SURVEILLANCE REPORT

Seasonal influenza 2021–2022

Annual Epidemiological Report

Key facts

- The 2021–2022 influenza season in the EU/EEA marked the return of influenza virus activity after a low-level circulation following the onset of the COVID-19 pandemic.
- Despite increased influenza activity in 2021–2022 compared to the 2020–2021 season, the circulation and timing were not comparable with any annual influenza epidemic activity observed before the COVID-19 pandemic or after the 2009 influenza pandemic.
- The seasonal pattern showed an unprecedented late onset, crossing the epidemic threshold in week 08/2022, with an overall shorter duration compared to all seasons since 2009.
- The overall low and late onset of influenza virus circulation during the 2021–2022 season might have been influenced by the COVID-19 pandemic and measures implemented in the countries during the winter period, leading to late activity when measures were lifted.
- As Member States move towards integrating surveillance of SARS-CoV-2, influenza and other relevant respiratory viruses, underlying systems may change and in the future reported data may not be comparable with historical data.

Methods

For a detailed description of methods used to produce this report, please refer to the Methods chapter [1].

An overview of the national surveillance systems is available online [2].

Additional data on influenza are available from ECDC's online 'Surveillance atlas of infectious diseases' [3].

Surveillance of influenza in EU/EEA countries is carried out by the European Influenza Surveillance Network (EISN), coordinated by the European Centre for Disease Prevention and Control (ECDC).

EU/EEA influenza surveillance is based on weekly data reported to ECDC by sentinel general practitioners (in some countries also by other physicians, such as paediatricians) and national influenza reference laboratories from week 40 to week 20 of the following year.

Surveillance data include:

- Qualitative indicators of influenza activity, namely intensity, geographical spread and trend. Intensity - ranging from low activity (i.e. no activity or activity at baseline level) to very high - is an indicator of the level of influenza activity. Geographical spread - ranging from no activity to widespread - refers to the number of affected areas in a given country. Trend – increasing, stable or decreasing – compares the level of ILI/ARI sentinel consultations with the previous week.

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Stockholm, December 2022

- The aggregate number of influenza-like illness (ILI) and/or acute respiratory infection (ARI) cases reported by sentinel physicians[1] [2]. Each country also reports denominator data (population covered by sentinel surveillance) to enable calculation of weekly ILI and ARI consultation rates.
- The aggregate number of sentinel specimens obtained from a systematic sample of ILI/ARI patients testing positive for influenza, by type, A subtype and B lineage [2]. Overall positivity rates of sentinel specimens are used to estimate the start, duration and end of influenza activity; a 10% threshold is used to indicate the start of the seasonal epidemic.
- Antigenic and genetic characterisation and strain-based antiviral susceptibility data for a subset of influenza viruses detected in sentinel and non-sentinel specimens [2].
- Case-based hospital data reported by a subset of countries on a voluntary basis[2], including demographic, clinical and virological data [2].

Since the 2014–15 season, influenza surveillance in the 53 countries of the WHO European Region has been jointly coordinated by ECDC and WHO's Regional Office for Europe. Results are disseminated through a joint weekly bulletin (www.FlunewsEurope.org) [4].

This report presents data from EU/EEA countries. Archived weekly data from October 2014 onwards are available from: http://www.flunewseurope.org/Archives [4].

Seasonal data in this report, covering the period from week 40/2021 to 20/2022, were extracted from the database during week 38/2022 for the reporting week 20/2021.

