Key facts

- In 2015, 21,118 confirmed cases of invasive pneumococcal disease (IPD) were reported to TESSy.
- The notification rate for 2015 was 5.6 cases per 100,000 population, which is higher than in 2014.
- Age-specific rates were highest in those aged 65 years and over (16.1 cases per 100,000 population), followed by infants under one year of age (12.9 cases per 100,000 population).
- The 10 most common serotypes were 8, 3, 22F, 12F, 19A, 9N, 7F, 15A, 33F, 10A (in order of frequency), accounting for 62% of typed isolates.
- Of all cases <5 years of age, 72% were caused by a serotype not included in any PCV vaccine.
- Among cases aged 65 years and over, 71% were caused by a PPV23 serotype, and 32% were caused by a PCV13 serotype.

Methods

This report is based on data for 2015 retrieved from The European Surveillance System (TESSy) on 26 October 2016. 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, please refer to the Methods chapter [1].

An overview of the national surveillance systems is available online [2].

Additional data on this disease are accessible from ECDC’s online Surveillance atlas of infectious diseases [3].

In 2015, a total of 29 Member States reported data; Portugal reported data for the first time.

Twenty-five Member States used the EU case definition that was published in 2008 and again, in unchanged form, in 2012 [4]. One Member State used the EU-2002 case definition, and three Member States used alternative case definitions. The 2012/2008 case definition differs from the EU 2002 case definition by not including possible and probable cases and by including detection of *S. pneumoniae* antigen at a normally sterile site as a confirmed case.
National IPD surveillance systems are heterogeneous. Of the 29 countries reporting data, 22 countries conduct surveillance with compulsory reporting and national coverage. Four countries perform surveillance by voluntary sentinel systems. Among these four countries, France, the Netherlands and Spain have surveillance systems which cover 72%, 25% and 80% of the national population, respectively. The population coverage of the Belgian surveillance system is unknown, therefore notification rates were not calculated for Belgium. Germany has a voluntary, laboratory-based surveillance system and does not report data to ECDC [5].

All countries – except for Belgium, Bulgaria and Croatia – reported case-based data [6]. Analysis by serotype was performed for Member States that provided serotype data.

IPD data from France are 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 are used for the analysis related to serotype and antimicrobial susceptibility while data reported from FR-EPIBAC are included in the rest of the analysis not related to serotype or antimicrobial susceptibility.

**Epidemiology**

In 2015, 21,118 confirmed cases of IPD were reported by 29 countries. The notification rate was 5.6 cases per 100,000 population, which was higher than in 2014 but similar to the notification rate in 2011–2013 (Table 1). The United Kingdom had the highest number of confirmed cases (5,796), followed by France (3,299) (Figure 1). The highest notification rates were reported in Slovenia, the Netherlands, Finland and Denmark, with 16.1, 15.8, 14.9 and 14.3 confirmed cases per 100,000 population, respectively (Figure 2).

**Table 1. Distribution of confirmed cases of invasive pneumococcal disease, EU/EEA, 2011–2015**

<table>
<thead>
<tr>
<th>Country</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>National coverage</th>
<th>Reported cases</th>
<th>Confirmed cases</th>
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<td>Rate</td>
<td>Number</td>
<td>Rate</td>
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<td>Rate</td>
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<td>19</td>
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</table>

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

The national coverage in France is calculated based on the entire French population; in reality, however, the 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 were collected through the FR-EPIBAC surveillance system.
Figure 1. Reported confirmed cases of invasive pneumococcal disease, EU/EEA, 2015

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

Figure 2. Rates of reported confirmed cases of invasive pneumococcal disease per 100,000 population, EU/EEA, 2015

Source: Country reports from Austria, Belgium, 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, the United Kingdom.
Age and gender distribution

In 2015, invasive pneumococcal disease was predominantly reported in infants and the elderly, with 16.1 confirmed cases per 100,000 population in adults aged 65 years or older and 12.9 confirmed cases per 100,000 population in children under one year of age (Figure 3). As in previous years, the rates of disease were lowest in people between 5 and 44 years. There was a predominance of cases in males in all age groups, resulting in an overall male-to-female ratio of 1.2:1.

