SURVEILLANCE REPORT

Invasive pneumococcal disease

Annual Epidemiological Report for 2017

Key facts

- In 2017, 23 886 confirmed cases of invasive pneumococcal disease (IPD) were reported in the EU/EEA.
- The notification rate was 6.2 cases per 100 000 population, continuing the increase observed since 2014.
- Age-specific rates were highest in those aged 65 years and over (18.9 cases per 100 000 population), followed by infants under one year of age (14.5 cases per 100 000 population), with higher rates in males compared to females.
- The 10 most common serotypes were 8, 3, 22F, 19A, 12F, 9N, 15A, 10A, 11A and 23B (in order of decreasing frequency), accounting for 66% of typed isolates.
- Of all 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, 72% were caused by serotypes in the 23-valent polysaccharide vaccine and 30% were caused by serotypes in the 13-valent PCV.

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. EU Member States and EEA countries contribute to the system by uploading their infectious disease surveillance data at regular intervals.

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 2017, 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 defining a confirmed case [4].

Suggested citation: European Centre for Disease Prevention and Control. Invasive pneumococcal disease. In: ECDC. Annual epidemiological report for 2017. Stockholm: ECDC; 2019.

Stockholm, May 2019

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), the other based on laboratories (FR-PNEUMO-NRL). Data reported from FR-PNEUMO-NRL were used for the analysis of 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].

Epidemiology

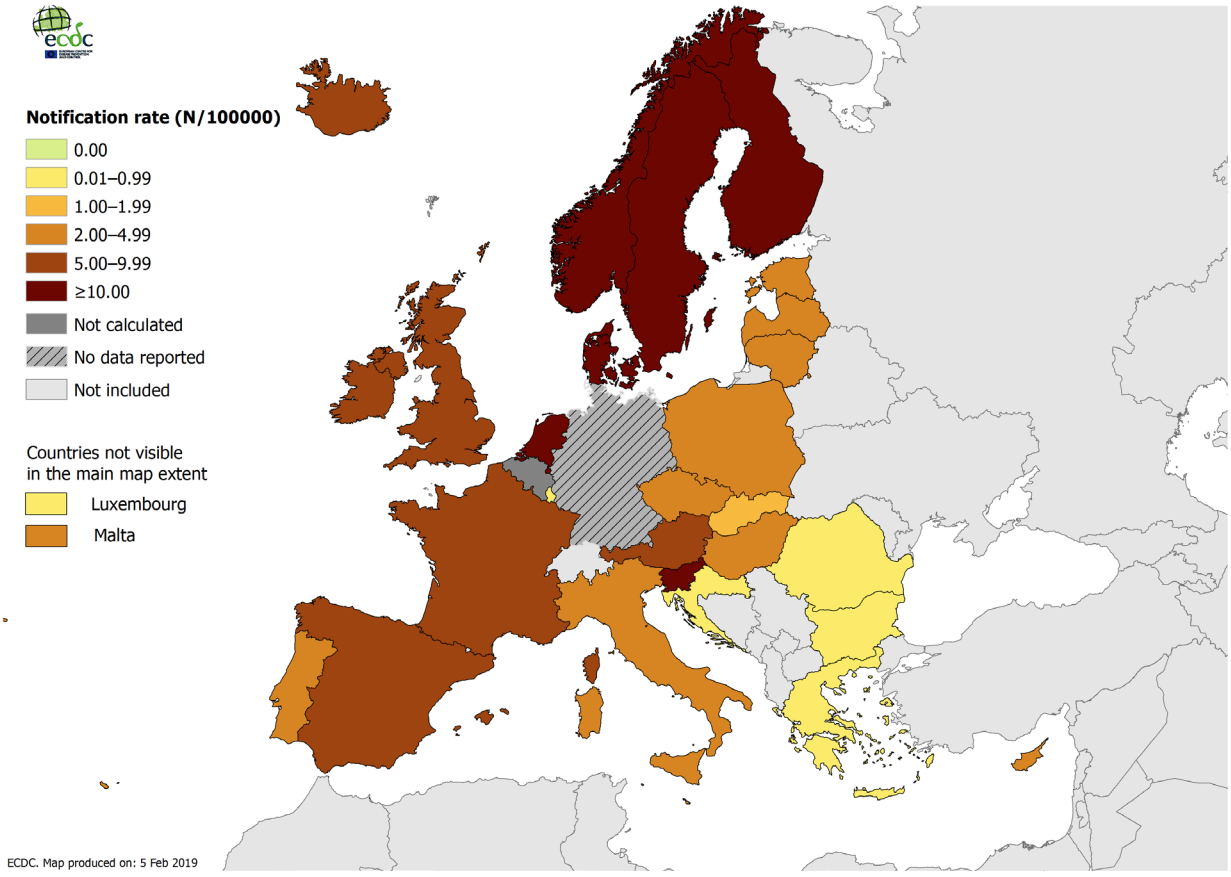
For 2017, 23 886 confirmed cases of IPD were reported by 29 countries. The notification rate was 6.2 cases per 100 000 population (Table 1). The United Kingdom had the highest number of confirmed cases, followed by France. The highest notification rates were reported in Denmark, Finland, the Netherlands, 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, 2013–2017

