NIPH
Norwegian Institute of Public Health

REPORT

2022

**NORWAY:**

# Influenza Virological and Epidemiological season report prepared for the WHO Consultation on the Composition of Influenza Virus Vaccines for the Southern Hemisphere 2023

September 2022

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# Norwegian Institute of Public Health

## Influenza Virological and Epidemiological season report prepared for the WHO Consultation on the Composition of Influenza Virus Vaccines for the Southern Hemisphere 2023,

## September 2022


Division of Infection Control

Department of Virology;

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and

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Contents

Contents 2

**The 2021-2022 influenza season, Norway 3**

Summary 3

**Influensasesongen 2021-2022 i Norge (summary in Norwegian) 4**

Hovedbudskap 4

**A look back at the preceding 2020/2021 season 6**

**The 2021/2022 season 7**

Influenza-like illness (ILI) in primary health care 7

Outbreaks in health care institutions 7

Influenza hospitalisations based on registry data 8

Influenza patients in intensive care units 9

Laboratory confirmed influenza: Virological surveillance 10

Genetic characterisation of the viruses in circulation 15

Influenza A(H3N2) 15

Influenza A(H1N1) 16

Influenza B/Victoria lineage 17

Antiviral susceptibility 18

**Population immunity against recent influenza viruses, August 2021 18**

**Vaccine distribution and coverage 21**

**References 23**

**Acknowledgements 24**

**Appendices 25**

Methods 25

Influenza-like illness 25

Virological surveillance. 25

Registry-based surveillance of influenza hospitalisations 25

Influenza patients in intensive care units 26

Influenza seroepidemiology 26

# The 2021-2022 influenza season, Norway

## Summary


- There was no influenza outbreak in Norway during the preceding 2020-2021 season.
- Consistent with the very low influenza activity during the preceding two seasons, seroprevalence against contemporary influenza viruses in August 2021 had declined and the susceptibility of the unvaccinated part of the population had increased.
- The vaccine coverage in the national immunisation programme reached the highest level ever recorded. Approximately 1.4 million doses were distributed to risk groups and health care personnel, and the number of discarded doses was estimated to 150.000. According to the national immunisation registry SYSVAK, the vaccine coverage among persons 65 years or older was at least 64 percent. The estimated number of doses used (private market included) has increased by 27 % compared to the preceding 2020/21 season
- A slight increase in influenza virus detections, predominantly A(H3N2), was seen during the autumn and early winter, but only in early March did this start to develop into a medium-magnitude outbreak. The frequency of detections peaked just before Easter, in week 14, and subsequently by early June had returned to very low, where it remained through summer with around 1 % positivity rate.
- The proportion of influenza-like illness (ILI) increased from mid-March and crossed the epidemic threshold in week 13, 2022. The ILI rate then indicated low-level influenza intensity for five weeks before returning down to very low level. Due to effects of the COVID-19 pandemic there is uncertainty concerning how well the ILI indicators now perform.
- The trends of influenza hospitalisations and ICU admissions reflected the trends in influenza detections well, with a late peak around week 14-16 in 2022. Between week 2021-40 and 2022-34, a total of 2,631 patients were admitted to hospital with influenza, and 62 patients were admitted to ICU. Seven influenza outbreaks in long-term care facilities were notified.
- As of week 34/2022, 13,940 cases of influenza have been laboratory confirmed, out of 562,953 patients tested during this season. During December-February the weekly number of persons tested for influenza was unprecedented, to a large extent due to testing for both SARS-CoV-2 and influenza on specimens taken for COVID-19 screening or verification, thus often without any clinical indication for influenza. After the relaxation of SARS-CoV-2 screening measures the weekly number of influenza test have returned to normal.
- Among the 13,825 detected influenza A viruses, 2598 have been subtyped as H3 and 170 as H1. Among the 115 recorded detections of influenza B, 26 have been identified in the National Influenza Centre as B/Victoria lineage and none as B/Yamagata.
- About 74 % of all samples received for surveillance have been whole genome sequenced for genetic characterisation. The H3N2 viruses driving the influenza this season were characterized as A/Bangladesh/4005/2020-like viruses, i.e. belonging to the genetic group 3C.2a1b.2a.2. The majority of the viruses possessed the antigen drift substitution

H156S in the HA protein. These viruses correspond well to the H3 vaccine component for the Northern hemisphere 2022/23 season, A/Darwin/6/2021.

- No resistance to neuraminidase inhibitors or adamantanes has been detected, but one single case with a baloxavir resistance mutation in the PA gene was found, not treatment related.

## Influensasesongen 2021-2022 i Norge (summary in Norwegian)

### Hovedbudskap

- Influensautbruddet i Norge uteble i den foregående 2020-2021 sesongen.
- I samsvar med at det hadde vært svært lite influensa de siste sesongene, var også forekomsten av beskyttende antistoff mot aktuelle influensavirus lavere i august 2021 enn i tidligere år. Dette tydet på at den uvaksinerte del av befolkningen var mer mottakelig for fremtidige influensautbrudd.
- Det var rekordhøy oppslutning om vaksinasjonsprogrammet. Det ble sendt ut omtrent 1,4 millioner doser til bruk for målgruppene, men med en meldt kassasjon på omtrent 150.000 doser. Vaksinasjonsdekningen blant personer over 65 år var ifølge SYSVAK på 64 prosent på landsbasis. Estimert antall brukte doser totalt (både program og vanlig salg) var 27 % høyere enn i sesongen 2020/21.
- Høsten og forvinteren 2021/2022 ble det påvist litt mer influensavirus, primært influensa A(H3N2), uten at det utviklet seg til noe utbrudd av betydning. Først i begynnelsen av mars 2022 kom det en klar økning. Antall og andel influensapositive prøver kulminerte i en middelstor topp like før påske, i uke 14. Deretter var det fallende forekomst inntil det var nede rundt 1% av de testede tidlig i juni, en andel som har holdt seg gjennom sommeren.
- Nivået av influensalignende sykdom økte medio mars 2022. Influensautbruddet krysset utbruddsterskelen i uke 13 og lå på lavt nivå i fem uker før nivået returnerte til svært lavt. Det er usikkerhet knyttet til hvor godt ILI-indikatoren måler influensaaktiviteten som følge av endringer i diagnosepraksis i primærhelsetjenesten i kjølvannet av covid-19-pandemien.
- Trendene i antall innleggelser i sykehus og intensivavdeling med influensa har gjenspeilet trenden i influensapåvisninger, med en topp rundt uke 14-16. Mellom uke 2021-40 og 2022-34 var det rapportert om totalt 2 631 innleggelser i sykehus og 62 innleggelser i intensivavdeling. FHI er varslet om syv utbrudd av influensa i helseinstitusjoner denne sesongen.
- Til og med uke 34/2022 er det denne sesongen laboratoriepåvist 13 940 influensatilfeller, etter at 562 953 personer er testet. I perioden desember 2021-februar 2022 lå antallet testede rekordhøyt, i stor grad fordi influensatest også ble gjort på prøver for covid-19 screening eller bekreftelse, dvs. for det meste uten klinisk mistanke om influensa. Etter at testing for covid-19 ble trappet ned har det ukentlige antallet influensatester returnert til nivå som var vanlig før pandemien.

- Blant 13 825 influensa A-påvisninger er 2598 virus subtypet som A(H3) og 170 som A(H1). Av de 115 registrerte influensa B-påvisninger er 26 bekreftet ved det nasjonale influensasenteret som genotype B/Victoria mens ingen har vært B/Yamagata.
- Cirka 74 % av de influensapositive prøvene oversendt til det nasjonale influensasenteret har blitt genetisk karakterisert ved helgenomsekvensering. Influensa A(H3N2)-virus, som dominerte hele denne sesongen, tilhørte den genetiske gruppen 3C.2a1b.2a.2 (A/Bangladesh/4005/2020-gruppen). De fleste av disse hadde antigen drift-mutasjonen H156S i HA-proteinet. Disse virusene samsvarer godt med H3N2-komponenten i kommende sesongs influensavaksine, A/Darwin/6/2021.
- Det er ikke funnet influensavirus med resistensmutasjoner mot neuraminidasehemmere eller adamantaner. Det ble imidlertid funnet ett enkelt virus med mutasjon i PA-proteinet som gir resistens mot baloxavir. Dette tilfellet var ikke behandlingsrelatert.

## A look back at the preceding 2020/2021 season

The 2020/21 season in Norway was characterized by a virtual absence of influenza detections. The proportion of influenza-like illness (ILI) in primary health care never exceeded the epidemic threshold; no outbreaks of influenza in health care institutions were reported, and the numbers of influenza hospitalisations and ICU admissions were very low.

That season, only 20 sporadic cases of influenza were detected out of 155,198 tested. Of these, 7 were A(H3N2), 2 A(H1N1), 8 B (not genotyped) and 3 B/Victoria. No B/Yamagata lineage viruses were detected.

