SURVEILLANCE REPORT

Invasive pneumococcal disease

Annual Epidemiological Report for 2018

Key facts

- In 2018, 24 663 confirmed cases of invasive pneumococcal disease (IPD) were reported in the EU/EEA.
- The crude notification rate was 6.4 cases per 100 000 population, continuing the increasing trend observed since 2014.
- Age-specific rates were highest in adults aged 65 years or older (18.7 confirmed cases per 100 000 population) and in infants under one year (14.4 confirmed cases per 100 000 population), with higher rates reported in males than females.
- The 10 most common serotypes were 8, 3, 19A, 22F, 12F, 9N, 15A, 10A, 23B and 6C (in order of decreasing frequency), accounting for 70% of typed isolates.
- Of all the cases under five years of age, 75% were caused by a serotype not included in any pneumococcal conjugate vaccine (PCV).
- Among cases aged 65 years and over, 73% were caused by serotypes included in the 23-valent polysaccharide vaccine and 29% were caused by serotypes in the 13-valent PCV.

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. 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].

Additional data on the disease are accessible from ECDC's online *Surveillance atlas of infectious diseases* [3].

In 2019, 29 Member States reported data on invasive pneumococcal disease (IPD). Twenty-four Member States used the EU-2008/2012 case definition. One Member State used the EU-2002 case definition and for four Member States, the case definition was unknown/not specified. The EU-2008/2012 case definition differs from the EU-2002 case definition by excluding possible and probable cases and including detection of *S. pneumoniae* antigens at a normally sterile site as the definition of a confirmed case [4].

National IPD surveillance systems were heterogeneous. Of the 29 countries reporting data, 22 countries conducted surveillance with compulsory reporting and national coverage. Six countries had voluntary sentinel systems. The Netherlands and Spain had surveillance systems that covered 25% and 80% of the national population respectively. The population coverage of the Belgian surveillance system was unknown, so notification rates were not calculated. IPD data from France were reported through two different systems: one relying on reports from physicians (FR-EPIBAC) and the other based on laboratories (FR-PNEUMO-NRL). Data reported from FR-PNEUMO-NRL were used to analyse serotype and antimicrobial susceptibility, while data reported from FR-EPIBAC provided epidemiological and clinical information. Germany had a voluntary laboratory-based surveillance system and did not report data to ECDC [5]. All countries except Belgium, Bulgaria, Croatia and Poland reported case-based data [2].

Suggested citation: European Centre for Disease Prevention and Control. Invasive pneumococcal disease. In: ECDC. Annual epidemiological report for 2018. Stockholm: ECDC; 2020.

Stockholm, September 2020

Epidemiology

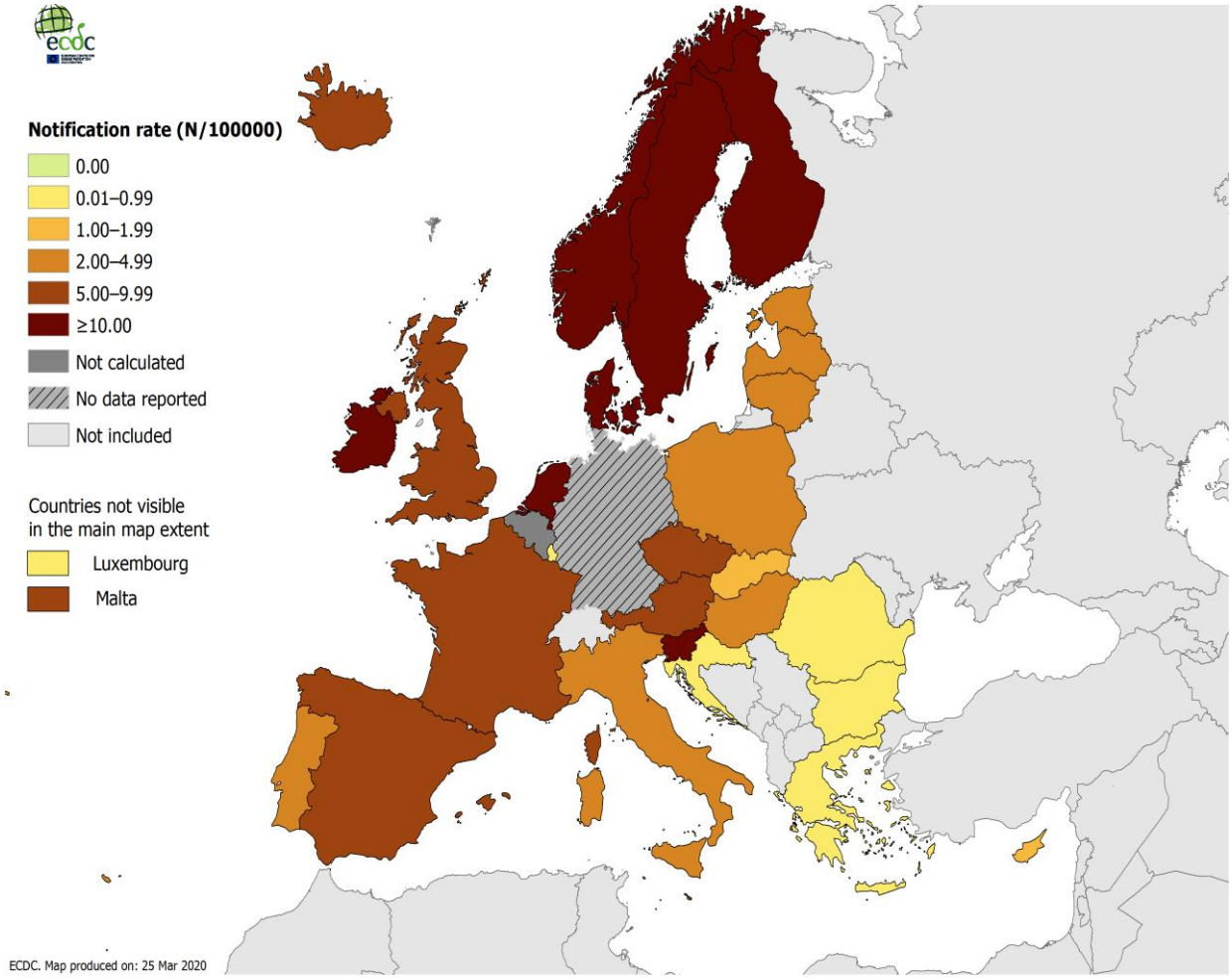
In 2018, 24 663 confirmed cases of IPD were reported by 29 countries. The crude notification rate was 6.2 cases per 100 000 population (Table 1). The United Kingdom reported the highest number of confirmed cases, followed by France. The highest notification rates were reported in Denmark, Ireland, Finland, the Netherlands, Norway, Slovenia and Sweden (Table 1, Figure 1). Many countries in the southern and eastern parts of the EU had low notification rates.

