RAPID RISK ASSESSMENT

Intensified circulation of respiratory syncytial virus (RSV) and associated hospital burden in the EU/EEA

12 December 2022

Summary

In recent weeks, respiratory syncytial virus (RSV) circulation in the EU/EEA has intensified, with increasing transmission rates in all population groups and an earlier-than-usual start of the season. Several EU/EEA countries are experiencing high RSV circulation and the number of severe acute respiratory infections (SARI) due to RSV is increasing. At this time of the year RSV infections are not unusual, however this year there is more RSV activity and it began earlier than in pre-COVID-19 seasons.

RSV infection generally causes mild disease, but the severity of clinical manifestations varies considerably. Those most affected by RSV-associated severe disease are children below five years (particularly infants under six months), adults aged 65 years and above and individuals with specific comorbidities. Hospitalisations caused by RSV and other respiratory pathogens, such as influenza virus and SARS-CoV-2, are increasing in a number of Member States, and are already placing pressure on healthcare systems.

Although several vaccine candidates are in clinical development for infants, pregnant women and older adults, there are currently no licensed vaccines available to prevent RSV infection. Effective passive immune prophylaxis is available and this is recommended for high-risk infants. At present, there are no specific therapeutic options for RSV infection, and treatment of hospitalised patients is mainly supportive.

Combining the probability of infection and the impact of the associated disease, the risk from RSV infection is assessed as **low** for the general population, and **high** for infants under six months, adults 65 years and above and individuals with specific comorbidities.

The risk that co-circulating RSV, influenza virus and SARS-CoV-2 will place pressure on EU/EEA healthcare systems in the coming weeks is assessed as **high**.

Given the increased circulation of respiratory viruses, including RSV, the main options for response for EU/EEA national public health authorities are set out below.

- Implement risk communication activities for the public, including active promotion of vaccinations against seasonal influenza and COVID-19.
- Increase awareness among healthcare professionals to ensure timely diagnosis of cases and enhance hospital preparedness to manage increased patient load in outpatient and inpatient settings. This is particularly important for paediatric hospitals and intensive care units, but also for long-term care facilities (LTCF).
- Provide RSV prophylaxis for high-risk infants in accordance with national guidelines.
- Implement appropriate infection prevention and control (IPC) measures based on the local epidemiological situation, particularly for vulnerable groups within healthcare facilities, including LTCFs.
- Promote good hygienic practices in the community and consider appropriate non-pharmaceutical interventions (NPIs), including targeted guidance for risk groups and care-givers of vulnerable groups. This includes staying home when ill; good hand and respiratory hygiene, including appropriate use of face masks; appropriate ventilation of indoor spaces; use of teleworking where possible, and avoiding crowded public spaces, including public transportation, to reduce the spread of RSV and other respiratory viruses.
- Where possible, implement and improve surveillance of RSV and testing for respiratory pathogens. ECDC encourages Member States to continue reporting influenza, SARS-CoV-2, and RSV infection and hospitalisation data from sentinel and non-sentinel sources.

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Event background

Since the end of October 2022 and as of week 47, media and national reports from official public sources in various EU/EEA countries have indicated an increase in paediatric hospitalisations and growing pressure on hospitals due to respiratory syncytial virus (RSV) infections causing bronchiolitis. Meanwhile, there is concurrent circulation of other respiratory pathogens, such as influenza virus and SARS-CoV-2. National data reported to ECDC's European Surveillance System (TESSy) also show an increased level of RSV circulation (see below). Data on RSV detections, total number of specimens tested, and positivity rates are also publicly available in ECDC's Surveillance Atlas of Infectious Diseases [1].

In Denmark, as of 1 December 2022, the cumulative number of RSV related admissions was 3 323, with 71 deaths. The current season began later than the 2021/2022 season, but both have been characterised by an extraordinarily high RSV circulation and an earlier peak than in pre-COVID-19 seasons. Over 45% of all hospitalisations involved children under the age of one year, with one-third (1 216/3 323) involving infants under six months [2].

In France, according to Santé Publique France, current RSV circulation and related childhood hospitalisations far exceed the epidemics of the previous years. As of week 47 in 2022, bronchiolitis was responsible for 56% of hospitalisations in the 0–2 years age group following an emergency room visit. This represents a 16% increase within a week since week 46. On 9 November, Santé Publique France published a press release alerting clinicians and the general public to the upcoming epidemic season for RSV, describing preventive measures and giving advice on the most common symptoms in children [3].

In Ireland, as of week 47 the cumulative number of notified RSV cases for the current season was 4 470, an increase of 35% compared to the previous season. Thirty-seven percent of RSV cases were hospitalised, with an age-specific hospitalisation rate of 36.8/100 000 population in the 0–4 years age group. One outbreak was also reported in a nursing home during week 47/2022. Overall, the RSV epidemic in Ireland exhibits the same early onset as in the previous season, occurring several weeks earlier than the median for seasons during the period 2014–2020 [4].

In the Netherlands, as of 1 December, a sharp increase has been reported in laboratory-confirmed RSV cases. In addition, increasing detections of RSV have been reported in samples from patients with acute respiratory infections (ARI) in primary care sentinel surveillance (up to 22% positive in week 47). There has also been an increase in paediatric hospitalisations due to (RSV-) bronchiolitis in young children [5].

In Portugal, as of week 47, authorities reported an increasing trend in RSV-related hospitalisations of children under two years. In this age group, there have been 171 cumulative hospitalisations during the current season, with approximately 50% of cases aged under three months [6].

In Spain, RSV-related hospitalisation rates up to week 47 remained high and, although they were decreasing in the 0–4 years age group (100 cases per 100 000 population), they were increasing in those aged over 79 years (29.6 cases per 100 000 population) [7]. The Spanish Society of Paediatric Emergency Medicine published a statement expressing their concern about the increased volume of admissions in paediatric emergency departments [7].

In Germany, as of week 47, according to the Robert-Koch Institute, there has been a continuous increase in severe acute respiratory illness (SARI) in the 0–4 years age group during the current season. The levels are comparable to those seen in seasons with higher RSV activity (2018/2019 and 2021) [8]. In addition, German media have reported that there is reduced paediatric hospital staff capacity due to sick leave caused by influenza, SARS-CoV-2 and RSV infections [9].

In the USA, in late October and November 2022, media reported an unusually high RSV circulation associated with an increase in paediatric hospitalisations [10,11]. As of week 47, official public sources are describing an earlier-than-usual start to the current season and higher hospitalisation rates for RSV compared to pre-pandemic seasons, with cumulative hospitalisation rates of 318 per 100 000 population in children aged 0–4 years [12].

