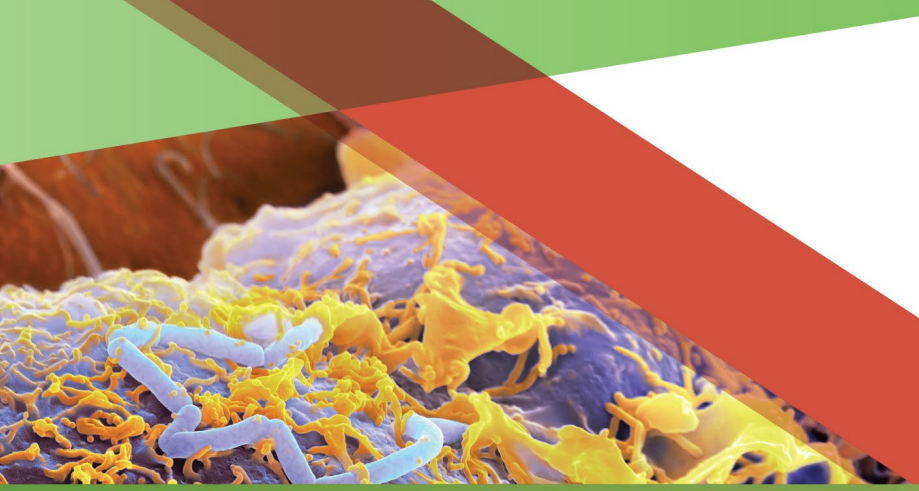

SURVEILLANCE REPORT

Listeriosis

Annual Epidemiological Report for 2021

Key facts

- In 2021, 30 Member States reported 2 268 confirmed listeriosis cases in the EU/EEA.
- The age-standardised EU/EEA notification rate was 0.44 cases per 100 000 population.
- The highest rate was detected among elderly people over 64 years of age (1.7 cases per 100 000 population).
- Number of confirmed listeriosis cases reported per year is stable in the EU/EEA.

Introduction

Listeriosis is a disease caused by *Listeria monocytogenes*. The disease primarily causes problems in pregnant women, newborns, and adults with a weakened immune system. After exposure, most healthy adults do not develop any symptoms, except in the case of pregnant women. After an incubation period of about three weeks pregnant women may suffer from a self-limiting influenza-like illness which may affect the uterus. In addition, listeriosis in adults with weakened immune system and the elderly may lead to meningitis, brain infection, and severe blood infection.

Methods

This report is based on data for 2021 retrieved from The European Surveillance System (TESSy) on 9 October 2022. TESSy is a system for the collection, analysis and dissemination of data on communicable diseases.

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].

A subset of the data used for this report is available through ECDC's online Surveillance Atlas of Infectious Diseases [3].

The notification of listeriosis in humans is mandatory in all EU/EEA Member States except Belgium. The surveillance systems for listeriosis have full national coverage in all Member States except in Belgium and Spain. In Belgium, the population coverage is estimated to be 80% since 2015. The variation in coverage over time was taken into consideration when calculating the national notification rates. No information on estimated coverage was provided by Spain, so no notification rates were calculated. For 2020 and 2021, Spain has not received data from all regions so the case numbers might therefore not be complete for these years. Fifteen of the 30 Member States used the

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Stockholm, December 2022

EU case definition from 2018, four used the one from 2012 and six the one from 2008; four Member States used another case definition, and one did not specify which case definition was used. The majority of the Member States (27 of 30) conducted passive surveillance; in 22 Member States, cases were reported by both laboratories and physicians and/or hospitals. All Member States provide case-based data except Bulgaria, which reported aggregate data. Both reporting formats were included to calculate numbers of cases, notification rates, disease trends, and distributions by age and gender.

EpiPulse, a new ECDC-run portal integrating several former ECDC applications, including the Epidemic Intelligence Information System (EPIS) platform, was launched on 22 June 2021. The portal facilitates the collection, analysis, and dissemination of indicator- and event-based surveillance data on infectious diseases and associated health issues.

Since 2021, it has been possible to report the seven-gene multi-Locus sequence type (ST) via case-based data collection. ST for *L. monocytogenes* has a higher discriminatory power than serogroup/type. In addition, ST was derived *in silico* from whole genome sequencing (WGS) data for Member States that routinely submit sequences for WGS-enhanced listeriosis surveillance but did not report STs via case-based data collection.

