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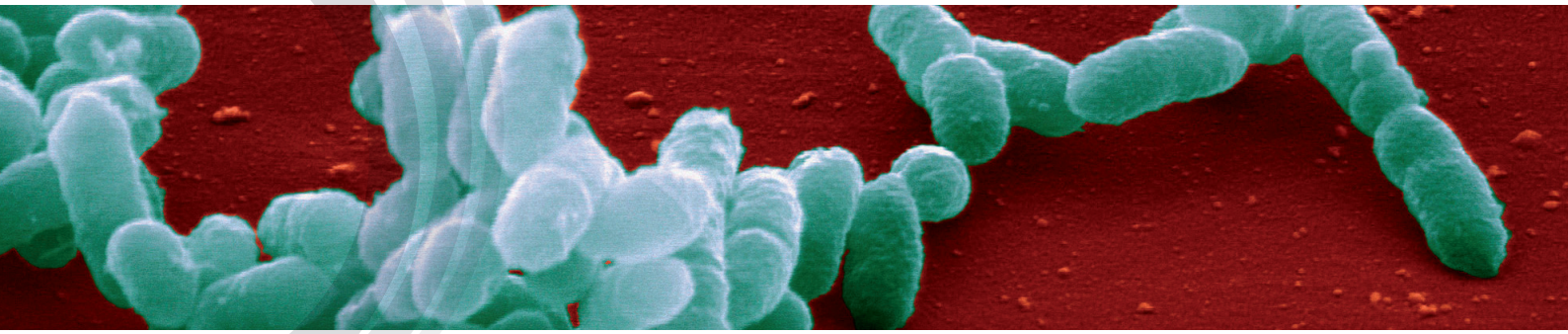

Surveillance of invasive bacterial diseases in Europe

Invasive pneumococcal disease, invasive *Haemophilus influenzae* disease and invasive meningococcal disease

2012

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ECDC SURVEILLANCE REPORT

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This report of the European Centre for Disease Prevention and Control (ECDC) was coordinated by Sabrina Bacci and Robert Whittaker.

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Abbreviations

CC	Clonal complex
CFR	Case fatality rate
CSF	Cerebrospinal fluid
CTX	Cefotaxime
CFX	Ceftriaxone
EEA	European Economic Area
ERY	Erythromycin
EU	European Union
EUCAST	European Committee on Antimicrobial Susceptibility Testing
IBD	Invasive bacterial disease
IMD	Invasive meningococcal disease
IPD	Invasive pneumococcal disease
Hi	*Haemophilus influenzae*
Hib	*Haemophilus influenzae* type b
MCC	Meningococcal C conjugate vaccine
MIC	Minimum inhibitory concentration
PCV7	Heptavalent pneumococcal conjugate vaccine
PCV10	10-valent pneumococcal conjugate vaccine
PCV13	13-valent pneumococcal conjugate vaccine
PEN	Penicillin
PPV23	23-valent pneumococcal polysaccharide vaccine
SIR	Susceptible, intermediate, resistant classification (final interpretation of antimicrobial susceptibility to penicillin, erythromycin and cefotaxime/ceftriaxone)
TESSy	The European Surveillance System
WHO	World Health Organization

Executive summary

This report describes the occurrence of invasive bacterial diseases (IBD) in Europe during 2012, based on data collected through The European Surveillance System (TESSy).

Invasive bacterial diseases remain an important public health issue across Europe and continue to cause serious disease in several countries, particularly among young children and the elderly. The main aim of this report is to provide information on the morbidity, epidemiological trends and circulating strains of invasive bacterial diseases caused by *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Neisseria meningitidis* in Europe.

All three diseases were characterised by a clear seasonal distribution of cases with a noticeable rise during the winter months, which is typical of respiratory diseases. There may be a number of factors involved in this seasonal pattern including co-infection with respiratory viruses or temperature and environmental conditions.

For invasive pneumococcal disease (IPD), 20 785 confirmed cases were reported in 2012 by 27 EU/EEA Member States for an overall notification rate of 5.2 cases per 100 000. Infants and the elderly were most affected. During 2008–12, a steady decreasing trend was observed for cases below five years of age. Trends remained stable across all other age groups. The majority of infections were caused by serotypes covered by the 13-valent pneumococcal conjugate vaccine PCV13, while a decline in the proportion of PCV7-serotypes was observed. Non-vaccine serotypes 6C and 15A are becoming more common. Erythromycin is the antibiotic with the highest level of non-susceptibility, while some serotypes exhibit higher levels of antibiotic non-susceptibility than others. The emergence of non-vaccine serotypes remains an important issue and continued monitoring of serotype replacement in Europe is essential to assess changing trends and the effectiveness of interventions, and to inform the development of new vaccines.

For invasive *H. influenzae* (Hi) disease, 3 545 confirmed cases were reported in 2012 by 27 EU/EEA Member States, for an overall notification rate of 0.6 cases per 100 000. The highest notification rate was observed in non-capsulated strains among cases below one year of age. During 2008–12, the notification rate increased for non-capsulated strains, remained stable for non-b serotypes and decreased for Hib, especially below the age of five years. Due to the success of Hib vaccination programmes, Hib has substantially decreased in Europe and continues to do so, being a rare disease in the majority of Member States, with age-specific rates < 1 per 100 000 population in children younger than five years. At a European level, more robust surveillance data are needed for serotype replacement to be accurately assessed.

For invasive meningococcal disease (IMD), 3 463 confirmed cases were reported in 2012 by 27 EU/EEA Member States for an overall notification rate of 0.7 cases per 100 000. Serogroup B was predominant, especially in young children, with the rate 10 times that of of serogroup C infection. However, distribution of serogroups varied considerably between countries, partly depending on whether routine meningococcal serogroup C conjugate vaccination (MCC) had been introduced. Overall, a consistent decreasing trend was observed for serogroup B and C during 2008–12, while there was an increase in the notification rates of serogroup Y, affecting mainly infants and the elderly. Serogroup A has largely disappeared from Europe. However, sporadic cases continue to be reported. The availability of the serogroup B vaccine provides the potential to further reduce the incidence of this disease. Surveillance of this serogroup is essential before and after the introduction of this vaccination in any country. Additionally, enhanced surveillance of serogroup C must be maintained.

Surveillance systems undergo various changes over time that may have an impact on the data reported by individual countries or overall including: changes in case definitions, representativeness, data collection and validation as well as the implementation of laboratory methods and standards. Data heterogeneity across Member States may also be attributable to differences between disease surveillance systems, such as sensitivity or laboratory capacities and practices. The completeness of some variables, such as vaccination status, outcome, clinical presentation and antimicrobial resistance, needs to be improved. These limitations must be considered when interpreting the data presented in this report.

Key facts

Invasive pneumococcal disease (IPD)

- In 2012, 20 785 confirmed cases of IPD were reported by 27 EU/EEA countries. Germany, Liechtenstein and Portugal did not submit data on IPD.
- The notification rate across Europe was 5.22 cases per 100 000 population, ranging from 0.19 to 15.8. Nordic countries reported the highest country-specific rates.

- Infants (11.9 per 100 000) and the elderly (15.4 per 100 000) were most affected. A steady decline in notification rates for cases below five years of age was observed in Europe during 2008–12. There were higher rates for males in all age groups.
- Bacteraemia was the reported clinical presentation in 53% of cases, followed by bacteraemia associated with pneumonia (24%); data on clinical presentation were missing for 50% of cases.
- The overall case fatality rate (CFR) in EU/EEA countries was 11% (95% CI: 10%–12%). Age-specific CFRs were highest among meningitis cases and among cases above 65 years of age. Serotype 3 accounted for the highest number of deaths (n=83). CFR data should be interpreted with caution as data on outcome were missing for 70% of cases. Also, in Europe there is no common approach to the follow-up time or endpoint for a fatal outcome.
- 73 immunologically unique serotypes have been reported across European countries. The 10 most common serotypes in 2012 were, in ranking order, 3, 7F, 19A, 1, 22F, 8, 14, 12F, 6C and 15A.
- Between 2010–12, a proportional decrease in infections due to serotypes included in PCV7 was observed, the occurrence of serotypes 3 and 7F remained stable, and serotypes 6C, 8, 12F, 22F and 15A increased.
- Serotypes 6C and 15A are not covered by any licensed vaccine. Serotypes 7F, 19A and 1, the most prevalent serotypes in children under 15 years, are included in PCV13. Serotypes 3, 8 and 22F occurred mainly in older age groups. They are all included in PPV23, and serotype 3 is also included in PCV13.
- In theory, vaccinating with PCV13 could potentially have prevented about 50% of cases occurring in all age groups. Vaccinating with PCV7 can prevent < 15% of cases. These results support the decision to shift to a vaccine with higher valence.
- Resistance against erythromycin was the most prevalent, followed by penicillin. Serotype 19A represented the greatest proportion of resistant isolates, followed by serotype 14. Compared with 2011, multidrug-resistant strains increased.
- Results in this report corroborate the sustained reduction in vaccine-type IPD partially offset by the increase of non-vaccine type disease. Results should be interpreted with caution, however, since surveillance systems changed over time, which may have biased the observed trends.
- The completeness of some variables needs to be improved, and data should be as homogeneous across countries as possible to enable comparisons and properly assess the impact of different public health strategies.
- The emergence of non-vaccine serotypes and the prevalence of antimicrobial-resistant strains remain an important issue. Continued monitoring in Europe is essential for assessing interventions and informing the development of new vaccines.

Invasive *Haemophilus influenzae* disease

- In 2012, 2 545 confirmed cases of invasive *H. influenzae* (Hi) disease were reported by 26 EU Member States and one EEA country. Liechtenstein, Luxembourg and Iceland did not submit data on Hi.
- The overall notification rate was 0.57, ranging from 0.04 to 2.26 cases per 100 000. Countries in the north-west of Europe reported the highest rates.
- Septicaemia was the most common clinical presentation across most age groups, except for those between one and four years of age in whom meningitis was the most common presentation (missing information for 60% of cases).
- Only 53% (n=1 352) of confirmed cases had serotype information. Overall, non-capsulated strains made up 77% of cases.
- Serotype b was isolated from 108 confirmed invasive Hi cases, mainly in children and adolescents. Hib was responsible for about 20% of all meningitis cases. The greatest decline during 2008–12 was observed in children younger than 1 year of age. A significantly declining trend was also observed in adults. The notification rate of Hib in children under 5 years of age dropped by almost 50% between 2008 and 2012.
- Capsulated non-b serotypes were responsible for 206 confirmed cases in 2012, and Hif (62%) was the serotype most commonly isolated. Notification rates were highest among cases under one year of age. During 2008–12, trends were stable in all age groups, except in children younger than one year, in whom notification rates decreased significantly.
- Non-capsulated strains were reported in more than 50% of cases for all age groups and had the highest CFR (12%). Notification rates were highest among cases below one year of age. During 2008–12, there was

an upward trend in non-capsulated strains; age-specific trends were fluctuating with a slight but significant increase in cases between 15 and 44 years of age.

- Despite the overwhelming success of Hib vaccination programmes, invasive Hi disease still remains a public health problem, affecting mainly infants and children.
- Increased incidence of non-capsulated strain infection has been observed in Europe; however this may be partly explained by the extension of enhanced surveillance and an increased awareness.
- More robust surveillance data are needed, particularly with regard to serotype, clinical presentation, outcome and vaccination status data of confirmed cases to better assess changes in the epidemiology of the disease.

Invasive meningococcal disease (IMD)

- For 2012, 3 463 confirmed cases of IMD were reported by 27 EU Member States and one EEA country. Liechtenstein and Iceland did not submit data on IMD.
- The notification rate across Europe was 0.68 cases per 100 000 population, ranging from 0.11 to 1.76. IMD appears to be rare in the majority of Member States.
- As in previous years, children under one year of age were most affected (11.4 cases per 100 000), followed by children between one and four years of age (3.7 per 100 000). In both age groups, rates decreased between 2008 and 2012. A small peak in notification rates was also observed in young adults between 15 and 24 years of age.
- Meningitis was the clinical presentation in 43% of cases. No relationship was observed between clinical presentation and serogroup.
- The overall CFR in EU/EEA countries was 7.9% and was highest in cases 65 years or older (14%). The CFRs for serogroups B and C were 7% and 14%, respectively.
- Serogroup B was responsible for 68% of confirmed cases. The highest age-specific notification rate was reported for children younger than one year. The decline in rates observed during 2008–12 in this age group was driven by dwindling case numbers in the United Kingdom.
- Serogroup C accounted for 17% of cases in 2012. Notification rates were highest in children under five years of age, but were 10-fold lower than in cases of serogroup B infection in the same age groups.
- Countries without meningococcal C conjugate vaccination reported higher serogroup C IMD rates than countries with MCC vaccination across all age groups. This difference was most pronounced in cases between one and four years of age.
- During the period 2008–12, a slight decrease in serogroup C rates was observed in countries with MCC. In countries without MCC vaccination, the serogroup C rate remained stable.
- Notification rates of serogroup Y increased between 2008 and 2012. In 2012, the highest notification rates were observed in cases under one year of age (0.16 per 100 000), 65 years or older (0.11), and between 15 and 24 years (0.10). A significant increasing trend was observed in cases older than 15 years.
- Improvements in case ascertainment, data reporting and molecular typing may have led to better characterisation of serogroup Y isolates in Europe.
- A large majority of isolates tested in 2012 were susceptible to the antibiotics currently used for treatment and prophylaxis (ciprofloxacin, rifampicin, penicillin G and cefotaxime/ceftriaxone).
- In 2012, the bacterial population was highly diverse; however three main clones seem responsible for severe IMD in Europe: ST-32 was the most frequent, followed by ST-11 and ST-41/44.
- Serogroup B was mostly associated with CC ST-41/44, ST-32 and ST-269. Clone CC ST-11 was mostly associated with serogroup C cases, and 86% of serogroup Y cases were due to ST-23 strains.
- The highest variability in PorA genotypes was associated with isolates of serogroup B, and the lowest with serogroup W.
- There was a high proportion of missing data for some variables including vaccination status, clinical presentation, antimicrobial resistance and molecular characterisation. Results based on any of these variables must be interpreted with caution. Differences between surveillance systems should be considered for all variables.

Background

The European Centre for Disease Prevention and Control (ECDC), an EU agency based in Stockholm, Sweden, was established in 2005 to strengthen Europe's defences against infectious diseases. According to Article 3 of its founding regulation[1], ECDC's mission is to identify, assess and communicate current and emerging threats to human health posed by infectious diseases. ECDC works in partnership with national public health bodies across Europe to strengthen and develop EU-wide disease surveillance and early warning systems.

The surveillance of invasive pneumococcal disease (IPD), invasive *H. influenzae* disease and invasive meningococcal disease (IMD) is important to estimate disease incidence and monitor disease trends and changes in serogroup/serotype and genotype distribution in order to guide policymakers in the definition of national immunisation schedules. The pooling of European data increases the precision of estimates for diseases in which the number of reported cases is steadily decreasing.

From 1999 to 2007, the European Union Invasive Bacterial Infections Surveillance Network (EU-IBIS) carried out surveillance of invasive bacterial diseases caused by *Neisseria meningitidis* and *H. influenzae*. The surveillance of IPD was not included at the time. In October 2007, coordination of the EU-IBIS surveillance activities was transferred to ECDC. After this transition, enhanced EU/EEA surveillance for IPD was identified as one of the top priorities by both Member State representatives and ECDC and was introduced in 2007.

Today, the surveillance of IBD relies on a range of networks operated through ECDC. Data on IBD are submitted to ECDC by operational contact points in Member States for the European Surveillance System (TESSy). Vaccination schedules in European countries can be found through the recently launched ECDC vaccine schedule query tool[2]. Data on antimicrobial resistance are collected and analysed by the European Antimicrobial Resistance Surveillance Network (EARS-Net). For *S. pneumoniae*, data on antimicrobial resistance are also collected through the IBD surveillance network.

This report describes and discusses data on IBD submitted by Member States to ECDC through TESSy for 2012.

Surveillance methods common to all IBD

Case definitions

For the 2012 data collection, data providers were requested to report cases of IBD applying the 2012 EU case definition[3] and specify in their data source description which case definition was actually used. Details on country-specific use of case definitions are provided in the disease chapters.

Laboratory diagnosis of IBD requires the bacterium to be isolated and cultured from a normally sterile body site, or for bacterial nucleic acid to be detected at a normally sterile body site. Diagnosis may also be performed by the detection of bacterial antigen from a sterile body site for IPD, and from the CSF for IMD. Sterile body sites include: cerebrospinal fluid (CSF), blood, joint fluid, synovial, pleural effusion, pericardial effusion, peritoneal fluid, subcutaneous tissue fluid, placenta, amniotic fluid or petechial skin.

Data submission and validation

This report includes confirmed cases of IPD, invasive *H. influenzae* disease and IMD reported by the national public health institutes and ministries of health in the EU/EEA countries for 2012 and uploaded to TESSy up to 23 January 2014. The system accepts aggregate data, although case-based reporting is favoured by ECDC.

In addition to data submission, countries were asked to provide a description of their national surveillance systems to help interpret their data. Tables containing this information are included in the report (see Annex 1 – Table A1, Annex 2 – Table B1, Annex 3 – Table C1). A description of national surveillance systems is provided for all three types of bacteria.

[1] Regulation (EC) No 851/2004 of the European Parliament and of the Council of 21 April 2004 establishing a European Centre for Disease Prevention and Control. OJ L 142, 30.4.2004, pp. 1–11.

[2] Available from: http://vaccine-schedule.ecdc.europa.eu/Pages/Scheduler.aspx

[3] See Commission Implementing Decision 2012/506/EU of 8 August 2012 amending Decision 2002/253/EC laying down case definitions for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and of the Council: Available from: http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:262:0046:0090:EN:PDF

The competent bodies[4] in the Member States have designated national operational contact points for IBD surveillance who work together with ECDC on the reporting of IBD data to TESSy. These contact points were requested to submit data to TESSy and include the latest metadataset agreed by the Member States. The IBD dataset consists of a core group of variables common to all diseases and an enhanced dataset specific for each disease.

Twenty-seven EU/EEA Member States submitted data on IPD and invasive *H. influenzae* disease, and 28 Member States provided data on IMD. Liechtenstein did not submit data for any of the three diseases. Iceland only submitted data on IPD. Portugal and Germany did not submit data for IPD. Luxembourg did not submit data for invasive Hi disease. Since this report refers to 2012, it only includes data from countries which were EU/EEA Member States by 2012. Croatian data were therefore not included.

The data cleaning and validation process included automatic and manual checks aiming to identify and remove any obvious mistakes or inconsistency in the data. Validation rules were based on the 2012 EU case definition. The draft report was shared with all Member States for comments and confirmation of national figures.

Data analysis

Data are presented with the 'date used for statistics' as the preferred date. This is the date the country chooses as its preferred date for reporting and could be date of disease onset, date of diagnosis, date of notification, or any other date the country may use nationally.

Distributions were expressed as absolute and relative frequencies. We analysed the categorical variables using Pearson's chi-squared test or Fisher's exact test, as appropriate.

Annual notification rates were calculated by using numbers of confirmed cases as the numerator and the population on 1 January of 2013 as the denominator. If the surveillance system was comprehensive, population data were obtained from Eurostat (http://epp.eurostat.ec.europa.eu). If data were reported through a sentinel surveillance system, notification rates were calculated only if relevant subpopulation figures or their extrapolation to national coverage were provided by the country. Otherwise, cases of those countries were not included in the calculation of pooled EU/EEA notification rates. Similarly, populations of countries not reporting were excluded, whereas populations of countries reporting 0 cases were included.

Notification rates over time (trends) were considered for the period 2008–12. Poisson regression with a log-linear model was used to test for trend variations over time. When needed, negative binomial models were used as an extension of Poisson models to correct for overdispersion of data. Only countries reporting consistently over several years were included and listed in the corresponding figures and tables. Populations of countries not reporting were excluded.

To estimate case fatality rates (CFR), only countries reporting outcome for at least one case were included. Only cases with known outcome were considered. CFR was calculated as the number of deaths divided by the number of cases with known outcome. Acknowledging the differences in IBD surveillance systems and reporting across Europe, CFR and relative confidence intervals (95% CI) were also calculated for each country. Serotype-specific CFR was calculated following the same rule. Consequently, only cases with known outcomes and serotype were considered.

For clinical presentation, cases reported as 'not under surveillance' were excluded. Unless presented, all other 'unknown' and 'missing' responses were excluded from analysis. The vaccination status 'fully vaccinated' and 'partly vaccinated' were defined by the reporting country according to its immunisation schedule.

All analyses were performed with STATA 13.0 and Microsoft Excel 2010.

[4] The ECDC founding regulation states that in its relations with the Member States, ECDC shall cooperate with the competent bodies operating in its technical field, particularly in the area of surveillance [Regulation (EC) No 851/2004 of the European Parliament and of the Council, Art. 3, Par. 2]. Available from: http://ecdc.europa.eu/en/aboutus/Key%20Documents/0404_KD_Regulation_establishing_ECDC.pdf

1 Invasive pneumococcal disease

1.1 Summary

Serotypes covered by licensed PCV vaccine

- PCV7 protects against serotypes 4, 6B, 9V, 14, 18C, 19F and 23F
- PCV10 protects against serotypes 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5 and 7F
- PCV13 protects against serotypes 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F, 3, 6A and 19A

Invasive pneumococcal disease (IPD) is an acute and life-threatening disease caused by *Streptococcus pneumoniae*, a common commensal of the upper respiratory tract that can cause local and invasive infection. The pneumococcal vaccines that are currently available in Europe are a 23-valent polysaccharide vaccine for adults (PPV23) and three conjugate vaccines (PCVs), covering 7, 10 and 13 serotypes, respectively (PCV7, PCV10, PCV13). Pneumococcal conjugate vaccines are available in 29 EU/EEA countries and are part of routine vaccination in 23 countries (VENICE II[5,6]).

In 2012, 20 785 confirmed cases of IPD were reported by 27 EU/EEA countries, giving a notification rate of 5.2 cases per 100 000 population (ranging from 0.2 to 15.8). The Nordic countries reported the highest country-specific rates, although their rates were lower than in 2010. Slovakia and Slovenia reported the highest proportion of cases between one and four years of age (16.3%). In Slovenia, PCV is not routinely administered.

As in previous years, there was a clear seasonal distribution of cases with a noticeable rise during the winter months. Infants (11.9 per 100 000) and the elderly (15.4 per 100 000) were affected the most. Among confirmed IPD cases for which age information was provided, 49% (n=10 186) were 65 years or older and 39% (n=8 049) were 25 to 64 years old. During 2008–12, a steadily decreasing trend in notification rate was observed for cases below five years of age, while trends remained stable across all other age groups. Notification rates among males were higher than among females in all age groups, with clear predominance in children younger than one year and patients 65 years and older.

Bacteraemia was reported in 53% of cases, followed by bacteraemia associated with pneumonia (24%), although data on clinical presentation were missing for 50% of cases and could be biased by the type of surveillance system in place (for example, not all the countries use the clinical presentation of bacteraemia associated with pneumonia). The overall CFR in EU/EEA countries was 11% (95% CI: 10%–12%). Age-specific CFR were highest among meningitis cases and cases 65 years or older. Serotype 9N was associated with the highest serotype-specific CFR (23%) followed by serotype 11A (21%). Data on CFR should be interpreted with caution, however, since outcome was missing for 70% of cases, and there is no common approach to the follow-up time or endpoint for a fatal outcome across European countries.

Vaccination status was reported for 18% of all confirmed IPD cases: 90% of them were unvaccinated and 2% were fully vaccinated. The vaccine type administered was known for about 40% of vaccinated cases (n=153) and reported by 6 countries.

In 2012, 73 different serotypes were reported, the 10 most common ones being, in ranking order: 3, 7F, 19A, 1, 22F, 8, 14, 12F, 6C and 15A. Twenty-five serotypes accounted for 90% of all the isolates typed, and the ten most frequently reported were responsible for 63% of confirmed cases with serotype information.

Serotypes 3, 7F, 19A and 1 have been the four most common causative agents of IPD since 2010, although they are partly included in PCV10 and fully covered by PCV13. Overall, a decline in the proportion of serotypes included in PCV7 has been observed since 2010. Serotypes 8, 12F and 22F are not covered by any of the PCV vaccines and their occurrence has been increasing, although they are included in PPV23. Serotypes 6C and 15A are currently not covered by any licensed vaccine, but there is evidence that PCV13 vaccination can potentially confer cross-protection against serotype 6C [19]. Among PCV7-serotypes, only serotype 14 still occurs in the ten most common serotypes in 2012, while unlike 2010, serotypes 4, 19F and 23F are no longer among the ten most common reported.

Serotypes 19A, 7F and 1 were most frequently reported in children younger than five years. Serotype 1 was also predominant in the 5–14 year-old age group (37%). All of these serotypes are covered by PCV13, but not by PCV7. Serotypes 8 and 22F occurred mainly in cases who were 15 years or older, serotype 7F in cases between 15 and 44 years, and serotype 3 in cases 45 years or older. Both serotypes affecting older age groups (7F and 3) are

[5] http://venice.cineca.org/VENICE_Survey_PNC_1_2012-02-24.pdf

[6] http://vaccine-schedule.ecdc.europa.eu/Pages/Scheduler.aspx

included in PPV23 and PCV13. In 2012, overall, about 50% of cases were caused by a PCV13 serotype and < 15% by a PCV7 serotype.

IPD surveillance systems in EU/EEA reporting countries, 2012

- 27 countries reported IPD cases at EU level in 2012.
- 27 reported data from a single source.
- 26 reported case-based data.
- 22 countries had a passive surveillance system.
- 19 had a compulsory and comprehensive surveillance system in place.
- 4 countries had a sentinel surveillance system.
- 16 countries applied the EU 2008 case definition.
- 18 countries submitted data reported by laboratories as well as physicians and/or hospitals
- 6 countries had a laboratory-based surveillance system
- 3 submitted data reported only by physicians and/or hospitals

The emergence of non-vaccine serotypes remains an important issue. Currently, the majority of IPD infections in Europe are caused by PCV13 serotypes. However, as observed with PCV7, the effectiveness of PCV13 may decrease over time, as new pneumococcal serotypes emerge. The completeness of some variables, such as clinical presentation, outcome, vaccination status, and antimicrobial resistance needs to be improved, so results must be interpreted with caution. Continued monitoring of serotype replacement in Europe is essential to assess changing trends and the effectiveness of interventions and to inform the development of new vaccines.

1.2 Introduction

Invasive pneumococcal disease (IPD) is an acute and life-threatening disease caused by *Streptococcus pneumoniae*, a common commensal of the upper respiratory tract that can cause local and invasive infection. Invasive disease encompasses severe syndromes including meningitis, pneumonia/empyema and bacteraemia and may result in serious sequelae including permanent impairment. Children are at major risk as are immunocompromised patients and the elderly. WHO estimates that 1.6 million people, including one million children younger than five years, die of IPD annually [1].

Based on immunological properties of the capsule, pneumococci are divided into 46 serogroups, 26 of which have only one serotype and 20 are further divided into two to four serotypes. Ninety-four immunologically unique serotypes have so far been described, with 20 to 30 being responsible for the majority of IPD worldwide [2].

Pneumococcal disease can be prevented by vaccination. A 23-valent pneumococcal polysaccharide vaccine (PPV23) for adults based on the main serotypes causing IPD was licensed in 1983. This vaccine is effective at preventing IPD in adults, but its effectiveness wanes over time [10]. Moreover, many of the 23 serotypes included in the vaccine are poorly immunogenic in infants and children under two years of age, the age group with the highest incidence of IPD [10].

The first pneumococcal vaccine for infants and young children licensed in Europe in 2001 was a 7-valent pneumococcal conjugate vaccine (PCV7), offering protection against serotypes 4, 6B, 9V, 14, 18C, 19F and 23F. The introduction of the vaccine markedly decreased the incidence of IPD caused by vaccine serotypes [3, 4]. Moreover, the vaccination of infants has resulted in herd immunity by reducing nasopharyngeal carriage and transmission of the bacterium, contributing to a decrease in pneumococcal morbidity and mortality among the older age groups [5, 6]. However, the emergence of complicated pneumococcal pneumonia caused by non-PCV7 serotypes has gradually reduced the effectiveness of PCV7 [7].

Serotype replacement implied that a new generation of vaccines was needed to prevent IPD. A 10-valent conjugate vaccine (PCV10), licensed in 2009, included the seven serotypes of PCV7 plus serotypes 1, 5 and 7F, which are known for their propensity to cause IPD [67]. A 13-valent conjugate vaccine (PCV13) was licensed in 2010, adding serotypes 3, 6A, and 19A to the PCV10 serotypes. PCV7 has not been distributed since the introduction of PCV13. Infections due to serotype 3 are increasingly being reported, especially in association with severe pneumonia [35]. Serotypes 6A and 19A have long been important causes of IPD, and 19A in particular has become more prevalent and resistant to antibiotics over the past 10 years [25–26]. Continued serotype replacement remains an important challenge in the development of future vaccines [8].

Community-acquired respiratory infections in general, and those caused by *S. pneumoniae* in particular, are the main indications for prescribing antimicrobial agents in young children. Antimicrobial use and abuse is, in turn, one of the main reasons for the emergence of antimicrobial resistance in respiratory pathogens. Individuals that carry and hence potentially transmit resistant pneumococci are also at higher risk of developing IPD caused by resistant strains [9].

1.3 Data sources and case definitions

For 2012, 25 EU Member States and two EEA countries notified cases of IPD to TESSy. Germany, Liechtenstein and Portugal did not report.

According to the data provided, all countries reported data from a single source. Nineteen countries had a compulsory and comprehensive surveillance system in place. Italy had a voluntary comprehensive surveillance system, and four countries (Belgium, Cyprus, France and the Netherlands) had a voluntary sentinel surveillance system. Hungary had a voluntary but comprehensive system, and in Spain the system was voluntary and representative, with a national coverage of 80%. There was no single surveillance system in the United Kingdom, with data submitted separately by England and Wales, Scotland and Northern Ireland. Data from the United Kingdom were reported through one data source to TESSy, although surveillance methodologies in these three systems may differ (Annex 1, Table A1).

Among countries with a sentinel system in place, France reported the size of the population covered by the system. In the Netherlands, the surveillance system calculated national coverage, while in Belgium and Cyprus the extent of the national coverage was unknown.

Most countries reported having a passive surveillance system in place for IPD, but only five countries (Belgium, Cyprus, the Czech Republic, France and Slovakia) described their system as active.

Data on IPD were reported by laboratories as well as physicians and/or hospitals in 18 countries. In six countries (Cyprus, Belgium, Denmark, Finland, Hungary and the Netherlands) data were only reported by laboratories, and in three countries (Italy, Luxembourg and Romania) only physicians and/or hospitals reported. Case-based data were submitted by all countries except for Bulgaria. Greece had a surveillance system with national coverage for meningitis only.

Case definitions differed between countries, with the majority (n=16) applying the 2008 EU case definition. Luxembourg still uses the 2002 EU case definition, and five countries (Latvia, Italy, Slovakia, Sweden and the United Kingdom) had moved to the 2012 EU case definition. The remaining five countries did not report which case definition they had applied.

A key difference between the 2002 and 2008 versions of the EU case definition is that the latter no longer contains clinical criteria and only defines confirmed cases based on laboratory criteria. The 2012 EU case definition is the same as in 2008.

In 2012, all countries reported data from a single source. During 2008–12, nine countries reported data through multiple data sources. There was no overlapping in Denmark, Greece, Hungary, Ireland and Spain. In Spain, the two systems have different national coverage. Population coverage was provided for both data sources. In the majority of countries this change occurred between 2009 and 2010. There was overlap in reporting data sources in Cyprus and the Czech Republic for 2010, in France for 2010–11, and in the Netherlands for 2009–11. In Latvia, the surveillance system did no change, but notification of IPD cases became mandatory in 2010.

1.4 Methods

This report describes invasive disease due to *S. pneumoniae* through epidemiological and laboratory variables. Only laboratory-confirmed cases of IPD reported by Member States were considered for inclusion in the analysis, independently of the case definition applied by countries for reporting at national level. Any person meeting the laboratory criteria of any version of the EU case definition was considered a confirmed case of IPD. Data were analysed according to the methods and rules previously described in this report (chapter 'IBD data submission, validation and analysis', page 6).

Aggregated data, reported only by Bulgaria, were included where possible. For Belgium and Cyprus, notification rates could not be calculated, since the population covered by their sentinel surveillance systems was unknown.

The trend analysis by age included the period from 2008 to 2012 and excluded the following countries:

- Belgium and Cyprus, since calculation of rates was not possible;
- Bulgaria because of aggregate reporting;
- Latvia and Lithuania because of aggregate reporting in 2008–09;
- Poland because of aggregate reporting in 2008;
- Malta and Romania, as they only started reporting in 2009; and
- France, Iceland and Luxembourg, as they only started reporting in 2010.

Member States were asked to provide results of antimicrobial susceptibility testing (AST), i.e. the minimum inhibitory concentration (MIC) values and the final interpretation based on one or more test results. The final interpretation was expressed as susceptible (S), intermediate (I) or resistant (R) in accordance with protocols and clinical breakpoints used for antimicrobial susceptibility testing at national level. However, some countries

submitted data on MIC but did not provide any interpretation, and conversely, other countries only reported the final interpretation, but no MIC values.

It was recommended that all European reference laboratories switch to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines for interpretation of results on antimicrobial resistance in *S. pneumoniae*. However, at present, some countries or laboratories use the EUCAST criteria, others use the Clinical and Laboratory Standards Institute (CLSI) guidelines and some are following their own national guidelines. There are major differences between the EUCAST and CLSI guidelines for *S. pneumoniae*, both in terms of media and defined breakpoints for a number of antimicrobials, and this is especially true for the beta-lactam antimicrobials (Table 1.8). Therefore, and because information on national standards and methods for antimicrobial susceptibility testing was lacking, MIC results and their final interpretation (SIR) were described separately. Data on interpretation of antimicrobial susceptibility are presented by country. As a general rule, data are expressed as a percentage, i.e. the percentage of R isolates out of all isolates with AST information, and an isolate is considered non-susceptible to an antimicrobial agent when tested and found resistant (R) or with intermediate susceptibility (I). MIC data are presented in a standard format by serial dilutions to be interpreted according to the standards used at national level. If the MIC value was associated with a '> ' or '≥ ' symbol, the record was allocated to the closest higher dilution. Multidrug resistance is defined as resistance to penicillin, erythromycin and cefotaxime/ceftriaxone.