Table 1. Distribution of confirmed invasive pneumococcal 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	322	3.8	422	4.9	439	5.0	545	6.2	611	6.9	6.4	611
Belgium	1 192	-	1 362	-	1 329	-	1 461	-	1 553	-	-	1 553
Bulgaria	21	0.3	31	0.4	35	0.5	34	0.5	24	0.3	0.3	24
Croatia	27	0.6	24	0.6	14	0.3	16	0.4	21	0.5	-	21
Cyprus	14	1.6	9	1.1	5	0.6	20	2.3	17	2.0	2.0	18
Czech Republic	337	3.2	413	3.9	323	3.1	389	3.7	535	5.0	4.7	535
Denmark	725	12.9	807	14.3	731	12.8	771	13.4	799	13.8	12.7	799
Estonia	12	0.9	24	1.8	30	2.3	45	3.4	43	3.3	3.1	43
Finland	703	12.9	815	14.9	817	14.9	822	14.9	761	13.8	12.5	761
France	3 184	6.6	3 299	6.9	3 800	7.9	3 862	8.0	3 862	7.7	7.2	3 862
Germany	.	.	.	.	.	.	.	.	.	.	.	.
Greece	30	0.3	55	0.5	52	0.5	52	0.5	42	0.4	0.4	42
Hungary	150	1.5	189	1.9	226	2.3	268	2.7	331	3.4	3.1	331
Iceland	24	7.4	25	7.6	19	5.7	27	8.0	30	8.6	9.7	30
Ireland	342	7.4	370	7.9	378	8.0	414	8.7	514	10.6	11.8	514
Italy	957	1.6	1 248	2.1	1 529	2.5	1 705	2.8	1 555	2.6	2.2	1 555
Latvia	51	2.5	87	4.4	65	3.3	75	3.8	76	3.9	3.5	76
Liechtenstein	.	.	.	.	.	.	.	.	.	.	.	.
Lithuania	6	0.2	25	0.9	56	1.9	76	2.7	65	2.3	2.1	65
Luxembourg	1	0.2	0	0.0	0	0.0	1	0.2	1	0.2	0.2	1
Malta	22	5.1	9	2.0	11	2.4	18	3.9	31	6.5	6.2	31
Netherlands	546	13.0	667	15.8	631	14.9	616	14.4	688	16.0	14.8	693
Norway	569	11.1	522	10.1	599	11.5	560	10.6	581	11.0	11.0	581
Poland	705	1.9	979	2.6	967	2.5	1 192	3.1	1 350	3.6	-	1 350
Portugal	-	-	142	1.4	163	1.6	301	2.9	397	3.9	3.5	420
Romania	62	0.3	53	0.3	50	0.3	50	0.3	74	0.4	0.4	74
Slovakia	78	1.4	68	1.3	59	1.1	100	1.8	98	1.8	1.8	98
Slovenia	276	13.4	332	16.1	281	13.6	328	15.9	276	13.4	12.2	276
Spain	1 856	5.0	2 037	5.5	1 825	4.9	2 443	6.6	2 365	6.3	5.9	2 365
Sweden	1 159	12.0	1 314	13.5	1 351	13.7	1 367	13.7	1 408	13.9	12.9	1 408
United Kingdom	4 157	6.5	5 796	8.9	6 205	9.5	6 333	9.6	6 555	9.9	9.5	6 555
EU/EEA	**17 528**	**4.8**	**21 124**	**5.6**	**21 990**	**5.8**	**23 891**	**6.2**	**24 663**	**6.4**	**6.2**	**24 692**

Source: Country reports.
ASR: age-standardised rate
.: no data reported
-: no notification rate calculated.
Note: The national coverage in France is calculated based on the entire French population. However, the actual surveillance system only collects data from metropolitan France, thus the coverage of the surveillance system shown here for France is underestimated.
The number of cases presented from France in Table 1 was collected through the FR-EPIBAC surveillance system.