Sentinel surveillance

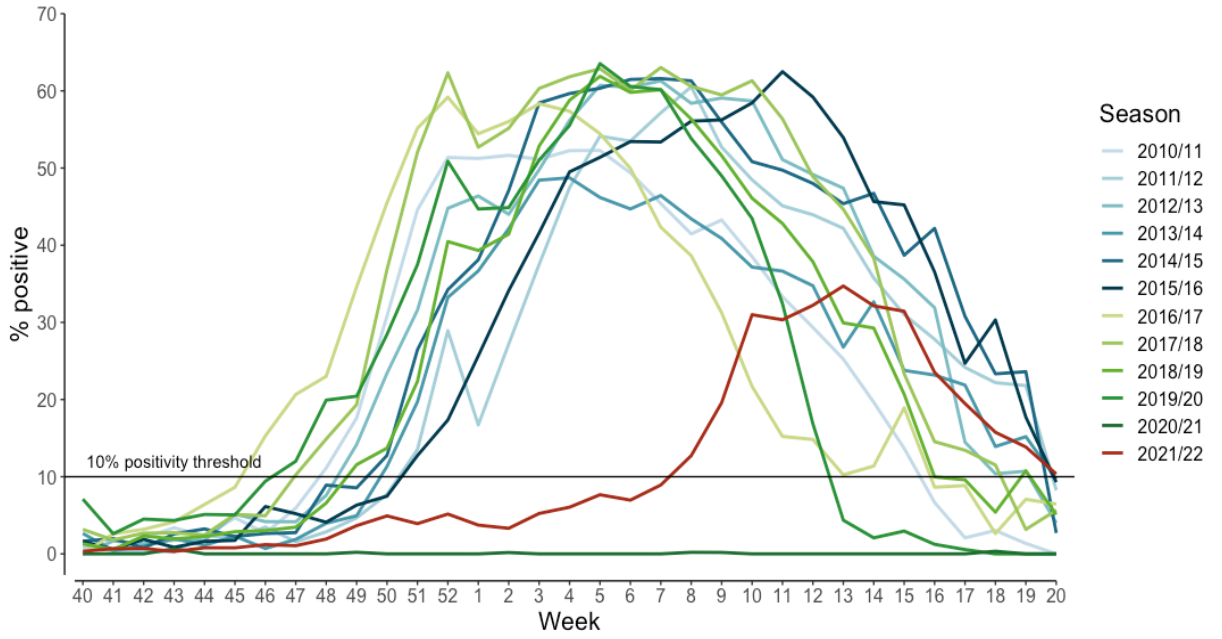
During the 2021–2022 season, 35 096 specimens from sentinel primary care providers were tested for influenza in EU/EEA countries and 4 609 (13%) of the specimens tested positive for influenza virus. The number of influenza virus detections from sentinel sources (n=4 609) increased compared to the 2020–2021 season (n=10), however, it was still lower than that of any earlier season - e.g. 2019–2020 (n=11 978) and 2018–2019 (n=16 472) [5-7].

In week 8/2022, the weekly percentage of sentinel specimens positive for influenza crossed the 10% threshold, signalling that the seasonal epidemic was beginning later than usual in the EU/EEA countries (based on data from 2018–2019 and 2019–2020). Furthermore, the 2021–2022 season was much shorter than previous seasons, excluding the 2020–2021 season, with only 13 weeks above the 10% positivity threshold. Between 2010–2011 and 2019–2020, seasonal influenza seasons lasted between 18 and 24 weeks. The percentage of positive specimens peaked at 36% in week 13/2022, with influenza activity decreasing from this point onwards. At no point in the season were influenza viruses circulating at high levels (based on proportions of 40% and above of sentinel specimens testing positive for influenza virus). The peak of the 2021–2022 season was lower and occurred later than in previous seasons, excluding the 2020–2021 season (Figure 1).

Of 4 609 positive sentinel specimens, 98.7% were type A and 1.3% were type B virus. Of 4 548 influenza A viruses, 4 105 were subtyped with 348 (8.5%) reported as A(H1N1)pdm09 and 3 757 (91.5%) as A(H3N2). Of 61 influenza B viruses reported, only 11 were ascribed to a lineage; of these all were B/Victoria viruses, and no B/Yamagata viruses were reported (Figure 2). Different proportions of type A subtypes were observed among the countries.

