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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 2019–2020 Beijing, February 2019

**NORWAY: National Influenza Centre**

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Division of Infection Control and Environmental Health;

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# Content

# The 2018-2019 influenza season, Norway

## Summary


- Seroepidemiology data from August 2018 indicate that immunity in Norway against circulating influenza A(H1N1) and A(H3N2) viruses is quite strong. Also for the B/Yamagata-lineage virus that caused last winter's influenza outbreak, there was a marked increase in people with antibody at protective levels.
- Added to this comes the immunity due to the subsequent influenza vaccination campaign in the autumn. Rates of vaccination were raised considerably this year.
- The influenza activity crossed the outbreak threshold during Christmas (week 52/2018) after showing a stagnating trend in the first weeks of the year it was again increasing in week 4/2019. The level of influenza activity at that point remained low.
- In week 4, the number of hospitalisations and ICU admissions was increasing, but the number of admissions was lower compared to the two previous seasons. The highest hospitalisation rates were found in young children (0-4 years) followed by the elderly (60 years or older). So far the hospitalisation rate in young children is similar to the rates observed in 2015-16 and 2017-18. There are fewer hospitalised elderly so far this season compared with the previous two seasons.
- No excess all-cause mortality has been observed.
- Influenza A(H1N1) virus predominates, constituting approximately 75% of detections. The remainder is A(H3N2) virus, with unusually few (<2%) influenza B virus, with B/Yamagata lineage more common than B/Victoria.
- As in earlier A(H1N1)pdm09 dominated seasons, a high proportion of cases are children.
- Two genetically different groups of influenza A(H1N1)pdm09 viruses circulates in Norway, both are assigned to the H1 6B.1 clade.
- Most H3N2 viruses belonged to the 3C.2a1b clade, but separated into two subgroups.
- Only three influenza B-Victoria viruses have been detected so far, the two that have been characterised both were triple deletion variants, but genetically different from each other.
- All influenza B-Yamagata viruses were clade 3 viruses.

## A look back at the previous season

The previous influenza outbreak of 2017/18 started in mid-December and lasted for an unusually long period. Although intensity, measured as weekly incidence of ILI, only reached medium level, the cumulative magnitude was larger than in the preceding seasons. The outbreak was dominated by influenza B Yamagata-lineage viruses, antigenically similar to the reference/vaccine virus B/Phuket/3073/2013. A lower number of influenza A(H3N2) (clade 3C.2a2 in majority) circulated at the same time. By week 12/2018, influenza B cases had decreased significantly, while influenza A(H3N2) persisted longer and was predominant until the end of the season. The older segments of the population accounted for a high proportion of both the B/Yamagata and A(H3N2) cases. A significantly larger number was hospitalised with influenza that season compared to the preceding three seasons due to the protracted outbreak. Excess mortality was observed in the elderly during several weeks.

Despite very few cases of influenza B/Victoria-lineage infection that season, the novel two-amino acid HA deletion variant represented a larger proportion than in the preceding 2016/17 season, and increased during the outbreak. The moderate number of H1N1 viruses that circulated belonged to subclade 6B.1.

The last time influenza A(H1N1)pdm09 viruses predominated was in the 2015/16 season.

# The 2018/19 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 MEM-levels) in week 52. From week 52 throughout week 4 the ILI-rates showed only a small cumulative increase of 0.3 % (Figure 1).

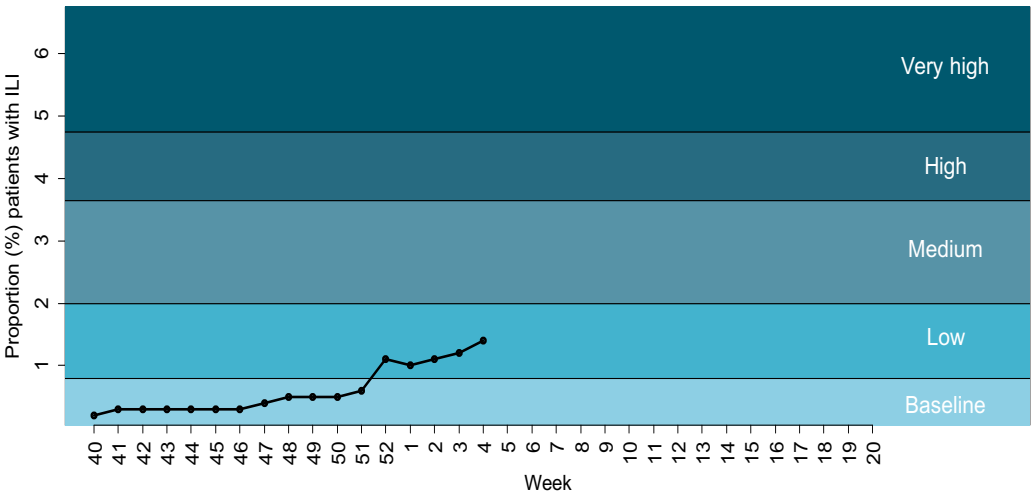



**Figure 1: Level of influenza intensity (by present-season MEM intensity thresholds) depicted as weekly proportion of patients in general practice and emergency clinics presenting with ILI, Norway 2018-2019 season**

We suspect the epidemic curve has not yet peaked, based on historical data (Figure 2). Earlier seasons with a similar development have reached the peak in late February or March.

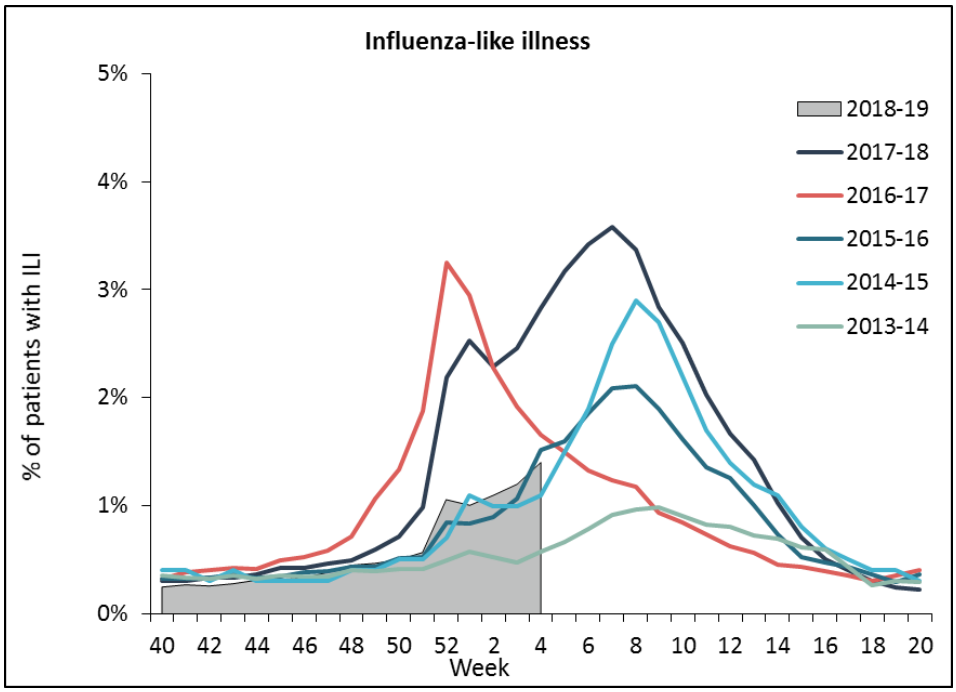



**Figure 2: Weekly incidence of ILI, Norway 2018-2019 season (grey). The graph shows the proportion of patients in general practice and emergency clinics presenting with ILI, by calendar week. The five previous seasons are also shown.**

## Severe influenza: laboratory confirmed hospitalised cases

The number of laboratory confirmed influenza cases among hospitalised patients began to increase in week 49, reached a temporary peak in week 1 and started to increase again in week 3 (Figure 3). In week 4, the total number of hospitalised patients was lower than it was at the same time during the two preceding seasons and comparable to those of the 2014-15 and 2015-16 seasons (Figure 4[1].) 99% of the detections have been Influenza A. The highest weekly incidence rates were found in young children (0-4 years), followed by the elderly (60 years or older) (Figure 3). So far, the cumulative incidence rate in young children has been similar to that of 2015-16 and 2017-18. In the elderly, the rate has been much lower than the rates from the two previous seasons.

[1] 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.