During 2021, ECDC continued EU/EEA-wide WGS-enhanced surveillance of listeriosis through isolate-based data collection which was first started in March 2019. The objectives of this activity are:

In the short term:

- early detection and delineation of multi-country listeriosis outbreaks and/or dispersed clusters to trigger outbreak investigations and contribute to food trace back and forward investigations so that appropriate control and preventive measures can be implemented in the food chain.

In the medium term:

- detection of (re-)emergence and monitoring the spread of *L. monocytogenes* strains;
- identification of persistent *L. monocytogenes* strains causing human infections in EU/EEA and likely originating from continuous sources; and
- identification of transmission chains, new risk factors for infection and severity of disease.

In the long term:

- monitoring of EU/EEA trends by selected indicators.

For cluster detection, raw reads or assemblies were submitted by the participating Member States. Sequences were analysed at ECDC with BioNumerics version 7.6.3 (Applied-Maths, Sint-Martens-Latem, Belgium). The analysis of raw reads included trimming using the default Bionumerics 7.6.3 settings; de novo assembly using SPAdes v.3.7.1; post-assembly optimisation by mapping reads back onto the assembly and keeping the consensus (using MismatchCorrector implemented in SPAdes v3.7.1). The default settings of BLAST parameters for allele calling were used. Core genome multi-locus sequence typing (cgMLST) analysis was performed using assembly-based allele calling using Institut Pasteur scheme [4] in BioNumerics. Isolates were retained in the analysis if at least 1 574 (90%) of the 1 748 core loci were detected.

A multi-country core cluster of *L. monocytogenes* was defined as at least two different Member States reporting at least one isolate each with maximum four differing alleles in cgMLST in single-linkage analysis. To further investigate the detected clusters, a threshold of seven core genome alleles was used to search for possibly epidemiologically linked isolates. All Member States that have isolates in a cluster or have submitted sequences can visualise and contextualise the data interactively through EpiPulse.

In addition to the WGS data submitted by the Member States for the listeriosis cluster detection, ECDC also collects and centrally analyses sequence data during multi-country outbreak investigations that are mainly initiated by Member State public health institutes in EpiPulse.

