Invasive Haemophilus influenzae disease

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Key facts

- In 2014, 2 799 confirmed cases of invasive Haemophilus influenzae (H. influenzae) disease were reported to TESSy.
- The notification rate was 0.6 cases per 100 000 population, a similar rate as in previous years.
- Age-specific rates were highest in infants (4.0 cases per 100 000) and the elderly (1.7 cases per 100 000).
- The H. influenzae type b (Hib) vaccine has led to a progressive and sustained reduction of type b serotype infections. In 2014, 6% of cases with a known serotype were caused by serotype b, 57% of which were aged 25 years and over.
- Non-capsulated strains caused the majority of cases in all age groups and 82% of all cases for which serotyping results were available.
- Serotype f caused 9% of all cases and 72% of cases among non-b capsulated serotypes (serotypes a, c, d, e and f).
- The changing epidemiology of invasive H. influenzae disease should be carefully monitored; disease surveillance should include all age groups, serotypes and clinical presentations.

Methods

Click here for a detailed description of the methods used to produce this annual report

ECDC has coordinated the surveillance of invasive H. influenzae disease at the European level since the transfer of EU-IBIS (European Union Invasive Bacterial Infections Surveillance Network) to ECDC in 2007.

• In 2014, 29 EU/EEA Member States routinely report data on invasive H. influenzae disease to TESSy.

• All Member States report 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 use a case definition that is compatible with the EU case definition for confirmed cases.

• The majority of Member States report data from comprehensive, passive surveillance systems with national coverage. Belgium, France and Spain report data from sentinel surveillance systems. For a summary of the surveillance systems characteristics in each Member State, please refer to the Annex.

Epidemiology

In 2014, 2 799 confirmed cases of invasive H. influenzae disease were reported by 29 countries (Table 1, Figure 1). No confirmed cases were reported by Malta. Liechtenstein and Luxembourg reported no data (Table 1). In 2014, the overall confirmed case notification rate was 0.6 cases per 100 000 population, comparable to the rates observed from 2010 to 2013, but showing a slightly upward trend. The highest rates were reported by Sweden (2.1 cases per 100 000), Denmark (1.5) and Norway (1.4) (Table 1, Figure 2).

Table 1. Reported, confirmed cases of invasive Haemophilus influenzae disease: number and rate per 100 000 population, EU/EEA, 2010–2014

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Country	2010		2011		2012		2013		2014					
	Confirmed cases	Rate	Con-firmed cases	Rate	Con-firmed cases	Rate	Con-firmed cases	Rate	Nation-al data	Report type	Re-ported cases	Con-firmed cases	Rate	ASR
Austria	2	0.0	3	0.0	6	0.1	25	0.3	Y	C	28	28	0.3	0.3
Belgium	70	-	96	-	78	-	67	-	N	C	56	56	-	-
Bulgaria	10	0.1	2	0.0	3	0.0	1	0.0	Y	C	2	2	0.0	0.0
Croatia	.	.	.	.	2	0.0	4	0.1	Y	C	1	1	0.0	0.0
Cyprus	3	0.4	9	1.1	8	0.9	2	0.2	Y	C	1	1	0.1	0.1
Czech Republic	22	0.2	15	0.1	11	0.1	22	0.2	Y	C	19	19	0.2	0.2
Denmark	43	0.8	47	0.8	65	1.2	69	1.2	Y	C	82	82	1.5	1.4
Estonia	1	0.1	2	0.2	3	0.2	2	0.2	Y	C	4	4	0.3	0.3
Finland	41	0.8	66	1.2	81	1.5	48	0.9	Y	C	59	59	1.1	1.0
France	371	0.8	492	1.0	491	1.0	489	1.0	74%	C	453	453	0.9	0.9
Germany	209	0.3	267	0.3	321	0.4	414	0.5	Y	C	461	458	0.6	0.5
Greece	4	0.0	7	0.1	6	0.1	9	0.1	Y	C	6	6	0.1	0.1
Hungary	5	0.0	8	0.1	4	0.0	2	0.0	Y	C	7	7	0.1	0.1
Iceland	0	0.0	2	0.6	0	0.0	0	0.0	Y	C	4	4	1.2	1.2
Ireland	26	0.6	44	1.0	41	0.9	41	0.9	Y	C	61	61	1.3	1.3
Italy	62	0.1	36	0.1	60	0.1	78	0.1	Y	C	103	101	0.2	0.2
Latvia	0	0.0	0	0.0	1	0.0	0	0.0	Y	C	1	1	0.0	0.1
Liechtenstein	.	.	.	.	.	.	.	.	.	.	.	.	.	.
Lithuania	1	0.0	2	0.1	3	0.1	2	0.1	Y	C	3	2	0.1	0.1
Luxembourg	0	0.0	0	0.0	.	.	.	.	.	.	.	.	.	.
Malta	2	0.5	0	0.0	5	1.2	0	0.0	Y	C	0	0	0.0	0.0
Netherlands	144	0.9	137	0.8	135	0.8	159	0.9	Y	C	160	160	1.0	0.9
Norway	89	1.8	85	1.7	78	1.6	86	1.7	Y	C	71	71	1.4	1.4
Poland	25	0.1	22	0.1	35	0.1	25	0.1	Y	C	41	41	0.1	0.1
Portugal	10	0.1	23	0.2	45	0.4	28	0.3	Y	C	60	40	0.4	0.4
Romania	19	0.1	10	0.0	9	0.0	5	0.0	Y	C	2	2	0.0	0.0
Slovakia	3	0.1	0	0.0	3	0.1	5	0.1	Y	C	4	4	0.1	0.1
Slovenia	15	0.7	22	1.1	18	0.9	16	0.8	Y	C	15	15	0.7	0.7
Spain	76	0.3	115	0.5	87	0.4	90	0.4	50%	C	130	130	0.6	0.5
Sweden	179	1.9	203	2.2	214	2.3	196	2.1	Y	C	204	204	2.1	1.9
United Kingdom	664	1.1	739	1.2	726	1.1	715	1.1	Y	C	787	787	1.2	1.2
EU/EEA	**2096**	**0.5**	**2454**	**0.5**	**2539**	**0.5**	**2600**	**0.6**		**C**	**2823**	**2799**	**0.6**	**0.6**