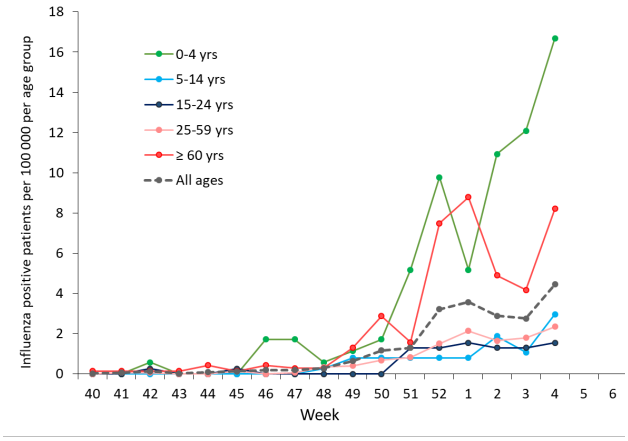



**Figure 3: The estimated incidence of positive influenza samples in the different age groups of hospitalised patients per week, until week 4 of the 2018/2019 influenza season. The estimation is based on reports from nine sentinel medical microbiology laboratories.**

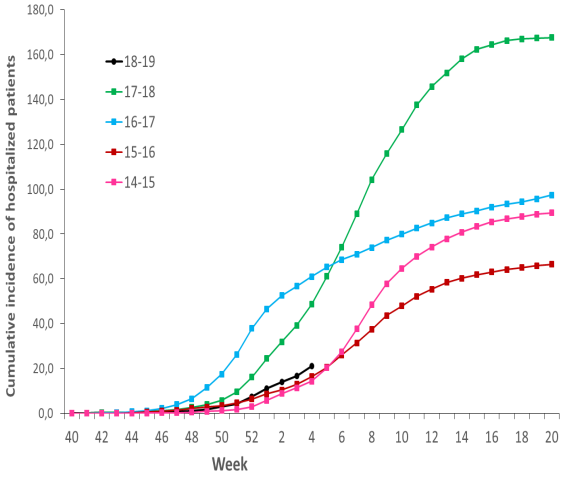



**Figure 4: Estimated cumulative incidence of hospitalised patients with confirmed influenza per week compared to the previous four influenza seasons.**

## Influenza patients in intensive care units

So far in the influenza season, the number of patients with laboratory confirmed influenza admitted to ICUs has been lower than in the previous two seasons (Figure 5).

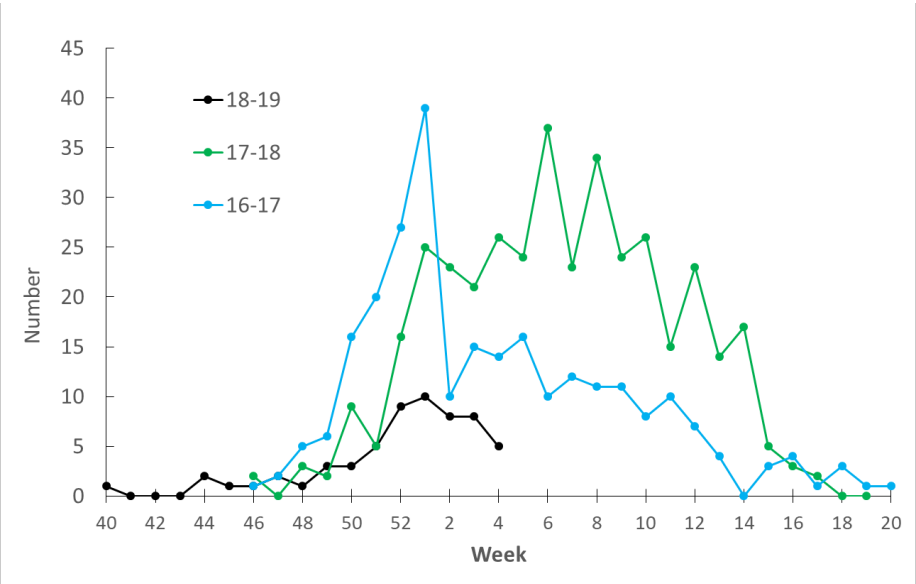



**Figure 5. The number of patients admitted to ICUs during the current and previous two influenza seasons. Data source: The Norwegian Intensive Care Registry (NICR). The number for week 4 is likely to be incomplete.**

## Excess all-cause mortality

With a few exceptions, from week 40 2018 to week 4 2019, the all-cause mortality was within expected levels.

## Laboratory confirmed influenza: Virological surveillance

Altogether, 82885 patients in Norway have been tested for influenza during weeks 40/2018-4/2019, resulting in 5430 detections of influenza A and 77 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 49 – 52/2018. After this, there was some stagnation during the first weeks of January, after which the increase has resumed in weeks 3 and 4/2019. Weekly totals and proportions of influenza positives are now at an intermediate level (Figure 6). Historically, seasons with a corresponding development of proportion positives have had outbreaks peaking in late February or March (e.g., 2011/2012; 2014/2015; 2015/2016).

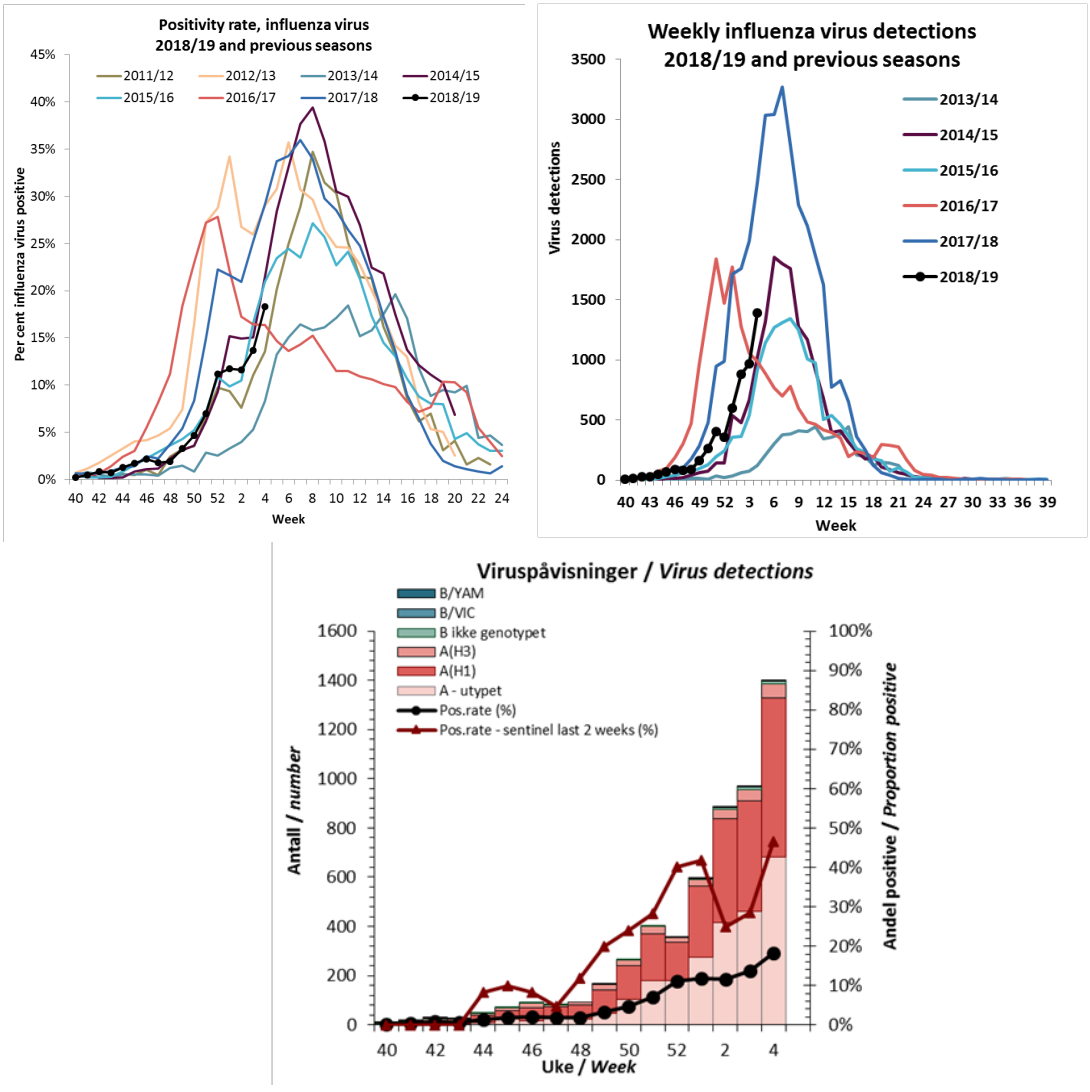



**Figure 6: Laboratory detections, Norway 2018-2019. Upper left-hand panel: Weekly proportion of influenza virus positive specimens, with previous season proportions shown for comparison. Upper right-hand panel: Weekly number of influenza virus detections, with previous season numbers shown for comparison. 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 proportion of type B viruses is unusually low. During the first few weeks, there was a slight majority of A(H3N2) viruses. This has, however, increasingly shifted toward A(H1N1) predominance(Figure 7, 8).