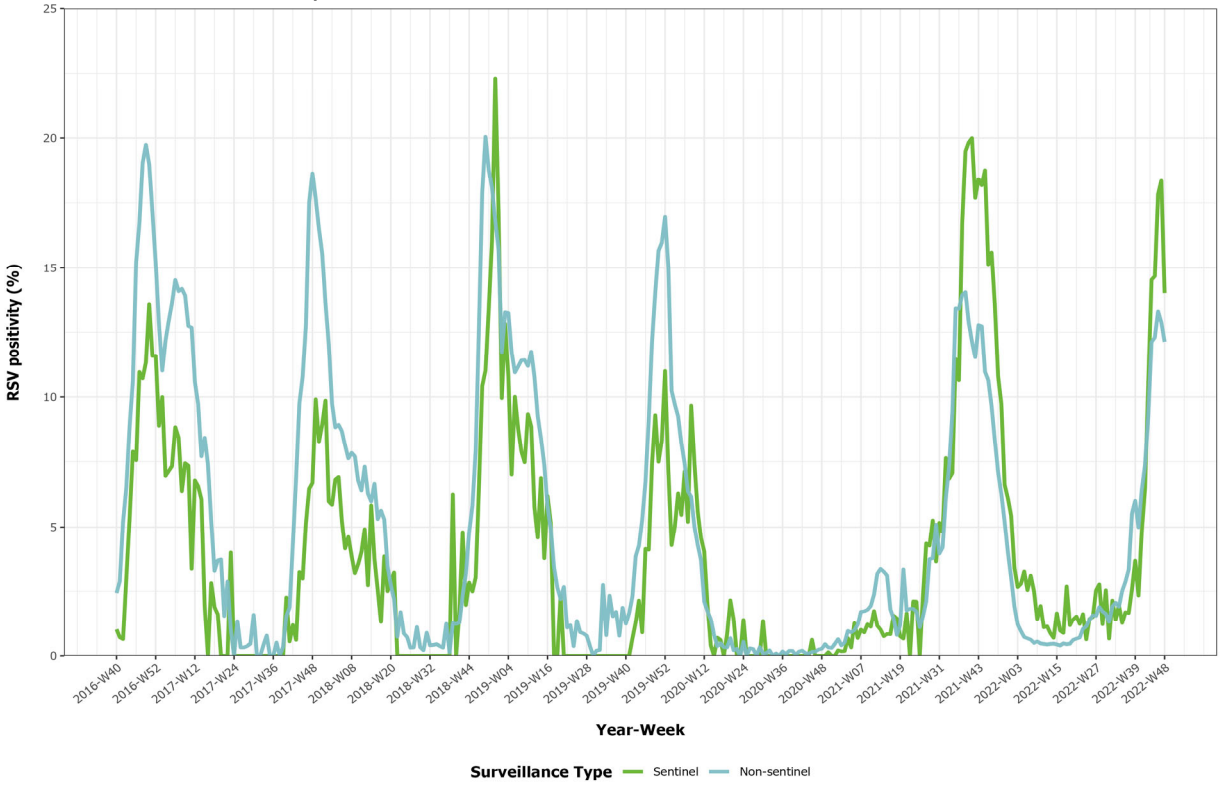
In Australia, during the past winter season, the national public health authorities reported that RSV infections exceeded the quarterly and annual rolling mean from mid-May and June 2022 [13].

RSV data reported to The European Surveillance System (TESSy)

Since week 40/2022, the start of the reporting period for respiratory viruses, and for the weeks up to week 47/2022, 23 EU/EEA countries reported 25 838 RSV detections to TESSy from 244 325 specimens tested (pooled test positivity 11%) by primary care sentinel and non-sentinel sources (i.e. hospitals, schools, primary care facilities not involved in sentinel surveillance, or nursing homes and other institutions). Of these, 1 498 detections (pooled test positivity 12%) were from sentinel sources, and 24 340 (pooled test positivity 11%) from non-sentinel sources.

The percentage of all sentinel primary care specimens that tested positive for RSV has remained above 3% since week 41/2022 and above 10% since week 43 (Figure 1). The percentage positive of all non-sentinel specimens from patients tested for RSV has remained above 3% [14] since week 37 and above 10% (used as influenza season start threshold) since week 44.

Figure 1. Percentage of sentinel and non-sentinel surveillance specimens testing positive for RSV, weeks 40/2016–47/2022, EU/EEA



Source: TESSy, INFLVIRWAGGR record type

When comparing the test positivity and the number of positive RSV detections across the seasons, the pre-COVID-19 seasons provide the most reliable comparison, as they were relatively stable in terms of start, length, and test positivity in both sentinel and non-sentinel surveillance (Tables 1-2 and Figure 1). We therefore looked at the first seven and 11 weeks of sentinel and non-sentinel specimens for all the seasons since 2016/17, respectively, which had an RSV positivity above the 3% season threshold [14]. When comparing the current sentinel surveillance data with the pre-COVID-19 seasons, the average test positivity is at the levels of 2018/19 season, while the overall test positivity is somewhat higher and also above the levels for seasons 2016/17–2017/18 and 2019/20. Based on the pooled test positivity data, the start of the current season was five weeks earlier than in the last three pre-COVID-19 seasons 2017/18–2019/20, but 14 weeks later than the 2021/22 season, with differences between countries. The number of sentinel specimens tested in the countries has increased on average five times since the pre-COVID-19 seasons. This could be due to an increased number of general practitioner (GP) practices taking part in the surveillance systems, however, as yet the changes in national surveillance systems due to COVID-19 pandemic are not fully known to ECDC (Table 1).

For the non-sentinel data, the number of specimens tested has increased on average three-fold since the pre-COVID-19 seasons, although the average weekly and the overall test positivity are still below pre-COVID-19 levels (Table 2). Nevertheless, the pooled test positivity data from non-sentinel sources show that this season started about five weeks earlier than the last two seasons pre-COVID-19 and only nine weeks later than the 2021/22 season, with differences between countries (Table 2).

