

SURVEILLANCE REPORT

Haemophilus influenzae disease

Annual Epidemiological Report for 2021

Key facts

- In 2021, 1 698 confirmed cases of invasive *Haemophilus influenzae* disease were reported in the European Union/European Economic Area (EU/EEA). The number of cases is similar to 2020 (1 849 cases) but less than that for previous years. The low number of cases observed during the COVID-19 pandemic may be a result of the public health measures introduced, the repurposing of healthcare services and the under-reporting of cases during the period.
- The notification rate in 2021 was 0.4 cases per 100 000 population, which is a decrease from 2019 when it was 0.7 per 100 000 population.
- Age-specific rates were highest in infants below one year (4.0 cases per 100 000 population for males and females), followed by people aged 65 years and over (1.0 cases per 100 000 population for males and 0.6 for females).
- Serotyping data were available for 54% of confirmed cases. Non-capsulated strains were presented in 62% of cases and were the most common in all age groups.
- In 2021, serotype b (Hib) was the most common capsulated serotype observed (20%), and this represented a slight increase on previous years.

Introduction

Invasive *Haemophilus influenzae* is a bacterium that can cause serious bacterial infections, particularly the type B strain that affects both children and adults, with young children being most at risk. *Haemophilus influenzae* can cause a number of serious conditions including meningitis, septicemia, pneumonia, and epiglottitis, and it remains the leading cause of meningitis deaths in unvaccinated people around the world [1].

Methods

This report is based on data for 2021 retrieved from The European Surveillance System (TESSy) on 26 April 2023. TESSy is a system for the collection, analysis, and dissemination of data on communicable diseases. 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].

In 2021, 30 EU/EEA Member States reported data on invasive *H. influenzae* disease to ECDC. Most of the Member States reported data using the EU case definition (Commission Implementing Decision 2018/945/EU of 22 June 2018 of the European Parliament and of the Council) or a case definition compatible with the EU case definition for confirmed cases. For two Member States, the case definition was not specified/unknown (Greece, Belgium), and one Member State used another case definition (Germany) [2]. The majority of Member States reported data from comprehensive, passive surveillance systems with national coverage [3]. Belgium reported aggregated data.

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Epidemiology

In 2021, 30 EU/EEA countries reported a total of 1 698 confirmed cases of invasive *H. influenzae* disease, which was a similar number when compared to 2020 (1 849), but lower than that for previous years (Table 1). France, Germany, and the Netherlands accounted for (56.8%) of the confirmed cases, reporting 434, 361 and 171 cases respectively. Bulgaria, Croatia, Malta, and Romania reported zero cases. In 2021, the overall notification rate was 0.4 per 100 000 population, which is similar to 2020 (0.4 per 100 000) but lower than the rate for previous years (0.7 in 2019, 0.8 in 2018 and in 2017). The highest rates were reported by Lichtenstein and Iceland (5.7 and 1.9 per 100 000 respectively). Figure 1 represents the notification rate per 100 000 in EU/EEA.