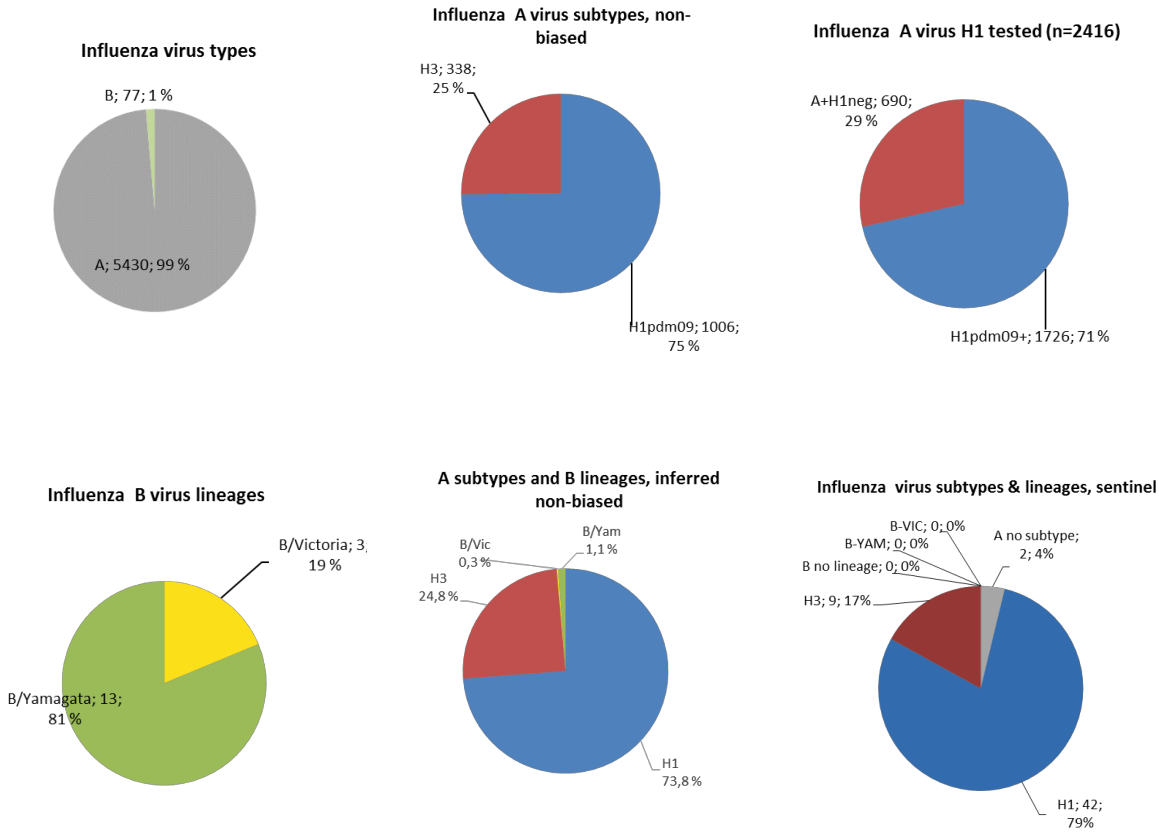



**Figure 7. Proportions of 2018/19 season influenza virus subtypes and lineages among viruses analysed in Norway, by 19th December 2018. All-laboratories proportions of A/B type, A subtypes and B lineages are shown in the first four diagrams. The subtype and lineage frequencies are superimposed on type distributions in the lower middle 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. A similar proportion is obtained through an alternative approach that uses data from a higher number of laboratories that test all A positives for H1 but not H3, shown in the top-right diagram, where A positives testing negative for H1 serve as a proxy for H3. The sentinel data are not subtype biased in this way but the numbers are more limited at this point.**

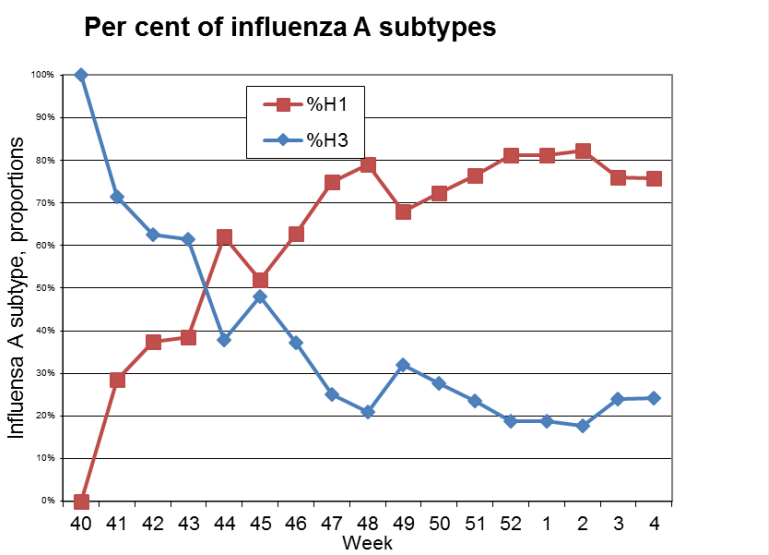



**Figure 8. Weekly proportions of subtype H1 and H3, respectively, among influenza A viruses that have been tested for both H1 and H3.**

The A(H1N1)pdm09 predominance represents a continuation of a pattern of H1N1 predominance every third season since the virus emerged with the 2009 pandemic (Figure 9). In addition to these 3-year-interval major H1N1pdm09 outbreaks, this virus also predominated during the 2013-14 season but that was a very small outbreak (cf. Fig 6), with little expected impact on population immunity.

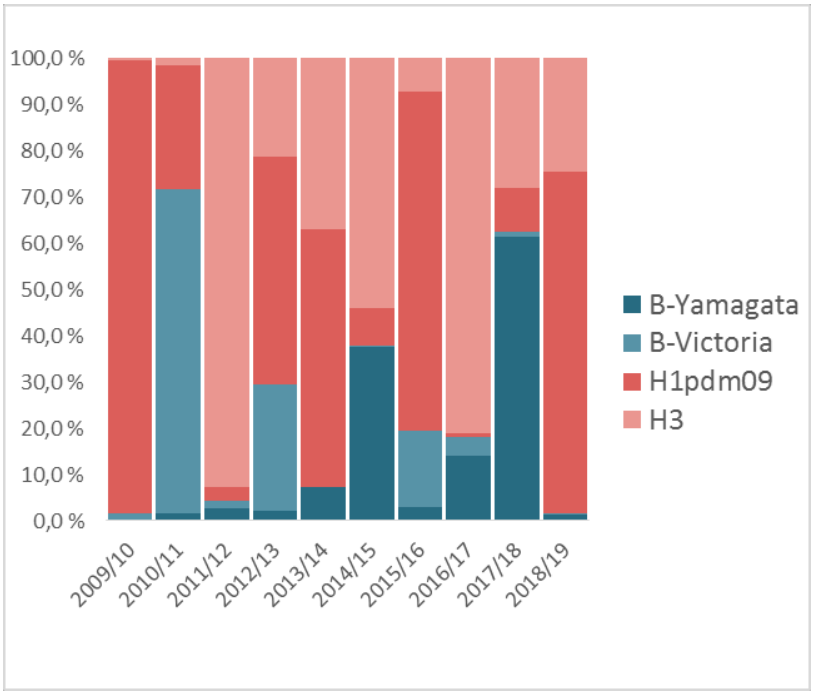



Figure 9: Predominance of influenza viruses in Norway, seasons 2009 to2019. Proportions of influenza A subtypes and B lineages were superimposed on type A and B proportions, as described for figure 7.