Figure 1. Distribution of confirmed invasive pneumococcal disease cases per 100 000 population by country, EU/EEA, 2018

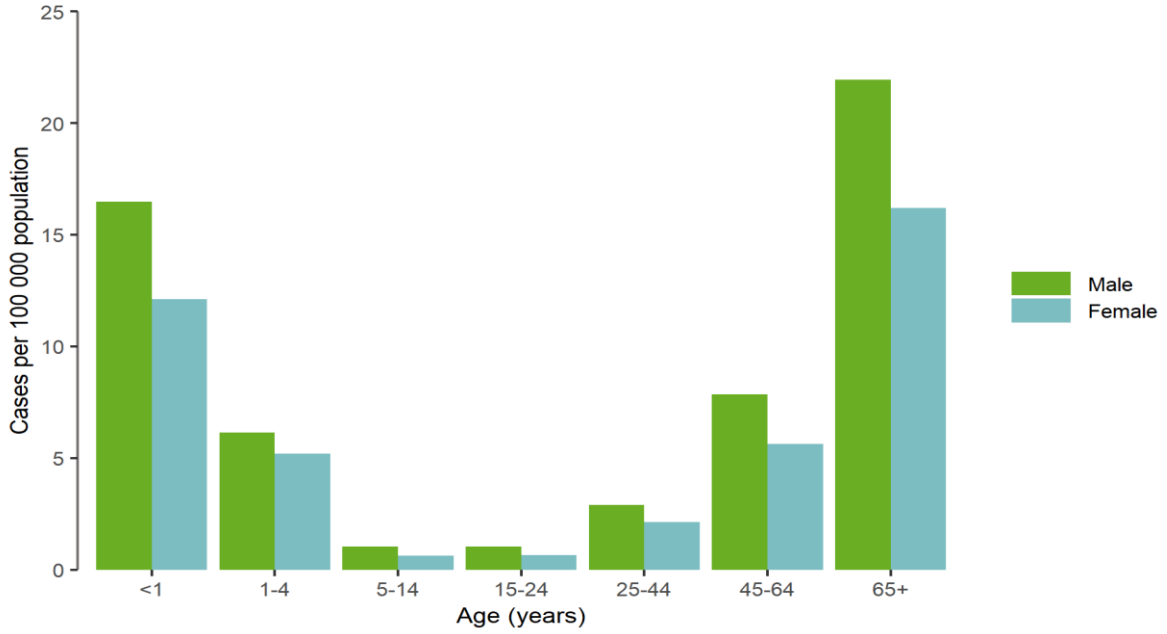


Source: Country reports from Austria, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United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

Age and gender distribution

In 2018, IPD was predominantly reported in the elderly and in infants, with 18.7 confirmed cases per 100 000 population in adults aged 65 years and above, and 14.4 confirmed cases per 100 000 population in infants under one year (Figure 2). The rates of disease were the lowest in persons aged 5–24 years (0.8 confirmed cases per 100 000 population). The notification rate was higher in males in all age groups. The overall male-to-female ratio was 1.2:1.

