THREAT ASSESSMENT BRIEF

Assessing the risk of influenza for the EU/EEA in the context of increasing circulation of A(H3N2) subclade K

21 November 2025

Summary

Circulating respiratory viruses, including influenza viruses, SARS-CoV-2 and RSV, all contribute to winter pressures on healthcare systems in the EU/EEA. In a typical season, influenza causes substantial morbidity in the European population, with up to 50 million symptomatic cases and 15 000 – 70 000 deaths annually. All age groups are affected, although children have higher illness rates and are usually the first to become sick and transmit the disease in their households, driving transmission in the community. It is estimated that up to 20% of the population are infected annually. This results in absence from school and work and a significant impact on health systems. Higher impact is seen in closed settings e.g. LTCFs, where outbreaks of seasonal influenza can have high a morbidity and mortality.

In the context of early circulation of seasonal influenza in EU/EE and the recently emerged influenza A(H3N2) subclade K that is circulating globally, ECDC decided to assess the risk of influenza for the EU/EEA to raise awareness of the potential implications and provide recommendations to public health authorities. Considerable uncertainty remains around the likely public health impact of this subclade on the influenza season.

Epidemiological situation

Compared to previous years, influenza is increasing unusually early in the EU/EEA, dominated by influenza A, with A(H3N2) driving the increases in recent weeks. This situation reflects developments recently reported by other northern hemisphere countries.

The newly emerged A(H3N2) subclade K (former J.2.4.1) has been now detected in all continents and accounts for a third of all A(H3N2) sequences deposited in GISAID between May and November 2025 globally, and almost half in the EU/EEA. Phylogenetic analysis shows a significant divergence of subclade K from the northern hemisphere A(H3N2) vaccine strain. In-vitro antigenic and serological analyses also suggest a mismatch between the vaccine and this new subclade. Real-world vaccine effectiveness (VE) data are currently limited.

A(H3N2) has not been the dominant virus in recent seasons which may lead to lowered immunity in populations without recent exposure, although serological data are not yet available to assess this further. Countries in east Asia who now report declining epidemics of A(H3N2) have not experienced unusually high disease severity and phylogenetic analysis suggest that the A(H3N2) subclade K strains circulating in these

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countries are no different from those present in the EU/EEA. Even if a less well-matched A(H3N2) virus dominates this winter, the vaccine is still expected to provide some protection against severe disease and so it remains a vital public health tool.

Risk Assessment

Based on currently available information, ECDC assesses the risk from of an influenza season dominated by A(H3N2) subclade K for the general EU/EEA population as moderate and for populations at higher risk for severe disease (people over 65 years of age, people with underlying metabolic, pulmonary, cardiovascular, neuromuscular and other chronic diseases, pregnant women or persons who are immunocompromised, and people living in closed settings such as long-term care facilities (LTCF)), as high. Even if the individual risk of severe illness remains similar to previous years, a larger epidemic driven by lower immunity to infection could result in a higher absolute number of hospitalisations and increased pressure on healthcare services. This assessment may change as more data become available.

Recommendations

- Vaccination should proceed without delay. An early influenza season means that those eligible for vaccination, especially those at higher risk of severe disease, should not wait to get vaccinated.
- Early treatment of affected individuals with influenza antivirals is essential to reduce the likelihood of complications and progression in populations at higher risk of severe disease. Antivirals become even more important in the context of a circulating influenza strain that may be poorly matched to the vaccine. Testing should guide antiviral treatment where possible, but strong clinical suspicion and the local epidemiology should also guide decisions to avoid delays that may reduce effectiveness.
- Antiviral prophylaxis can be considered in outbreaks detected in closed settings regardless of vaccination status.
- Hospitals and long-term care facilities (LTCFs) should review their preparedness plans and enhance their infection prevention and control practices to mitigate against pressure to the healthcare system during the influenza season. Use of face masks is advised for staff and visitors within hospitals and LTCFs in periods of increased respiratory virus circulation.
- Countries should provide tailored communication on how people can reduce transmission and the impact of severe disease through clear messages on vaccination, hand hygiene and respiratory etiquette.
- Countries should continue to report epidemiological and virological surveillance findings promptly via EpiPulse to support rapid assessment and response across the EU/EEA.