**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 40/2018 through week 4/2019.**

| | | Virus detections | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| week | % ILI | Specimens | % positive | A not subtyped | A(H1) pdm09 | A(H3) | B not lineage typed | B/ Victoria lineage | B/ Yamagata lineage |
| 40 | 0.2 % | 3459 | 0,2 % | 0 | 0 | 4 | 3 | 0 | 1 |
| 41 | 0.3 % | 3465 | 0,5 % | 4 | 5 | 5 | 2 | 0 | 1 |
| 42 | 0.3 % | 3531 | 0,8 % | 3 | 11 | 10 | 4 | 0 | 2 |
| 43 | 0.3 % | 3698 | 0,7 % | 5 | 12 | 8 | 0 | 0 | 2 |
| 44 | 0.3 % | 3852 | 1,3 % | 8 | 29 | 11 | 2 | 0 | 0 |
| 45 | 0.3 % | 4140 | 1,7 % | 23 | 34 | 12 | 2 | 0 | 0 |
| 46 | 0.3 % | 4312 | 2,1 % | 16 | 55 | 19 | 2 | 0 | 0 |
| 47 | 0.4 % | 4541 | 1,8 % | 35 | 39 | 6 | 2 | 0 | 0 |
| 48 | 0.4 % | 4832 | 1,9 % | 22 | 60 | 9 | 0 | 0 | 0 |
| 49 | 0.5 % | 5015 | 3,3 % | 48 | 93 | 23 | 1 | 1 | 0 |
| 50 | 0.5 % | 5636 | 4,7 % | 104 | 137 | 21 | 2 | 0 | 0 |
| 51 | 0.6 % | 5804 | 7,0 % | 180 | 191 | 28 | 6 | 0 | 0 |
| 52 | 1.0 % | 3178 | 11,2 % | 181 | 155 | 18 | 0 | 1 | 1 |
| 1 | 1.0 % | 5081 | 11,7 % | 275 | 288 | 27 | 5 | 0 | 2 |
| 2 | 1.1 % | 7615 | 11,6 % | 415 | 423 | 37 | 8 | 0 | 1 |
| 3 | 1.2 % | 7093 | 13,7 % | 461 | 450 | 45 | 11 | 0 | 2 |
| 4 | 1.4 % | 7633 | 18,3 % | 683 | 647 | 55 | 11 | 1 | 1 |
| Total | Total | 82885 | | 2463 | 2629 | 338 | 61 | 3 | 13 |
| | | | Type A: | 5430 | | Type B: | 77 | | |

## Age distribution of the different viruses

Preliminary age profiles for the A(H1N1) and A(H3N2) viruses 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. Age profiles for influenza B/Yamagata and B/Victoria are not available due to the very low number of viruses analysed.

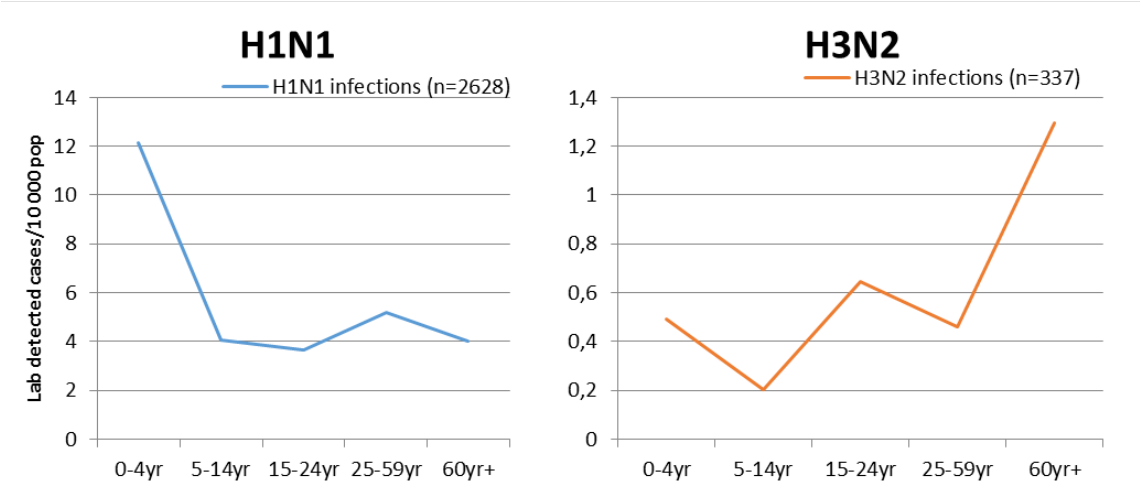



**Figure 10. Cumulative incidence per 10 000 population of subtype/lineage detections by age group, based on viruses subtyped in Norwegian laboratories in the 2018/19 influenza season. Since the number of viruses subjected to type, subtype and variant testing differs widely, the incidences are comparable between age groups in the same panel, but incidences are not comparable between the panels.**

## Monthly reported non-influenza respiratory viruses

Human metapneumovirus and RSV were major causes of respiratory illness in the Norwegian population during the first months of 2018. From June to November, Rhinoviruses were prevalent. It is noteworthy that *Chlamydophila pneumoniae* was detected in higher numbers than usual in the autumn and winter months, whereas *Mycoplasma pneumoniae* was detected in smaller numbers than in the previous two years (Figure 11).

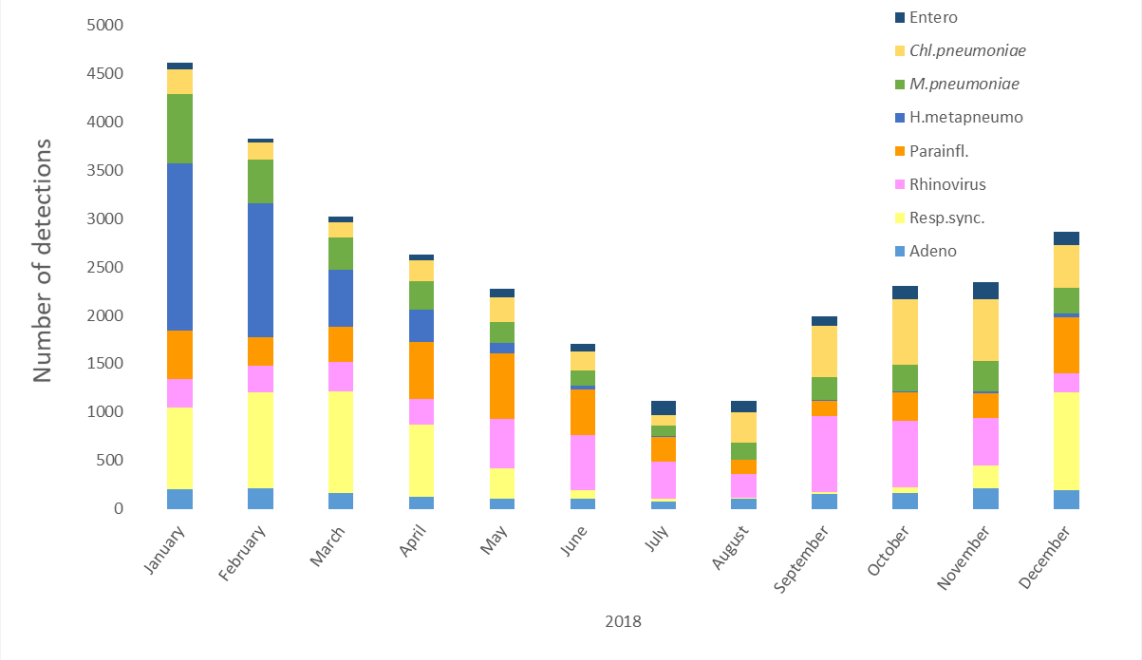
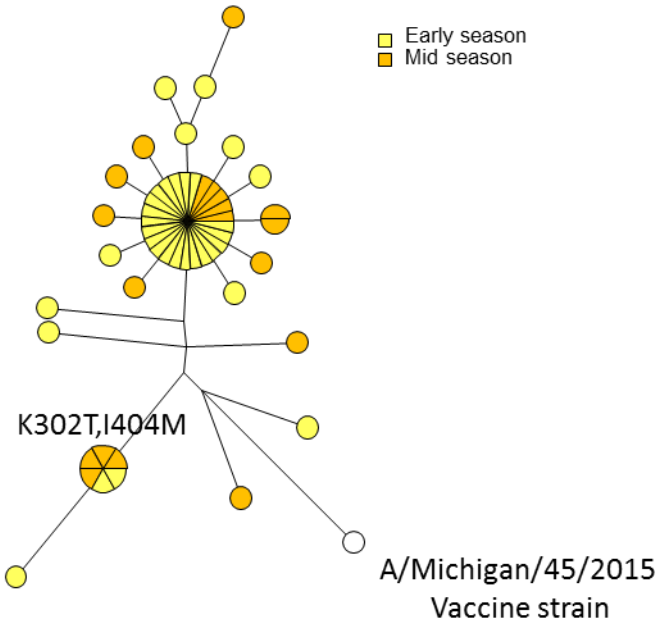



**Figure 11: Respiratory viruses, *Mycoplasma* and *Chlamydophila* detections in Norway reported monthly, from January 2018 through December 2018. Respiratory viruses with very low detection frequencies have been omitted. The number of patients tested for the different viruses varies, thus the figures displayed do not accurately portray the actual proportions of infections.**

## Genetic characterisations of the viruses in circulation

The analysed H1N1 viruses are all characterised as clade 6B.1 A/Michigan/45/2015 viruses and the major group of H1 viruses currently possesses the following substitutions: S74R, N129D, S183P, S185I, R223Q and N260D and group phylogenetically together with the A/Switzerland/3330/2017, or even closer to the A/Ukraine/7993/2018 reference strain (see phylogenetic tree at the end of the report). There is also a smaller group of H1 viruses circulating possessing the key substitutions K302T, I404M and N496S (Figure 12), grouping together with clade A/Dnipro/409/2018 reference strain. Also; the NA of these two groups of H1 viruses differ.