Epidemiology

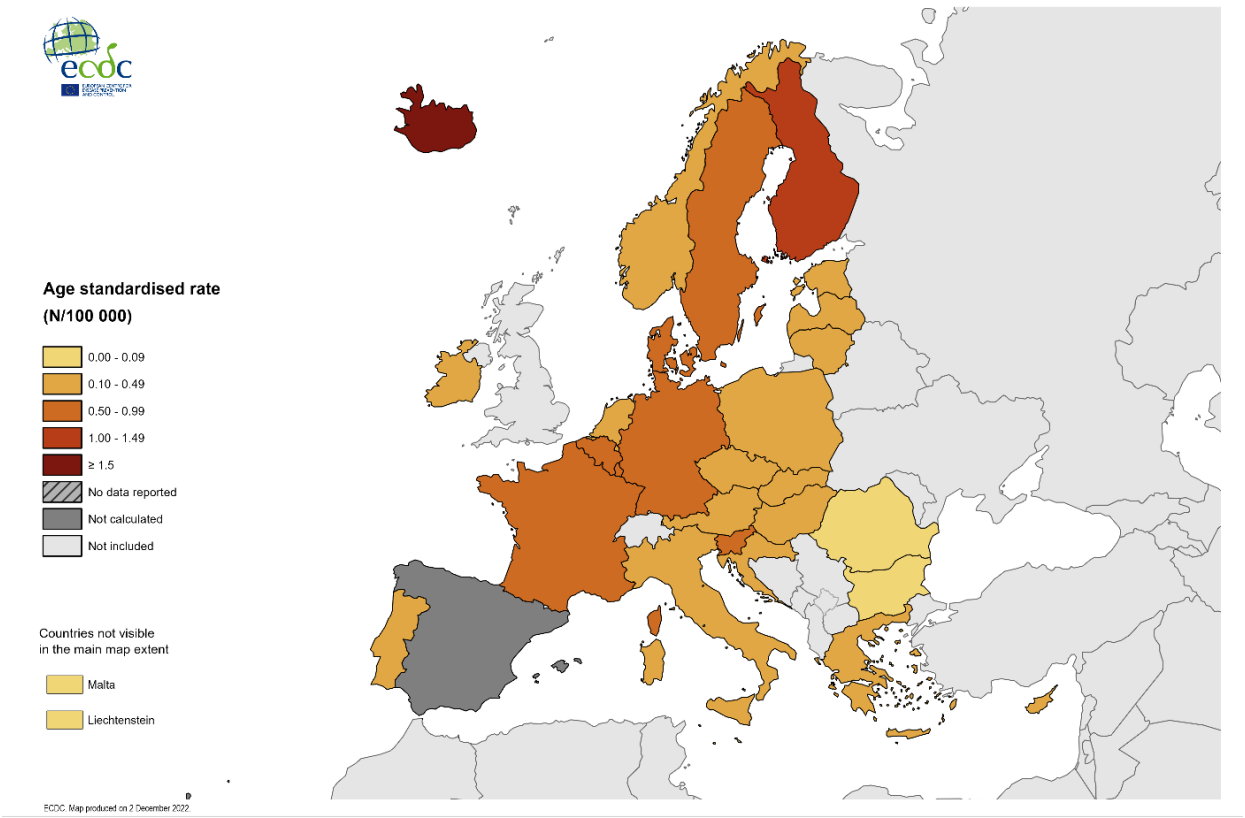
In 2021, 2 268 confirmed cases of listeriosis were reported by 30 EU/EEA Member States. The EU/EEA notification rate was 0.51 per 100 000 population. Germany, France, and Italy had the highest numbers of reported cases (560, 435 and 241, respectively), corresponding to 54.5% of all cases reported in the EU/EEA. The highest incidence rates were observed in Iceland, Finland, and Denmark. Figure 1 illustrates the country-specific age-standardised rates per 100 000 population.

Table 1. Distribution of confirmed listeriosis cases and rates per 100 000 population by country and year, EU/EEA, 2017–2021

Country	2017		2018		2019		2020		2021		
	Number	Rate	Number	Rate	Number	Rate	Number	Rate	Number	Rate	ASR
Austria	32	0.36	27	0.31	38	0.43	41	0.46	38	0.43	0.38
Belgium	73	0.80	74	0.81	66	0.72	54	0.59	68	0.73	0.67
Bulgaria	13	0.18	9	0.13	13	0.19	4	0.06	3	0.04	0.04
Croatia	8	0.19	4	0.10	6	0.15	5	0.12	8	0.20	0.20
Cyprus	0	0.00	1	0.12	1	0.11	2	0.23	1	0.11	0.11
Czechia	30	0.28	31	0.29	27	0.25	16	0.15	24	0.22	0.21
Denmark	57	0.99	49	0.85	61	1.05	43	0.74	62	1.06	0.95
Estonia	4	0.30	27	2.05	21	1.59	3	0.23	5	0.38	0.33
Finland	89	1.62	80	1.45	50	0.91	94	1.70	70	1.26	1.01
France	370	0.55	338	0.50	373	0.56	334	0.50	435	0.64	0.57
Germany	721	0.87	678	0.82	571	0.69	546	0.66	560	0.67	0.54
Greece	20	0.19	19	0.18	10	0.09	20	0.19	21	0.20	0.17
Hungary	36	0.37	24	0.25	39	0.40	32	0.33	35	0.36	0.31
Iceland	6	1.77	2	0.57	4	1.12	4	1.10	5	1.36	1.50
Ireland	14	0.29	21	0.43	17	0.35	6	0.12	14	0.28	0.31
Italy	164	0.27	178	0.29	202	0.34	155	0.26	241	0.41	0.33
Latvia	3	0.15	15	0.78	6	0.31	8	0.42	10	0.53	0.42
Liechtenstein	ND	NR	ND	NR	ND	NR	ND	NR	0	0.00	0.00
Lithuania	9	0.32	20	0.71	6	0.21	7	0.25	7	0.25	0.25
Luxembourg	5	0.85	5	0.83	3	0.49	4	0.64	4	0.63	0.73
Malta	0	0.00	1	0.21	5	1.01	5	0.97	0	0.00	0.00
Netherlands	108	0.63	69	0.40	103	0.60	90	0.52	86	0.49	0.44
Norway	16	0.30	24	0.45	27	0.51	37	0.69	20	0.37	0.35
Poland	116	0.31	128	0.34	121	0.32	57	0.15	120	0.32	0.29
Portugal	42	0.41	64	0.62	56	0.54	47	0.46	57	0.55	0.47
Romania	10	0.05	28	0.14	17	0.09	2	0.01	11	0.06	0.05
Slovakia	12	0.22	17	0.31	18	0.33	7	0.13	13	0.24	0.23
Slovenia	13	0.63	10	0.48	20	0.96	26	1.24	19	0.90	0.77
Spain	284	NR	370	NR	504	NR	191	NR	224	NR	NR
Sweden	81	0.81	89	0.88	113	1.10	88	0.85	107	1.03	0.90
United Kingdom	160	0.24	168	0.25	154	0.23	ND	ND	ND	NR	NR
EU/EEA	**2 496**	**0.47**	**2 570**	**0.47**	**2 652**	**0.46**	**1 928**	**0.43**	**2 268**	**0.51**	**0.44**

