

Haemophilus influenzae

Annual Epidemiological Report for 2018

Key facts

- In 2018, 3 982 confirmed cases of invasive *Haemophilus influenzae* disease were reported in the EU/EEA.
- The notification rate was 0.8 cases per 100 000 population, which is an increase compared to 2014 when it was 0.6.
- Age-specific rates were highest in infants under one year (4.0 cases per 100 000 population), followed by people aged 65 years and over (2.4 cases per 100 000 population).
- Serotyping data were available for 57% of confirmed cases. Non-capsulated strains caused 78% of cases overall and the majority of cases in all age groups.
- Serotype f was the most common capsulated serotype observed (9%).
- The *H. influenzae* serotype b (Hib) vaccination has led to a sustained reduction in serotype b infections. In 2018, 7% of cases with known serotype were caused by serotype b.

Methods

This report is based on data for 2018 retrieved from The European Surveillance System (TESSy) on 11 March 2020. 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 2018, 30 EU/EEA Member States reported data on invasive *H. influenzae* disease to ECDC. The majority of Member States reported data using the EU case definition (Commission Implementing Decision 2012/506/EU of 8 August 2012 of the European Parliament and of the Council) or a case definition compatible with the EU case definition for confirmed cases. For three Member States, the case definition was not specified/unknown. The majority of Member States reported data from comprehensive, passive surveillance systems with national coverage. Belgium and France reported data from sentinel surveillance systems in 2017 [2]. Belgium reported aggregated data.

Epidemiology

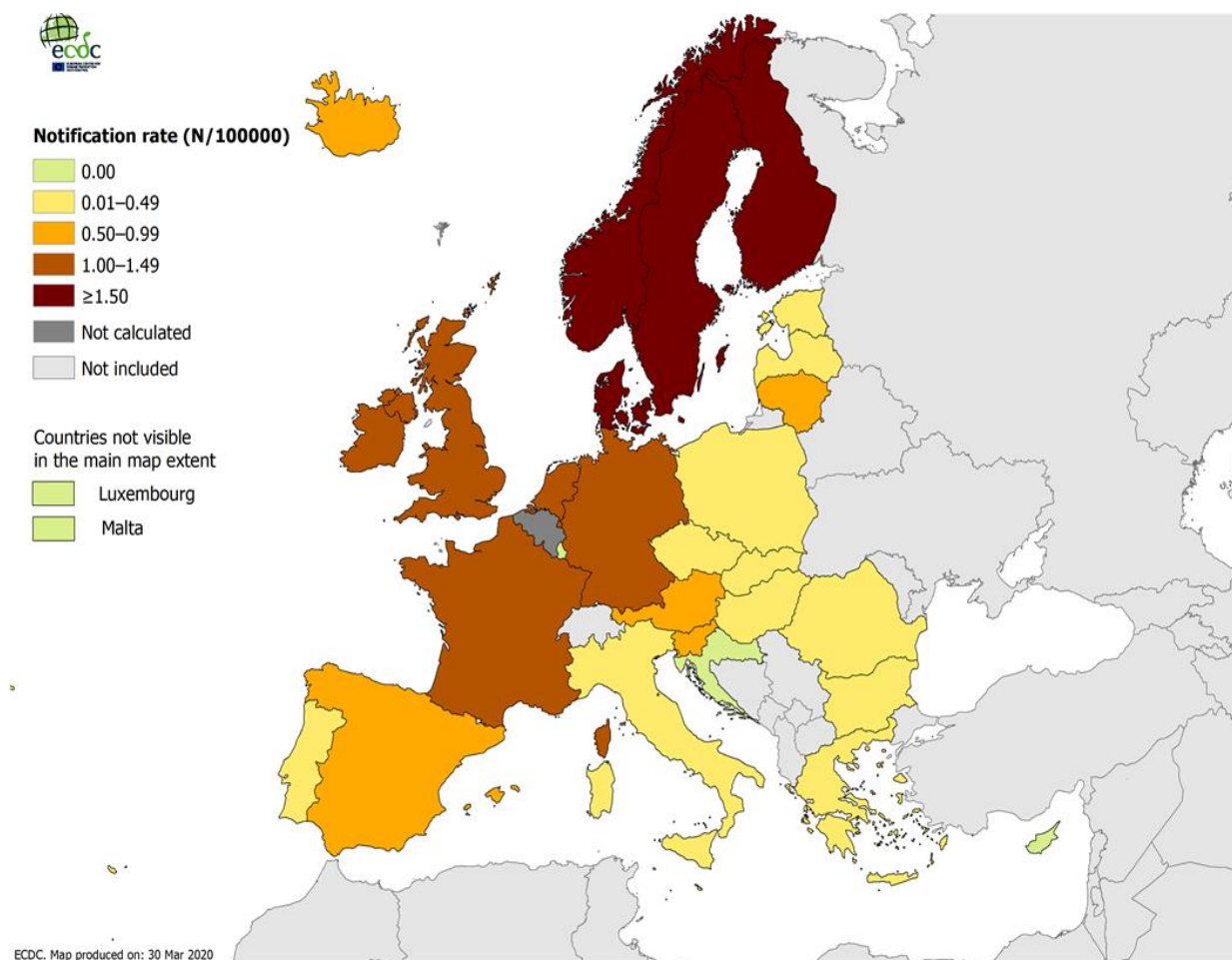
For 2018, 30 countries reported 3 982 confirmed cases of invasive *H. influenzae* disease in the EU/EEA (Table 1). France, Germany and the United Kingdom accounted for 57% of all confirmed cases. Croatia, Cyprus, Luxembourg, and Malta reported zero cases, while Liechtenstein did not report data on *H. influenzae* (Table 1). In 2018, the notification rate was 0.8 confirmed cases per 100 000 population in the EU/EEA, with the highest rates reported by Denmark and Sweden (2.1 and 2.0 cases per 100 000 population respectively) (Table 1, Figure 1). The notification rate of invasive *H. influenzae* in the EU/EEA increased from 0.6 in 2014 to 0.8 per 100 000 population in 2017 and in 2018. In 2010–12 the annual notification rate was 0.5 per 100 000 population [4].

