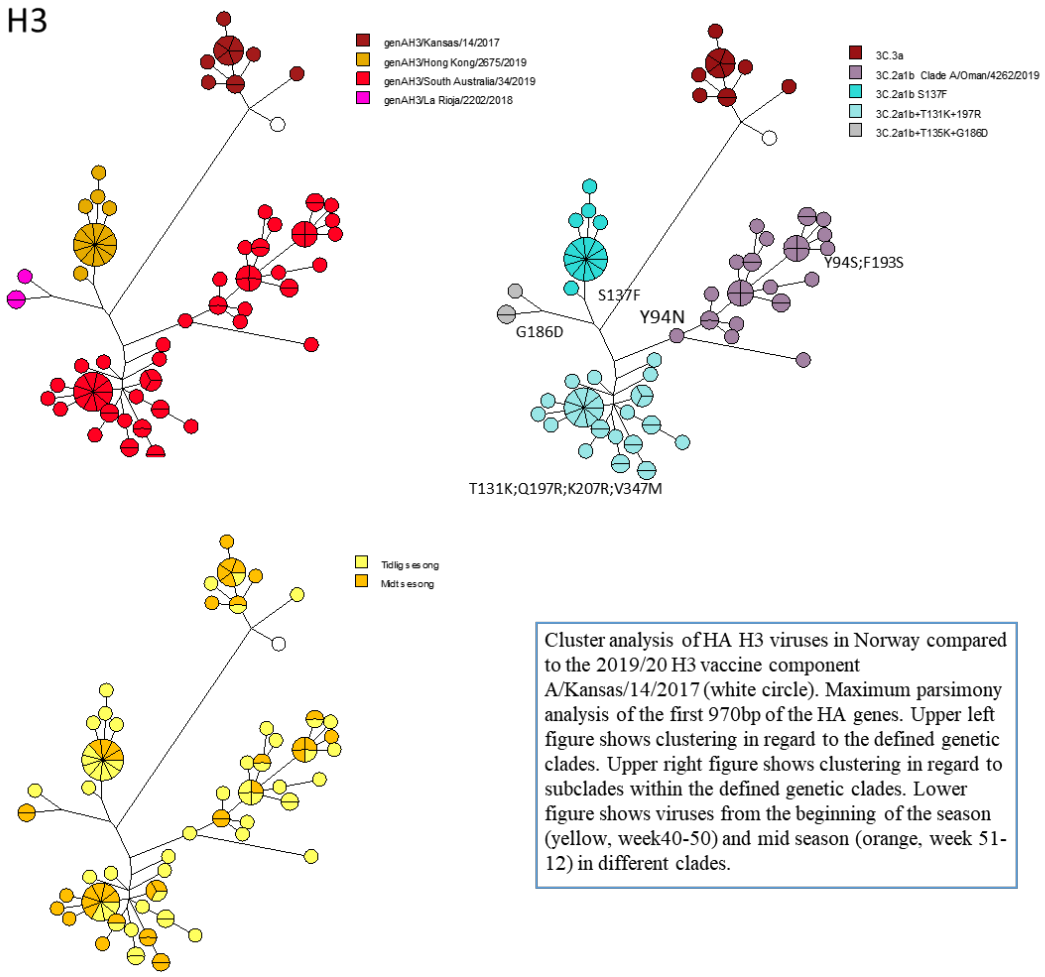
From week 40/2019 to week 4/2020, the influenza laboratory received 2541 influenza positive samples for further analysis. 13.4% (341) of these were further characterised to look at genetic markers for genetic drift and virulence. 15% (382) of the positive samples were tested for antiviral resistance either genetically (247) or by neuraminidase inhibitor susceptibility (134). 133 viruses were shipped to the WHO Collaborative Centre in London (Francis Crick Institute) for further analysis (making up 5% of all positive samples received at NIPH). In addition, 191 HA gene sequences were published in the GISAID (Global Initiative on Sharing All Influenza Data) sequence database (constituting 7.5% of all positive samples at NIPH).

H3N2

The most prevalent influenza H3N2 viruses so far this season have been the 3C.2a1b genetic group, A/South Australia/34/2019-like viruses, with the T131K substitution. The most prevalent subgroups were the H3N2 viruses appearing in Norway during the summer months of 2019, 3C. 2a1b viruses possessing Q197R and K207R in addition in HA and the 3C.2a1b Clade A/Oman/4262/2019 group of viruses possessing Y94N and some

also with Y94S instead, and with F193S. Most of the recent H3 viruses have been in the Q197R+K207R 3C2a.1b group (Figure 11) and although numbers are small, there appears to be a slight excess of people vaccinated yet infected with this subgroup of H3 viruses. A few viruses in the 3C.2a1b+T135K-A group have also possessed the substitution G186D (See also phylogenetic analysis at the end of the report).

We did see a somewhat higher proportion of hospitalised patients infected with the 3C.3a viruses than other subgroups of H3N2 viruses (not shown). The A/Hong Kong/2875/2019-like viruses possessing the S137F substitution caused a small local outbreak in the southern part of Norway early in the season.



Cluster analysis of HA H3 viruses in Norway compared to the 2019/20 H3 vaccine component A/Kansas/14/2017 (white circle). Maximum parsimony analysis of the first 970bp of the HA genes. Upper left figure shows clustering in regard to the defined genetic clades. Upper right 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 51-12) in different clades.

Figure 11. Cluster analysis of the HA gene of influenza A(H3N2) viruses season 2019/20 in Norway, up to week 4 2020.