In this report, EUCAST clinical breakpoints[7] were used as reference for interpreting MIC results (Table 8). Following these guidelines, we calculated the overall proportion of isolates non-susceptible to penicillin using different breakpoints for meningitis and non-meningitis IPD cases.

1.4.1 Data sources

Countries with sentinel surveillance of IPD included Belgium, Cyprus, France and the Netherlands.

- For Belgium and Cyprus, the population coverage was unknown, so data were excluded from the notification rates analysis.
- For France, the population coverage was provided (Annex 1, Table A2) and was used as denominator for the analysis of notification rates.
- The Netherlands reported the population coverage of their data source to be 25% of the total population in 2012, which was applied to the analysis of notification rates.

Due to the potential overlap of data sources or changes in the surveillance system, the following choices were made:

- Cyprus reported from two different data sources in 2010, when the surveillance system changed to the current sentinel system (CY-LABNET). Only IPD cases reported through 'CY-LABNET' were included in this report, as in previous reports.
- The Czech Republic reported from two data sources in 2010, when the surveillance system changed to the current system (CZ-NRL-STR). In this report only data from 'CZ-NRL-STR' were included, as in previous reports
- France reported data on IPD from two sources in 2010–11: 'FR-EPIBAC' data were used for the general variables (e.g. age, gender, notification rates), whereas data from 'FR-PNEUMO-NRL' were taken into account for the analysis of laboratory variables (e.g. laboratory methodology and serotype). In 2012, only FR-EPIBAC data were used for reporting.
- The Netherlands reported from two data sources for 2009–11. After consultation with national representatives, the data source 'NL-NRBM' was included in this report, while data from 'NL-OSIRIS' were excluded as the data were not complete. In 2012, only 'NL-NRBM' was used for reporting.
- In Spain, two different data sources were used for reporting IPD cases during 2008–12. There was no overlapping in reporting, but the systems have different coverage. In 2008–09, 'ES-MICROBIOLOGICAL', (33% national coverage) was used; in 2010–12, 'ES-NRL' data were used (80% national coverage).

Notification rates for France, the Netherlands and Spain should be interpreted with caution.

[7] http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/Breakpoint_table_v_3.1.xls

1.5 Results

1.5.1 Number of cases

For 2012, 20 785 confirmed cases of IPD were reported to TESSy by 27 EU/EEA countries. The overall notification rate was 5.22 cases per 100 000, ranging from 0.19 (Luxembourg) to 15.8 (Denmark). Nordic countries (Denmark, Finland, Norway and Sweden) presented the highest notification rates, although their rates were lower than in 2010. A high notification rate (15.18) was also observed through sentinel surveillance in the Netherlands, where the system covers 25% of the population. Fourteen countries presented notification rates lower than four cases per 100 000 population. From 2008–12, the overall trend in the EU has remained relatively stable. Increasing trends were observed in the Czech Republic, Hungary, Latvia and Poland; decreasing trends were reported by Finland, Greece, Lithuania, Norway, Spain and Sweden (Table 1.1).

Table 1.1. Number of confirmed IPD cases and notification rates per 100 000 population in EU/EEA countries, 2008–12

Country	2008		2009		2010		2011		2012	
	N	NR	N	NR	N	NR	N	NR	N	NR
Austria	133	1.60	296	3.54	325	3.88	158	1.88	235	2.79
Belgium^	1875	-	2051	-	1851	-	1836	-	1738	-
Bulgaria*	35	0.47	46	0.62	26	0.35	37	0.50	19	0.26
Cyprus^	21	-	9	-	11	-	12	-	10	-
Czech Republic	117	1.13	143	1.37	300	2.87	384	3.66	335	3.19
Denmark	120	2.19	129	2.34	960	17.34	924	16.62	882	15.80
Estonia	32	2.39	14	1.05	14	1.05	18	1.35	20	1.50
Finland	925	17.45	855	16.05	836	15.62	779	14.49	752	13.92
France#	-		-		5117	10.76	5037	10.62	4430	9.20
Greece	63	0.56	66	0.59	38	0.34	41	0.37	43	0.39
Hungary	65	0.66	49	0.50	108	1.10	107	1.09	186	1.88
Ireland	401	9.11	357	8.02	304	6.80	357	7.81	350	7.64
Italy	694	1.16	738	1.23	854	1.42	713	1.18	787	1.29
Latvia	7	0.32	7	0.32	16	0.75	51	2.46	56	2.74
Lithuania	18	0.56	16	0.50	9	0.29	9	0.29	7	0.23
Luxembourg	0	0.00	0	0.00	2	0.40	2	0.39	1	0.19
Malta	0	0.00	9	2.19	11	2.66	11	2.65	15	3.59
Netherlands#	609	14.85	605	14.68	571	13.78	622	14.94	635	15.18
Poland	212	0.56	274	0.72	333	0.87	351	0.91	402	1.04
Romania	0	0.00	122	0.60	80	0.40	90	0.45	79	0.39
Slovakia	36	0.67	29	0.54	18	0.33	57	1.06	49	0.91
Slovenia	204	10.15	253	12.45	224	10.94	255	12.44	245	11.92
Spain##	1648	10.94	1339	8.78	2212	5.95	2220	5.95	2260	6.04
Sweden	1789	19.48	1618	17.48	1456	15.59	1361	14.45	1387	14.63
United Kingdom~	5514	9.02	5019	8.15	5616	9.05	4632	7.40	5209	8.27
EU total**	14518	4.43	14044	4.19	21292	5.45	20064	5.10	20132	5.12
Iceland	-		-		32	10.07	33	10.36	27	8.45
Norway	855	18.05	799	16.65	748	15.40	729	14.82	626	12.56
EU/EEA total**	15373	4.65	14843	4.39	22072	5.59	20826	5.23	20785	5.22

^ Sentinel surveillance with unknown population coverage, so notification rate not calculated

** Aggregate reporting*

 # Sentinel surveillance, population coverage known

Sentinel surveillance in 2008–09. Voluntary surveillance system in 2010–12. Known population coverage, but systems have different coverage.

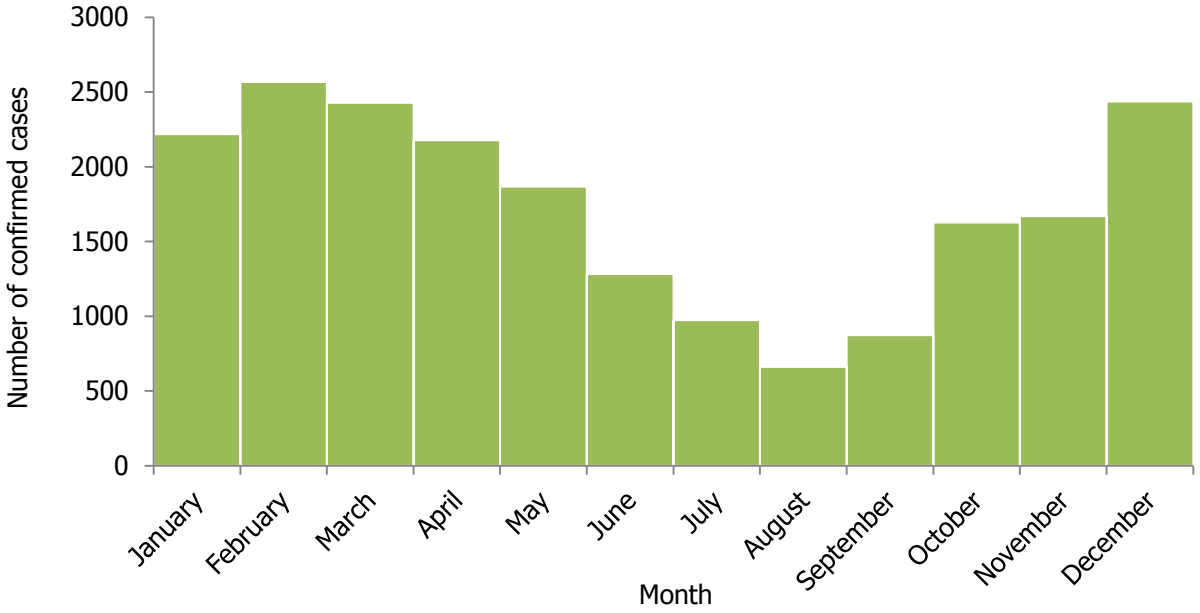
~ No single surveillance system in the UK. Data are representative (as submitted by England, Wales, Scotland and Northern Ireland), but surveillance systems use different approaches.

*** Notification rates were calculated excluding cases and populations of countries with unknown population coverage and populations non-reporting countries. Populations of countries reporting 0 cases were included.*

1.5.2 Seasonality

The seasonal distribution of IPD cases followed a pattern similar to other respiratory diseases. In 2012, the highest number of cases was observed during the winter months, peaking in February and decreasing in summer, as in previous years (Figure 1.1). Seasonality by country is presented in Annex 1, Table A3.

Figure 1.1. Distribution of confirmed IPD cases by calendar month, EU/EEA countries, 2012 (n=20 778)



1.5.3 Age and gender

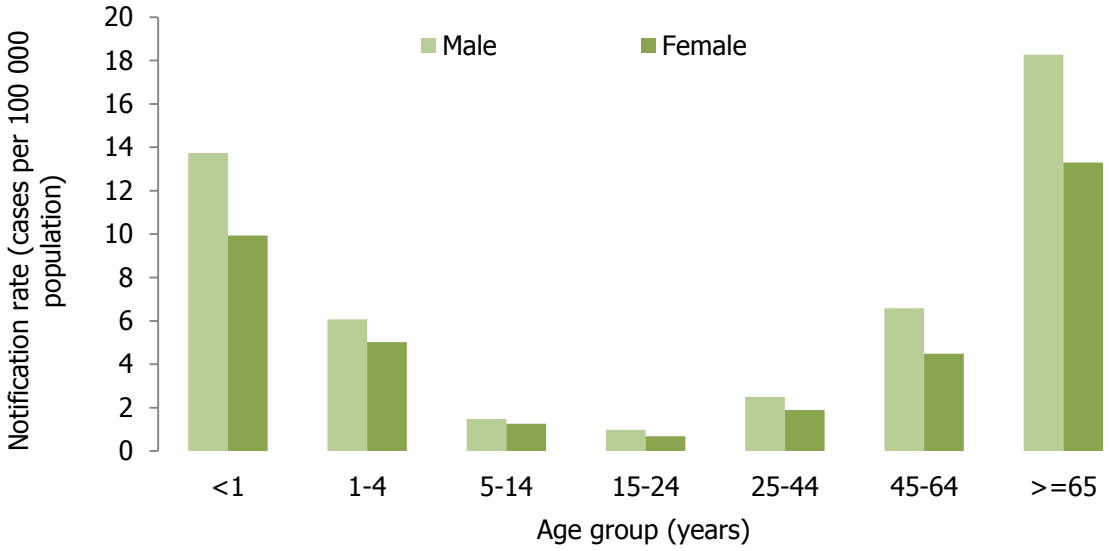
Of the 20 694 confirmed IPD cases for which age information was provided (excluding aggregated data), 49% (n=10 186) were 65 years or older and 39% (n=8 049) were 25 to 64 years of age. Only 2% of cases were young adults between 15 and 24 years of age. Children under 14 years of age accounted for 10% (n= 2 094), with the majority between one and four years of age (Annex 1, Table A4). The highest notification rates of IPD were seen in cases 65 years and older (15.4 per 100 000) and in children under one year of age (11.9 per 100 000) (Figure 1.2).

Most countries reported a low proportion of cases in children (0–14 years) and higher proportions in adolescents and adults. Younger age groups accounted for more than 20% of cases in six countries (Cyprus, Lithuania, Poland, Romania, Slovakia and Slovenia). Among countries reporting age for more than 20 confirmed IPD cases, Romania had the highest proportion of cases under one year (10%) and between 5 and 14 years (10%). Slovenia and Slovakia reported the highest proportion of cases between one and four years of age (16.3%) (Annex 1, Table A4).

Of the 20 707 reported cases with gender information, 54% (n=11 219) were male and 46% (n=9 488) were female, corresponding to a male–female ratio of 1.2. There were slightly higher rates for males in all age groups, but male overrepresentation was especially evident in children under one year and in adults 65 years or over (Figure 1.2).

Between 2008 and 2012, the notification rate of cases under one year of age and between one and four years steadily declined. Across all other age groups, the trend was stable (Figure 1.3, Annex 1, Table A5).

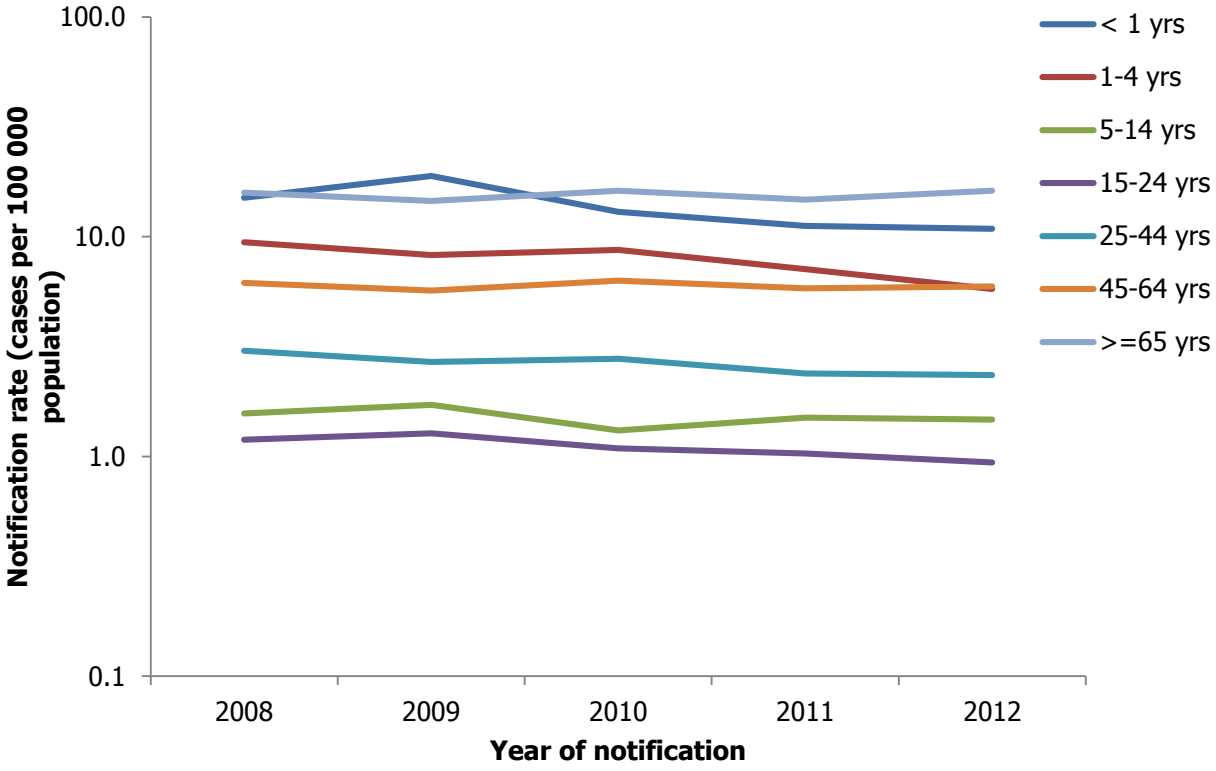
Figure 1.2. Notification rate of confirmed IPD cases by age group and gender, EU/EEA countries, 2012 (n=18 964*)



** Excludes data from Belgium and Cyprus, for which population coverage was unknown, and aggregated data where different age groups were reported.*

Contributing countries: Austria, 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 1.3. Notification rate of confirmed IPD cases by age group and year, EU/EEA countries, 2008–12 (n=67 203)



Contributing countries: Austria, the Czech Republic, Denmark, Estonia, Finland, Greece, Hungary, Ireland, Italy, the Netherlands, Norway, Slovakia, Slovenia, Spain, Sweden and the United Kingdom

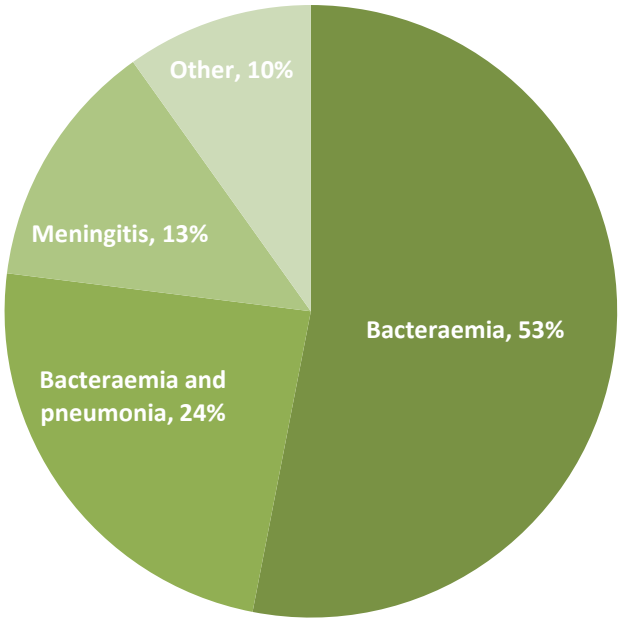
1.5.4 Clinical presentation

Information on clinical presentation was reported by 21 of 27 countries. Of the 10 383 cases for which clinical presentation was known (50% missing), bacteraemia was the most frequent clinical presentation, accounting for

53% of all cases, followed by bacteraemia and pneumonia, observed in 24% of confirmed cases (Figure 1.4). Spain and the United Kingdom contributed 67% of these data: the United Kingdom accounted for 69% of cases with bacteraemia and Spain for 55% of all cases with bacteraemia and pneumonia. Clinical presentation data from France were the least complete (9%), and meningitis was the only presentation reported. All confirmed IPD cases reported by Greece (n=43) and Luxembourg (n=1) were reported as having had meningitis (Annex 1, Table A6).

Bacteraemia was the most common clinical presentation across all age groups, with meningitis equally as common among children under one year of age. Among all cases of bacteraemia, those aged ≥ 45 accounted for 76%, while newborns, infants and toddlers up to 24 months of age accounted for 11%. Bacteraemia associated with pneumonia was the second most frequent clinical presentation for all age groups (Table 1.2).

Figure 1.4. Distribution of confirmed IPD cases by clinical presentation, 2012 (n=10 383)



Contributing countries: Austria, Belgium, Cyprus, the Czech Republic, Estonia, France, Greece, Hungary, Iceland, Ireland, Latvia, Lithuania, Luxembourg, Malta, Norway, Poland, Romania, Slovakia, Slovenia, Spain and the United Kingdom.

Table 1.2. Distribution of reported IPD cases by clinical presentation and age group, EU/EEA countries, 2012 (n=10 335)

Age group (years)	Bacteraemia		Meningitis		Bacteraemia and pneumonia		Other		Total
	N	%	N	%	N	%	N	%	N
< 1	114	37%	115	37%	53	17%	28	9%	310
1–4	263	42%	82	13%	175	28%	106	17%	626
5–14	133	38%	68	19%	89	26%	59	17%	349
15–24	106	50%	31	15%	53	25%	23	11%	213
25–44	705	52%	223	17%	301	22%	115	9%	1 344
45–64	1 505	53%	428	15%	625	22%	296	10%	2 854
≥ 65	2 667	57%	412	9%	1 169	25%	391	8%	4 639
Total	**5 493**	**53%**	**1 359**	**13%**	**2 465**	**24%**	**1 018**	**10%**	**10 335**

Contributing countries: Austria, Belgium, Cyprus, Czech Republic, Estonia, France, Greece, Hungary, Iceland, Ireland, Latvia, Lithuania, Luxembourg, Malta, Norway, Poland, Romania, Slovakia, Slovenia, Spain and United Kingdom.

1.5.5 Case fatality rate

In 2012, 21 countries reported data on outcome for 6 328 confirmed IPD cases, but the completeness for this variable differed widely from country to country. The overall CFR was 11% (95% CI: 10%–12%). Cyprus, Lithuania and Luxembourg reported no deaths, but provided information on outcome for less than 10 confirmed cases (Annex 1, Table A7). Among countries reporting outcome for more than 20 IPD cases (n=15), the highest case fatality was observed in Hungary (CFR: 29%; 95% CI: 16%–44%) and the lowest in Ireland (CFR: 4%; 95% CI: 1%–8%) (Annex 1, Table A7). Age-specific CFR was highest among cases 65 years and over (15%) (Annex 1, Table A8) and among cases with meningitis (19%) (Annex 1, Table A9).

1.5.6 Vaccination status

Vaccination status was reported by only 17 countries for 18% of all confirmed IPD cases. Of the 3 750 cases for which vaccination status was reported, 90% (n=3 374) were unvaccinated. The vaccine type administered was reported by six countries, accounting for 4% of cases (n=153). Among these cases, 44% (n=68) had received at least one dose of PPV23. Forty-two cases (27%) were vaccinated with PCV7, 32 of which had received three doses of the vaccine and one had received four doses. Only two cases that had been vaccinated with three or four doses of PCV7 became infected with a PCV7-preventable serotype. Two cases had received three doses of PCV10. Forty-one cases (27%) had received at least one dose of PCV13, with 19 receiving three doses and two cases receiving four doses. Only three cases that had been vaccinated with three or four doses of PCV13 became infected with a PCV7-preventable serotype.

1.5.7 Serotypes

Of the 20 785 confirmed cases of IPD notified in 2012, 13 837 (67%) from 23 countries had information on serogroup/serotype. Thirty-five serogroups were identified, 17 of which had only one serotype and 18 had more than one serotype (Annex 1, Table A10). For 751 IPD cases, only the serogroup, but no serotype, was reported. Overall, 73 immunologically unique serotypes, responsible for 13 034 confirmed IPD cases, were reported in 2012. Three cases were reported as serotype 'other' and 49 as 'not typeable' (Annex 1, Table A10).

Most common serotypes

Twenty-five serotypes[8] accounted for 90% (n=11 697) of the typed isolates and the ten most frequently reported were responsible for 63% (n=8 187) of cases with known serotype (Table 1.3, Annex 1, Table A11). The most prevalent serotypes were 3 (n=1 374), 7F (n=1 189) and 19A (n=1 116), accounting for 10.5%, 9.1% and 8.6% of the total number of serotyped-confirmed cases, respectively. These three serotypes were also the three most common in 2011. Serotype 1 was the fourth most common, accounting for 7.8% of cases (n=1 018) (Table 1.3, Figure 1.5).

Since 2010, a decline in the proportion of serotypes included in PCV7 (4, 6B, 9V, 14, 18C, 19F and 23F) has been observed (Figure 1.5). Only serotype 14 still ranks among the ten most common serotypes in 2012. The prevalence of serotypes 3 and 7F has remained almost the same between 2010 and 2012 (Figure 1.5). The remaining five serotypes in the top 10 (6C, 8, 12F, 22F and 15A) are not covered by any of the PCV vaccines, and their prevalence has increased between 2010 and 2012, although serotypes 22F, 8 and 12F are covered by PPV23 (Figure 1.5). Among countries reporting typed isolates for more than 20 confirmed IPD cases, serotype 14 was particularly prevalent in Slovenia, followed by Latvia, Austria and Finland. The most prevalent serotypes were serotype 3 in Hungary, serotype 7F in Norway, serotype 19A in Slovakia, and serotype 1 in Denmark (Annex 1, Table A11).

Table 1.3. The 10 most common IPD serotypes reported in 2012, EU/EEA countries (n=13 034*)

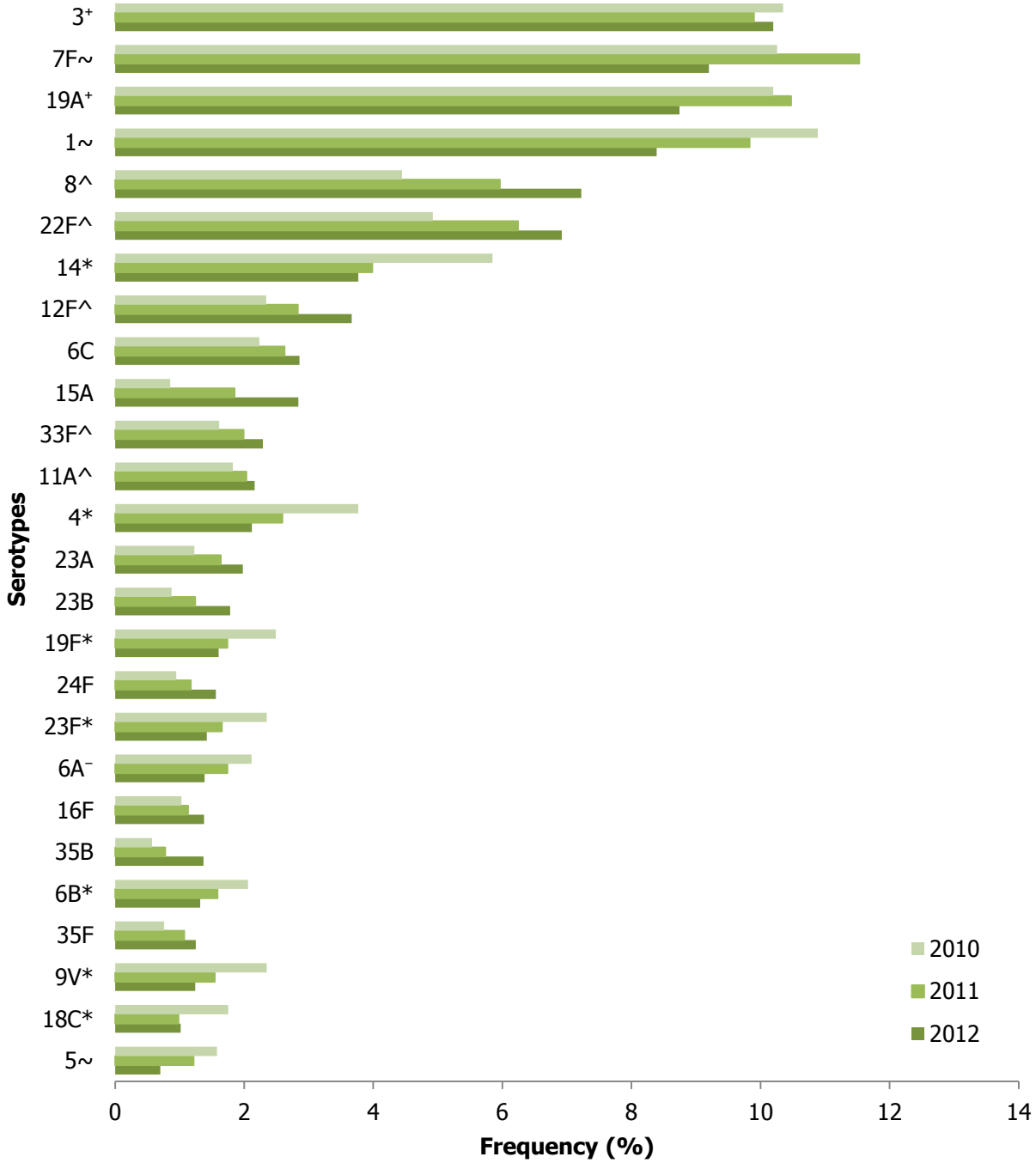
Rank	Serotype	Confirmed IPD cases (N)	Frequency (%)
1	3	1374	10.5
2	7F	1189	9.1
3	19A	1116	8.6
4	1	1018	7.8
5	22F	963	7.4
6	8	885	6.8
7	14	477	3.7
8	12F	444	3.4
9	6C	375	2.9
10	15A	346	2.7

Contributing countries: Austria, Belgium, Cyprus, the Czech Republic, Denmark, Estonia, Finland, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, the Netherlands, Norway, Poland, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom

** Total refers to the total number of typed isolates*

[8] Top 25 serotypes reported in 2012: 3, 7F, 19A, 1, 22F, 8, 14, 12F, 6C, 15A, 9N, 33F, 11A, 4, 23A, 10A, 23B, 19F, 23F, 24F, 35F, 6A, 9V, 6B and 16F.

Figure 1.5. Distribution of confirmed IPD cases by most common serotype in 2012 (n=11 835), 2011 (n=11 838) and 2010 (n=8 550), EU/EEA countries



** Covered by PCV7, PCV10, PCV13 and PPV23*

~ Covered by PCV10, PCV13 and PPV23

+ Covered by PCV13 and PPV23

^ Covered by PPV23 only

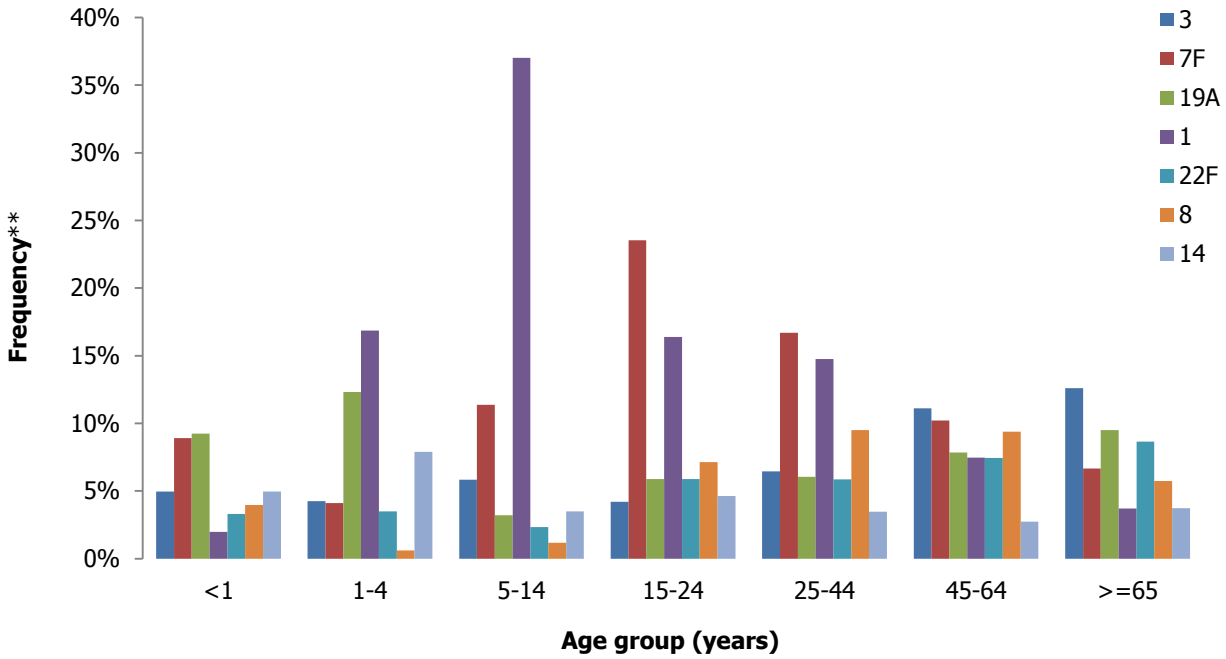
- Covered by PCV13 only

Contributing countries: Austria, Belgium, Cyprus, the Czech Republic, Denmark, Finland, Greece, Hungary, Iceland, Ireland, Italy, Lithuania, the Netherlands, Norway, Poland, Romania, Slovakia, Slovenia, Spain and the United Kingdom

Serotype and age

Among the 12 992 cases for which serotype and age were reported, the most frequently reported serotypes in children younger than one year were 19A and 7F (Figure 1.6, Annex 1, Table A12). In children between 1 and 14 years of age, serotype 1 was the most commonly reported. Among cases between 15 and 44 years, serotype 7F was the most prevalent. In cases 45 years or older, serotype 3 was the most prevalent. Serotypes 8 and 22F were mainly observed in persons 15 years or older. Serotypes 7F, 19A and 1 – the most prevalent serotypes in children under 15 years – are not covered by PCV7.

Figure 1.6. Distribution of seven most frequent IPD serotypes by age group, EU/EEA countries, 2012 (n=12 992*)



** Total number of cases for which information on serotype and age was available.*

*** Frequency refers to the proportion of the total number of cases for which serotype information was available by age group: < 1 year, n=303; 1–4 years, n=658; 5–14 years, n=343; 15–24 years, n=238; 25–44 years, n=1504; 45–64 years, n=3557; ≥ 65 years, n=6389*

Serotype and clinical presentation

Information on clinical presentation was available in 60% of confirmed IPD cases for which serotype was known. Among these cases, serotype 7F was the most frequently reported serotype for cases with bacteraemia. Serotype 3 was the most frequently reported serotype among meningitis cases, followed by serotype 19A. Serotypes 3 and 1 were the most frequent in cases with bacteraemia and pneumonia (Table 1.4).