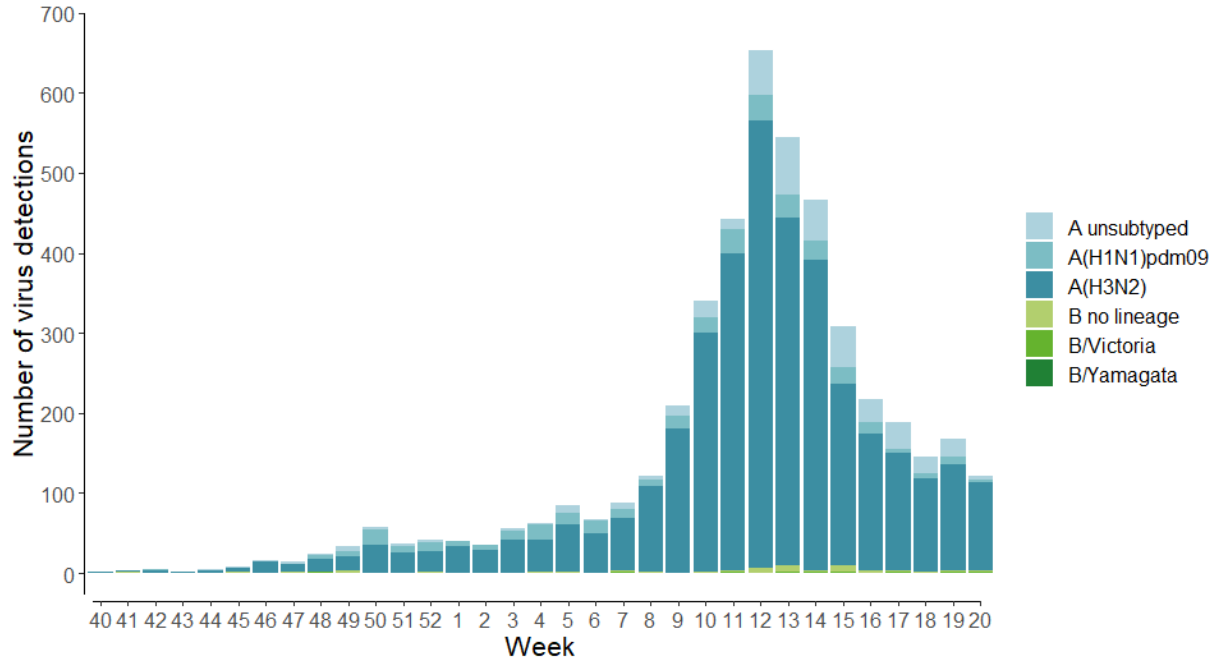
[1] ILI and a denominator were reported by Austria, Belgium, Croatia, Czechia, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, and Slovenia. ARI and a denominator were reported by Belgium, Bulgaria, Czechia, Denmark, Estonia, Finland, France, Germany, Latvia, Lithuania, Luxembourg, Malta, Portugal, the Netherlands, Romania, Slovakia, Slovenia, and Spain.

Figure 1. Weekly proportion of sentinel specimens positive for influenza virus by season and week of reporting, EU/EEA, 2010–11 to 2021–22



**Seasons 2015–2016 and 2020–21 have 53 weeks of reporting.*

Figure 2. Influenza virus detections from sentinel surveillance by virus (sub)type and lineage and week of reporting, weeks 40/2021 to 20/2022, EU/EEA