H1N1

The analysed H1N1 sequences were all characterised as clade 6B.1A A/Brisbane/02/2018-like viruses. The major group of H1 viruses fell in the A/Norway/3433/2018 6B.15A subgroup of viruses and only a small proportion of viruses

belonged to the 6B.1A7 subgroup, mainly viruses from the north of Norway. Some viruses were also seen belonging to the 6B.1A5B subgroup (Figure 12, and phylogeny at the end of the report)

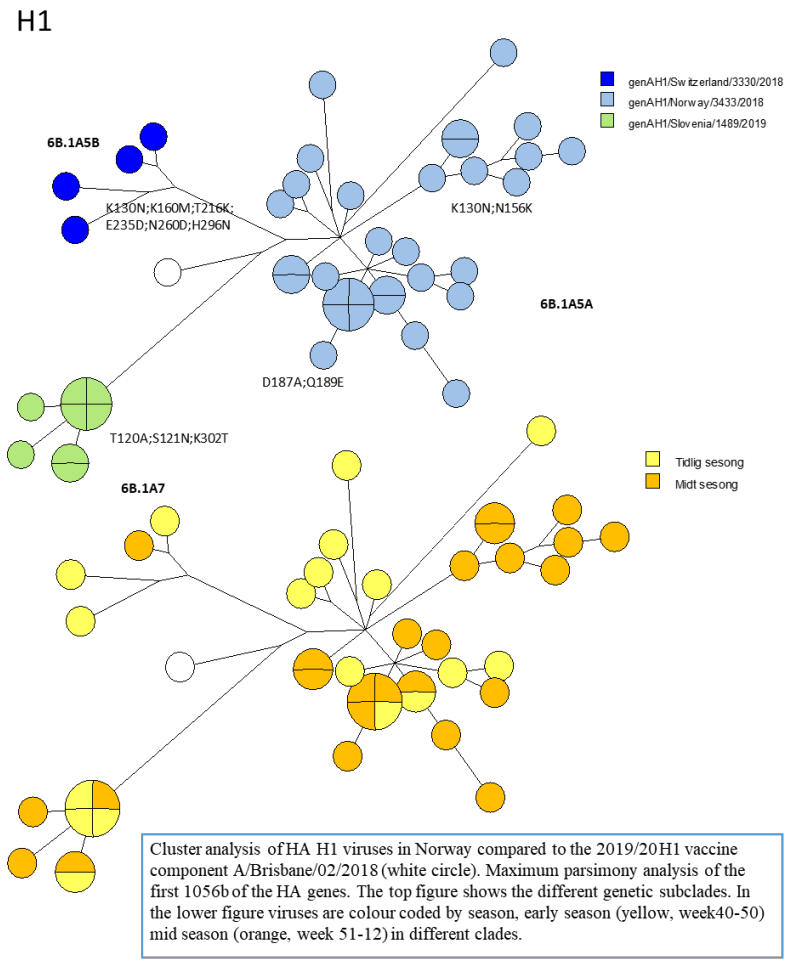
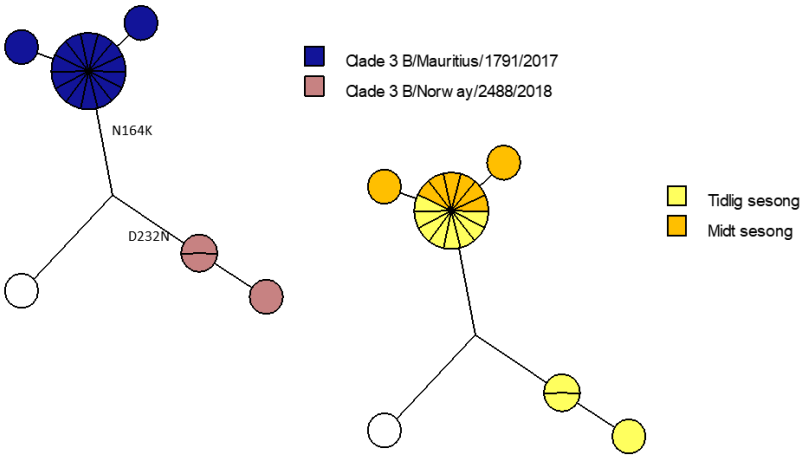


Figure 12. Cluster analysis of the HA gene of influenza A(H1N1)pdm09 viruses season 2019/20 in Norway, up to week 4 2020.

B-Yamagata

Influenza B-Yamagata viruses characterised are all clade 3 viruses with a few amino acid differences. Most of the viruses possessed the N164K substitution. A smaller group of viruses from the beginning of the season possessed D232N (Figure 13).

HA B-Yamagata



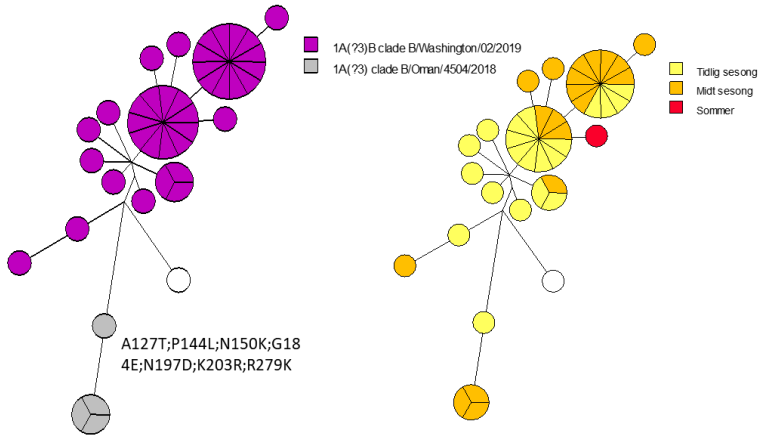
Cluster analysis of HA B-Yamagata viruses in Norway compared to the 2019/20 B-Yamagata vaccine component B/Phuket/3073/2013 (white circle). Maximum parsimony analysis of the first 1010b of the HA genes. The left figure shows the different genetic subclades. In the right figure viruses are colour coded by season, early season (yellow, week40-50) mid season, in different clades.