The N1 gene of the major clade of A/Switzerland/330/2017-like viruses possessed the key amino acid substitutions: Q51K, V67I, F74S and S95N and formed the same phylogenetic clustering as the HA genes (see phylogenetic tree at the end of the report). The closest relative is the A/Ukraine/7992/2018 reference strain. The NA of the minority group of H1 viruses possessed I188 and M314I with or without S12L in NA. Two other viruses possessed P93H, I216V and I264T, this was viruses characterised by T120A and S185I in the HA.




Cluster analysis of HA H1 viruses in Norway compared to the 2018/19 H1 vaccine component A/Michigan/45/2014 (white circle). Maximum parsimony analysis of the first 1096b of the HA genes. Viruses are colour coded by season, early season (yellow, week40-50) and mid season (orange, week 51-2).

**Figure 12. Cluster analysis of the HA gene of influenza A(H1N1)pdm09 viruses season 2018/19 in Norway, up to week 2 2019.**

The characterised H3N2 viruses are almost all 3C.2a1b A/Alsace/1746/2018 viruses, however these divide into two equally prevalent subgroups; the clade A/Iceland/78/2018 subgroup with the A106V and T131K key substitutions and the clade A/LaRioja/2202/2018 subgroup with the T128A and T135K substitutions together with either I48R, D53N or S198P (Figure 13)(see also phylogenetic tree at the end of the report). The most recent viruses also grouped together with the 3C.2a1b Clade A/LaRioja/2202/2018 viruses. This is also the group of H3 viruses with most genetic variation. A small group of H3 viruses was assigned to the 3C.2a2 clade A/Switzerland/8060/2017 and one single virus from week 50 was 3C.2a4 clade A/Valladolid/182/2017.

The N2 gene of all 3C.2a1b viruses possessed P126L in NA. The A/Iceland/78/2018-like viruses possessed in addition the key amino acid substitution S315R while the A/LaRioja/2202/2018 viruses possessed wither G93S or Y155H in NA (see also phylogenetic tree at the end of the report).

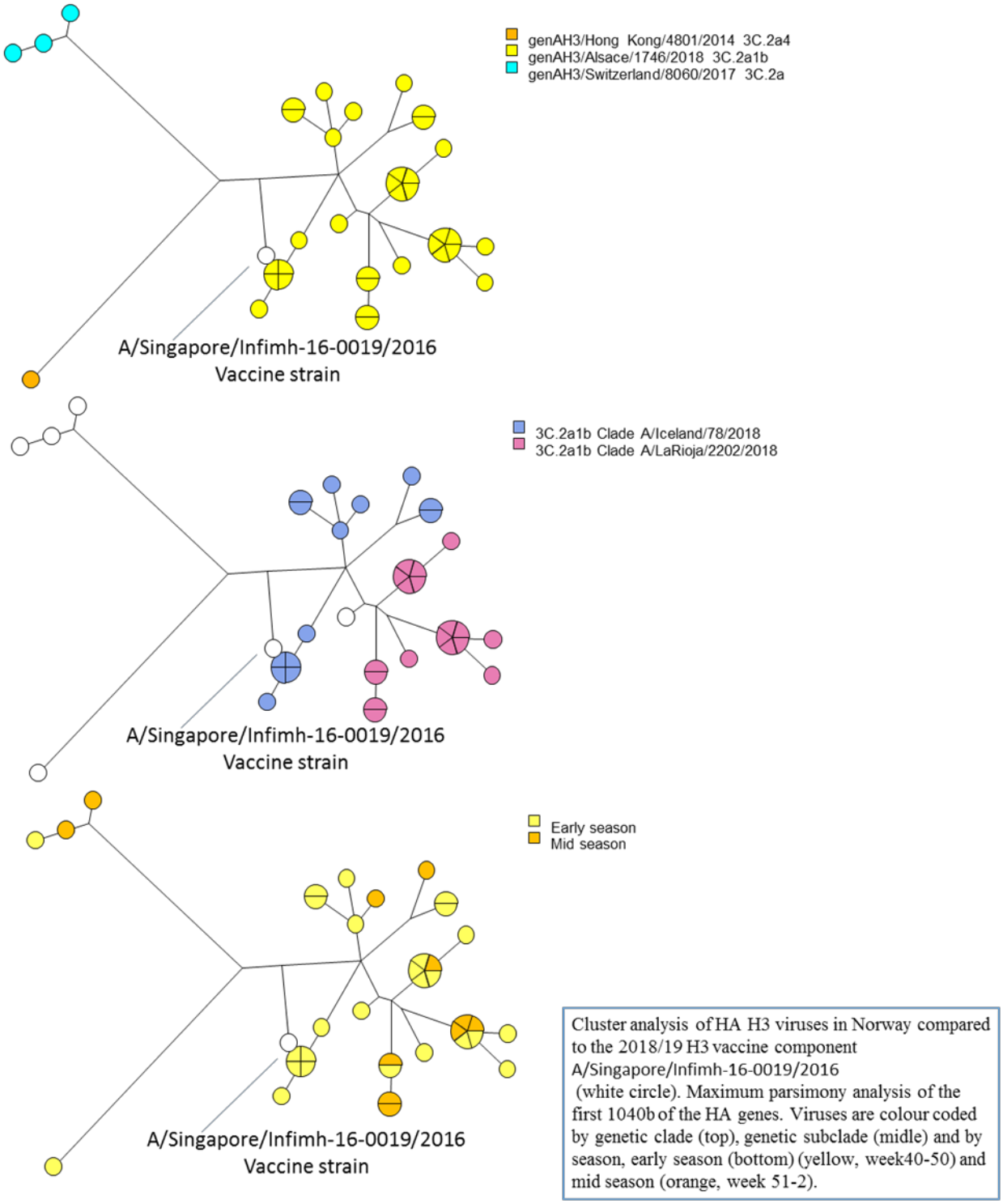



**Figure 13. Cluster analysis of the HA gene of influenza A(H3N2) viruses season 2018/19 in Norway, up to week 2 2019.**

Influenza B-Yamagata viruses characterised this far seem to be the same as previous season, all clade 3 viruses. One virus possessed the S120T and S229D substitutions in HA not seen in other viruses from Norway. As there are few B-Yamagata viruses and few characterised no phylogeny is shown.

Only two influenza B-Victoria viruses has been detected this far. Both are triple deletion variants with a deletion in HA1 positions 162-164, but they are also genetically distinct; one belongs to the Asian B/Hong Kong/269/2017 clade and the other is closer to the African triple-deletion viruses B/Niger/5592/2018.

Very few samples from vaccinated persons analysed at NIC Norway have been positive for influenza so far this season, compared to the frequency of influenza-positive samples from unvaccinated persons. Numbers are too low, however, to calculate meaningful VE estimates. Furthermore, there is no clear genetic difference between viruses from outpatients or hospitalised patients.

## Antiviral susceptibility

No resistance towards neuraminidase inhibitors like oseltamivir and zanamivir has so far been detected, out of 151 viruses analysed (Table 2).

**Table 2: Resistance to neuraminidase inhibitor drugs**

| pr. 30/01-19 | Oseltamivir (Tamiflu®) | | Zanamivir (Relenza®) | |
|---|---|---|---|---|
| Virus | Tested | Oseltamivir-resistant virus | Tested | Zanamivir-resistant virus |
| H3 | 52 | 0 / (0 %) | 52 | 0 / (0 %) |
| B | 4 | 0 / (0 %) | 4 | 0 / (0 %) |
| H1 | 95 | 0 / (0 %) | 59 | 0 / (0 %) |
| Resistance to oseltamivir and zanamivir detected either by sequence analysis or by neuraminidase susceptibility assay | | | | |

## Vaccine distribution and coverage

A total of 883 000 influenza vaccine doses have been distributed so far this season; 714 000 of these were specifically meant for persons in medical risk groups and health care personnel involved in direct patient care. These numbers represent an increase in distributed doses of 55-60 % over the last two years (Figure 14).