Country	2013		2014		2015		2016		2017			
	Number	Rate	Number	Rate	Number	Rate	Number	Rate	Confirmed cases	Rate	ASR	Reported cases
Austria	350	4.1	322	3.8	422	4.9	439	5.0	545	6.2	5.7	545
Belgium	1 604	-	1 192	-	1 362	-	1 329	-	1 461	-	-	1 461
Bulgaria	17	0.2	21	0.3	31	0.4	35	0.5	34	0.5	0.5	34
Croatia	16	0.4	27	0.6	24	0.6	14	0.3	16	0.4	-	16
Cyprus	8	0.9	14	1.6	9	1.1	5	0.6	20	2.3	2.4	20
Czech Republic	424	4.0	337	3.2	413	3.9	323	3.1	389	3.7	3.4	389
Denmark	842	15.0	725	12.9	807	14.3	731	12.8	771	13.4	12.3	771
Estonia	24	1.8	12	0.9	24	1.8	30	2.3	45	3.4	3.2	45
Finland	724	13.3	703	12.9	815	14.9	817	14.9	822	14.9	13.4	822
France	3 687	7.8	3 184	6.6	3 299	6.9	3 800	7.9	3 862	8.0	7.4	3 862
Germany	.	.	.	.	.	.	.	.	.	.	.	.
Greece	40	0.4	30	0.3	55	0.5	52	0.5	52	0.5	0.5	52
Hungary	202	2.0	150	1.5	189	1.9	226	2.3	268	2.7	2.6	270
Iceland	19	5.9	24	7.4	25	7.6	19	5.7	27	8.0	8.8	27
Ireland	347	7.5	342	7.4	370	7.9	378	8.0	414	8.7	9.5	414
Italy	977	1.6	957	1.6	1 248	2.1	1 529	2.5	1 705	2.8	2.4	1 705
Latvia	56	2.8	51	2.5	87	4.4	65	3.3	75	3.8	3.6	75
Liechtenstein	.	.	.	.	.	.	.	.	.	.	.	.
Lithuania	17	0.6	6	0.2	25	0.9	56	1.9	76	2.7	2.4	76
Luxembourg	1	0.2	1	0.2	0	0.0	0	0.0	1	0.2	0.2	1
Malta	6	1.4	22	5.1	9	2.0	11	2.4	18	3.9	3.6	18
Netherlands	652	15.5	546	13.0	667	15.8	631	14.9	616	14.4	13.2	629
Norway	620	12.3	569	11.1	522	10.1	599	11.5	560	10.6	10.6	560
Poland	540	1.4	705	1.9	979	2.6	962	2.5	1 187	3.1	-	1 187
Portugal	-	-	-	-	142	1.4	163	1.6	301	2.9	2.6	302
Romania	92	0.5	62	0.3	53	0.3	50	0.3	50	0.3	0.3	50
Slovakia	84	1.6	78	1.4	68	1.3	59	1.1	100	1.8	1.8	100
Slovenia	278	13.5	276	13.4	332	16.1	281	13.6	328	15.9	14.4	328
Spain	2 026	5.4	1 856	5.0	2 037	5.5	1 825	4.9	2 443	6.6	6.1	2 443
Sweden	1 316	13.8	1 159	12.0	1 314	13.5	1 351	13.7	1 367	13.7	12.4	1 367
United Kingdom	5 045	7.9	4 157	6.5	5 796	8.9	6 205	9.5	6 333	9.6	9.2	6 333
EU/EEA	**20 014**	**5.5**	**17 528**	**4.8**	**21 124**	**5.6**	**21 985**	**5.8**	**23 886**	**6.2**	**6.1**	**23 902**