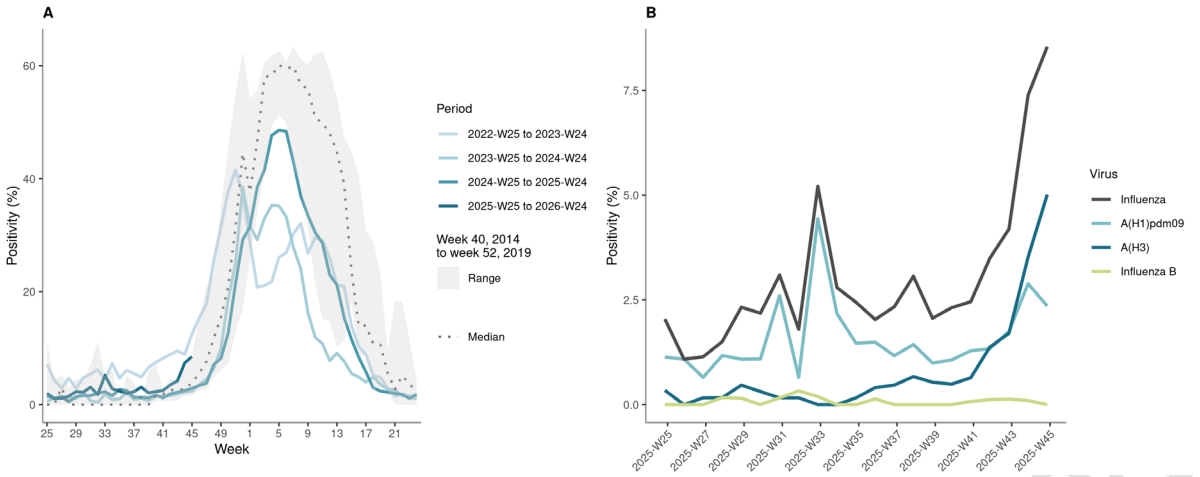
Epidemiological situation

Early increases in influenza in the EU/EEA driven by A(H3N2)

As of week 45, 2025, the number of patients presenting to primary care with symptoms of respiratory illness, including influenza-like illness, was at baseline or low levels. Although the threshold for influenza season start had not yet been reached in the EU/EEA, virological data showed an earlier than expected increasing trend, with a timing three to four weeks earlier than the two most recent seasons and at the earliest range of five pre-COVID-19 pandemic seasons (Figure 1A). To date, all EU/EEA countries with sufficient data have reported a dominance of influenza A, with A(H3N2) overtaking A(H1N1)pdm09 to drive the increasing trend in test positivity in primary care surveillance in recent weeks [1] (Figure 1B). Test positivity in primary care surveillance, an indicator of transmission, is currently highest in children aged 5-14 years, which is typical at the start of seasonal activity.

Figure 1. A. Historical comparison of influenza test positivity, 2014/25 to 2025/26 seasons.

B. Virus-specific test positivity, week 25 to 45, 2025 from primary care ILI/ARI virological surveillance, EU/EEA [2]



Virological and antigenic data concerning influenza A(H3N2) subclade K

Phylogenetic analysis of A(H3N2) subclade K strains shows a substantial divergence from the northern hemisphere vaccine strain A/Croatia/10136RV/2023 (see technical annex) and from the viruses that circulated in 2024-2025 influenza season in the EU/EEA. The newly emerged A(H3N2) subclade K (former J.2.4.1) belong to the dominating clade 2a.3a.1 and have K2N, T135K S144N(+CHO), N158D, I160K, Q173R, K189R, T328A and S378N (haemagglutinin subunit 2: S49N) substitutions in haemagglutinin gene compared to A/Croatia/10136RV/2023, the WHO recommended vaccine virus for the 2025-2026 northern hemisphere influenza season. This is a substantially higher number of mutations than has been observed in the evolution previous seasons. Subclade K accounts for 47% of the A(H3N2) virus sequences deposited on GISAID EpiFlu from 19 EU/EEA countries between 1 May and 17 November 2025. This subclade is also widespread globally. Strains belonging to subclade K have been deposited on GISAID EpiFlu from countries in Oceania, Asia, Africa, Europe and North America – and accounts for 33% of all A(H3N2) sequences deposited in GISAID (technical annex) in the same period**.**