Non-sentinel surveillance

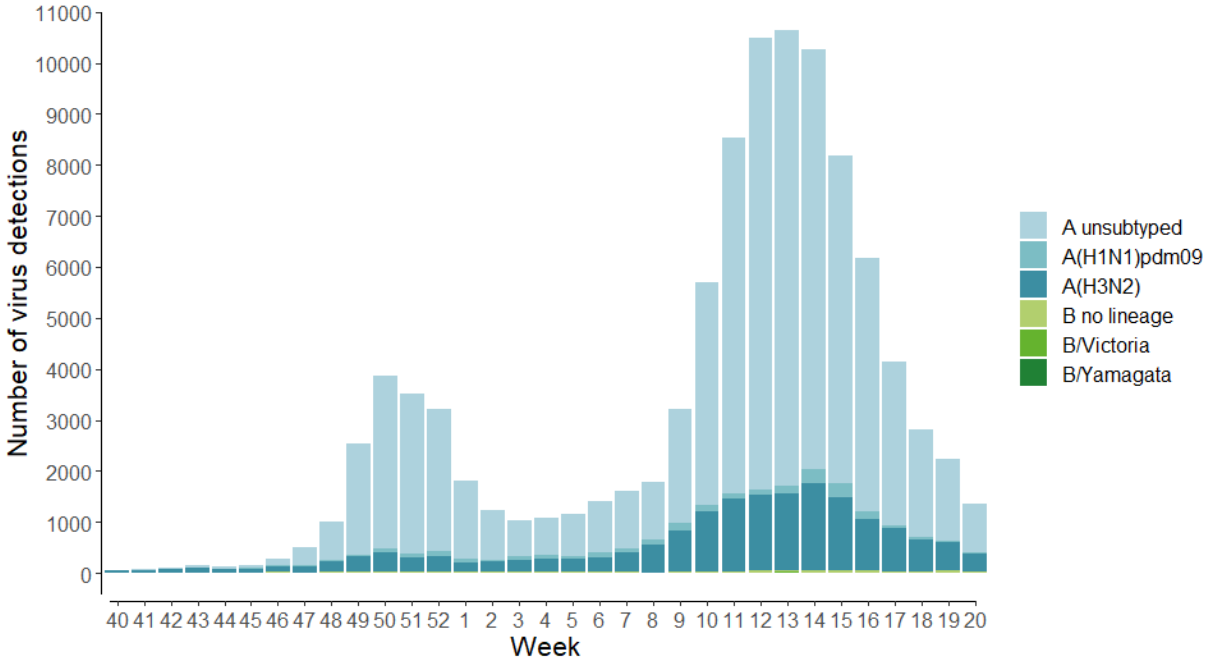
During the 2021–2022 season, 2 016 434 specimens from non-sentinel sources were tested for influenza in EU/EEA countries and 100 453 (5%) of them tested positive. The highest number of virus detections was observed during similar reporting periods in sentinel and non-sentinel surveillance – week 12 and 13, respectively. (Figures 2 and 3).

Of 100 453 positive sentinel specimens, 99.2% were type A and 0.8% were type B viruses; comparable proportions were seen in sentinel surveillance data. Of 99 614 influenza type A viruses, 19 724 (19.8%) were

subtyped with 17 263 (87.5%) reported as influenza A(H3N2) and 2 461 (12.5%) were A(H1N1)pdm09. There was a much higher proportion of un-subtyped type A viruses (80.2%) in non-sentinel surveillance data than in sentinel surveillance (9.7%). Of 839 influenza type B viruses, 94 (11.2%) were assigned to a lineage: 92 (97.9%) were B/Victoria and two (2.1%) were B/Yamagata (Figure 3). The reported Yamagata viruses were most likely vaccination-related detections following live attenuated virus vaccination (LAIV) of children (personal communication) [8].

The number of specimens tested in sentinel and non-sentinel sources was comparable to previous seasons.

Figure 3. Influenza virus detections from non-sentinel surveillance by virus (sub)type and lineage and week of reporting, weeks 40/2021 to 20/2022, EU/EEA



Hospitalisations due to influenza

Laboratory-based surveillance from intensive care units (ICU) and other wards (non-ICU)

