

Haemophilus influenzae

Annual Epidemiological Report for 2017

Key facts

- In 2017, 3 888 confirmed cases of invasive *Haemophilus influenzae* disease were reported in the EU/EEA.
- The notification rate was 0.8 cases per 100 000 population, and this has increased since 2013 when it was 0.6 and since the period 2010–12 when the annual rate was 0.5 per 100 000 population.
- Age-specific rates were highest in infants below one year of age (4.1 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 45% of confirmed cases. Non-capsulated strains caused 76% of cases overall and represented 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 2017, 8% of cases with known serotype were caused by serotype b.

Methods

This report is based on data for 2017 retrieved from The European Surveillance System (TESSy) on 31 January 2019. 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, 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].

In 2017, 29 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.

Suggested citation: European Centre for Disease Prevention and Control. *Haemophilus influenzae*. In: ECDC. Annual epidemiological report for 2017. Stockholm: ECDC; 2019.

Stockholm, April 2019

© European Centre for Disease Prevention and Control, 2019. Reproduction is authorised, provided the source is acknowledged.

Epidemiology

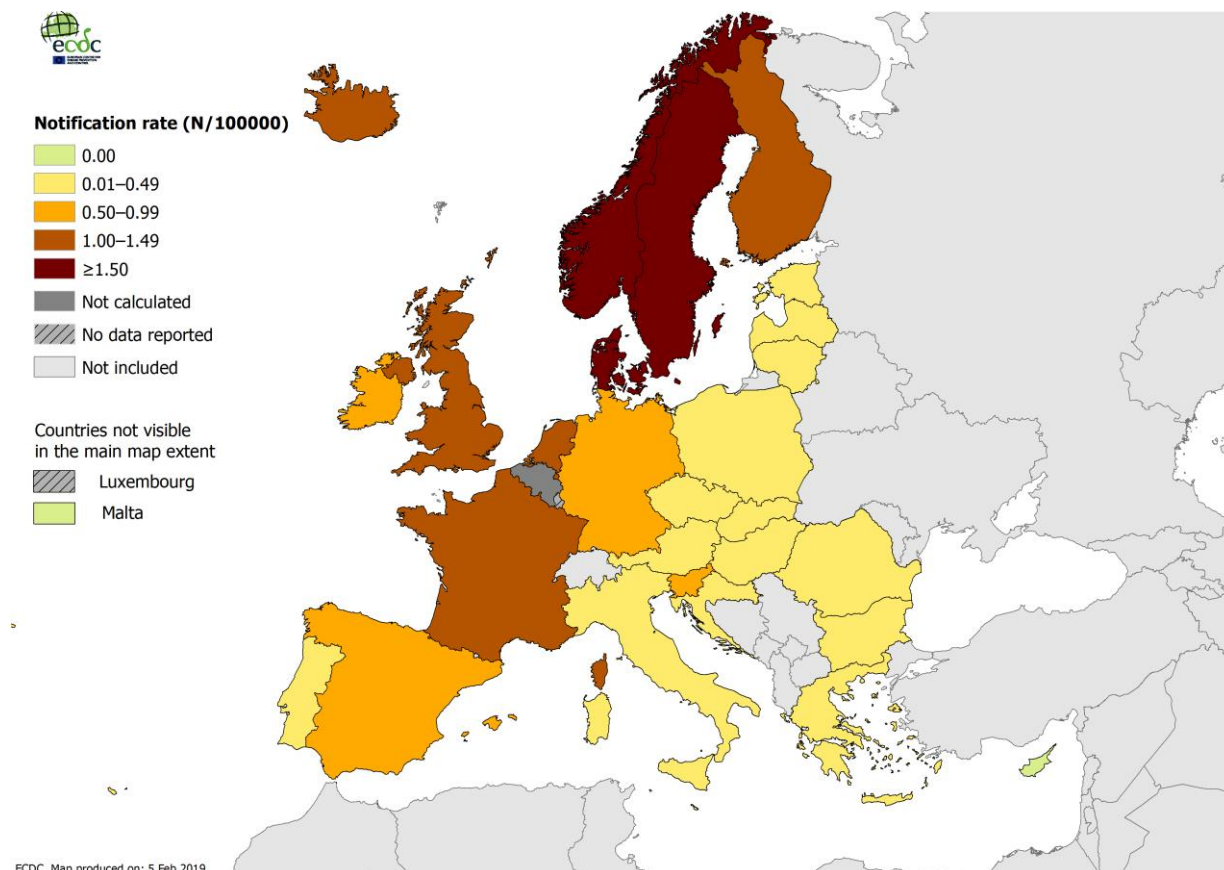
For 2017, 29 countries reported 3 888 confirmed cases of invasive *H. influenzae* disease in the EU/EEA (Table 1). France, Germany and the United Kingdom accounted for 58% of all confirmed cases. Cyprus and Malta reported zero cases, while Luxembourg and Liechtenstein did not report data on *H. influenzae* (Table 1). In 2017, the notification rate was 0.8 confirmed cases per 100 000 population in the EU/EEA, with the highest rates reported by Norway and Sweden (2.3 cases per 100 000 population), and Denmark (2.0) (Table 1, Figure 1). The notification rate for invasive *H. influenzae* in the EU/EEA increased from 0.6 per 100 000 population in 2013, to 0.8 in 2017. During the period 2010–12 the annual notification rate was 0.5 per 100 000 population [4].