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

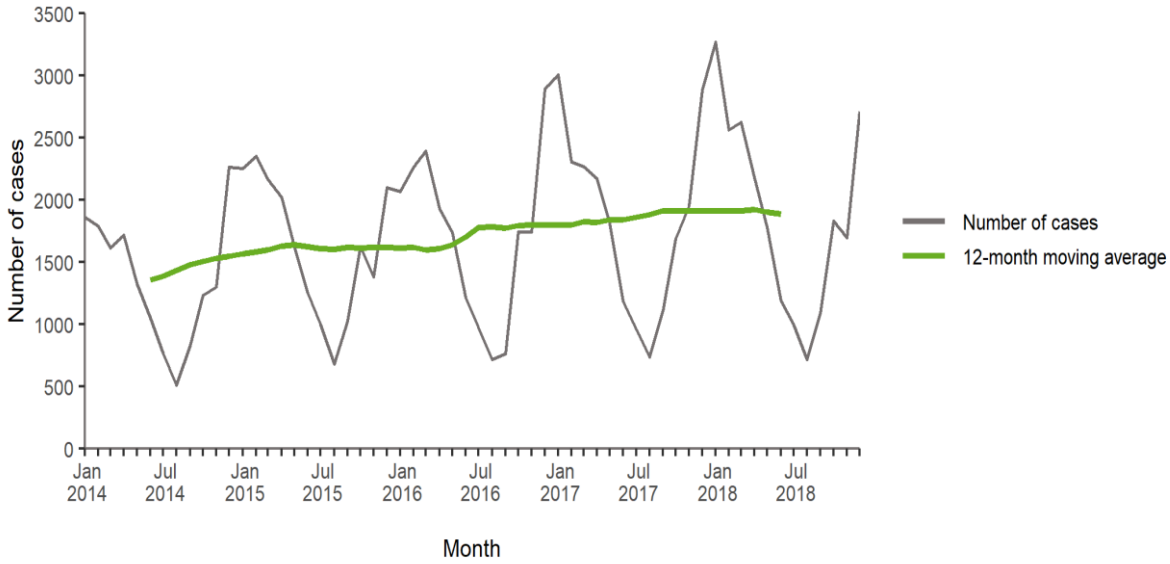


Source: Country reports from Austria, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United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

Seasonality and trend

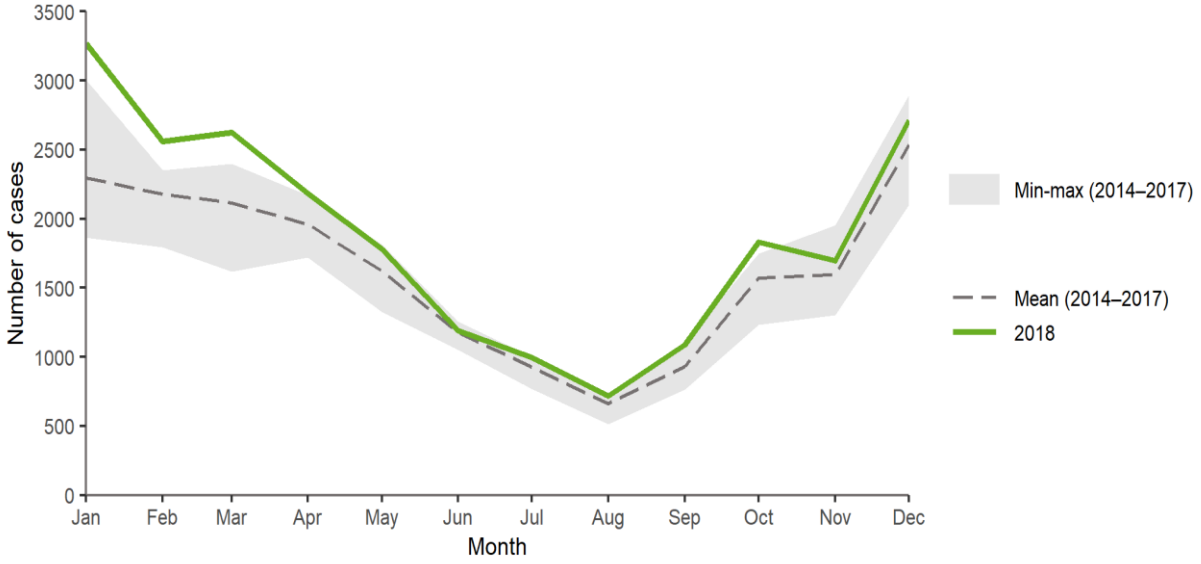
The seasonal distribution of IPD cases followed a pattern similar to many other respiratory diseases. Case numbers were lowest during summer, increased rapidly with the onset of autumn, and peaked during the winter months (Figures 3, 4). There was an increasing trend in reported cases during the period 2014–2017 (Figure 4). The notification rate increased to 6.2 cases per 100 000 population in 2017, compared to 4.8 in 2014 (Table 1).

Figure 3. Distribution of confirmed invasive pneumococcal disease cases by month, EU/EEA, 2014–2018



Countries included: Austria, Cyprus, Czechia, Denmark, Estonia, Finland, France, Greece, Hungary, Ireland, Iceland, Italy, Latvia, Lithuania, Malta, the Netherlands, Norway, Poland, Romania, Slovenia, Slovakia, Spain, Sweden and the UK.

Figure 4. Distribution of confirmed invasive pneumococcal disease cases by month, EU/EEA, 2018 and 2014–2017