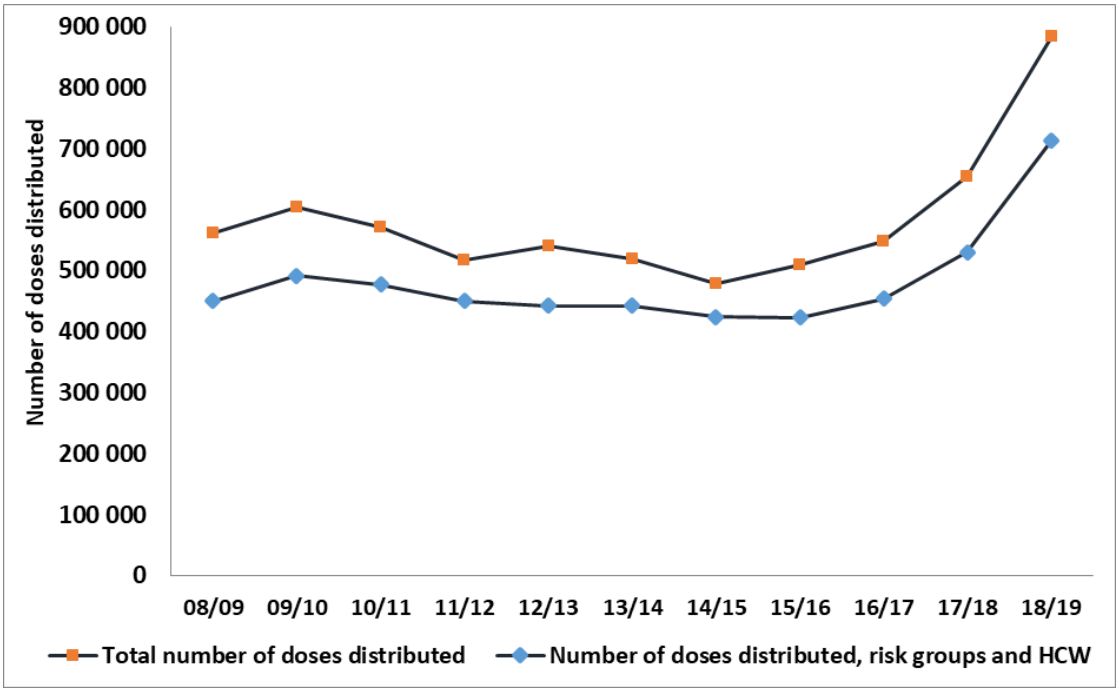



**Figure 14: Influenza vaccine doses (seasonal) distributed in Norway, 2008 through 2018 as per 21st January. HCW = Health Care Workers.**

Estimates of vaccine coverage in the various risk groups in the current season will not be available until October/November 2019.

# Population immunity against recent influenza viruses, August 2018

The National Influenza Seroepidemiology Programme annually in August collects about 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 1178 sera were analysed this year. The main findings are shown in figure 15, table 3, and summarised as follows:

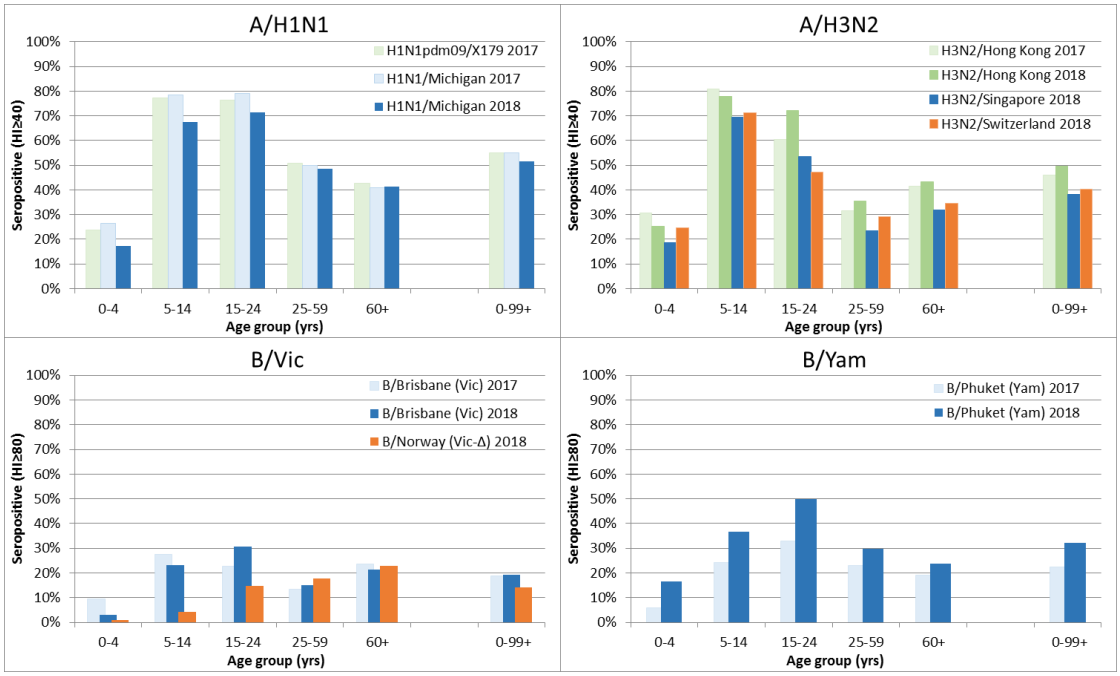



**Fig 15. Seroprevalence in August 2018 to current influenza A and B reference and vaccine strains for 'All ages' (0-99+) and in various age groups. For comparison, seroprevalences to some virus strains in August 2017 are also shown. X179A= A/California/07/2009 (H1N1)pdm09; Michigan= A/Michigan/45/2015 (H1N1)pdm09 clade 6B.1; Hong Kong = A/Hong Kong/5738/2014 (H3N2) clade 3C.2a; Singapore= A/Singapore/INFIMH-16-0019/2016 (H3N2) clade 3C.2a1 ; Switzerland= A/Switzerland/8060/2017 (H3N2) clade 3C.2a2; B/Brisbane= B/Brisbane/60/2008 (Victoria lineage); B/Norway= B/Norway/2409/2017 (Victoria lineage, amino acid 162-163 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, even though circulation of this virus was limited during the previous season. However, for those below 25 years old, the proportion of people with protective antibody levels (seroprevalence) had fallen by 10 percentage points since 2017.

Similarly, for A(H3N2) viruses, the comparatively strong population immunity observed in 2017, stemming from previous outbreaks and vaccination, was essentially maintained. The seroprevalence may be somewhat lower against some more recent genetic variants, particularly in the 15-24 years age group.

The seroprevalence against B/Victoria-lineage viruses remained low with overall seroprevalence of 20 % against the previous B/Victoria vaccine component B/Brisbane/60/2008.

Interestingly, the seroprevalence against a newly emerged "double deletion" variant, represented by B/Norway/2409/2017 in our analysis, shows a different and reduced pattern for those below 25 years old, and particularly those younger than 15 years. For those 25 years and older the seroprevalence against the two virus variants was similar.

B/Yamagata-lineage viruses predominated last winter, and the seroprevalence against the current variant B/Phuket/3070/2013 increased since 2017 in all age groups. The largest increase occurred in people younger than 25 years, with more modest increases in other age groups.

**Table 3. Influenza seroepidemiological results in August 2018 - Comparison between age groups.**
For comparison data from studies performed for the preceding years 2014-2017 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 |
| ***H1 Michigan/45/15 (2018)**** | ***17*** | ***67*** | ***71*** | ***58*** | *48* | ***41*** | *51* |
| 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 |
| ***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* |
| 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/Vic Brisbane/60/08 (2018)*** | ***3*** | *23* | ***31*** | ***22*** | ***15*** | *21* | *19* |
| ***B/VicΔ Norway/2409/17 (2018)**** | ***1*** | ***4*** | *15* | ***7*** | ***18*** | ***23*** | *14* |
| 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 |
| ***B/Yam Phuket/3073/13 (2018)**** | ***17*** | *37* | ***50*** | ***38*** | *30* | ***24*** | *32* |
| *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 |
| ***Sera analysed (n): 2018 Aug*** | 155 | 251 | 236 | 642 | 501 | 275 | 1418 |
| *[1)]Sub-panel (n) of 2018 sera (Hong Kong/5738/14)* | 84 | 125 | 114 | 323 | 251 | 137 | 711 |
| *[1)]Sub-panel (n) of 2018 sera (Switz./8060/17)* | 50 | 85 | 84 | 218 | 166 | 92 | 477 |