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

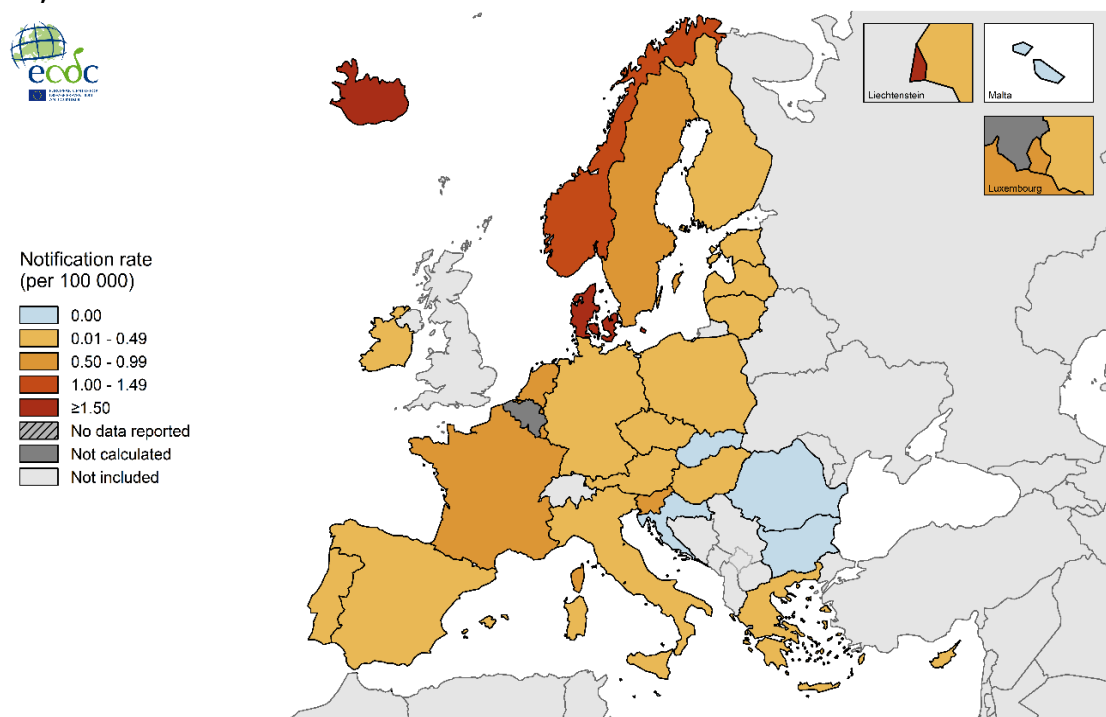
Country	2017		2018		2019		2020		2021	
	Number	Rate	Number	Rate	Number	Rate	Number	Rate	Number	Rate
Austria	39	0.4	49	0.6	64	0.7	28	0.3	31	0.3
Belgium	67	NRC	77	NRC	76	NRC	27	NRC	38	NRC
Bulgaria	2	0.0	1	0.0	3	0.0	0	0.0	0	0.0
Croatia	1	0.0	0	0.0	1	0.0	0	0.0	0	0.0
Cyprus	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
Czechia	23	0.2	26	0.2	25	0.2	22	0.2	15	0.1
Denmark	113	2.0	121	2.1	115	2.0	59	1.0	101	1.7
Estonia	2	0.2	1	0.1	3	0.2	2	0.2	1	0.1
Finland	73	1.3	89	1.6	77	1.4	41	0.7	15	0.3
France	603	1.2	594	1.2	694	1.0	399	0.6	434	0.6
Germany	804	1.0	832	1.0	940	1.1	520	0.6	361	0.4
Greece	7	0.1	7	0.1	5	0.0	2	0.0	6	0.1
Hungary	21	0.2	32	0.3	24	0.2	10	0.1	15	0.2
Iceland	4	1.2	3	0.9	8	2.2	5	1.4	7	1.9
Ireland	45	0.9	59	1.2	63	1.3	31	0.6	16	0.3
Italy	153	0.3	169	0.3	185	0.3	76	0.1	66	0.1
Latvia	2	0.1	4	0.2	4	0.2	1	0.1	1	0.1
Liechtenstein	NDR	NDR	NDR	NDR	NDR	NDR	NDR	NDR	2	5.1
Lithuania	8	0.3	14	0.5	3	0.1	0	0.0	2	0.1
Luxembourg	0	0.0	0	0.0	0	0.0	3	0.5	3	0.5
Malta	0	0.0	0	0.0	3	0.6	0	0.0	0	0.0
Netherlands	224	1.3	237	1.4	227	1.3	203	1.2	166	0.9
Norway	120	2.3	91	1.7	98	1.8	40	0.7	58	1.1
Poland	108	0.3	115	0.3	102	0.3	78	0.2	52	0.1
Portugal	46	0.4	35	0.3	42	0.4	35	0.3	42	0.4
Romania	2	0.0	1	0.0	0	0.0	1	0.0	0	0.0
Slovakia	5	0.1	6	0.1	8	0.1	5	0.1	1	0.0
Slovenia	20	1.0	19	0.9	24	1.2	11	0.5	15	0.7
Spain	308	0.8	364	0.9	245	0.6	161	0.4	171	0.4
Sweden	229	2.3	201	2.0	259	2.5	89	0.9	78	0.8
United Kingdom	863	1.3	835	1.3	NDR	NDR	NDR	NDR	NDR	NDR
EU-EEA	3 892	0.8	3 982	0.8	3 298	0.7	1 849	0.4	1 698	0.4

Source: Country reports.