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, 2017

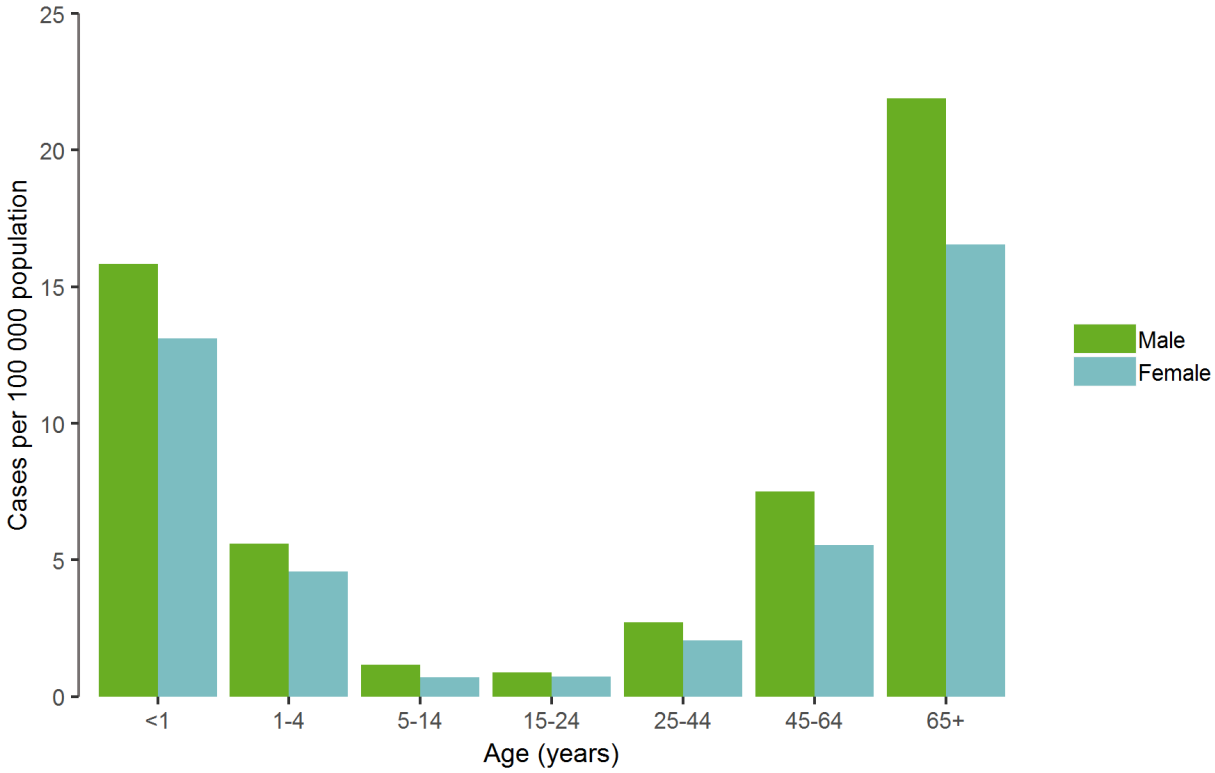


Source: Country reports from Austria, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United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

Age and gender distribution

In 2017, IPD was predominantly reported in the elderly and in infants, with 18.9 confirmed cases per 100 000 population in adults aged 65 years or older and 14.5 confirmed cases per 100 000 population in infants under one year of age (Figure 2). As in previous years, the rates of disease were lowest in persons from 5–44 years of age. The notification rate was higher in males in all age groups. The overall male-to-female ratio was 1.1:1.

Figure 2. Distribution of confirmed invasive pneumococcal disease cases per 100 000 population by age and gender, EU/EEA, 2017