The antigenic data published in the southern hemisphere vaccine composition meeting suggest that the northern hemisphere vaccine A(H3N2) component poorly recognises viruses from J.2.3, J.2.4 (which is the parent strain of subclade K) and J.2.5 HA subclades [3]. The findings of human serology studies also showed that, after vaccination, antibody levels against many of the recently circulating A(H3N2) viruses—especially those in J.2.2, J.2.3, J.2.4, and J.2.5 subclades —were much lower than against the vaccine reference virus [3].

There is currently limited real-world effectiveness data for available 2025–26 seasonal influenza vaccines, including their performance against influenza A(H3N2) subclade K. Available antigenic characterisation data are based primarily on ferret assays, which have known constraints. Ferret antigenic-drift indicators correlate only moderately with reductions in vaccine effectiveness (VE) against infection, and their relationship with VE against severe disease is weaker. Broader human immune responses—including cellular immunity and cross-reactive antibodies from prior infection or vaccination (including with antigenically mismatched vaccines)—may still provide meaningful protection against severe outcomes despite antigenic differences observed in vitro. This underscores the importance of robust real-world VE studies as the season progresses. In England, where A(H3N2) subclade K has dominated the early 2025–26 season, preliminary VE estimates against hospital attendance and admission are broadly similar to end-of-season estimates from recent years [4]. However, these early findings will need to be monitored closely as VE data become available from additional countries over the course of the season.

Genotypic data from TESSy in the WHO European Region showed no evidence of A(H3N2) viruses with reduced susceptibility to neuraminidase inhibitors oseltamivir or zanamivir or polymerase acidic (PA) protein inhibitor baloxavir marboxil [1]. Similar geno- and phenotypic data have been shown earlier globally [3].

A(H1N1)pdm09 and B/Vic vaccine components

A(H1N1)pdm09 and B/Victoria viruses have also continued to diversify genetically [5]. WHO data show that A(H1N1)pdm09 viruses from the D.3.1 subgroup have now become dominant worldwide, replacing earlier 5a.2a and related subgroups. The current northern hemisphere vaccine strain (Victoria/4897/2022-like) still reacts well with viruses from the older 5a.2a and 5a.2a.1 groups. However, tests using ferret antisera indicate reduced recognition of the D.3.1 viruses [3].

Antigenic testing showed that antibodies from ferrets infected with B/Austria/1359417/2021-like viruses (subgroup 3a.2), which represent the vaccine virus for the 2025–26 northern hemisphere season, reacted well with most B/Victoria lineage viruses. This included viruses that had amino acid changes in their HA protein within the C.5.1, C.5.6, C.5.6.1, and C.5.7 subclades [3].

To our knowledge, no published VE data are yet available for A(H1N1)pdm09 or B/Victoria viruses.