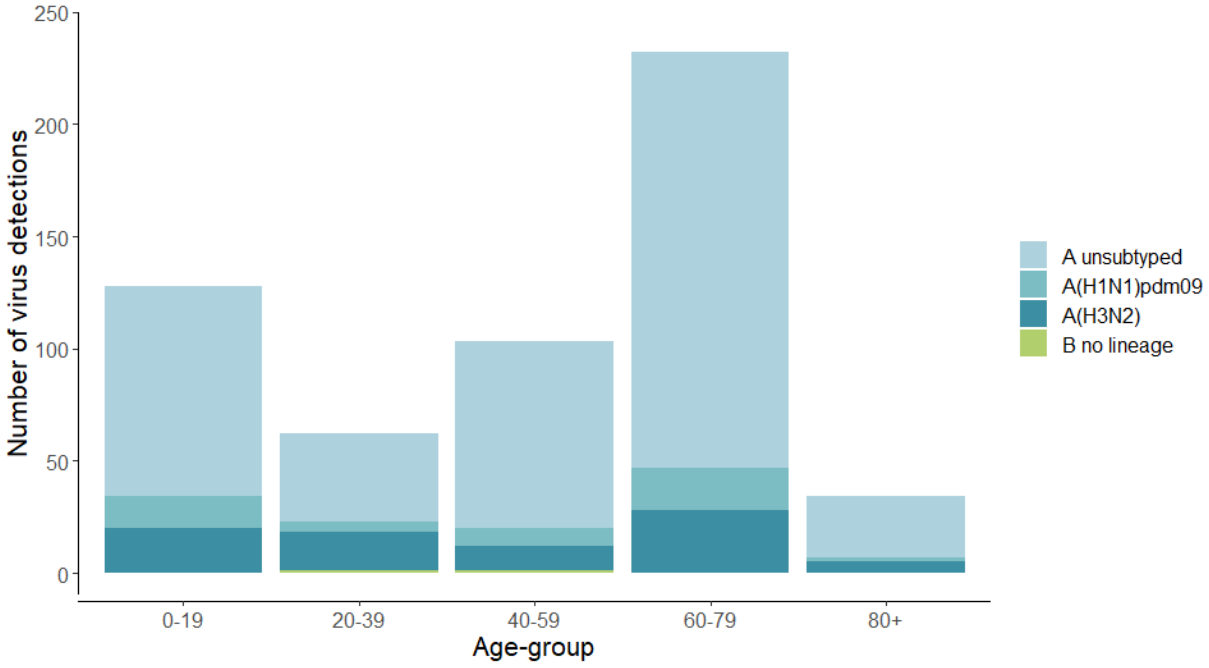
Four countries (Czechia, France, Ireland, and Sweden) reported a total of 1 105 laboratory-confirmed hospitalised influenza cases during the 2021−2022 influenza season. All four countries reported intensive care unit (ICU) cases while only Czechia and Ireland reported non-ICU cases. Most hospitalised cases (1 100; 99.5%) were due to influenza type A viruses and five were reported as type B without lineage determination.

In laboratory-confirmed influenza cases reported from ICU (n=565), influenza virus type A and type B viruses were detected in 99.6% and 0.4% of all patients, respectively. France reported 426 (75%) of the cases in ICU, followed by Sweden (110; 19%), Ireland (17; 3%) and Czechia (12; 2%). The majority of severe cases occurred in individuals aged 60−79 years (41.5%) followed by 0−19 (22.9%), 40−59 (18.4%), 20−39 (11.1%) and 80+ years (6.1%). In all age groups, influenza A viruses, specifically those reported without subtype, constituted most of the virus detections in ICU (n=428); of the subtyped viruses (n=129), more influenza A(H3N2) infections (62.8%) were detected than A(H1)pdm09 (37.2%) (Figure 4).

In laboratory-confirmed influenza cases reported from non-ICU wards (n=540), most of the viruses detected were type A viruses (537; 99.4%), with only three (0.6%) type B viruses. Among the influenza A detections, most viruses were reported as un-subtyped (401; 74.7%) followed by A(H3N2) (133; 24.8%) and A(H1N1)pdm09 (3; 0.6%).