Figure 13. Cluster analysis of the HA gene of influenza B-Yamagata viruses season 2019/20 in Norway, up to week 4 2020.

B-Victoria

All of the few influenza B-Victoria viruses collected and analysed this season were the triple deletion variant viruses, amino acids 162 to 164 (Δ3), belonging to the clade 1A(Δ3)B subgroup of viruses B/Washington/02/2019. The majority of the viruses possessed the E128K and G133R substitutions in HA. A smaller more recent group of viruses possessed a number of substitutions: A127T;P144L;N150K;G184E;N197D;K203R;R279K. This far, these have only been seen in central Norway (Figure 14)

HA B-Victoria



Cluster analysis of HA B-Victoria viruses in Norway compared to the 2019/20 B-Victoria vaccine component B/Colorado/06/2017 (white circle). Maximum parsimony analysis of the first 1056b of the HA genes. The left figure shows the different genetic subclades. In the right figure viruses are colour coded by season, early season (yellow, week40-50) mid season, in different clades.

Figure 14. Cluster analysis of the HA gene of influenza B-Victoria viruses season 2019/20 in Norway, up to week 4 2020.

Antiviral susceptibility

No resistance towards neuraminidase inhibitors like oseltamivir and zanamivir has so far been detected, out of 134 viruses analysed (Table 2).

Table 2: Resistance to neuraminidase inhibitor drugs

pr. 29/01-20	Oseltamivir (Tamiflu®)		Zanamivir (Relenza®)	
Virus	Tested	Oseltamivir-resistant virus	Tested	Zanamivir-resistant virus
H3	45	0 / (0 %)	45	0 / (0 %)
B	21	0 / (0 %)	21	0 / (0 %)
H1	68	0 / (0 %)	14	0 / (0 %)
Resistance to oseltamivir and zanamivir detected either by sequence analysis or by neuraminidase susceptibility assay				

Vaccine distribution and coverage

A total of 1 019 276 influenza vaccine doses have been distributed so far this season; 812 190 of these were specifically meant for persons in medical risk groups and health care personnel involved in direct patient care. The number of distributed doses has increased by 14 % since last season (Figure 15).

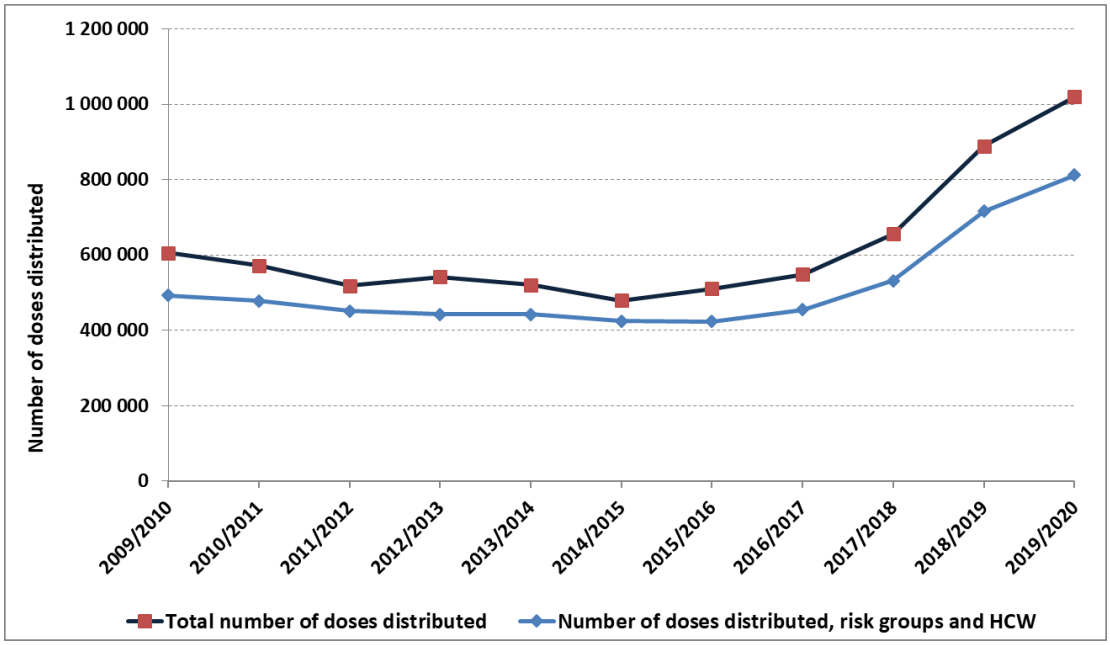


Figure 15: Influenza vaccine doses (seasonal) distributed in Norway, 2008 through 4th of February 2020. HCW = Health Care Workers.

Estimates of vaccine coverage in the various risk groups in the current season will not be available until October 2020.