Source: Country reports.
ASR: age-standardised rate.
NR: no rate calculated. No information on estimated coverage was provided by Spain, so no notification rates were calculated.
ND: no data reported. Data have not been collected from the UK since 2020, as the country left the EU on 31 January 2020.

Figure 1. Distribution of confirmed listeriosis cases per 100 000 population by country, EU/EEA, 2021

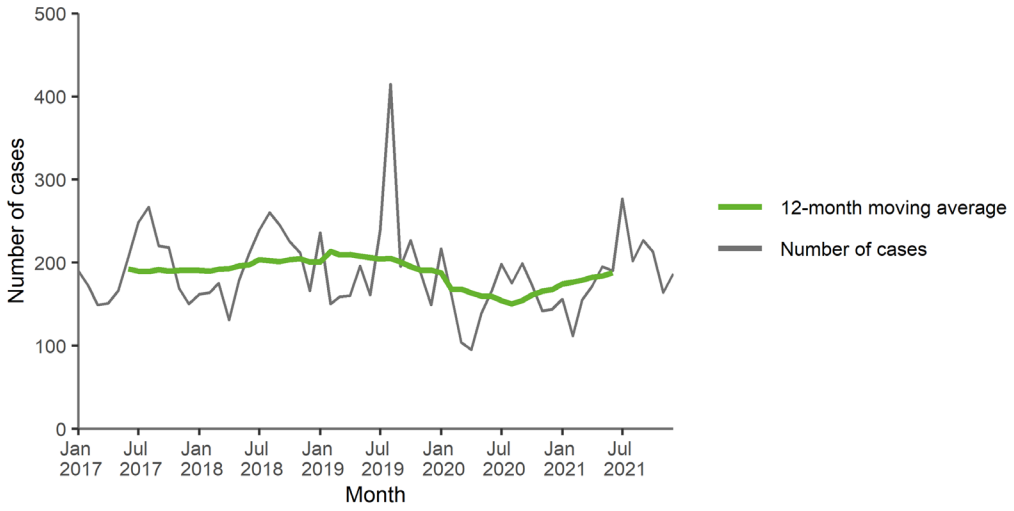


Number of listeriosis cases per 100 000 population, 2021.
Source: Country reports from Austria, Belgium, Bulgaria, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Sweden.

Member States reporting listeriosis cases consistently from 2017 to 2021 show a stable trend, with a decrease in 2020 (Figure 2).