Table 1. Distribution of confirmed cases of invasive *Haemophilus influenzae* disease and rates per 100 000 population by country and year, EU/EEA, 2013–2017

Country	2013		2014		2015		2016		2017			
	Number	Rate	Number	Rate	Number	Rate	Number	Rate	Confirmed cases	Rate	ASR	Reported cases
Austria	25	0.3	28	0.3	45	0.5	41	0.5	39	0.4	0.4	39
Belgium	67	-	56	-	64	-	85	-	67	-	-	67
Bulgaria	1	0.0	2	0.0	4	0.1	3	0.0	2	0.0	0.0	2
Croatia	4	0.1	1	0.0	0	0.0	1	0.0	1	0.0	0.0	1
Cyprus	2	0.2	1	0.1	0	0.0	2	0.2	0	0.0	0.0	0
Czech Republic	22	0.2	19	0.2	32	0.3	22	0.2	23	0.2	0.2	23
Denmark	69	1.2	82	1.5	90	1.6	106	1.9	113	2.0	1.8	113
Estonia	2	0.2	4	0.3	1	0.1	0	0.0	2	0.2	0.1	2
Finland	48	0.9	59	1.1	52	1.0	69	1.3	73	1.3	1.2	73
France	489	1.0	453	0.9	508	1.1	588	1.2	603	1.2	1.2	603
Germany	415	0.5	458	0.6	539	0.7	613	0.7	800	1.0	0.8	807
Greece	9	0.1	6	0.1	10	0.1	4	0.0	7	0.1	0.1	7
Hungary	2	0.0	7	0.1	8	0.1	16	0.2	21	0.2	0.2	21
Iceland	0	0.0	4	1.2	1	0.3	12	3.6	4	1.2	1.4	4
Ireland	41	0.9	61	1.3	51	1.1	58	1.2	45	0.9	1.0	45
Italy	78	0.1	101	0.2	123	0.2	141	0.2	153	0.3	0.2	153
Latvia	0	0.0	1	0.0	2	0.1	2	0.1	2	0.1	0.1	2
Liechtenstein	*	*	*	*	*	*	*	*	*	*	*	*
Lithuania	2	0.1	2	0.1	14	0.5	7	0.2	8	0.3	0.2	8
Luxembourg	-	-	-	-	0	0.0	-	-	-	-	-	-
Malta	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0.0	0
Netherlands	159	0.9	160	1.0	195	1.2	190	1.1	224	1.3	1.2	224
Norway	86	1.7	71	1.4	98	1.9	85	1.6	120	2.3	2.3	120
Poland	25	0.1	41	0.1	62	0.2	69	0.2	108	0.3	0.3	108
Portugal	28	0.3	40	0.4	18	0.2	17	0.2	46	0.4	0.4	49
Romania	5	0.0	2	0.0	4	0.0	5	0.0	2	0.0	0.0	2
Slovakia	5	0.1	4	0.1	7	0.1	1	0.0	5	0.1	0.1	5
Slovenia	16	0.8	15	0.7	31	1.5	20	1.0	20	1.0	0.9	20
Spain	90	0.4	130	0.6	147	0.6	242	0.6	308	0.8	0.7	308
Sweden	196	2.1	204	2.1	221	2.3	178	1.8	229	2.3	2.1	229
United Kingdom	715	1.1	787	1.2	850	1.3	807	1.2	863	1.3	1.2	863
EU/EEA	2601	0.6	2799	0.6	3177	0.7	3384	0.7	3888	0.8	0.7	3898