The influenza A(H3N2) viruses belonged to the antigenically distinct 3C.2a1b.2a.2 subgroup and most closely resembled viruses like A/Bangladesh/100009/2020.

The influenza B-viruses belonged to the B-Victoria lineage (Δ162-164) and the antigenic different group of viruses originating from West Africa.

The H1N1 viruses belonged to 6B.1A/183P-7.

# The 2021/2022 season

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

## Influenza-like illness (ILI) in primary health care

The proportion consultations for ILI in primary health care started to increase in mid-March and crossed the epidemic threshold in week 13 2022 (Figure 1). Never before has an outbreak of seasonal influenza been registered this late in a season in Norway. The outbreak remained at low level for five weeks before crossing the threshold back to very low level, where it remains at present.

The coding practices for influenza in primary health care has been altered due to the COVID-19 pandemic. Therefore, there has been uncertainties as to how well the ILI indicator would perform to measure influenza activity in this new setting. This season, a rise in laboratory confirmed influenza preceded the increase in ILI by three weeks. How the ILI indicator will perform in future influenza outbreaks must be evaluated continuously in the coming years.

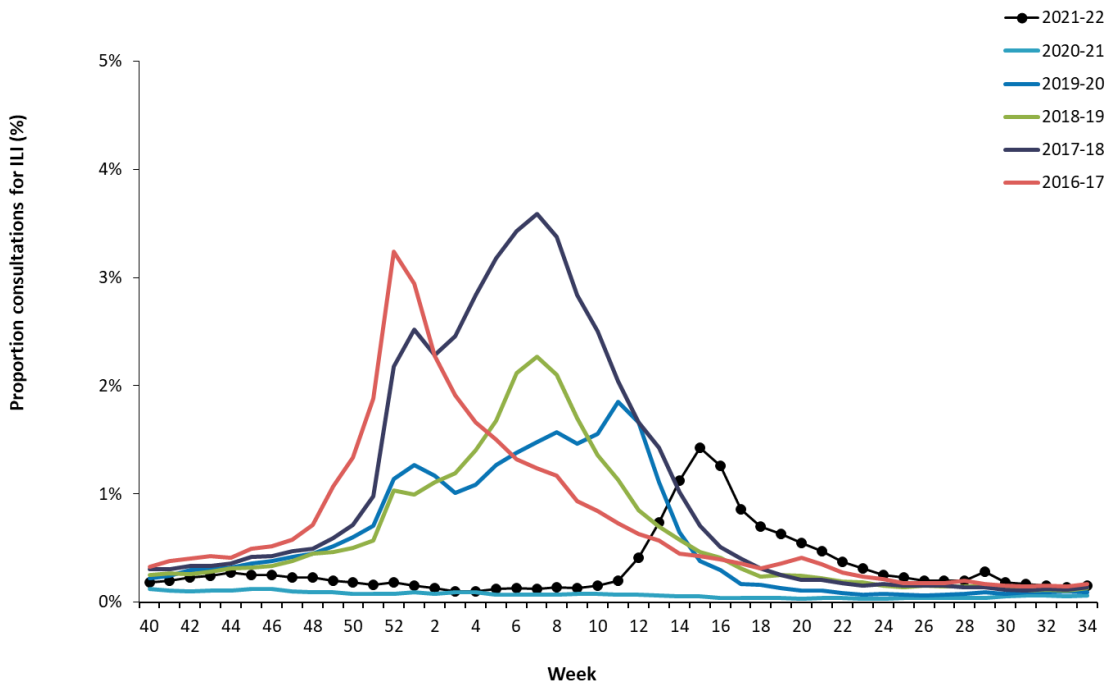



**Figure 1. Weekly proportion of patients in general practice and emergency clinics diagnosed with ILI, Norway, 2021-2022 season (black dotted line) and previous five seasons. Source: Sykdomspulsen with data from KUHR, NIPH.**

## Outbreaks in health care institutions

Seven outbreaks of influenza were reported from health care institutions throughout week 13-22 this season through VESUV, the national web-based outbreak alert system.

## Influenza hospitalisations based on registry data

Between week 40-2021 and 34-2022, altogether 2,631 (48.5 per 100,000 population) patients were hospitalised with influenza. The weekly number of new patients admitted varied from 0 to 20 between week 2021-40 and week 2022-9, after which the weekly number of new patients admitted rapidly increased, reaching a peak of 417 in week 2022-15 (figure 2). Since week 2022-24, the weekly number of new patients admitted has remained <20 again. The median age of the 2,631 patients was 66 years (interquartile range 29-79 years), and 1,324 (50 %) of them were male.

In comparison, in season 2020-2021 there was no circulation of influenza in Norway, and this registry-based surveillance system identified <5 patients hospitalised with influenza during the entire season.

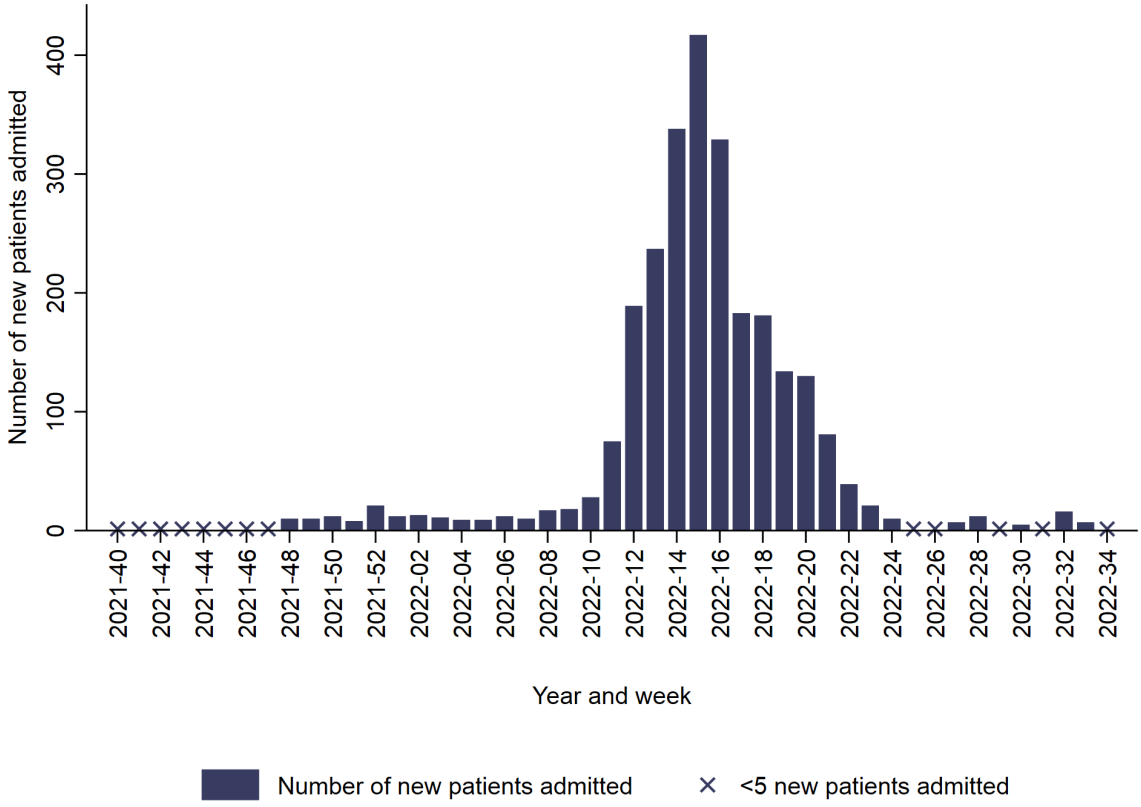



**Figure 2. Weekly number of patients hospitalised with laboratory confirmed influenza and influenza diagnosis, Norway, 4 October 2021 – 28 August 2022. Source: The Norwegian Emergency Preparedness Register (Beredt C19) with data from the Norwegian Patient Register and the Norwegian Surveillance System for Communicable Diseases (MSIS) laboratory database**

While registry data on influenza-positive PCR tests have been available only since the start of the COVID-19 pandemic, registry data based on hospital discharge codes alone show that the age groups 5-14 and 15-29 years had an exceptionally high incidence of hospital admissions in season 2021-2022 compared to previous seasons for which data is available (figure 3). Nevertheless, the incidence was highest among the elderly and youngest children, as usual.