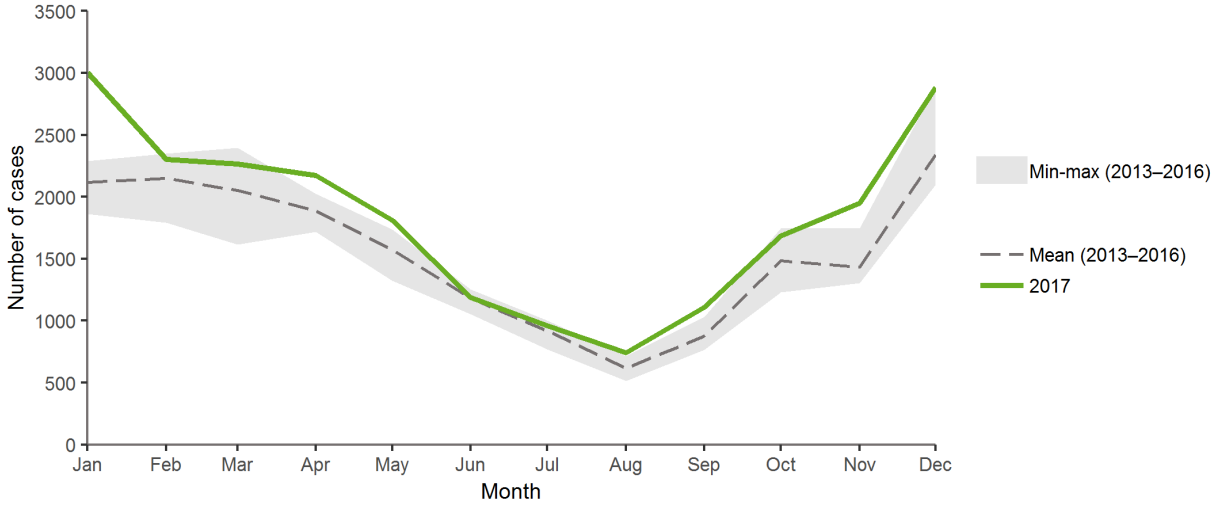


Source: Country reports from Austria, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United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

Seasonality and trend

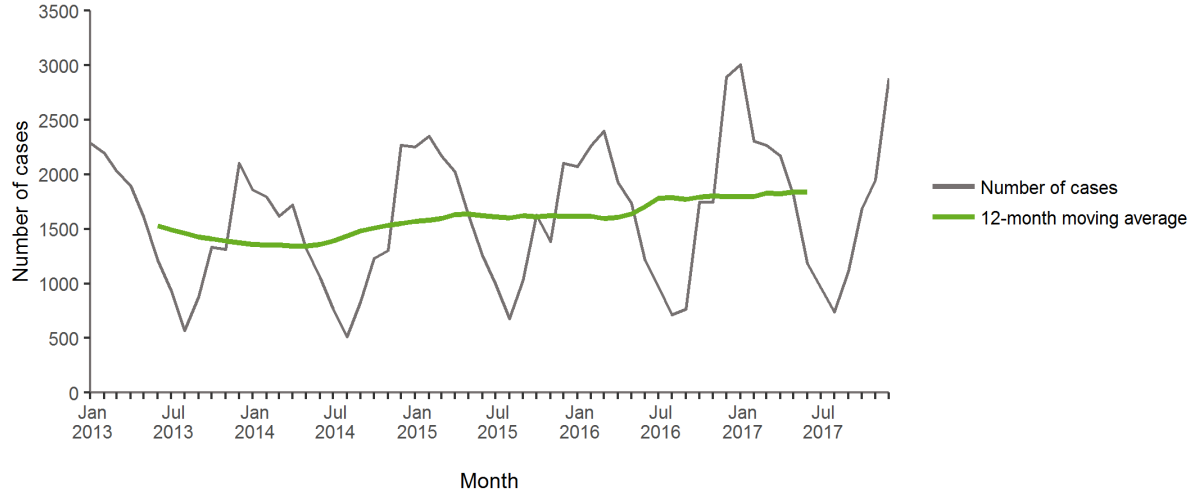
The seasonal distribution of IPD cases followed a pattern similar to that of many other respiratory diseases. Case numbers were lowest during summer, increased rapidly with the onset of autumn, and peaked during the winter months (Figures 3, 4). There was an increasing trend of reported cases from 2014–2017 (Figure 4) and the notification rate increased to 6.2 cases per 100 000 population in 2017 from 5.8 and 5.6 cases per 100 000 population respectively in 2016 and 2015 (Table 1).

Figure 3. Distribution of confirmed invasive pneumococcal disease cases by month, EU/EEA, 2013–2016 and 2017



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

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



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

Serotype

Data on serotype were reported for 16 191 (68%) of 23 886 cases in the EU/EEA countries for 2017. The 10 most common serotypes were 8, 3, 22F, 19A, 12F, 9N, 15A, 10A, 11A and 23B (ordered by decreasing frequency), accounting for 66% of all cases with a known serotype. The distribution of these serotypes from 2013–2017 is presented in Figure 5 for countries that reported serotyping data for each of the years. When comparing frequencies in 2017 and 2013, serotypes 8, 12F and 9N, increased by 120%, 87% and 85% respectively.

Different serotypes are covered by the:

- 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.