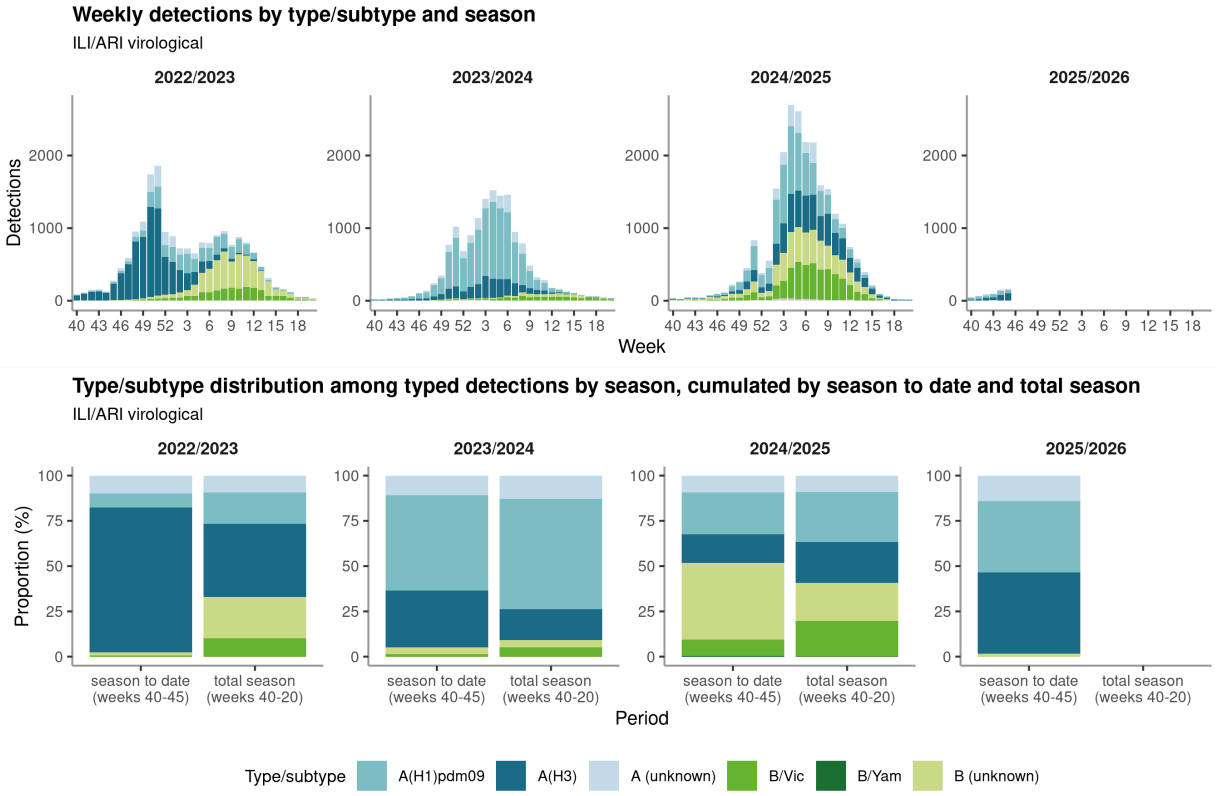
Disease severity and impact

It remains uncertain whether influenza A(H3N2) will dominate throughout the 2025/26 season or whether co-circulation with A(H1N1)pdm09 and/or B/Victoria will occur. The EU/EEA has not experienced dominant circulation of A(H3N2) since the first half of the 2022/23 influenza season (Figure 2). The 2021/22 season was also dominated by A(H3N2) but with low overall levels of activity, following 2020/21 in which circulation of influenza was interrupted due to the COVID-19 pandemic [6].

Reduced recent exposure may lower population-level protection against infection with A(H3N2), particularly among young children who may have had little or no prior exposure to this subtype. However, protection against severe disease is likely to remain more robust due to cross-reactive immunity from previous influenza infections and vaccination, consistent with observations from past seasons and post-pandemic periods.

Even if the individual risk of severe illness remains similar to previous years, a larger epidemic driven by lower immunity to infection could still result in a higher absolute number of hospitalisations and increased pressure on healthcare services. Serological data for the 2025/26 season are not yet available, and these assessments therefore remain uncertain.

Figure 2. Weekly influenza detections (top panel) and distribution of type/subtype by season in primary care ILI/ARI virological surveillance (lower panel), EU/EEA, 2022/23 to 2025/26 seasons [2]



The UK reported an unusually early start to its influenza season, dominated by A(H3N2) subclade K [4], although by week 45 indicators of transmission and severity remained at low levels [7]. Hong Kong also reported an A(H3N2)-dominated epidemic, which is now declining, with hospital admission rates that peaked at levels no higher than in previous seasons [8]. A similar picture has been reported by Taiwan [9]. Phylogenetic analysis suggests that the A(H3N2) subclade K strains circulating in these countries are no different from those present in the EU/EEA (data not shown).

In the EU/EEA, there has been limited impact of severe influenza to date, with increasing hospital admissions observed in a small number of countries as expected given the early rise in transmission. A combination of circulating influenza, RSV and SARS-CoV-2 viruses will all contribute to the overall impact of respiratory viruses on healthcare this winter. As of week 45, 2025, SARS-CoV-2 transmission continued to decrease following a summer epidemic. RSV activity remained low, with increases restricted to individual countries [1].