Table 1.4. Distribution of the 10 most frequent IPD serotypes by clinical presentation, EU/EEA countries, 2012 (n=7 819*)

Serotype	Bacteraemia		Meningitis		Bacteraemia and pneumonia		Other	
	N	%	N	%	N	%	N	%
3	432	9.0	69	10.4	307	14.4	30	13.2
7F	528	11.0	46	6.9	137	6.4	7	3.1
19A	429	8.9	58	8.8	207	9.7	21	9.2
1	269	5.6	6	0.9	288	13.5	20	8.8
22F	387	8.1	35	5.3	89	4.2	7	3.1
8	441	9.2	29	4.4	121	5.7	8	3.5
14	111	2.3	15	2.3	132	6.2	8	3.5
12F	143	3.0	16	2.4	107	5.0	8	3.5
6C	169	3.5	14	2.1	58	2.7	7	3.1
15A	191	4.0	19	2.9	35	1.6	9	3.9
Total*	**4 794**		**662**		**2 135**		**228**	

** Total number of cases for which serotype information is available by clinical presentation*

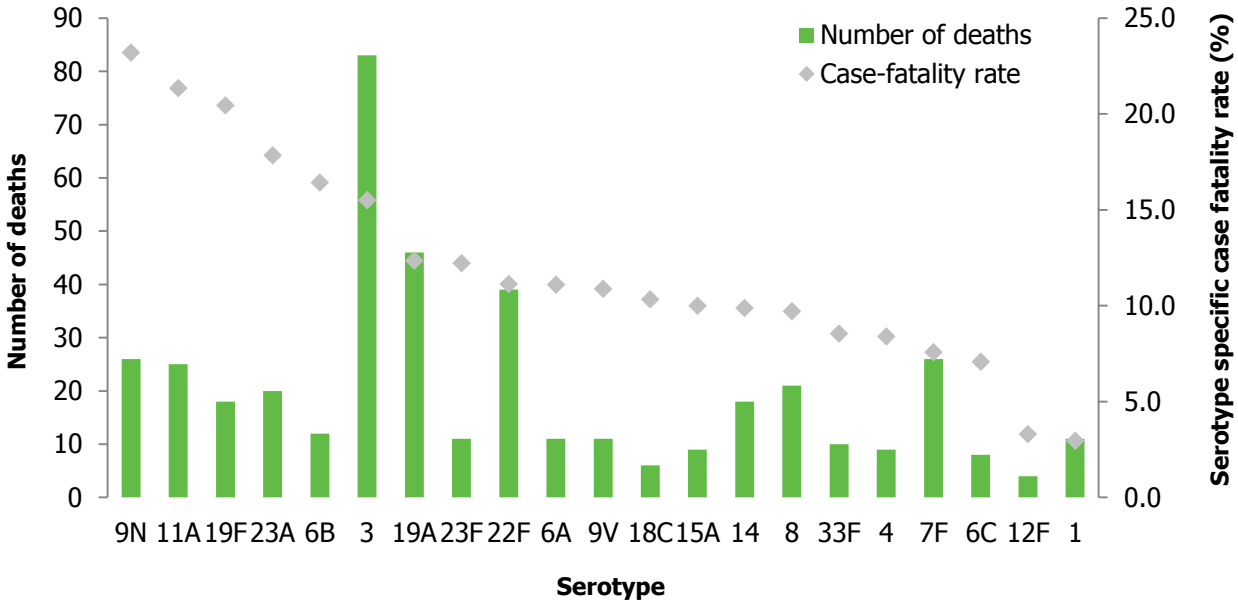
Contributing countries: Austria, Belgium, Cyprus, the Czech Republic, Estonia, Greece, Hungary, Iceland, Ireland, Latvia, Lithuania, Norway, Poland, Romania, Slovakia, Slovenia, Spain and the United Kingdom

Serotype and case fatality

Of the reported cases with fatal outcome, 75% (n=520) had serotype information available. Serotype 3 accounted for the majority of reported deaths (n=83), followed by serotype 19A (n=46) and 22F (n=39) (Figure 1.7).

Among serotypes with outcome information for more than 50 confirmed IPD cases, serotype 9N presented the highest serotype-specific case fatality rate (23%), followed by serotypes 11A (21%), 19F (20%) and 23A (18%). Serotype 23A is not covered by any of the licensed vaccines.

Figure 1.7. Distribution of reported IPD cases with fatal outcome (n=4 527*) and case fatality rate by serotype, EU/EEA countries, 2012



** N refers to the total number of cases for which outcome and serotype information was known. Information on outcome was available for 68 of 73 serotypes, and 45 different serotypes were linked to at least one case with fatal outcome in 2012. Only 21 serotypes are shown here.*

Serotype and vaccines

Across all age groups, 13% (n=1 683) of IPD cases were due to serotypes included in PCV7, 31% (n= 3 963) were due to serotypes included in PCV10, and 51% (n= 6 632) to serotypes covered by PCV13 (Table 1.5). PCV13 could have potentially prevented about 50% of the cases in children under one year of age (Figure 1.8). The potential coverage of PCV13 is higher than 45% in all age groups, while the coverage of PCV7 is below 20% for all age groups.

In the 15–64 year age range, 84% (n= 5 299) of the reported cases would have been covered by PPV23; among confirmed IPD cases aged 65 years or over, PPV23 would have covered 70% (n= 6 839). Overall, serotypes included in the PPV23 vaccine were responsible for 79% of cases (n=10 244) for which information on serotype and age was available (Table 1.6).

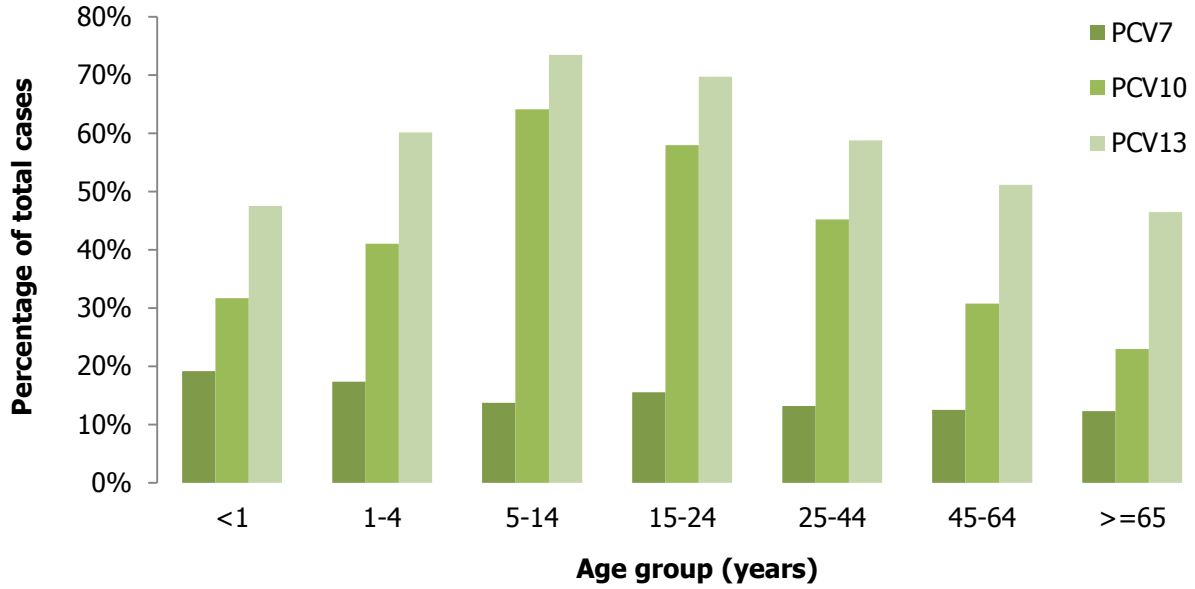
Table 1.5. Distribution of reported PCV serotype cases of IPD by age group for the three licensed PCV, EU/EEA countries, 2012 (n=12 992*)

PCV7 serotypes	PCV10 serotypes	PCV13 serotypes	Number and % of cases							
			< 1 year		1–14 years		≥ 15 years		Total	
			N	%	N	%	N	%	N	%
4	4	4	3	1.0	3	0.3	292	2.5	298	2.3
6B	6B	6B	11	3.6	17	1.7	150	1.3	178	1.4
9V	9V	9V	3	1.0	14	1.4	166	1.4	183	1.4
14	14	14	15	5.0	64	6.4	398	3.4	477	3.7
18C	18C	18C	7	2.3	19	1.9	110	0.9	136	1.0
19F	19F	19F	13	4.3	23	2.3	176	1.5	212	1.6
23F	23F	23F	6	2.0	21	2.1	172	1.5	199	1.5
	1	1	6	2.0	238	23.8	764	6.5	1 008	7.8
	5	5	5	1.7	25	2.5	54	0.5	84	0.6

PCV7 serotypes	PCV10 serotypes	PCV13 serotypes	Number and % of cases							
			< 1 year		1–14 years		≥ 15 years		Total	
			N	%	N	%	N	%	N	%
	7F	7F	27	8.9	66	6.6	1 095	9.4	1 188	9.1
		3	15	5.0	48	4.8	1 307	11.2	1 370	10.5
		6A	5	1.7	18	1.8	165	1.4	188	1.4
		19A	28	9.2	92	9.2	991	8.5	1 111	8.6
Total			**303**		**1 001**		**11 688**		**12 992**	

** Total number of cases for which serotype information is available by age group*

Figure 1.8. Percentage of cases potentially covered by PCV, by age group, EU/EEA countries, 2012 (n=12 992*)



** Total cases in each age group for which serotype and age information in available*

Table 1.6. Percentage of cases potentially covered by PPV23, EU/EEA countries, 2012 (n=12 992*)

PPV23 serotypes	Number and % of cases					
	15–64 years		≥ 65 years		All age groups	
	N	%	N	%	N	%
1	527	9.9	237	3.5	1 008	7.8
2	0	0.0	2	0.0	3	0.0
3	502	9.5	805	11.8	1 370	10.5
4	183	3.5	109	1.6	298	2.3
5	35	0.7	19	0.3	84	0.6
6B	67	1.3	83	1.2	178	1.4
7F	670	12.6	425	6.2	1 188	9.1
8	494	9.3	367	5.4	881	6.8
9N	147	2.8	184	2.7	339	2.6
9V	65	1.2	101	1.5	183	1.4
10A	79	1.5	111	1.6	224	1.7
11A	101	1.9	185	2.7	302	2.3
12F	226	4.3	163	2.4	440	3.4
14	160	3.0	238	3.5	477	3.7
15B	48	0.9	81	1.2	156	1.2
17F	31	0.6	33	0.5	72	0.6
18C	57	1.1	53	0.8	136	1.0
19A	384	7.2	607	8.9	1 111	8.6
19F	81	1.5	95	1.4	212	1.6
20	42	0.8	56	0.8	100	0.8
22F	367	6.9	552	8.1	960	7.4
23F	67	1.3	105	1.5	199	1.5
33F	106	2.0	174	2.5	323	2.5
Total*	**5 299**		**6 839**		**12 992**	

** Total cases for which serotype and age information is available*

1.5.8 Antimicrobial resistance

Resistance to penicillin

For 2012, 17 countries (Table 1.7) reported antimicrobial susceptibility testing (AST) data for penicillin in 11 222 confirmed cases, with three countries (Belgium, Spain and the United Kingdom) reporting 71% (n=7 923) of the data. The completeness for this variable differs considerably among countries; in eight countries, it was above 95% (Cyprus, Belgium, Denmark, Finland, Iceland, Norway, Slovenia and Spain), while in six it was below 45% (Austria, Estonia, Italy, Lithuania, Poland and Slovakia).

Country-specific numbers for isolates with information on AST ranged between three (Lithuania) and 3927 (United Kingdom) (Table 1.7). Among countries reporting 10 or more isolates, the percentage of non-susceptible isolates was below 1% in one country (Belgium), between 1% and 5% in four countries (Denmark, Iceland, Slovakia and the United Kingdom) and between 5% and 20% in seven countries (Austria, Hungary, Ireland, Italy, Norway, Slovenia and Spain). A percentage of non-susceptibility higher than 20% was reported by three countries (Cyprus, Finland and Poland) (Table 1.7).

Resistance to erythromycin

Sixteen countries (Table 1.7) reported AST data on erythromycin for 8 682 confirmed cases, with two countries (Spain and the United Kingdom) reporting 62% (n=5 394) of the data. In six countries, completeness below 45% (Austria, Estonia, Italy, Lithuania, Poland and Slovakia).

Country-specific numbers for isolates with information on AST ranged between three (Lithuania) and 3134 (United Kingdom) (Table 1.7). Among countries reporting 10 or more isolates, the percentage of isolates reported as non-susceptible was below 5% in one country (Austria), between 5% and 10% in four countries (Denmark, Iceland, Norway and the United Kingdom) and above 20% in seven countries (Finland, Hungary, Italy, Poland, Slovakia, Slovenia and Spain) (Table 1.7).

Resistance to cefotaxime/ceftriaxone

Fifteen countries (Table 1.7) reported AST data for cefotaxime/ceftriaxone in 5 443 confirmed cases, with one country (Spain) reporting 42% (n=2 259) of the data. In seven countries, completeness was below 45% (Austria, Denmark, Estonia, Lithuania, Poland, Slovakia and the United Kingdom).

Country-specific numbers of isolates with information on AST ranged between one (Lithuania) and 2259 (Spain) (Table 1.7). Among countries reporting 10 or more isolates, the percentage of non-susceptible isolates was below 1% in three countries (Iceland, Norway and Spain), between 1 and 5 per cent in four countries (Finland, Hungary, Slovenia and the United Kingdom) and between 5 and 10% in six countries (Austria, Cyprus, Denmark, Ireland, Poland and Slovakia). No countries reported a percentage of non-susceptibility above 10% (Table 1.7).

Table 1.7. Distribution of confirmed IPD cases, by antimicrobial susceptibility to penicillin, erythromycin and cefotaxime/ceftriaxone as interpreted by the countries (susceptible, intermediate or resistant), EU/EEA countries, 2012 (PEN n=11 222, ERY n=8 682, CTX/CFX n=5 443)

Antimicrobial agent	Penicillin				Erythromycin				Cefotaxime/ceftriaxone			
	%			N	%			N	%			N
Country	S	I	R	Total	S	I	R	Total	S	I	R	Total
Austria	93.1	3.4	3.4	29	95.2	0.0	4.8	21	90.9	9.1	0.0	22
Belgium	99.5	0.1	0.4	1 736	-	-	-	-	-	-	-	-
Cyprus	70.0	20.0	10.0	10	66.7	0.0	33.3	9	90.0	0.0	10.0	10
Denmark	95.0	4.8	0.2	882	94.7	0.0	5.3	882	90.9	9.1	0.0	66
Estonia	100.0	0.0	0.0	7	100.0	0.0	0.0	7	100.0	0.0	0.0	4
Finland	72.3	26.9	0.8	743	77.4	0.3	22.3	743	95.0	4.8	0.1	743
Hungary	84.2	11.2	4.6	152	77.6	0.0	22.4	152	98.7	1.3	0.0	152
Iceland	96.2	0.0	3.8	26	92.3	0.0	7.7	26	100.0	0.0	0.0	15
Ireland	80.9	14.8	4.4	298	83.2	0.0	16.8	298	91.3	8.4	0.3	298
Italy	86.3	1.1	12.6	95	74.2	1.1	24.7	93	-	-	-	-
Lithuania	66.7	0.0	33.3	3	66.7	0.0	33.3	3	100.0	0.0	0.0	1
Norway	93.9	6.1	0.0	607	94.2	0.0	5.8	607	99.7	0.3	0.0	607
Poland	75.7	13.8	10.5	181	67.4	0.0	32.6	181	91.7	7.2	1.1	181
Slovakia	95.2	0.0	4.8	21	76.2	0.0	23.8	21	91.7	0.0	8.3	12
Slovenia	89.4	0.0	10.6	245	79.2	0.8	20.0	245	95.5	4.5	0.0	245
Spain	93.9	2.4	3.6	2 260	74.6	0.0	25.4	2 260	99.1	0.6	0.3	2 259
United Kingdom	95.7	3.1	1.3	3 927	90.6	0.4	9.0	3 134	98.9	0.6	0.5	828
Total	**93.1**	**4.9**	**2.0**	**11 222**	**84.5**	**0.2**	**15.4**	**8 682**	**97.6**	**2.1**	**0.3**	**5 443**

- = No data reported

Minimum inhibitory concentration (MIC)

In 2012, 13 countries reported MIC values for penicillin, 11 countries for erythromycin and 12 countries for cefotaxime/ceftriaxone. In this report, results on MIC have been interpreted according to the EUCAST Guidelines (Table 1.8)

A total of 4 959 confirmed IPD cases had information on MIC results for penicillin. Overall, 7% of tested isolates were non-susceptible to penicillin. Among pneumococcal meningitis cases with MIC results, 33% were due to penicillin-resistant *S. pneumoniae*. Penicillin-resistant serotypes mainly responsible for pneumococcal meningitis were 14, 19A, 19F, 23B and 23F. The proportion of penicillin-resistant isolates was lower in non-meningitis pneumococcal cases (0.7%), and resistance was related to serotypes 14 and 19A (Table 1.9).

For erythromycin, information on MIC results was available for 4 776 isolates, of which 21% were classified as resistant (> 0.5 mg/L). Resistance to erythromycin was related mainly to serotypes 6B, 6C, 14, 15A, 19A, 19F and 24F. Among the antimicrobial agents tested, erythromycin showed the highest prevalence of resistance (Table 1.9).

For cefotaxime/ceftriaxone, information on MIC results was available for 4 864 isolates. Overall, 2% of tested isolates were resistant (> 2 mg/L). Resistance to cefotaxime/ceftriaxone was reported for 3.3% of pneumococcal meningitis cases and was mainly related to serotypes 14 and 19A (Table 1.9).

Resistance and serotype

Information on MIC results for the three antimicrobial agents was provided for 4 625 typed isolates. For all three antimicrobial agents, serotype 19A represented the greatest proportion of resistant isolates, followed by serotype 14.

Combined resistance to penicillin, erythromycin and cefotaxime/ceftriaxone (multidrug resistance) was observed in serotypes 6A, 6B, 6C, 9V, 14, 15A, 19A, 19F, 23A, 23F, 24F and 35B. In 2011, multidrug resistance was reported for serotypes 6B, 14, 19, 19A, 19F and 23F9.

Dual resistance to penicillin and erythromycin was reported in serotypes 3, 4, 14, 38, 11A, 12F, 15A, 15B, 15C, 18C, 19A, 19F, 22F, 23A, 23B, 23F, 24A, 24F, 35B, 6A, 6B, 6C, 9N and 9V.

Table 1.8. Comparison of interpretative standards for minimum inhibitory concentration (MIC) determination (mg/L) with *S. pneumoniae* in EUCAST and CSLI guidelines

Antimicrobial agent	EUCAST MIC breakpoint (mg/L)		CLSI MIC interpretive standard (mg/L)		
	S	R	S	I	R
Penicillin parenteral (meningitis)	≤ 0.06	> 0.06	≤ 0.06		≥ 0.12
Penicillin parenteral (non-meningitis)	≤ 0.06	> 2.00	≤ 2.00	4.00	≥ 8.00
Cefotaxime/ceftriaxone (meningitis)	≤ 0.50	> 2.00	≤ 0.50	1.00	≥ 2.00
Cefotaxime/ceftriaxone (non-meningitis)	≤ 0.50	> 2.00	≤ 1.00	2.00	≥ 4.00
Erythromycin	≤ 0.25	> 0.50	≤ 0.25	0.50	≥ 1.00
Ciprofloxacin	≤ 0.12	> 2.00			
Clindamycin	≤ 0.50	> 0.50	≤ 0.25	0.50	≥ 1.00

[9] http://ecdc.europa.eu/en/publications/Publications/invasive-pneumoccocal-disease-surveillance-2011.pdf

Table 1.9. Distribution of reported IPD cases by antibiotic, clinical presentation and MIC, EU/EEA countries, 2012

MIC (mg/L)	Penicillin				Erythromycin		Cefotaxime/ceftriaxone			
	Meningitis		Non-meningitis*		N	%	Meningitis		Non-meningitis**	
	N	%	N	%			N	%	N	%
≤ 0.032	298	66.7	2357	76.0	38	0.8	303	67.6	2368	76.4
0.064	26	5.8	130	4.2	244	5.1	21	4.7	131	4.2
0.125	15	3.4	73	2.4	3041	63.7	31	6.9	126	4.1
0.25	31	6.9	93	3.0	436	9.1	16	3.6	84	2.7
0.5	16	3.6	102	3.3	2	0.0	40	8.9	130	4.2
1	32	7.2	179	5.8	27	0.6	22	4.9	208	6.7
2	19	4.3	147	4.7	49	1.0	15	3.3	54	1.7
4	8	1.8	18	0.6	21	0.4				
8	2	0.4	3	0.1	56	1.2				
16					77	1.6				
32					38	0.8				
64					64	1.3				
> 64					683	14.3				
Total	**447**		**3 102**		**4 776**		**448**		**3 101**	

** Excludes 1410 cases for which clinical presentations were unknown*

*** Excludes 1315 cases for which clinical presentations were unknown*

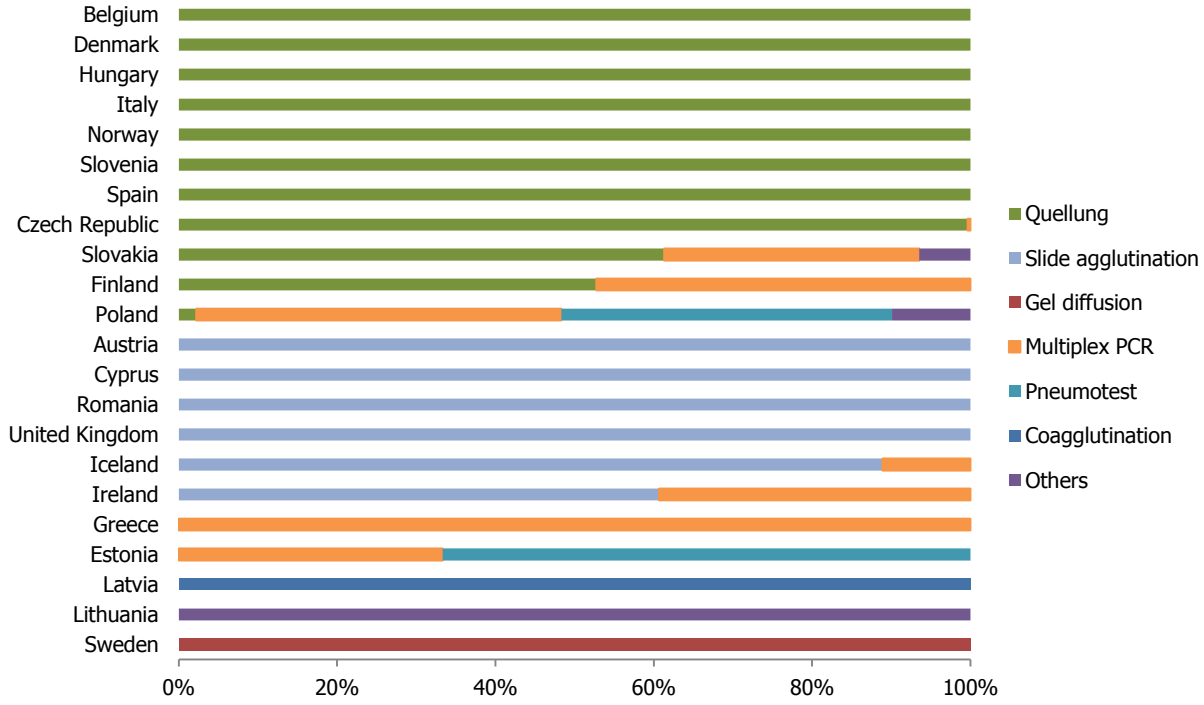
1.5.9 Laboratory methods used for strain identification

All but one reporting country (Bulgaria) included information on specimen, and the completeness for this variable was 99% (Annex 1, Table A13). Blood samples accounted for 88% (n=18 059) of the total number of cases for which the specimen was reported, and CSF for 8% (n=1 590) (Annex 1, Table A13). Blood samples made up ≥ 80% of specimens in all age groups, except in children younger than one year and between 5 and 14 years. In these two age groups, the proportion of blood specimens was about 72%, and the proportion of CSF specimens highest, accounting for 24% and 15%, respectively (Annex 1, Table A14).

Serotyping methods

In Europe, a variety of laboratory methods are used to serotype strains, such as the standard quellung reaction test, slide agglutination, coagglutination, multiplex PCR, gel diffusion and Pneumotest (SSI Diagnostica, Denmark). In 2012, information on test methods was available for 61% of confirmed IPD cases (n= 12 592), it was reported by 22 countries, but the completeness for this variable differed widely from country to country. Quellung was the preferred technique for serotyping and was used in 56% of all cases for which a serotype was reported. This was followed by slide agglutination (29%) and Pneumotest (10%), a commercial kit that uses either latex agglutination or quellung (Figure 1.9). Fourteen countries reported using only one method to type IPD isolates, with seven using the quellung test. Only Poland and Slovakia reported that they performed two or more laboratory tests for typing (Figure 1.9).

Figure 1.9. Proportion of reported serotyping test methods used in confirmed IPD cases by country, EU/EEA countries, 2012 (n=12 582*)



Contributing countries: Belgium, Cyprus, the Czech Republic, Denmark, Estonia, Finland, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Norway, Poland, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom

** Excludes Austria, which only reported information for one isolate (typed by slide agglutination)*

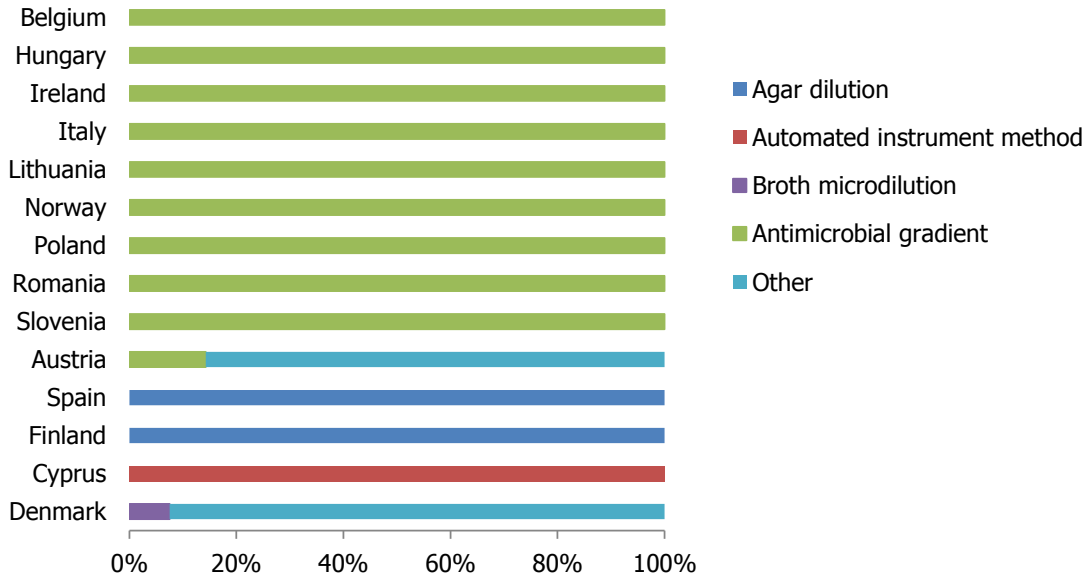
Antimicrobial susceptibility testing methods

In Europe, a variety of laboratory methods are used to test for antimicrobial susceptibility, including antimicrobial gradient tests, agar dilution, broth microdilution and automated instrument method. Member States reported antimicrobial susceptibility testing results, expressed as minimum inhibitory concentration (MIC) and/or categorised as S, R, I: susceptible (S), intermediate (I), or resistant (R), in accordance with national standards and protocols.

In 2012, only 14 countries reported which antimicrobial susceptibility testing methods they used. Overall, the level of completeness was very low (27%), with considerable differences between countries. Only Cyprus, Slovenia and Spain reported AST information for all confirmed cases. Data from Spain represented 40% of all cases for which information was available.

Antimicrobial gradient was the method of choice for the majority of countries (n=9) who only used one test method, while only two countries used agar dilution. Austria and Denmark reported that they used more than one test method (Figure 1.10).

Figure 1.10. Proportion of reported MIC test methods used for isolates in confirmed IPD cases, by country, EU/EEA countries, 2012 (n=4 851)



Contributing countries: Austria, Belgium, Cyprus, Denmark, Finland, Hungary, Ireland, Italy, Lithuania, Norway, Poland, Romania, Slovenia and Spain

1.5.10 Data quality

In 2012, 25 EU Member States and two EEA countries notified 20 785 confirmed cases of IPD to TESSy. Non-reporting countries were Germany, Liechtenstein and Portugal.

Overall, data on age, age in months (required for cases younger than two years), gender, classification and specimen were complete, or almost complete, with a proportion of missing values lower than 1% (Annex 1, Table A15). Data on clinical presentation were reported by 21 of 27 reporting countries. The level of data completeness was the same as in 2011, approximately 50%.

Data on serotypes were reported by 23 countries: Austria, Belgium, Cyprus, the Czech Republic, Denmark, Estonia, Finland, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, the Netherlands, Norway, Poland, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom. Data completeness for serotype significantly improved (67% complete, up from 47% in 2010), but completeness for the serotyping method remained low (60% complete).

Data on vaccination status were reported by 17 countries for less than 20% of all cases. Data on outcome were supplied by 21 countries for about 30% of cases. However, the completeness for this variable differed widely from country to country.

MIC data were reported in approximately 20–30% of all cases. MIC results for penicillin were the most complete, with 13 countries reporting data. Antimicrobial resistance data expressed as susceptible (S), intermediate (I) and resistant (R) were marginally more complete for some antimicrobials (Annex 1, Table A15). SIR data were submitted by 17 countries for penicillin (missing 46%), by 16 for erythromycin (missing 58%) and by 15 countries for cefotaxime/ceftriaxone (missing 74%) (Annex 1, Table A15).

1.6 Discussion

In 2012, 20 785 confirmed cases of invasive pneumococcal disease were reported in Europe, with an overall notification rate of 5.2 per 100 000 population. Nordic countries (Denmark, Finland, Norway and Sweden) presented the highest notification rates, although rates in these countries were lower than in 2010. Over the last five years, several changes occurred in the surveillance of IPD, at both the European and national levels, such as changes in representativeness, national coverage, reporting procedure, which could have biased the results. Consequently, national notification rates and trends over time must be interpreted with caution.

The highest IPD notification rates were among children under one year of age (11.9 per 100 000) and among adults 65 years and over (15.4 per 100 000). This pattern, which has been seen in data from Europe since 2006 as well as from other parts of the world [10–15], supports the recommendations for targeting these age groups for vaccination. Pneumococcal vaccination is currently carried out in 28 EU/EEA countries. For more details on the

vaccine schedules in each Member State please consult the ECDC vaccine scheduler[10]. During 2008–12, a steady decline in notification rates for cases below five years of age was observed in Europe, while the trend was stable across all other age groups. Slovenia and Slovakia reported the highest proportion of cases between one and four years of age (16.3%). In Slovenia, PCV is not part of the routine immunisation schedule.

S. pneumoniae is considered to be the leading bacterial cause of pneumonia and is reported as a major cause of hospital admissions for children and adults [15]. In 2012, the most frequent clinical presentation in the EU/EEA was bacteraemia, accounting for 53% of cases, followed by bacteraemic pneumonia (24%).

Data on clinical presentation can be biased by the surveillance system and its implementation, the level of data completeness (50% missing in 2012) and by data representativeness (Spain and the United Kingdom contributed 67% of clinical presentation data in 2012). The overall CFR in EU/EEA countries was 11% (95% CI: 10%–12%), in line with other published data [11]. However, all data and analyses on CFR should be interpreted with caution because data for the variable 'outcome' were largely incomplete (70% missing), the level of completeness differed widely from country to country, and there is no common European approach to the follow-up time or endpoint for fatal IPD.

Of the *S. pneumoniae* isolates that underwent susceptibility testing, erythromycin resistance was the most prevalent, followed by penicillin resistance, which was in line with previously published data [11]. Compared with 2011, an increased number of multidrug-resistant strains (combined resistance to penicillin, erythromycin and cefotaxime) was reported. For all three antimicrobial agents, serotype 19A represented the greatest proportion of resistant isolates, followed by serotype 14. Of the pneumococcal meningitis cases with available MIC results, 33% were due to penicillin-resistant *S. pneumoniae*. Of the serotypes that are frequently responsible for pneumococcal meningitis, the following were penicillin resistant: 14, 19A, 19F, 23B and 23F. Serotypes 19A, 14, 19F and 23F are considered to be the most antimicrobial-resistant *S. pneumoniae* serotypes [33,34]. The comparison of AST results between countries is problematic due to the use of different guidelines, media and break points.

Vaccination status was only reported for 18% of all confirmed IPD cases, 90% of whom were unvaccinated. The vaccine type administered was known for 41% of vaccinated cases (n=153). This information was reported by very few countries. For the few cases for which information on both vaccine type and serotype were available, IPD in the vast majority of vaccinated cases was caused by non-vaccine serotypes. The completeness of this variable needs to be improved.

In 2012, 73 immunologically unique serotypes were reported across European countries. This information was only available for approximately 65% of all confirmed IPD cases, and data on serogroup/serotype were not reported by all countries. Despite the high variability, 25 serotypes accounted for 90% of all typed isolates, and the ten most frequently reported serotypes were responsible for 63% of the confirmed cases with serotype information. The four most prevalent serotypes since 2010 were 3, 7F, 19A and 1, which are included in either PCV10 (7F and 1) or PCV13 (3, 7F, 19A and 1). Overall, a decline in the proportion of serotypes included in the PCV7 vaccine has been observed since 2010, and in 2012 only serotype 14 still ranked among the ten most common serotypes. Overall, 51% of cases were caused by a PCV13 serotype, 31% by a PCV10 serotype and 13% by a PCV7 serotype. This supports the decision to shift to a vaccine of higher valence. The continued circulation of some PCV7 serotypes may reflect the fact that the vaccine is not recommended in all countries in Europe and is only recommended for risk groups in some countries. In general, the current serotype distribution of IPD in Europe appears to differ from other regions of the world [37] although this may reflect current vaccine policies and differences in the year of data collection [38].

Among serotypes with more than 50 confirmed cases for which information on outcome was available, serotype 9N accounted for the highest serotype-specific CFR in 2012 (23%), followed by serotype 11A (21%). Serotypes 3, 9N and 11A are all included in PPV23, with serotype 3 also included in PCV13, although none of these three serotypes are included in PCV7 or PCV10. A high serotype-specific CFR was observed also in serotype 23A (18%), which is not covered by any licensed vaccine. Serotype 3, which accounted for the highest number of deaths (n=83), has been associated with a high invasive capacity [31] and increased case fatality [32]. This information should be interpreted with caution due to the small number of cases for which serotype and outcome were reported.

One of the major challenges in pneumococcal vaccination is serotype replacement. This phenomenon has been widely described [26–30]. The occurrence of serotypes 8, 12F and 22F has been increasing over the years, although they are included in the PPV23 vaccine; serotypes 8 and 22F occurred mainly in the older age groups.