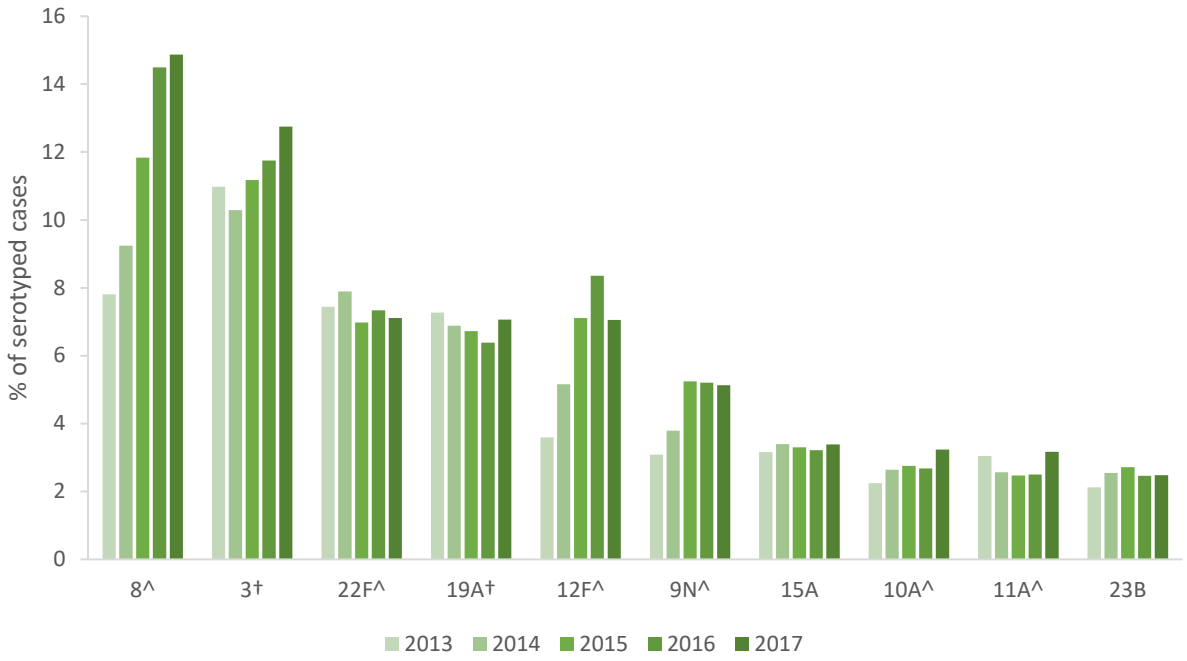
The five most common serotypes by age group are presented in Table 2. Serotypes 3 and 19A, which are included in PCV13, were among the most common in all age groups. The proportion of serotype 8 was higher among persons aged 15–64 years compared with the other age groups.

Of all cases in children aged under five years in 2017, 8% 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), 15% by a PCV13/non-PCV10 serotype (3 and 19A) and 76% by a serotype not included in any PCV vaccine. For countries that reported serotype data during each year from 2013–2017, there was a decrease in the proportion of PCV7 serotypes from 13% to 8% and in the proportion of PCV10/non-PCV7 serotypes from 9% to 1% (Figure 6). There was no substantial difference in the proportion of PCV13/non-PCV10 serotypes in 2013 and 2017, 16% and 15% respectively, and there was an increase of non-PCV serotypes from 63% to 76%.

In 2017, among cases aged 5–64 years, 7% were caused by a PCV7 serotype, 4% by a PCV10/non-PCV7 serotype, 18% by a PCV13/non-PCV10 serotype and 72% by non-PCV serotypes.

Among adults 65 years and over in 2017, 72% were caused by PPV23 serotypes and 30% were caused by PCV13. For countries that reported serotype data during each year from 2013–2017, there was a decrease in the proportion of PCV13 serotypes from 40% to 30% (Figure 7). The proportion caused by PPV23 serotypes fluctuated between 70% and 73%. The proportion caused by PPV23/non-PCV13 serotypes (2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F and 33F) increased from 33% in 2013 to 43% in 2017.

Figure 5. Distribution of confirmed serotyped cases of invasive pneumococcal disease: most common *S. pneumoniae* serotypes in 2017