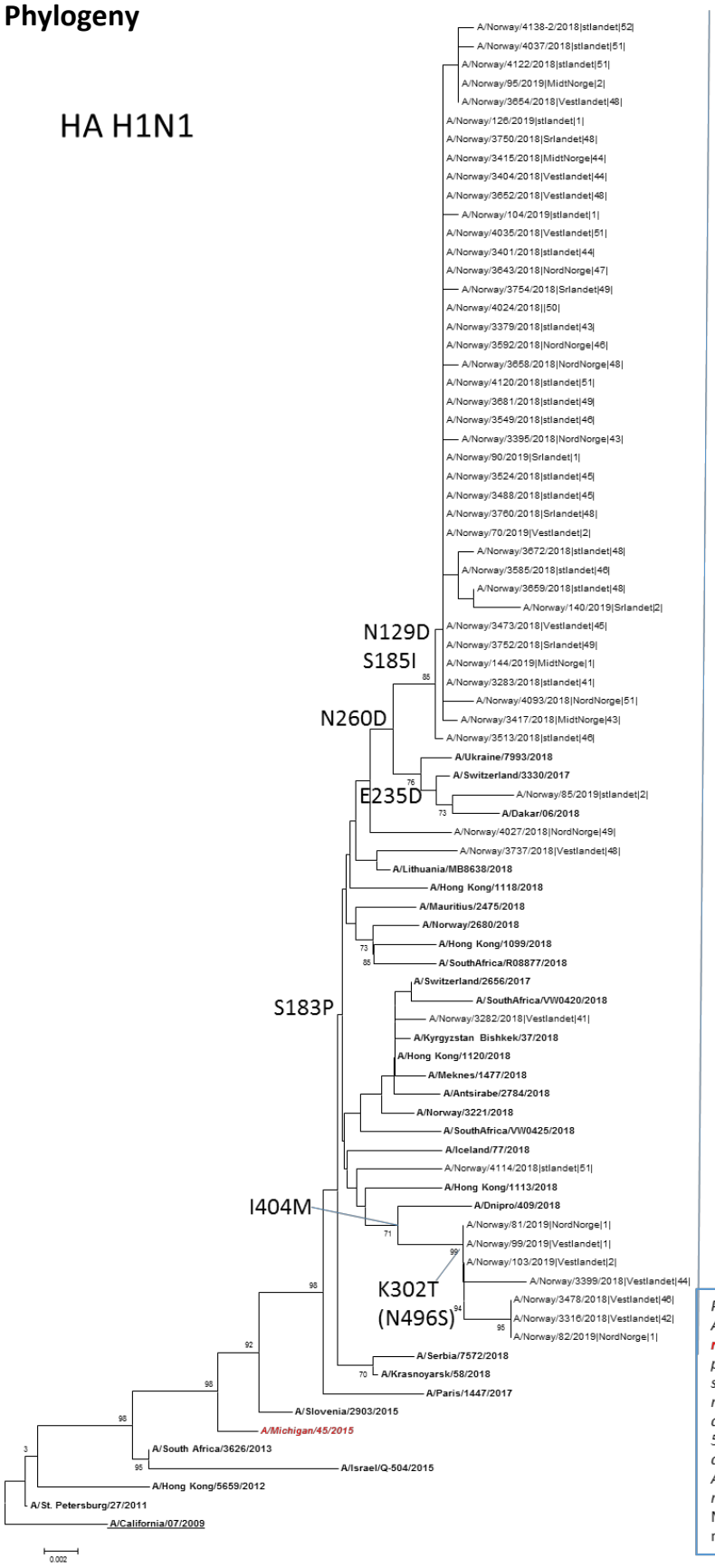
[$]Year of serum collection and HI analysis.

*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.

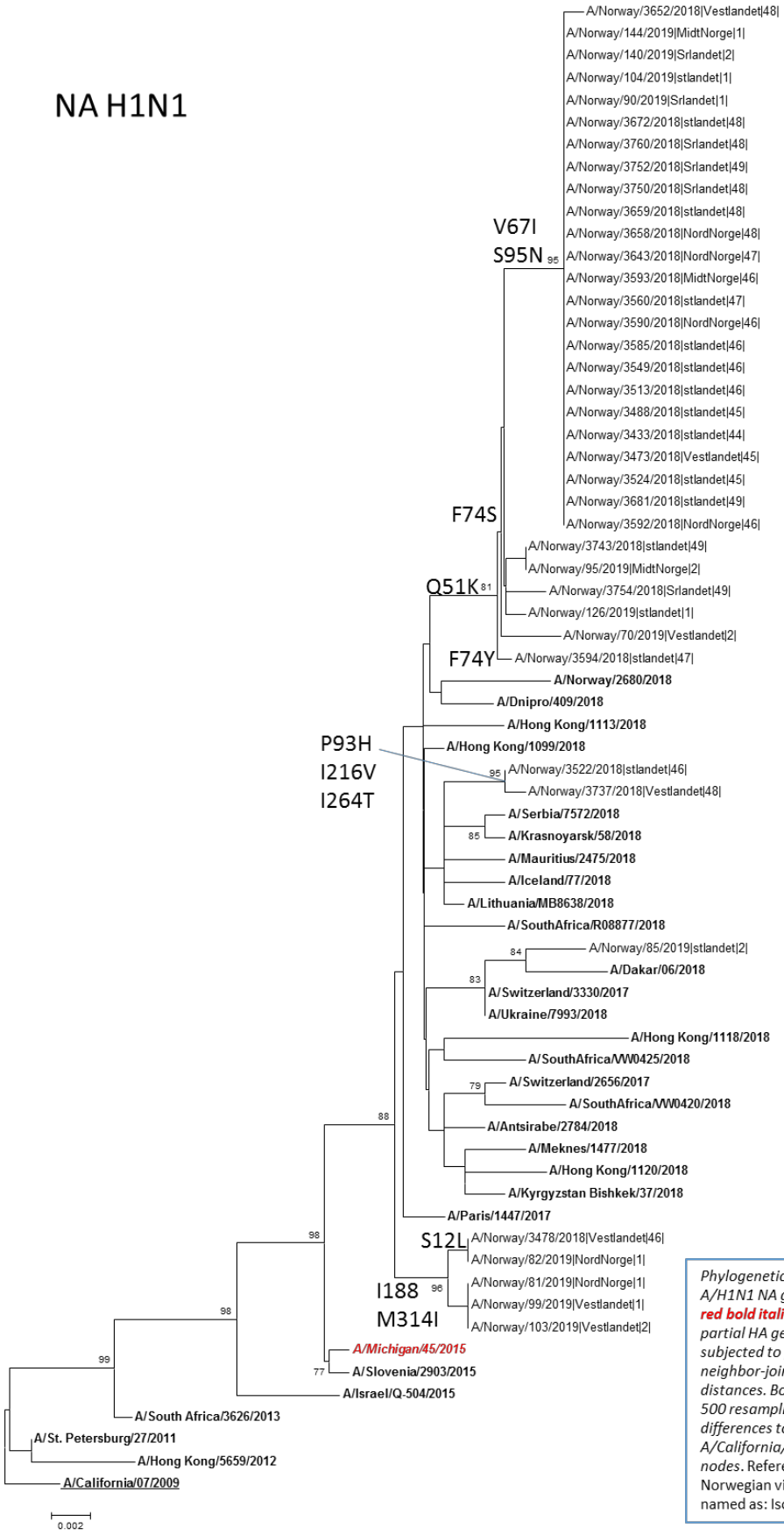
**(Corresponding to) components of the Northern hemisphere influenza vaccine (trivalent/quadrivalent) for the season 2018-2019.