Table 1. RSV surveillance data for six previous and current seasons from the sentinel surveillance system, week 40/2016 to week 47/2022, EU/EEA

Season	Total number of specimens*	Number of RSV positive*	Pooled test positivity (%)*	Country median positivity % (Range)*†	First week of RSV test positivity above 3%*	Minimum and maximum number of countries reporting per week*
2016/17	1775	162	9.1	4.9 (0-17.5)	w43	5, 7
2017/18	2253	183	8.1	4.7 (0-25.0)	w46	7, 11
2018/19	1865	213	11.4	11.8 (0-25.0)	w46	9, 11
2019/20	2289	170	7.4	4.0 (0-33.3)	w46	9, 13
2020/21	1202	1	0.1	-	Season threshold not exceeded during autumn 2020#	4, 8
2021/22	1069	53	5.0	0 (0-32.2)	w27	4, 6
2022/23	11299	1445	12.8	12.8 (1.7-35.7)	w41	15, 16

Source: TESSy, INFLVIRWAGGR record type

**in the first 7 weeks above 3% test positivity. †Median test positivity includes only EU/EEA countries reporting both numerators (RSV positive results) and denominators (number of specimens tested for RSV) in the period. #Calculated from weeks 40-47, 2020.*

Table 2. RSV surveillance data for six previous and current seasons from the non-sentinel surveillance system, week 40/2016 to week 47/2022, EU/EEA

Season	Total number of specimens*	Number of RSV positive*	Pooled test positivity (%)*	Country median positivity % (Range)*†	First week of RSV test positivity above 3%*	Minimum and maximum number of countries reporting per week*
2016/17	60403	9562	15.8	4.8 (0-22.5)	w42	5, 12
2017/18	73098	10386	14.2	5.9 (0-29.5)	w42	10, 14
2018/19	88196	12955	14.7	13.1 (1.3-57.1)	w43	12, 14
2019/20	97614	12089	12.4	4.5 (0-37.7)	w43	9, 13
2020/21	40755	90	0.2	-	Season threshold not exceeded during autumn 2020#	9, 13
2021/22	94732	8404	8.9	1.9 (0-12.5)	w28	8, 13
2022/23	261187	24999	9.6	9.3 (0-39.1)	w37	13, 18

Source: TESSy, INFLVIRWAGGR record type

**in the first 11 weeks above 3% test positivity. † Median test positivity includes only EU/EEA countries reporting both numerators (RSV positive results) and denominators (number of specimens tested for RSV) during the period. # Calculated from weeks 40–47, 2020.*

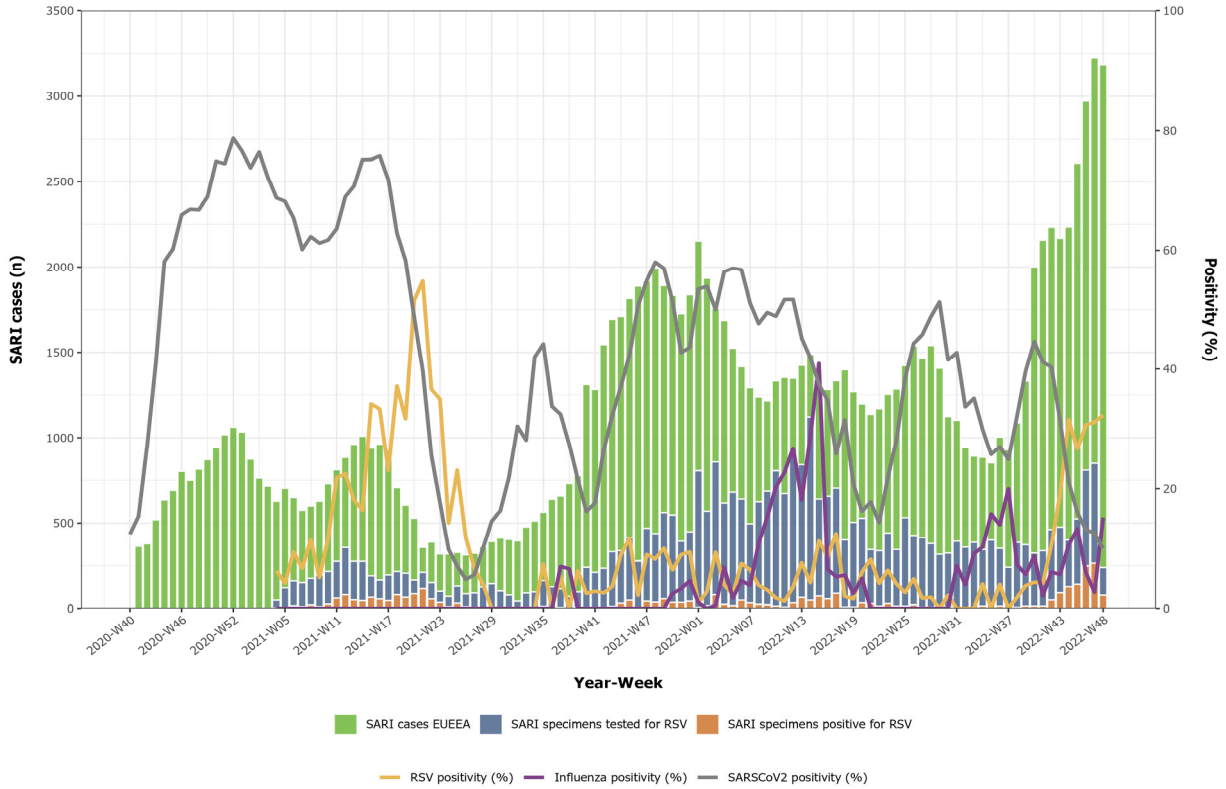
Since week 40/2022, 11 countries (Czechia, Croatia, Denmark, France, Germany, Ireland, the Netherlands, Norway, Portugal, Slovenia and Spain) have reported three or more consecutive weeks of RSV positivity above 3% [14] from their sentinel sources and 12 countries (Bulgaria, Czechia, Denmark, France, Ireland, Iceland, Lithuania, Latvia, Portugal, Slovenia, Spain and Sweden) from their non-sentinel systems.

A few countries additionally monitor severe disease related to RSV infection through surveillance of hospitalised laboratory-confirmed RSV cases in intensive care units (ICUs) or other wards, or severe acute respiratory infections (SARI).

Since week 40/2020, 126 869 SARI cases have been reported to TESSy (in record types INFLSARIAGGR and SARISURV) by eight EU countries (Belgium, Croatia, Germany, Ireland, Lithuania, Malta, Romania and Spain). Of these, 4 945 cases from six countries (Belgium, Croatia, Ireland, Lithuania, Malta, and Romania) were reported to have been tested for RSV and 436 were found positive (overall positivity 8.8%).

Positivity for RSV has been increasing in SARI cases since week 40/2022, reaching 39% in week 47/2022 (of 46 cases tested in Ireland and Romania) (Figure 2). This figure should be interpreted with caution given the small number of countries reporting severe RSV data and risk of selection bias (i.e. related to the age of tested patients). An increase of this type has not been observed for influenza and SARS-CoV-2 (Figure 2).