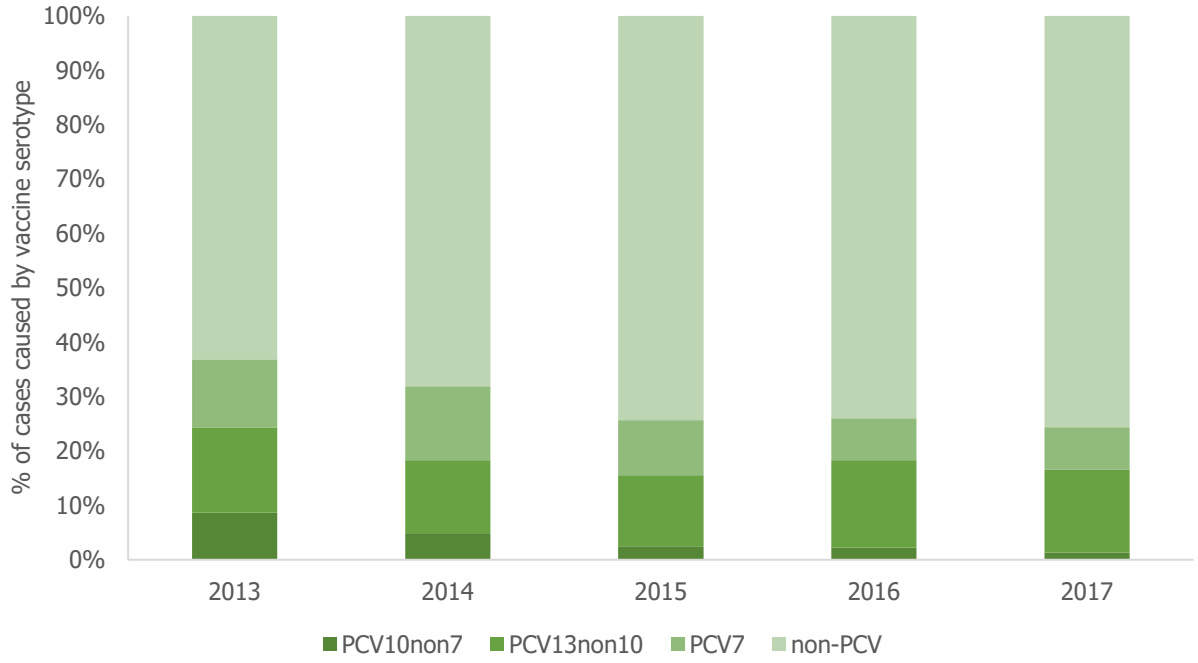
Source: Country reports from Austria, the Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, the Netherlands, Norway, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.
^: covered by PPV23.
†: covered by PCV13 and PPV23

Table 2. Proportion of the five most frequent serotypes of *S. pneumoniae* from confirmed cases of invasive pneumococcal disease, by age group, 2017

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)	3 (10.0%)	24F (12.1%)	3 (8.1%)	8 (24.8%)	8 (24.1%)	8 (18.3%)	3 (14.1%)
	10A (8.9%)	12F (9.2%)	8 (8.7%)	12F (13.7%)	12F (12.0%)	3 (12.4%)	8 (12.3%)
	8 (8.7%)	19A (7.6%)	19A (6.9%)	3 (9.8%)	3 (9.7%)	12F (8.6%)	22F (8.1%)
	24F (8.1%)	3 (7.4%)	12F (5.7%)	19A (7.7%)	19A (6.2%)	22F (7.2%)	19A (7.3%)
	19A (6.5%)	23B (6.4%)	10A (5.2%)	1 (3.9%)	9N (5.6%)	19A (6.6%)	9N (5.2%)

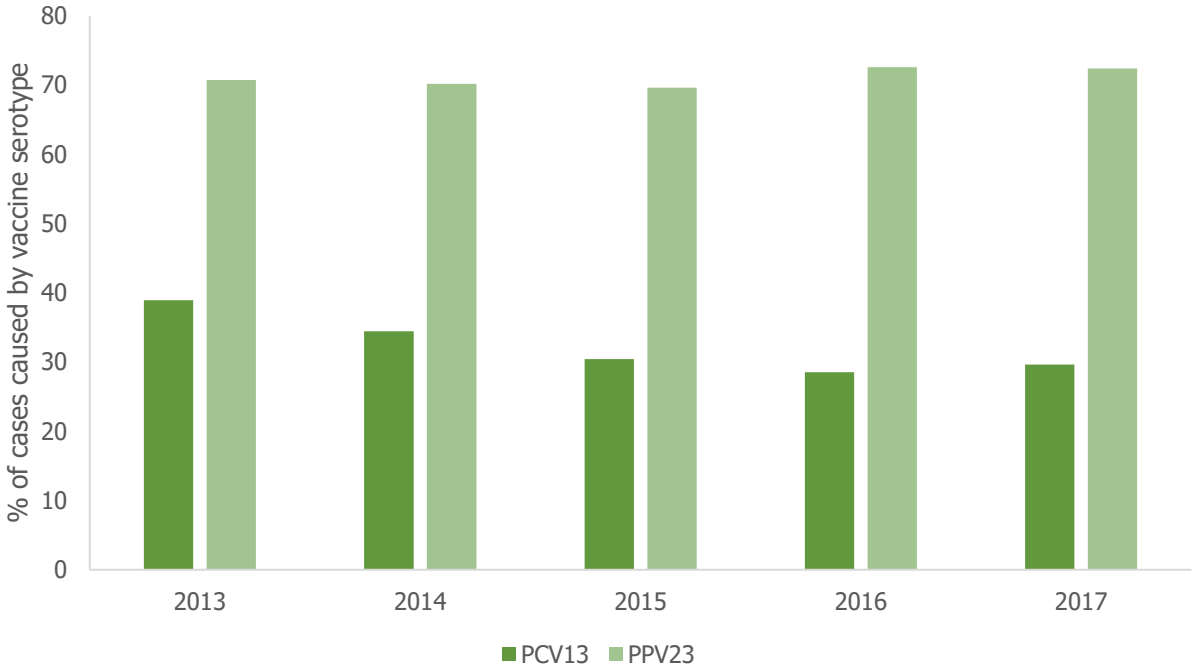
Source: Country reports from Austria, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, the Netherlands, Norway, Portugal, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