ECDC risk assessment for the EU/EEA

This Threat Assessment Brief has been developed based on the data available at the time of publication and follows the ECDC Rapid Risk Assessment methodology, where the overall risk is determined by a combination of the probability of infection and its impact [10].

What is the public health risk of influenza for the EU/EEA population in the current season considering the increasing circulation of A(H3N2) subclade K?

In a typical season, influenza causes substantial morbidity in the European population, with up to 50 million symptomatic cases and 15 000 – 70 000 deaths annually. All age groups are affected, although children have higher illness rates and are usually the first to become sick and transmit the disease in their households, driving transmission in the community. It is estimated that up to 20% of the population are infected annually [11]. This results in absence from school and work and a significant impact on health systems, from primary up to tertiary care, where patients with severe influenza or other complications can remain hospitalised for many days. Higher impact can be expected in closed settings e.g. LTCFs, where outbreaks of seasonal influenza can have high a morbidity and mortality. Transmission rates fluctuate during the season, so the highest rates of hospitalisations and pressure to the health system are expected for a limited number of weeks when circulation is high. There are effective pharmaceutical and public health and social measures that countries can implement during high circulation to mitigate this impact.

Risk for individuals in the general population

As in past influenza seasons, the probability of infection is considered high. For most individuals in the general population, influenza is usually a self-limiting illness, even asymptomatic for a significant percent (up to 60%), so the impact of influenza infection for individuals in the general population is estimated as low.

Therefore, the risk posed to individuals in the general population in the current season is estimated as moderate based on currently available information.

Risk for individuals at a higher risk of severe disease

The probability of infection is considered high, as in the general population. The impact of severe influenza disease from A(H3N2) subclade K for individuals with chronic conditions is currently estimated as moderate. Persons older than 65 years of age, persons with underlying metabolic, pulmonary, cardiovascular, neuromuscular and other chronic diseases as well as immunocompromised and persons living in closed settings e.g. long-term care facilities (LTCF) are at higher risk for severe influenza and complications of their chronic conditions. In addition, pregnant women are at increased risk of severe influenza disease, which can lead to severe complications for themselves and their babies [12,13]. Severe influenza leads to hospitalisation due to complications such as bronchitis, pneumonia and respiratory distress, or worsening of a chronic disease, and more rarely encephalitis and myocarditis. Hospitalisations in ICU for severe influenza disease are associated with significant mortality estimated up to 1 in 4 patients [14].

Therefore, the overall risk to individuals in this population group is assessed as high based on currently available information.

Limitations and uncertainties posed by A(H3N2) subclade K

While the above assessment is typical of the risk associated with seasonal influenza, there may be additional challenges posed specifically by A(H3N2) subclade K circulation, in terms of early season start and A(H3N2) dominance across the season, that could increase the overall risk. Key knowledge gaps that could alter our assessment include: the level of population immunity to A(H3N2), the severity of disease associated with A(H3N2) subclade K; the durability of vaccine effectiveness against severe disease outcomes for A(H3N2) subclade K; and the relative proportion of A(H3N2) viruses versus other subtypes over the course of the whole season. These uncertainties underscore the importance of preparedness, timely surveillance, and ongoing response measures.

ECDC continues to monitor the situation and may update this assessment as needed during the season.

ECDC recommendations

Vaccination

Vaccination should proceed without delay. Vaccination is the most effective measure to protect against severe influenza. ECDC scenario modelling conducted for September 2024–May 2025 using EU/EEA primary-care consultation data for influenza-like illness in adults aged 65 years and over, showed that higher influenza vaccine

uptake is strongly associated with lower disease burden—a finding that remains relevant for the 2025–26 season [15]. An early season means individuals—particularly those at higher risk, including older adults, individuals with chronic medical conditions, pregnant women, and healthcare workers—should receive the influenza vaccine as soon as possible. Vaccination of healthcare workers may also reduce transmission to patients and limit pressure on healthcare systems due to staff absence. Even if a less well-matched A(H3N2) virus dominates this winter, the vaccine is still expected to provide protection against severe disease [4]. Most EU/EEA Member States now recommend seasonal influenza vaccination for children [16]. Vaccinating children—according to national guidelines—helps protect them from severe influenza and its complications, with the greatest benefit seen in those younger than five years of age. Childhood vaccination against influenza has been shown to offer indirect protection of other age groups in some settings, which is important given the role children play in transmission [17]

Use of antivirals

Where indicated, early treatment is essential. Antivirals are most effective when given promptly (ideally within the first 48 hours of symptom onset, or within 36 hours in the case of zanamivir in children) and can help reduce the likelihood of complications and progression to severe outcomes, particularly in groups at higher risk. Countries should ensure timely availability and simple access pathways for antiviral treatment in the community and in hospitals for these groups, irrespective of vaccination status [18].