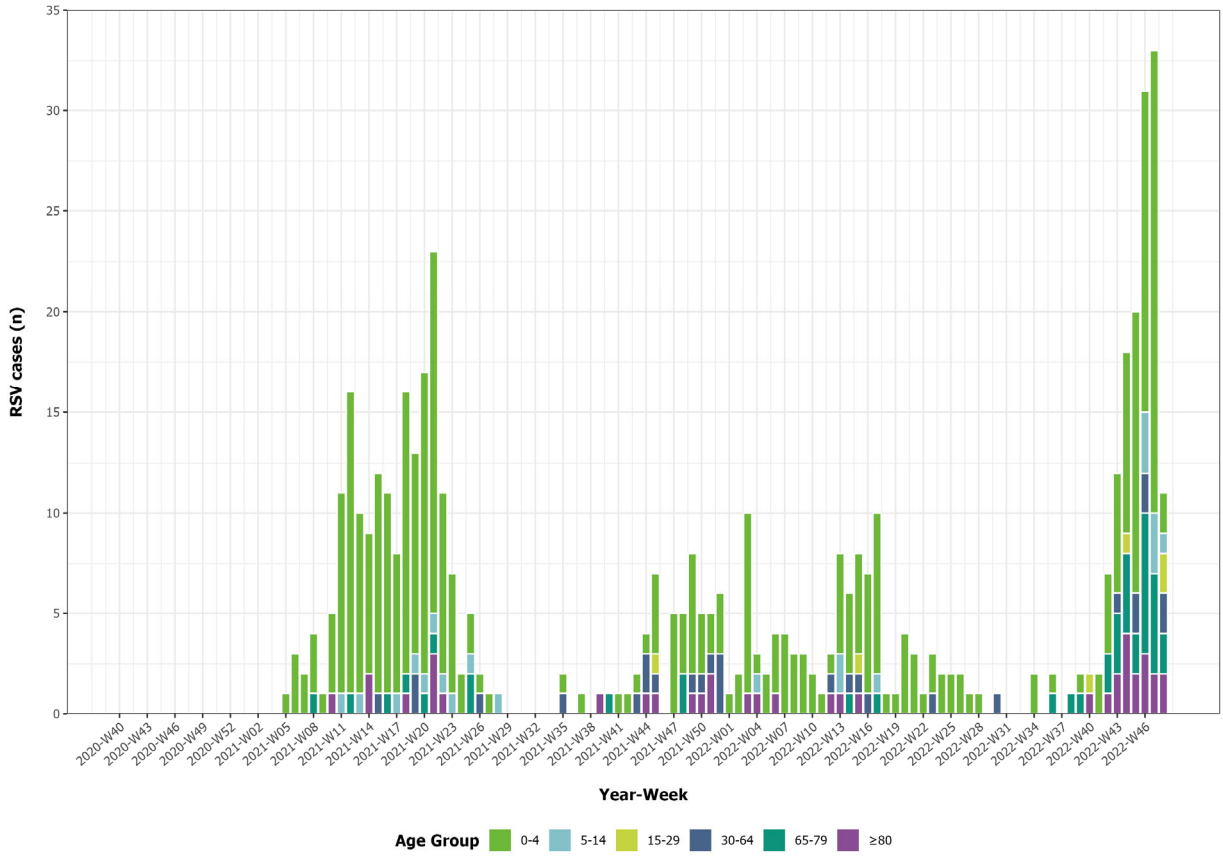
Figure 2. SARI cases and testing results for RSV and overall positivity for RSV, influenza and SARS-CoV-2, week 40/2020–week 47/2022, eight EU/EEA countries (Belgium, Croatia, Germany, Ireland, Lithuania, Malta, Romania, Spain)



Source: TESSy, INFLSARIAGGR and SARISURV record types

Of 83 RSV-positive SARI cases with known age reported by four countries (Croatia, Ireland, Malta and Romania) between weeks 40 and 47/2022, 38 (46%) were under five years and 34 (41%) were in adults aged 65 years or above (Figure 3). In data reported to TESSy from week 40/2020 to week 39/2022, 261 RSV-positive SARI cases aged under five years and 36 cases aged 65 years or above were reported (79% and 11%, respectively, of 332 SARI cases tested for RSV in five countries – Belgium, Croatia, Ireland, Malta and Romania).

Figure 3. SARI cases testing positive for RSV by age group in five EU/EEA countries (Belgium, Croatia, Ireland, Malta, Romania), 2021-w40 to 2022-w47



Source: TESSy, INFLSARIAGGR and SARISURV record types.

Further visualisations of TESSy reported data can be found in ECDC's 'Surveillance Atlas of infectious diseases' online [15].

Disease background

Virus and disease characteristics

RSV is an enveloped virus, with a linear negative-sense single-stranded RNA genome, belonging to the species *Human orthopneumovirus*. There are two antigenically distinguishable subtypes, RSV-A and RSV-B. RSV is transmitted via droplets, but the most common route is direct contact with contaminated respiratory secretions followed by self-inoculation of nasopharyngeal or ocular membranes. RSV can survive on fomites (toys, paper tissues and beds) for several hours and on hands for up to 25 minutes. The incubation period is approximately five days, and the period of shedding is one week, although longer periods have also been documented, especially in young children and immunocompromised patients [16]. Unrecognised asymptomatic RSV individuals play an important role in the transmission of RSV within the household and the community [17].

RSV is a major contributor to lower respiratory tract infections (LRTI) worldwide. By the age of two years almost all children have been infected, but natural infection does not provide long-lasting immunity. Reinfection is common although it usually only affects the upper respiratory tract. RSV clinical manifestations vary in different age groups. Symptoms range from mild influenza-like presentations to severe LRTIs, including bronchiolitis and pneumonia, possibly requiring acute care admission and mechanical ventilation [18].

In children, the typical clinical picture consists of low-grade fever, cough, rhinitis, respiratory distress and apnoea in infants. During the first year of life, especially if it is the primary infection, bronchiolitis and/or pneumonia may develop as the respiratory disease progresses to the lower respiratory tract. Infants often experience feeding difficulty due to nasal congestion and increased breathing workload which may result in dehydration and lethargy – hence the subsequent need for hospitalisation [19].

Nevertheless, most RSV infections result in relatively mild illness. Factors that increase the risk of severe RSV infection include young age (infants under six months are more prone, particularly during their first three months), prematurity, haemodynamically-significant congenital heart disease, bronchopulmonary dysplasia, immunosuppression, Down syndrome, chronic pulmonary disease, passive parental cigarette smoke and advanced age [19-22]. In addition, siblings, attendance of a daycare institution, absence of breastfeeding and family history of asthma contribute to an increased risk of hospitalisation due to RSV infection [23]. Morbidity of high-risk patients is significant, with prolonged length of hospital stay and the need for advanced management in an intensive care unit [19].