Table 1. Distribution of confirmed *Haemophilus influenzae* disease cases and rates per 100 000 population by country, EU/EEA, 2014–2018

Country	2014		2015		2016		2017		2018			
	Number	Rate	Number	Rate	Number	Rate	Number	Rate	Confirmed cases	Rate	ASR	Reported cases
Austria	28	0.3	45	0.5	41	0.5	39	0.4	49	0.6	0.5	49
Belgium	56	-	64	-	85	-	67	-	77	-	-	77
Bulgaria	2	0.0	4	0.1	3	0.0	2	0.0	1	0.0	0.0	1
Croatia	1	0.0	0	0.0	1	0.0	1	0.0	0	0.0	0.0	0
Cyprus	1	0.1	0	0.0	2	0.2	0	0.0	0	0.0	0.0	0
Czech Republic	19	0.2	32	0.3	22	0.2	23	0.2	24	0.2	0.2	26
Denmark	82	1.5	90	1.6	106	1.9	113	2.0	121	2.1	2.0	121
Estonia	4	0.3	1	0.1	0	0.0	2	0.2	1	0.1	0.1	1
Finland	59	1.1	52	1.0	69	1.3	73	1.3	89	1.6	1.5	89
France	453	0.9	508	1.1	588	1.2	603	1.2	594	1.2	1.1	594
Germany	458	0.6	539	0.7	613	0.7	804	1.0	834	1.0	0.8	851
Greece	6	0.1	10	0.1	4	0.0	7	0.1	7	0.1	0.1	7
Hungary	7	0.1	8	0.1	16	0.2	21	0.2	32	0.3	0.3	33
Iceland	4	1.2	1	0.3	12	3.6	4	1.2	3	0.9	0.9	3
Ireland	61	1.3	51	1.1	58	1.2	45	0.9	59	1.2	1.3	59
Italy	101	0.2	123	0.2	141	0.2	153	0.3	169	0.3	0.2	169
Latvia	1	0.0	2	0.1	2	0.1	2	0.1	4	0.2	0.2	4
Liechtenstein
Lithuania	2	0.1	14	0.5	7	0.2	8	0.3	14	0.5	0.5	14
Luxembourg	-	-	0	0.0	0	0.0	0	0.0	0	0.0	0.0	0
Malta	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0.0	0
Netherlands	160	1.0	195	1.2	190	1.1	224	1.3	237	1.4	1.3	237
Norway	71	1.4	98	1.9	85	1.6	120	2.3	91	1.7	1.7	91
Poland	41	0.1	62	0.2	69	0.2	108	0.3	115	0.3	0.3	115
Portugal	40	0.4	18	0.2	17	0.2	46	0.4	35	0.3	0.3	37
Romania	2	0.0	4	0.0	5	0.0	2	0.0	1	0.0	0.0	1
Slovakia	4	0.1	7	0.1	1	0.0	5	0.1	6	0.1	0.1	6
Slovenia	15	0.7	31	1.5	20	1.0	20	1.0	19	0.9	0.9	19
Spain	130	0.6	147	0.6	242	0.6	308	0.8	364	0.9	0.9	364
Sweden	204	2.1	221	2.3	178	1.8	229	2.3	201	2.0	1.8	201
United Kingdom	787	1.2	850	1.3	807	1.2	863	1.3	835	1.3	1.2	883
EU/EEA	2 799	0.6	3 177	0.7	3 384	0.7	3 892	0.8	3 982	0.8	0.8	4 052

Source: Country reports. Legend: = no data reported, ASR: age-standardised rate, - = no notification rate calculated.

Figure 1. Distribution of confirmed *Haemophilus influenzae* disease cases per 100 000 population by country, EU/EEA, 2018