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, 2017

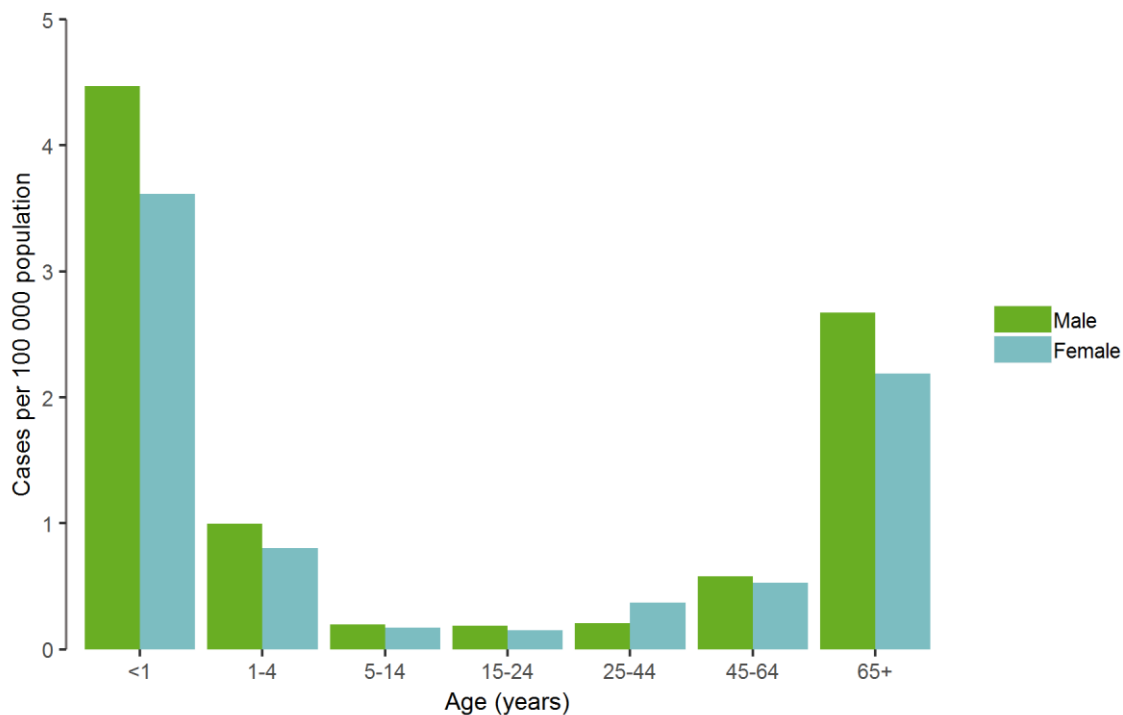


Source: Country reports from Austria, Belgium, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the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

Age and gender distribution

In 2017, invasive *H. influenzae* disease was predominantly reported in infants and the elderly, with a notification rate of 4.1 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 Portugal (9.2 cases per 100 000 population), the United Kingdom (7.3), Ireland (7.0) and France (6.0). In adults aged 65 years and over, the highest rates were reported in Sweden (7.4 per 100 000 population) and Denmark (7.3). Stratified by gender, rates were higher among males in all the 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 invasive *Haemophilus influenzae* disease cases per 100 000 population, by age and gender, EU/EEA, 2017