RSV is a leading cause of acute LRTIs in infants and young children, but it is also considered a cause of morbidity and mortality comparable to influenza in adults aged 65 years and above and high-risk individuals [24]. RSV outbreaks in long-term care facilities (LTCFs) have significant case fatality rates [25].

Seasonality

RSV epidemics present in Europe with clear annual seasonality and a west-to-east gradient observed in the season onset. In general, countries in the eastern part of Europe have a later start to the RSV season (about four weeks) than those in the western part of Europe [26]. Lower temperature and higher relative humidity have been shown to be associated with higher RSV activity [26].

Based on historical RSV surveillance data from 15 EU/EEA countries, all RSV seasons from 2010/11 to 2015/16 had a similar timing and epidemic course across Europe, with some variation within and between countries. During this period, each year, the RSV epidemic in Europe progressed rapidly after week 40 (beginning of October) and the median start of the RSV season was in week 49 (beginning of December) in sentinel and non-sentinel surveillance systems (ranging from week 41 to week 3 for the sentinel and from week 42 to week 8 for the non-sentinel data). The median length of the RSV season was 16−18 weeks and the peak was around week 4 (end of January) [27].

Introduction of non-pharmaceutical interventions (NPI) to control SARS-CoV-2 circulation caused a change to the regular seasonality of RSV activity in Europe. Soon after NPIs were introduced, in February–March 2020, the circulation of RSV stopped, and in the 2020/2021 season the RSV epidemics began several weeks later than usual, if at all [28,29]. In the summer of 2021, out-of-season RSV activity was observed in several countries, however, the reasons have not been fully explored [29,30]. In Belgium, analysis of the winter seasons during the period 1999−2020 identified all the RSV peaks between weeks 47 and 52. The only exception was winter 2020, with no peak, resulting in delayed RSV peaks during spring 2021 and a plateau from early spring to mid-summer [30].

The seasonality of RSV may affect optimal health system performance. The RSV epidemics, occurring mostly between October and March in Europe, result in acute pressure on primary care providers, emergency services and paediatric hospital capacity [31,32].

Disease burden

Each year, RSV is estimated to cause 33 million cases and 66 000–199 000 deaths in children under five years worldwide [33]. RSV accounts for approximately two thirds of acute LRTIs in infants and is the most common cause of bronchiolitis and pneumonia in this group. RSV is also a leading cause of hospitalisations for infants in their first year of life [34], often not because of the severity of the disease, but because of the care required, and the significant burden it places on outpatient care services [31]. Approximately three quarters of infants hospitalised for RSV were previously healthy and born at term [35].

In the USA, where these data are available, RSV accounts for an estimated 96 deaths in infants <12 months old each year and in this age group infant mortality is five times higher for RSV than for influenza [35]. US mortality rates for infants <12 months old were estimated to be 561 due to RSV (with 64% occurring in infants aged 1–4 months) and 1 603 due to bronchiolitis per 1 000 000 live births, respectively. Overall, 21–54% of RSV, bronchiolitis and influenza deaths in infants happen outside the hospital setting [36].

In Europe, estimates of hospitalisations due to RSV in children under five years, based on national RSV-associated hospitalisation estimates, literature review, multiple imputation and the nearest neighbour matching approaches, show an average of 213 014 (95% Confidence Interval (CI):192 181–233 844) hospital admissions per winter associated with RSV in the EU, Norway and the United Kingdom [37]. In a multi-centre, prospective, observational birth cohort study of healthy term-born infants in four European countries (Finland, the Netherlands, Spain and the United Kingdom (England and Scotland)), incidence of RSV-associated hospitalisations in the total cohort was 1.8% (95% CI 1.6–2.1), incidence of RSV infection was 26.2% (24.0–28.6) and incidence of medically-attended RSV was 14.1% (12.3–16.0) [38].

On average, annual hospitalisations for adults have been shown to be 158 185 (95% CI: 140 651–175 742) for those aged 18 years and above [39]. The highest proportion of hospitalisations for adults (47%) occurred among those aged 75–84 years, with an annual average of 75 013 (95% CI: 70 466–79 580) at a rate of 2.25 (95% CI: 2.12–2.39) per 1 000 adults. For adults ≥85 years, the rate was 3.09 (95% CI: 2.63–3.55) per 1 000, with an average of 39 153 (95% CI: 33 368–44 939) hospitalisations per year.

In a study published in 2022, 28 to 60% of the respiratory tract infection hospitalisations of children under three months were associated with RSV in five European countries (Denmark, Finland, Norway, the Netherlands, and the United Kingdom (England and Scotland)) [40]. In these countries, annual incidence of RSV-associated hospitalisations was >40 (range 42–90) per 1 000 people in the age group 0–2 months. In 1–2 years age group the incidence rate ranged from 1.3 to 10.5 hospitalisations per 1 000. Overall, incidence declined with age and increased again in those aged 65 years and above [40]. In a prospective study of neonates in Finland, a seasonal incidence rate of RSV hospitalisation was 22.1 per 1 000 (95% CI, 10.1–41.9) [41].

In the short-term, RSV infection in children is associated with an increased incidence of acute otitis media (inflammation or infection located in the middle ear), pneumonia and excessive antibiotic usage [41,42]. In the long-term, RSV-associated LRTI is a significant risk factor for long-term respiratory morbidity, and is characterised by early transient or recurrent wheezing, asthma and impaired lung function [43,44].

Although rates of severe RSV illness appear highest among children with high-risk conditions, including premature birth, a large number of severe infections have been reported among otherwise healthy young children [45]. RSV has also been associated with moderate-to-severe disease among adults aged over 65 years, especially among those with co-morbidities [46,47].

Disease surveillance for RSV in the EU/EEA

RSV is not a mandatory reportable disease at the EU level, however the World Health Organization (WHO) established RSV case definitions in 2018 [48] and many EU/EEA countries have respiratory sentinel surveillance in place, with random or systematic sampling approaches. In addition, to our knowledge, based on an unpublished survey conducted by the Preparing for RSV Immunisation and Surveillance in Europe consortium (PROMISE) group in 2022, twelve EU/EEA countries have made RSV a notifiable disease.