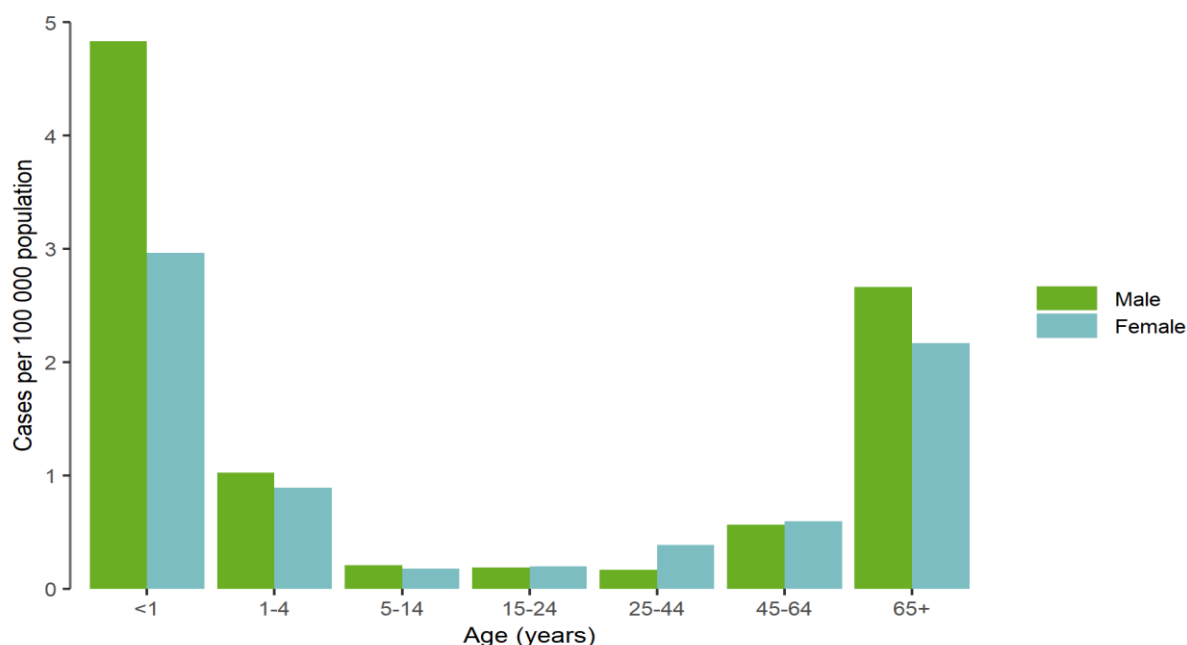


Source: Country reports from Austria, Belgium, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom.

Age and gender distribution

In 2018, invasive *H. influenzae* disease was predominantly reported in infants and the elderly, with a notification rate of 4.0 confirmed cases per 100 000 population in children under one year of age, and 2.4 confirmed cases per 100 000 population in adults aged 65 years and over (Figure 2). The highest rates among infants were reported in the Netherlands (12.4 cases per 100 000 population), Slovenia (9.9), the United Kingdom (7.5) and Spain (6.0). In adults aged 65 years and over, the highest rates were reported in Denmark (5.9 per 100 000 population) and Ireland (4.3). Stratified by gender, rates were higher among males in all age groups except adults aged 25-44 years. The overall male-to-female ratio of the frequency of reported cases was 0.9:1.

Figure 2. Distribution of confirmed *Haemophilus influenzae* disease cases per 100 000 population, by age and gender, EU/EEA, 2018

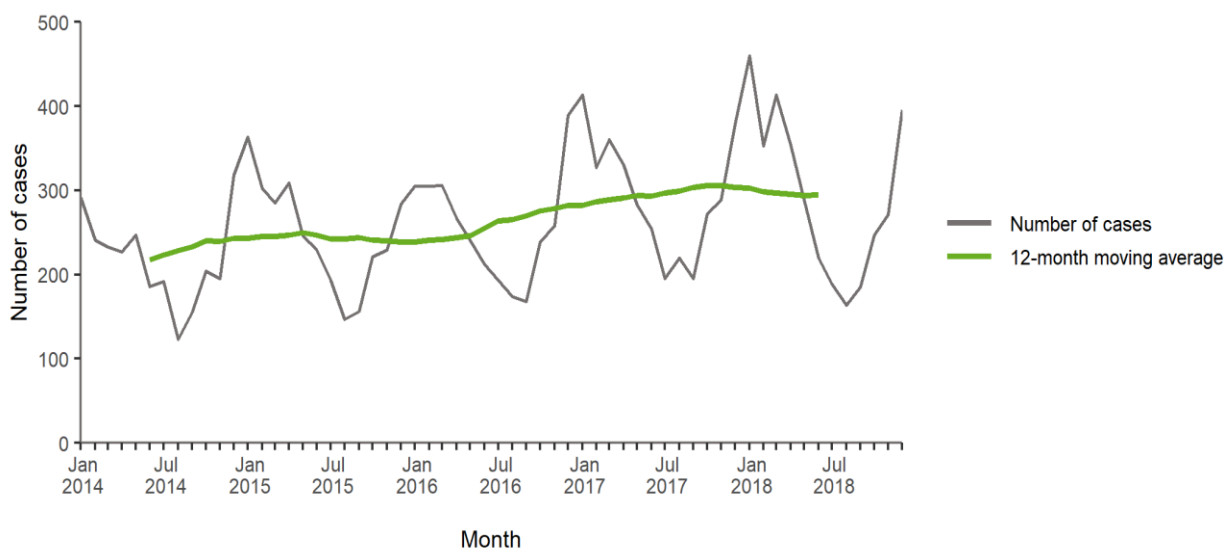


Source: Country reports from Austria, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom.