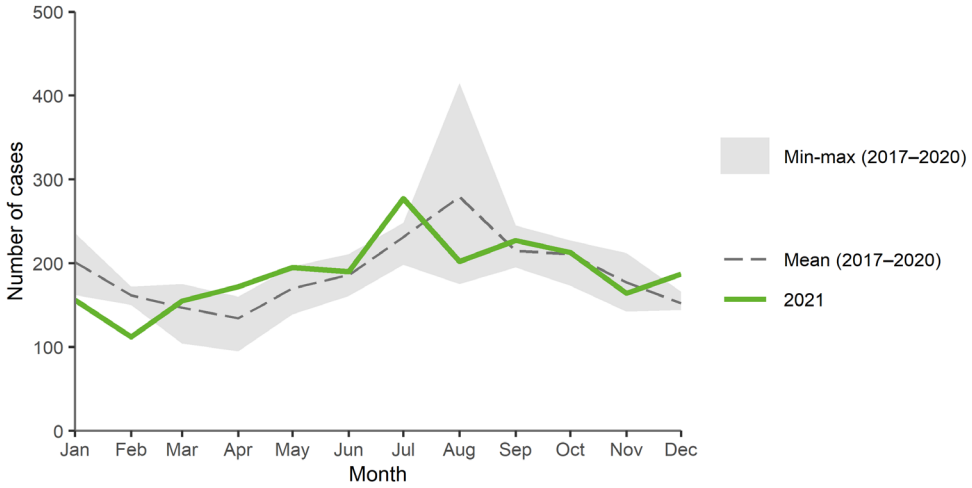
Listeriosis cases typically peak during the summer months and to a lesser degree during winter, but in 2021 the winter peak was relatively small.

Figure 2. Distribution of confirmed listeriosis cases by month, EU/EEA, 2017–2021



Source: Country reports from Austria, Belgium, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden.

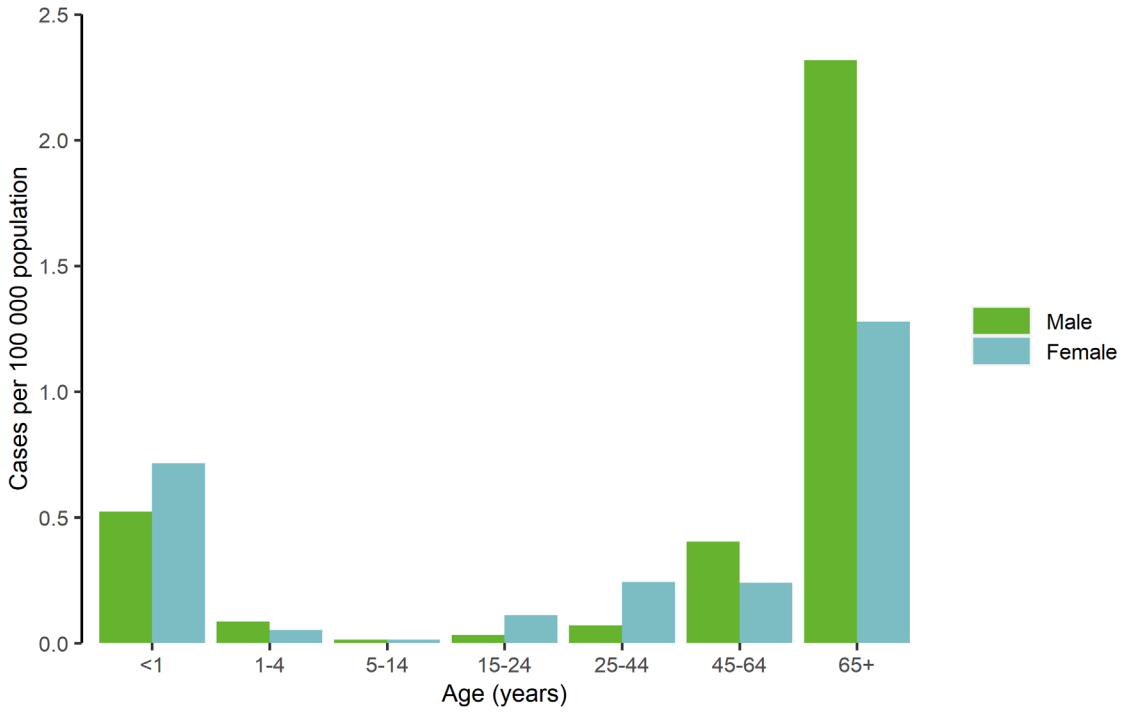
Figure 3. Distribution of confirmed listeriosis cases by month, EU/EEA, 2021 and 2017–2020



Source: Country reports from Austria, Belgium, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden.