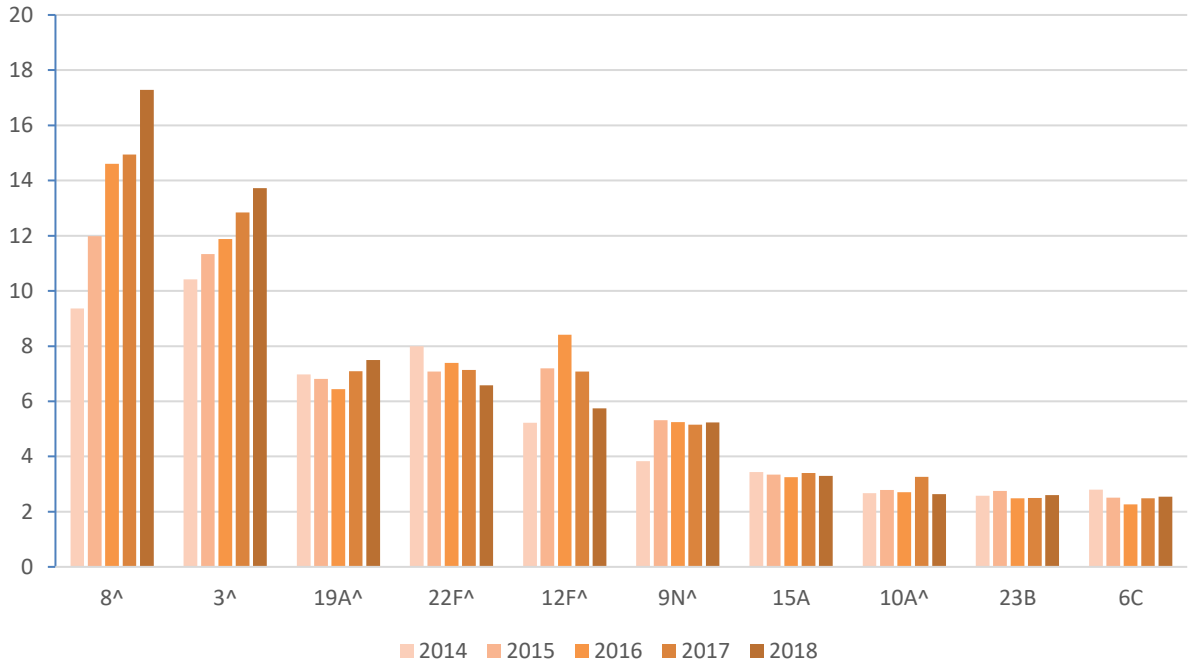
Countries included: Austria, Cyprus, Czechia, Denmark, Estonia, Finland, France, Greece, Hungary, Ireland, Iceland, Italy, Latvia, Lithuania, Malta, the Netherlands, Norway, Poland, Romania, Slovenia, Slovakia, Spain, Sweden and the UK.

Serotype

Data on serotype were reported from 16 371 sampled cases in EU/EEA countries in 2018. The ten most common serotypes were 8, 3, 19A, 22F, 12F, 9N, 15A, 10A, 23B, 6C, 11A (in order of decreasing frequency), accounting for 70% of all cases with a known serotype in 2018.

The distribution of these serotypes during the period 2014–2018 is presented in Figure 5 for countries that reported serotyping data consistently for each year of the reporting period. When comparing distribution in 2018 and 2014, there was a sharp increase in serotypes 8 and 3 during the reporting period (by 184% and 131% respectively).

Figure 5. Distribution of confirmed serotyped cases of invasive pneumococcal disease: most common *S. pneumoniae* serotypes in 2018[1]



Source: Country reports from Austria, the Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, the Netherlands, Norway, Portugal, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.
^: covered by PPV23.
†: covered by PCV13 and PPV23

The distribution of serotypes varied according to the age groups affected. The five most common serotypes in each age group are presented in Table 2. For cases under one year of age, serotypes 8, 10A, 3, 19 A and 24F were predominant. Serotypes 24F, 3 and 19A were the most common in the 1-4 year age group. Serotype 8 was the most common for those aged 5–64 years. Serotype 8 and 3 were the most common serotypes for those over 25 years. Serotype 19A was among the top five serotypes in all age groups.

In 2018, of all cases in children aged under five years, 7% were caused by a PCV7 serotype (4, 6A, 6B, 9V, 14, 18C, 19F and 23F), 1% by a PCV10/non-PCV7 serotype (1, 5 and 7F), 16% by a PCV13/non-PCV10 serotype (3 and 19A) and 75% by a serotype not included in any current PCV vaccine. In 2018, among cases aged 5–64 years, 6% were caused by a PCV7 serotype, 2% by a PCV10/non-PCV7 serotype, 20% by a PCV13/non-PCV10 serotype and 71% by non-PCV serotypes. Among adults aged 65 years and over, 71% were caused by PPV23 serotypes and 29% were caused by PCV13 serotypes.

In the under-fives, for countries that reported serotype data consistently each year from 2013–2017, there was a decrease in the proportion of PCV7 serotypes from 14% to 6%, and in the proportion of PCV10/non-PCV7 serotypes from 5% to 1% (Figure 6). There was a slight increase in the proportion of PCV13/non-PCV10 serotypes between 2013 and 2017 (13% to 16% respectively) and an increase in non-PCV serotypes from 68% to 75%.

In those aged 65 years and above, in countries that reported serotype data consistently each year during the period 2014–2018, there was a decrease in the proportion of PCV13 serotypes from 35% to 29% (Figure 7). The proportion caused by PPV23 serotypes fluctuated between 67% and 73%. The proportion caused by PPV23/non-PCV13 serotypes (2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F and 33F) increased from 34% in 2013 to 40% in 2018.