Population immunity against recent influenza viruses, August 2019

In August each year, the National Influenza Seroepidemiology Programme solicits approximately 2000 anonymised convenience sera from clinical/microbiological laboratories across Norway. The sera, aimed to be representative of the Norwegian population geographically and by age composition, are tested by the haemagglutination-inhibition (HI) test to determine the antibody immunity against relevant circulating influenza viruses. As an austerity measure, only a subset of 1054 sera were analysed this time. The main findings are shown in figure 16, table 3, and summarised as follows:

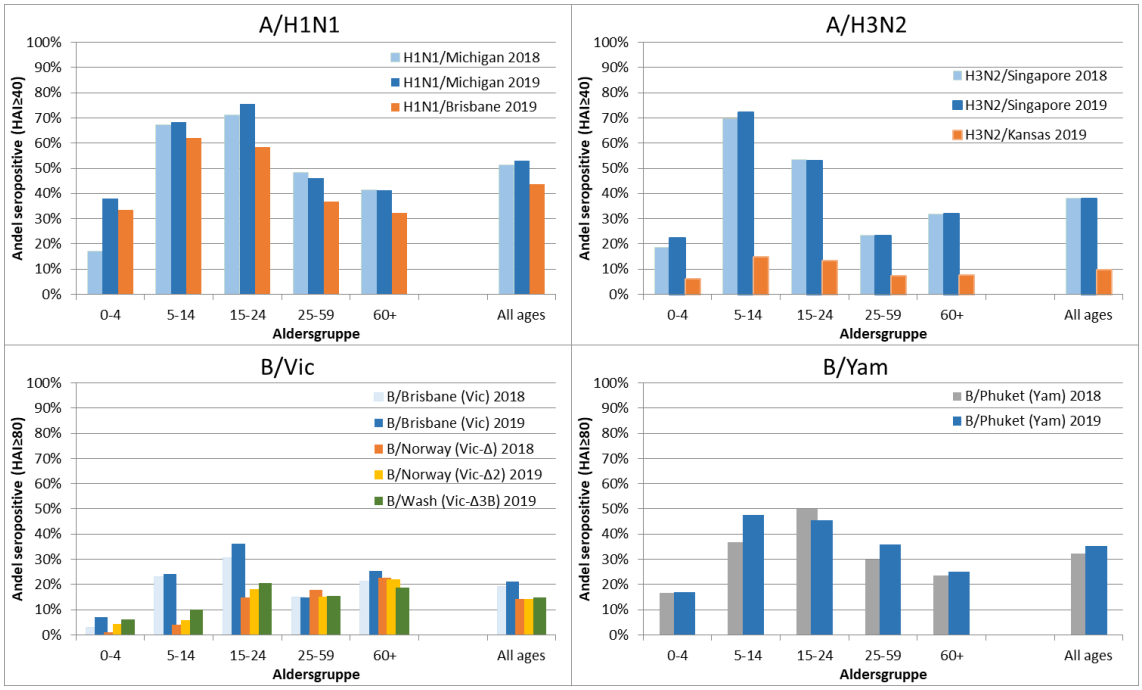


Fig 15. Seroprevalence in August 2019 to current influenza A and B reference and vaccine strains for 'All ages' and in various age groups. For comparison, seroprevalences to some virus strains in August 2018 are also shown. Michigan= A/Michigan/45/2015 (H1N1)pdm09 clade 6B.1; H1N1/Brisbane= A/Brisbane/02/2018 (H1N1)pdm09 clade 6B.1A1; Singapore= A/Singapore/INFIMH-16-0019/2016 (H3N2) clade 3C.2a1 ; Kansas= A/Kansas/14/2017 (H3N2) clade 3C.3a; B/Brisbane= B/Brisbane/60/2008 (Victoria lineage); B/Norway= B/Norway/2409/2017 (Victoria lineage, amino acid 162-163 deletion variant); B/Wash=B/Washington/02/2019 (Victoria lineage, amino acid 162-164B deletion variant); B/Phuket= B/Phuket/3073/2013 (Yamagata lineage).

For A(H1N1) viruses, the comparatively strong population immunity that has been accumulated in recent years had been maintained in most age groups. There was a marked increase since 2018 in the proportion of people with protective antibody levels (seroprevalence) in the youngest age group in which many individuals would have experienced their first A(H1N1) exposure last winter. Seroprevalence against the more recent subclade 6B.1A1 A/Brisbane/02/2018 variant was slightly lower than against the clade 6B.1 virus A/Michigan/45/2015.

For A(H3N2) viruses, the seroprevalence against clade 3C.3a viruses observed in 2017 and 2018 was essentially maintained. The seroprevalence was quite high in the 5-24 year olds. Perhaps importantly, our data appear to indicate that population immunity against recent

clade 3C.3a viruses, represented by the current vaccine virus A/Kansas/14/2017, is very poor (10% seroprevalence overall). If this is so, the current vaccine virus is well placed to address a significant vulnerability in the population immunity.

The seroprevalence against B/Victoria-lineage viruses remained low with overall seroprevalence of 21 % against the previous B/Victoria vaccine component B/Brisbane/60/2008. Interestingly, in most age groups there was little difference in seroprevalence against the mother variant B/Brisbane/60/2008, and against the two newly emerged deletion variants, represented by B/Norway/2409/2017 (1A(Δ2) group) and the current vaccine virus B Washington/02/2019 (1A(Δ3)B group). The exception was for those between 5 and 25 years old, where seroprevalence against B/Brisbane/60/2008 was markedly higher. The seroprevalences differed little between the 1A(Δ2) group and 1A(Δ3)B groups, and individual sera tended to have similar titres against the two antigens (data not shown).

For the B/Yamagata-lineage viruses, represented by the vaccine virus for tetravalent vaccines, B/Phuket/3070/2013, the seroprevalence changed little from 2018. Overall seroprevalence was 35%, with highest proportions in the 5-24 year olds.