NDR: No data reported.

NRC: No rate calculated.

Figure 1. Confirmed *Haemophilus influenzae* disease cases per 100 000 population by country, EU/EEA, 2021



Administration boundaries: ©EuroGeographics

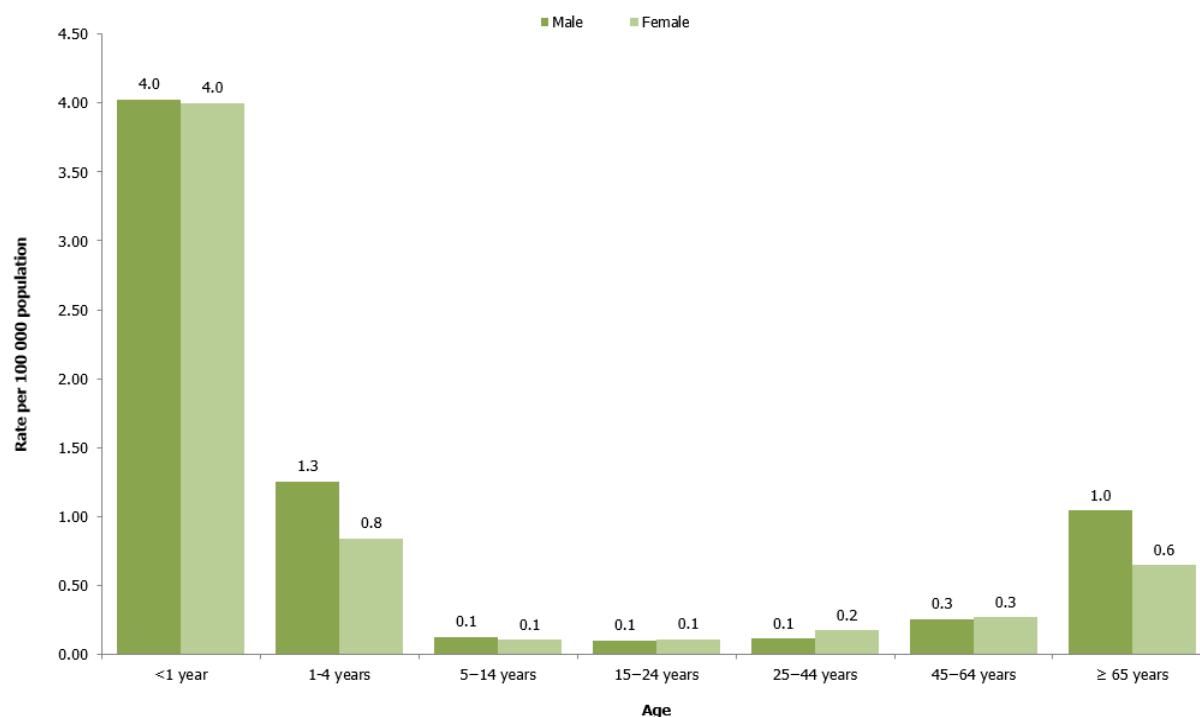
The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union. ECDC. Map produced on 3 May 2023.

Age and gender distribution

In 2021, the invasive *H. influenzae* disease notification rate for infants under one year was 4.0 confirmed cases per 100 000 population for both males and females. Among adults aged 65 years and over, the rates were 1.0 confirmed case per 100 000 population for males and 0.6 for females. For the age group 25–44 years, there was a higher notification rate for females than males (0.2 versus 0.1 per 100 000 population respectively) (see Figure 2).

The highest rates among infants were reported in Luxembourg (30.2 cases per 100 000 population), Portugal (11.5), and France (11.1).