[1] Different serotypes are covered by different vaccines, as follows:

- 7-valent pneumococcal conjugate vaccine (PCV7): 4, 6B, 9V, 14, 18C, 19F and 23F
- 10-valent pneumococcal conjugate vaccine (PCV10): 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5 and 7F
- 13-valent pneumococcal conjugate vaccine (PCV13): 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F, 3, 6A and 19A. Although serotype 6A is included in PCV13 and not in PCV7, it is considered to be a PCV7 serotype in the analysis due to documented cross-protection provided by the serotype 6B antigen in PCV7.
- 23-valent pneumococcal polysaccharide vaccine (PPV23): 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F and 33F.

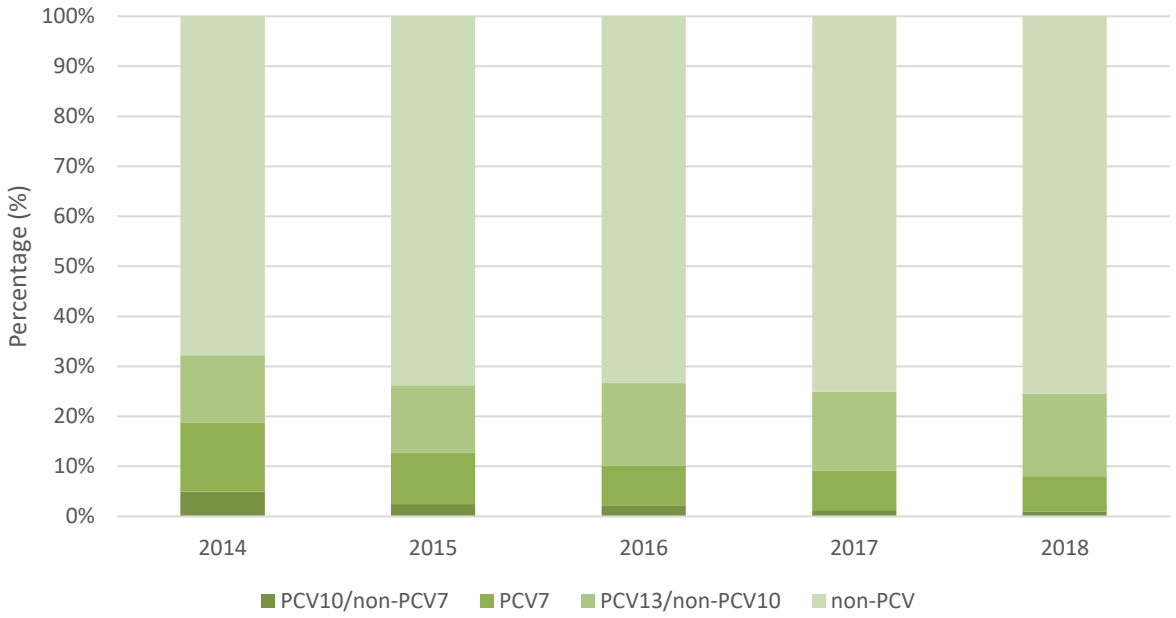
Table 2. Proportion of the five most frequent serotypes of *S. pneumoniae* from confirmed cases of invasive pneumococcal disease, by age group, 2018

Age group (years)	<1	1–4	5–14	15–24	25–44	45–64	≥65
Five most common serotypes by age group (% of all cases per age group)	8 (11.0%)	24F (12.2%)	8 (10%)	8 (32.5%)	8 (28%)	8 (21.5%)	3 (14.7%)
	10A (8.4%)	3 (9.2%)	19A (8.3%)	12F (10%)	3 (11.3)	3 (14.6%)	8 (14.0%)
	3 (7.6%)	19A (8.4%)	12F (7.5%)	19A (8.7%)	12F (9.5%)	19A (7.2%)	19A (7.6%)
	19A (7.0%	12F (7.3%)	23B (7.1%)	3 (7.3%)	19A (7.6%)	12F (7.1%)	22F (7.4%)
	24F (6.5%)	23B (7.3%)	3 (5%)	33F (4.7%)	9N (4.5%)	22F (6.4%)	9N (5.4%)

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

* Number of cases for which information on serotype and age was available : <1 year: n=368; 1–4 years: n=606; 5–14 years: n= 240; 15–24 years: n=231; 25–44 years: n=1 632; 45–64 years: n=3 481; ≥65 years: n=8 864.

Figure 6. Confirmed cases of invasive pneumococcal disease aged <5 years: serotype distribution by PCV type and year, 2014–2018