Table 3. Influenza seroepidemiology results in August 2019 - Comparison between age groups.
For comparison data from studies performed for the preceding years 2015-2018 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 (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
H1 Michigan/45/15 (2018)	17	67	71	58	48	41	51
H1 Michigan/45/15 (2019)	***38***	***68***	***75***	***64***	***46***	***41***	***53***
H1 Brisbane/02/18 (2019)*	***34***	***62***	***58***	***54***	***37***	***32***	***44***
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
H3 Hong Kong/5738/14 (2018)	25	78	72	63	36	43	50
H3 Sing/INFIMH-16-19/2016 (2018)	19	70	54	52	23	32	38
H3 Switzerland/8060/17(2018)	25	71	47	51	29	34	40
H3 Sing/INFIMH-16-19/2016 (2019)	***22***	***72***	***53***	***53***	***27***	***34***	***40***
H3 Kansas/14/17 (2019)*	***6***	***15***	***13***	***12***	***7***	***8***	***10***
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/Vic Brisbane/60/08 (2018)	3	23	31	22	15	21	19
B/VicΔ2 Norway/2409/17 (2018)	1	4	15	7	18	23	14
B/Vic Brisbane/60/08 (2019)	***7***	***24***	***36***	***24***	***15***	***25***	***21***
B/VicΔ2 Norway/2409/17 (2019)	***4***	***6***	***18***	***10***	***15***	***22***	***14***
B/VicΔ3B Wash/02/19 (2019)*	***6***	***10***	***20***	***13***	***15***	***19***	***15***
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
B/Yam Phuket/3073/13 (2018)	17	37	50	38	30	24	32
B/Yam Phuket/3073/13 (2019)*	***17***	***48***	***46***	***39***	***36***	***25***	***35***
Sera analysed (n): 2015 Aug	178	353	363	894	788	409	2091
Sera analysed (n): 2016 Aug	188	351	333	874	745	411	2028
Sera analysed (n): 2017 Aug	189	318	353	860	797	436	2093
Sera analysed (n): 2018 Aug	155	251	236	642	501	275	1418
Sera analysed (n): 2019 Aug	**113**	**187**	**171**	**471**	**375**	**208**	**1054**

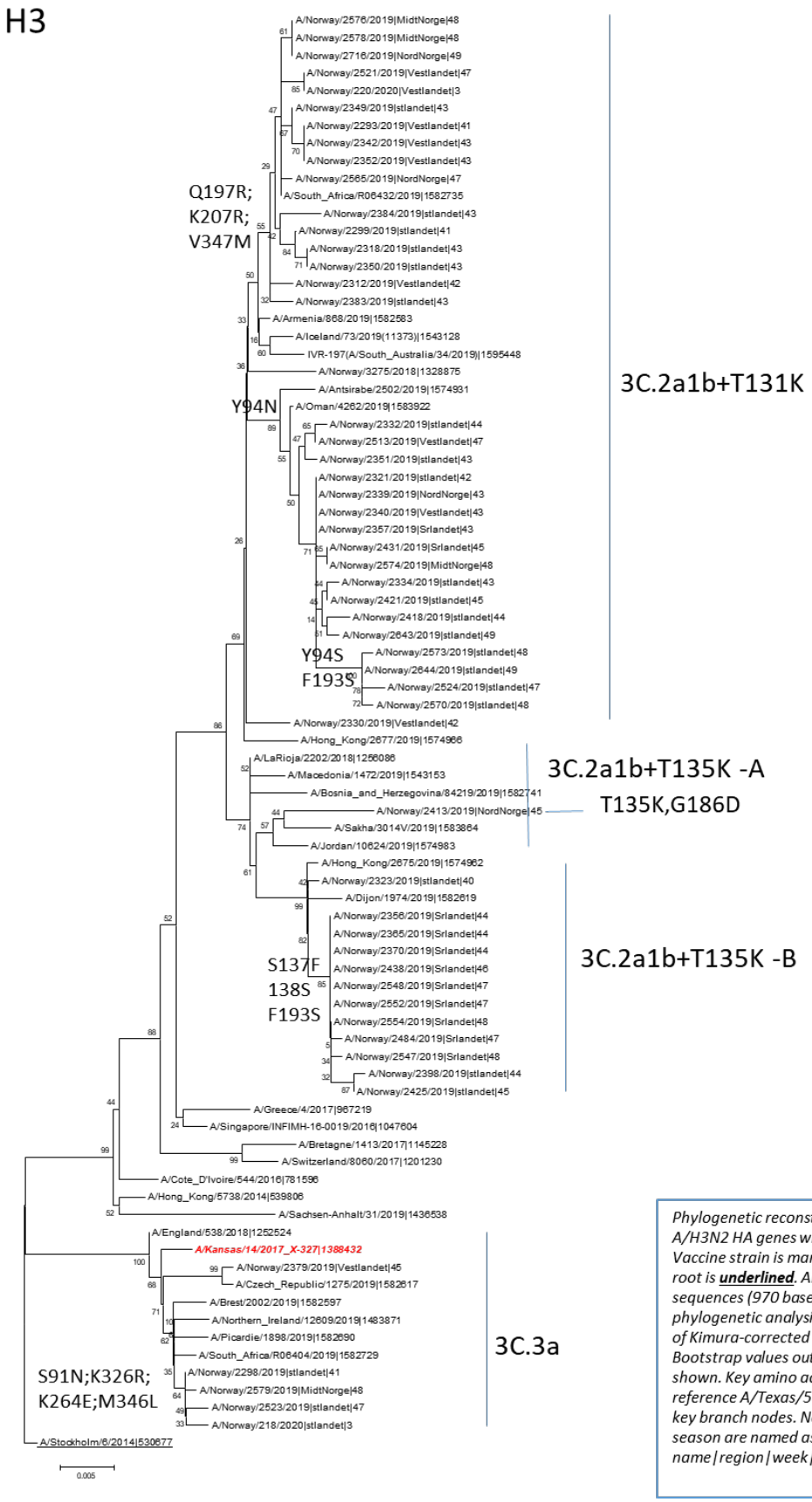
[$]Year of serum collection and HI analysis.