Seasonality and trend

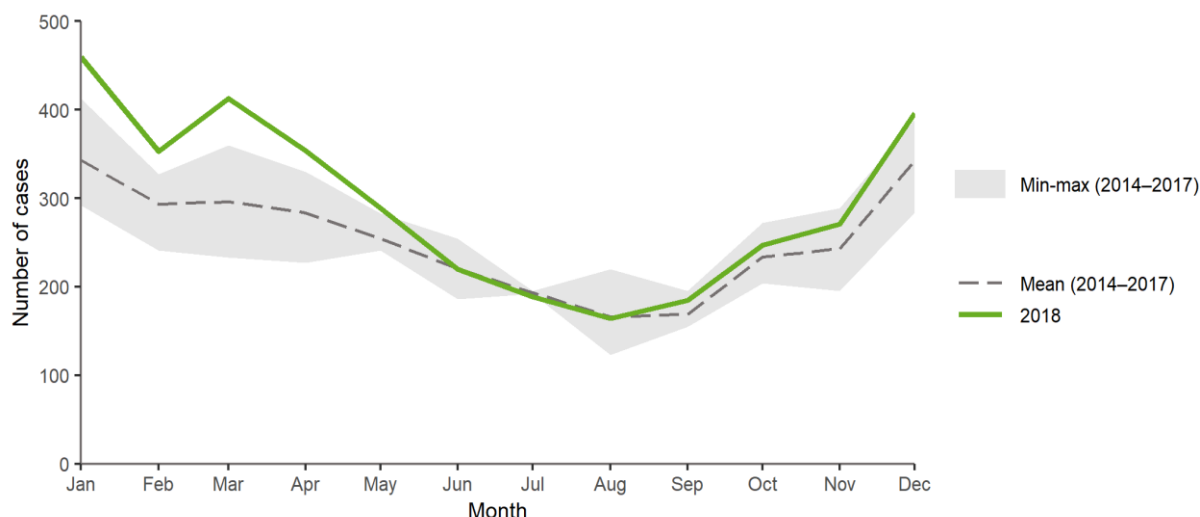
The distribution of invasive *H. influenzae* cases by month follows a seasonal pattern, with the highest number of cases reported in the winter months, followed by a steady decrease until September and an increasing trend towards the end of the year, reaching a peak in December. Compared with the mean number of cases reported during the period 2014–2017, a higher number of cases were reported in 2018 (Figure 3). Figure 4 shows an increasing trend in the number of cases reported from 2014 to 2018.

Figure 3. Distribution of confirmed *Haemophilus influenzae* disease cases by month, EU/EEA, 2014–2018



Source: Country reports from Austria, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Sweden, and the United Kingdom.

Figure 4. Distribution of confirmed *Haemophilus influenzae* disease cases by month, EU/EEA, 2018 and 2014–2017



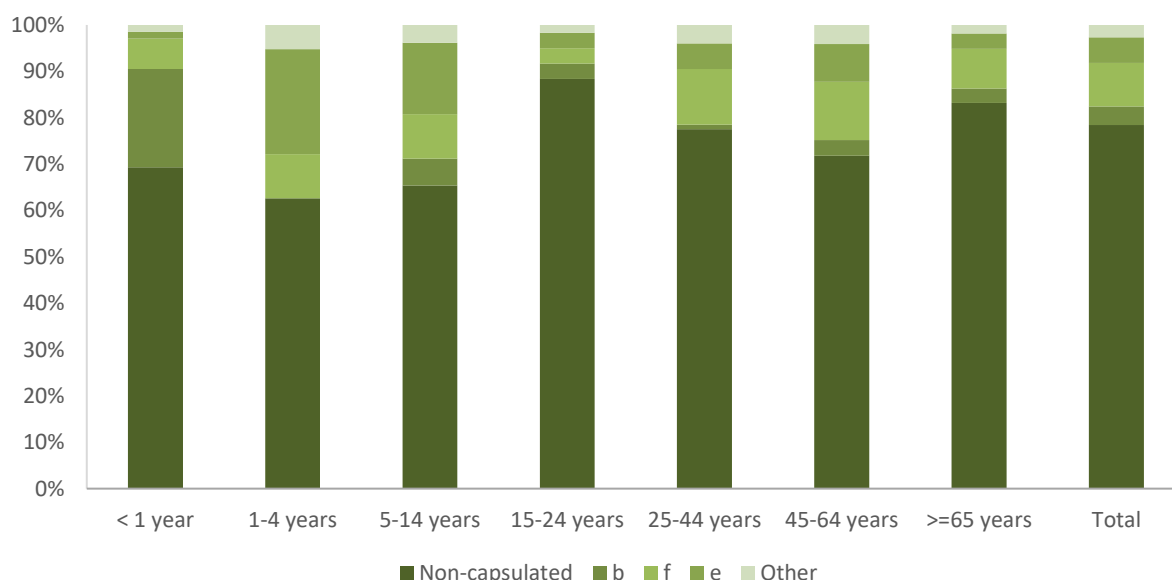
Source: Country reports from Austria, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Sweden, and the United Kingdom.