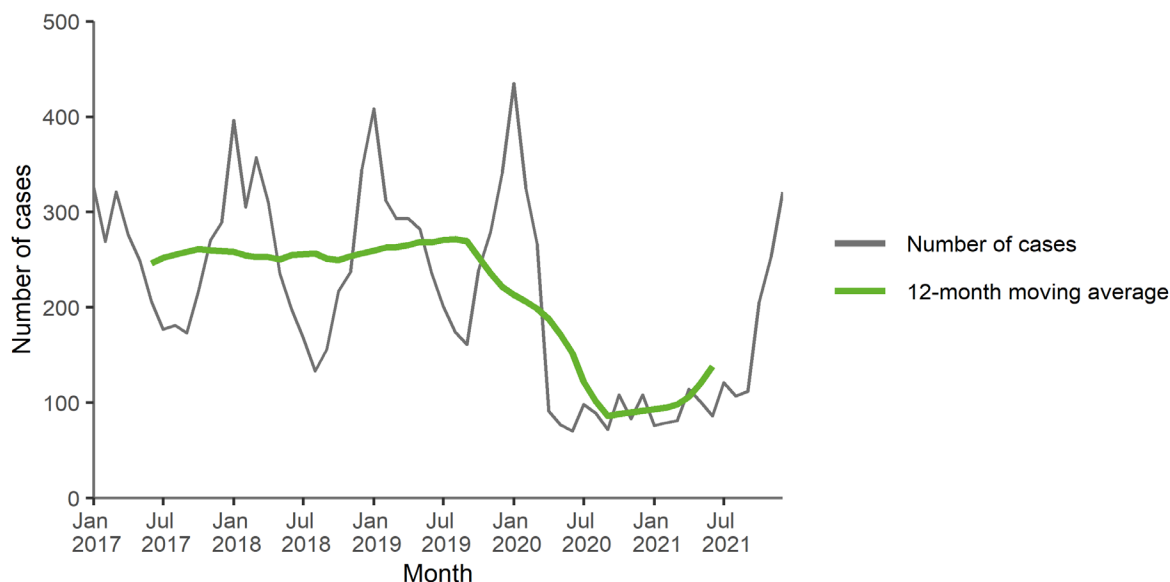
Figure 2. Confirmed *Haemophilus influenzae* disease cases per 100 000 population, by age and gender, EU/EEA, 2021



Seasonality and trend

The distribution of invasive *H. influenzae* cases in the EU/EEA by month typically follows a seasonal pattern, with peaks during the winter months (as displayed in January 2019, January 2018 and January 2017). However, the data from 2020 and 2021 show a significant deviation from this historical pattern, which can most probably be attributed to the COVID-19 restrictions that reduced the transmission of respiratory infections. These measures appear to have caused a decrease in the number of cases during periods when they would typically rise, which is particularly noticeable in the decrease during early 2020 and a sustained low throughout that year. As shown in the graph, after an initial decrease, following a peak in early 2020, cases remained significantly lower than in previous years, until a slight resurgence occurred in mid-2021 (Figure 3).

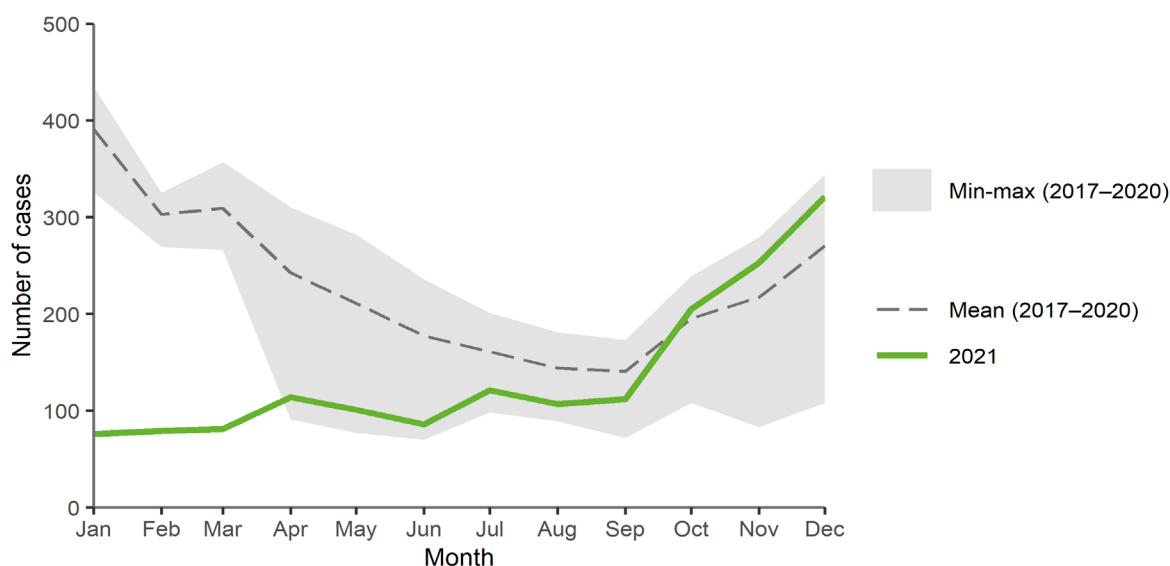
Figure 3. Confirmed *Haemophilus influenzae* disease cases by month, EU/EEA, 2017–2021