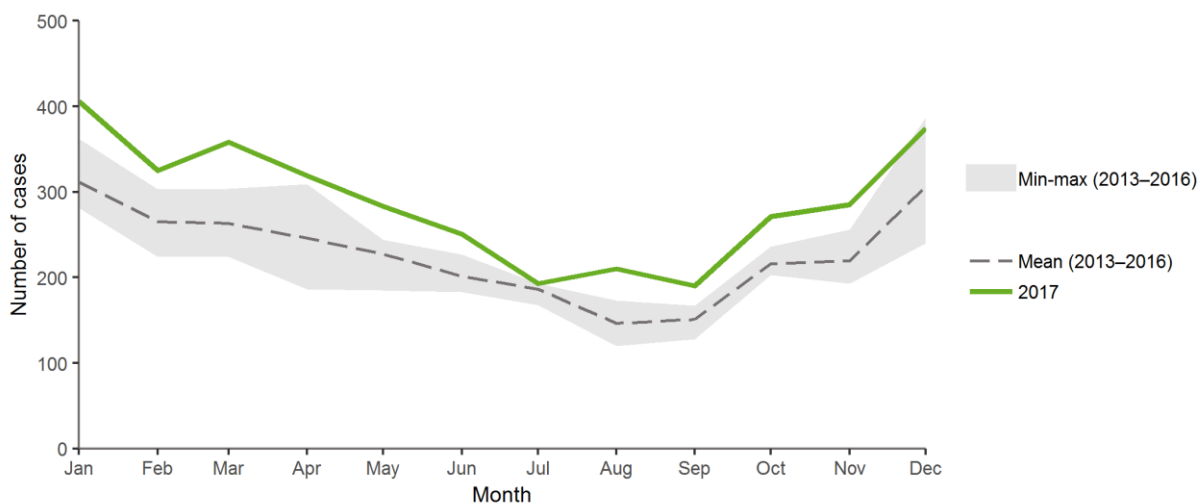


Source: Country reports from Austria, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom.

Seasonality and trend

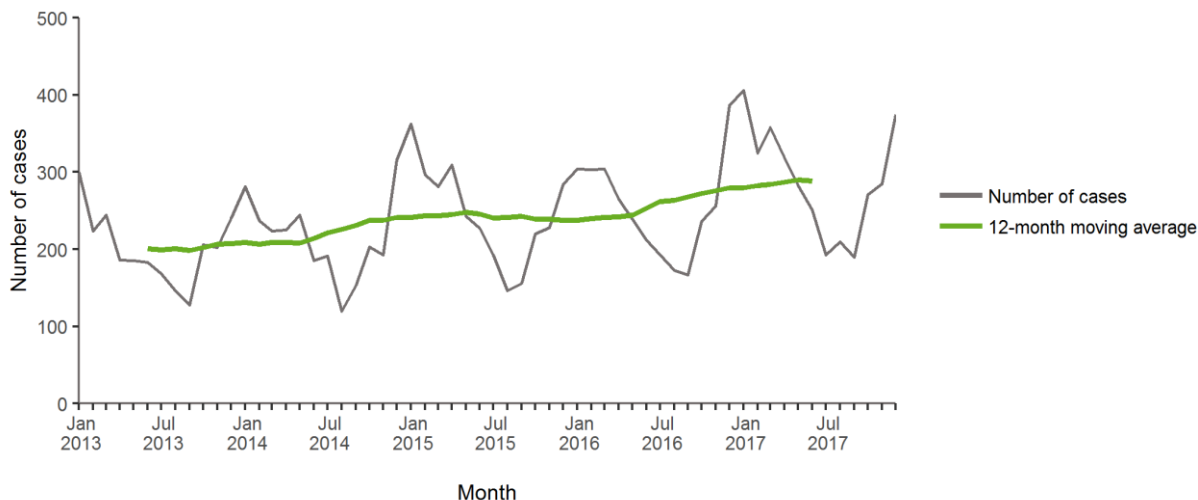
The distribution of invasive *H. influenzae* cases by month follows a seasonal pattern, with the highest number of cases reported in the winter months, followed by a steady decrease until September and an increasing trend towards the end of the year reaching a peak in December. Compared with the mean number of cases reported during 2013–2016, a larger number was reported in 2017 (Figure 3). Figure 4 shows an increasing trend in the number of cases reported between 2013 and 2017.