Of 1 093 hospitalised patients with laboratory-confirmed influenza, 87 were reported to have died; 78 deaths occurring in ICU and nine in non-ICU wards. Most deaths were attributed to un-subtyped influenza A virus (68; 78.2%), followed by A(H3N2) (14; 16.1%) and A(H1N1)pdm09 A(H3N2) (5; 5.7%). No fatalities were caused by influenza type B viruses. Similarly, of 78 reported deaths in ICU, 62 (79.5%) were reported as un-subtyped influenza A virus, 11 (14.1%) as A(H3N2) and five (6.4%) as A(H1N1)pdm09. Overall, the majority of deaths occurred in individuals aged 60−79 (54; 62.1%) years followed by 40−59 (15; 17.2%), 80+ years (11; 12.6%), 0-19 (4; 4.6%), and 20−39 years (3; 3.4%). Comparable proportions were seen in ICU fatalities.

Figure 4. Distribution of virus types, subtypes and lineages by age group in ICU, weeks 40/2021 to 20/2022, EU/EEA



Severe acute respiratory infection (SARI) based surveillance

Eight countries (Belgium, Ireland, Romania, Croatia, Germany, Lithuania, Malta and Spain) reported 51 291 SARI patients from hospital settings, 2 822 of which resulted in fatal cases. Samples from 3 533 SARI patients were taken for influenza testing and 314 (8.9%) were positive. All known influenza type cases (301) were due to influenza type A.

Virus characterisations

For specimens collected since week 40/2021, genetic characterisation data of 4 973 viruses were reported to TESSy. Among the genetically characterised viruses, 4 880 (98%) were influenza A and 93 (2%) influenza B viruses.

Of the 410 characterised A(H1N1)pdm09 viruses (8% of all influenza A viruses), only 45 (11%) were represented by clade 6B.1A.5a.2 viruses, such as A/Victoria/2570/2019, the virus component for 2022–2023 northern hemisphere vaccine, or A/India/Pun-NIV312851/2021, while the remaining 365 (89%) belonged to the 6B.1A.5a.1 group, represented by A/Guangdong-Maonan/SWL1536/2019.

For the 4 470 genetically characterised A(H3N2) viruses (92% of influenza A viruses), the majority, 4 448 (99%), belonged to clade 3C.2a1b.2a.2, represented by A/Bangladesh/4005/2020, which is in the same clade as the recommended vaccine virus strain A/Darwin/9/2021 for the 2022–2023 northern hemisphere influenza season. Of the remainder, 20 (<1%) belonged to the subclade 3C.2a1b.1a, represented by A/Denmark/3264/2019, and two (<1%) were 3C.2a1b.2a.1, represented by A/Cambodia/e0826360/2020.

The B/Victoria lineage constituted 93 characterised viruses. Most of these, 63 (68%) viruses belonged to clade V1A.3a.2, represented by B/Austria/1359417/2021, the recommended vaccine virus strain for the 2022–2023 northern hemisphere influenza season. The remaining 30 (32%) belonged to clade V1A.3, represented by B/Washington/02/2019 and these were only reported by the Netherlands.

There were no reports of B/Yamagata lineage virus characterisations.

Antiviral susceptibility

Since week 40/2021, 3 425 viruses were assessed genotypically and/or phenotypically for susceptibility to oseltamivir (388 A(H1N1)pdm09, 2 940 A(H3N2) and 97 B viruses) and 3 389 viruses for susceptibility to zanamivir (387 A(H1N1)pdm09, 2 905 A(H3N2) and 97 B viruses). During this period, 2 775 viruses were assessed genotypically for susceptibility to baloxavir marboxil (302 A(H1N1)pdm09, 2 415 A(H3N2) and 58 type B viruses). Genotypically, one A(H1N1)pdm09 virus was found to carry H275Y in NA which is associated with highly reduced inhibition by oseltamivir. Four A(H3) viruses were carrying S331R in NA which has been reported to be associated

with reduced inhibition by both oseltamivir and zanamivir. However, S331R has been also associated with altered sialidase kinetics and resistance has not been tested phenotypically. One A(H3) virus was carrying E23G in PA and one A(H3) virus was carrying I38T in PA that are associated with reduced susceptibility to baloxavir marboxil. Phenotypically no viruses were identified with reduced susceptibility.