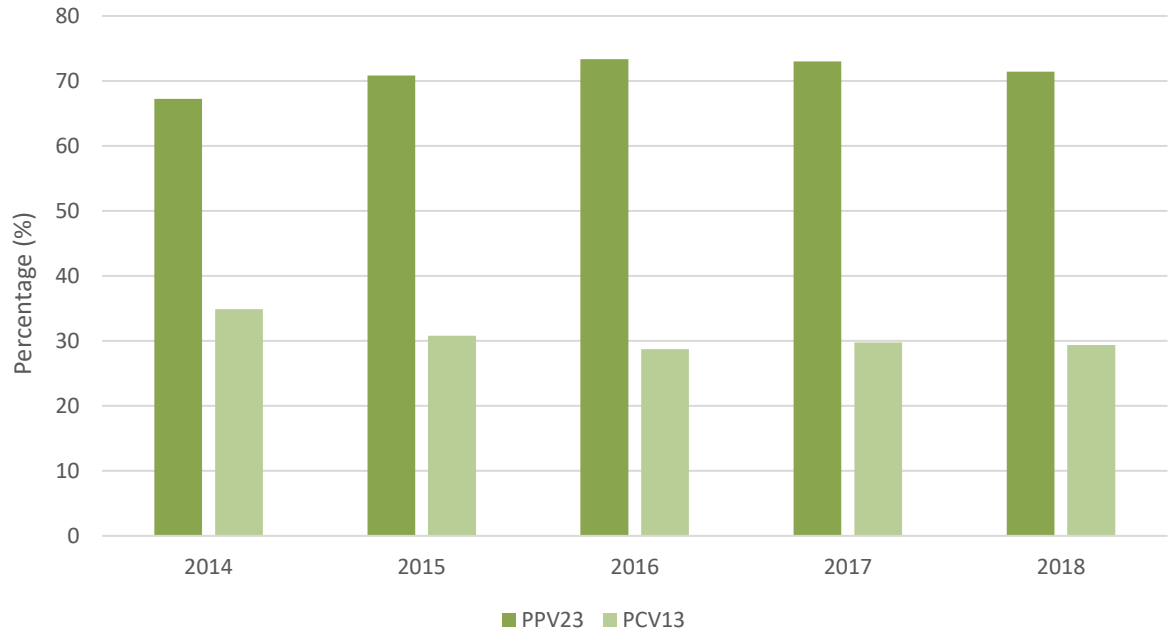


Source: Country reports from Austria, the Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, the Netherlands, Norway, Portugal, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

**: Although serotype 6A is included in PCV13 and not in PCV7, for the purposes of this analysis it is considered a PCV7 serotype due to documented cross-protection provided by the serotype 6B antigen in PCV7.*

PCV7 serotypes: 4, 6A, 6B, 9V, 14, 18C, 19F and 23F
PCV10non7 serotypes: 1, 5 and 7F
PCV13non10 serotypes: 3 and 19A
Non-PCV serotypes: all remaining serotypes.

Figure 7. Confirmed cases of invasive pneumococcal disease aged ≥65 years: serotype distribution by pneumococcal vaccine type and year, 2013–2017



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

**: PCV13 serotypes: 1, 3, 5, 4, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F; PPV23 serotypes: 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, 33F.*

Antimicrobial susceptibility

Antimicrobial susceptibility data were based on the reporting of Sensitive, Intermediate and Resistant (SIR) and Minimum Inhibitory Concentration (MIC) data. MIC data were converted to SIR data based on EUCAST breakpoints. Ten countries reported antimicrobial susceptibility data in 2018. Penicillin susceptibility data were reported for 5 001 of all IPD cases. Of these, 82% (n=4 081) were reported as sensitive, 16% (n=825) as intermediate and 2% (n=95) as resistant. Erythromycin susceptibility data were reported for 5 003 of all IPD cases. Of these, 82% (n=4 090) were reported as sensitive, 0.6% (n=29) as intermediate and 18% (n=883) as resistant. Cephalosporin susceptibility data were reported for 4 112 of all IPD cases. Of these, 93% (n=3 815) were reported as sensitive, 6% (n=262) as intermediate and 1% (n=31) as resistant.

Clinical presentation

Clinical presentation was known for 8 423 (34%) of all cases. Of these, septicaemia was reported in 2 964 cases (35%), bacteraemic pneumonia in 3 611 (43%), meningitis in 1 627 (19%), meningitis and septicaemia in 56 (1%) and a further 165 (2%) had other clinical presentations.

The most common clinical presentation in <1 year and 5–14-year-olds was meningitis; in 1–4 year olds septicaemia and bacteraemic pneumonia were equally frequent and among those aged 15 years and over, bacteraemic pneumonia was the most common clinical presentation.

Outcome

Among 10 486 cases with known outcome (42%) in 2018, 1 609 (15%) died. The case fatality rate increased with age: 4% in children <15 years of age, 6% in 15–44-year-olds, 11% in 45–64-year-olds and 21% in those aged 65 years and above.

Discussion

The crude notification rate of 6.4 cases per 100 000 population of confirmed IPD in 2018 is slightly higher than in previous years. The elderly and infants continue to be the most affected age groups. Notification rates varied by country, ranging from 0.2 to 16.0 cases per 100 000 population. The variation may be due to differences in healthcare systems, vaccination programmes, case ascertainment and reporting, as well as implementation of enhanced surveillance systems in a number of countries in recent years [6].