*All entries are per cent of sera having HI titres ≥ 40 for the A strains and ≥ 80 for the ether-treated B strains.

**(Corresponding to) components of the Northern hemisphere influenza vaccine (trivalent/quadrivalent) for the season 2019-2020.

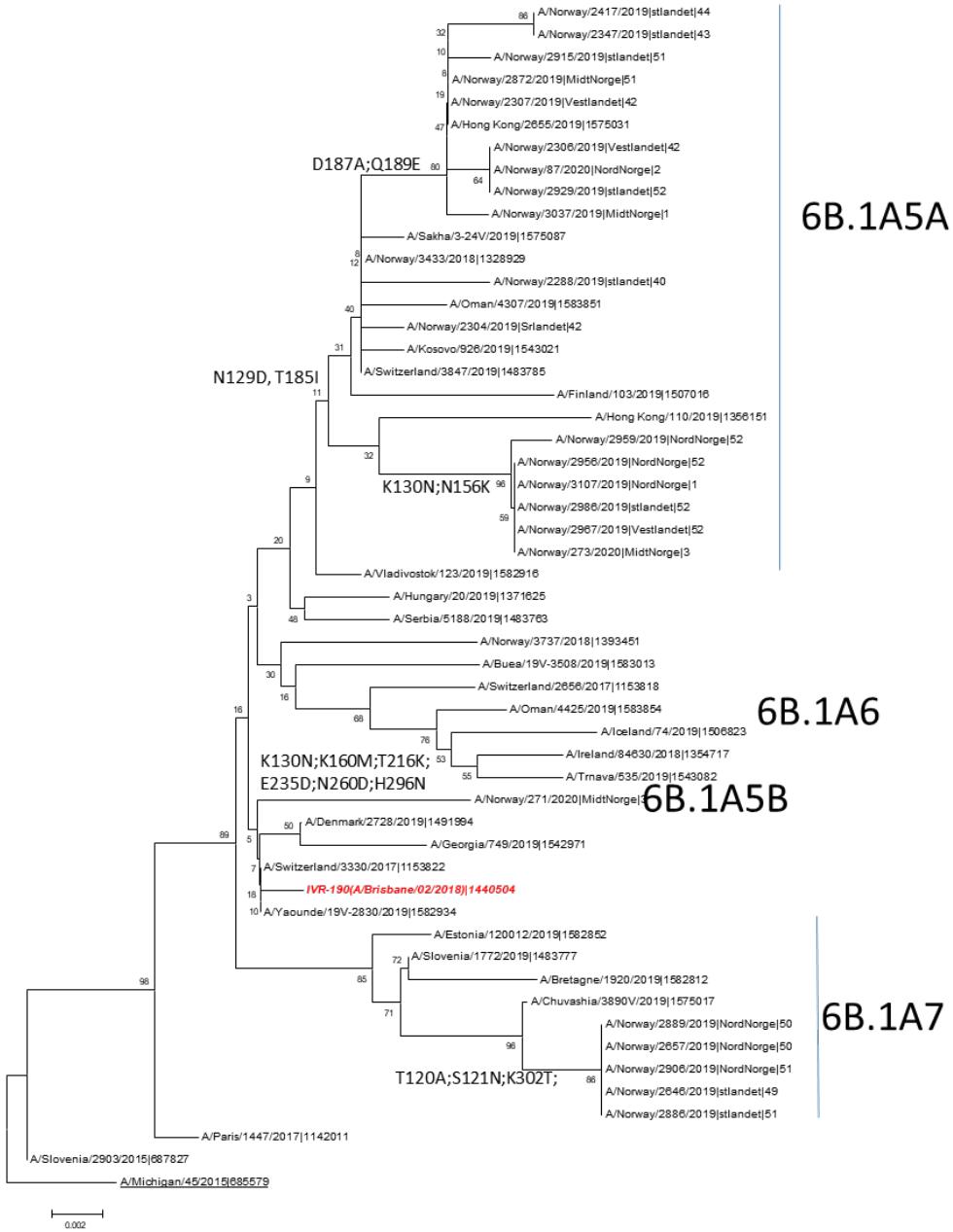
B/Yam: B/Yamagata/16/1988 lineage; **B/Vic**: B/Victoria/2/1987 lineage