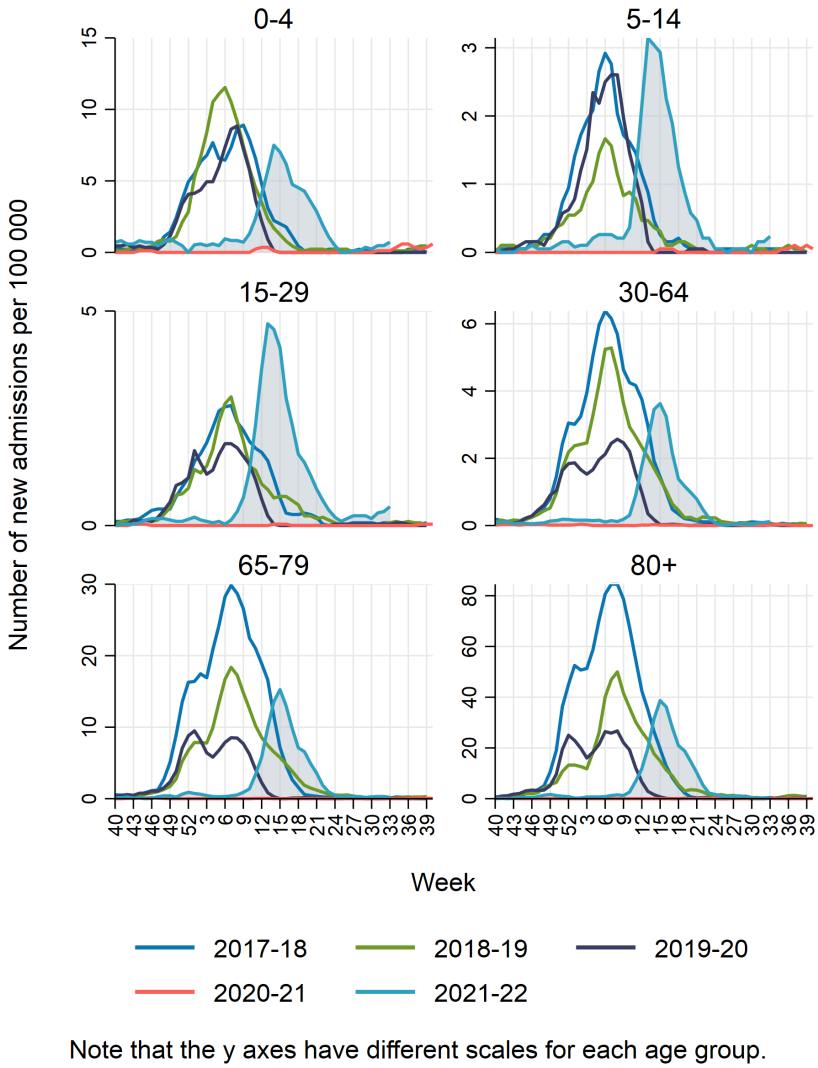



**Figure 3. Three-week moving average of hospital admissions with influenza diagnosis per 100,000 by age group and season, Norway, 2 October 2017 – 28 August 2022. Source: The Norwegian Emergency Preparedness Register (Beredt C19) with data from the Norwegian Patient Register**

## Influenza patients in intensive care units

Between week 40-2021 and 24-2022, 62 patients were admitted to ICU with confirmed influenza. The highest numbers of weekly admissions were registered in weeks 13-17, with 6-9 admissions per week. During the remaining weeks, less than 5 new patients were admitted per week. The median age of the 62 patients was 71.5 years (interquartile range 57-78 years), and 30 (48 %) were male. In comparison, less than five patients with influenza were admitted to ICU in Norway during the entire preceding 2020-2021 season, which is very low.

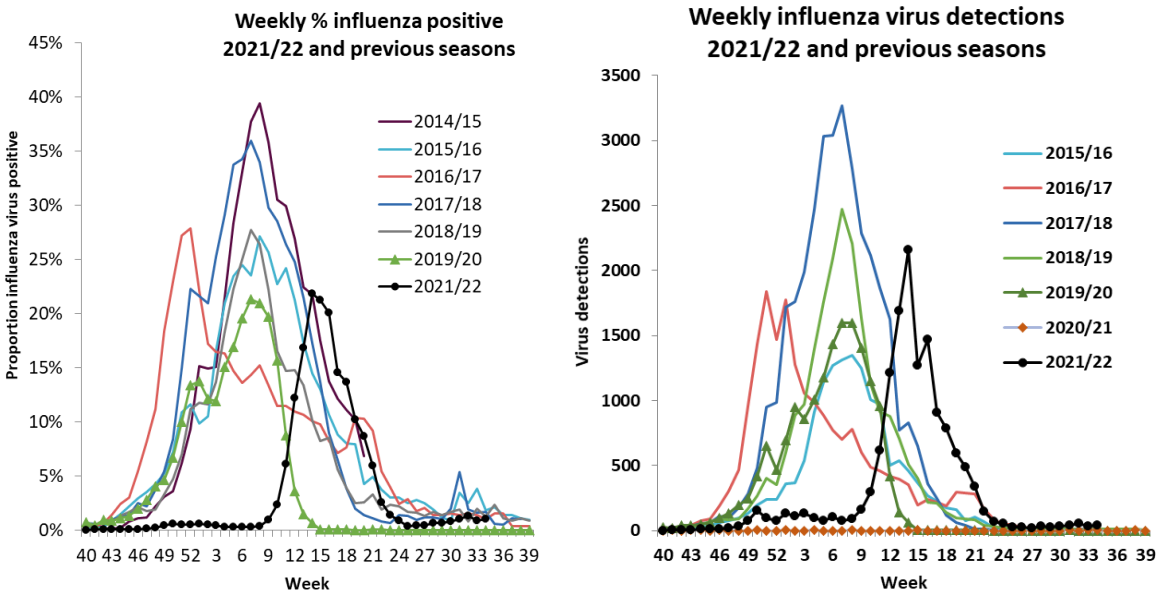
## Laboratory confirmed influenza: Virological surveillance

Altogether, 562,953 patients in Norway were tested for influenza during weeks 40/2021-34/2022, resulting in 13,825 recorded detections of influenza A virus and 115 influenza B virus (Figure 3, Table 1).

In a few instances in the autumn, trace amounts of virus RNA representing three or four different subtypes/lineages were detected in a sample, this has been interpreted as likely contamination with tetravalent influenza vaccine.

During the periods with extremely low prevalence of influenza in the population, the positive predictive value of the tests is expected to be poorer than usual, and in accordance with this, more positive results than usual could not be confirmed in the National Influenza Centre (NIC). This has particularly been the case for the type B virus detections, among which more than 10% of 39 referred specimens could not be verified as influenza B positive in the NIC. It is thus possible that a considerable proportion of the 115 recorded influenza B virus infections are spurious.
In contrast, less than 1% of the almost 1800 referred influenza A positive specimens could not be confirmed and/or subtyped in the NIC.

The number of detections started to rise in late November and levelled out after a small peak in week 50 when 157 out of 25,077 specimens (0.6%) tested positive for influenza. Only in week 9/2022 the numbers again started to rise, leading up to a medium-magnitude peak around Easter, weeks 14-16 (Figure 4). In several decades of virological influenza surveillance, this is the latest time of winter/spring we have had a sizeable influenza peak.



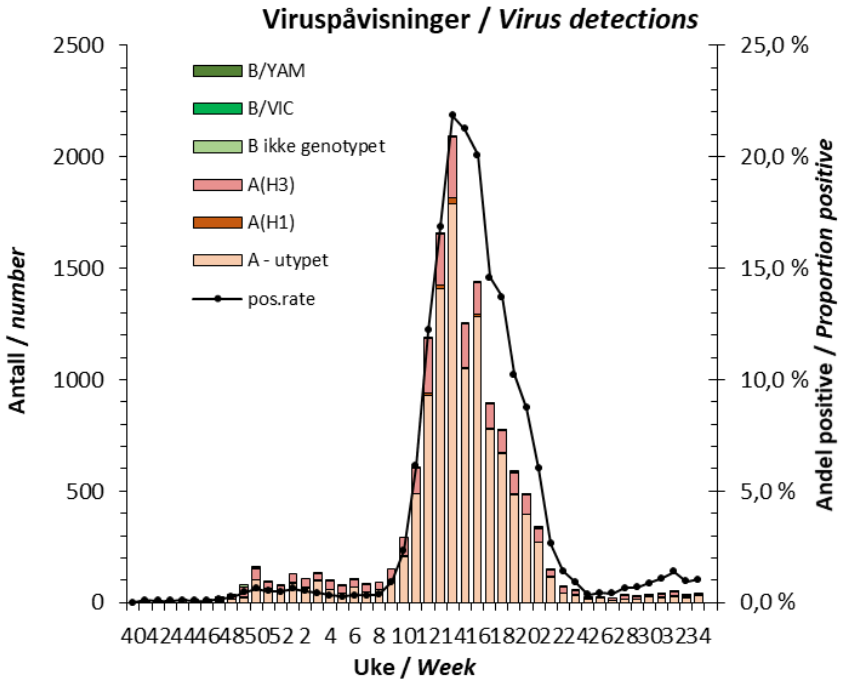




**Figure 4. Laboratory detections, Norway 2021-2022. Upper left-hand panel: Weekly proportion of influenza virus positive specimens, with previous season proportions shown for comparison. Upper right-hand panel: Weekly number of influenza virus detections, with previous season numbers shown for comparison. Seasons impacted by Covid-19 are marked with symbols.**
**Lower panel: Weekly number of the different influenza viruses, displayed as stacked bars.**

Influenza A(H3N2) viruses were strongly predominant throughout the season. (figure 5). Among the 13,818 detected influenza A viruses, 2562 have been subtyped as H3 and 166 as H1, either in the primary laboratory or in the NIC. However, in the most recent weeks the field may have started to open up, with H3 predominance declining and also the proportion of type B detections rising slightly.