Although PCV13 has been authorised for use in adults over 50 years of age, the data suggest that PPV23 continues to be relevant for the vaccination in older age groups, since PCV13 does not cover all the relevant serotypes. Serotypes 6C and 15A are the only two top-10 serotypes not yet covered by any licensed vaccine. Serotype 6C was first described only a few years ago [16] and prevalence in nasopharyngeal carriage of this serotype in certain settings has increased after vaccination [17, 18]. Previous studies showed that PCV7 vaccination provides some

[10] http://vaccine-schedule.ecdc.europa.eu/Pages/Scheduler.aspx

cross protection against serotype 6A, but not against serotype 6C [20]. There is evidence, however, that PCV13 vaccination has the potential to confer cross-protection against this serotype [19]. This finding also supports the introduction of PCV13 into national vaccination schemes. Serotype 15A was not observed among the 10 most frequently reported serotypes in Europe before 2012. The increase of serotype 15A after introduction of PCV7 vaccination has already been documented and was often associated with an increased non-susceptibility to penicillin and erythromycin [21].

As only three years of serotype data were available for IPD (2010–12), it is difficult to draw conclusions on serotype replacement at the European level or secular trends of specific serotypes [29]. Moreover, changes in national data sources and reporting, better ascertainment of cases, improvements in laboratory methods and enhanced surveillance for IPD may have biased the results and complicated their interpretation. However, results in this report do corroborate the sustained reduction in vaccine-type IPD, although this has been partially thwarted by the increase of non-vaccine type disease. Continued surveillance of invasive pneumococcal serotypes in Europe is essential to monitor serotype replacement and the prevalence of antimicrobial-resistant strains to document changes in characteristics of the disease, guide treatment decisions, and inform future vaccine development.

2 Invasive *Haemophilus influenzae* disease

2.1 Summary

Prior to the introduction of the *H. influenzae* type b (Hib) conjugate vaccine, Hib caused the majority of cases of invasive *H. influenzae* infections, mainly in children younger than five years of age, whereas non-capsulated strains (ncHi) were involved in respiratory tract infections and otitis media but would also cause invasive disease, especially in adults. From the late 1990s, EU/EEA countries began introducing routine early childhood Hib vaccination into their national schedules. The vaccine has proven to be effective in reducing b-serotype infection; however, concerns remain about possible changes in the epidemiology of invasive disease, such as serotype replacement and shift towards older age groups.

In 2012, 26 EU Member States and one EEA country notified 3 545 confirmed cases of invasive Hi disease. The notification rate across Europe was 0.57 cases per 100 000 population, ranging from 0.04 (Bulgaria, Hungary and Romania) to 2.26 (Sweden). Countries in the northwest of Europe reported the highest rates. There was a clear seasonal distribution of cases with a noticeable rise during the winter months. Of all cases reported in 2012, 55% were among adults 65 years of age and older. Infants (4.2 cases per 100 000) and the elderly (1.9 per 100 000) were the predominant age groups affected, as observed in previous years. Males were more affected than females in these age groups. Notification rates across all age groups remained relatively stable during 2008–12.

Septicaemia was the most common clinical presentation across most age groups, except for children between one and four years in whom meningitis was the most common presentation. Pneumonia was the second most common clinical presentation in cases aged 45 year or older, while in those younger than 45 years meningitis was the second most common presentation. Data on clinical presentation was missing for 60% of cases. The overall CFR in EU/EEA countries was 9.6% (95% CI: 8.2%–11.3%). The greatest CFR was observed among in cases ≥ 65 years (12%), followed by cases < 1 year of age (11%). When analysed by serotype, infections caused by non-capsulated strains had the highest CFR (12%). Vaccination status was only known in 42% (n=45) of all cases with serotype b invasive Hi disease, 71% of which (n=37) were unvaccinated, and three cases had received four vaccine doses

Overall, non-capsulated strains made up 77% of cases, followed by non-b serotypes (15%). Hib was responsible for 8% of cases. During 2008–12, notification rates for serotype b decreased significantly. The trend for non-b serotypes remained stable, whereas non-capsulated strains constantly increased since 2010.

Serotype b was responsible for about 21% of all meningitis cases, while representing less than 5% of septicaemia or pneumonia cases. Cases below one year of age were the most affected. Over time, notification rates showed a decreasing trend, particularly in cases below five years of age, in whom notification rates almost halved from 2008 to 2012. During this period, almost all countries reported notification rates < 1 per 100 000 population except for Estonia (2011–12), although the number of reported cases in this country was very low. Among serotype non-b infections, Hif was the most common strain (62%). Non-b serotype notification rates were highest among cases under one year of age. Trends were stable in all age groups except in children younger than one year, in whom notification rates decreased significantly. Non-capsulated strains (ncHi) were isolated in > 50% of cases in all age groups, with proportions exceeding 80% in the 15–24-year age group and among those 65 years and older. Non-capsulated serotype notification rates were highest among cases below one year of age. Overall, there was an upward trend in disease caused by ncHi strains during 2008–12; age-specific trends were fluctuating, with a slight increase in cases between 15 and 44 years.

Increased incidence of non-capsulated strain infection has been observed in recent years. However, this may be partly explained by the extension of enhanced surveillance systems to include all serotypes greater awareness of the disease and an increase in the culturing of blood isolates. More robust surveillance data are needed for serotype replacement in invasive Hi disease to be accurately assessed, particularly with regard to serotype data.

Surveillance systems for *H. influenzae* in EU/EEA reporting countries, 2012

- 27 countries reported invasive Hi cases at the EU/EEA level in 2012.
- 26 countries reported data from a single source; 26 reported case-based data.
- 23 countries described a passive surveillance system.
- 21 countries have a compulsory and comprehensive surveillance system in place.
- Three countries have a sentinel surveillance system.
- 16 countries applied the EU 2008 case definition.
- 18 countries submitted data reported by laboratories, physicians and/or hospitals.
- 5 countries have laboratory-based surveillance systems.
- 5 countries submitted data reported only by physicians and/or hospitals.

2.2 Introduction

Invasive *H. influenzae* (Hi) disease is a severe form of a bacterial infection caused by *Haemophilus influenzae*. Most strains of *H. influenzae* are opportunistic pathogens, residing in the upper respiratory tract as constituents of the normal flora of humans. Nasopharyngeal carriage is usually asymptomatic. Invasive Hi disease occurs when the bacterium reaches a normally sterile site, resulting in serious conditions including bacteraemia, pneumonia, epiglottitis, and acute bacterial meningitis.

H. influenzae is divided into two major categories: capsulated and non-capsulated strains. Capsulated strains of *H. influenzae* generally cause invasive disease and are classified into six different serotypes (a–f) on the basis of their distinct capsular antigens [2]. *H. influenzae* serotype b (Hib) is the serotype most pathogenic to humans, affecting mainly infants and young children. The remaining capsulated serotypes rarely cause invasive disease and usually affect people with co-morbidities. Non-capsulated strains are also termed 'non-typable' (ncHi) because they lack a capsular serotype. They usually cause non-invasive milder respiratory tract infections, such as otitis media and sinusitis. However, ncHi can cause invasive disease, mainly in elderly patients and individuals with underlying medical conditions [44].

In the late 1990s, EU/EEA countries began introducing routine early childhood Hib vaccination into their national schedules. Before routine vaccination with *Haemophilus influenzae* type b (Hib) conjugate vaccine was introduced, *H. influenzae* serotype b (Hib) caused > 80% of invasive Hi disease and was a leading cause of bacterial meningitis in young children < 5 years of age [39]. Hib vaccination is now part of the routine immunisation schedule in all EU/EEA Member States[11]. The vaccine has proven to be effective and has led to a sharp decrease in Hib infections in most countries worldwide [40]. Furthermore, conjugate Hib vaccine reduces pharyngeal carriage, thus resulting in indirect protection (herd protection) [5].

However, vaccination with Hib conjugate vaccine does not prevent infection with ncHi strains or non-b capsulated serotypes, and concerns remain about possible changes in the epidemiology of invasive disease, such as shift in predominance of serotypes, which would have an impact on the long-term effectiveness of the vaccine [41–44], or a shift of the disease's age predilection toward adults.

This report describes surveillance data collected across European countries for 2012 and time trends in different age groups and Hi serotypes to understand the burden of invasive Hi disease and monitor the strain distribution in Europe.

2.3 Data sources and case definitions

In 2012, 26 EU Member States and one EEA country notified cases of invasive Hi disease to the European Surveillance System (TESSy), excluding Liechtenstein, Luxembourg and Iceland.

According to the data provided, 21 countries had a compulsory and comprehensive surveillance system in place, three countries (Belgium, France and Spain) had a voluntary sentinel surveillance system, and Italy and the Netherlands had a voluntary but comprehensive surveillance system. There is no single surveillance system in United Kingdom as data are collected separately in England, Northern Ireland, Scotland and Wales. Data from the United Kingdom were reported through one data source to TESSy, although surveillance systems in these four countries differ (Annex 2, Table B1).

Among countries with a sentinel system in place, France reported the size of the population covered by the system, Spain reported national coverage. In Belgium, the national coverage was unknown.

Most countries reported to have a passive surveillance system for invasive Hi in place, except for Belgium, the Czech Republic, France and Slovakia, which described their systems as active surveillance systems.

Data on invasive Hi infections were reported by laboratories as well as physicians and/or hospitals in 17 countries. In five countries, data were only reported by laboratories (Belgium, Denmark, Finland, the Netherlands and Spain), and in five countries only physicians and/or hospitals supplied data (Cyprus, the Czech Republic, Italy, Poland and Romania). Case-based data were submitted by all countries, with the exception of Bulgaria.

Case definitions differed from country to country, with the majority (n=16) applying the 2008 EU case definition. Two countries (Portugal and the United Kingdom) applied the 2002 EU case definition and five (Italy, Latvia, Norway, Slovakia and Sweden) had moved to the 2012 EU case definition. The case definition applied was defined as 'other' in two countries and 'unknown' in the remaining two countries.

The 2002 EU case definition only covered the notification of invasive *H. influenzae* type b. Taking into account clinical criteria, the 2002 case definition differentiated between confirmed, possible and probable cases. Starting in 2008, the EU case definition included all serotypes responsible for invasive Hi disease. Clinical criteria were no

[11] http://vaccine-schedule.ecdc.europa.eu/Pages/Scheduler.aspx

longer considered relevant for surveillance purposes, and the case definition focussed only on laboratory-confirmed cases. Apart from that, there are only minor differences between the 2008 and 2012 versions of the EU case definition.

In 2012, all countries reported data from a single source except for Cyprus. Apart from Cyprus, another two countries reported data through multiple data sources during 2008–12. In Denmark, data sources did not overlap. In the Netherlands, they overlapped in 2010–11.

2.4 Methods

This report describes invasive disease due to all serotypes of *H. influenzae* by epidemiological and laboratory variables. Only laboratory-confirmed cases of invasive Hi disease reported by Member States were considered for inclusion in the analysis, regardless of the case definition applied by countries for reporting at the national level. According to all three versions of the EU case definition, any person who meets the laboratory criteria is considered a confirmed case of invasive Hi disease. Data were analysed in accordance with the methods and rules previously described in this report (chapter 'IBD data submission, validation and analysis').

Aggregated data, reported only by Bulgaria, were included where possible. Notification rates were not calculated for Belgium because the population coverage of the Belgian sentinel surveillance system is unknown.

Trends in notification rate over time excluded countries where calculation of rates was not possible (Belgium for 2012, Cyprus for 2011, Iceland only reported in 2011, and Bulgaria uses aggregate reporting).

Serotype-specific trends only included countries that had reported information on serotype for the entire period covered in this report. The following countries were excluded:

- Austria and Spain, as they did not report serotype data in 2012.
- Lithuania, as they did not report serotype data from 2010 to 2012.
- Slovakia, as they did not report serotype information from 2009 to 2011.
- Germany and Portugal, as they did not report serotype data from 2008 to 2010.
- Latvia, as they did not report serotype data in 2009.
- France, as they did not report serotype data from 2008 to 2009.

2.4.1 Data sources

Invasive Hi disease data from countries with sentinel surveillance were treated differently depending on the availability of information on the denominator:

- For France, the population covered was available (Annex 2, Table B2) and was used as denominator for the analysis of notification rates.
- For Spain, the population coverage was reported as 33% of the total population in 2012, which was applied to the analysis of notification rates.
- For Belgium, the population coverage was unknown, so data from Belgium were excluded from the notification rates analysis.

Due to the potential overlap of data sources or changes in the surveillance system, the following criteria were applied to specific countries:

- Cyprus reported from two different data sources in 2012. Only data reported through the data source CY-NOTIFIED_DISEASES were included in this report, while data from CY-LABNET were excluded as the data were less complete. Data for 2011 were reported only from the sentinel data source CY-LABNET, for which the population coverage was unknown, thus data from Cyprus were excluded from any trend analysis.
- Denmark changed its data source used for reporting of invasive Hi cases in 2012 (DK-LAB). From 2008 to 2011 the data source DK-MIS was used. There was no difference in representativeness and no overlapping in reporting between the two data sources, thus data from both sources were included in this report.
- For the Netherlands, only data reported from the data source NL-NRBM were included in this report, while data from NL-OSIRIS were excluded because data were less complete. The NL-NRBM data source is described as voluntary and comprehensive, thus data were included in the analysis of notification rates.

2.5 Results

2.5.1 Number of cases

For 2012, 2 545 confirmed cases of invasive Hi disease were reported by 26 EU Member States and one EEA country, excluding Liechtenstein, Luxembourg and Iceland.

The overall notification rate was 0.57 cases per 100 000, ranging from 0.04 (Bulgaria, Hungary and Romania) to 2.26 (Sweden). High rates were also observed in Finland (1.50) and Norway (1.56) (Table 2.1).

Table 2.1. Number of confirmed cases and notification rates (cases per 100 000 population) of invasive *H. influenzae* disease reported in EU/EEA countries, 2008–12

Country	2008		2009		2010		2011		2012	
	N	NR	N	NR	N	NR	N	NR	N	NR
Austria	5	0.06	14	0.17	2	0.02	3	0.04	6	0.07
Belgium^	49	-	76	-	68	-	96	-	78	-
Bulgaria*	14	0.19	15	0.20	10	0.13	2	0.03	3	0.04
Cyprus+	0		2	0.25	3	0.37	1	-	8	0.93
Czech Republic	7	0.07	10	0.10	22	0.21	15	0.14	11	0.10
Denmark	32	0.58	31	0.56	43	0.78	47	0.85	65	1.16
Estonia	1	0.07	1	0.07	1	0.07	2	0.15	3	0.22
Finland	45	0.85	47	0.88	41	0.77	66	1.23	81	1.50
France#	442	0.90	417	0.86	371	0.78	492	1.04	491	1.02
Germany	160	0.20	199	0.24	224	0.27	268	0.33	319	0.39
Greece	4	0.04	13	0.12	4	0.04	1	0.01	6	0.05
Hungary	6	0.06	3	0.03	5	0.05	8	0.08	4	0.04
Ireland	22	0.50	43	0.97	26	0.58	44	0.96	41	0.89
Italy	50	0.08	56	0.09	69	0.11	47	0.08	59	0.10
Latvia	1	0.05	1	0.05	0		0		1	0.05
Lithuania	3	0.09	1	0.03	1	0.03	2	0.07	3	0.10
Malta	0		3	0.73	2	0.48	0		0	
Netherlands	109	0.66	124	0.75	144	0.87	133	0.80	139	0.83
Poland	28	0.07	19	0.05	25	0.07	22	0.06	35	0.09
Portugal	5	0.05	8	0.08	10	0.10	23	0.22	45	0.43
Romania	2	0.01	22	0.11	19	0.09	10	0.05	9	0.04
Slovakia	4	0.07	5	0.09	3	0.06	0		3	0.06
Slovenia	12	0.60	18	0.89	15	0.73	22	1.07	18	0.88
Spain#	73	0.48	53	0.35	78	0.51	77	0.50	90	0.58
Sweden	163	1.78	146	1.58	179	1.92	203	2.16	214	2.26
United Kingdom~	773	1.26	742	1.20	622	1.00	746	1.19	735	1.17
EU total	**2 010**	**0.46**	**2 069**	**0.47**	**1 987**	**0.45**	**2 330**	**0.54**	**2 467**	**0.56**
Iceland	0		0		0		2	0.63	-	-
Norway	75	1.58	71	1.48	89	1.83	85	1.73	78	1.56
Total	**2 085**	**0.47**	**2 140**	**0.48**	**2 076**	**0.47**	**2 417**	**0.55**	**2 545**	**0.57**

^ Sentinel surveillance, population coverage unknown: notification rate not included

** Aggregate reporting*

+ Cyprus in 2011 reported cases from a different sentinel data source; population coverage unknown: notification rate not included

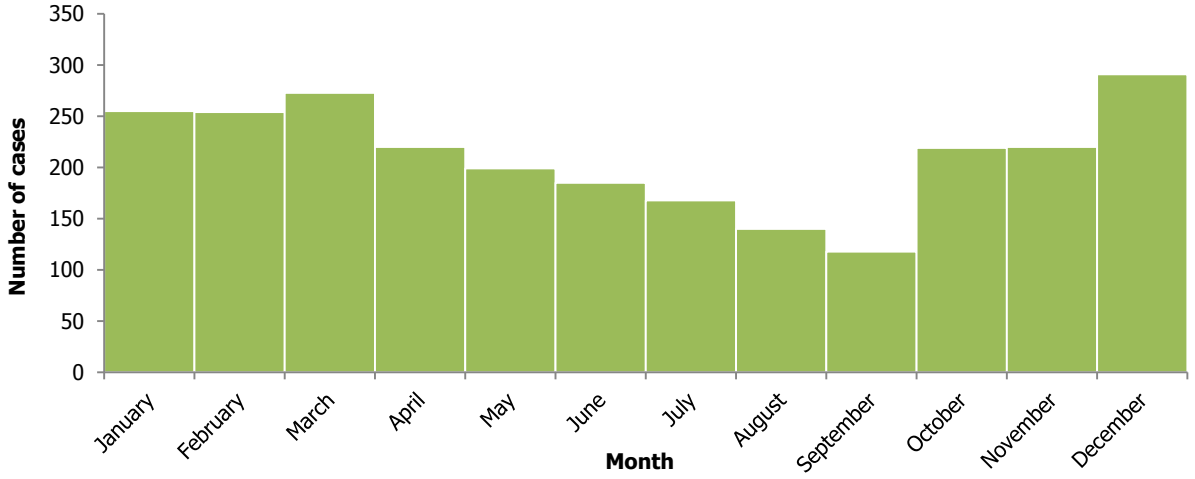
 # Sentinel surveillance, population coverage known

~ There is no single surveillance system in the UK. Representative data were submitted by England and Wales, Scotland and Northern Ireland; surveillance systems differ.

2.5.2 Seasonality

The seasonal distribution of cases of invasive Hi disease followed a pattern similar to other respiratory diseases. In 2012, the highest number of cases was observed during the winter months, peaking in March and December (Figure 2.1). Case numbers decreased in summer, as observed in previous years. Seasonality by country is presented in Annex 2, Table B3.

Figure 2.1. Distribution of confirmed invasive *H. influenzae* cases by month, in EU/EEA countries, 2012 (n=2 542)



2.5.3 Age and gender

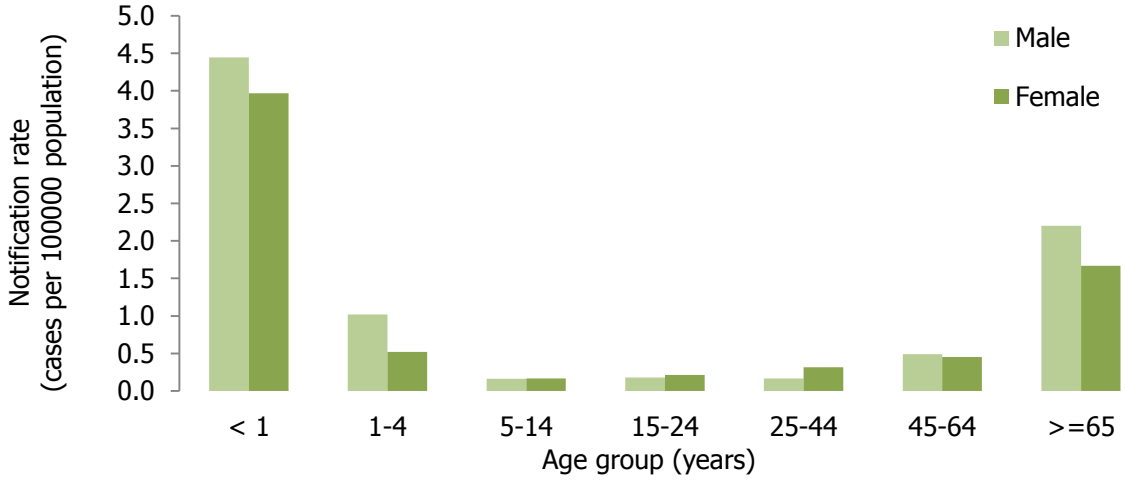
Of the 2 533 confirmed cases for which age information was provided, 55% (n=1 385) were in people 65 years or older, 30% (n=757) in adults between 25 and 64 years, and 10% (n=264) in children younger than five years. Cases 5 to 24 years of age accounted for 5% (n=127) (Annex 2, Table B4).

In countries that reported more than 20 confirmed cases, the highest proportion of cases ≥ 65 years was observed in Germany (63.3%), followed by Finland (63%), Sweden (62%) and Norway (60%). Those countries also reported that the proportion of confirmed cases in children under five years of age was below the European average, with Norway reporting the lowest proportion (0.03%). In Portugal and Poland, 20% of the confirmed cases were younger than five years. Most countries that reported a high proportion of younger cases also had a proportion of cases in older age groups below the European average (Annex 2, Table B4).

As observed in previous years, the notification rate was highest among cases < 1 year (4.2 per 100 000), followed by those ≥ 65 years (1.9 per 100 000). In other age groups, notification rates were lower than 1 case per 100 000 population (Figure 2.2; Annex 2, Table B5). During the period 2008–11, trends were stable across all age groups, with a slight increase in those 65 years and older (Figure 2.3; Annex 2, Table B6).

The overall male–female ratio was almost one, but males were overrepresented in children under five years and adults 65 years or older (Figure 2.2; Annex 2, Table B5).

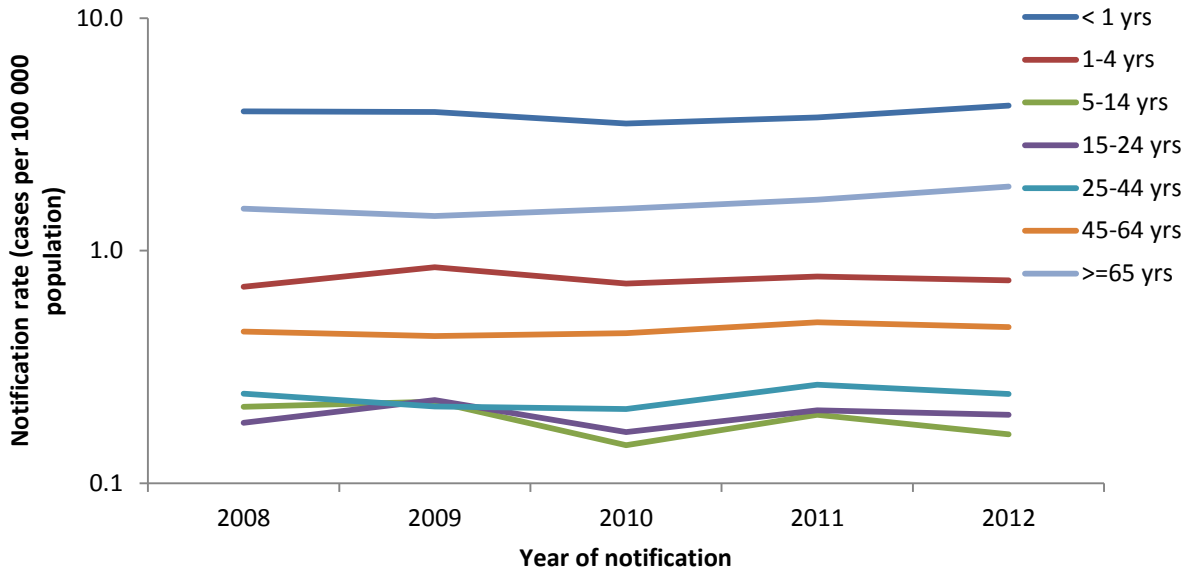
Figure 2.2. Notification rate of confirmed invasive *H. influenzae* cases by age group and gender, EU/EEA countries, 2012 (n=2 456*)



** Data from Belgium were excluded because population coverage was unknown.*

Contributing countries: Austria, Bulgaria, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

Figure 2.3. Notification rate of confirmed invasive *H. influenzae* cases by age group and year, EU/EEA countries, 2008–12 (n=10 706)



Contributing countries: Austria, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom

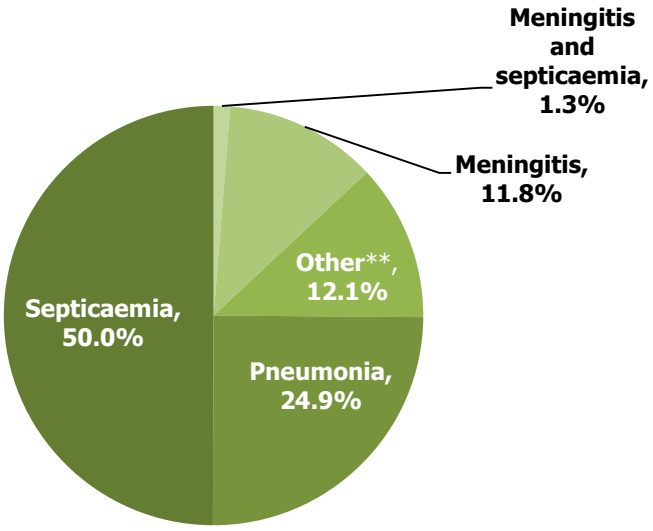
2.5.4 Clinical presentation

Data on clinical presentation were reported by 18 of 27 countries for 1 019 confirmed cases (60% missing or recorded as being 'not under surveillance').

Septicaemia was the most frequent clinical presentation accounting for 50% of cases, followed by pneumonia (25%) (Figure 2.4). France, Germany and the United Kingdom contributed 76% of these data. The United Kingdom alone contributed 68% of septicaemia cases. France reported the highest number of cases with meningitis (n=30), and about 57% of all pneumonia cases were reported by Germany. Nine of the 18 countries submitting data on clinical presentation reported less than 10 cases (Annex 2, Table B7).

Septicaemia was the most common clinical presentation across age groups, except for children between one and four years of age, in whom meningitis was the most common presentation. Pneumonia was the second most common clinical presentation in those 45 years or older, while in cases younger than 45 years meningitis was the second most common presentation (Table 2.2).

Figure 2.4. Distribution of reported invasive *H. influenzae* cases by clinical presentation, 2012 (n=1019*)



** Excludes cases with unknown clinical presentation and cases with clinical presentation reported as 'not under surveillance'.*

*** 'Other' includes cases where clinical presentation was recorded as 'other' (n=113), osteomyelitis/septic arthritis (n=5), cellulitis (n=4) or epiglottitis (n=1).*

Table 2.2. Distribution of reported invasive *H. influenzae* cases by clinical presentation and age group, EU/EEA countries, 2012 (n=1019*)

Age group (years)	Septicaemia		Meningitis		Pneumonia		Other**		Meningitis and septicaemia		Cellulitis		Osteomyelitis/ septic arthritis		Total
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N
< 1	44	65.7	10	14.9	3	4.5	7	10.4	3	4.5		0.0		0.0	67
1–4	22	34.9	23	36.5	4	6.3	11	17.5	2	3.2		0.0	1	1.6	63
5–14	10	33.3	8	26.7	4	13.3	6	20.0	1	3.3	1	3.3		0.0	30
15–24	18	72.0	1	4.0		0.0	5	20.0	1	4.0		0.0		0.0	25
25–44	54	54.5	17	17.2	13	13.1	13	13.1		0.0	1	1.0	1	1.0	99
45–64	79	44.4	25	14.0	43	24.2	26	14.6	4	2.2		0.0	1	0.6	178
≥ 65	282	50.6	36	6.5	187	33.6	46	8.3	2	0.4	2	0.4	2	0.4	557
Total	**509**	**50.0**	**120**	**11.8**	**254**	**24.9**	**114**	**11.2**	**13**	**1.3**	**4**	**0.4**	**5**	**0.5**	**1 019**

Contributing countries: Austria, the Czech Republic, Estonia, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Norway, Poland, Portugal, Romania, Slovakia, Slovenia and the United Kingdom

** Excludes 'unknown' and cases reported as NUS (not under surveillance)*

*** 'Other' includes cases where clinical presentation was recorded as 'other' (n=113) and one case reported with epiglottitis (age group 45–64 years)*

2.5.5 Case fatality rate

In 2012, 19 of 27 countries reported data on outcome. The completeness for this variable differed from country to country: in 11 countries information on CFR was available for all confirmed cases, in four countries the completeness was approximately 50% or lower.

Overall, 1 422 confirmed cases had information on outcome. The CFR in EU/EEA countries was 9.6% (95% CI: 8.2–11.3%). In eight countries, no deaths were reported. All but one country reported outcome information even if the total number of cases was below 20. Among countries reporting outcome information for 20 or more cases, the lowest CFR was observed in Portugal (CFR: 0%; 95% CI: 0–15%). The highest CFRs were reported by Italy (CFR: 18%; 95% CI: 8–34%) and Sweden (CFR: 18%; 95% CI: 13–24%), followed by Poland (CFR: 17%; 95% CI: 7–34%) (Annex 2, Table B8).

The highest CFR was observed among cases ≥ 65 years of age (12%), followed by cases < 1 year (11%) (Annex 2, Table B9). Cases with meningitis and septicaemia had the highest CFR (25%), followed by pneumonia cases (13%) and septicaemia cases (9%) (Annex 2, Table B10).

2.5.6 Vaccination status

Vaccination status was reported by 16 countries for 293 confirmed cases (missing for 88%). Vaccination status was only known for 42% (n=45) of all cases with invasive Hi disease, 71% of which (n=37) were unvaccinated, and three cases had received four vaccine doses.

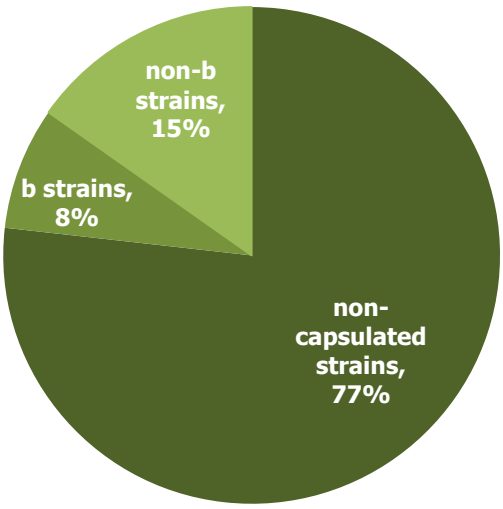
2.5.7 Serotypes

Of the 2 545 reported confirmed cases of invasive Hi disease, only 1 352 (53%) included serotype information. Non-capsulated isolates made up 77% of these cases (n=1 038), followed by non-b serotypes (15%, n=206) (Figure 2.5; Annex 2, Table B11).

Twenty countries reported serotype data, but the completeness for this variable differed widely from country to country. For 11 of these countries, non-capsulated strains made up more than 70% of the cases, with Poland and Finland reporting more than 90% of isolates as non-capsulated strains. Among countries reporting serotype information for 20 or more cases, the highest proportion of serotype b isolates was observed in the Netherlands (n=28, 20%) (Annex 2, Table B11).

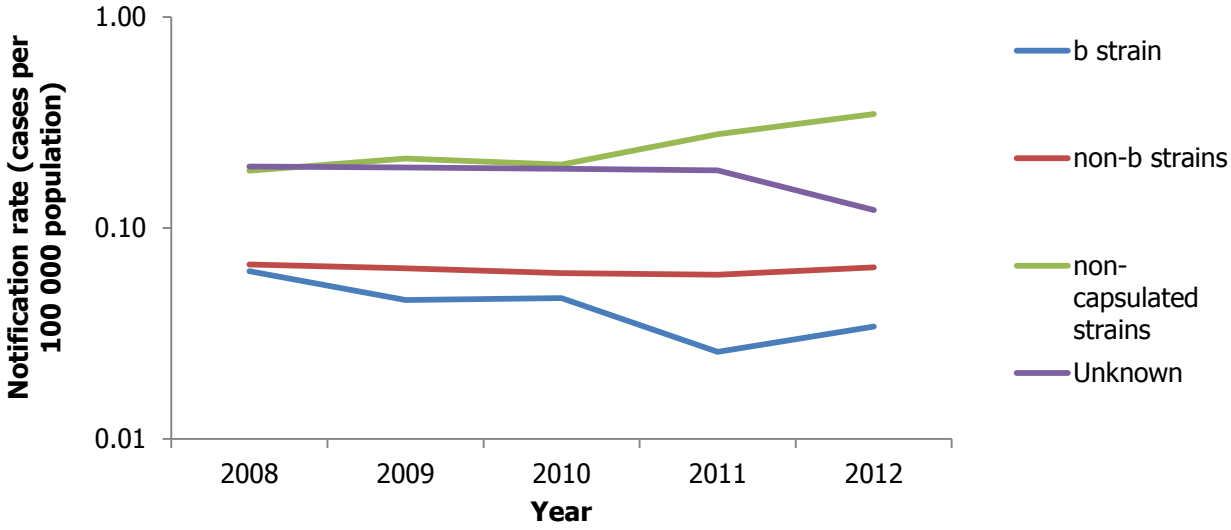
Between 2008 and 2012, a significant decrease in notification rates for serotype b was observed while rates for non-b isolates remained stable over time. The notification rate for non-capsulated strains increased from 2010 to 2012 (Figure 2.6; Annex 2, Table B12). A slight but significant decline was observed in isolates reported with unknown serotype.