In most countries and areas, the surveillance of mild acute respiratory infection (ARI) or influenza-like illness (ILI) in primary care, mainly due to RSV, influenza virus or SARS-CoV-2, is based on nationally organised sentinel networks of primary care physicians, mainly general practitioners (GPs), covering at least 1–6% of the population in their country or area. Depending on the country or area, physicians may report the weekly number of patients seen with ILI and/or ARI, including data on RSV testing if applicable. For severe disease associated with RSV, influenza virus or SARS-CoV-2, countries conduct sentinel surveillance for hospitalised cases presenting with SARI, according to standard case definitions. Depending on the country, all or a subset of SARI patients are tested. Furthermore, many EU/EEA countries have laboratory non-sentinel surveillance in place. Case definitions, populations under surveillance, and data formats differ among countries or areas and only a subset of specimens from ILI, ARI or SARI patients is routinely tested for RSV [49].

In 2022 an ECDC/WHO Regional Office for Europe survey conducted among EU/EEA countries showed that 20 of 29 responding countries have an ILI or ARI-based integrated primary care RSV sentinel surveillance system in place and seven more countries have plans to implement this. Furthermore, 20 countries have non-sentinel

laboratory-based RSV surveillance in place and two countries have plans to implement this. Ten countries have SARI-based integrated secondary care RSV sentinel surveillance systems in place, and 12 others are planning to implement this [50]. The respiratory syncytial virus consortium in Europe (RESCEU) [51] has facilitated RSV surveillance development across EU/EEA countries and developed recommendations for national RSV surveillance together with public health experts from EU/EEA countries [52].

Diagnostics and genomic surveillance

A testing and diagnostic algorithm for RSV surveillance through community and hospital surveillance has previously been proposed, based on ARI and extended SARI case definitions [52]. Laboratory diagnostics of RSV infection are usually based on molecular detection using nucleic acid amplification (PCR) techniques, direct or indirect immunofluorescence assay (DFA/IFA), rapid antigen detection tests (RADT) or virus culture [53]. Diagnostics are often carried out by (multiplex) PCR systems for several respiratory virus infections (influenza, SARS-CoV-2, RSV) based on tests from different commercial manufacturers or are included in in-house (multiplex) PCR panels of centralised sentinel diagnostics. In addition to PCR-based assays, antigen detection is also frequently used for primary diagnostics. The recommended specimen type for RSV is nasopharyngeal swab [52], however any upper respiratory specimen type can be used for detection. Virus isolation and serology are carried out at some laboratories [54], mainly for studies of the phenotypic properties of the virus and for sero-epidemiological studies and research purposes [52]. In addition to determination of RSV as a causative agent, PCR assays allow also for differentiation of RSV antigenic groups A and B. The attachment glycoprotein (G) gene is usually sequenced to further determine genotypes [55,56], but the fusion glycoprotein (F) gene and whole genome sequencing are also recommended options [52].

Data from the most recent survey among EU/EEA countries by ECDC/WHO's Regional Office for Europe showed that genomic surveillance of emerging respiratory pathogens in eight of 29 countries already includes RSV and eight more countries are planning to implement this [50]. The joint ECDC/WHO guidance on operational considerations for respiratory virus surveillance in Europe provides further recommendations for integrated respiratory virus surveillance and sample size calculations [57]. In order to achieve a seasonal overview of circulating strains, the RESCEU consortium formulated the following additional recommendations specifically for RSV:

- sequence a minimum of 10% of the detected viruses with a minimum of 20 randomly selected specimens per RSV type per country or institute per season;
- if possible, these specimens should be randomly selected from each age group <3 months, 3–5 months, 6–11 months, 12–23 months, 2–4 years, 5–14 years, 15–64 years and 65+ years [52].

Further recommendations for specimen collection, transport, and storage as well as timing of sampling, detection methods and phenotypic characterisation are described by Teirlinck et al [52].

Case management

At present, there are no specific therapeutic options for RSV infection. Management of hospitalised children is mainly supportive, including hydration, oxygen supplementation and, if necessary, intubation and mechanical ventilation. Antimicrobials are only indicated if there is evidence of a co-existing bacterial infection. Ribavirin has in vitro antiviral activity against RSV but has not been recommended for routine clinical use due to potential toxicity and minimal clinical benefit.

Prevention

Despite extensive research efforts, there are no licensed vaccines to prevent RSV infection. However, multiple promising vaccine candidates are in clinical development for infants, pregnant women and older adults. Potential vaccines currently being evaluated include live attenuated, gene-based vector, nucleic acid, chimeric, particle and subunit vaccines [58].

Effective passive immune prophylaxis is available. Palivizumab is a short-acting monoclonal antibody (mAb), which needs to be administered intramuscularly to infants every month (half-life of approximately one month) for a total of five months from the onset of the RSV season. It has been shown to reduce the risk of hospitalisation of infants at high-risk of severe RSV disease. The cost of Palivizumab is around EUR 3 400–5 600 per child [59]) and therefore it is mainly administered to high-risk infants in high-income countries, in accordance with national recommendations.

On 31 October 2022, the European Medicines Agency (EMA) recommended a marketing authorisation in the European Union for nirsevimab, a recombinant human monoclonal antibody with prolonged half-life that can be given as a single intramuscular injection [60]. Data from two randomised, double-blind, placebo-controlled multicentre clinical trials demonstrated favourable efficacy and safety of nirsevimab in healthy infants, both preterm and full-term, entering their first RSV season [61]. Administration of nirsevimab is indicated for infants at high-risk, in accordance with the national recommendations of each country.

ECDC risk assessment for the EU/EEA

This assessment is based on evidence available to ECDC at the time of publication. It follows the ECDC rapid risk assessment methodology, where the overall risk is determined by a combination of the probability of infection and the impact of the disease on affected populations [62]. ECDC will continue to monitor the event and reassess the risk depending on its evolution and the implemented response measures.

What is the risk of RSV infection in the EU/EEA for the general population and high-risk groups in the coming weeks?

In many areas of the EU/EEA, RSV circulation has intensified in recent weeks, with increasing transmission rates in all population groups and an earlier-than-usual start to the RSV season. Based on recent RSV detections and test positivity, the probability of becoming infected with RSV in the coming weeks is assessed as **MODERATE** for all population groups.

RSV infection generally causes mild disease, but the severity of clinical manifestations varies considerably. In infants, the elderly and individuals with specific comorbidities RSV may lead to severe complications, often associated with hospitalisation [18]. In infants under six months, RSV symptoms can also be associated with dehydration, increasing the chance of hospitalisation and ICU admission [19]. In summary, the impact of RSV infection is assessed as **VERY LOW** in the general population and **HIGH** in high-risk groups, such as infants under six months, adults aged 65 years and above and individuals with specific comorbidities.