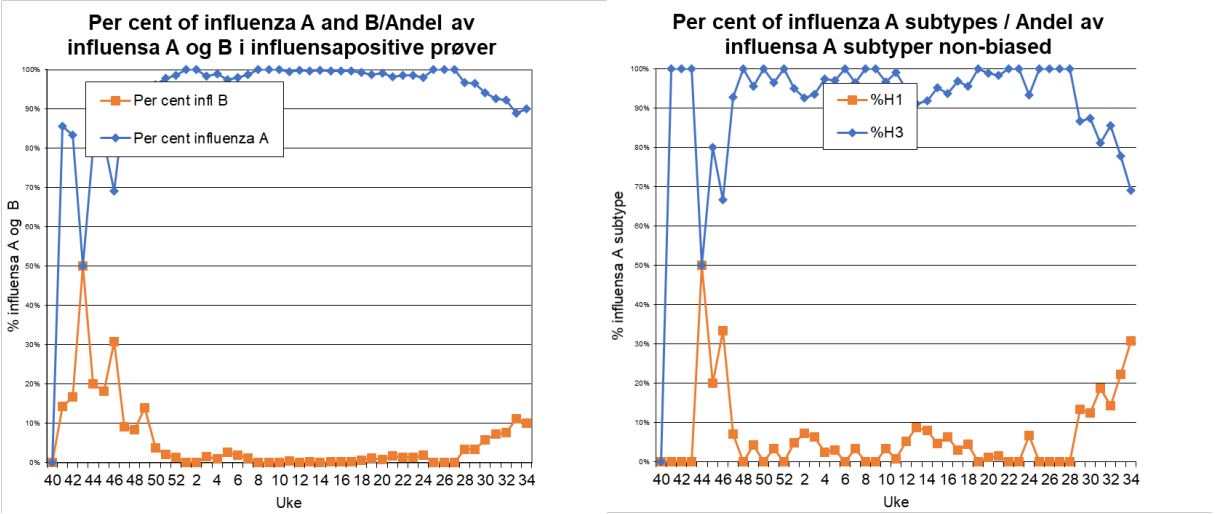



**Figure 5. Weekly proportions of influenza virus type A and B (left) and subtype H1 and H3 among influenza A viruses that have been tested for both H1 and H3 (right).**

## Virological sentinel surveillance

Due to the redirection since March 2020 of respiratory infection specimen collection away from general practices and emergency wards to Covid-19 testing stations, the virological sentinel system for influenza was not operable between mid-March 2020 and mid-February 2022. However, with the return of patients to general practices the sentinel system was reactivated and strengthened by including more GPs and engaging sentinel laboratories for testing. From week 7, 2022, physicians send specimens to their routine laboratory and the NIC receives the data as well as influenza and SARS_CoV-2 positive specimens for subtyping and characterisation.

From the reactivation in week 7 and through week 34/2022, 1047 sentinel specimens were tested, with 232 detections of influenza virus A (200 subtype H3, 5 subtype H1, and 27 not subtyped), and 7 influenza virus B (of which 3 were Victoria-lineage and 4 were not lineage identified). In addition, 80 SARS-CoV-2, 2 RSV,161 rhinovirus, 56 hMpV, 37 parainfluenza virus and 24 other human coronaviruses were detected. Influenza detections increased and peaked simultaneously to the detections in the non-sentinel virological surveillance.

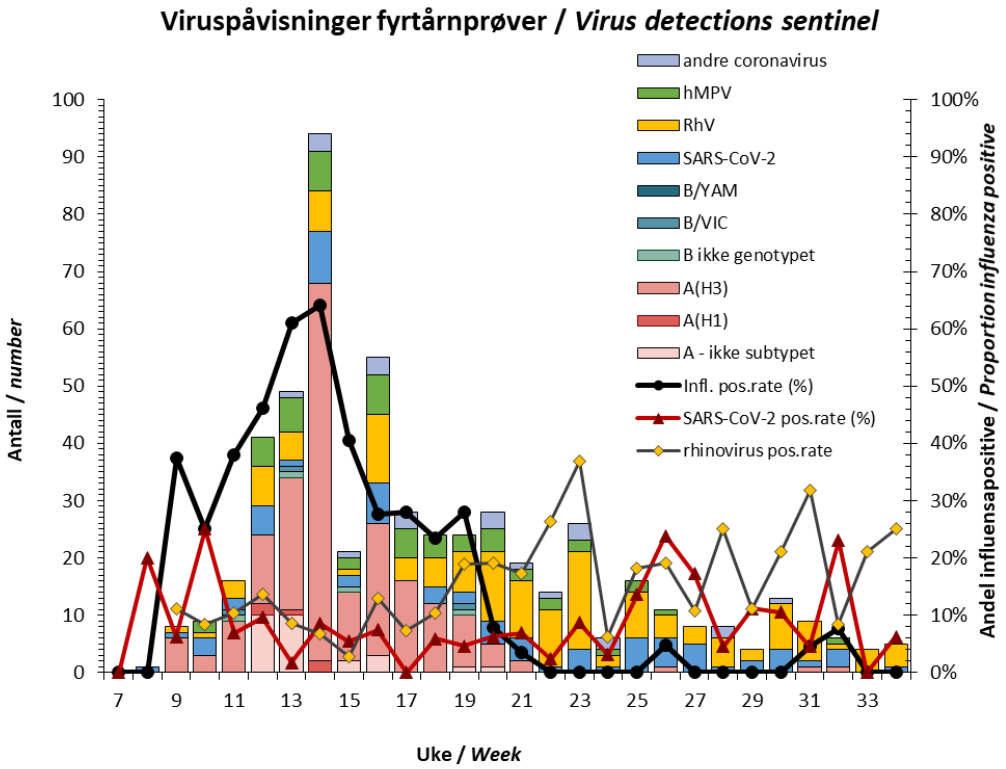



**Figure 6. Weekly numbers of detections and per cent positives of respiratory viruses in the respiratory sentinel surveillance.**

**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 (non-sentinel and sentinel combined), in Norway from week 40/2021 through week 34/2022.**