Figure 2.5. Distribution of reported invasive *H. influenzae* cases by serotype, EU/EEA countries, 2012 (n=1 352)



** Non-b includes serotypes A, E, F and isolates classified as 'non-b'*

Figure 2.6. Notification rates of invasive *H. influenzae* disease in EU and EEA countries, by serotype and year, 2008–12 (n=6 933)



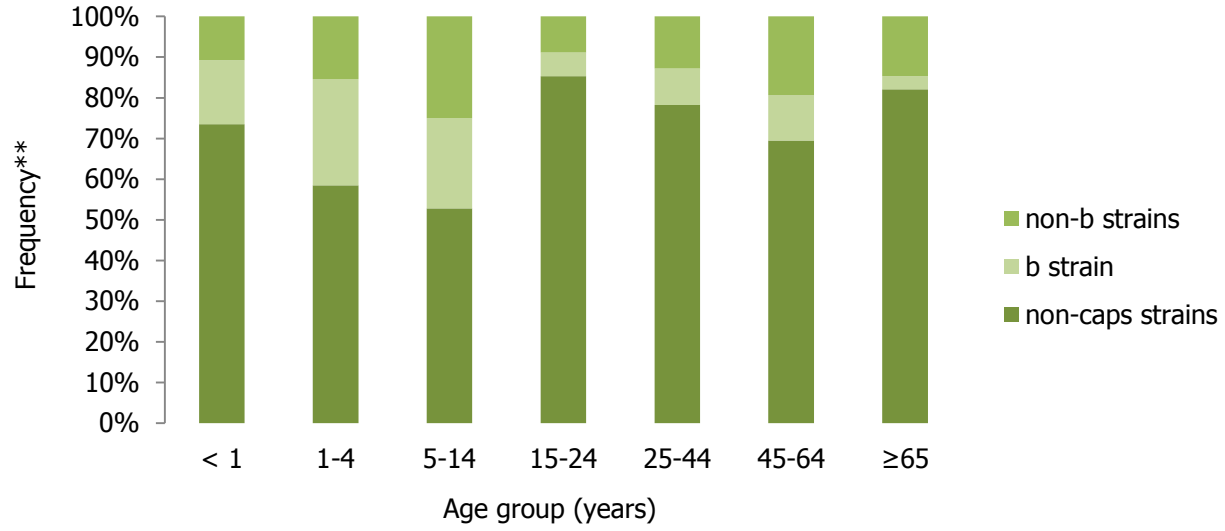
Contributing countries: Czech Republic, Denmark, Estonia, Finland, Greece, Hungary, Ireland, Italy, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovenia, Sweden and the United Kingdom

Non-b strains include serotypes A, C, D, E, F and isolates classified as 'non-b'.

Serotype and age

Non-capsulated strains were reported in > 50% of cases in all age groups, with proportions greater than 80% in those between 15 and 24 years of age (85%) and 65 years and older (82%). Serotype b was isolated in 20% of cases < 15 years and in 6% of cases ≥ 15 years of age. The highest proportion of serotype non-b cases was observed in children 5 to 14 years of age (25%), followed by adults between 45 and 64 years (19%) (Figure 2.7, Annex 2, Table B13). Serotype distribution was comparable between genders (Annex 2, Table B14).

Figure 2.7. Distribution of invasive H. influenzae serotypes by age group, EU/EEA countries, 2012 (n=1 348*)



** Four cases with missing age information had non-capsulated strains.*

*** Frequency refers to the proportion of cases for which serotype information was available by age group.*

Serotype and clinical presentation

Information on clinical presentations was available in 45% of confirmed cases with known serotype. Among cases with septicaemia and pneumonia, the serotype distribution was similar, with over 80% of cases being due to non-capsulated strains and less than 5% to serotype b. Among cases with meningitis, non-capsulated strains still accounted for the majority of cases, however serotype b was responsible for 21% (Table 2.3).

Table 2.3. Distribution of invasive *H. influenzae* serotypes by clinical presentation, EU/EEA countries, 2012 (n=615*)

Serotype	Septicaemia		Meningitis		Pneumonia		Other^		Meningitis and septicaemia		Cellulitis		Total
	N	%	N	%	N	%	N	%	N	%	N	%	N
Non-capsulated strains	331	81.1	50	61.7	60	82.2	30	75.0	4	44.4	1	25.0	476
Non-b strains**	63	15.4	14	17.3	12	16.4	6	15.0	1	11.1	1	25.0	97
b strain	14	3.4	17	21.0	1	1.4	4	10.0	4	44.4	2	50.0	42
Total	**408**		**81**		**73**		**40**		**9**		**4**		**615**

Contributing countries: Czech Republic, Estonia, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Norway, Poland, Portugal, Romania, Slovakia, Slovenia and the United Kingdom

** Clinical presentation missing in 737 cases and 'not under surveillance' in 81 cases.*

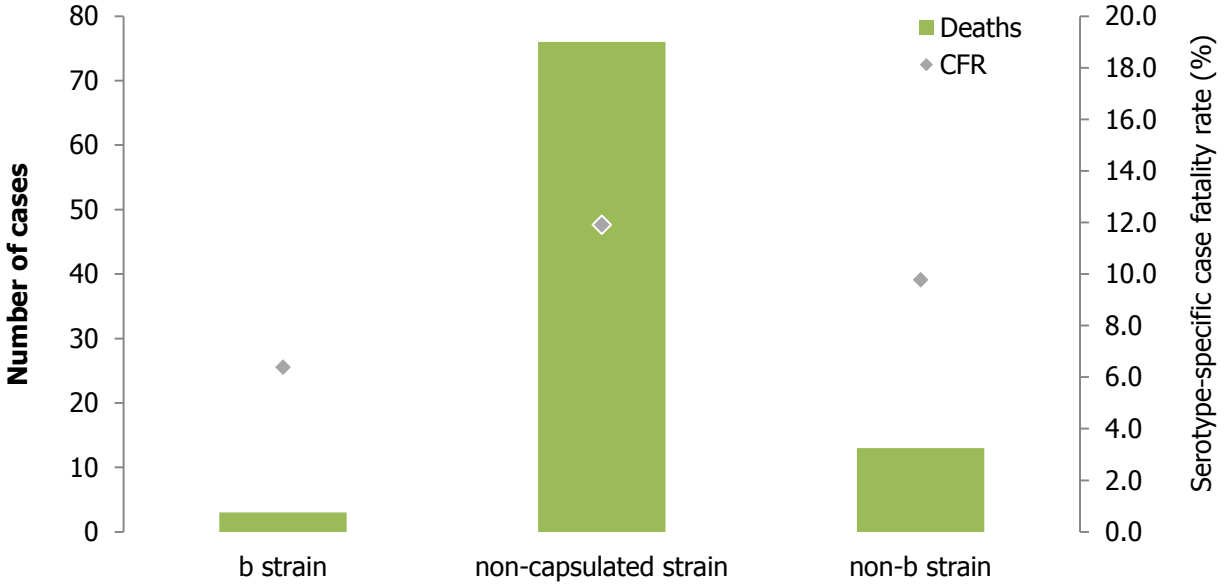
*** Non-b includes serotypes a, e, f and isolates classified as 'non-b'.*

^ 'Other' includes cases where clinical presentation was recorded as 'other' (n=39) and one non-b case reported with epiglottitis.

Serotype and case fatality

Of 137 reported deaths, 67% (n=92) had available serotype data. Non-capsulated isolates accounted for the majority of reported deaths (n=76) and had the highest CFR (12%, (95% CI: 9.5%–14.7%)), followed by non-b isolates (10%, ((95% CI: 5.3%–16.1%)). The case fatality rate for serotype b cases was (6.4%, (95% CI: 1.3%–17.5%)) (Figure 2.8).

Figure 2.8. Distribution of fatal outcome of confirmed invasive *H. influenzae* disease by serotype, and serotype-specific case fatality rate, EU/EEA countries, 2012 (n=818*)



Contributing countries: Czech Republic, Estonia, Germany, Greece, Hungary, Ireland, Italy, Latvia, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Sweden and the United Kingdom

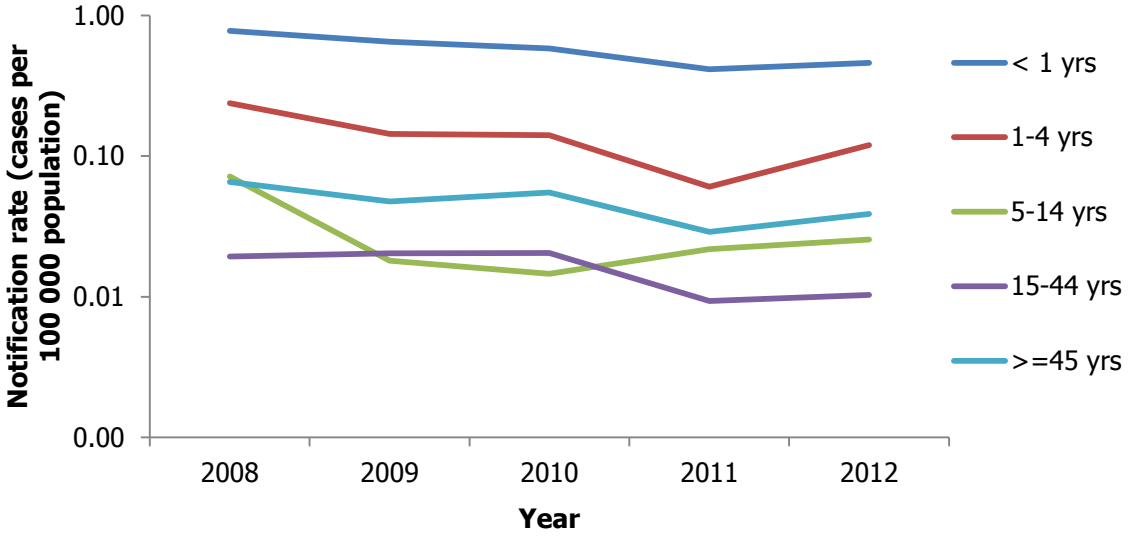
** Cases for which outcome and serotype were known.*

Serotype b strains

During 2008–12, cases below one year of age were the age group most affected by invasive Hib disease, followed by children between one and four years. Over time, notification rates decreased significantly in all age groups, except for the age group from 5 to 14 years. The largest absolute decline in notification rates was observed in children younger than one year of age (Figure 2.9; Annex 2, Table B15).

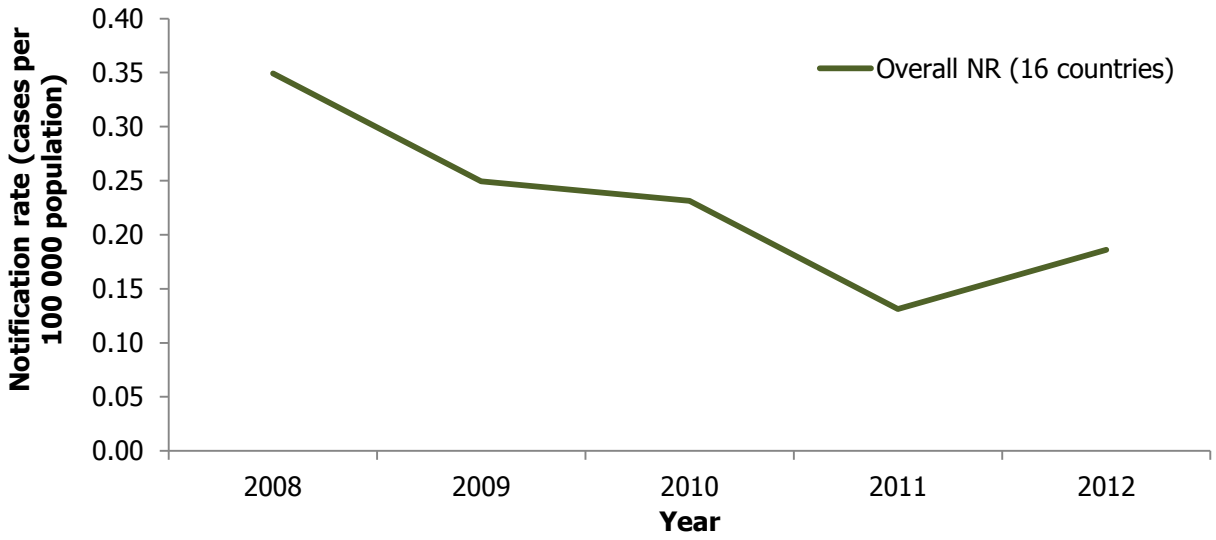
Sixteen countries reported data on serotype for all years from 2008 to 2012. The rate of invasive Hib disease among < 5-year-olds decreased by almost 50% in these countries during this period, and almost all countries reported notification rates < 1 per 100 000 population. Among these countries, Hungary, Malta and Slovenia never reported any Hib cases (Figure 2.10, Table 2.4)

Figure 2.9. Notification rate of invasive *H. influenzae* serotype b disease by age group and year, EU/EEA countries, 2008–12 (n=555)



Contributing countries: Czech Republic, Denmark, Estonia, Finland, Greece, Hungary, Ireland, Italy, Malta, the Netherlands, Norway, Poland, Romania, Slovenia, Sweden and the United Kingdom

Figure 2.10. Notification rate of invasive *H. influenzae* serotype b disease in children younger than five years of age, by year, EU/EEA countries, 2008–12 (n=162)



Contributing countries: Czech Republic, Denmark, Estonia, Finland, Greece, Hungary, Ireland, Italy, Malta, the Netherlands, Norway, Poland, Romania, Slovenia, Sweden and the United Kingdom

Table 2.4. Number of reported cases and notification rate of invasive *H. influenzae* serotype b disease in children younger than five years of age, by country and year, EU/EEA countries, 2008–12 (n=162)

Country	2008		2009		2010		2011		2012	
	N	NR	N	NR	N	NR	N	NR	N	NR
Czech Republic	1	0.19	1	0.18	0	0.00	0	0.00	0	0.00
Denmark	2	0.61	1	0.31	0	0.00	1	0.31	2	0.63
Estonia	0	0.00	0	0.00	0	0.00	1	1.27	2	2.54
Finland	1	0.34	2	0.68	0	0.00	1	0.33	3	0.99
Greece	0	0.00	2	0.36	0	0.00	1	0.18	2	0.36
Hungary	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Ireland	3	0.93	1	0.30	0	0.00	0	0.00	2	0.54
Italy	1	0.04	1	0.04	1	0.04	0	0.00	3	0.11
Malta	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00

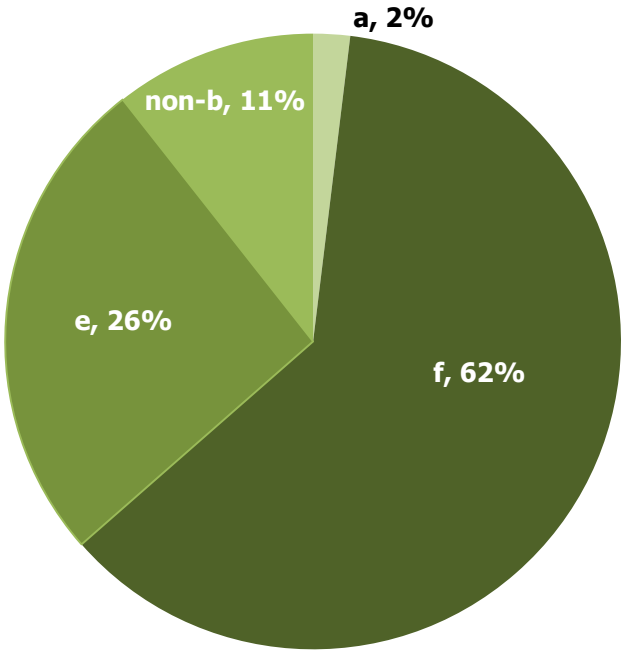
Country	2008		2009		2010		2011		2012	
	N	NR	N	NR	N	NR	N	NR	N	NR
Netherlands	7	0.74	9	0.97	9	0.97	5	0.54	7	0.76
Norway	1	0.34	1	0.34	0	0.00	1	0.32	0	0.00
Poland	7	0.38	7	0.37	7	0.36	2	0.10	0	0.00
Romania	2	0.19	0	0.00	3	0.28	1	0.09	3	0.29
Slovenia	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Sweden	0	0.00	1	0.19	5	0.91	1	0.18	1	0.18
United Kingdom	23	0.63	9	0.24	8	0.21	5	0.13	2	0.05
Total	**48**	**0.35**	**35**	**0.25**	**33**	**0.23**	**19**	**0.13**	**27**	**0.19**

Non-type b strains

In 2012, 206 cases with non-b serotypes were reported: *H. influenzae* type f was the most common non-b strain (62%), followed by serotype e (26%) (Figure 2.11).

During the period 2008–12, notification rates of Hi disease due to non-type b strains were highest among cases < 1 year of age, followed by adults 45 years and older. Trends were stable in all age groups, except in children younger than one year, in whom notification rates decreased significantly (Figure 2.12, Annex 2, Table B16).

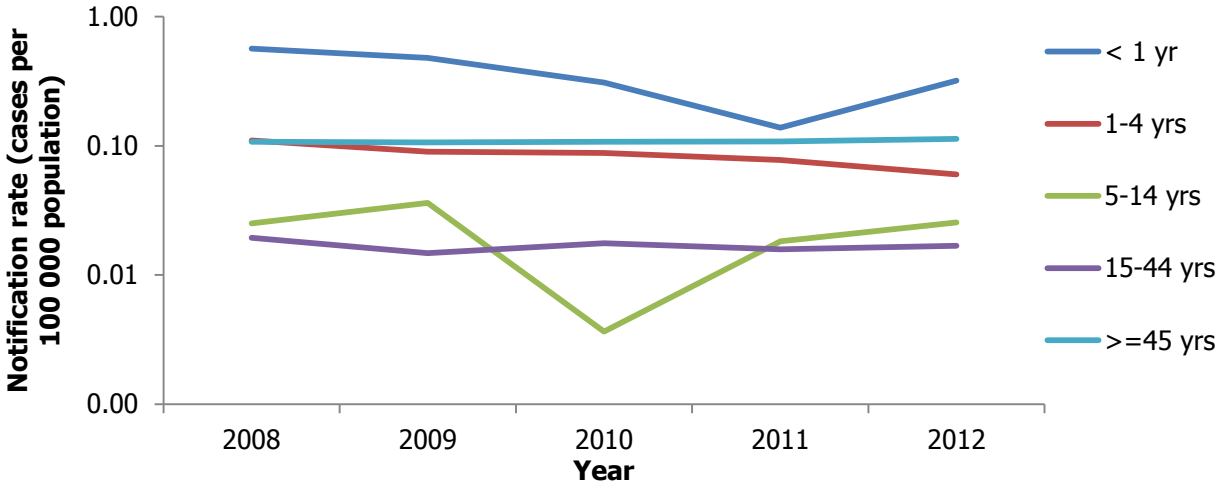
Figure 2.11. Distribution of non-b serotypes of invasive *H. influenzae* disease (n=206), EU/EEA countries, 2012



** Non-b includes all isolates that were classified just as 'non-b'.*

No cases of serotype c or serotype d H. influenzae were reported.

Figure 2.12. Notification rate of invasive *H. influenzae* non-b disease, by age group and year of reporting, EU/EEA countries, 2008–12 (n=832)

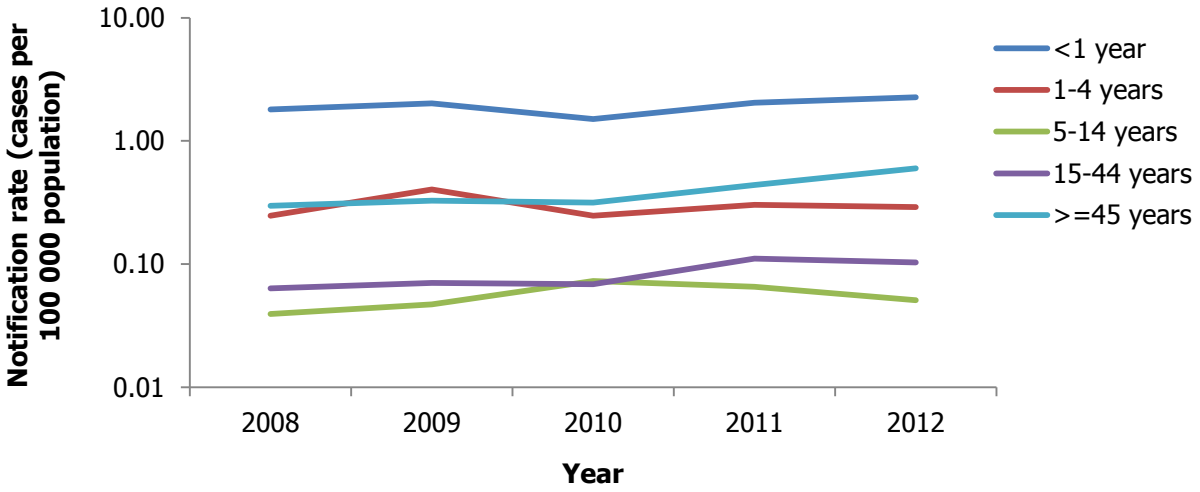


Contributing countries: Czech Republic, Denmark, Estonia, Finland, Greece, Hungary, Malta, Ireland, Italy, the Netherlands, Norway, Poland, Romania, Slovenia, Sweden and the United Kingdom

Non-capsulated strains

During 2008–12, notification rates of Hi disease due to non-capsulated strains were highest among cases < 1 year. Children between one and four years and adults older than 45 years of age were the second most affected age groups and presented similar notification rates. Age-specific trends were fluctuating and not significant, except in cases between 15 and 44 years of age, in whom a slight significant increase was observed (Figure 2.13, Annex 2, Table B17).

Figure 2.13. Notification rate of invasive *H. influenzae* (non-capsulated) disease, by age group and year of reporting, EU/EEA countries, 2008–12 (n=3 211)



Contributing countries: Czech Republic, Denmark, Estonia, Finland, Greece, Hungary, Ireland, Italy, the Netherlands, Norway, Poland, Romania, Slovenia, Sweden and the United Kingdom

2.5.8 Laboratory methods used for strain identification

Specimens

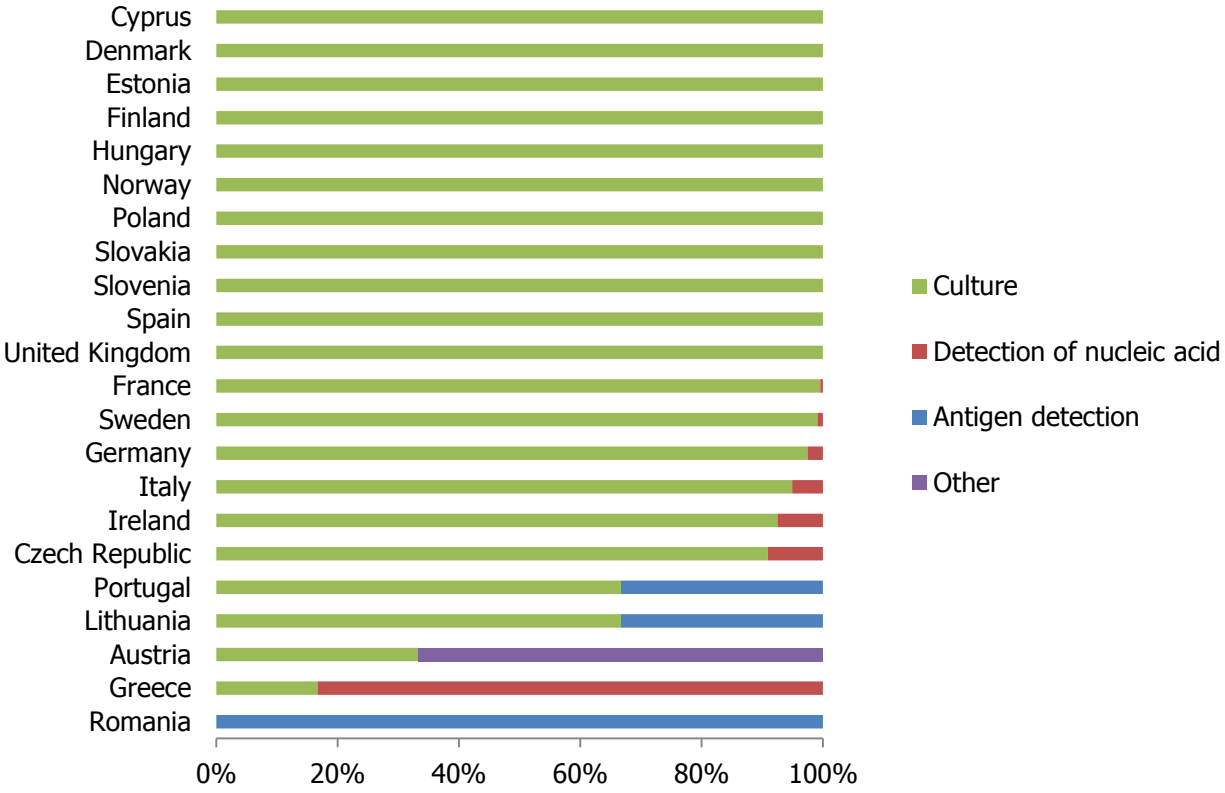
Blood isolates accounted for 89.1% (n=2 148) of cases for which the specimen was reported (n=2 410). Cerebrospinal fluid was reported in 7.5% (n=181) of cases, bronchoalveolar lavage was reported in 0.1% (n=2) of cases and 'other sterile site' in 3.3% (n=79). Seventeen countries reported specimen information for 100% of confirmed cases (Annex 2, Table B18). Blood specimens made up ≥ 80% of specimens in all age groups, except in children between one and four years of age, where the proportion of blood specimens was about 70% and the highest proportion of CSF specimens was observed (24%) (Annex 2, Table B19).

Test methods

Information on test methods was available for 85% of cases (n=2 162) from 22 countries. In 18 of 22 countries information on test methods was reported for more than 90% of confirmed cases. Laboratory methods used to detect the pathogen included: culture, serology, immunology tests, antigen detection, detection of nucleic acid, genotyping and sequencing. Among these, only culture, antigen detection and detection of nucleic acid were reported by European laboratories as primary test method used for diagnosis.

Culture was the most frequently reported method, accounting for 98% of tests, and the only method performed on all types of specimens and reported by 22 countries (Figure 2.14). The second most frequent diagnostic test was detection of nucleic acid, which accounted for a mere 1% of performed tests.

Figure 2.14. Proportion of diagnostic tests used on primary specimen for cases reported as invasive *H. influenzae* disease by country, EU/EEA countries, 2012 (n=2 162)



2.5.9 Data quality

Data on serotypes were reported by 20 countries for 53% of confirmed cases: Austria, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Ireland, Italy, the Netherlands, Norway, Poland, Portugal, Romania, Slovenia, Spain, Sweden and the United Kingdom.

In 2012, data on age, age in months, gender, classification and specimen were complete, or almost complete, although there was a slight increase in the amount of missing data for these and other variables. Only 20 countries reported outcome, accounting for 56% of cases. Test method, vaccination status and clinical presentation were highly incomplete, with information missing for more than 60% of cases (Annex 2, Table B20).

2.6 Discussion

In 2012, 2 545 confirmed cases of invasive Hi disease were reported by 27 EU/EEA countries. Invasive Hi disease has become rare in Europe, with an overall notification rate of 0.57 per 100 000 population. As in previous years, higher rates were observed in north-west Europe. This may be due to better case ascertainment and reporting. The highest notification rates for invasive Hi disease are still reported for children under one year of age (4.2 per 100 000), followed by adults ≥ 65 years of age (1.9 per 100 000). Notification rates in all countries should be interpreted and compared cautiously due to the diversity of surveillance systems and variations in the representativeness of their data.

As in the previous years, the majority of cases suffered from septicaemia. It was the most common clinical presentation in all age groups, except for cases between one and four years of age, for whom meningitis was the most common presentation. Pneumonia was the second most common clinical presentation in cases above 45 years of age; in cases below 45 years of age, meningitis was the second most common clinical presentation. Capsulated serotypes were more prominent in cases of meningitis, whereas non-capsulated strains were more commonly associated with septicaemia and pneumonia. Clinical presentation is known to be associated with different serotypes and strongly related to age [52,53]. However, these results must be interpreted with caution as data on clinical presentation were missing for 60% of cases. Moreover, the reported clinical presentations may be affected by the data collection and reporting procedures in place at the national level.

The overall case fatality rate was 9.6% (95% CI: 8.2%–11.3%), slightly lower than what has been observed in other surveillance systems [11]. CFR varied markedly between different countries, however, 11 countries reported CFR even if case numbers were below 20. These figures should be interpreted cautiously as data for outcome were only reported for 56% of cases and only by 19 of 27 countries. Moreover, there is no common definition of the point in time at which a fatal outcome is determined. Regarding vaccination status, the completeness of the variable also needs to be improved so that more accurate conclusions can be drawn.

Prior to the introduction of conjugate vaccines, Hib was the predominant serotype causing invasive disease in children and accounted for more than 80% of patients with invasive Hib disease [15]. Non-b serotypes were only of anecdotal interest in Europe [39], and ncHi strains were a minor cause of invasive disease [14, 16], mainly affecting adults.

In 2012, the overall notification rate for serotype b infection in Europe was 0.03 per 100 000. However, Hib still caused 20% of all invasive Hi infections in children younger than five years. During 2008–12, Hib rates continued to decrease, particularly in cases below five years of age. No increasing trends have been observed in adults. The rate of invasive Hib disease among children below five years of age is used as the main indicator of the burden of disease; between 2008–12, almost all countries reported notification rates < 1 per 100 000 population in young children.

In agreement with other studies [45,50,51], data presented in this report confirm the sustained declines in invasive Hib infection in children and across all age groups due to the introduction of the Hib conjugate vaccine into national immunisation schedules in Europe. The success of Hib conjugate vaccines raises the important question about serotype replacement as a consequence of the conjugated Hib vaccine [41–44].

Among encapsulated non-b Hi serotypes reported in 2012, Hif was predominant (62%), as observed elsewhere [42,45,48,49], however, the overall notification rates for non-b isolates remained stable over time, with the exception of a significant decrease observed in children under one year of age.

In the Hib vaccine era, ncHi strains have become the main cause of invasive Hi infection in Europe, as observed in several countries [2–5, 8–12]. In 2012, ncHi strains were responsible for 77% of all confirmed invasive Hi cases. They were predominant across all age groups and associated with the highest serotype-specific CFR (12%) [39,44]. The increasing trend in notification rates for ncHi strains between 2008 and 2012 may be partly explained by the slight decline observed in the number of reported isolates with unknown serotype. An upward trend was observed in cases between 15 and 44 years, but not in other age groups. The emerging role of invasive disease due to ncHi strains is intriguing because such strains have traditionally been considered relatively non-invasive [55]. The increase may be partly explained by changes in surveillance systems overtime, particularly the extension of enhanced surveillance, greater awareness of the disease and an increase in the culturing of blood isolates [56].

A better understanding of the epidemiology of ncHi serotypes is needed, especially since a licensed 10-valent pneumococcal vaccine conjugated to the immunogenic outer membrane protein D of *H. influenzae* may potentially prevent ncHi disease in children and high-risk adults [48].

The prevention of invasive Hib disease through immunisation is a great public health achievement; however *H. influenzae* still represents an important public health problem, particularly in infants and children, and invasive Hi disease remains a major source of illness and death.

Surveillance of Hi disease is essential to monitor shifts in disease incidence, understand the burden of invasive Hi disease, and develop public health prevention strategies. At the European level, more robust surveillance data are needed if serotype replacement, Hib vaccine failure, and the epidemiology of ncHi and non-b strains are to be accurately assessed, particularly with regard to data on serotype, clinical presentation, outcome and vaccination status.

3 Invasive meningococcal disease

3.1 Summary

Overall, 3 463 confirmed cases of invasive meningococcal disease (IMD) were reported by 28 EU/EEA countries for 2012. The notification rate was 0.68 cases per 100 000 population, with the majority of Member States reporting < 1 case per 100 000. There was a notable decrease among cases under one year of age (21.7 per 100 000 in 2008, 11.4 in 2012) and also a small decrease in cases between one and four years (4.7 in 2008, 3.7 in 2012); however, infants remained the most affected age group. Notification rates were lower in older age groups, with a small peak in adolescents and young adults (15–24-year-olds).

Data on clinical presentation were missing for 52% of cases. Meningitis occurred in 43% of cases with known clinical presentation. There was no association between clinical presentation and serogroup. The overall CFR in EU/EEA countries was 7.9% (95% CI: 7.0%–8.9%). Case fatality was highest in the elderly (14%). This observation should be interpreted with caution, as there is no common approach in Europe to the follow-up time or endpoint for fatal outcome of IMD.

Sixty-eight percent of all cases of IMD were caused by serogroup B, although this serogroup showed an overall decreasing trend and has decreased in all age groups since 2008. The dominance of serogroup B was most pronounced in infants (83% of cases, 8.9 per 100 000) and 1–4-year-olds (9% of cases, 2.9 per 100 000). Among infants, the downwards trend was associated particularly with a reduction in cases in the United Kingdom.

Serogroup C accounted for 17% of cases in 2012. Notification rates were highest in infants < 1 year (1.1 per 100 000) and in 1–4-year-olds (0.31 per 100 000), but were significantly lower than for cases of serogroup B infection in the same age groups. The CFR among cases with serogroup C IMD (14%) was almost twice as high as for serogroup B. During 2008–12, a slight overall decrease in the number of serogroup C infections was observed. In 2012, 15 of 28 reporting EU/EEA countries recommended immunisation against IMD. Notification rates of serogroup C disease were higher in countries without meningococcal C conjugate (MCC) vaccination. This difference was greatest in the 1–4-year-old age group. From 2008 to 2012, a downward trend was observed in cases of serogroup C infection below five years of age. The same downward trend was observed in the 5–14-years age group in countries that introduced MCC after 2008. A stable trend was observed in countries without MCC vaccination.