Combining the probability of infection and the impact of the disease, the risk derived from RSV infection is assessed as **LOW** for the general population and **HIGH** for infants under six months, adults aged 65 years and above and individuals with specific comorbidities.

What is the risk posed by co-circulation of RSV, influenza virus and SARS-CoV-2 for EU/EEA healthcare systems in the coming weeks?

The current early RSV season is occurring alongside an early influenza season and intensifying circulation of other respiratory viruses, including SARS-CoV-2 [19]. Against this background, the overall probability of infection with RSV, influenza virus or SARS-CoV-2 in the general population is assessed as **HIGH**. A high level of respiratory virus circulation leads to an increased number of hospitalisations and increased healthcare staff absenteeism due to sickness [63]. Given these factors, the impact of the circulation of RSV and other respiratory viruses (e.g. influenza and SARS-CoV-2) on healthcare systems could be **MODERATE.** Considering both the probability and the impact, there is a **HIGH risk** of significant pressure on healthcare systems in some areas of the EU/EEA in the coming weeks.

Options for response

In view of the increased circulation of respiratory viruses, including RSV, the following options for response are proposed for public health authorities in the EU/EEA:

- implement risk communication activities for the public including active promotion of vaccinations against seasonal influenza and COVID-19;
- increase healthcare professionals' awareness and enhance hospital preparedness;
- Provide RSV prophylaxis to high-risk infants in accordance with national guidelines;
- implement appropriate infection prevention and control (IPC) measures based on the local epidemiological situation, particularly for vulnerable groups within healthcare facilities, including LTCFs;
- promote good hygiene practices in the community and consider non-pharmaceutical interventions (NPIs), including targeted guidance for risk groups and care-givers of vulnerable groups;
- where possible, implement and improve surveillance of RSV and testing for respiratory pathogens.

Risk communication activities

Risk communication to the public should enhance appropriate healthcare consultation, with sufficient information about the disease, causes, and potential outcomes.

In the absence of specific vaccine and treatment for RSV, and in order to reduce the pressure on healthcare services, public health efforts should also aim to actively promote vaccinations against seasonal influenza and COVID-19 [63]. Information campaigns should be in place to promote these vaccinations for healthcare workers and eligible population groups. Specific communication may be designed to address vulnerable people for whom these vaccinations (including booster dose) may not provide strong protection.

Communication and educational strategies should be implemented to raise awareness and knowledge of RSV bronchiolitis among parents of young infants and children. Information on which symptoms are severe or should give cause for concern and what action should be taken will alleviate parental anxiety. This may also help reduce the number of unnecessary visits to emergency departments for mild cases.

Emphasis should also be placed on reinforcing basic hygiene measures in kindergartens and nurseries, such as more thorough cleaning of the facilities, appropriate ventilation and advice to parents that children with respiratory symptoms should remain at home, when possible.

Increase awareness among healthcare professionals and hospital preparedness

Healthcare workers should be sensitised to ensure timely diagnosis of RSV in patients at increased risk of a severe outcome when presenting with symptoms compatible with respiratory tract infection. The clinical symptoms for RSV are similar to those for other respiratory viruses (e.g. seasonal influenza, SARS-CoV-2, etc.) and RSV is usually considered to be a paediatric disease, meaning that it is often under-diagnosed as a cause of severe respiratory disease in adults.

During the epidemic months, RSV can exert strong pressure on healthcare systems, as it is currently reported in many EU/EEA countries. It is expected that this will place a significant burden on both community and hospital patient care settings. Increased RSV-related consultations in primary healthcare settings, along with increased visits to emergency departments lead to higher utilisation of healthcare resources and significant pressure on hospital services. This is particularly true for paediatric wards and paediatric/neonatal ICUs (PICU/NICU), whose bed capacity is much smaller than that for adult units. Reinforcement of healthcare systems and support of healthcare workers should be prioritised in the coming months, as the co-circulation of RSV, influenza virus, SARS-CoV-2 and other respiratory viruses may lead to staff shortages due to sick leave. Maintaining an adequate ratio of staff to patients, especially in ICUs, is critical for patient safety and quality of care. Planning for increased capacity should be reviewed, in order to manage the expected higher number of cases, and then re-assessed frequently according to the epidemiological situation. This should include access to pharmaceuticals for the prophylaxis and management of RSV infection, oxygen supplies and staffing.

In areas experiencing high circulation of RSV or other respiratory viruses, healthcare facilities and LTCFs should consider appropriate use of face masks for healthcare workers and visitors [64,65].

As seen during the pandemic, healthcare worker fatigue in terms of stress, anxiety and burn-out can further affect staff shortages. Interventions to support healthcare workers should consider the organisational, social, personal and psychological aspects. Patients need to be guided towards appropriate consultation for first-line and hospital care. Nursing and other helplines can be considered to help provide advice to parents and triage for sick children.

Provide RSV prophylaxis for high-risk infants

The local epidemiological situation and national recommendations should be considered for the use of prophylactic treatment. A humanised neutralising antibody, palivizumab, has been shown to be effective as prophylaxis in infants at higher risk of severe RSV disease, although its use is limited due to high cost and the need for monthly administration during the epidemic season. The EMA recently approved a second long-acting monoclonal antibody, nirsevimab, to be administered as a single dose each season [60]. This prophylactic should be used where available in accordance with national guidelines. It is available in some EU/EEA countries and could be considered in order to reduce the RSV burden for the current season.

Infection prevention and control practices

During the period of increased RSV circulation, healthcare facilities, including LTCFs, should apply measures to minimise the risk of RSV transmission within their facilities and especially in the units with high-risk patients. They should also ensure that personal protective equipment (PPE) is available and used appropriately to protect those providing patient and resident care. Nosocomial spread of RSV is a major problem in hospital wards and LTCFs during RSV epidemics [66]. RSV outbreaks in LTCFs can have devastating effects since the residents are already vulnerable due to their age and frequent underlying health problems, resulting in a high probability of unfavourable outcomes. LTCF staff should be prepared to manage RSV outbreaks.

RSV can survive for several hours on surfaces [16]. Strict infection control practices in healthcare facilities should be implemented, including rapid diagnosis and isolation or cohorting of patients with RSV infection. Both standard and contact precautions are recommended for prevention of RSV in healthcare settings. Hand hygiene and use of PPE (gloves, single use aprons, face masks and goggles) are the most important infection prevention and control measures to avoid transmission of RSV to patients at increased risk of a severe outcome (e.g. premature infants or elderly patients). Ventilation plays a key role for the prevention of all respiratory infections in healthcare settings. During seasonal outbreaks of respiratory pathogens, hospitals and LTCFs should limit the number of visitors and group activities may be reduced. Parents of hospitalised children with RSV and visitors to elderly patients or LTCF residents should be made aware of the need for good hand hygiene and strict respiratory etiquette, including wearing a well-fitting surgical mask, during close contact.