Serotype

Of the 3 982 confirmed cases of invasive *H. influenzae* disease, 2 266 (57%), reported by 23 Member States, had a known serotyping result. Of these cases, 78% (n=1 777) were non-capsulated (non-typable), 9% (n=213) were serotype f, 7% (n=153) were serotype b (Hib) and 3% (n=63) were serotype e; 60 cases were reported as serotype a, c, d or non-b. Non-capsulated strains were the most common cause in all age groups (Figure 5). Hib accounted for 21% and 23% of invasive disease in children <1 year of age, and 1-4 years of age, respectively.

Notification rates of confirmed invasive *H. influenzae* cases in the 18 Member States that consistently reported serotype data from 2014 to 2018, by serotype and year, are shown in Figure 6.

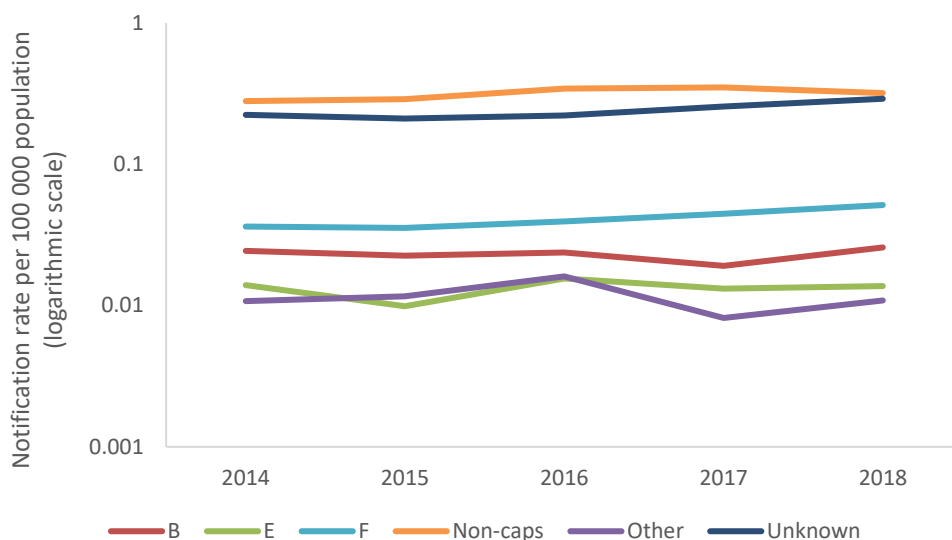
Figure 5. Serotype distribution of confirmed invasive *Haemophilus influenzae* cases by age group, EU/EEA, 2018



Other' refers to all cases reported as serotype a, c, d or 'non-b'.

Source: Country reports from Austria, the Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

Figure 6. Notification rate of confirmed invasive *Haemophilus influenzae* cases per 100 000 population, by serotype and year, EU/EEA, 2014–2018



'Other' refers to all cases reported as serotype a, c, d or 'non-b'.

Source: Country reports from Austria, the Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, the Netherlands, Norway, Poland, Portugal, Slovakia, Slovenia, Spain, and the United Kingdom.