There was an increasing trend in serogroup Y, although the notification rate remains very low. Improved surveillance and the availability of molecular typing for this serogroup may be partly responsible for this increase. Serogroup A has largely disappeared from Europe.

In 2012, three main clones were responsible for severe IMD in Europe: ST-32, ST-11 and ST-41/44. Serogroup B was mostly associated with clonal complex ST-41/44, ST-32 and ST-269, serogroup C cases with clonal complex ST-11, and serogroup Y cases with clonal complex ST-23 (86%). The highest variability in PorA genotypes was associated with isolates of serogroup B and the lowest with serogroup W.

IMD appears to be rare in Europe, and the development of a serogroup B vaccine provides the potential to further reduce the incidence of this disease. There was a high proportion of missing data for some variables including vaccination status, clinical presentation, antimicrobial resistance and molecular characterisation. Results based on any of these variables must be interpreted with caution, and reporting of these variables should be improved.

Surveillance systems for IMD in EU/EEA countries, 2012

- 28 countries reported invasive IMD cases at EU level in 2012.
- 28 reported data from a single source.
- 27 reported case-based data.
- 24 countries described a passive surveillance system.
- 23 have a compulsory and comprehensive surveillance system in place.
- One country has a sentinel surveillance system.
- 15 countries applied the EU 2008 case definition.
- 21 countries submitted data reported by laboratories, physicians and/or hospitals.
- Three countries have laboratory-based surveillance systems.
- Four countries submitted data reported only by physicians and/or hospitals.

3.2 Introduction

Invasive meningococcal disease (IMD) is caused by the bacterium *Neisseria meningitidis*, a common commensal of the upper respiratory tract, for which human carriers are the only reservoir. *N. meningitidis* is a major cause of meningitis and septicaemia in children and adults throughout the world and is also carried in the nasopharynx of otherwise healthy humans.

IMD is an acute disease, rare but severe and potentially life-threatening. It occurs most frequently in young children and the elderly, with smaller peaks often reported in adolescents and young adults. It may be characterised by meningitis, bacteraemia, sepsis, or, less commonly, pneumonia, arthritis and pericarditis. The case fatality rate is high, and 10–20% of survivors suffer from long-term sequelae including loss of limbs, hearing loss and mental retardation [57]. Timely, appropriate antibiotic therapy can cure IMD. Moreover, timely detection of cases is important to prevent secondary cases by offering prophylaxis to close contacts of cases.

The capsular polysaccharide, which is the immunological basis for serogrouping, plays an important role in virulence. At least 13 serogroups have been defined by the serological specificity of the bacterial polysaccharide capsule, with five (A, B, C, Y and W) being responsible for over 90% of severe meningitis and septicaemia cases [71]. All five serogroups have the potential to cause outbreaks under the right circumstances [71]. Besides the capsular polysaccharide serogroup antigens, other important structures widely studied in meningococci are the outer membrane proteins (OMP), subcapsular proteins which contain the serotype, and serosubtype antigens, useful markers which form the basis for strain characterisation [76].

The epidemiology of meningococcal disease varies throughout the world. Most disease in Africa is caused by serogroup A, although serogroup C, W-135 and X outbreaks have been described [71]. In Europe and other industrialised regions, serogroups B and C remain the major cause of IMD.

Primary prevention through implementation of effective vaccination programmes is seen as key to controlling IMD. Polysaccharide vaccines against serogroups A and C are available and have been widely used, often in combination with serogroup Y and W-135 components. These vaccines, however, are poorly immunogenic in young children and infants due to their inability to mount mature anamnestic immune responses to the meningococcal capsule [71]. This has been overcome by conjugating the capsular polysaccharide to a protein carrier, which forms the basis of the meningococcal serogroup C conjugate (MCC) vaccines.

In 1999, in response to the increasing incidence of serogroup C disease from the mid-1990s, the UK became the first country to introduce MCC vaccines into the routine schedule. MCC vaccine has since proved effective in reducing the burden of serogroup C IMD. Evidence suggests that MCC vaccination in adolescents and young adults contributes to maintaining herd immunity within the population [62,77]. In 2012, 15 European countries recommended vaccination with MCC vaccine in their routine national immunisation programmes, eight of them offering vaccination after 11 years of age[12]. Since several countries have introduced MCC vaccine into their immunisation programmes, a decrease has been observed in the burden of IMD [58–60].

A quadrivalent protein–polysaccharide conjugate vaccine offering protection against serogroups A, C, W and Y, has also been licensed for persons between 11 and 55 years of age in the USA and in Europe and provides effective protection against these serogroups [78]. Recently, a vaccine against group B disease was granted a licence from the European Commission[13] and was approved in the UK in March 2014 by the Joint Committee on Vaccination and Immunisation (JCVI) but has not yet been implemented in the UK childhood vaccination programme.

3.3 Data sources and case definition

In 2012, 27 EU Member States and one EEA country notified cases of IMD to TESSy. Liechtenstein and Iceland did not report to TESSy.

According to the data provided, 24 countries had a compulsory and comprehensive surveillance system in place; in Belgium, Denmark and Italy the system was voluntary and comprehensive, and only Cyprus had a voluntary sentinel surveillance system with unknown national coverage. There was no single surveillance system in the United Kingdom, with data collected separately in England, Northern Ireland, Scotland, and Wales. Data from the United Kingdom were reported through one data source to TESSy, although surveillance systems in these four countries differ (Annex 3, Table C1).

Most countries reported to have a passive surveillance system for IMD, but four countries (Belgium, Cyprus, the Czech Republic and Slovakia) described their systems as active.

[12] http://vaccine-schedule.ecdc.europa.eu/Pages/Scheduler.aspx

[13] http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/002333/WC500137857.pdf

Data on IMD were reported by laboratories as well as physicians and/or hospitals in 20 countries. In three countries, data were reported only by laboratories (Belgium, Cyprus and Denmark), and in five only by physicians and/or hospitals (Italy, Luxembourg, Romania and Spain). Case-based data were submitted by all countries except for Bulgaria.

Case definitions differed from country to country, with the majority (n=15) applying the 2008 EU case definition. Two countries (Luxembourg and Portugal) were still applying the 2002 EU case definition, and six (Italy, Latvia, Norway, Slovakia, Sweden and the United Kingdom) have moved to the 2012 EU case definition. The case definition was not reported or reported as 'other' in the remaining five countries.

The 2002 EU case definition required a clinical picture compatible with IMD in addition to laboratory confirmation to constitute a confirmed case. Possible cases and asymptomatic carriers were not supposed to be reported. Starting in 2008, the clinical presentation was better defined and considered relevant for classification of possible and probable cases, but not for confirmed cases, which had to meet the laboratory criteria. In 2012, clinical criteria for case classification were redefined; the laboratory criteria did not change.

In 2012, all countries reported data from a single source. During 2008–12, five countries (Cyprus, Denmark, Spain, Latvia and the Netherlands) reported through multiple data sources. In Cyprus and Denmark, there was no overlap between these sources.

3.4 Methods

This report describes invasive disease due to *N. meningitidis* (IMD) by epidemiological and laboratory variables. Only laboratory-confirmed cases of IMD were considered for inclusion in the analysis, independently of the case definition applied by countries for reporting at national level. According to all three EU case definitions, any person meeting the laboratory criteria is considered a confirmed case of IMD. Data were analysed in accordance with the methods and rules previously described in this report (chapter 'IBD data submission, validation and analysis').

Aggregated data, reported only by Bulgaria, were included where possible. Notification rates were not calculated for Cyprus which operates a sentinel surveillance system with unknown population coverage.

Age-specific trends were analysed for the period 2008–12 but only for countries for which rates could be calculated. The following countries were excluded from trend analysis:

- Cyprus, as calculation of rates was not possible for 2011–12
- Bulgaria because of aggregate reporting
- Iceland, as it did not report for 2012.

For serogroup-specific trends, the same rules were applied. Moreover, only countries reporting information on serogroup for all years covered in this report were included.

3.4.1 Data sources

Due to the potential overlap of data sources or system changes over time, data from certain countries were treated as follows:

- Cyprus changed its surveillance system after 2010. The sentinel system in place in 2012 had unknown coverage, thus data from Cyprus were excluded from the trend analysis.
- Denmark changed the data source used for reporting IMD in 2012. The representativeness did not change and data sources did not overlap, so data from both sources were included in this report.
- In Spain, data were reported from two different sources during 2008–11. Data from 'ES-STATUTORY_DISEASES' were used for the analysis (2008–11) of variables such as number of confirmed cases, age, gender, clinical presentation and vaccination status. Data from 'ES-NRL' were used for the analysis (2008–11) of laboratory variables, such as MIC results, strain characterisation, specimens and test methods. In 2012, Spanish data were submitted only from the 'ES-STATUTORY_DISEASES' data source.
- In Latvia, two data sources overlapped during 2008–09 leading to cases being duplicated, thus the data source 'LV-Laboratory' was excluded from analysis.
- In the Netherlands two data sources overlapped during 2008–11. As in previous reports, only data reported from the data source 'NL-OSIRIS' were included in this report. 'NL-OSIRIS' was the only data source used for reporting in 2012.

3.5 Results

3.5.1 Number of cases

For 2012, 3 463 confirmed cases of IMD were reported by 27 EU Member States and 1 EEA country, excluding Liechtenstein and Iceland.

The overall notification rate for confirmed cases was 0.68 per 100 000, ranging from 0.11 (Bulgaria) to 1.76 (Lithuania). High rates were also observed in the United Kingdom (1.37) and Ireland (1.31) (Table 3.1).

Table 3.1. Number and notification rate (per 100 000 population) of confirmed IMD cases by year and country, EU/EEA, 2008–12

Country	2008		2009		2010		2011		2012	
	N	NR	N	NR	N	NR	N	NR	N	NR
Austria	84	1.01	89	1.07	85	1.01	49	0.58	56	0.67
Belgium	110	1.03	104	0.97	96	0.89	111	1.01	115	1.04
Bulgaria*	20	0.27	16	0.21	8	0.11	13	0.18	8	0.11
Cyprus^	2	-	1	-	1	-	1	-	6	-
Czech Republic	82	0.79	80	0.77	60	0.57	63	0.60	59	0.56
Denmark	63	1.15	71	1.29	66	1.19	72	1.29	56	1.00
Estonia	6	0.45	5	0.37	2	0.15	7	0.52	6	0.45
Finland	28	0.53	33	0.62	34	0.64	34	0.63	33	0.61
France	657	1.03	606	0.94	511	0.79	563	0.87	550	0.84
Germany	451	0.55	493	0.60	384	0.47	370	0.45	354	0.43
Greece	78	0.70	77	0.68	55	0.49	52	0.47	59	0.53
Hungary	30	0.30	37	0.37	37	0.38	67	0.68	51	0.52
Ireland	152	3.45	134	3.01	98	2.19	89	1.95	60	1.31
Italy	178	0.30	181	0.30	150	0.25	152	0.25	136	0.22
Latvia	7	0.32	4	0.18	5	0.24	2	0.10	4	0.20
Lithuania	48	1.49	39	1.23	48	1.53	42	1.38	53	1.76
Luxembourg	2	0.41	3	0.61	1	0.20	2	0.39	3	0.57
Malta	3	0.74	5	1.22	2	0.48	6	1.45	3	0.72
Netherlands	162	0.99	150	0.91	143	0.86	106	0.64	109	0.65
Poland	321	0.84	301	0.79	228	0.60	282	0.73	238	0.62
Portugal	60	0.58	65	0.63	79	0.76	77	0.74	69	0.65
Romania	104	0.51	102	0.50	52	0.26	68	0.34	71	0.35
Slovakia	48	0.89	39	0.72	37	0.69	21	0.39	31	0.57
Slovenia	24	1.19	15	0.74	9	0.44	13	0.63	9	0.44
Spain#	590	1.29	533	1.15	404	0.87	431	0.92	335	0.72
Sweden	49	0.53	65	0.70	67	0.72	68	0.72	103	1.09
United Kingdom~	1 355	2.22	1190	1.93	1 008	1.62	1 036	1.66	862	1.37
EU total	**4 714**	**0.95**	**4 438**	**0.89**	**3 670**	**0.74**	**3 797**	**0.76**	**3 439**	**0.69**
Iceland	2	0.63	5	1.57	2	0.63	2	0.63	-	-
Norway	36	0.76	44	0.92	39	0.80	37	0.75	24	0.48
Total	**4 752**	**0.95**	**4 487**	**0.89**	**3 711**	**0.74**	**3 836**	**0.76**	**3 463**	**0.68**

** Aggregated reporting*

^ Sentinel surveillance, population coverage unknown, so notification rate not included.

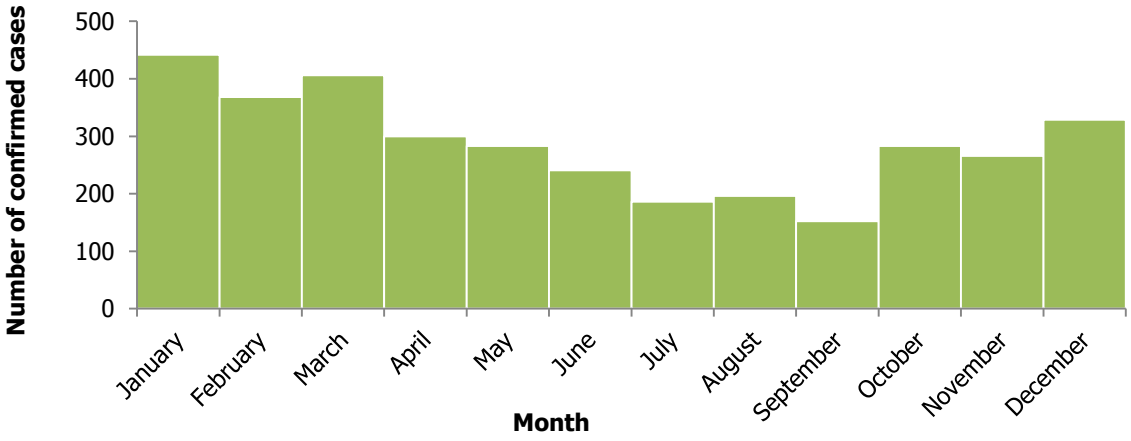
 # Only data from the data source 'ES-STATUTORT_DISEASES' were included in this report

~ There is no single surveillance system in the UK. Data are representative (as submitted by England, Wales, Scotland and Northern Ireland), but surveillance systems are different.

3.5.2 Seasonality

In 2012, most confirmed IMD cases occurred in winter, similar to other respiratory diseases. IMD cases peaked in January, and the lowest number of cases was reported in September (Figure 3.1). Previous years were characterised by a similar seasonal pattern, with the highest notification rates during winter and a marked decrease during summer. Seasonality by country is presented in Annex 3, Table C2.

Figure 3.1. Distribution of confirmed IMD cases by month, EU/EEA countries, 2012 (n=3 452*)



** 'Number of cases by month' was not reported by Luxembourg (three cases) and Bulgaria (eight cases).*

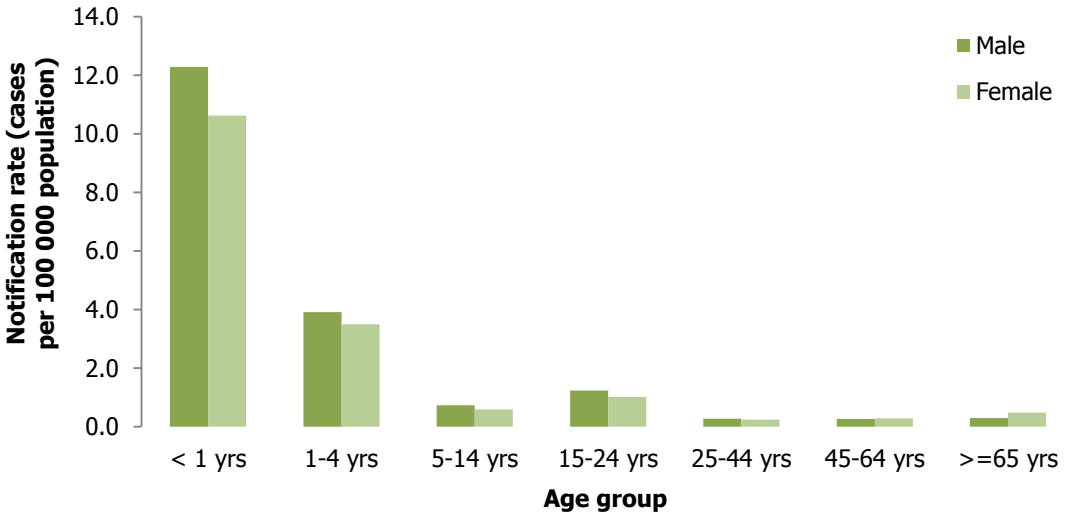
3.5.3 Age and gender

Information on age was available for 3 450 confirmed cases. The highest proportion of confirmed cases was in children younger than five years of age (40%, n=1381), followed by the age group 15–24 years of age (19%, n=672) (Annex 3, Table C3). The highest notification rate was reported among children below one year of age (11.4 cases per 100 000) and between one and four years of age (3.7 cases per 100 000) (Annex 3, Table C4).

Of the 3 449 confirmed cases where gender information was specified, 51.9% (n=1 789) were male, corresponding to a male–female ratio of almost 1. Males showed higher rates than females in all age groups ≤ 24 years of age, especially in children younger than one year (Figure 3.2; Annex 3, Table C5).

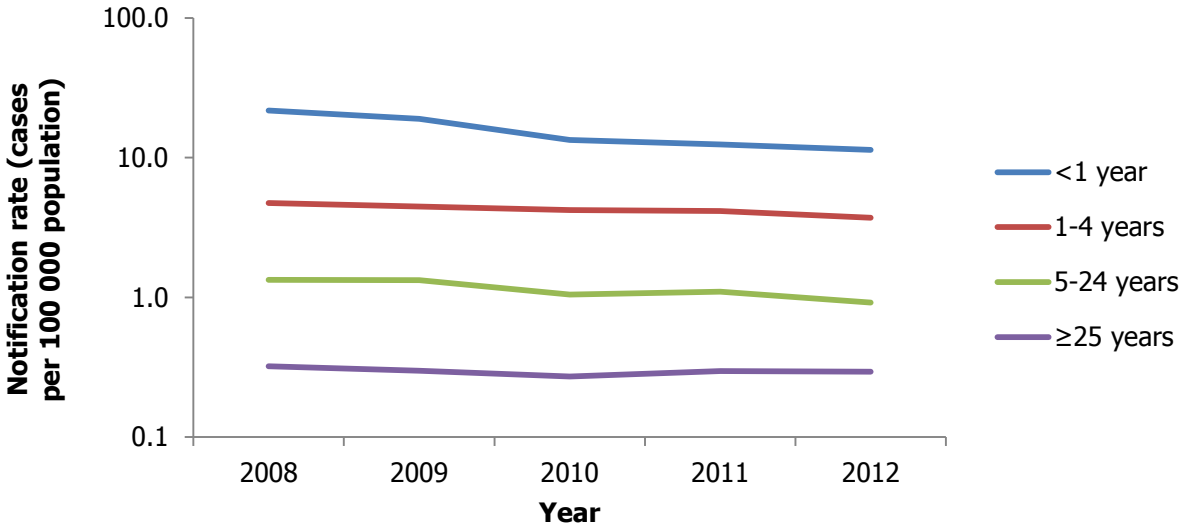
There was no change in age distribution over the period 2008–12, characterised by a decrease in rates with increasing age (Figure 3.3; Annex 3, Table C4). A significant steady decrease in notification rates was observed in cases younger than 1 year of age. Notification rates in children between one and four years of age and in the 5–24-year age group showed a similar trend, with a slight decrease observed after 2010. No changes in trend were observed in age groups above 24 years.

Figure 3.2. Notification rate of confirmed IMD cases by age group and gender, EU/EEA countries, 2012 (n=3 439)



Contributing countries: all reporting countries except for Cyprus (population coverage unknown)

Figure 3.3. Notification rate of confirmed IMD cases by age group and year, EU/EEA countries, 2008–12 (n=20 055*)



Contributing countries: Austria, Belgium, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom

** Excludes aggregated data if different age groups were reported.*

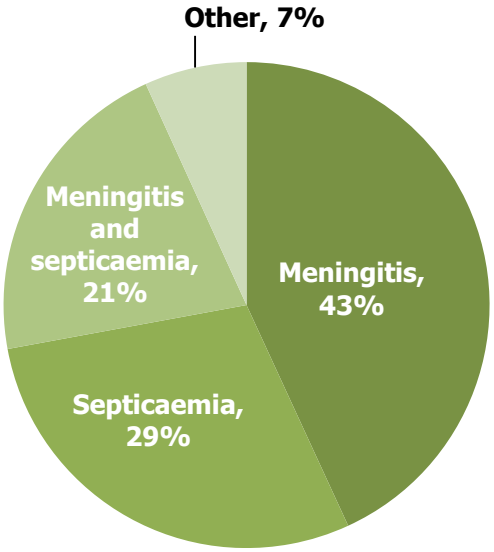
3.5.4 Clinical presentation

Of the 1 674 cases for which the clinical presentation was known (52% missing or recorded as 'not under surveillance'), meningitis was the most frequent clinical presentation, accounting for 43% of all cases, followed by septicaemia (29%) (Figure 3.4). In two countries, clinical presentation was not under surveillance, and five countries did not collect this information.

Among countries reporting clinical presentation (21 out of 28 IMD-reporting countries), all countries reported at least one meningitis case. Eighteen countries reported at least one case of septicaemia, the second most frequent clinical presentation (Annex 3, Table C6). Only two confirmed IMD cases (18 and 84 years of age) presented with pneumonia and were described together with cases whose clinical presentation was reported as 'other'.

Meningitis was the most common clinical presentation in almost all age groups, followed by septicaemia. In those over 64 years of age, septicaemia was the most and meningitis the second most frequently reported clinical presentation (Table 3.2).

Figure 3.4. Distribution of confirmed IMD cases by clinical presentation, EU/EEA countries, 2012 (n=1 674*)



** Excludes cases reported as 'clinical presentation not under surveillance' and aggregated data if different age groups were reported.*

Contributing countries: Austria, Belgium, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom

Table 3.2. Distribution of confirmed IMD cases by clinical presentation and age group, EU/EEA countries, 2012 (n=1 666)

Age group (years)	Septicaemia		Meningitis		Meningitis and septicaemia		Other		Total
	N	%	N	%	N	%	N	%	N
< 1	87	31	106	38	72	26	14	5	279
1–4	120	32	134	36	97	26	19	5	370
5–14	54	29	84	46	34	18	12	7	184
15–24	71	21	178	53	61	18	28	8	338
25–44	43	22	111	56	32	16	12	6	198
45–64	42	27	68	43	34	22	14	9	158
≥ 65	66	47	38	27	20	14	15	11	139
Total	**483**	**29**	**719**	**43**	**350**	**21**	**114**	**7**	**1 666**

3.5.5 Case fatality rate

Twenty-five of 28 countries reported data on outcome for 92% of confirmed IMD cases. In 20 countries, the completeness was higher than 90%, and in one country it was lower than 70%. Deaths were reported from 20 countries (Annex 3, Table C7). The overall CFR in EU/EEA countries was 7.9%, calculated on the basis of 3 185 confirmed IMD cases with known outcome. Among countries reporting outcome for more than 10 confirmed cases and with a completeness exceeding 90%, 5 of 15 reported a CFR lower than 8%, and seven a CFR ranging between 10% and 14%. In all countries reporting outcome for more than 100 confirmed cases, the CFR was lower than 10% (range 4.2%–9.7%). The highest CFR was observed in Latvia (25%), but the number of cases reported was very low (n=4).

Among confirmed cases with information on clinical presentation and outcome (n= 1 563), the highest CFR was reported among cases presenting with septicaemia (18.8%), followed by cases with meningitis and septicaemia (11.1%). One of the two confirmed cases presenting with pneumonia died (Annex 3, Table C8). Information on age and outcome was available for 3 175 confirmed cases. The highest age-specific CFR was observed among cases over 64 years (14.1%) whereas in those younger than 25 years, it was 6.3% (Annex 3, Table C9).

3.5.6 Vaccination status

Information on vaccination status was available for 32% of confirmed IMD cases. Among reporting countries where immunisation was not recommended (countries without MCC[14]), reporting of vaccination status was 65% complete, and 5 of 15 countries did not report vaccination status at all.

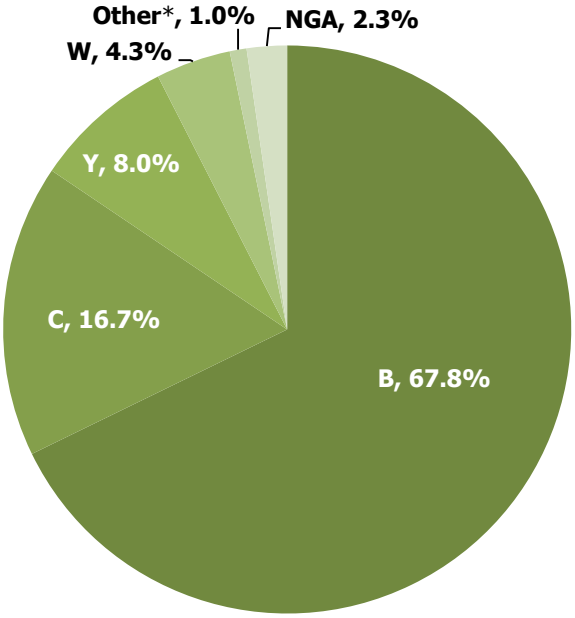
Among reporting countries where immunisation against IMD was recommended (countries with MCC[15]), reporting of vaccination status was 23% complete. Three countries did not report on vaccination status, and in 6 of 13 countries, the information was available for less than 35% of cases. Only Ireland reported vaccination status with 100% completeness. Vaccination status was known for 48% of all confirmed IMD cases of serogroup C IMD (n=539), 95% of which (n=265) were unvaccinated and 5% (n=14) had received at least one dose.

3.5.7 Serogroups

In 2012, information on serogroup was reported for 3 234 confirmed IMD cases by 27 of 28 reporting countries. Serogroup B was responsible for 68% of confirmed meningococcal infections, followed by serogroup C (17%). Serogroups B and C, together with serogroup Y, made up 93% of confirmed IMD cases with known serogroup (Figure 3.5). The notification rate of serogroup B cases (0.44 per 100 000) was four times higher than for serogroup C cases (0.11). Serogroup B was observed in all countries that reported on serogroup, and only four countries did not report any cases of serogroup C. The highest country-specific proportion of cases of serogroup Y was reported in Sweden (44%; n=45), followed by Norway (25%, n=6) and Finland (24%, n=8) (Annex 3, Table C10).

Between 2008 and 2012, a steadily decreasing trend in notification rates for serogroup B and C infection was observed while notification rates for serogroups Y and W increased only slightly (Figure 3.6; Annex 3, Table C11).

Figure 3.5. Percentage distribution of IMD by serogroup, EU/EEA, 2012 (n=3 234)



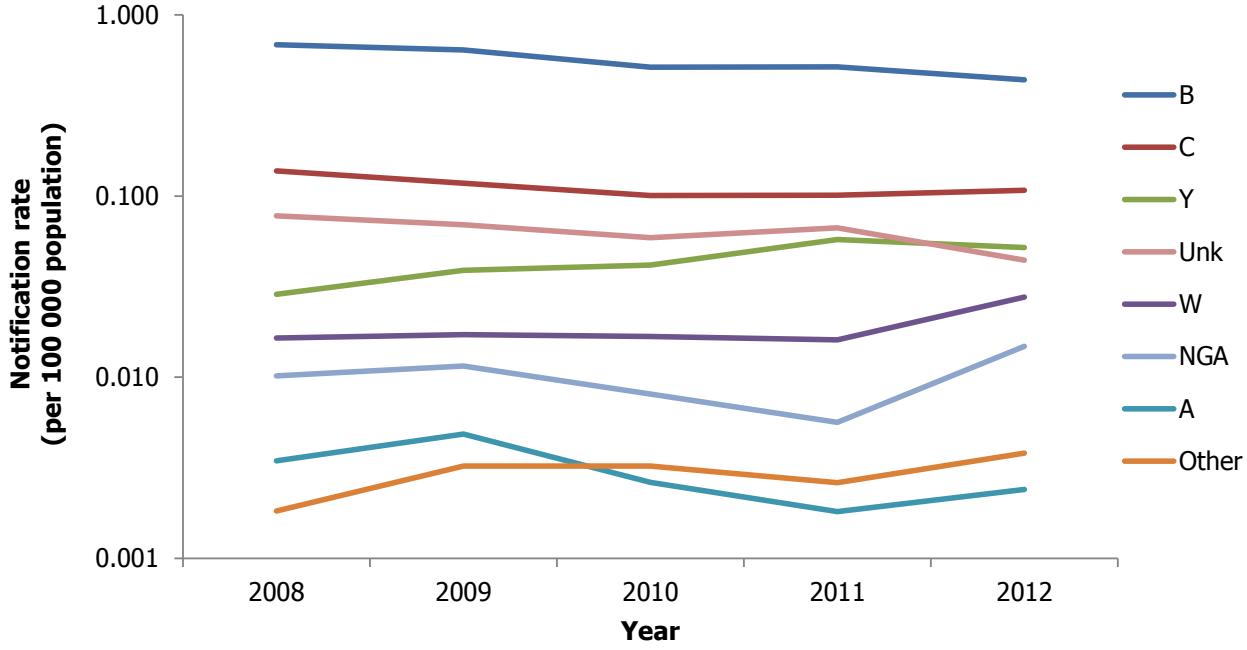
NGA = not groupable

** 'Other' includes confirmed cases reported as serogroup 'other' (0.5%; n=15), serogroup A (0.4%; n=12), serogroup 29E (0.1%; n=3) and serogroup Z (0.03%; n=1).*

[14] Countries without MCC: Bulgaria, the Czech Republic, Denmark, Estonia, Finland, Hungary, Latvia, Lithuania, Malta, Norway, Poland, Romania, Slovakia, Slovenia and Sweden

[15] Countries with MCC: Austria, Belgium , Cyprus, France, Germany, Greece, Ireland, Italy, Luxembourg, the Netherlands, Portugal, Spain and the United Kingdom

Figure 3.6. Notification rates of IMD cases, by serogroup and year, EU/EEA countries, 2008–12 (n=20 161)



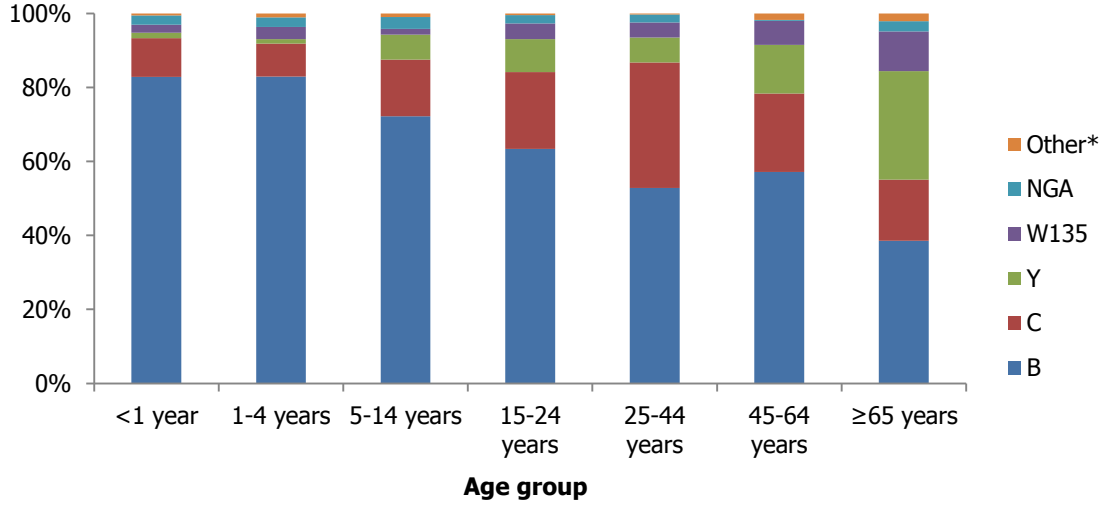
NGA = not groupable. Unk = unknown. 'Other' refers to the remaining reportable serogroups that should be reported. In addition to serogroups reported as 'other' (n=42), cases of serogroup 29E (13), serogroup X (n=13) and serogroup Z (n=5) reported during 2008–12 are included.

Contributing countries: Austria, Belgium, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom

Serogroup and age

The proportion of cases of serogroup B infection decreased with increasing age, while the proportions of serogroups Y and W were higher in the older age groups. In infants under one year of age (n=554), 83% of cases were due to serogroup B and 10% to serogroup C. The same serotype distribution was observed in children between one and four years of age (n=733). In those older than 64 years (n=327), 39% of cases were due to serogroup B, and serogroups Y and W were responsible for 29% and 11% of cases, respectively. Serogroup C was mostly reported in adults, affecting 34% of IMD cases in the 25–44-year age group (Figure 3.7, Annex 3 Table C12). Serogroup distribution was similar in both genders.

Figure 3.7. Percentage distribution of IMD by serogroup and age group, EU/EEA, 2012 (n=3 233)



NGA = not groupable. 'Other' includes confirmed cases reported as serogroup 'other' (n=15), serogroup A (n=12), serogroup 29E (n=3) and serogroup Z (n=1).

Serogroup and clinical presentation

Confirmed IMD cases of serogroup B and serogroup C showed similar percentages in the amount of clinical presentations. In both serogroups, meningitis was the most common clinical presentation reported. Almost half of the confirmed serogroup Y cases presented with septicaemia. Among serogroup W the proportion of cases with septicaemia or meningitis was the same (Table 3.3).