Source: Country reports. Legend: Y = yes, N = no, C = case based, A = aggregated, - = no data reported, ASR: age-standardised rate, . = no notification rate calculated

Figure 1. Number of reported, confirmed cases of invasive Haemophilus influenzae disease, EU/EEA, 2014

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, the United Kingdom.

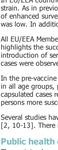
Figure 2. Number of reported, confirmed cases of invasive Haemophilus influenzae disease per 100 000 population, EU/EEA, 2014

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, the United Kingdom.

Age and gender distribution

In 2014, invasive H. influenzae disease was predominantly found in infants and the elderly (Figure 3), with a notification rate of 4.0 confirmed cases per 100 000 population in children under one year of age, and 1.7 confirmed cases per 100 000 population in adults aged 65 years or over. For both age groups, higher rates were observed in males (Figure 3). The overall notification rate was 0.6 cases per 100 000 population for males and 0.6 for females, with a male-to-female ratio of 1.03:1.

Figure 3. Reported, locally acquired Invasive Haemophilus influenzae disease cases, by age and gender, EU/EEA, 2014



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

Seasonality

The distribution of invasive H. influenzae cases by month follows a seasonal pattern, with the highest number of reported cases in the winter months, followed by a steady decrease until August and an increasing trend towards the end of the year. Compared to previous years, a higher peak was seen in May. This peak may be due to random variation as the number of reported cases was small (Figure 4). Figure 5 shows an increasing trend in the number of cases reported from 2010–2014.

Figure 4. Seasonal distribution of reported, confirmed cases of invasive Haemophilus influenzae disease, EU/EEA, 2014 compared with 2010–2013

Source: Country reports from Austria, Belgium, 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, the United Kingdom.

Figure 5: Trend and number of reported cases of invasive Haemophilus influenzae disease, EU/EEA, 2010–2014

Source: Country reports from Austria, Belgium, 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, the United Kingdom.

Serotype

Of the 2 799 reported confirmed cases of invasive H. influenzae disease, 1 706 (61%) – reported by 20 Member States – had a known serotyping result. Of these 1 706 cases, 82% (n=1 394) were non-capsulated (non-typeable). Non-capsulated strains were the most common cause of infection in all age groups (Figure 6). The majority of invasive non-capsulated strains were observed among cases 65 years or over (Figure 7). Serotype b caused 6% (n=104) of cases in 2014. Among cases of serotype b invasive H. influenzae disease, 57% were aged 25 years or over (Figure 7).

Among non-b capsulated serotypes (serotypes a, c, d, e and f), f was the most commonly reported serotype (72%, n=150) and the second most common cause of invasive H. influenzae disease overall (9%). Serotype e contributed to 23% (n=47) of non-b capsulated infections and 3% of all cases. The majority of cases of serotypes e and f infection were in persons aged 45 years and over (Figure 7). Eight cases of serotype a, one case of serotype c, and two cases of serotype d were reported (Figure 6).

Among 17 Member States that consistently reported serotype data from 2010 to 2014, there was a consistent upward trend in non-capsulated strains, with a 61% increase in the number of reported cases between 2010 (n=862) and 2014 (n=1 393). No increasing trends were observed among other serotypes (Figure 8).