| | | *Virus detections* | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| *week* | Clinical surveillance % ILI | *Specimens* | % positive | A *not subtyped* | A(H1) pdm09 | A(H3) | B *not lineage typed* | B/Victoria lineage | B/Yamagata lineage |
| 40 | 0,2 % | 5975 | 0,00 % | 0 | 0 | 0 | 0 | 0 | 0 |
| 41 | 0,2 % | 6198 | 0,11 % | 0 | 0 | 6 | 1 | 0 | 0 |
| 42 | 0,2 % | 7628 | 0,08 % | 3 | 0 | 2 | 1 | 0 | 0 |
| 43 | 0,2 % | 8866 | 0,09 % | 3 | 0 | 1 | 4 | 0 | 0 |
| 44 | 0,3 % | 14421 | 0,10 % | 10 | 1 | 1 | 3 | 0 | 0 |
| 45 | 0,3 % | 15295 | 0,07 % | 4 | 1 | 4 | 2 | 0 | 0 |
| 46 | 0,3 % | 14014 | 0,09 % | 3 | 2 | 4 | 4 | 0 | 0 |
| 47 | 0,2 % | 13916 | 0,16 % | 6 | 1 | 13 | 2 | 0 | 0 |
| 48 | 0,2 % | 15068 | 0,24 % | 17 | 0 | 16 | 3 | 0 | 0 |
| 49 | 0,2 % | 17242 | 0,46 % | 22 | 2 | 44 | 11 | 0 | 0 |
| 50 | 0,2 % | 24959 | 0,63 % | 102 | 0 | 49 | 5 | 1 | 0 |
| 51 | 0,2 % | 17907 | 0,53 % | 64 | 1 | 28 | 2 | 0 | 0 |
| 52 | 0,2 % | 14811 | 0,50 % | 45 | 0 | 28 | 1 | 0 | 0 |
| 1 | 0,2 % | 20591 | 0,63 % | 87 | 3 | 39 | 0 | 0 | 0 |
| 2 | 0,1 % | 21320 | 0,51 % | 63 | 7 | 38 | 0 | 0 | 0 |
| 3 | 0,1 % | 30089 | 0,44 % | 97 | 3 | 29 | 2 | 0 | 0 |
| 4 | 0,1 % | 30043 | 0,32 % | 57 | 1 | 38 | 1 | 0 | 0 |
| 5 | 0,1 % | 29371 | 0,27 % | 42 | 1 | 33 | 2 | 0 | 0 |
| 6 | 0,1 % | 31351 | 0,33 % | 71 | 0 | 30 | 1 | 1 | 0 |
| 7 | 0,1 % | 24537 | 0,32 % | 49 | 2 | 28 | 1 | 0 | 0 |
| 8 | 0,1 % | 25480 | 0,36 % | 61 | 0 | 32 | 0 | 0 | 0 |
| 9 | 0,1 % | 16989 | 0,93 % | 104 | 0 | 54 | 0 | 0 | 0 |
| 10 | 0,2 % | 12689 | 2,34 % | 206 | 4 | 87 | 0 | 0 | 0 |
| 11 | 0,2 % | 10086 | 6,12 % | 488 | 3 | 123 | 2 | 1 | 0 |
| 12 | 0,4 % | 9904 | 12,22 % | 937 | 15 | 257 | 1 | 0 | 0 |
| 13 | 0,7 % | 10007 | 16,86 % | 1417 | 22 | 247 | 3 | 2 | 0 |
| 14 | 1,1 % | 9892 | 21,84 % | 1789 | 28 | 340 | 3 | 0 | 0 |
| 15 | 1,4 % | 5967 | 21,27 % | 1050 | 9 | 205 | 4 | 0 | 0 |
| 16 | 1,3 % | 7301 | 20,07 % | 1287 | 12 | 164 | 4 | 0 | 0 |
| 17 | 0,9 % | 6227 | 14,56 % | 778 | 4 | 125 | 1 | 1 | 0 |
| 18 | 0,7 % | 5739 | 13,70 % | 671 | 4 | 108 | 4 | 1 | 0 |
| 19 | 0,6 % | 5839 | 10,2 % | 485 | 2 | 104 | 5 | 2 | 0 |
| 20 | 0,6 % | 5642 | 8,7 % | 396 | 3 | 89 | 1 | 3 | 0 |
| 21 | 0,5 % | 5663 | 6,0 % | 270 | 3 | 62 | 4 | 2 | 0 |
| 22 | 0,4 % | 5568 | 2,6 % | 111 | 5 | 29 | 0 | 2 | 0 |
| 23 | 0,3 % | 5067 | 1,4 % | 42 | 1 | 27 | 1 | 0 | 0 |
| 24 | 0,3 % | 5721 | 0,9 % | 34 | 3 | 14 | 1 | 0 | 0 |
| 25 | 0,2 % | 6727 | 0,3 % | 17 | 1 | 5 | 0 | 0 | 0 |
| 26 | 0,2 % | 5829 | 0,4 % | 22 | 0 | 4 | 0 | 0 | 0 |
| 27 | 0,2 % | 5071 | 0,4 % | 10 | 0 | 11 | 0 | 0 | 0 |
| 28 | 0,2 % | 4630 | 0,6 % | 15 | 1 | 13 | 1 | 0 | 0 |
| 29 | 0,3 % | 4295 | 0,67 % | 12 | 3 | 13 | 1 | 0 | 0 |
| 30 | 0,2 % | 3926 | 0,84 % | 24 | 1 | 7 | 1 | 1 | 0 |
| 31 | 0,2 % | 3765 | 1,04 % | 21 | 4 | 13 | 1 | 2 | 0 |
| 32 | 0,2 % | 3747 | 1,36 % | 24 | 6 | 18 | 2 | 2 | 0 |
| 33 | 0,1 % | 3727 | 0,86 % | 19 | 6 | 7 | 1 | 3 | 0 |
| 34 | 0,2 % | 3853 | 1,04 % | 22 | 5 | 9 | 2 | 2 | 0 |
| Total | | 562953 | | 11057 | 170 | 2598 | 89 | 26 | 0 |
| *week* | % ILI | *Specimens* | % positive | A *not subtyped* | A(H1) pdm09 | A(H3) | B *not lineage typed* | B/Victoria lineage | B/Yamagata lineage |
| | | | Type A: 13825 | | Type B: 115 | | | | |

## Genetic characterisation of the viruses in circulation

This season, the NIC at the Norwegian Institute of Public Health has received 1,990 influenza virus positive samples for further analysis in the national monitoring. Of these 824 (41 %) have been subjected to further in-depth analysis with whole genome sequencing.

### *Influenza A(H3N2)*

At the start of the season in 2021 almost all cases were similar to the A (H3N2) virus that caused outbreaks in South Asia summer of 2021 and early autumn. Most viruses detected in Europe at that time appeared to be this genetic variant. This virus has somewhat altered antigenic properties in relation to the influenza A(H3N2) virus we have had in circulation in Norway before. The viruses were characterized as A/Bangladesh/4005/2020-like viruses belonging to the genetic group 3C.2a1b.2a.2 with the following defining mutations in HA1: Y159N, T160I, L164Q, D190N, F193S and Y195F. The majority of H3 viruses detected in Norway had the E50K substitution as well and some with and without the antigenic drift substitution H156S. This is a potential key mutation for antigenic drift and has been shown in functional studies to be somewhat antigenically different from the vaccine of the northern hemisphere. However, the main H3N2 virus causing the late influenza outbreak in Norway spring 2022 was a slightly different 3C.2a1b.2a.2 virus, A/Darwin/6/2021-like (Figure 7). Compared to the H3 vaccine strain for the Northern hemisphere 2021-22, most of these viruses possessed the HA1 amino acid mutations: D53G, D104G, **H156S**, Y159N, K160I, L164Q, N171K, R186D, D190N, P198S, K276R. During summer additional single substitutions have occurred in small groups of viruses; S124N has appeared in some of the viruses, L164Q in others, I140M, T164S, R299K and E50K in others. E50K was dominating in the early season version of the A/Bangladesh/4005/2020 viruses. Some new Bangladesh-like viruses have reappeared during summer, but with additional substitutions: F79V, I140K, S262N and loss of R269K. Only five cases have been identified as 3C.2a1b.1a (A/Denmark/3264/2019-similar).

The H3 component of the Northern Hemisphere vaccine was changed in February from 3C.2a1b.2a1 to the new Darwin-like H3 virus 3C.2a1b.2a.2. This is a good match compared to the circulating viruses in Norway this season. Viruses have been sent to the WHO Collaborating Centre for Influenza in London, UK for further analysis and genetic sequences deposited in the GISAID EpiFlu database.