Figure 6. Confirmed cases of invasive pneumococcal disease aged <5 years: serotype distribution by PCV 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, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.
**: Although serotype 6A is included in PCV13 and not in PCV7, it is considered a PCV7 serotype for the purpose of this analysis 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, 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 SIR and MIC data. MIC data were converted to SIR data based on EUCAST breakpoints. Fourteen countries reported antimicrobial susceptibility data in 2017. Penicillin susceptibility data were reported for 6 281 (26%) of all IPD cases. Of these, 83% (n=5 208) were reported as sensitive, 14% (n=880) as intermediate and 3% (n=193) as resistant. Erythromycin susceptibility data were reported for 6 279 (26%) of all IPD cases. Of these, 83% (n=5 229) were reported as sensitive, 0.2% (n=12) as intermediate and 17% (n=1 038) as resistant. Cephalosporin susceptibility data were reported for 5 766 (24%) of all IPD cases. Of these, 94% (n=5 418) were reported as sensitive, 4.0% (n=242) as intermediate and 2% (n=106) as resistant.

Clinical presentation

Clinical presentation was known for 8 055 (34%) of all cases. Of these, septicaemia was reported in 2 848 cases (35%), bacteraemic pneumonia in 3 414 (42%), meningitis in 1 499 (19%), meningitis and septicaemia in 74 (1%) and a further 220 (3%) 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 10 006 cases with known outcome (42%) in 2017, 1 548 (15%) died. The case fatality rate increased with age: 3% in children <15 years of age, 6% in 15–44-year-olds, 11% in 45–64-year-olds and 22% in persons 65 years and above.

Discussion

The notification rate of 6.2 cases per 100 000 population of confirmed IPD in 2017 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 0.2–15.9 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 an effect 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, 28 Member States have introduced conjugate vaccines to their routine national childhood immunisation programmes [11]. In TESSy, the proportion of IPD cases caused by PCV serotypes has decreased over time such that 75% and 72% of cases among children <5 years of age and in adults 65 years or above were caused by non-PCV serotypes in 2017. Serotype replacement has gradually reduced the impact of PCV as the rates of carriage and disease caused by non-vaccine serotypes have increased [12]. Among IPD cases in 2017 among infants and children aged 1–4 years, the most common serotypes included 8, 10A, 12F and 24F, which are not included in any of the currently licensed PCVs. These serotypes could be potential targets for future higher-valency vaccines. TESSy data support the success of PCV immunisation of children in reducing the burden of disease caused by PCV serotypes, as well as the need for alternative vaccination strategies that target non-PCV serotypes.

In order to provide further insight into the epidemiology of IPD, ECDC started funding SpIDnet (*Streptococcus pneumoniae* invasive disease network) in August 2012. This project aims 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 has 13 study sites in 10 Member States and covers around 20% of the total EU/EEA population. This project complements routine surveillance performed at the European level by actively collecting additional data and using a common protocol. A recent publication showed that the incidence of IPD caused by any serotype in children younger than five years decreased by 47% in the PCV10/13 period compared to the PCV7 period (i.e. before the introduction of PCV10/13) [13]. 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% compared to 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 decline of 9% of IPD cases in adults ≥65 years five years after the introduction of PCV10/13 vaccination in children [14]. On the other hand, an overall increase in IPD cases among older adults was observed from 2014–2015 in 12 of 13 project sites. The declines observed in IPD cases caused by PCV vaccines 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 [15].

Twenty-one Member States offer PPV23 and/or PCV13 for persons 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 [16]. The vaccine is safe and effective in preventing non-IPD and IPD caused by vaccine serotypes [16]. 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.

Public health implications

PCVs have provided significant protection against IPD due to 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 in order to guide vaccination strategies and antibiotic treatment. It would 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 likely give further information on the effects of vaccination on e.g. clonal expansion and capsular switching, and will also inform vaccination strategies.