Clinical presentation

The clinical presentation was known for 2 477 cases (49%). Of these cases, septicaemia was reported in 951 (38%), pneumonia in 647 (26%), meningitis or both septicaemia and meningitis in 186 (8%), and other clinical presentations (epiglottitis, cellulitis, and septic arthritis/osteomyelitis) in 29 cases (1%). For a further 664 cases (27%), the clinical presentation was reported as 'other'. Septicaemia was the most common clinical presentation among all age groups and the most common presentation for all serotypes.

Outcome

The outcome was known for 2 229 cases (56%). The case fatality was 11% (n=169). Six deaths were reported in children <1 year of age. Two deaths due to Hib were reported in 2018.

Vaccination status

In 2018, among 21 serotype B cases aged <1 year old with documented vaccination status, eight were unvaccinated while the other 13 reported being vaccinated with a number of doses varying from one (six cases) to four (one case). The number of doses was unknown for one case.

Among 23 cases aged one to four years with documented vaccination status, nine were unvaccinated while the other 14 reported being vaccinated with a number of doses varying from two (one case) to four (seven cases). The number of doses was unknown for one case.

Discussion

In EU/EEA countries, cases of invasive *H. influenzae* disease are rare, with the greatest burden in infants and the elderly. The majority of cases are caused by infection with a non-capsulated strain. As in previous years, the disease was most commonly reported in the north of Europe, possibly due to better case ascertainment. The results should be interpreted with caution because the completeness of data for some variables, such as clinical presentation, outcome, and serotype, remains low.

The World Health Organization recommends the inclusion of conjugate Hib vaccines in all infant immunisation programmes, either as three primary doses without a booster or as two (alternatively three) primary doses with a booster, depending on age-specific disease burden in different settings [5]. The introduction of Hib vaccines has led to substantial reduction in invasive Hib disease and in pharyngeal Hib carriage, resulting in herd protection [5]. Before the introduction of Hib vaccination, invasive *H. influenzae* disease was predominantly caused by serotype b infections in healthy young children [6]. While Hib vaccination has markedly reduced the incidence of invasive Hib disease in all age groups, this reduction has been greatest in young children [7-10]. The majority of Hib cases now occur in older adults with underlying co-morbidities [9]. Since 2010, Hib vaccination has been part of the national immunisation programme in all EU/EEA Member States, and high coverage has been maintained [11]. The sustained low number of Hib cases reported in all age groups highlights the success of this intervention. Serotype f is now the most common capsulated serotype observed in Europe, accounting for 9% of all cases reported for 2017.

A high proportion of cases had no reported information on serotype. However, non-capsulated *H. influenzae* is now the leading cause of invasive *H. influenzae* disease in all age groups, particularly among groups more susceptible to infection, for example neonates, the elderly, and persons with underlying co-morbidities [11-14]. Between 2012 and 2015, the notification rate of non-capsulated cases steadily increased in the EU/EEA [4]. An analysis of data in twelve European countries between 2007 and 2014 showed significant increasing trends in non-capsulated invasive *H. influenzae* disease among infants under one month and people aged 20 years and above [11]. The notification rate of non-capsulated invasive *H. influenzae* disease remained steady. Several studies have reported increasing trends in non-capsulated *H. influenzae*, as well as in capsulated serotypes a, e and f, following the introduction of routine Hib vaccination [11, 15-18]. However, most studies do not report evidence of strain replacement as a result of the introduction of routine Hib vaccination [7, 15, 17, 19].

Public health implications

The sustained success of Hib vaccination is evident. Maintaining high vaccination coverage in young children across Europe is essential to ensure the protection of all age groups against Hib.

The increasing recognition of non-capsulated *H. influenzae* as an important invasive pathogen warrants continuous monitoring of all strains and genetic typing to assess their genetic diversity. Improvements in the collection of serotype and clinical presentation data in routine surveillance systems for invasive *H. influenzae* disease would improve the possibility of detecting changes in epidemiology and inform preventive interventions.

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