Figure 6: Serotype distribution of reported, confirmed cases of invasive H. influenzae disease by age group, EU/EEA, 2014

'Non-caps' refers to non-capsulated strains, 'other' refers to all cases reported as serotype a, c or d.

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

Figure 7: Age group distribution of reported, confirmed cases of invasive H. influenzae disease by serotype, EU/EEA, 2014

'Non-caps' refers to non-capsulated strains, 'other' refers to all cases reported as serotype a, c or d.

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

Figure 8: Trend and number of reported, confirmed cases of invasive H. influenzae disease by serotype, EU/EEA, 2010–2014

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

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

Clinical presentation

The clinical presentation was known for 1 519 cases (54% of all cases) reported in 2014. Of these cases, septicaemia was reported in 764 cases (50%), pneumonia in 444 (29%) and meningitis in 161 (11%). Seventeen cases presented with both septicaemia and meningitis. Three cases of epiglottitis, six cases of cellulitis, and eight cases of septic arthritis/osteomyelitis were reported. For 116 cases, the clinical presentation was reported as 'other'. Septicaemia was the most common clinical presentation across age groups and serotypes.

Outcome

The outcome was known for 1 445 cases, 52% of all cases. There were 107 fatal cases reported, a case fatality of 7%, considering only cases with known outcome. Case fatality was highest among cases of serotype e (13%, n=4/31), followed by non-capsulated strains (8%, n=67/823), serotype b (7%, n=3/44) and serotype f (5%, n=5/100). Eighty percent of deaths occurred in persons aged ≥45 years, and 65% in those ≥65 years.

Discussion

In EU/EEA countries, cases of invasive H. influenzae disease are rare with the greatest burden in infants and the elderly, the majority caused by infection with a non-capsulated strain. As in previous years, the disease was most commonly reported in the north of Europe. This observation is possibly due to better case ascertainment and the implementation of enhanced surveillance systems. The results should be interpreted with caution because the completeness of data for some variables, such as clinical presentation and outcome, was low. In addition, there is currently no common definition of fatal outcome due to invasive H. influenzae disease in Europe.

All EU/EEA Member States have made serotype b vaccination part of their routine child immunisation schedule, and the sustained low number of serotype b cases reported highlights the success of this intervention. Indeed, serotype f is now the most common capsulated serotype observed in Europe and accounts for 9% of all cases. Before the introduction of serotype b vaccination, invasive H. influenzae disease was predominantly caused by serotype b infections in healthy young children [1]. The majority of serotype b cases were observed in ≥25 year olds, an expected shift in the age distribution, considering the impact of routine serotype b vaccination [2-5].

In the pre-vaccine era, non-capsulated H. influenzae was not a known common cause of invasive infection, however it is now the leading cause of invasive H. influenzae disease in all age groups, particularly among groups who are more susceptible to infection, e.g. neonates, the elderly, and immunocompromised persons [6-8]. The number of non-capsulated cases reported has steadily increased over the past five years, although many potential explanations exist for this increase, such as increasing survival rates among persons more susceptible to infection, the increased use of immunosuppressive therapy [8], and changes in data reporting or laboratory practices [9].

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 [2, 10-13]. There is, however, still no evidence of serotype replacement in the EU following the introduction of routine Hib vaccination [3, 4, 10, 12, 14-16].

Public health conclusions

The sustained success of serotype b vaccination is clear. Maintaining high vaccination coverage across Europe is therefore essential.

The predominance of cases caused by non-capsulated strains shows the importance of continuous monitoring for all strains, for example by genetic typing of non-capsulated strains. All age groups and clinical presentations should be monitored in order to accurately assess changes in the epidemiology and develop preventative interventions.

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Additional information

ECDC Surveillance Atlas of Infectious Diseases

ECDC surveillance report on invasive bacterial diseases in Europe 2012: http://ecdc.europa.eu/en/publications/_layouts/forms/Publication_DispForm.aspx?List=4f55ad51-4aed-4d32-b960-af70113dbb90&ID=1261

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ECDC surveillance report on invasive bacterial diseases in Europe 2008/2009: http://www.ecdc.europa.eu/en/publications/_layouts/forms/Publication_DispForm.aspx?List=4f55ad51-4aed-4d32-b960-af70113dbb90&ID=436

Network background and EU-IBIS reports: http://www.ecdc.europa.eu/en/activities/surveillance/EU_IBD/background/Pages/Background.aspx

Annex

Table. Invasive Haemophilus influenzae disease, surveillance systems overview, 2014

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* The European Surveillance System (TESSy) is a system for the collection, analysis and dissemination of data on communicable diseases. EU Member States and EEA countries contribute to the system by uploading their infectious disease surveillance data at regular intervals.