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

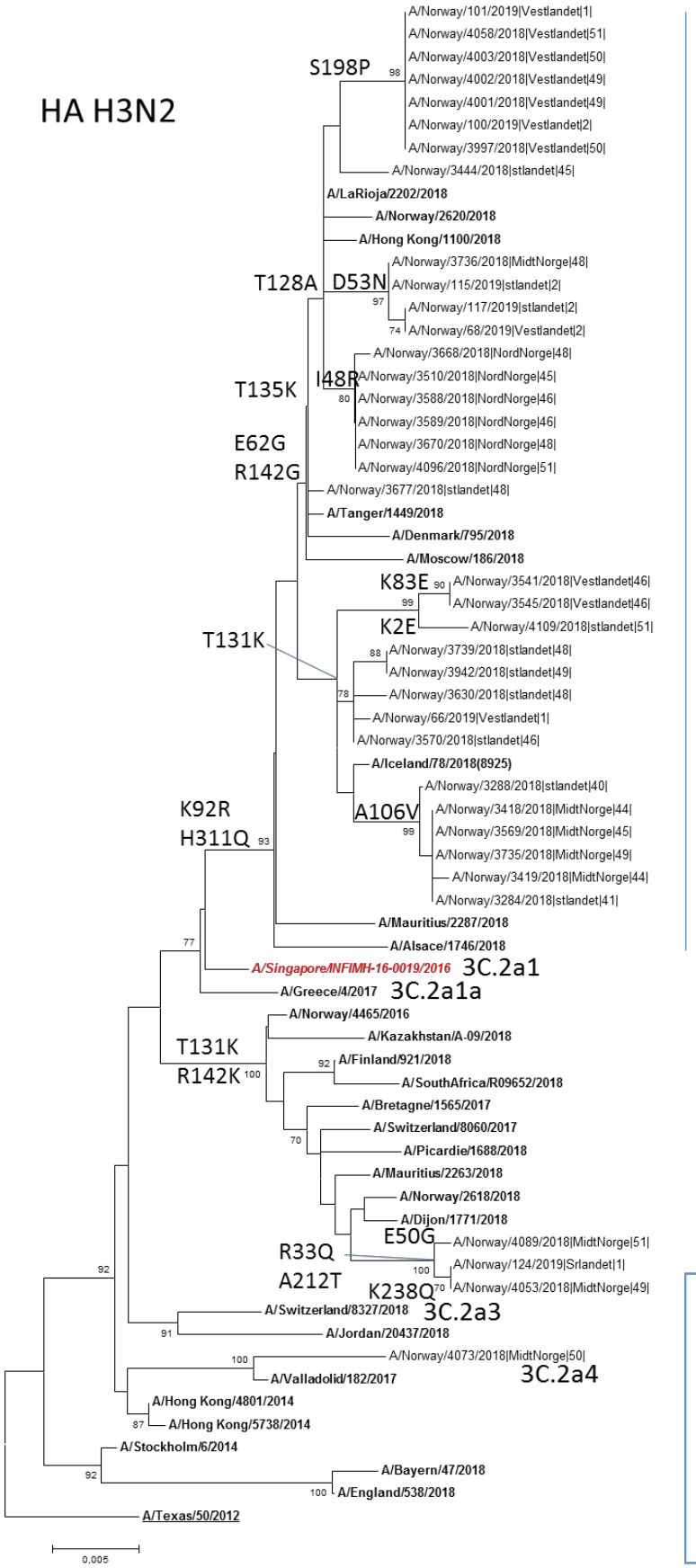
## Phylogeny



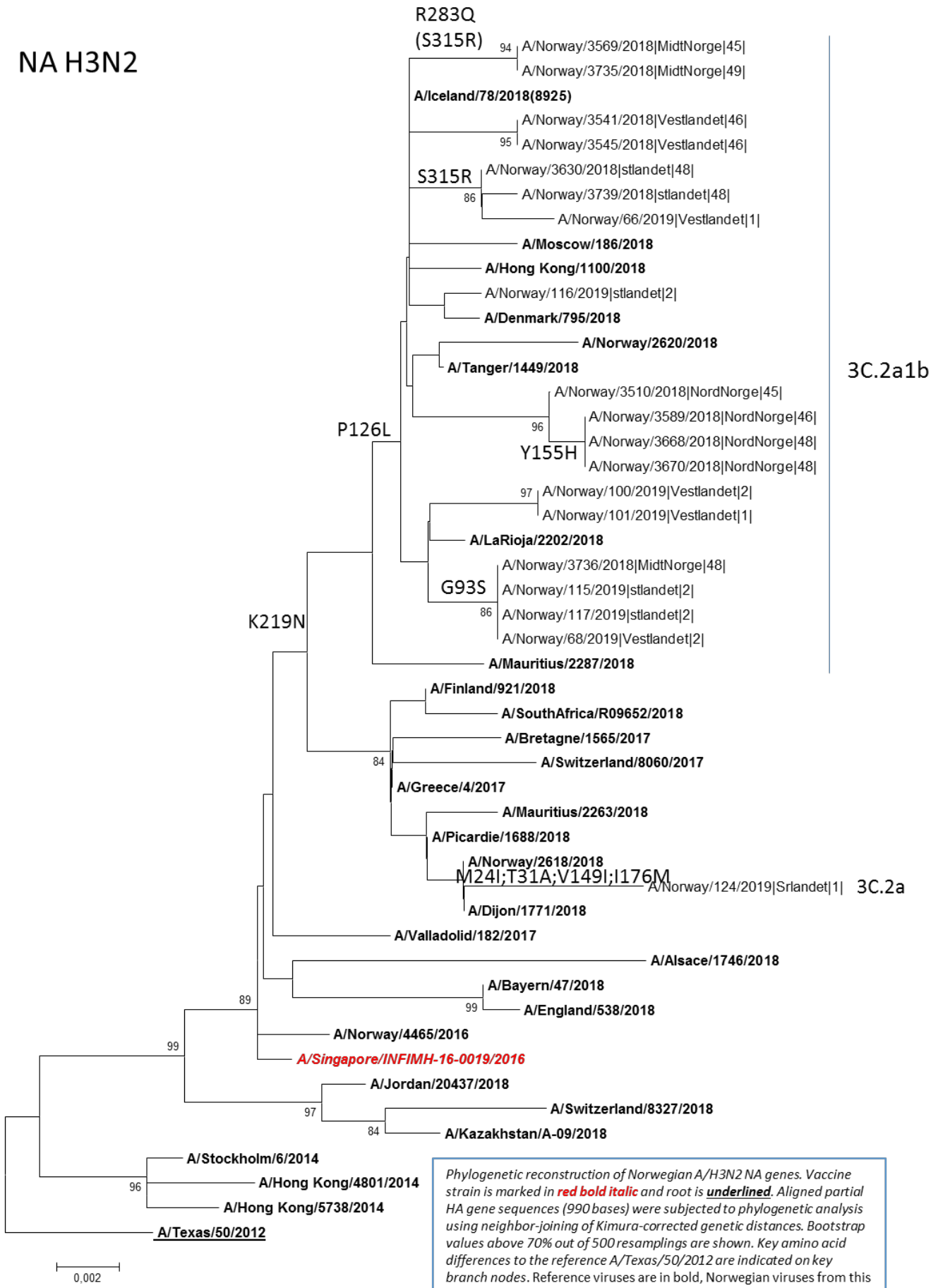

*Phylogenetic reconstruction of Norwegian A/H1N1 HA genes. Vaccine strain is marked in **red bold italic** and root is **underlined**. Aligned partial HA gene sequences (1096 bases) were subjected to phylogenetic analysis using neighbor-joining of Kimura-corrected genetic distances. Bootstrap values above 70% out of 500 resamplings are shown. Key amino acid differences to the reference A/California/07/2009 are indicated on branch nodes.* Reference viruses are in bold, Norwegian viruses from this season are named as: Isolate name|region|week|.




*Phylogenetic reconstruction of Norwegian A/H1N1 NA genes. Vaccine strain is marked in **red bold italic** and root is **underlined**. Aligned partial HA gene sequences (1096 bases) were subjected to phylogenetic analysis using neighbor-joining of Kimura-corrected genetic distances. Bootstrap values above 70% out of 500 resamplings are shown. Key amino acid differences to the reference A/California/07/2009 are indicated on branch nodes*. Reference viruses are in bold, Norwegian viruses from this season are named as: Isolate name|region|week|.




*Phylogenetic reconstruction of Norwegian A/H3N2 HA genes. Vaccine strain is marked in* ***red bold italic*** *and root is* ***underlined****. Aligned partial HA gene sequences (1040 bases) were subjected to phylogenetic analysis using neighbor-joining of Kimura-corrected genetic distances. Bootstrap values above 70% out of 500 resamplings are shown. Key amino acid differences to the reference A/Texas/50/2012 are indicated on key branch nodes.* Reference viruses are in bold, Norwegian viruses from this season are named as: Isolate name|region|week|.




*Phylogenetic reconstruction of Norwegian A/H3N2 NA genes. Vaccine strain is marked in **red bold italic** and root is **underlined**. Aligned partial HA gene sequences (990 bases) were subjected to phylogenetic analysis using neighbor-joining of Kimura-corrected genetic distances. Bootstrap values above 70% out of 500 resamplings are shown. Key amino acid differences to the reference A/Texas/50/2012 are indicated on key branch nodes.* Reference viruses are in bold, Norwegian viruses from this season are named as: Isolate name|region|week|.

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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.

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With best regards,

Karoline Bragstad, Kristian Waalen, Trine Hessevik Paulsen, Ragnhild Tønnessen, Torstein Aune, Birgitte Klüwer, Kjersti Rydland, and Olav Hungnes

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8 February 2019

# 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 60% 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 fifth 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. For the 2018-19 season an electronic form has been developed that will enable the reporting of data that are more detailed. 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.

### *Monthly reported non-influenza respiratory viruses*

The national monthly reporting scheme for laboratory diagnoses of viruses was based on a voluntary partnership arrangement between medical microbiology laboratories in Norway. The scheme was in operation between 1969-2018. The purpose of these reports was 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 were collected at the Norwegian Institute of Public Health and then compiled into a summation form for the current year. In 2019, this scheme has been discontinued.

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