Figure 3. Rate per 100,000 population of confirmed cases of invasive pneumococcal disease, by age and gender, EU/EEA, 2015

Seasonality and trend

The seasonal distribution of IPD cases followed a pattern similar to that of many other respiratory diseases. The lowest rates were observed during summer. Case numbers increased rapidly with the onset of autumn and winter, showing a peak in February (Figure 4). A similar pattern was observed during 2011–2014 (Figures 5). The notification rates of IPD remained stable over the same period (Figure 5), with the lowest values reported in 2014.

Source: Country reports from Austria, Belgium, 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, the United Kingdom.
Figure 4. Seasonal distribution of reported confirmed cases of invasive pneumococcal disease, EU/EEA, 2015

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

Figure 5. Trend of reported confirmed cases of invasive pneumococcal disease, EU/EEA, 2011–2015

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

Different serotypes are covered by the pneumococcal vaccines:

- 7-valent pneumococcal conjugate vaccine (PCV7): 4, 6B, 9V, 14, 18C, 19F, 23F
- 10-valent pneumococcal conjugate vaccine (PCV10): 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F
- 13-valent pneumococcal conjugate vaccine (PCV13): 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F, 3, 6A*, 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, 33F

For 2015, 25 EU/EEA countries reported data on serotype for 15,396 (73%) of 21,118 cases. The 10 most common serotypes were 8, 3, 22F, 12F, 19A, 9N, 7F, 15A, 33F, 10A (ordered by frequency), accounting for 62% of all cases with known serotype. This was similar to the 10 most common serotypes observed in 2013 and 2014. A gradual increase in the frequency of serotypes 8, 12F, 9N, 15A, 33F, 10A, 23B was observed from 2013 to 2015; for the same period a gradual decrease in the frequency was seen for 7F (Figure 6).

Among cases aged <1 year, serotype 8 was the most common (9%), followed by 19A (8%). Among children aged 1–4 years, serotypes 24F (11%) and 12F (10%) were the most common (Table 2). Of all cases aged <5 years in 2015, 13% were caused by a PCV7 serotype (4, 6A, 6B, 9V, 14, 18C, 19F, 23F), 2% by a PCV10non7 serotype (1, 5, 7F), and 13% by a PCV13non10 serotype (3, 19A) (Figure 7). The proportion of cases caused by PCV10non7 and PCV7 serotypes has decreased since 2012. In 2015, 72% of cases <5 years of age were caused by a serotype not included in any PCV vaccine, a gradual increase from 48% in 2012 (Figure 7).

Among cases aged 5–64 years, 9% were caused by a PCV7 serotype, 8% by a PCV10non7 serotype, and 17% by a PCV13non10 serotype. The proportion of cases caused by PCV7 and PCV10non7 serotypes has gradually decreased since 2012, when 13% of cases were caused by a PCV7 serotype, and 23% by a PCV10non7 serotype. The proportion of cases caused by PCV13non10 serotypes has increased from 15% in 2012 to 17% in 2015.

Among adults 65 years and over, the most frequent serotypes were 3 (13%) and 8 (10%) (Table 2). Seventy-one percent were caused by a PPV23 serotype, and 32% were caused by a PCV13 serotype. The proportion (32%) caused by a PCV13 serotype has gradually declined since 2012 when 43% of cases aged 65 years and over were caused by a PCV13 serotype. Twenty-nine percent of cases aged 65 years and over were caused by a serotype not covered by either PCV13 or PPV23 in 2015, similar to previous years (Figure 8). The proportion of cases among adults > 65 years caused by a PPV23 serotype has remained stable over 2013–15 (Figure 8).
Figure 6. Distribution of confirmed cases of invasive pneumococcal disease: most common *S. pneumoniae* serotypes in 2015 (n=15 396), 2014 (n=12 980) and 2013 (n=14 811)

Table 2. Proportion of the five most frequent serotypes of *S. pneumoniae* from confirmed cases of invasive pneumococcal disease, by age group, 2015 (n= 15 384*)