Source: Country reports from Austria, Bulgaria, Croatia, 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 4 shows that the initial number of cases in January 2021 was lower than the historical trend, before starting to increase slowly as of October 2021.

Figure 4. Confirmed *Haemophilus influenzae* disease cases by month, EU/EEA, 2021 and 2017–2020

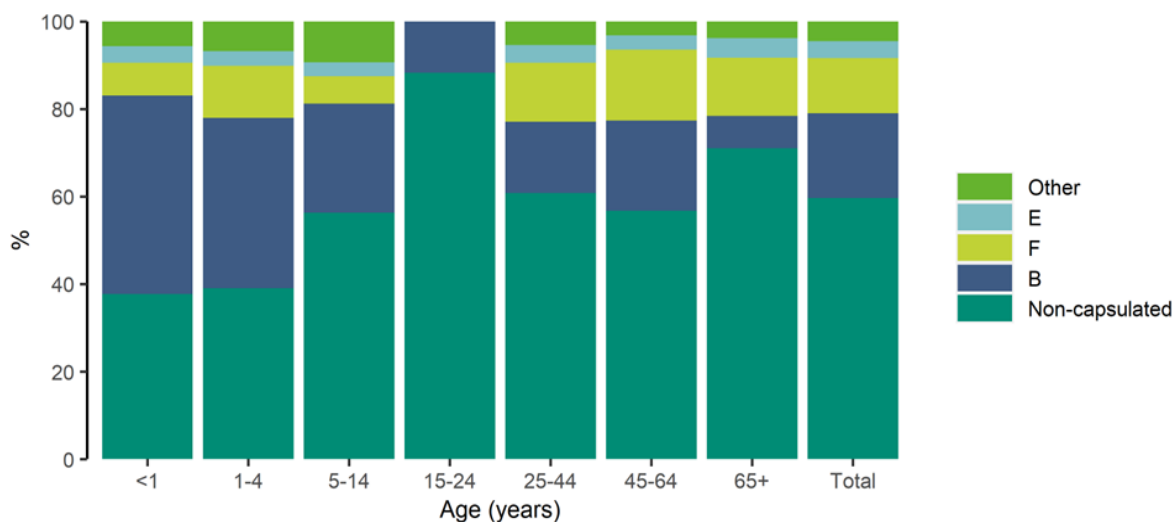


Source: Country reports from Austria, Bulgaria, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden.

Serotype

In 2021, there were 916 cases of invasive *H. influenzae* with known serotype out of 1 698 (54%). Of the known cases, 573 cases (62%) were non-capsulated (non-typable), 122 cases (13%) were serotype f and 185 cases (20%) were serotype b (Hib). Non-capsulated strains were the most common in most age groups. Serotype b was more common among infants under one year (46 cases), and among children aged 1–4 years (48 cases). (Figure 5).