References

1. European Centre for Disease Prevention and Control. Introduction to the Annual Epidemiological Report. In: ECDC. Annual epidemiological report for 2017 [Internet]. Stockholm: ECDC; 2017 [cited 31 January 2019]. Available from: http://ecdc.europa.eu/annual-epidemiological-reports/methods
2. European Centre for Disease Prevention and Control. Surveillance systems overview [Internet, downloadable spreadsheet]. Stockholm: ECDC; 2018 [cited 31 January 2019]. Available from: http://ecdc.europa.eu/publications-data/surveillance-systems-overview-2017
3. European Centre for Disease Prevention and Control. Surveillance atlas of infectious diseases [Internet]. Stockholm: ECDC; 2017 [cited 31 January 2019]. Available from: http://atlas.ecdc.europa.eu/public/index.aspx?Dataset=27&HealthTopic=40
4. European Centre for Disease Prevention and Control. EU case definitions [Internet]. Stockholm: ECDC; 2018 [cited 15 May 2018]. Available from: http://ecdc.europa.eu/en/aboutus/what-we-do/surveillance/Pages/case_definitions.aspx
5. van der Linden M, Falkenhorst G, Perniciaro S, Imohl M. Effects of Infant Pneumococcal Conjugate Vaccination on Serotype Distribution in Invasive Pneumococcal Disease among Children and Adults in Germany. PLoS One. 2015 Jul 1;10(7):e0131494.
6. Navarro Torné A, Dias JG, Quinten C, Hruba F, Busana MC, Lopalco PL, et al. European enhanced surveillance of invasive pneumococcal disease in 2010: data from 26 European countries in the post-heptavalent conjugate vaccine era. Vaccine. 2014 Jun 17;32(29):3644-50.
7. Flasche S, Van Hoek AJ, Sheasby E, Waight P, Andrews N, Sheppard C, et al. Effect of Pneumococcal Conjugate Vaccination on Serotype-Specific Carriage and Invasive Disease in England: A Cross-Sectional Study. PLoS Med. 2011 Apr;8(4):e1001017.
8. D'Ancona F, Caporali MG, Del Manso M, Giambi C, Camilli R, D'Ambrosio F, et al. Invasive pneumococcal disease in children and adults in seven Italian regions after the introduction of the conjugate vaccine, 2008–2014. Epidemiol Prev. 2015 Jul-Aug;39(4 Suppl 1):134-8.
9. Waight PA, Andrews NJ, Ladhani SN, Sheppard CL, Slack MP, Miller E. Effect of the 13-valent pneumococcal conjugate vaccine on invasive pneumococcal disease in England and Wales 4 years after its introduction: an observational cohort study. Lancet Infect Dis. 2015 May;15(5):535-43.
10. Tocheva AS, Jefferies JM, Rubery H, Bennett J, Afimeke G, Garland J, et al. Declining serotype coverage of new pneumococcal conjugate vaccines relating to the carriage of *Streptococcus pneumoniae* in young children. Vaccine. 2011 Jun 10;29(26):4400-4.
11. European Centre for Disease Prevention and Control. Vaccination Scheduler – Vaccine schedules in all countries of the European Union [Internet]. Stockholm: ECDC; 2019 [cited 22 March 2019]. Available from: http://vaccine-schedule.ecdc.europa.eu
12. Lynch JP 3rd, Zhanel GG. *Streptococcus pneumoniae*: epidemiology and risk factors, evolution of antimicrobial resistance, and impact of vaccines. Curr Opin Pulm Med. 2010 May;16(3):217-25.
13. Savulescu C, Krizova P, Lepoutre A, Mereckiene J, Vestrheim DF, Ciruela P, et al.. Effect of high-valency pneumococcal conjugate vaccines on invasive pneumococcal disease in children in SpIDnet countries: an observational multicentre study. Lancet Respir Med. 2017 Aug;5(8):648-656.
14. Hanquet G, Krizova P, Valentiner-Branth P, Ladhani SN, Nuorti JP, Lepoutre A, et al. Effect of childhood pneumococcal conjugate vaccination on invasive disease in older adults of 10 European countries: implications for adult vaccination. Thorax. 2019 May;74(5):473-482.
15. Feikin DR, Kagucia EW, Loo JD, Link-Gelles R, Puhan MA, Cherian T, et al. Serotype-Specific Changes in Invasive Pneumococcal Disease after Pneumococcal Conjugate Vaccine Introduction: A Pooled Analysis of Multiple Surveillance Sites. PLoS Med. 2013;10(9):e1001517.
16. Tomczyk S, Bennett NM, Stoecker C, Gierke R, Moore MR, Whitney CG, et al. Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine Among Adults Aged ≥65 Years: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep. 2014 Sep 19;63(37):822-5.