Phylogeny



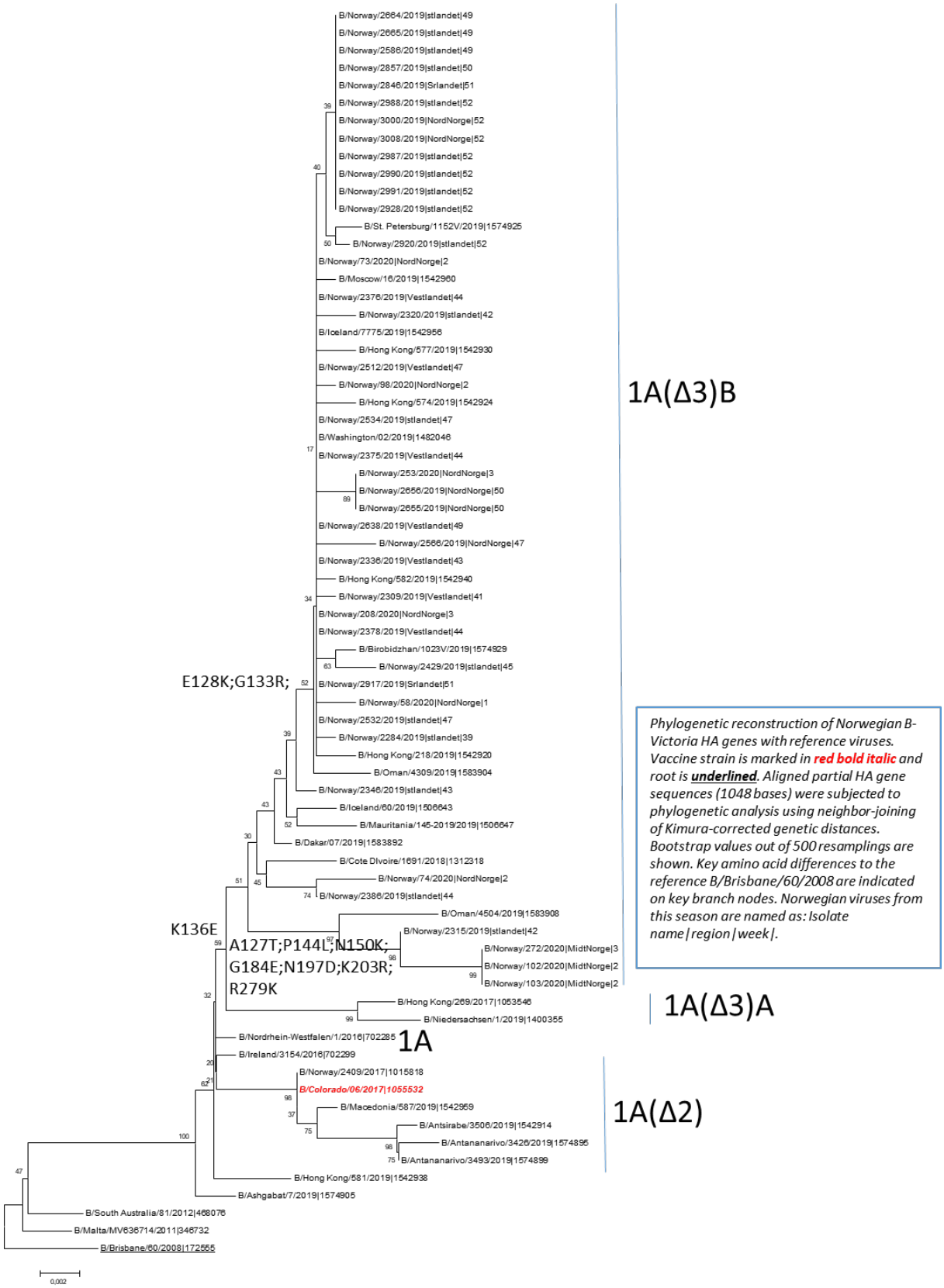
*Phylogenetic reconstruction of Norwegian A/H3N2 HA genes with reference viruses. Vaccine strain is marked in **red bold italic** and root is **underlined**. Aligned partial HA gene sequences (970 bases) were subjected to phylogenetic analysis using neighbor-joining of Kimura-corrected genetic distances. Bootstrap values out of 500 resamplings are shown. Key amino acid differences to the reference A/Texas/50/2012 are indicated on key branch nodes. Norwegian viruses from this season are named as: Isolate name|region|week|.*