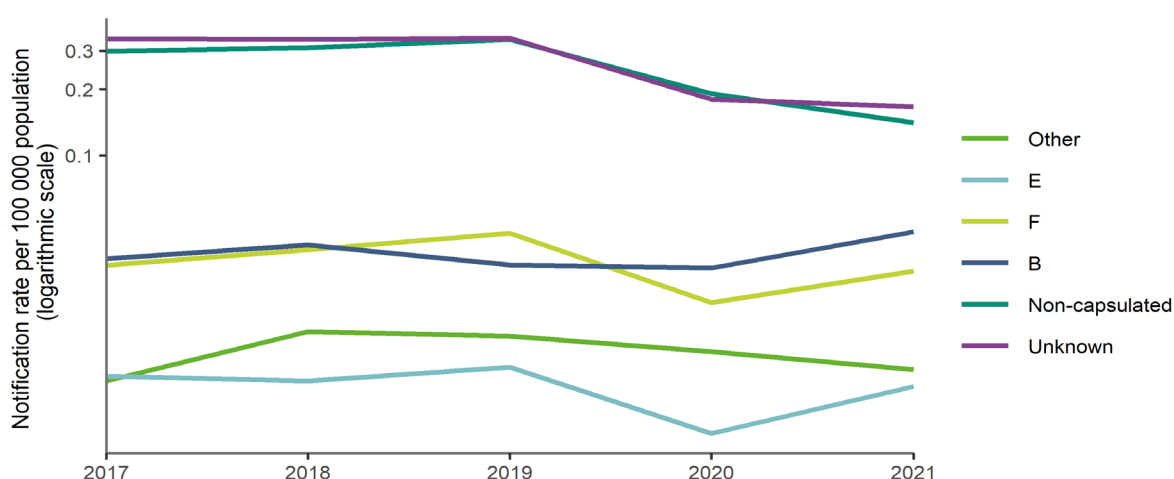
Figure 5. Serotype distribution of confirmed *Haemophilus influenzae* disease cases by age group, EU/EEA, 2021



In 2021, most of the cases had a non-capsulated serotype (0.14 per 100 000 population), and this trend has been the same since 2017. Serotype B (Hib) increased slightly between 2017 (0.03) and 2021 (0.04). In 2021, the notification rate for cases with unknown serotype remained high (0.16 per 100 000 population). However, when making comparisons with previous years, the proportion of different serotypes should be interpreted with caution due to the fact that the absolute numbers were much lower in 2021.

Figure 6 shows the notification rates per 100 000 population for different serotypes of invasive *H. influenzae* from 2017 to 2021. Among the different serotypes/groups of serotypes the rate for non-capsulated strains was highest for most of the years in the five-year period 2017–2021, and the rate for 2021 was the lowest in the five years (0.14 per 100 000 population). Serotype b showed a slight increase in 2021 compared to 2017 (0.04 versus 0.03 respectively). Although serotypes e and f have experienced fluctuations, in recent years they have displayed a general upward trend. The number of unknown serotype cases decreased in 2021 compared to 2017 (0.16 versus 0.33 respectively).

Figure 6. Notification rate of confirmed *Haemophilus influenzae* disease per 100 000 population, by serotype and year, EU/EEA, 2017–2021



Source: Country reports from Austria, Belgium, Czechia, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Liechtenstein, the Netherlands, Norway, Poland, Portugal, Slovenia, Spain, Sweden.

Clinical presentation

In 2021, clinical presentations were documented for a total of 1 295 (76%) cases of invasive *H. influenzae* disease. Among the known cases, the most prevalent presentations were septicaemia, reported in 305 cases (23.5%), and pneumonia, reported in 282 cases (21.7%). Meningitis was identified in 148 cases (11.4%), while a combination of meningitis and septicaemia was seen in 22 cases (1.7%). Other less frequent presentations included epiglottitis in 31 cases, cellulitis in two cases, and osteomyelitis in 18 cases. A total of 394 cases (30.4%) were classified as 'other presentation'. Finally, 403 cases were reported with unknown clinical presentations. Septicaemia remained the most common clinical presentation across all age groups and was consistently prevalent in reported cases.

Outcome

In 2021, the outcome was known for 803 cases (47%). For 78 (9.7%) cases this was not under surveillance and for 895 (53%) cases the outcome was unknown. The case fatality rate (CFR) for cases with known outcome was 7.09% (179 deaths), four deaths were reported in infants under one year, and six in children aged 1–4 years.