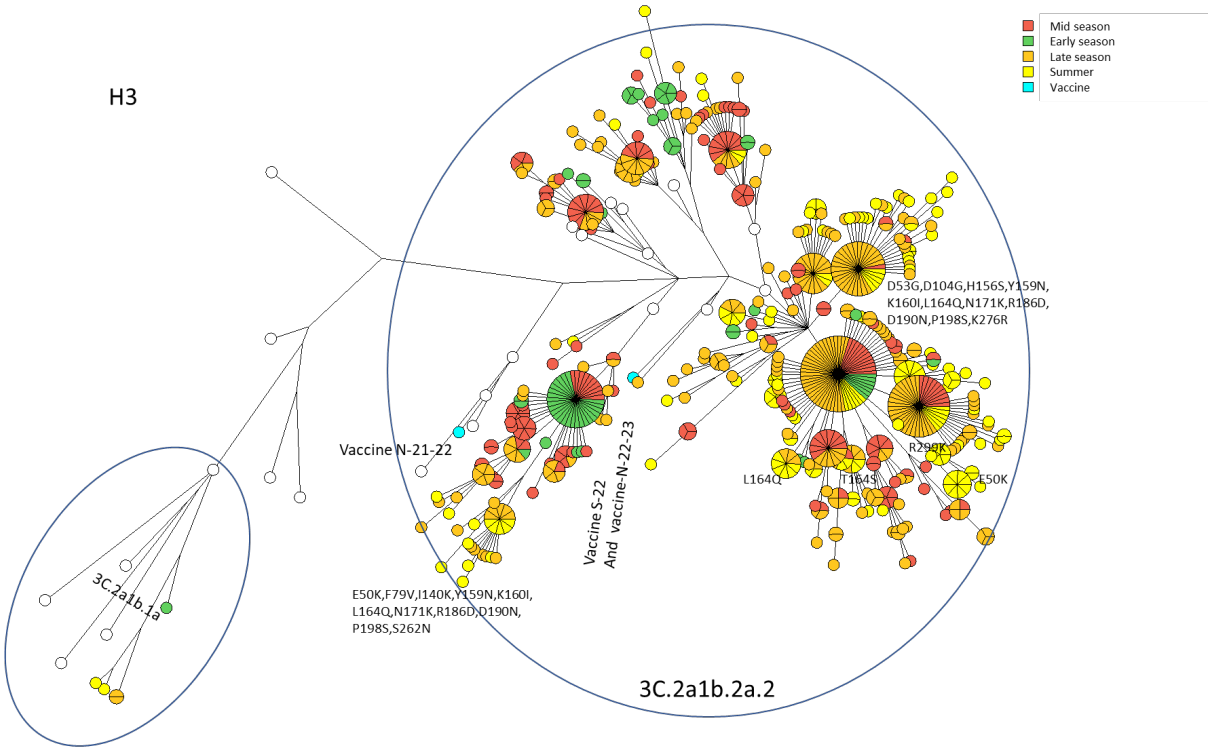



**Figure 7: Genetic relationship of Norwegian A(H3N2) virus together with the H3N2 vaccine component for the Northern hemisphere 2021/22 and Southern hemisphere 2022, HA-gene. Each circle or sector represents one virus, and the clusters show genetic relationship. Left: Norwegian samples colour coded on time for sampling, early season before week 51, and mid-season from week 51 to 11. Late season from week 12 to 22, summer from week 23 to 39.**

## *Influenza A(H1N1)*

Influenza A(H1N1) viruses of both clade 6B.1A.5a.2 and 6B1A.5a.1 have been detected during the season although at fairly low numbers. 6B.1A.5a.2 viruses like A H1/India/Pun-NIV312851/2021 have been dominating the H1 viruses (figure 8) possessing the HA substitutions (compared to the vaccine strain): K54Q, N129D, K130N, N156K, L161I, T185I, A186T, Q189E, T216A, E224A, D235E, V250A, R259K, K308R. During summer 2022 two cases of 6B.1A.5a.2 was detected that possessed some additional substitutions in HA1: P137S, K142R, D260E, and T277A.

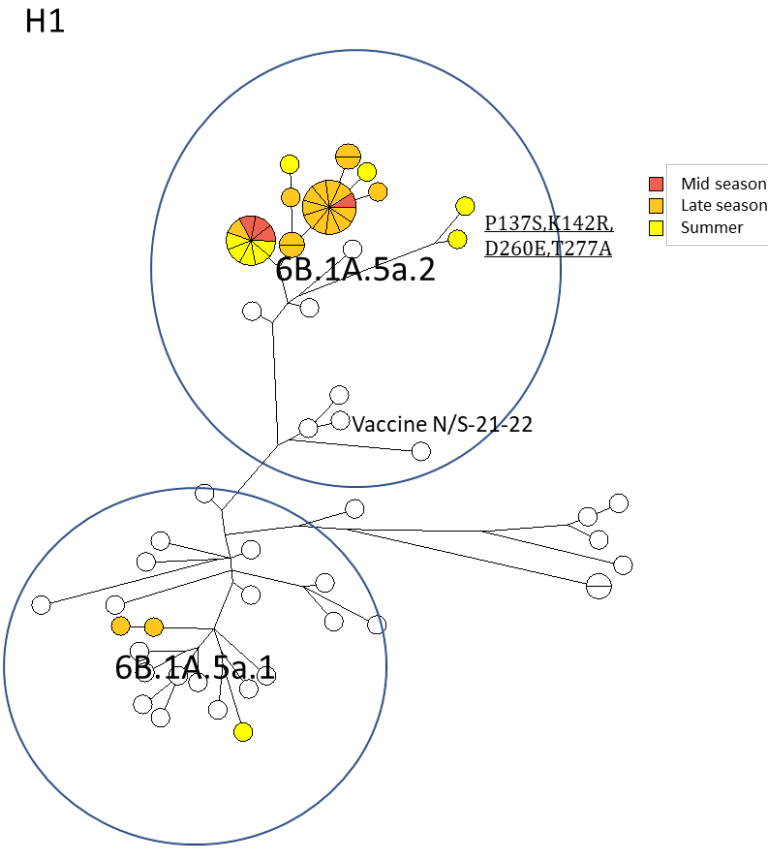



**Figure 8: Genetic relationship of Norwegian A(H1N1) virus together with the H1N1 vaccine component for the Northern hemisphere 2021/22 and Southern hemisphere 2022, HA-gene. Each circle or sector represents one virus, and the clusters show genetic relationship. Norwegian samples colour coded on time for sampling, early season before week 51, and mid-season from week 51 to 11. Late season from week 12 to 22, summer from week 23 to 39.**

### *Influenza B/Victoria lineage*

Only six cases of influenza B/Victoria could be genetically characterised, and they all belonged to the V1A.3a.2 clade B/Austria/1359417/2021 possessing D144G, E183K and G184E.

### Antiviral susceptibility

During the season 674 samples were genetically analysed for antiviral neuraminidase resistance at the reference laboratory. No neuraminidase resistance was detected. However, 3 H3N2 viruses had the I222V substitution in NA. This substitution is not associated with resistance in H3N2 viruses, but could infer resistance together with substitutions in position 119. Such substitutions were however not found in any of the Norwegian viruses.

As baloxavir got licensed in Norway in May 2021 also resistance towards baloxavir is investigated, although this antiviral is not in active use in Norway. This drug tends to have slightly higher degree of antiviral resistance developing. This has been the most widely used drug in Japan. In 2018 the resistance towards baloxavir in Japan was at 1,5 % and in 2019 at 9.5 %, mainly found in treated children. However, human to human transmission has also been detected (Takashita *et al*., 2019; Imai *et al*., 2020). Out of 442 influenza viruses in Norway investigated for baloxavir resistance one single case (0.23 %) from week 19 was detected. This is the first potential baloxavir resistance case in Norway. The sample was from an elderly (>80 years old) hospitalized case, not undergone antiviral treatment, infected with influenza A(H3N2), possessing the I38T substitution in the PA protein.

No samples had neuraminidase susceptibility phenotypic testing performed as antiviral resistance testing of influenza virus has been deprioritized during the COVID-19 pandemic.

For many years all circulating influenza viruses have been resistant to adamantanes, thus the antiviral is not used for treatment in Norway and most other countries. However, in recent years there has been reports of single cases that is susceptible again. Therefore, NIPH has again resumed testing for adamantane resistance. All cases investigated for adamantane resistance (476) possessed the S31N substitution in the M2 protein indicating high resistance towards adamantanes. .

## Population immunity against recent influenza viruses, August 2021

In August each year, the National Influenza Seroepidemiology Programme solicits approximately 2000 anonymised residual 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. Due to COVID-19 workload, the analysis of sera was not carried out in 2020, and from the August 2021 collection only a subset of ca. 660 sera was analysed. The main findings are shown in figure 5, table 2, and summarised as follows:

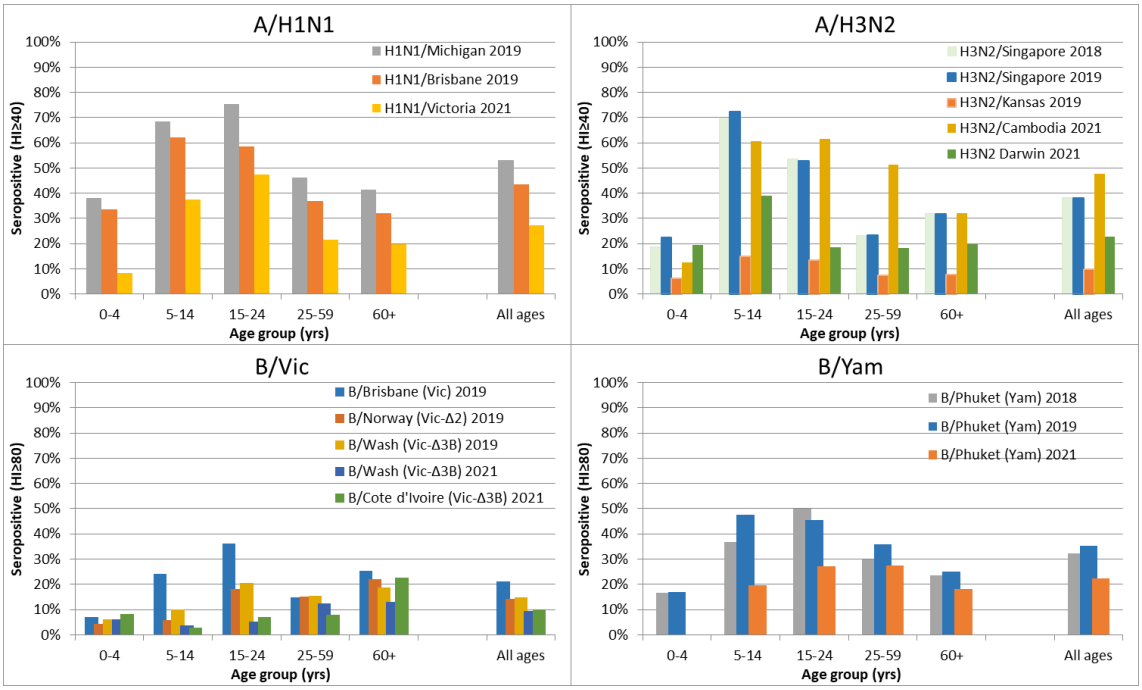



**Fig 5. Seroprevalence in August 2021 to current influenza A and B reference and vaccine strains for 'All ages' and in various age groups. For comparison, seroprevalences to some virus strains in August 2019 are also shown.**
**H1N1/Michigan= A/Michigan/45/2015 (H1N1)pdm09 clade 6B.1; H1N1/Brisbane= A/Brisbane/02/2018 (H1N1)pdm09 clade 6B.1A1; H1N1/Victoria= A/Victoria/2570/2019(H1N1); H3N2/Singapore= A/Singapore/INFIMH-16-0019/2016 (H3N2) clade 3C.2a1 ; Kansas= A/Kansas/14/2017 (H3N2) clade 3C.3a.1; H3N2/Cambodia= A/Cambodia/e0826360/2020(H3N2), 3C.2a1b.2a.1; H3N2/Darwin= A/Darwin/9/2021(H3N2), 3C.2a1b.2a.2; B/Brisbane= B/Brisbane/60/2008 (Victoria lineage, V1.A); B/Norway= B/Norway/2409/2017 (Victoria lineage, V1A.1); B/Wash=B/Washington/02/2019 (Victoria lineage, V1A.3); B/Cote d'Ivoire= B/Cote d'Ivoire/948/2020 (Victoria lineage, V1A.3a.1); B/Phuket= B/Phuket/3073/2013 (Yamagata lineage).**

For A(H1N1) viruses, there has been a drop in seroprevalence in all the age groups, leading to less than 30 % prevalence in all ages and, notably, less than 10% prevalence in children less than five years old.

For A(H3N2) viruses, the seroprevalence against the 3C.2a1b.2a.1 ("Cambodia-like") was substantial in 5-59 years age group and in all ages. The seroprevalence against the recently predominant 3C.2a1b.2a.2 ("Bangladesh-like") subgroup was much lower.

The seroprevalence against contemporary B/Victoria-lineage viruses was low in 2019 and had declined further in August 2021, with overall seroprevalence of only 10 % against recent B/Victoria variants represented by B/Washington/02/2019 (V1A.3) and B/Cote d'Ivoire/948/2020 (V1A.3a.1).

For the B/Yamagata-lineage viruses, represented by the vaccine virus for tetravalent vaccines, B/Phuket/3070/2013, the seroprevalence had declined since 2019, with overall seroprevalence at 22%, and similar proportions in all age groups except 0-4 year olds for whom the seroprevalence was zero.

**Table 2. Influenza seroepidemiology results in August 2019 – Seroprevalence* in age groups.**
For comparison data from studies performed for the preceding years 2016-2019 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 (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 |
| ***H1 Victoria/2570/19 (2021)**** | ***8*** | ***37*** | ***47*** | ***36*** | ***22*** | ***20*** | ***27*** |
| 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) | 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 |
| ***H3 Cambodia/e0826360/20 (2021)**** | ***13*** | ***61*** | ***61*** | ***52*** | ***51*** | ***32*** | ***48*** |
| ***H3 Darwin/9/21 (2021)***** | ***20*** | ***39*** | ***18*** | ***28*** | ***18*** | ***20*** | ***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/Wash/02/19 (Vic-Δ3B) (2021)**** | ***6*** | ***4*** | ***5*** | ***5*** | ***12*** | ***13*** | ***10*** |
| ***B/Cote d'Ivoire/948/20 (Vic-Δ3B) (2021)*** | ***8*** | ***3*** | ***7*** | ***6*** | ***8*** | ***23*** | ***10*** |
| 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 |
| ***B/Yam Phuket/3073/13 (2021)**** | ***0*** | ***20*** | ***27*** | ***19*** | ***28*** | ***18*** | ***22*** |
| *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 |
| ***Sera analysed (n): 2019 Aug*** | ***48*** | ***107*** | ***114*** | ***269*** | ***250*** | ***137*** | ***656*** |

[$]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 2021-2022.

***(Corresponding to) components of the Southern hemisphere influenza vaccine (trivalent/quadrivalent) for the season 2022.

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

## Vaccine distribution and coverage

A total of 1.8 million influenza vaccine doses have been distributed in the 2021/22 season; 1,4 million of these were distributed from NIPH specifically intended for persons in medical risk groups and health care personnel involved in direct patient care. Municipalities and hospitals have reported that 150.000 of these doses were not used. The estimated number of doses used has increased by 27 % compared to the 2020/21 season and has doubled in four years (Figure 7).

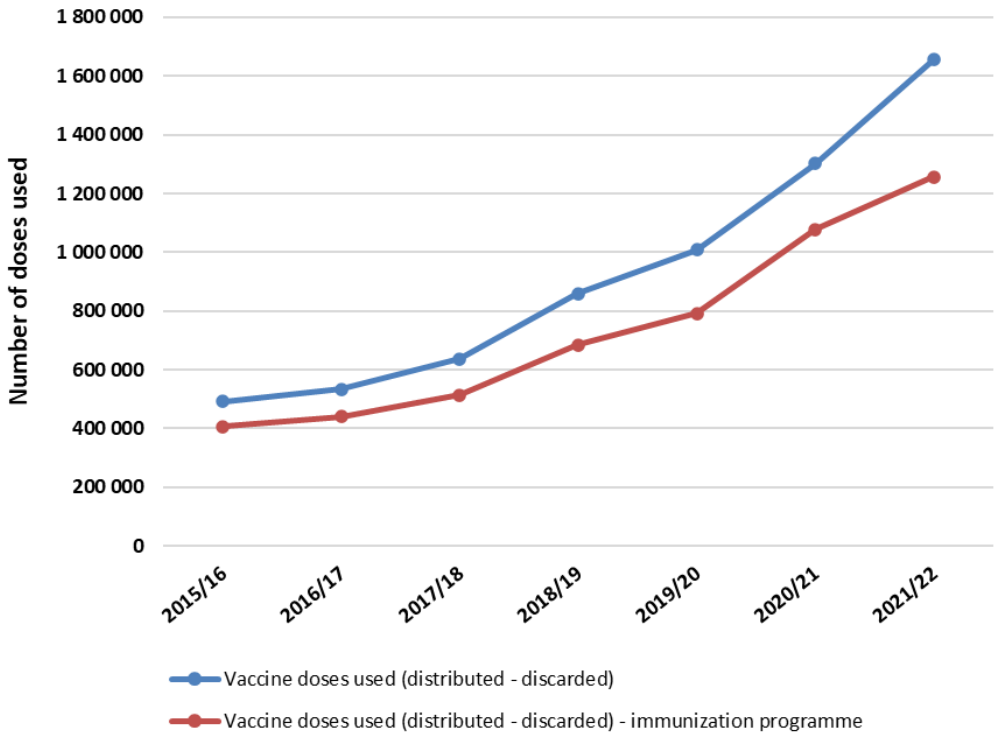



**Figure 7. Estimated number of influenza vaccine doses used in the Norwegian Influenza Immunization Programme, September 2015 through May 2022.**

According to the Norwegian Immunization Registry SYSVAK (SYSVAK), at least 64 % of the population above 65 years of age received an influenza vaccine this season.