Figure 3. Distribution of confirmed *Haemophilus influenzae* disease cases by month, EU/EEA, 2017 and 2013–2016



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

Figure 4. Distribution of confirmed invasive *Haemophilus influenzae* disease cases by month, EU/EEA, 2013–2017



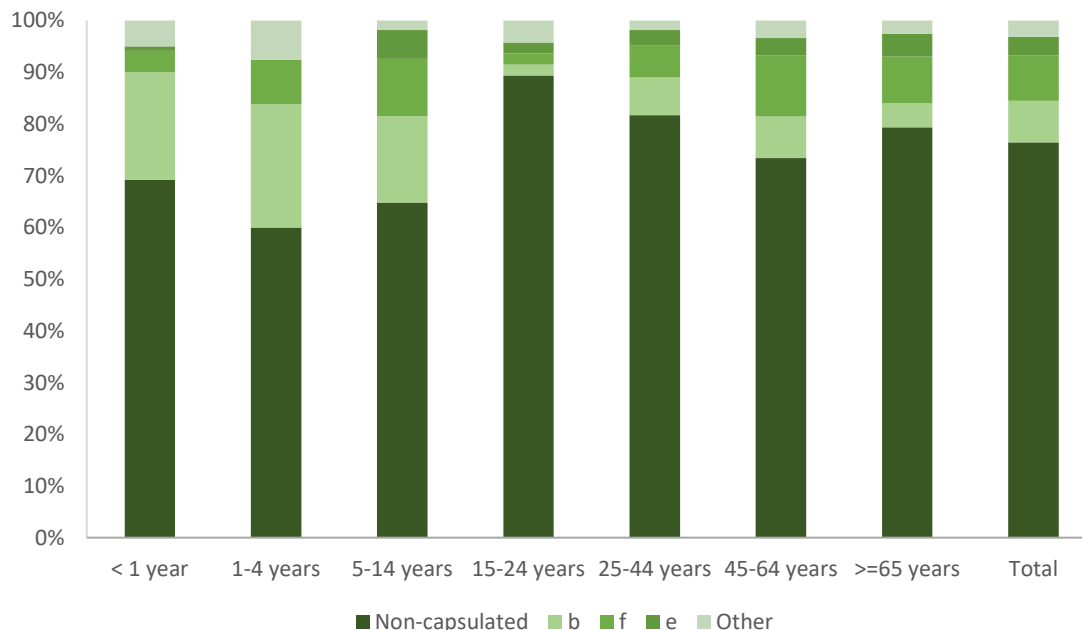
Source: Country reports from Austria, Bulgaria, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, the Netherlands, Norway, Poland, Romania, Slovakia, Slovenia, Sweden, and the United Kingdom.

Serotype

Of the 3 888 confirmed cases of invasive *H. influenzae* disease, 1 742 (45%) reported by 22 Member States had a known serotyping result. The number of cases without a known serotype increased from 41% in 2016 to 55% in 2017. Of the cases with known serotype in 2017, 76% (n=1 331) were non-capsulated (non-typeable), 9% (n=153) were serotype f, 8% (n=141) were serotype b (Hib) and 4% (n=62) were serotype e. Fifty-five 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 24% of invasive disease in children <1 year of age, and 1–4 years of age, respectively.

Notification rates of confirmed invasive *H. influenzae* cases are shown in Figure 6 for 19 Member States that consistently reported serotype data from 2013 to 2017, by serotype and year. An upward trend in non-capsulated strains was observed between 2013 and 2015, followed by a decrease in 2016 and 2017.

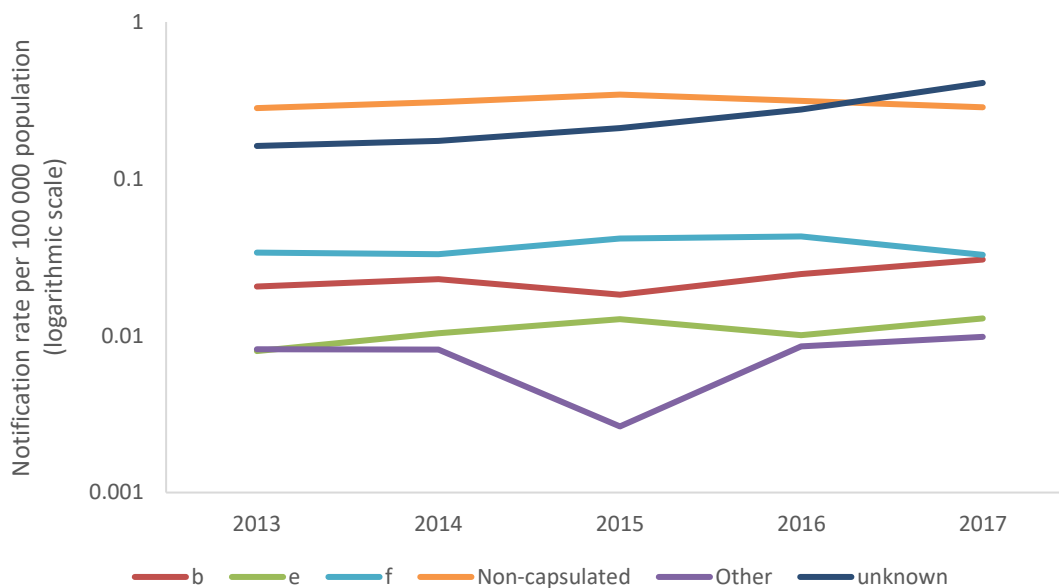
Figure 5. Serotype distribution of confirmed invasive *Haemophilus influenzae* cases by age group, EU/EEA, 2017