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>&lt;1</th>
<th>1–4</th>
<th>5–14</th>
<th>15–24</th>
<th>25–44</th>
<th>45–64</th>
<th>≥65</th>
</tr>
</thead>
<tbody>
<tr>
<td>Five most common serotypes by age group (% of all cases)</td>
<td>8 (8.5%)</td>
<td>24F (10.8%)</td>
<td>1 (14.3%)</td>
<td>8 (15.1%)</td>
<td>8 (16.4%)</td>
<td>8 (14.3%)</td>
<td>3 (13.4%)</td>
</tr>
<tr>
<td>19A</td>
<td>12F (10.1%)</td>
<td>8 (9.6%)</td>
<td>7F (13.9%)</td>
<td>12F (11.0%)</td>
<td>3 (11.9%)</td>
<td>8 (10.2%)</td>
<td></td>
</tr>
</tbody>
</table>
Age group (years) | <1 | 1–4 | 5–14 | 15–24 | 25–44 | 45–64 | ≥65
--- | --- | --- | --- | --- | --- | --- | ---
12F | 19A | 12F | 12F | 3 | 12F | 22F
(7.4%) | (7.9%) | (7.5%) | (5.7%) | (13.0%) | (8.9%) | (4.9%)
10A | 22B | 23B | 9N | 7F | 22F | 19A
(6.8%) | (7.1%) | (7.2%) | (6.0%) | (6.4%) | (7.0%) | (7.0%)
33F | 3 | 3 | 19A | 19A | 19A | 12F
(6.5%) | (6.1%) | (6.1%) | (8.3%) | (5.9%) | (6.4%) | (4.9%)

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

* Number of cases for which information on serotype and age was available. Number of cases for which serotype information was available by age group: <1 year: n=352; 1–4 years: n=622; 5–14 years: n=293; 15–24 years: n=238; 25–44 years: n=1639; 45–64 years: n=4162; ≥65 years: n=8078.

Figure 7. Invasive pneumococcal disease, reported confirmed cases aged <5 years: serotype distribution by PCV vaccine type, 2012–2015 (n= 4 185)

* Although serotype 6A is included in PCV13 and not in PCV7, it is considered to be 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, 23F; PCV10non7 serotypes: 1, 5, 7F; PCV13non10 serotypes: 3, 19A; non-PCV serotypes: all remaining serotypes.
Antimicrobial susceptibility

Data on antimicrobial susceptibility against at least one antimicrobial was known for 16 097 (76%) of all cases and was reported by 24 countries. The prevalence of non-susceptibility (combined intermediate and resistant categories) to penicillin increased from 11% in 2013 to 14% in 2015. In 2015, non-susceptibility to erythromycin was 17%, increasing from 14% in 2014. Cefotaxime/ceftriaxone non-susceptibility decreased from 7% in 2013 to 5% in 2015 (Figure 9). In 2015, the prevalence of non-susceptibility varied between countries, with the highest percentages of non-susceptibility reported by Poland (erythromycin: 31.3%) and Spain (cefotaxime/ceftriaxone: 10.0%, penicillin: 23.8%).

Figure 9. Susceptibility of *S. pneumoniae* from confirmed cases of invasive pneumococcal disease to cefotaxime/ceftriaxone, penicillin and erythromycin, 2013–2015


Note: SIR values (susceptible, intermediate, and resistant) are displayed as interpreted by the reporting countries. ‘Intermediate’ and ‘resistant’ were categorised as ‘non-susceptible’.

Clinical presentation

The clinical presentation was known for 15 403 (78%) of all cases. Septicaemia was reported in 8 089 cases (41%), bacteraemic pneumonia in 5 098 cases (26%), meningitis in 1 711 cases (9%), meningitis and septicemia in 104 cases (1%); a further 401 cases (2%) had other clinical presentations. Septicaemia was the most common clinical presentation in all age groups and with 9 of the 15 most common serotypes (22F, 23B, 11A, 6C, 24F, 10A, 15A, 33F and 23A). The other six most common serotypes (8, 3, 12F, 19A, 9N and 7F) were most commonly associated with bacteraemic pneumonia. For serotypes 12F, 22F and 33F, the proportion of septicaemia and bacteraemia were similar (range: 43%–46%).

Outcome

The outcome was known for 9 052 (48%) of all cases. Among cases with known outcome, 1 312 (14%) were reported as fatal. However, due to the poor completeness of this variable, these results must be interpreted with caution. The true case fatality is expected to be considerably lower.

Discussion

In 2015, the notification rate of 5.6 cases per 100 000 population of confirmed IPD was within the range observed between 2011 and 2014 (4.8–5.8 per 100 000). The notification rates varied by country, ranging from 0 to 16.1 cases per 100 000 population. The elderly and infants continue to be the most affected age groups.