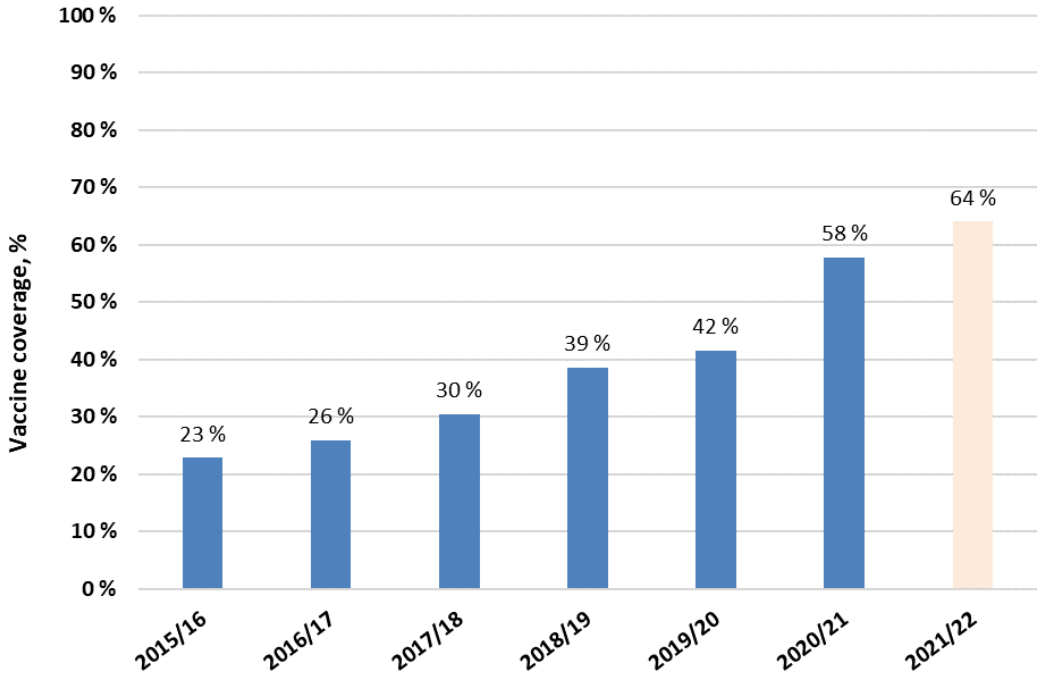



**Figure 8. Vaccine coverage among residents above 65 years in Norway, 2015/16 season through to 2021/22 season as of May 2022.**

According to Emergency preparedness register for COVID-19 (Beredt C19), the vaccine coverage in risk groups 18-64 years and 0-17 years per 24th of May 2022 are 39 % and 8 %, respectively. Vaccine coverage among health care workers was 59 % in specialist health care services (mainly hospitals) and 39 % in primary healthcare. 81 % of the doses used is registered in the national immunisation registry SYSVAK, due to underreporting and technical issues. Vaccine coverage is therefore also estimated for the various risk groups based on survey data from Statistics Norway. However, these estimates will not be available until October 2022.

## Animal influenza

Highly pathogenic avian influenza (HPAI) was detected for the first time in wild birds in Norway in 2020 (1). In November 2021, there were outbreaks of HPAIV A(H5N1) in two holdings of laying hens in Southern-Norway. This was the first ever outbreak of highly pathogenic avian influenza in commercial poultry holdings in Norway. In the 2021-2022 season, HPAIVs were detected in wild birds all across Norway, including in high arctic areas such as Spitzbergen and Jan Mayen. Two different viruses predominated: H5N1 and H5N5. In June 2022, a large number of sick or dead seabirds (mainly Northern gannets) were found along the Norwegian coast, and in July and August three instances of HPAIV H5N1 infection were also detected wild red foxes that probably had fed on such birds. This was the first detection of avian influenza in mammals in Norway. All HPAIVs detected in Norway so far have belonged to clade 2.3.4.4b. No cases of avian influenza have been detected in humans in Norway. The Norwegian Institute of Public Health has assessed the risk for human infection as very low (2), but increased awareness and precautionary infection control measures are recommended to prevent zoonotic infection.

## References

1 Veterinærinstituttet: https://www.vetinst.no/fugleinfluensa-i-norge

2 Folkehelseinstituttet. Vurdering av risiko for smitte til mennesker med høypatogen fugleinfluensa A(H5N1) i Norge. Available from: https://www.fhi.no/publ/2021/vurdering-av-risiko-for-smitte-til-mennesker-med-hoypatogen-fugleinfluensa--/

Previous **Norwegian reports prepared for the WHO vaccine consultation meeting:**

WHO-rapporter - FHI (https://www.fhi.no/sv/influensa/influensaovervaking/who-rapporter/)

# Acknowledgements

The work presented relies heavily on the essential contributions by the Norwegian medical microbiology laboratories, the Norwegian Intensive Care Registry and intensive care units, 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 is provided by the Department of Infectious Disease Epidemiology and Modelling, Norwegian Institute of Public Health. We would also like to thank our colleagues at NIPH working with the MSIS laboratory database for providing valuable data on laboratory results for influenza and also the National Immunisation Registry (SYSVAK) for data about influenza vaccination uptake. The Emergency preparedness register for COVID-19 is of great value in the epidemiological surveillance of influenza disease and vaccination coverage, where data from the Norwegian Patient Registry (NPR) provided by the Norwegian Directorate of Health is of great value.

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With best regards,

Karoline Bragstad, Trine Hessevik Paulsen, Elina Marjukka Seppälä, Ragnhild Tønnessen, Birgitte Klüwer, Kjersti Rydland, Torstein Aune, and Olav Hungnes

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Division for Infection Control

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11 September 2022

# Appendices

## Methods

### *Influenza-like illness*

Norwegian ILI surveillance data is provided by Sykdomspulsen (sKUHR data). Sykdomspulsen receives data from the KUHR-system (hosted by the Norwegian Directorate of Health), which daily provides anonymised data on influenza diagnosed in primary health care consultations. The information is admitted to KUHR through doctors' reimbursement claims to the health authorities. Sykdomspulsen has been receiving KUHR data since 2014 and is supported by retrospective data from the 2006-07 season and onwards.

### *Virological surveillance.*

Virological sentinel surveillance: Usually, a network of volunteer sentinel physicians throughout the country collects specimens from patients with ILI for analysis at the National Influenza Centre. During the first two years of COVID-19 pandemic this sentinel network was unable to operate, because community respiratory illness testing was almost completely redirected to the SARS-CoV-2 testing infrastructures. From February 2022, an improvised virological sentinel surveillance has been reactivated, in which the participating practices send the specimens to a routine primary laboratory for rapid-turnaround testing for influenza, SARS-CoV-2 and some other respiratory viruses. The patient data and outcomes are provided to the NIC, and positive specimens forwarded for further work and biobanking.

Comprehensive virological surveillance: In addition, medical microbiology laboratories that perform influenza diagnostics report all testing outcomes in real-time to the newly established national MSIS laboratory database. Surveillance statistics for laboratory confirmed influenza has been harvested from this database. 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, and, during the COVID-19 pandemic, SARS-CoV-2 testing stations.

### *Registry-based surveillance of influenza hospitalisations*

In the 2021-2022 season, surveillance of influenza-related hospital admissions continued to be registry-based and nationwide. In the previous season, this system relied solely on data from the Norwegian Patient Registry, counting inpatient hospital admissions with ICD-10 codes for influenza (J09-J11). Since the beginning of the 2021-2022 season, the data on hospital discharge codes from NPR have been linked to data on PCR tests positive for influenza obtained from the Norwegian Surveillance System for Communicable Diseases (MSIS) laboratory database to enhance the specificity of the registry-based surveillance. Case-based data on PCR-positive influenza tests is available from season 2020-2021 onward, while historical data from the Norwegian Patient Registry is available from the beginning of year 2017. A patient hospitalised with influenza is defined as a person who has an influenza-related diagnosis code registered in NPR, who has been hospitalised overnight, and who has tested positive for influenza with a PCR test within 14 days before or up to 2 days after hospital admission. Only the first admission per season is included (readmissions excluded). The previously used, laboratory-based surveillance system for influenza-related hospitalisations was discontinued after the 2020-2021 season.

### *Influenza patients in intensive care units*

Since the 2018-19 season, almost all intensive care units (ICUs) in Norway have reported data on patients receiving intensive care with suspected or confirmed influenza to the Norwegian Intensive Care Registry (NICR) using an electronic form. Up to the 2020-2021 season, only anonymised data were reported from NICR to the NIPH. In the season 2021-2022 the NIPH has begun to receive case-based data on a daily basis, with historical data since the 2018-2019 season.

### *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. In normal times these sera are tested by the haemagglutination-inhibition (HI) test to determine the antibody immunity to relevant circulating influenza viruses. However, due to capacity limitations imposed by the response to COVID-19, the sera collected in 2020 were only tested for antibody against SARS-CoV-2 and not against influenza, and only a subset of the 2021 sera were tested against influenza.

### *Vaccine distribution and coverage*

Distribution data is gathered from Department of Infection Control and Vaccine at NIPH and from IQVIA Solutions (distribution from other wholesalers). Vaccine coverage data is gathered from the Norwegian immunisation registry SYSVAK. SYSVAK is a national, electronic immunisation registry that records an individual's vaccination status and vaccination coverage in Norway. It is mandatory to register all influenza vaccination. However, the last years the rate of registration has been around 75 % of the doses distributed (adjusted for the number of discarded doses). Coverage rates from SYSVAK is therefore minimum rates.

Coverage rate for people in risk groups under 65 years is captured from the emergency preparedness register for COVID-19 (Beredt C19). Beredt C19 includes information that has already been collected in the healthcare service, national health registries and medical quality registers, as well as other administrative registers with information about the Norwegian population.

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