Of confirmed listeriosis cases with known sex (N=2 267, i.e. all except one case), 55.4% were in males and 44.6% in females, corresponding to a male-to-female ratio of 1.2:1. The most affected age group were those over 64 years (1 594 cases; 70.4%, notification rate: 1.7 per 100 000 population). Ninety-four cases of pregnancy-associated listeriosis were reported in 2021. Of these, 10 resulted in miscarriage or fatal outcome of the newborn (pregnancy outcome reported for 44.7% of pregnancy-associated cases).

Figure 4. Distribution of confirmed listeriosis cases per 100 000 population, by age and gender, EU/EEA, 2021



Microbial surveillance

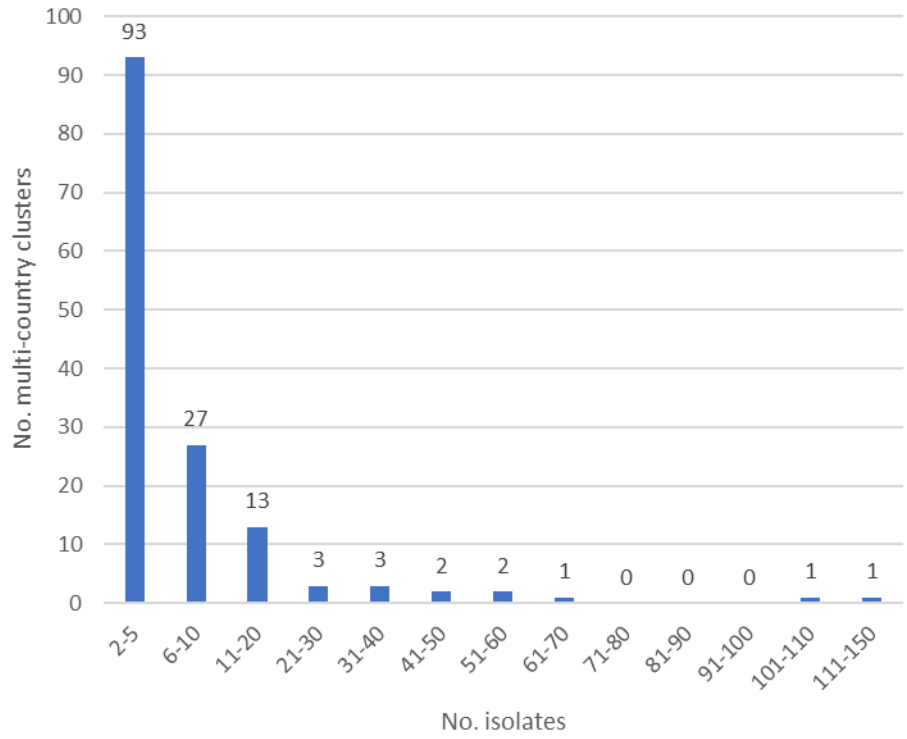
Subtyping of *L. monocytogenes* is either performed by phenotypic methods where serotypes are assigned, or by PCR where corresponding serogroups are assigned or can be derived from WGS data. In 2021, 12 Member States reported serotype and serogroup data (Austria, Belgium, Czechia, France, Germany, Hungary, Ireland, Luxembourg, Norway, Slovakia, Spain, and Sweden). This data is compiled in the EU surveillance reporting system, where e. g. serotype ½a is compiled with data reported as serogroup Iia. The most common type was Ivb (414) followed by Iia (339), Iib (80), and Iic (24).

In 2021, 11 Member States (Austria, Belgium, Czechia, Estonia, Ireland, Luxembourg, the Netherlands, Norway, Romania, Sweden, and Slovenia) reported ST data for a total of 381 isolates through TESSy case-based reporting. In addition to these, the ST could be determined *in silico* from WGS data submitted by Spain, Finland, and Portugal for a total of 216 isolates. In total, 26% (597 isolates) of the confirmed cases had information on ST. The most common ST was ST1 (n=90), followed by ST6 (n=37) and ST8 (n=36).