When considering the outcome of the cases with known serotype, 2021 data showed that the case fatality rate for serotype e was 9.5% (two deaths from 21 cases), and the CFR for serotype a was 9.1% (two deaths from 20 cases). The CFR for the non-capsulised cases was 7.6% (23 deaths from 301 cases) and the CFR for serotype b was 9.2% (10 deaths from 98 cases).

Vaccination status

In 2021, the vaccination status was known for 443 of the 1 698 confirmed cases (26%) of invasive *H. influenzae* disease. Among those with known vaccination status, 133 cases (30%) were vaccinated, and 310 (70%) were unvaccinated. The number of doses of vaccine received varied, with 13 cases having received one dose, 32 having received two doses, 37 having received three doses and 21 having received four doses.

In total, 47 of 158 (29.7%) cases among infants under one year were vaccinated, 47 of 175 cases among children aged 1–4 years (26.8%) were vaccinated, and only eight of 745 (0.93%) cases aged over 65 years were vaccinated.

Discussion

In 2021, the EU/EEA reported a total of 1 698 confirmed cases of invasive *H. influenzae* disease, similar to the number for 2020 (1 849 cases), but a notable decrease compared to 2019 (3 298) and 2018 (3 982). This decline is in line with the reduced incidence observed for many respiratory diseases, probably as a result of the extensive public health measures implemented during the COVID-19 pandemic, such as mask-wearing, social distancing, and lockdowns [4,5]. These measures not only decreased the spread of SARS-CoV-2 but also inadvertently reduced the transmission of other respiratory pathogens, including *H. influenzae* [5].

The pandemic also had an impact on routine healthcare activities, potentially disrupting vaccination programmes, especially on a global basis [6]. It is possible that these interruptions contributed to the relatively high proportion of invasive Hib cases observed in 2021 [7]. In fact, in 2021 Hib was responsible for 20% of the cases with known serotyping, a slight increase on previous years, reflecting the importance of maintaining vaccination continuity [8,9].

Clinical presentations of invasive *H. influenzae* disease in 2021 varied, with septicaemia and pneumonia being the most common, reported in 305 cases (23.5%) and 282 cases (21.7%) respectively. Meningitis was also present in 148 cases (11.4%). The predominance of septicaemia across all age groups underscores the severity of this infection. The diversity in clinical manifestations highlights the pathogen's capacity to cause significant morbidity across different demographic groups, results which were similar in the report for 2018 [10].

Serotyping results showed that among all the serotypes, non-capsulated strains remained the most prevalent, particularly among the elderly, indicating a shift in the epidemiology of the disease. Non-capsulated strains accounted for 62% of cases with known serotyping. In contrast, serotype f and serotype b (Hib) accounted for 13% and 20% respectively. This distribution suggests that the trend in dominant non-capsulated strains continues, highlighting the importance of the Hib vaccination and the need to reinforce efforts to maintain it [11-15].

The low number of cases in 2021, compared to previous years, coincided with the introduction of COVID-19 measures, hinting at the complex interplay between public health interventions and the epidemiology of other infectious diseases. This observation emphasises the broader impact of such public health measures, extending beyond their immediate target diseases [16].

The year 2021 illustrated how intertwined infectious disease dynamics can be, influenced by both direct interventions against specific pathogens and broader public health strategies. It also underscored the critical need for robust infectious disease surveillance and adaptable public health strategies to manage the spectrum of respiratory pathogens alongside emerging threats such as COVID-19.

Public health implications

The significant decrease in invasive *H. influenzae* cases in the EU/EEA during 2021 compared to pre-pandemic levels, with 1 698 reported cases, underscores the profound impact of COVID-19 public health measures. These interventions not only reduced SARS-CoV-2 spread, but also affected other respiratory pathogens. However, pandemic-induced disruptions in routine healthcare, particularly vaccinations, probably contributed to an increased proportion of invasive Hib cases, which will need to be monitored carefully in future surveillance data. The clinical diversity and severity, including septicaemia and pneumonia, highlight the pathogen's morbidity potential. The dominance of non-capsulated strains among the elderly indicates a shift in epidemiology, necessitating continuous surveillance and adaptable public health strategies in the EU/EEA to manage respiratory pathogens alongside emerging threats, such as COVID-19.

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