Testing should guide treatment where possible. Ideally, a confirmed influenza diagnosis (rapid antigen test or laboratory confirmation) should support prescribing. Where confirmation is delayed or unavailable, antiviral treatment for individuals at high risk for severe influenza should be considered based on strong clinical suspicion and local epidemiology indicating influenza circulation, to avoid delays that may reduce effectiveness.

Prophylactic use is indicated in specific contexts. While protection from severe disease at the onset of infection and symptoms is the primary indication for antiviral use, they can also be considered for preventing transmission and severe disease in certain high-risk settings, such as healthcare facilities or long-term care facilities (LTCFs) during confirmed or suspected outbreaks, regardless of vaccination status [18,19].

Prepare for winter pressures to the healthcare system

Review preparedness plans for healthcare facilities. While there are uncertainties regarding the likelihood and impact of an earlier influenza season, as well as the dominance of A(H3N2) influenza viruses relative to other subtypes over the course of the season, countries are advised to activate and implement winter preparedness plans for their healthcare facilities, including staffing arrangements, in anticipation of potential increases in patient demand driven by influenza as well as other respiratory viruses that will circulate this winter.

Strengthen infection prevention and control (IPC) measures. During periods of high respiratory-virus activity, staff and visitors in healthcare and long-term care settings should follow a layered approach, as outlined in ECDC infection prevention and control guidance [20]. This includes early identification and separation of symptomatic patients, cohorting where appropriate, using testing to guide patient placement, and implementing mask use (a properly fitted FFP2 respirator or surgical mask according to the clinical task) for all staff when in contact with patients and visitors. Healthcare workers exhibiting respiratory symptoms should be promptly tested, provided with antiviral treatment, as needed, and, if possible, removed from clinical duties until their symptoms resolve. Maintaining strict hand hygiene, regular environmental cleaning, optimised ventilation of closed spaces, and the appropriate use of personal protective equipment all help reduce healthcare-associated transmission of influenza.

Risk communication

Provide clear, targeted communication to support protective behaviours. Risk communication efforts should prioritise timely, audience-specific messaging through accessible channels, ensuring that both the public and professionals understand the evolving situation and know how to reduce risk. Communication should reinforce key protective behaviours, such as regular handwashing, covering the mouth and nose when coughing or sneezing, staying at home when ill, and ventilating closed spaces, alongside strong promotion of seasonal influenza vaccination. Tailored messaging for high-risk groups, parents of young children, healthcare workers and LTCF staff should be prioritised, using channels appropriate to each audience.

Surveillance and reporting

Maintain strong, timely reporting. Countries should continue to report epidemiological and virological surveillance findings promptly via TESSy—according to ECDC's operational guidance for integrated respiratory virus surveillance [21] – especially signals relating to antiviral resistance and disease severity, to support rapid assessment and response across the EU/EEA. Subtyping of detections from virological ILI/ARI/SARI surveillance remains important.