H1



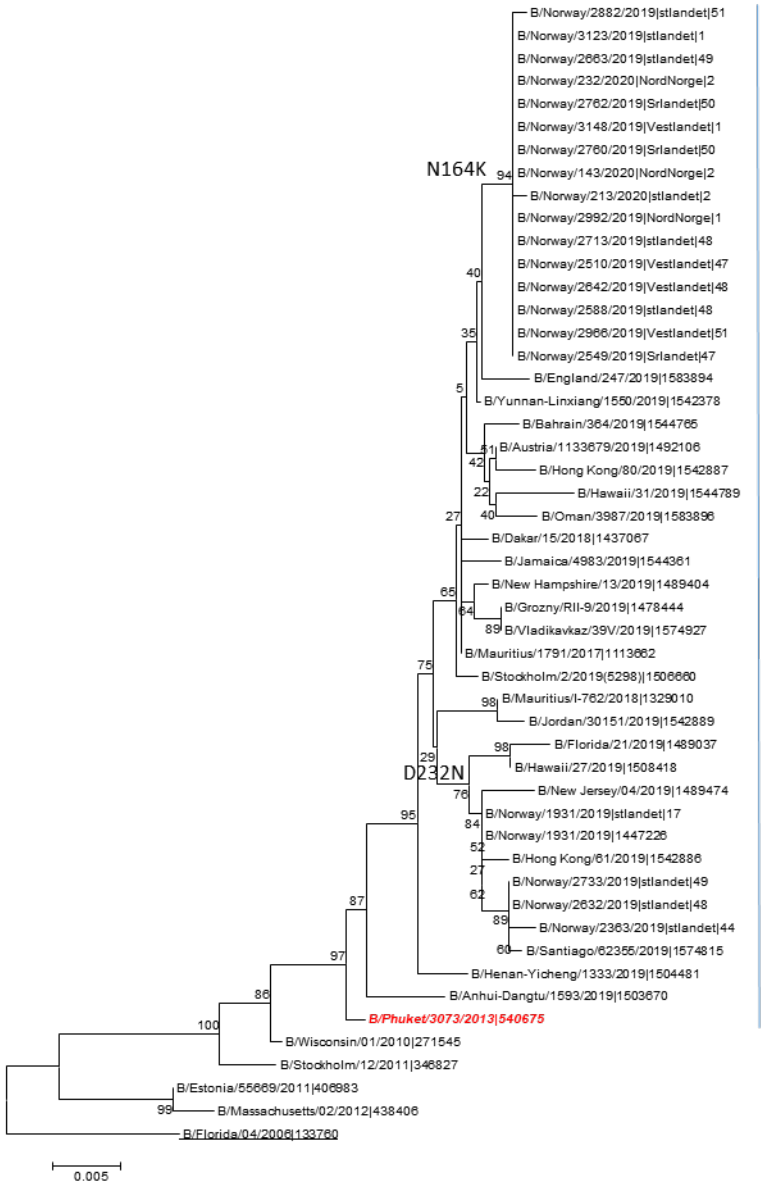
*Phylogenetic reconstruction of Norwegian A/H1N1 HA genes with reference viruses. Vaccine strain is marked in **red bold italic** and root is **underlined**. Aligned partial HA gene sequences (1056 bases) were subjected to phylogenetic analysis using neighbor-joining of Kimura-corrected genetic distances. Bootstrap values out of 500 resamplings are shown. Key amino acid differences to the reference A/Michigan/45/2015 are indicated on key branch nodes. Norwegian viruses from this season are named as: Isolate name|region|week|.*

HA B-Victoria



*Phylogenetic reconstruction of Norwegian B-Victoria HA genes with reference viruses. Vaccine strain is marked in **red bold italic** and root is **underlined**. Aligned partial HA gene sequences (1048 bases) were subjected to phylogenetic analysis using neighbor-joining of Kimura-corrected genetic distances. Bootstrap values out of 500 resamplings are shown. Key amino acid differences to the reference B/Brisbane/60/2008 are indicated on key branch nodes. Norwegian viruses from this season are named as: Isolate name|region|week|.*

HA B-Yamagata



3

*Phylogenetic reconstruction of Norwegian B-Yamagata HA genes with reference viruses. 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 out of 500 resamplings are shown. Key amino acid differences to the reference B/Phuket/3073/2013 are indicated on key branch nodes. Norwegian viruses from this season are named as: Isolate name|region|week|.*

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1 Bragstad K, Paulsen TH, Tønnessen R, Klüwer B, Rydland KM, Hungnes O. "Norway National Influenza Centre – Influenza Virological and Epidemiological Information prepared for the WHO Consultation on the Composition of Influenza Virus Vaccines for the Southern Hemisphere 2020., September 2019 ". Report 2019. Oslo: Norwegian Institute of Public Health, 2019. https://www.fhi.no/publ/2019/influenza-virological-and-epidemiological-information-prepared-for-the-who-/

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With best regards,

Karoline Bragstad, Trine Hessevik Paulsen, Ragnhild Tønnessen, Birgitte Klüwer, Kjersti Rydland, and Olav Hungnes

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6 February 2020

Appendices

Methods

Influenza-like illness

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.

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, according to virus type/subtype, detection method and patient age group. These laboratories also contribute influenza positive specimens to the NIC for further characterisation. Even though most of these laboratories are affiliated to hospitals, a large proportion of specimens tested for influenza virus are from outpatients visiting general practitioners.

Surveillance of laboratory-confirmed influenza in hospitalised patients

As an extension to the basic weekly reporting of influenza diagnostic testing outcomes, nine medical microbiology laboratories stratify their report into hospitalised patients and outpatients. Together, these laboratories cover approximately 68% of the Norwegian population, and report each week the number of influenza virus detections in hospitalised patients (all wards) as well as outpatients according to influenza type (A, B) and age group. This extended reporting constitutes the basis for the surveillance of laboratory confirmed influenza in hospitalised patients. This is the seventh year this surveillance system is in operation.

Influenza patients in intensive care units

In the 2016-17 and 2017-18 seasons, the Norwegian Intensive Care Registry (NICR) and NIPH carried out a pilot study to see whether national surveillance of influenza patients in intensive care units is feasible. As part of the pilot, NICR asked all ICUs from week 46/2017 to report weekly numbers 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. Almost all ICUs in Norway reported data to NICR. Since the 2018-19 season, an electronic form has been used. Currently, only anonymised data are reported from NICR to the NIPH.

Mortality monitoring

The Norwegian Mortality Monitoring system (NorMOMO) is used for weekly monitoring of all-cause mortality. The system has been in operation since 2015 and it is based on the algorithm developed by the EuroMOMO network.

Influenza seroepidemiology

The National Influenza Seroepidemiology Programme annually in August solicits about 2000 serum samples collected during the weeks 31-35 from clinical/microbiological laboratories covering the 19 counties of Norway. These anonymised convenience sera are aimed to be representative of the Norwegian population geographically and by age composition. The sera are tested by the haemagglutination-inhibition (HI) test to determine the antibody immunity to relevant circulating influenza viruses. HI titres ≥40 against the influenza A strains and ≥80 against ether-treated influenza B strains are considered as protective levels and recorded as seropositive in the analysis.

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