A number of studies have demonstrated the impact of PCVs in reducing the incidence of IPD. They have also provided evidence of increases in non-vaccine serotypes as a result of introducing PCV10 and PCV13 [7–9]. Moreover, the vaccination of infants and young children has resulted in indirect protection of older adults by reducing nasopharyngeal carriage and transmission of the bacterium in children, contributing to a decrease in morbidity and mortality in older age groups [7,10]. PCV7 was first licensed in 2001 for use in infants and young children and EU/EEA Member States began introducing the vaccine into routine childhood immunisation schedules in 2006. In 2009, the higher-valency PCV10 and PCV13 vaccines were licensed and have progressively replaced PCV7.

To date, 29 Member States have introduced conjugate vaccines to their routine national childhood immunisation programmes (all except Estonia and Malta) [11]. The vaccination is mandatory in six countries (Bulgaria, France, Croatia, Hungary, Poland and Slovakia). In TESSy, the proportion of IPD cases caused by PCV serotypes has decreased over time to the extent that 75% of cases among children <5 years of age and 71% in adults 65 years or above were caused by non-PCV serotypes in 2018. Serotype replacement has gradually reduced the impact of PCV as the rates of carriage and disease caused by non-vaccine serotypes have increased [12].

In 2018, among infants and children aged 1–4 years, the most common serotypes included 8, 10A, 3, 19A and 24F. Those serotypes are not included in any of the currently licensed PCVs, with the exception of 19A. A better understanding of the epidemiology of serotype 19A in relation to vaccination strategies is necessary. While vaccination with PCV13 confers longer and better protection against serotype 19A, it may vary, depending on the vaccination scheme - 2+1 or 3+1. Longer enhanced surveillance projects are required to better understand factors associated with fluctuation of serotype 19A.

Twenty-one Member States offer PPV23 and/or PCV13 for persons aged 50 years and over and/or for risk groups in certain age groups [11]. Among the elderly, the majority of IPD cases continue to be caused by PPV23 serotypes, with less than a third of all cases caused by PCV13 serotypes. In 2011, PCV13 was approved for use in adults aged 50 years and over. Studies have shown that PCV13 vaccination for the elderly can induce an immune response against vaccine serotypes that is as good as or better than PPV23 [13]. The vaccine is safe and effective in preventing non-IPD and IPD caused by vaccine serotypes [13]. However, decreases in PCV13 serotypes and increases in non-PCV13 serotypes in the elderly as an indirect effect of routine childhood vaccination reduce the potential additional benefit of PCV13 vaccination in the elderly [14]. Further monitoring of IPD serotype trends in the elderly and post-marketing effectiveness and impact studies in adults are warranted.

The SpiDnet project

From August 2012 to January 2020, in order to obtain further insight into the epidemiology of IPD, ECDC provided funding for SpIDnet (*Streptococcus pneumoniae* invasive disease network). This project aimed to establish active enhanced surveillance of IPD in the EU/EEA in order to monitor changes in the epidemiology of IPD, estimate the effectiveness of PCV vaccines and evaluate the impact of PCV vaccination programmes. The project had 13 study sites in 10 Member States and covered around 20% of the total EU/EEA population. The project complemented routine surveillance performed at the European level by actively collecting additional data using a common protocol. A recent publication showed that during the PCV10/13 period, the incidence of IPD caused by any serotype in children under five years decreased by 47%, compared to the PCV7 period (i.e. before the introduction of PCV10/13) [15]. The decrease was even more substantial (55%) when the period after the introduction of PCV10/13 was compared to the period before the introduction of PCV7. This decline demonstrates the positive overall effect of PCV programmes on IPD incidence in children. However, the incidence of IPD caused by non-PCV13 serotypes in children below the age of five increased by 62% against the average incidence when PCV7 was used, and by 115% compared to the period before PCV7 was used. Another recent publication from the SpIDnet project showed a 9% decline in IPD cases in adults aged ≥65 years five years following the introduction of PCV10/13 vaccination in children [14]. On the other hand, during the period 2014–2015 an overall increase in IPD cases among older adults was observed at 12 out of 13 project sites. The decreases observed in IPD cases caused by PCV vaccine types (77% due to PCV7 serotypes, 73% due to PCV10/non-PCV7 serotypes and 38% due to PCV13/non-7 serotypes) were in fact countered by a large increase (63%) in IPD cases due to non-PCV13 vaccine types. These results suggest the occurrence of serotype replacement, probably due to the use of PCV [16].

Public health implications

PCVs have provided significant protection against IPD as a result of the vaccine serotypes, with effects extending to all age groups through the introduction of herd immunity. At the same time, limited serotype coverage of the vaccines has resulted in serotype replacement. It is therefore essential to continue monitoring circulating serotypes in order to evaluate current vaccination programmes and inform development of new vaccines. The decision to introduce a vaccine to a routine national immunisation programme depends on context-specific factors in each country such as disease burden, serotype distribution and cost-effectiveness. Further monitoring of antimicrobial resistance is also needed to guide vaccination strategies and antibiotic treatment. It would also be of great value to improve the completeness of serotyping and antimicrobial susceptibility data in TESSy. ECDC is working towards molecular surveillance of IPD using whole-genome sequencing, which will probably give further information on the effects of vaccination on clonal expansion and capsular switching, and also inform vaccination strategies.

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