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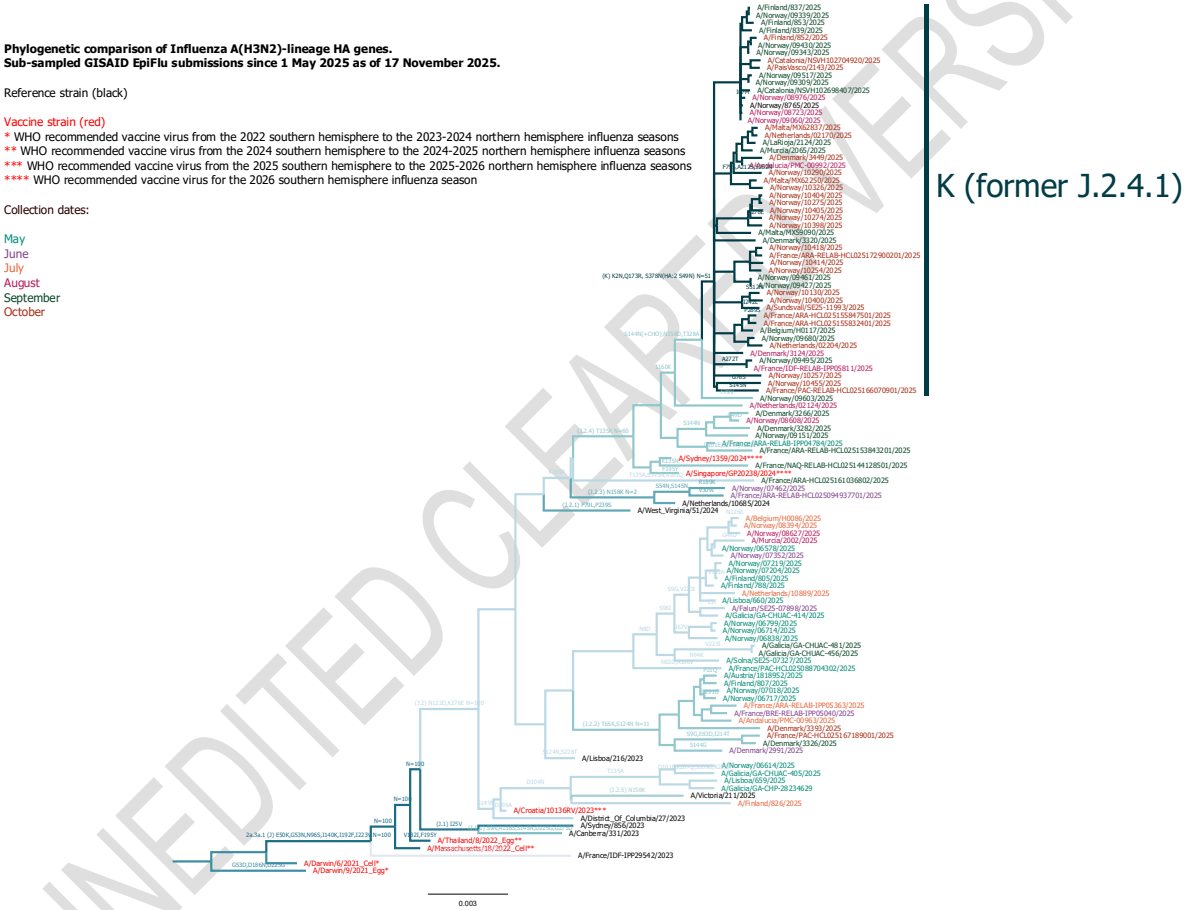
Technical annex

Phylogenetic analysis

The subclade K (formerly assigned as J.2.4.1 and represented by reference virus A/Norway/8765/2025), is a branch within the dominating clade 2a.3a.1 of subtype A(H3N2), characterised by a substantial number of amino-acid HA substitutions: K2N, S144N(+CHO), N158D, I160K, Q173R, T328A and S378N (HA:2 S49N) compared to A/Sydney/1359/2024 and A/Singapore/GP20238/2024, the WHO recommended vaccine viruses for the 2026 southern hemisphere influenza season, and additionally T135K and K189R compared to A/Croatia/10136RV/2023, the vaccine strain recommended for the 2025-2026 northern hemisphere (Fig A1). The rapid increase of K is reflected by GISAID EpiFlu submissions, from no detections included in virological surveillance data between week 40 2024 to week 33 2025 from 30 European Union and European Economic Area (EU/EEA) countries [5], to a total proportion since May 2025 of A(H3N2) of 47% (n=213) and 33% (n=1 506) globally as of 17 November 2025. Phylogenetic analysis was performed using the Nextstrain [22] build for seasonal influenza viruses as previously described [5].

Figure A1. Phylogenetic comparison of 100 sub-samples of influenza A(H3N2) HA gene data submissions to GISAID EpiFlu database for EU/EEA countries, 1 May-17 November 2025 (Source: GISAID).



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