Table 3.3. Distribution of invasive IMD serogroups by clinical presentation, EU/EEA countries, 2012 (n=1 487*)

Serogroup	Septicaemia		Meningitis		Meningitis and septicaemia		Other~		Total
	N	%	N	%	N	%	N	%	N
B	284	29.6%	387	40.3%	225	23.4%	64	6.7%	960
C	102	30.4%	154	46.0%	63	18.8%	16	4.8%	335
Y	33	49.3%	21	31.3%	8	11.9%	5	7.5%	67
W	16	40.0%	16	40.0%	5	12.5%	3	7.5%	40
A	1	9.1%	3	27.3%	5	45.5%	2	18.2%	11
Other#	2	12.5%	10	62.5%	2	12.5%	2	12.5%	16
NGA	17	29.3%	28	48.3%	9	15.5%	4	6.9%	58
Total	**455**		**619**		**317**		**96**		**1 487**

** Total number of cases for which serogroup information is available by clinical presentation. Overall 1 747 missing or 'not under surveillance' cases for clinical presentation among all reported serogroups. NGA = non groupable. The specific codes are kept for the most common serogroups.*

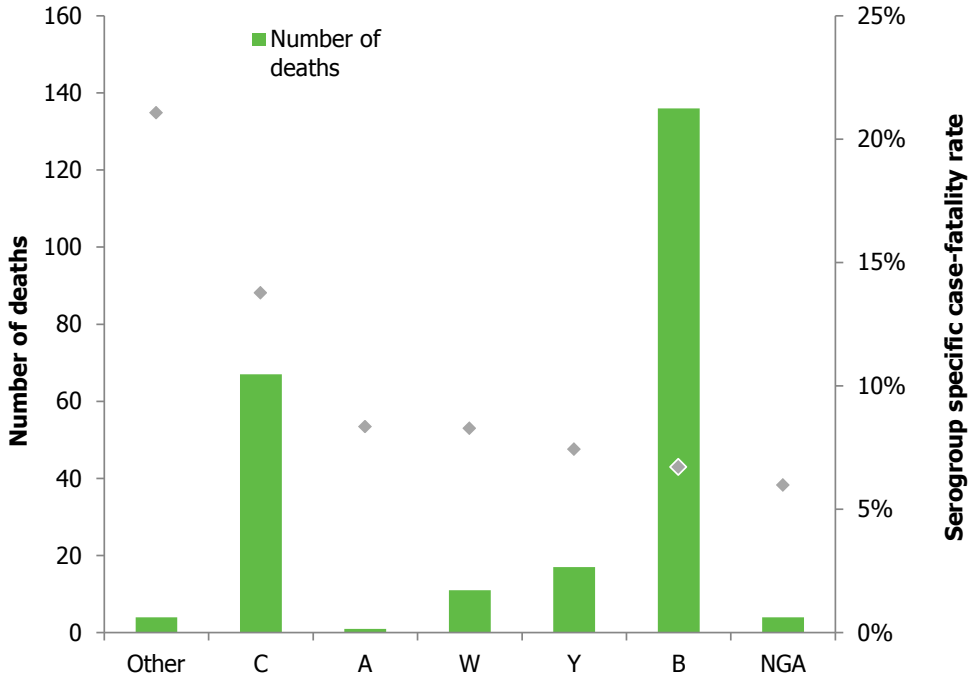
 # 'Other serogroups' are the remaining/other groupable serogroups that should be reported.

~ 'Other' in clinical presentations includes confirmed cases presenting pneumonia with known serogroup (n=1, serogroup Y).

Serogroup and case fatality

Information on outcome was available for 2 976 of 3 234 confirmed IMD cases with known serogroup. The highest CFR was found in cases grouped as serogroup 'other' (CFR: 21%, n=19). The CFR among cases with serogroup C IMD was twice as high as for serogroup B (Figure 3.8).

Figure 3.8. Distribution of reported IMD cases with fatal outcome (n=2 976*) and case–fatality rate by serogroup, EU/EEA countries, 2012



** N refers to the total number of cases for which outcome and serogroup information were known.*

NGA = not groupable

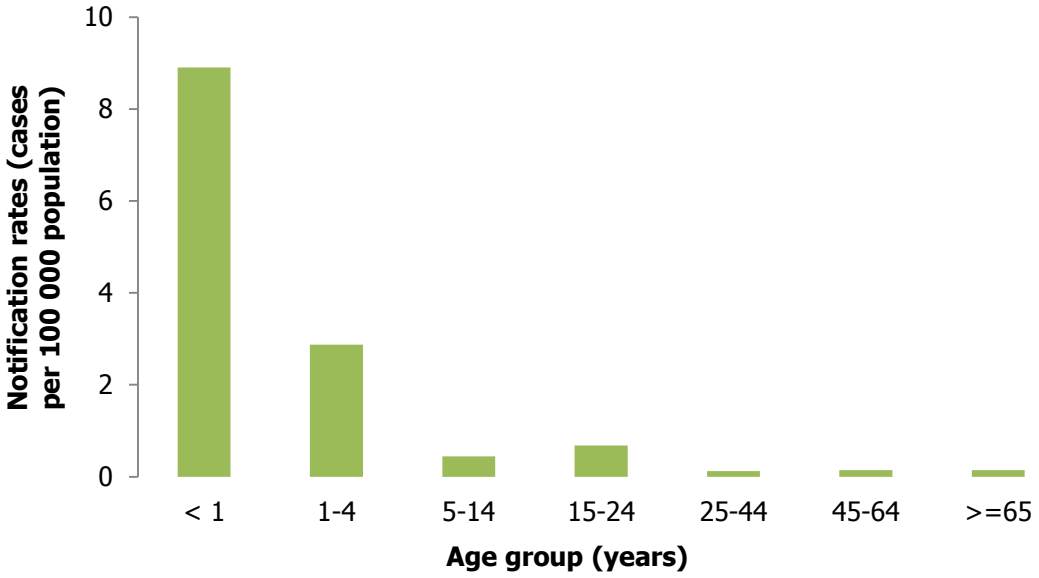
'Other' includes confirmed cases reported as serogroup 'other' (n=15) and other groupable serogroups, i.e. serogroup 29E (n=3) and serogroup Z (n=1).

Serogroup B

The highest notification rate for serogroup B IMD in 2012 was observed in cases < 1 year of age, followed by cases between one and four years of age. Notification rates decreased with increasing age, although a small peak was observed in adolescents and young adults (Figure 3.9; Annex 3, Table C13). Notification rates for cases aged < 1 year were highest in Ireland (23 cases per 100 000 population) and the United Kingdom (22 cases per 100 000 population). The United Kingdom (7.6 cases per 100 000 population) and Ireland (6.8 cases per 100 000 population) also presented high rates among cases between one and four years of age (Annex 3, Table C14).

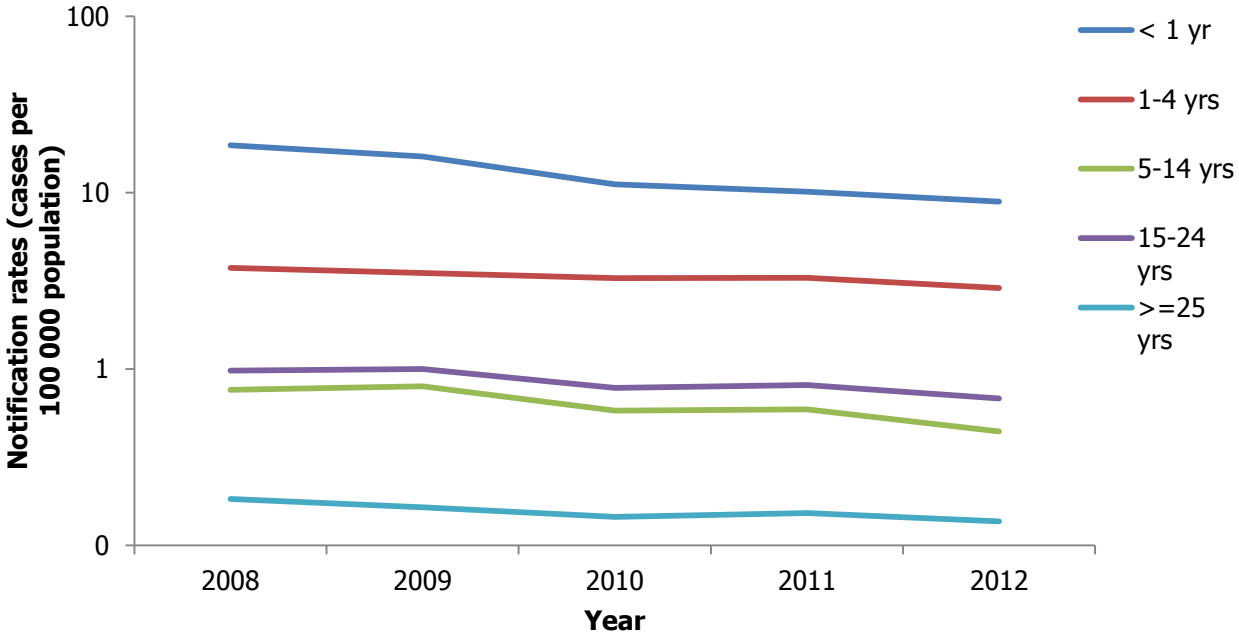
The notification rate of serogroup B cases did not show any increasing trend between 2008 and 2012 in any age group, with a notable decrease among children under one year of age. From 2010 onward, the decreasing trend in notification rates was significant in all age groups (Figure 3.10; Annex 3, Table C15). This trend was driven by the UK, where the notification rate for cases < 1 year of age dropped from 64 to 22 cases per 100 000 population between 2008 and 2012. Over the last five years, a strong reduction in notification rates in infants younger than one year of age was also observed in Ireland (from 50 to 23 cases per 100 000 population) and Spain (from 22 to 10 cases per 100 000 population). Among cases between one and four years of age, significant decreasing trends were observed in Ireland (from 22 to 7 cases per 100 000 population) and Spain (from six to three cases per 100 000 population).

Figure 3.9. Notification rates (cases per 100 000 population) of serogroup B IMD cases, by age group, EU/EEA countries, 2012 (n=2 182)



Contributing countries: Austria, Belgium, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom

Figure 3.10. Notification rate of serogroup B IMD by year and age group, EU/EEA countries, 2008–12 (n=13 765)



Contributing countries: Austria, Belgium, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Lithuania, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom

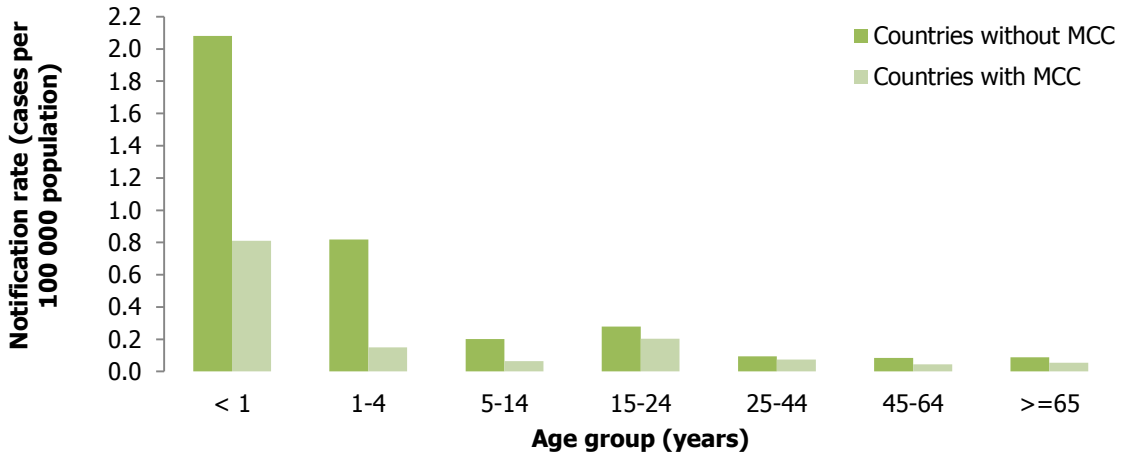
Serogroup C

In 2012, the age distribution of serogroup C IMD was very similar to serogroup B IMD, but age-specific rates in cases of serogroup C IMD were lower than for serogroup B, especially in cases below five years of age (Annex 3, Table C15). Notification rates of serogroup C IMD were higher across all age groups in countries without MCC compared to countries with MCC vaccination. This difference was most pronounced in cases between one and four years of age (0.1 cases per 100 000 in countries with MCC, 0.8 cases per 100 000 in countries without MCC) (Figure 3.11; Annex 3, Table C17).

Among countries without MCC vaccination, the highest notification rate in cases under one year of age was observed in Denmark (6.7 cases per 100 000), followed by Poland (3.9 cases per 100 000). Denmark, Poland and Sweden were the only countries to report notification rates > 1 per 100 000 among cases between one and four years of age (Annex 3, Table C16). Among countries with MCC, Austria reported the highest notification rates in those younger than one year of age (2.6 cases per 100 000) and between one and four years of age (0.6 cases per 100 000) (Annex 3, Table C16).

During 2008–12, notification rates for serogroup C IMD cases remained stable in countries without MCC vaccination, and no consistent trend was observed in any age group (Figures 3.12 and 3.13; Annex 3, Tables C18 and C19). A slight reduction in notification rates was observed in countries that introduced MCC vaccination (Figure 3.12; Annex 3, Table C19). In countries that introduced MCC after 2008, a slight decreasing trend was observed in children younger than five years of age and children between 5 and 14 years of age, although there was a slight increase in the notification rate in both age groups in 2012 (Figure 3.13; Annex 3, Table C19).

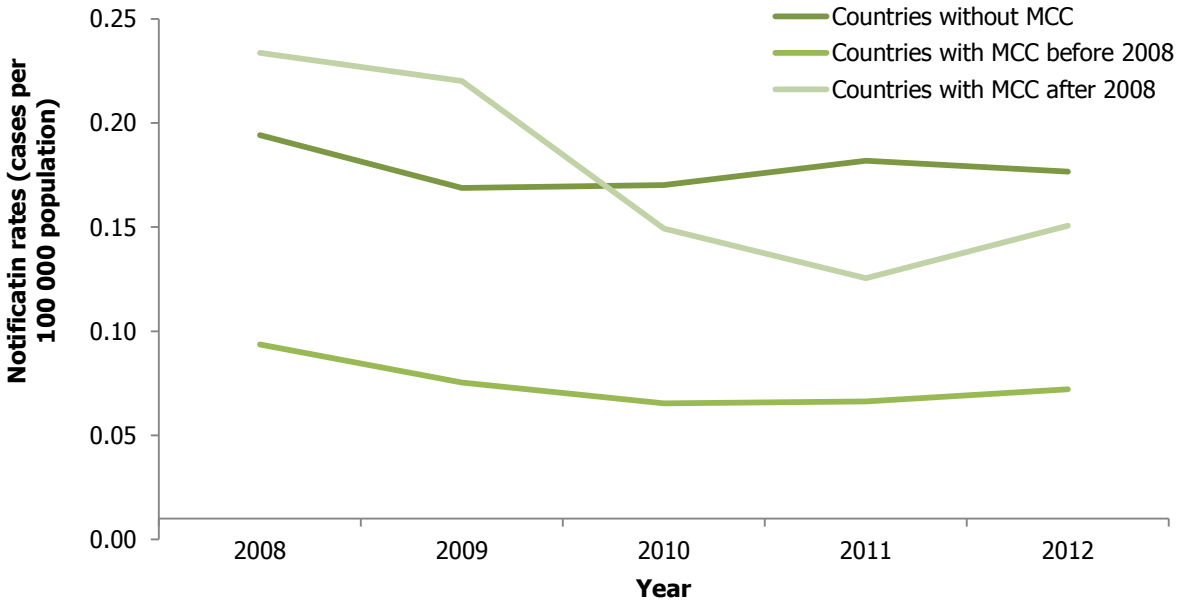
Figure 3.11. Notification rate of serogroup C IMD by age group, EU/EEA countries, 2012 (n=536)



Contributing countries with MCC: Austria, Belgium, France, Germany, Greece, Ireland, Italy, the Netherlands, Portugal, Spain and the United Kingdom

Contributing countries without MCC: Czech Republic, Denmark, Estonia, Finland, Hungary, Latvia, Lithuania, Malta, Norway, Poland, Romania, Slovakia, Slovenia and Sweden

Figure 3.12. Notification rate of serogroup C IMD by year and meningococcal C conjugate vaccination policy, EU/EEA countries, 2008–12 (n=2 792)



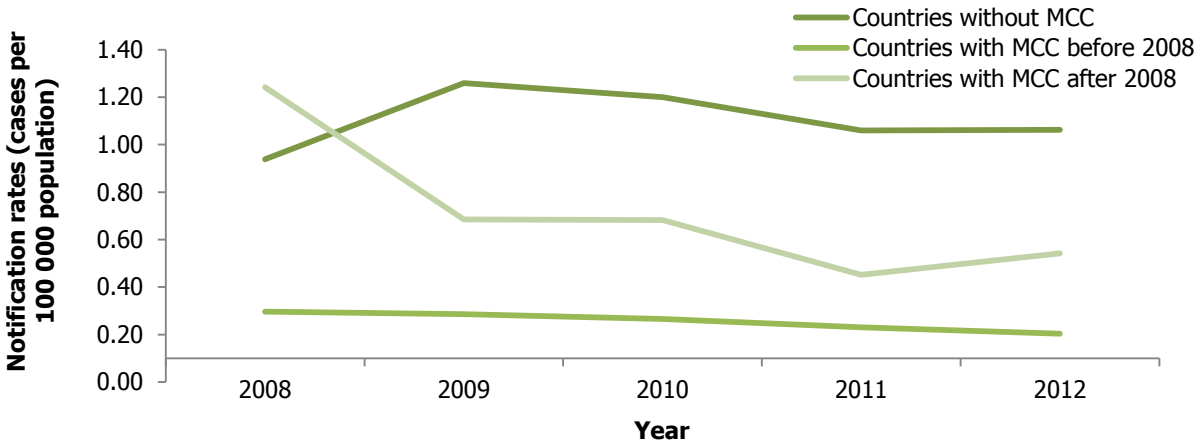
Contributing countries without MCC: Czech Republic, Denmark, Estonia, Finland, Hungary, Latvia, Lithuania, Malta, Norway, Poland, Romania, Slovakia, Slovenia and Sweden

Contributing countries with MCC before 2008: Belgium, Germany, Greece, Ireland, Italy, the Netherlands, Portugal, Spain and the United Kingdom

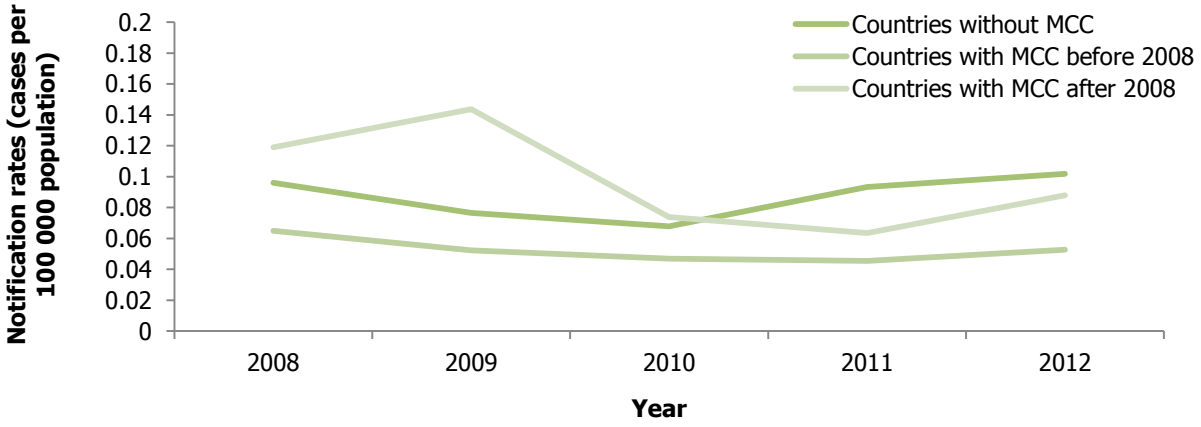
MCC after 2008: Austria, France

Figure 3.13. Notification rate (cases per 100 000 population) of serogroup C IMD by year, age group, and meningococcal C conjugate vaccination policy, EU/EEA countries, 2008–12 (n=2 792)

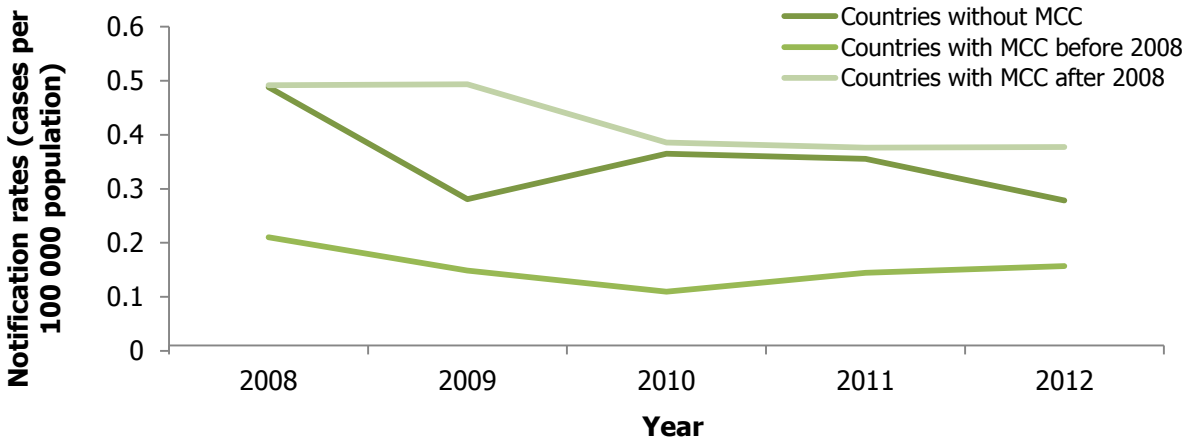
a) Under five years of age



b) Between 5 and 14 years of age



c) Older than 14 years of age



Contributing countries without MCC: Czech Republic, Denmark, Estonia, Finland, Hungary, Latvia, Lithuania, Malta, Norway, Poland, Romania, Slovakia, Slovenia and Sweden

Contributing countries with MCC before 2008: Belgium, Germany, Greece, Ireland, Italy, the Netherlands, Portugal, Spain and the United Kingdom

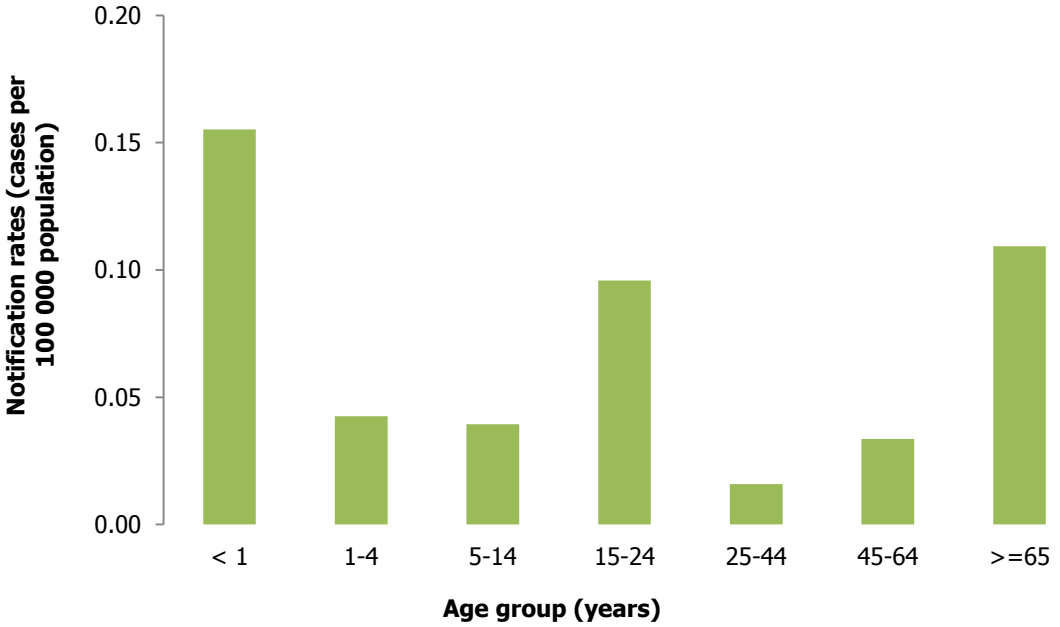
After 2008: Austria, France

Serogroup Y

The highest notification rate for serogroup Y IMD in 2012 was observed in cases under one year of age (0.16 cases per 100 000), followed by cases ≥ 65 years (0.11 cases per 100 000) and 15–24 years (0.10 cases per 100 000) (Figure 3.14, Annex 3 Table C13). The combined total of these cases accounted for more than 60% of confirmed serogroup Y IMD cases. Notification rates for cases under one year of age were highest in Austria (1.7 cases per 100 000), and notification rates for cases ≥ 65 years were highest in Sweden (1.3 cases per 100 000) (Annex 3, Table C20).

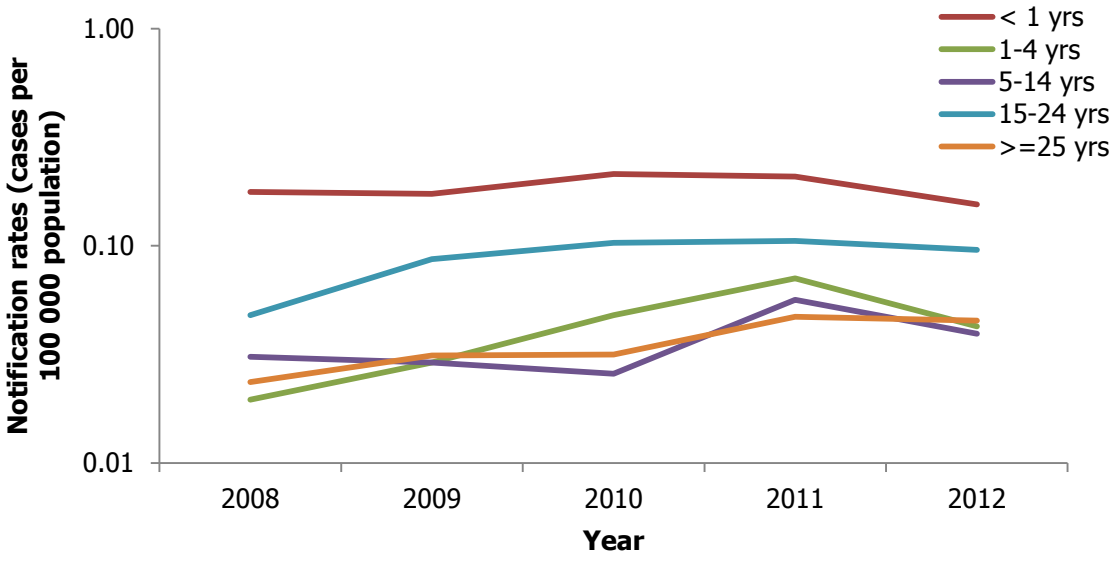
Serogroup Y was the only serogroup for which there was an increase during the period 2008–12 (Figure 3.6). A significant increasing trend was observed in cases between 15 and 24 years of age and cases older than 24 years (Figure 3.15; Annex 3, Table C21).

Figure 3.14. Notification rates of serogroup Y IMD cases, by age group, EU/EEA countries, 2012 (n=256)



Contributing countries: Austria, Belgium, the Czech Republic, Denmark, Finland, France, Germany, Greece, Ireland, Italy, the Netherlands, Norway, Poland, Portugal, Spain, Sweden and the United Kingdom

Figure 3.15. Notification rate of serogroup Y IMD by year and age group, EU/EEA countries, 2008–12 (n=1 080)



Contributing countries: Austria, Belgium, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Ireland, Italy, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom

3.5.8 Further characteristics of *N. meningitidis* strains

For 2012, 78 variants of the FetA variable region[16] (FetA VR) were reported by 18 of 28 countries for 1367 confirmed IMD cases. The most frequently reported variants were F3-3 (19%, n=259) and F1-5 (18%, n=243), followed by F4-1 (9%, n=125) (Annex 3, Table C22). In two countries, FetA VR variants were not under surveillance.

Variant F3-3 was isolated from 42% of serogroup C cases for which the information on FetA VR variants was available (n=306). Isolates of variant F1-5 were responsible for 27% of serogroup B cases with available information on FetA VR variants (n=842), and variant F4-1 represented 44% of FetA VR variants isolated from serogroup Y cases (Annex 3, Table C22).

Multilocus sequence typing (MLST)[17] data were reported for 23% (n=783) of confirmed IMD cases by 12 of 28 countries. The bacterial population was highly diverse, in line with findings from previous years. There were 23 clonal complexes (CC) isolated from 783 cases: 19.4% of isolates belonged to CC ST-32, followed by CC ST-11 (18.5%) and CC ST-41/44 (17.2%) (Annex 3, Table C23).

Among cases for which the information on MLS type and serogroup was available, ST-41/44 and ST-32 complex strains were reported in 30% and 25% of serogroup B cases (n=474), respectively. ST-11 complex strains were responsible for 65% of serogroup C cases (n=186), while 86% of serogroup Y cases (n=80) were due to ST-23 strains (Annex 3, Table C23).

In 2012, 19 countries reported subtyping results on the two main variable regions of the porA gene[18] (VR1 and VR2) for 1 496 confirmed IMD cases. There was more variation within porA VR2 gene segments (98 unique variants) than within VR1 (44 unique variants). The most frequently reported variants were P1.7-2, P1.22 and P1.5 in VR1 and P1.2, P1.4 and P1.14 in VR2 (Annex 3, Table C24). Eleven porA subtypes of *N. meningitidis* were responsible for 62% of IMD cases for which information was available, with the most prevalent variants being P1.5, 2 (19%, n=171) and P1.7-2,4 (16%, n=151) (Annex 3, Table C24).

Subtype information was available for 953 cases of serogroup B, 293 of serogroup C, 147 serogroup Y cases and 55 W IMD cases (Annex 3, Table C24). The association of serogroups, PorA genotypes and clonal groups is shown in Table 3.4.

Table 3.4. Predominant PorA genotypes of the ten most isolated clonal complexes from confirmed IMD cases, EU/EEA countries, 2012 (n=682)

Top ten complex clusters	Number of isolates*	Predominant PorA genotypes	Isolates (%)
ST-32	144	B:P1.7,16	35%
		B:P1.19,15	21%
		B:P1.7-2,16	12%
ST-11	140	C:P1.5,2	47%
		W:P1.5,2	11%
		Y:P1.5-1,10-8	18%
ST-41/44	129	B:P1.7-2,4	39%
ST-23	79	Y:P1.5-2,10-1	42%
		Y:P1.5-1,2-2	22%
ST-269	73	B:P1.19-1,15-11	53%
ST-213	37	B:P1.22,14	81%
ST-162	28	B:P1.7-2,4	54%
		B:P1.22,14	39%
ST-461	21	Eight different genotypes	NA
ST-103	18	C:P1.18-1,3	56%
ST-18	13	Six different genotypes	NA

** Refers to the number of isolates for which information on typing of PorA gene was available.*

Contributing countries: Czech Republic, Denmark, Estonia, France, Germany, Greece, Italy, Lithuania, Norway, Poland, Portugal, Sweden

[16] Coded values of the FetA VR variable region are available from: http://neisseria.org/nm/typing/tessy

[17] *N. meningitidis* MLST website: http://pubmlst.org/neisseria

[18] Details available from: http://neisseria.org/nm/typing/pora

3.5.9 Probable country of infection

In 2012, five cases with known probable country of infection were reported as acquired outside the EU: one case in China (serogroup B), one in the Dominican Republic (unknown serogroup), one in India (unknown serogroup), and two in Turkey (one unknown serogroup and one serogroup W).

3.5.10 Antimicrobial resistance

The large majority of isolates tested in 2012 were susceptible to the antibiotics currently used for treatment and prophylaxis (ciprofloxacin, rifampicin, penicillin G and cefotaxime/ceftriaxone). In total, information on antimicrobial resistance was available for 906 isolates tested for resistance to ciprofloxacin, 903 tested for rifampicin resistance, 1 186 tested for penicillin G resistance and 585 tested for cefotaxime resistance.

3.5.11 Laboratory methods used for strain identification

Specimens

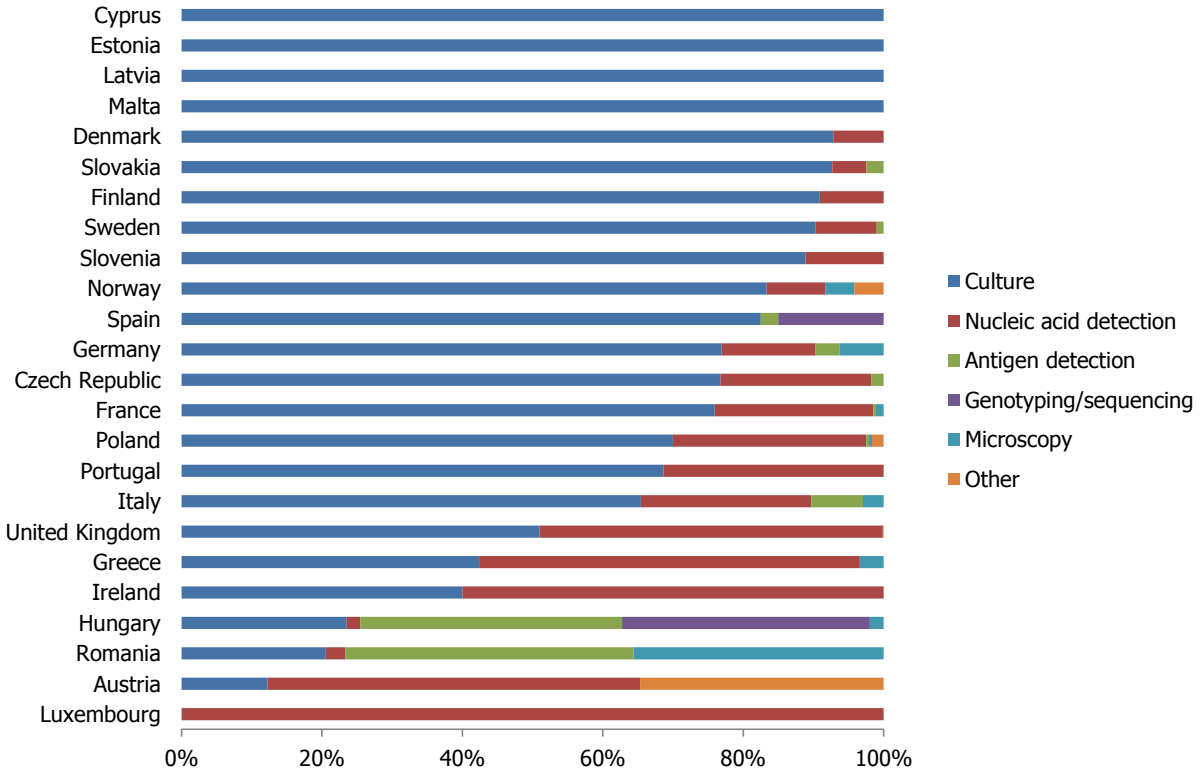
Blood isolates and CSF accounted for 53% and 45%, respectively, of the 2 581 cases for which the type of specimen was reported (Annex 3, Table C25). The proportions of blood and CSF specimens were similar in all age groups except in the age group ≥ 65 years, in whom blood specimens were predominant (86%) (Annex 3, Table C26).