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

Source: Country reports from Austria, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Lithuania, the Netherlands, Norway, Poland, Portugal, 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, 2013–2017



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

Source: Country reports from Austria, the Czech Republic, Denmark, Estonia, 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 1 904 cases (49%). Of these cases, septicaemia was reported in 841 (44%), pneumonia in 594 (31%), meningitis or both septicaemia and meningitis in 195 (10%), and other clinical presentations (epiglottitis, cellulitis, and septic arthritis/osteomyelitis) in 45 cases (2%). For a further 229 cases (12%) the clinical presentation was reported as 'other'. Septicaemia was the most common clinical presentation among all age groups. Among cases with reported clinical presentation and serotype, meningitis was the most common presentation for Hib (33%), while septicaemia was the most common presentation for serotype e, f, and non-capsulated invasive *H. influenzae* disease (76%, 66%, and 62% respectively).

Outcome

The outcome was known for 2 084 cases (54%). The case fatality was 8% (n=169). Ten deaths were reported in children <1 year of age. Three deaths due to Hib were reported in 2017.

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, continues to be 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 notably 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 programmes 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.

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]. The notification rate of non-capsulated cases steadily increased in the EU/EEA between 2012 and 2015 [15]. An analysis of data in twelve European countries from 2007 to 2014 showed significant increasing trends in non-capsulated invasive *H. influenzae* disease among infants under one month of age and people aged 20 years and above [11]. There was a decrease in the notification rate of non-capsulated invasive *H. influenzae* disease in 2016 and 2017, although the significance of this observation is unclear due to low notification of serotypes. 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, 16-19]. However, most studies do not report evidence of strain replacement due to the introduction of routine Hib vaccination [7, 16, 18, 20].

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 possibilities to detect changes in epidemiology and inform preventive interventions.