Vaccine effectiveness

On 25 February 2021, WHO published recommendations for the components of influenza vaccines for use in the 2021–2022 northern hemisphere influenza season [9]. Compared to the northern hemisphere 2020–2021 vaccines, three changes in the vaccine virus components were recommended. The A(H1N1)pdm09 component was replaced with A/Victoria/2570/2019 (H1N1)pdm09-like virus for egg-based vaccines, as well as A/Wisconsin/588/2019 (H1N1)pdm09-like virus for cell- or recombinant-based vaccines and the A(H3N2) component was replaced with A/Cambodia/e0826360/2020 (H3N2)-like virus for all vaccines [9,10]. The recommended vaccine composition for the 2022–2023 influenza season in the northern hemisphere is: an A/Victoria/2570/2019 (H1N1)pdm09-like virus, an A/Darwin/9/2021 (H3N2)-like virus, a B/Austria/1359417/2021 (B/Victoria lineage)-like virus, and a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus [11].

Preliminary influenza vaccine effectiveness (VE) for the 2021–2022 season against influenza A from seven study sites, reported by the European I-MOVE network, was 36% (95% CI: 14-71%) among all ages and 41% (95% CI: 15–59%) among those aged 18–64 years [12]. VE against influenza A(H3N2) specifically was 35% (95% CI: 6–54%) for all ages and 37% (95% CI: 3–59%) among those aged 18–64 years [12].

In Sweden, VE against laboratory-confirmed influenza for individuals over 65 years of age was estimated to be 47% [13]. In France, VE was estimated to be 50% (95% CI: 14-71%) against all circulating influenza viruses, 77% (95% CI: 36-92%) for A(H1N1)pdm09 and 31% (95% CI: -29-64%) for A(H3N2) [14].

Interim results on vaccine effectiveness (VE) in Denmark indicated 2021–2022 influenza VE estimates to be 62.7% and 64.2% in hospitalised and non-hospitalised children aged 2-6 years, respectively [15]. Furthermore, VE was 24.8% in non-hospitalised patients aged 7-44 years and non-significant in adults over 45 years [15].

A study from the United States, conducted among children, adolescents and adults, measured VE against medically attended outpatient ARI associated with influenza A(H3N2) virus and showed non-statistically significant effectiveness of 16% (95% CI = -16% to 39%) [16].

Discussion

The 2021–2022 influenza season marked the return of influenza virus activity after a period with very little circulation following the onset of the COVID-19 pandemic in the EU/EEA [5]. Unlike the previous season, 2021–2022 did have a seasonal pattern, however, onset was unprecedentedly late, as illustrated by the 10% positivity threshold only being crossed in week 08/2022. Furthermore, the season was of a shorter duration than any other season since the 2009 pandemic. In addition, influenza activity continued for a longer time at low levels and only returned to baseline in week 20 of 2022.

The overall low and late onset of influenza virus circulation during the season 2021–2022 might have been influenced by the COVID-19 pandemic and the measures implemented in countries during the winter period, leading to late activity when measures were lifted.

Circulation of influenza type A, mainly A(H3N2) viruses, dominated this season in primary care as well as in hospital settings. Following the return of influenza circulation, severe cases were reported, mostly among those aged 60 years or older.

Public health implications

Despite higher influenza activity in 2021–2022 than in the 2020-2021 season, the circulation and timing were not comparable with any annual influenza epidemic activity observed before the COVID-19 pandemic. As Member States move towards integrating surveillance of SARS-CoV-2, influenza and other relevant respiratory viruses, underlying systems may change and in the future reported data may not be comparable with historical data [17]. Continued surveillance activities for respiratory viruses, including influenza, are crucial for understanding the epidemiological situation as well as assessing pressure and burden on healthcare and population groups. In particular, severe disease surveillance in hospitals should be further developed and strengthened.

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