Sequencing-enhanced surveillance

Six Member States (Belgium, Czechia, Finland, Portugal, Slovenia, and Spain) submitted *L. monocytogenes* WGS data to TESSy for 319 isolates during 2021. In addition, 15 Member States submitted sequence data to contribute to ongoing multi-country outbreak investigations for 52 isolates. When analysed against historical sequences, a total of three multi-country clusters were detected throughout the year, including a total of nine isolates, and 43 isolates matched within pre-2021 detected multi-country clusters. Looking at all multi-country clusters detected by end of 2021, there were a total of 146, including 1 341 isolates with median four isolates per cluster (range 2–150), and median two involved Member States (range 2–11). The median cluster duration (time from oldest to newest isolate) was 2.3 years (range from 5 days to 14.8 years) for the 109 clusters with date information available for first and last isolate.

Figure 5. Numbers of isolates in *Listeria monocytogenes* microbiological multi-country clusters* detected by end of 2021



** All isolates within four alleles from at least one other isolate in the cluster by cgMLST.*
Source: Data from Belgium, Czechia, Finland, Portugal, Slovenia, Spain.

Outbreaks and other threats

In 2021, 23 urgent inquiries on listeriosis were launched in either ECDC's Epidemic Intelligence information System (EPIS) or EpiPulse by 10 different EU/EEA Member States, two non-EU/EEA countries, and ECDC. For 19 of these, no EU/EEA multi-country aspect was identified. For the four EU/EEA multi-country events, a probable source was found for two. One of the multi-country clusters involved ST1 (the most commonly reported ST in 2021), and the three others involved ST7, ST388, and ST451.

Discussion

Listeriosis is one of the most severe food- and waterborne diseases under EU surveillance and has the highest proportion of hospitalised cases of all zoonoses under EU surveillance [5]. The EU surveillance of listeriosis focuses on severe, invasive forms of the disease, for which the risk groups are mainly elderly and immunocompromised persons as well as pregnant women and infants. Notification of listeriosis cases in humans is compulsory in the vast majority of the EU/EEA Member States. Listeriosis can also manifest in milder forms causing gastrointestinal symptoms, but these cases are usually not notified, or even tested for at country-level and are also not in the scope of the EU/EEA-level surveillance.

Although a decrease in number of cases was observed at the EU level in 2020, the overall trend for listeriosis in 2017–2021 did not show a significant decrease or increase [5]. The decrease in 2020 likely has to do with the COVID-19 pandemic that has largely occupied the EU public health resources and hence might have affected surveillance capacity for other infectious diseases in some Member States. It is speculated that also COVID-19 control measures, such as the ones reducing peoples' outdoor activities and increasing the level of general hygiene, could have an effect in reducing foodborne diseases [6].

The year 2021 was the third year of EU/EEA-wide WGS-enhanced listeriosis surveillance, which started in March 2019. Overall, the COVID-19 pandemic did not seem to affect the number of Member States reporting listeriosis sequencing data proactively, although one Member State fewer submitted in 2021 than in 2019–2020. Microbiological clusters detected from these data show that although the multi-country clusters tend to be small and affect only a few Member States (skewed by the low number of Member States submitting data), they also often persist for several years, even decades. This indicates that microbiological cluster detection efforts combined with other relevant data, such as sequences from food isolates and exposure data, could help in locating sources of

the pathogen and allow the setting of control measures to reduce the EU/EEA burden of this notably severe disease.

In 2021, *L. monocytogenes* was identified as the causative agent in eight strong-evidence and 12 weak-evidence foodborne outbreaks that together affected 94 people in the EU, with 38 hospitalised cases and nine deaths, as reported to the European Food Safety Authority (EFSA) [5]. Four of the strong-evidence foodborne outbreaks were caused by fish products (two in the Netherlands and two in Sweden), three by meat products (reported by Austria, Finland, and Sweden) and one by broiler meat in Germany. The number of foodborne outbreaks reported for 2021 was the highest since EFSA first started collecting data, which might be explained by the implementation of high-discrimination typing methods based on WGS that greatly facilitate outbreak confirmation.

Public health implications

The persistently stable trend seen at the EU/EEA-level and the severity of listeriosis are worrying and call for more attention to be given to the prevention and control of the disease and outbreaks. It is important to raise awareness of listeriosis and risky foods among risk groups, currently especially among the elderly, where the majority of cases occur, but also among pregnant women. In addition, supranational cross-sectoral collaboration, including sequence data sharing, is essential in addressing the occurrence of persistent *L. monocytogenes* strains in humans.

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