References

1. European Centre for Disease Prevention and Control. Introduction to the Annual epidemiological report for 2016. In: ECDC. Annual epidemiological report for 2016. Stockholm: ECDC; 2017 [cited 2 April 2019]. Available from: <https://ecdc.europa.eu/en/annual-epidemiological-reports-2016/methods>.
2. European Centre for Disease Prevention and Control. Surveillance systems overview for 2017 [Internet, downloadable spreadsheet]. Stockholm: ECDC; 2018 [cited 2 April 2019]. Available from: <https://ecdc.europa.eu/en/publications-data/surveillance-systems-overview-2017>
3. European Centre for Disease Prevention and Control. Surveillance atlas of infectious diseases [Internet]. Stockholm: ECDC; 2017 [cited 30 January 2018]. Available from: <http://atlas.ecdc.europa.eu/public/index.aspx?Dataset=27&HealthTopic=22>
4. European Centre for Disease Prevention and Control. Annual Epidemiological Report 2016 – Invasive *Haemophilus influenzae* disease. [Internet]. Stockholm: ECDC; 2018. Available from: <https://ecdc.europa.eu/en/publications-data/haemophilus-influenzae-annual-epidemiological-report-2016>
5. World Health Organization. WHO position paper on *Haemophilus influenzae* type b (Hib) vaccination. Wkly Epidemiol Rec. 2013;88:413-28.
6. Peltola H. *Haemophilus influenzae* type b disease and vaccination in Europe: lessons learned. Pediatr Infect Dis J. 1998 Sep;17(9 Suppl):S126-32.
7. Georges S, Lepoutre A, Dabernat H, Levy-Bruhl D. Impact of *Haemophilus influenzae* type b vaccination on the incidence of invasive *Haemophilus influenzae* disease in France, 15 years after its introduction. Epidemiol Infect. 2013 Sep;141(9):1787-96.
8. Kastrin T, Paragi M, Kolman J, Cizman M, Kraigher A, Gubina M, et al. Characterisation of invasive *Haemophilus influenzae* isolates in Slovenia, 1993-2008. Eur J Clin Microbiol Infect Dis. 2010 Jun;29(6):661-8.
9. Collins S, Ramsay M, Campbell H, Slack MP, Ladhani SN. Invasive *Haemophilus influenzae* type b disease in England and Wales: who is at risk after 2 decades of routine childhood vaccination? Clinical infectious diseases: an official publication of the Infectious Diseases Society of America. 2013;57(12):1715-21.
10. Monge S, Mollema L, de Melker H, Sanders E, van der Ende A, Knol M. Clinical characterization of invasive disease caused by *haemophilus influenzae* serotype b in a high vaccination coverage setting. J Pediatric Infect Dis Soc. 2018 Mar 22. doi: 10.1093/jpids/piy020 [Epub ahead of print].
11. Whittaker R, Economopoulou A, Dias J, Bancroft E, Ramliden M, Celentano L, et al. Epidemiology of invasive *Haemophilus influenzae* disease, Europe, 2007–2014. Emerg Infect Dis. 2017;23(3):396-404.
12. Puig C, Grau I, Marti S, Tubau F, Calatayud L, Pallares R, et al. Clinical and molecular epidemiology of *Haemophilus influenzae* causing invasive disease in adult patients. PloS one. 2014;9(11):e112711.
13. van Wessel K, Rodenburg GD, Veenhoven RH, Spanjaard L, van der Ende A, Sanders EA. Non-typeable *Haemophilus influenzae* invasive disease in the Netherlands: a retrospective surveillance study 2001-2008. Clin Infect Dis. 2011 Jul 1;53(1):e1-7.
14. Collins S, Vickers A, Ladhani SN, Flynn S, Platt S, Ramsay ME, et al. Clinical and molecular epidemiology of childhood invasive non-typeable *Haemophilus influenzae* disease in England and Wales. Pediatr Infect Dis J. 2016 Mar;35(3):e76-84.
15. European Centre for Disease Prevention and Control. *Haemophilus influenzae*. In: ECDC. Annual epidemiological report for 2016. Stockholm: ECDC; 2018. [cited 2 April 2019]. Available from: <https://ecdc.europa.eu/en/publications-data/haemophilus-influenzae-annual-epidemiological-report-2016>
16. Ladhani S, Stark, M.E., Chandra, M., Slack, M.P. No evidence for *Haemophilus influenzae* serotype replacement in Europe after introduction of the Hib conjugate vaccine. Lancet. 2008;8:275-6.
17. Resman F, Ristovski M, Ahl J, Forsgren A, Gilsdorf JR, Jasir A, et al. Invasive disease caused by *Haemophilus influenzae* in Sweden 1997-2009; evidence of increasing incidence and clinical burden of non-type b strains. Clin Microbiol Infect. 2011 Nov;17(11):1638-45.
18. Ladhani S, Slack MP, Heath PT, von Gottberg A, Chandra M, Ramsay ME, et al. Invasive *Haemophilus influenzae* Disease, Europe, 1996-2006. Emerg Infect Dis. 2010;16(3):455-63.
19. Desai S, Jamieson FB, Patel SN, Seo CY, Dang V, Fediurek J, et al. The epidemiology of invasive *Haemophilus influenzae* non-serotype b disease in Ontario, Canada from 2004 to 2013. PloS one. 2015;10(11):e0142179.
20. Giufre M, Cardines R, Caporali MG, Accogli M, D'Ancona F, Cerquetti M. Ten years of Hib vaccination in Italy: prevalence of non-encapsulated *Haemophilus influenzae* among invasive isolates and the possible impact on antibiotic resistance. Vaccine. 2011;29(22):3857-62.