The variation in notification rates between countries may be due to better case ascertainment and the implementation of enhanced surveillance systems in a number of countries in recent years. Enhanced surveillance of invasive pneumococcal disease in Europe was established in 2010 [6], the latest addition to the list of European surveillance systems for vaccine-preventable diseases.

In 2010, invasive pneumococcal disease became mandatorily notifiable in Latvia. In 2012, Denmark reported cases related to the whole national population for the first time following the implementation of a nationwide laboratory surveillance system. Also in 2012, the Dutch system was expanded to include all age categories whereas previously it was restricted to children below the age of five.

Many of the surveillance systems for IPD in Europe were originally based on clinical and not laboratory data and focussed predominantly on the clinical presentation of meningitis.

The proportion of cases caused by PCV serotypes decreased across all age groups, and the majority of cases in 2015 were caused by non-PCV serotypes. PCV7 was first licensed in 2001 for use in infants and young children, and EU/EEA Member States began introducing the vaccine to their routine child immunisation schedules in 2006. In 2009, the higher valency PCV10 and PCV13 vaccines were licensed and have progressively replaced PCV7. To date, 26 Member States have introduced conjugate vaccines to their routine national childhood immunisation programmes [7].

In order to provide further insight into the epidemiology of invasive pneumococcal disease, ECDC started funding SpID-net (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 vaccine effectiveness of PCV vaccines, and evaluate the impact of PCV vaccination programmes. The project has study sites in ten Member States and covers around 20% of the total EU/EEA population. This type of project complements the routine surveillance performed at the European level by collecting additional data and using a common methodology. A recent report [14] shows that the incidence of invasive pneumococcal disease caused by any serotype in children younger than five years decreased by 47% when PCV10/13 was used predominately (as compared with predominant use of PCV7). The decrease is even more substantial when PCV10/12 is compared with vaccinations before the introduction of PCV7, namely 55%. This decline demonstrates the positive overall effect of the vaccination programmes. By contrast, the incidence of invasive pneumococcal disease caused by non-PCV13 serotypes in children below the age of five increased by 62% compared with the
average incidence when PCV7 was used, and by 115% compared with the period before PCV7 was used. These results suggest the occurrence of serotype replacement [8].

A number of other studies have demonstrated the effectiveness of pneumococcal conjugate vaccines in reducing the incidence of IPD [4]. Studies also provide evidence of increases in non-vaccine serotypes as an effect of the introduction of PCV10 and PCV13 [9-11]. Moreover, the vaccination of infants and young children has resulted in herd immunity by reducing nasopharyngeal carriage and transmission of the bacterium, contributing to a decrease in morbidity and mortality among the older age groups [9,12]. Over time, serotype replacement has gradually reduced the effectiveness of PCV7, as the rates of carriage and disease caused by non-vaccine serotypes have increased [13]. In the data reported to ECDC in 2015 in infants and children aged 1–4 years, the most common serotypes were 8, 24F and 12F, which are not included in any of the currently licensed pneumococcal conjugate vaccines. These serotypes could be potential targets for future higher valency vaccines.

Among the elderly, the majority of cases continue to be caused by PPV23 serotypes, with 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 in the elderly can induce an immune response against vaccine serotypes that is non-inferior or better than PPV23. The vaccine is safe and effective in preventing non-invasive pneumococcal pneumonia and invasive pneumococcal disease [14]. However, decreases in PCV13 serotypes and increases in non-PCV13 serotypes in the elderly as an indirect effect of routine childhood vaccination may decrease the potential benefit of elderly PCV13 vaccination [15]. Further monitoring of IPD serotype trends in the elderly and post-marketing impact studies in adults are essential. Twenty Member States offer different vaccines for persons 50 years and over, and/or for risk groups in certain age groups. Fifteen Member States offer PPV23, and nine offer PCV13 vaccination for the elderly [7].

**Public health implications**

The decision to introduce a vaccine to the routine national immunisation programme depends on context-specific factors in each country, such as the disease and serotype burden, cost-effectiveness, and feasibility. It is essential to continue to monitor circulating serotypes in order to evaluate current vaccination programmes and inform the development of new vaccines. Antimicrobial resistance should be further monitored in order to assess and guide treatment options.
References