Good hygienic practices and non-pharmaceutical interventions

Since March 2020, good hygienic practices and NPIs implemented in EU/EEA countries have proven to be an effective public health tool for reducing the spread of SARS-CoV-2 and other respiratory viruses, such as influenza virus and RSV, as indicated by the change in the seasonal patterns of circulation of these respiratory viruses during the 2020-2021 season.

Due to the current simultaneous circulation of influenza virus, SARS-CoV-2 and RSV in the community and given the upcoming end-of-year festive season, appropriate NPIs and targeted guidance for risk groups and caregivers of vulnerable groups should be considered in all countries. This guidance should be tailored according to the local epidemiological situation, the setting, and the pressure on the healthcare system and other essential services, bearing in mind the positive short-term and negative long-term effects of certain NPIs. Staying home when ill, good hand and respiratory hygiene, including appropriate use of face masks [65]; good ventilation in indoor spaces; teleworking where possible and avoidance of crowded public spaces, including public transport, are relevant measures. Siblings under two years to newborns and/or prematurely-born infants could possibly be kept at home from day-care during the epidemic weeks of RSV to avoid transmission to the newborn.

Overall, the key to NPI effectiveness is community engagement and prompt implementation of these measures when incidence of respiratory infections rises.

Surveillance of RSV and testing for respiratory pathogens

Where possible, RSV should be included in the ARI and SARI sentinel surveillance systems because effective integrated respiratory surveillance systems should provide sufficient data to monitor the intensity of circulation and spread of respiratory viruses, helping to guide control measures and mitigate their impact. These systems will also be important in the event of future respiratory pandemics.

As the clinical spectrum for COVID-19, RSV infection, and other respiratory virus infections does not always include high temperature, the ARI case definition is more sensitive than ILI for integrated sentinel surveillance[57], which is especially relevant for RSV since fever is not among the most dominant symptoms.

Where possible, upper respiratory specimens from patients with respiratory symptoms (ARI/ILI/SARI) via primary and secondary care sentinel surveillance should be tested using multiplex PCR assays to simultaneously detect RSV, influenza virus, SARS-CoV-2 and other relevant respiratory viruses [57]. Specimens from patients with respiratory symptoms that are not submitted from sentinel networks should still be tested in primary or secondary care laboratories for influenza viruses, SARS-CoV-2, and other relevant respiratory viruses. Countries should continue to collect these non-sentinel data, focusing on the epidemiological information relating to positive detections and the number of tests performed (denominator data) in each setting (primary or secondary care). Laboratory capacity to establish timely etiological diagnosis facilitates the appropriate room/bed assignment for admitted patients.

Consideration should be given to implementation of genomic surveillance, including RSV typing (RSV A and RSV B), and partial (most importantly the genome parts coding for the F and G proteins) or whole genome sequencing. Genomic surveillance should be integrated into overall respiratory virus monitoring strategies and objectives to ensure reliability and interpretability of findings. Sequencing data on RSV should be shared in a timely manner in publicly available databases, such as GenBank, European Nucleotide Archive and GISAID EpiRSV.

Discussions on the revision of the case definitions of EU communicable diseases under epidemiological surveillance are currently ongoing in accordance with the regular revision cycle and inclusion of RSV is being considered [67]. ECDC encourages Member States to start or continue reporting detection data from sentinel and non-sentinel sources through TESSy record types INFLVIRWAGGR and SARI data through SARISURV or INFLSARIAGGR. In addition, ECDC has initiated a new integrated respiratory surveillance system, where more detailed epidemiological data can also be collected for RSV cases in TESSy from the 2022 season onwards in the new record types RESPISURV and RESPISEVERE [68]. Introduction of these new record types also serves the need for simple adaptability of the surveillance system to additional respiratory viruses, as outlined in the joint WHO and ECDC guidance 'Operational considerations for respiratory virus surveillance in Europe' [57]. Countries can also share available data or assessments through EpiPulse (event id 2022-EIP-00086). A position paper by European public health experts and RESCEU is available, offering recommendations for setting up or enhancing existing national RSV surveillance strategies [52].

Limitations

This assessment is undertaken based on facts known to ECDC at the time of publication.

Since RSV is not yet notifiable at EU level, there are limitations to the RSV data that ECDC collects through TESSy. ECDC collects aggregate numbers for detections of laboratory-confirmed RSV cases from sentinel and non-sentinel surveillance systems, based on voluntary weekly reporting. The data do not include age or hospitalisation information. Only a few countries report hospital-based SARI data and only some of those provide case-based data. As a result of pooling surveillance data to calculate RSV positivity and other indicators, timing is driven by the country or countries reporting the highest number of specimens tested and positives. EU/EEA-level surveillance of RSV is based on case definitions used mostly for influenza and these do not target RSV specifically. Furthermore, the age groups most affected by RSV might not be properly captured by the surveillance system, especially with regard to infants as they would be brought directly to hospitals and paediatric ICUs might not be part of the national surveillance system.

During the COVID-19 pandemic, the strategies for testing RSV changed in many countries and are not fully known to ECDC at the present time.

These factors result in high heterogeneity among different surveillance systems providing RSV data to ECDC in terms of population, setting (primary care versus secondary care), sampling strategy, eligibility for testing and testing methods.

Source and date of request

ECDC internal decision, 28 November 2022.

Consulted experts

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All experts have submitted declarations of interest, and a review of these declarations did not reveal any conflict of interest.

Disclaimer

ECDC issues this risk assessment document based on an internal decision and in accordance with Article 10 of Decision No 1082/13/EC and Article 7(1) of Regulation (EC) No 851/2004 establishing a European Centre for Disease Prevention and Control (ECDC). In the framework of ECDC's mandate, the specific purpose of an ECDC risk assessment is to present different options on a certain matter. The responsibility on the choice of which option to pursue and which actions to take, including the adoption of mandatory rules or guidelines, lies exclusively with the EU/EEA countries. In its activities, ECDC strives to ensure its independence, high scientific quality, transparency and efficiency.

This report was written with the coordination and assistance of an Internal Response Team at ECDC. All data published in this risk assessment are correct to the best of our knowledge at the time of publication. Maps and figures published do not represent a statement on the part of ECDC or its partners on the legal or border status of the countries and territories shown.

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