Test method

Information on the first test method used for case confirmation and further characterisation of the disease was available for 81% of cases from 24 countries. Five countries reported the use of only one method and 13 reported the use of three test methods or more.

Culture was the most frequently reported method, accounting for 64% of tests (n=1 788), and was reported by all countries except for Luxembourg. The second most common method was nucleic acid detection (29%, n=811), reported by 19 countries. The use of genotyping/sequencing was reported only by Spain and Hungary. Antigen detection was the predominant method reported by Romania (42%, n=30) (Figure 3.16).

Figure 3.16. Proportion of strain identification methods used on primary specimens of IMD cases, by country, in EU/EEA countries, 2012 (n=2 789)



3.5.12 Data quality

Overall, data on age, age in months, gender, classification, outcome and serogroup were complete, or almost complete. The proportion of missing data decreased for all variables between 2010 and 2012. Data on serogroup were reported by all countries, except Luxembourg.

Data on antimicrobial resistance, molecular characterisation and vaccination status were less complete (< 45%). Information on clinical presentation was reported only for about 52% of confirmed cases (Annex 3, Table C27).

3.6 Discussion

IMD remains rare in Europe. Notification rates in most countries are below 1 per 100 000 population, and the overall notification rate was 0.68 per 100 000 population notification although this is higher than the rate observed in the United States (0.18 per 100 000) [11]. Overall, there has been a 28% reduction in cases in Europe since 2008. This may be the result of a range of factors including the success of vaccination campaigns against IMD, the success of other public health campaigns that target risk factors for IMD (e.g. smoking), secular trends in strains contributing to IMD, and better control against secondary cases [79]. As in previous years, the burden of meningococcal disease was highest in children below five years of age, but there is a smaller secondary peak in young adults between 15 and 24 years.

Over the last five years notable changes occurred in the surveillance of IMD, both at the national and European level. Changes such as representativeness, national coverage and reporting procedure could have biased the results, which is why notification rates in all countries and trends over time must be interpreted cautiously.

Meningitis was the most common clinical presentation in all age groups except those older than 65 years, for which septicaemia was the most frequent. There was no relationship observed between a specific clinical presentation and serogroup. Results on clinical presentation should be interpreted with caution as information was missing for 52% of cases and may be influenced by differences in clinical and surveillance practices in Member States. In some countries, meningitis is the main or only syndrome under surveillance, while the reported proportion of cases with septicaemia is heavily influenced by blood culture practices in Member States and it is therefore likely that the number of cases with septicaemia is underreported. However, a recent study carried out in the United Kingdom showed that *N. meningitidis* remains the most important cause of bacterial meningitis, accounting for more than a third of all cases of childhood bacterial meningitis [72].

The overall CFR was 7.9%, lower than what has been observed in other surveillance systems [11]. CFR varied markedly between countries. The highest CFR was observed among cases presenting with septicaemia, followed by cases with meningitis and septicaemia. Despite good completeness of outcome reporting, these figures should be interpreted cautiously as there is no common definition of the point in time at which a fatal outcome is determined.

The largest proportion of cases in 2012 was due to serogroup B, followed by serogroups C and Y, which together were responsible for 92% of all confirmed IMD cases. For serogroups B and C, the largest age-specific notification rate was observed in infants below one year of age and children between one and four years. However, rates for serogroup C were 10-fold lower than for cases of serogroup B infection in the same age groups. Overall, a constant decreasing trend was observed for serogroup B and C during 2008–12. Serogroup Y showed an overall increasing trend and was most common in the elderly.

The distribution of serogroups varied considerably between countries, partly depending on whether routine MCC vaccination had been introduced. In countries with routine MCC vaccination, serogroup B was always predominant. Currently, fifteen countries in Europe have MCC vaccination in their routine national immunisation programmes, two of which started MCC vaccination after 2008. Since its introduction, the MCC vaccine has proved effective in reducing the burden of serogroup C infection [58-60] and generating herd immunity [64]. In 2012, notification rates of serogroup C disease were higher across all age groups in countries without MCC vaccination. In countries that introduced MCC after 2008, a slight decreasing trend in children younger than 15 years was observed during 2008–12.

Serogroup Y infection was the only serogroup with an increasing trend, in line with recent findings from around Europe [69]. This increase could be partly due to increasing quality of surveillance, improving completeness of reporting, and the growing availability of molecular typing methods.

The observed decrease in serogroup B notification rates in Europe is predominantly driven by reduced numbers of cases in the UK [79]. This is consistent with secular trends in meningococcal group B disease and has also been observed elsewhere [72]. Despite this decreasing trend there are fears that the incidence may rise again as historically the incidence of IMD had fluctuated for reasons that are not well understood [79]. Serogroup B has been a strong candidate for vaccination and, following successful clinical trials [63], a multicomponent meningococcal serogroup B vaccine (4CMenB) against a large proportion of serogroup B strains was granted a licence from the European Commission. It has been recommended for the introduction in the childhood vaccination schedule in the UK by the JCVI [74]. Although meningococcal disease has been declining over the past decade, *N. meningitidis* remains a major cause of meningitis, especially in children, suggesting that the 4CMenB vaccine could have a substantial effect on disease burden.

Despite being common in Europe in the early half of the 20th century, serogroup A caused remarkably few cases of disease in Europe over the past few decades, and the reasons for the disappearance are not clear [73]. In 2012, only 12 serogroup A cases were reported, confirming that the disease has largely disappeared in Europe.

Precise characterisation of bacterial isolates from cases of invasive disease is essential for informed public health responses, providing the tools necessary for both enhanced surveillance and outbreak detection. Molecular surveillance provides a better understanding of the epidemiology of IMD, and in some cases, genotypic methods of characterisation are essential for identifying differences between phenotypically identical isolates [71]. Recommendations for the molecular typing of meningococci have been developed and molecular typing data for IMD have been collected at EU/EEA level. Currently, multi-locus sequence typing (MLST) and PorA and FetA typing data are reported to TESSy. MLST is recognised as the gold standard for accurate strain characterisation and epidemiological surveillance of this organism and plays a major part in defining its population biology [71].

In 2012, the bacterial population was highly diverse, in line with findings from previous years; however three main clones seem responsible for severe IMD in Europe: ST-32 was the most frequent, followed by ST-11 and ST-41/44. Certain clonal complexes were more frequently associated with particular serogroups, which also confirmed the findings from previous surveillance studies in Europe [75]. Eleven PorA subtypes of *N. meningitis* were responsible for 62% of IMD cases for which information was available. The highest variability in PorA genotypes was associated with isolates of serogroup B and the lowest with serogroup W. In 2012, a few countries submitted data on *N. meningitidis* strain characterisation, but doing so for less than 45% of confirmed IMD cases. As more Member States report on this variable, the accuracy of the findings will improve.

The rapid onset of disease, high case fatality and the high proportion of surviving patients with severe complications ensure that IMD remains prominent on the public health agenda throughout Europe. Surveillance at the European and national levels is important for quantifying the burden of IMD, identifying and describing trends to enable rational public health decision-making and evaluate the impact of interventions, such as vaccination.

4 Conclusions

Invasive bacterial diseases remain an important public health issue across Europe and continue to cause serious preventable disease in several countries, particularly among the young and the elderly.

Rates of invasive *H. influenzae* disease and IMD have been decreasing and both diseases remain rare in the majority of European countries. In the Hib conjugate vaccine era, the epidemiological characteristics of *H. influenzae* disease have undergone changes, and a shift in the distribution of capsular serotypes of invasive *H. influenzae* disease has occurred in Europe. Despite the decline, *N. meningitidis* remains an important cause of bacterial meningitis; therefore, the recently licensed protein-based MenB vaccine has the potential to have a major effect on the epidemiology of bacterial meningitis if introduced to the childhood immunisation programme.

Trends are stable for IPD, however serotype replacement among vaccine and non-vaccine serotypes does occur and needs to be carefully monitored.

Vaccines have proved effective in reducing the burden of disease of IPD (PCV7, 10, 13/PPV23), invasive *H. influenzae* disease (Hib vaccine) and IMD (MCC vaccine) across Europe. However, with the changing epidemiology of each disease come new challenges for vaccine policy, ranging from the introduction of a new vaccine (meningococcal group B) to the adjustment of current vaccine schedules (MCC vaccination in adolescents) to the development of new vaccines (PCV). Vaccine pre- and post-marketing surveillance must be maintained if the positive impact of vaccination is to be sustained in individuals and across populations.

The findings presented in this report are interesting both from an epidemiological and a public health perspective; they also underline the importance of standardised, reproducible laboratory and clinically based epidemiological surveillance.

Surveillance systems for IBD remain diverse across Europe, compromising the comparability of data between countries and impeding data interpretation on a European level. A stronger understanding of surveillance systems and laboratory practices in different Member States, as well as better linkage between notification and laboratory data at the national level, would facilitate interpretation of the data. The completeness of some variables needs to be improved, and the collected information should be as homogeneous across countries as possible in order to enable comparisons and properly assess the impact of the public health strategies implemented at the European level.

Continued enhanced IBD surveillance is vital for assessing the long-term effectiveness of vaccination, monitoring changes in the epidemiology of IBD, and informing the development of effective vaccines, and the establishment of a sensible vaccination policy.

5 Strengths and limitations

This report pools data on IPD, invasive *H. influenzae* disease and IMD from many Member States at a supranational level. The aim is to provide comprehensive baseline information on the epidemiology of IBD in EU/EEA countries and determine the burden of disease at the European level. This will in turn facilitate the prioritisation of policies, simplify the assessment of the impact of vaccination, and assist in the development of future vaccines. It also allows data to be compared with other regions of the world.

A certain degree of underdiagnosis and underreporting is suspected for all three diseases at the national and subnational level. A key challenge in IBD surveillance across Europe is that national surveillance systems for all three diseases are heterogeneous which hampers comparisons between Member States. Most data come from comprehensive surveillance systems, and in the majority of countries, epidemiological and laboratory data are merged at the national level. However, there are some countries where this is still not possible.

Healthcare systems, health-seeking behaviour, diagnostics, laboratory methods and medical practices (e.g. blood culture testing) also differ between Member States. Changes in surveillance systems (availability of new laboratory methods, comprehensiveness of the system, extension of age groups, a broader coverage of serogroups/serotypes, clinical forms of the disease under surveillance) and improvement in case ascertainment and reporting further complicate the analysis of data over time, even within countries.

On a positive note, most countries reported that they were applying the official European case definitions[19], mostly the 2008 version. The use of different versions of EU case definitions should not have negatively affected data analysis, as the criteria for a confirmed case of IPD, invasive *H. influenzae* disease or IMD have remained the same, or almost the same, over time, and only confirmed cases were included in this report.

One difference between countries is in the sensitivity and availability of laboratory methods used for case confirmation. This must be considered when comparing laboratory variables for IPD between countries. Furthermore, for IPD, some isolates were only characterised to the serogroup level (i.e. serogroup 7, 19, etc.), which points at limited capacity for serotyping in some laboratories.

For invasive *H. influenzae* disease and IMD, culture was the most frequently reported laboratory method used for confirming a case. Laboratory capacities have improved over the years, and Member States have increasingly reported results from nucleic acid detection methods and genotyping, although at this point in time, the majority of Member States do not use these techniques routinely for diagnostics and strain characterisation.

The completeness of reporting differed between variables and across countries. Although there are still important gaps in the data, data completeness is improving for all three diseases. Gaps in the surveillance data for serotype/serogroup data and other variables such as vaccination status, outcome, clinical presentation, antimicrobial resistance and molecular characterisation of strains remain, and data quality must continue to improve in order to allow more accurate conclusions.

With regard to outcome data, there is no common definition of the point in time at which a fatal outcome is determined and this may add variation to the figures throughout Europe. A high CFR in countries with low notification rates may indicate a bias towards reporting only the most severe outcomes. A low CFR in countries with high notification rates may in turn reflect a situation where deaths were occurring after the disease was notified. Outcome data accuracy might also be influenced by variations in surveillance systems: countries with hospital discharge data included in their routine surveillance might have higher outcome data completeness and, as a result, a higher case–fatality rate.

The absence of certain data from this report is another limitation. For example, serotype data was not available for IPD for the years before 2010. Serotype replacement is an important issue in the surveillance of IPD and for helping to inform future vaccine development and policy.

Caution must also be taken when comparing this report with other ECDC publications describing the epidemiology of IPD, invasive *H. influenzae* disease or IMD, as new countries may have started reporting to TESSy, also submitting information on cases notified in previous years (e.g. Germany and Luxembourg). There may be differences between reports in how data were analysed, which may result in different figures for otherwise very similar data. Countries may update their data at any time, which could account for additional variations in the figures between this and previous reports.

Finally, it is important to keep in mind that in countries with a small population, even small changes in numbers would lead to large differences in rates.

[19] Available from: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:159:0046:0090:EN:PDF

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Annex 1. Invasive pneumococcal disease

Table A1. Description of the data sources for surveillance of IPD, 2012

Country	Data source	Legal character	Comprehensive	Active/passive	Case-based/aggregated	Data reported by				National coverage	Case definition
						Labs	Physicians	Hosp.	Other		
Austria	AT-Epidemiegesetz	Cp	Co	P	C	Y	Y	Y	Y	Y	EU 2008
Belgium	BE-REFLAB	V	Se	A	C	Y	N	N	N	Y	EU 2008
Bulgaria	BG-NATIONAL_SURVEILLANCE	Cp	Co	P	A	Y	Y	Y	Y	Y	EU 2008
Croatia	HR-CNIPH	Cp	Co	P	C	Y	Y	Y	Y	Y	EU2012
Cyprus	CY-LABNET	V	Se	A	C	Y	N	N	N	N	none
Czech Republic	CZ-NRL-STR	Cp	Co	A	C	Y	Y	Y	N	Y	EU 2008
Denmark	DK-LAB	Cp	Co	P	C	Y	N	N	N	Y	Unk
Estonia	EE-PNEUMOCOCC	Cp	Co	P	C	Y	Y	Y	Y	Y	EU'08
Finland	FI-NIDR	Cp	Co	P	C	Y	N	N	N	Y	Unk
France	FR-EPIBAC	V	Se	A	C	Y	N	Y	N	Y	EU 2008
Greece	GR-Notification/Laboratory data	Cp	Co	P	C	Y	Y	Y	Y	Y	EU 2008
Hungary	HU-NRL_PNEU	V	Co	P	C	Y	N	N	N	Y	EU 2008
Iceland	IS-SUBJECT_TO_REGISTRATION	Cp	Co	P	C	Y	Y	Y	N	Y	EU 2008
Ireland	IE-PNEU	Cp	Co	P	C	Y	Y	Y	N	Y	EU 2008
Italy	IT-MENINGITIS	V	Co	P	C	N	Y	Y	N	Y	EU2012
Latvia	LV-BSN	Cp	Co	P	C	Y	Y	Y	Y	Y	EU2012
Lithuania	LT-COMMUNICABLE_DISEASES	Cp	Co	P	C	Y	Y	N	N	Y	EU 2008
Luxembourg	LU-SYSTEM1	Cp	Co	P	C	N	Y	N	N	Y	EU2002
Malta	MT-DISEASE_SURVEILLANCE	Cp	Co	P	C	Y	Y	Y	Y	Y	EU 2008
Netherlands	NL-NRBM	V	Se	P	C	Y	N	N	N	N	EU 2008
Norway	NO-MSIS_A	Cp	Co	P	C	Y	Y	Y	N	Y	Unk
Poland	PL-NATIONAL_SURVEILLANCE	Cp	Co	P	C	Y	Y	Y	N	Y	EU 2008
Romania	RO-RNSSy	Cp	Co	P	C	N	N	Y	N	Y	EU 2008
Slovakia	SK-EPIS	Cp	Co	A	C	Y	Y	Y	N	Y	EU2012
Slovenia	SI-SURVIVAL	Cp	Co	P	C	Y	Y	Y	N	Y	EU 2008
Spain	ES-NRL	V	O	P	C	Y	N	Y	N	U	Unk
Sweden	SE-SMINET	Cp	Co	P	C	Y	Y	N	N	Y	EU2012
United Kingdom	UK-PNEUMOCOCCAL	O	Co	P	C	Y	N	Y	Y	Y	EU2012

Cp: compulsory, V: voluntary, Co: comprehensive, O: other, Se: sentinel, P: passive, A: active, C: case-based, A: aggregated, Y: yes, N: no, Unk: unknown

Table A2. Population coverage of the FR-EPIBAC data source from France, 2010–12

Age-group	Population under surveillance, 2010			Population under surveillance, 2011			Population under surveillance, 2012		
	Female	Male	Both	Female	Male	Both	Female	Male	Both
< 1	292 337	304 734	597 071	289 992	303 065	593 057	283 924	298 083	582 007
1 to 4	1 149 157	1 196 485	2 345 642	1 139 941	1 189 930	2 329 871	1 157 326	1 205 333	2 362 659
5 to 14	2 818 916	2 960 405	5 779 321	2 818 951	2 957 650	5 776 601	2 899 630	3 033 769	5 933 399
15 to 24	2 888 589	2 977 796	5 866 385	2 851 593	2 945 889	5 797 482	2 864 892	2 956 651	5 821 543
25 to 44	6 215 743	6 138 592	12 354 335	6 168 748	6 082 890	12 251 724	6 203 150	6 103 685	12 306 835
45 to 64	6 433 081	6 127 310	12 560 391	6 384 443	6 071 711	12 456 068	6 472 125	6 160 645	12 632 769
≥ 65	4 731 817	3 321 250	8 053 067	4 790 599	3 421 240	8 211 839	4 943 947	3 586 926	8 530 873

Table A3. Distribution of confirmed IPD cases by country and month, EU/EEA countries, 2012 (n=20 778)

Country	Jan	Feb	Mar	Apr	May	June	July	Aug	Sept	Oct	Nov	Dec
Austria	20	26	29	21	20	13	9	6	1	22	22	46
Belgium	154	243	201	188	157	116	58	40	97	150	128	206
Bulgaria	4	3	4	2	1	0	0	2	0	0	2	1
Cyprus	1	1	2	1	2	0	0	1	1	1	0	0
Czech Republic	32	27	42	35	43	21	17	11	10	30	37	30
Denmark	98	95	74	90	78	50	50	16	50	67	74	140
Estonia	1	0	3	3	0	0	3	2	3	1	3	1
Finland	64	78	99	54	86	65	30	28	72	53	56	67
France	501	599	527	508	327	276	204	117	172	370	312	517
Greece	7	8	7	1	5	3	1	0	2	2	5	2
Hungary	15	15	21	21	28	14	5	11	10	16	18	12
Ireland	43	32	43	31	36	21	18	21	10	29	31	35
Italy	100	120	97	97	55	32	24	17	19	70	77	79
Latvia	1	7	12	11	3	2	3	6	2	0	6	3
Lithuania	0	1	1	0	0	2	0	1	0	0	0	2
Luxembourg	1	0	0	0	0	0	0	0	0	0	0	0
Malta	0	3	0	0	3	1	1	3	0	0	3	1

Country	Jan	Feb	Mar	Apr	May	June	July	Aug	Sept	Oct	Nov	Dec
Netherlands	67	69	79	68	75	44	22	18	14	58	54	67
Poland	44	42	34	40	31	33	23	20	9	44	37	45
Romania	4	7	6	11	7	5	5	2	3	6	5	18
Slovakia	8	5	5	4	6	1	3	2	3	2	4	6
Slovenia	20	29	41	22	23	13	9	8	14	17	25	24
Spain	301	359	307	223	198	101	77	60	59	157	188	230
Sweden	128	146	193	168	138	104	78	51	70	77	97	137
United Kingdom	546	590	535	505	487	318	301	197	210	415	424	674
EU total	**2 160**	**2 505**	**2 362**	**2 104**	**1 809**	**1 235**	**941**	**640**	**831**	**1 587**	**1 608**	**2 343**
Iceland	3	4	1	2	3	2	1	1	2	4	0	4
Norway	54	57	65	72	54	45	32	21	41	35	61	89
Total	**2 217**	**2 566**	**2 428**	**2 178**	**1 866**	**1 282**	**974**	**662**	**874**	**1 626**	**1 669**	**2 436**

Table A4. Distribution of confirmed IPD cases by country and age group (years), EU/EEA countries, 2012 (n=20 694)

Country	< 1		1–4		5–14		15–24		25–44		45–64		≥ 65		Total
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N
Austria	5	2.1	12	5.1	6	2.6	5	2.1	22	9.4	56	23.8	129	54.9	235
Belgium	57	3.4	151	9.0	61	3.6	30	1.8	189	11.2	438	26.0	760	45.1	1 686
Bulgaria*															
Cyprus	2	25.0									3	37.5	3	37.5	8
Czech Republic	2	0.6	13	3.9	17	5.1	9	2.7	46	13.7	108	32.2	140	41.8	335
Denmark	11	1.2	23	2.6	15	1.7	9	1.0	69	7.8	249	28.2	506	57.4	882
Estonia			3	15.0					2	10.0	6	30.0	9	45.0	20
Finland	8	1.1	24	3.2	11	1.5	14	1.9	95	12.6	257	34.2	343	45.6	752
France	134	3.0	187	4.2	90	2.0	70	1.6	493	11.1	1190	26.9	2 265	51.1	4 429
Greece	2	4.7	3	7.0	1	2.3			13	30.2	10	23.3	14	32.6	43
Hungary	5	2.7	4	2.2	15	8.1	2	1.1	17	9.1	68	36.6	75	40.3	186
Ireland	9	2.6	35	10.0	12	3.4	8	2.3	38	10.9	70	20.0	178	50.9	350
Italy	21	2.7	33	4.2	29	3.7	8	1.0	94	11.9	152	19.3	450	57.2	787
Latvia	2	3.6					1	1.8	14	25.0	20	35.7	19	33.9	56
Lithuania			2	28.6					2	28.6	2	28.6	1	14.3	7
Luxembourg													1	100.0	1
Malta			1	8.3	1	8.3			1	8.3	3	25.0	6	50.0	12
Netherlands	5	0.8	8	1.3	4	0.6	5	0.8	61	9.6	195	30.7	357	56.2	635
Poland	18	4.5	58	14.4	28	7.0	7	1.7	47	11.7	128	31.8	116	28.9	402
Romania	8	10.1	12	15.2	8	10.1	2	2.5	16	20.3	20	25.3	13	16.5	79
Slovakia	4	8.2	8	16.3	2	4.1	3	6.1	6	12.2	14	28.6	12	24.5	49
Slovenia	11	4.5	40	16.3	9	3.7	3	1.2	22	9.0	66	26.9	94	38.4	245
Spain	73	3.2	170	7.5	66	2.9	36	1.6	266	11.8	598	26.5	1 051	46.5	2 260
Sweden	7	0.5	20	1.4	16	1.2	13	0.9	134	9.7	387	27.9	810	58.4	1 387
United Kingdom	115	2.2	211	4.1	161	3.1	125	2.4	673	13.0	1 411	27.2	2 499	48.1	5 195
EU total	**499**	**2.5**	**1 018**	**5.1**	**552**	**2.8**	**350**	**1.7**	**2 320**	**11.6**	**5 451**	**27.2**	**9 851**	**49.2**	**20 041**
Iceland							3	11.1	8	29.6	8	29.6	8	29.6	27
Norway	5	0.8	14	2.2	6	1.0	12	1.9	76	12.1	186	29.7	327	52.2	626
Total	**504**	**2.4**	**1 032**	**5.0**	**558**	**2.7**	**365**	**1.8**	**2 404**	**11.6**	**5 645**	**27.3**	**10 186**	**49.2**	**20 694**

** Aggregated data reported, exact number of cases in these age groups could not be determined*

Table A5. Notification rate of confirmed IPD cases by age group and year, EU/EEA countries, 2008–12 (n=67 203)

Age group (years)	2008		2009		2010		2011		2012	
	N	NR	N	NR	N	NR	N	NR	N	NR
< 1	359	15.0	355	18.9	344	13.0	295	11.2	283	10.9
1–4	868	9.5	778	8.3	913	8.7	760	7.1	621	5.8
5–14	362	1.6	394	1.7	327	1.3	378	1.5	370	1.5
15–24	305	1.2	334	1.3	299	1.1	291	1.0	252	0.9
25–44	1 941	3.0	1 720	2.7	1 973	2.8	1 676	2.4	1 634	2.3
45–64	3 449	6.2	3 231	5.7	3 976	6.3	3 722	5.8	3 833	5.9
≥ 65	5 815	15.9	5 407	14.5	6 727	16.2	6 217	14.8	6 994	16.2
Total	**13 099**		**12 219**		**14 559**		**13 339**		**13 987**	

Contributing countries: Austria, the Czech Republic, Denmark, Estonia, Finland, Greece, Hungary, Ireland, Italy, the Netherlands, Norway, Slovakia, Slovenia, Spain, Sweden and the United Kingdom

Table A6. Distribution of IPD cases by clinical presentation and country, EU/EEA countries, 2012 (n=10 383)

Country	Bacteraemia		Meningitis		Bacteraemia and pneumonia		Other		Total
	N	%	N	%	N	%	N	%	N
Austria	73	46.2	32	20.3	50	31.6	3	1.9	158
Belgium	83	9.0	96	10.4	622	67.7	118	12.8	919

Country	Bacteraemia		Meningitis		Bacteraemia and pneumonia		Other		Total
	N	%	N	%	N	%	N	%	N
Cyprus	7	70.0			1	10.0	2	20.0	10
Czech Republic	129	39.7	73	22.5	118	36.3	5	1.5	325
Estonia	12	60.0	8	40.0		0.0			20
France			419	100.0					419
Greece			43	100.0					43
Hungary	98	58.0	66	39.1	5	3.0			169
Ireland	54	33.8	27	16.9	79	49.4			160
Latvia	18	32.1	15	26.8	21	37.5	2	3.6	56
Lithuania	7	100.0							7
Luxembourg			1	100.0					1
Malta							15	100.0	15
Poland	215	53.5	117	29.1	43	10.7	27	6.7	402
Romania			34	43.0	45	57.0			79
Slovakia	24	49.0	16	32.7	9	18.4			49
Slovenia	18	17.5	7	6.8	66	64.1	12	11.7	103
Spain	582	25.8	216	9.6	1367	60.5	95	4.2	2 260
United Kingdom	3 784	80.2	136	2.9	58	1.2	742	15.7	4 720
EU total	**5 104**	**51.5**	**1 306**	**13.2**	**2 484**	**25.1**	**1 021**	**10.3**	**9 915**
Iceland	22	81.5	4	14.8	1	3.7			27
Norway	382	86.6	56	12.7			3	0.7	441
Total	**5 508**	**53.0**	**1 366**	**13.2**	**2 485**	**23.9**	**1 024**	**9.9**	**10 383**

Table A7. Case fatality rate of IPD in EU/EEA countries*, 2012 (n=6 328)

Country	Confirmed cases (N)	Cases with known outcome (N)	Deaths (N)	CFR (%)	95% confidence interval (%)
Austria	235	235	15	6.4	3.6–10.3
Belgium	1738	1139	67	5.9	4.6–7.4
Cyprus	10	5	0	0.0	0–52.2
Czech Republic	335	328	61	18.6	14.5–23.2
Estonia	20	20	2	10.0	1.2–31.7
Greece	43	10	4	40.0	12.2–73.8
Hungary	186	45	13	28.9	16.4–44.3
Ireland	350	164	6	3.7	1.4–7.8
Italy	787	578	72	12.5	9.9–15.4
Latvia	56	56	8	14.3	6.4–26.2
Lithuania	7	4	0	0.0	0–60.2
Luxembourg	1	1	0	0.0	0–97.5
Malta	15	15	1	6.7	0.2–32
Poland	402	402	76	18.9	15.2–23.1
Romania	79	79	10	12.7	6.2–22.1
Slovakia	49	49	5	10.2	3.4–22.2
Slovenia	245	245	9	3.7	1.7–6.9
Sweden	1387	1387	183	13.2	11.5–15.1
United Kingdom	5209	1097	117	10.7	8.9–12.6
EU total	**11 154**	**5 859**	**649**	**11.0**	**10.2–11.8**
Iceland	27	27	2	7.4	0.9–24.3
Norway	626	442	45	10.2	7.5–13.4
Total	**11 807**	**6 328**	**696**	**11.0**	**10.2–11.8**

** Only 'unknown' outcomes reported by Bulgaria, Denmark, Finland, France, the Netherlands and Spain.*

Table A8. Number of confirmed cases, total number of deaths and case fatality rate of IPD by age group in EU/EEA countries, 2012 (n=6 291)

Age group (years)	Confirmed cases (N)	Cases with known outcome (N)	Deaths (N)	CFR (%)
< 1	496	152	10	6.6
1–4	1 008	399	20	5.0
5–14	547	198	9	4.5
15–24	351	107	2	1.9
25–44	2 309	739	35	4.7
45–64	5 388	1 682	166	9.9
≥ 65	9 843	3 014	453	15.0
Total	**19 942**	**6 291**	**695**	**11.0**

Table A9. Number of confirmed cases, total number of deaths and case fatality rate of IPD by clinical presentation in EU/EEA countries*, 2012 (n=3 451)

Clinical presentation	Confirmed cases (N)	Cases with known outcome (N)	Deaths (N)	CFR (%)
Meningitis	1 366	522	97	18.6
Bacteraemia	5 508	1 674	137	8.2
Bacteraemia and pneumonia	2 485	919	72	7.8
Other	1 024	336	18	5.4
Total	**10 383**	**3451**	**324**	**10.0**

Table A10. Distribution of serogroups and serotypes isolated from confirmed IPD cases, EU/EEA countries, 2012 (n=13 837)

Serogroup	Serotype	N isolates
1		1 018
2		3
3		1 374
4		298
5		85
6	na	44
	6A	188
	6B	178
	6C	375
	6D	2
7	na	133
	7A	5
	7B	3
	7C	9
	7F	1 189
8		885
9	na	53
	9A	3
	9L	1
	9N	339
	9V	183
10	na	11
	10A	227
	10B	16
	10F	8
11	na	49
	11A	302
	11B	4
	11C	2
	11F	3
12	na	90
	12A	1
	12B	5
	12F	444
13		12
14		477
15	na	32
	15A	346
	15B	157
	15B/C	5
	15C	80
	15F	6
16	na	23
	16A	3
	16F	177

Serogroup	Serotype	N isolates
18	na	11
	18A	7
	18B	5
	18C	136
	18F	4
19	na	104
	19A	1 116
	19B	1
	19C	2
	19F	212
20		100
21		25
22	na	75
	22A	1
	22F	963
23	na	26
	23A	281
	23B	223
	23F	199
24	na	38
	24A	3
	24B	4
	24F	190
25	25A	1
	25F	3
27		7
28	na	1
	28A	5
	28F	1
29		22
31		142
33	na	40
	33A	3
	33F	323
34		33
35	na	6
	35A	5
	35B	175
	35F	190
36		3
37		13
38		149
Other		3
Not typeable		49
Total		**13 837**

17	na	15
	17A	2
	17F	72

na = not available/not reported

Table A11. Distribution of ten most frequent IPD serotypes by country, EU/EEA countries, 2012 (n=13 034)**

Country	Top 10 serotypes																		Total**
	3~		7F*		19A~		1*		22F^		8^		14#		12F^		6C		15A		
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N
Austria	21	15.7	7	5.2	12	8.9	3	2.2	4	3.0	2	1.5	19	14.1			4	3.0	3	2.2	134
Belgium	114	10.7	17	1.0	119	6.8	286	16.5	5	0.3	68	3.9	21	1.2	102	5.9			21	1.2	1 069
Cyprus	2	100.0																			2
Czech Republic	47	17.0	16	5.8	11	4.0	26	9.4	13	4.7	5	1.8	18	6.5	2	0.7	4	1.4	6	2.2	277
Denmark	65	7.4	75	8.6	36	4.1	162	18.6	72	8.2	62	7.1	6	0.7	55	6.3	25	2.9	16	1.8	873
Estonia	2	50.0			1	16.7															4
Finland	76	10.4	44	5.9	38	5.1	3	0.4	72	9.7	5	0.7	103	13.9	4	0.5	20	2.7	6	0.8	731
Greece	5	83.3			1	5.6															6
Hungary	39	25.3	8	5.2	7	4.5	6	3.9	9	5.8	5	3.2	2	1.3	2	1.3	2	1.3	5	3.2	154
Ireland	20	6.7	46	15.3	27	9.0	10	3.3	31	10.3	19	6.3	9	3.0	3	1.0	5	1.7	11	3.7	298
Italy	56	12.9	40	8.8	44	9.7	30	6.6	25	5.5	20	4.4	22	4.9	21	4.6	8	1.8	6	1.3	435
Latvia	6	16.2	1	2.4			2	4.8			1	2.4	6	14.3	2	4.8			1	2.4	37
Lithuania		0.0					1	25.0					2	50.0							4
Netherlands	49	7.7	99	15.6	80	12.6	51	8.0	43	6.8	90	14.2	12	1.9	27	4.3	11	1.7	7	1.1	635
Poland	32	17.7	4	2.2	7	3.9	8	4.4	3	1.7	4	2.2	22	12.2	3	1.7	2	1.1			181
Romania	3	13.6			3	13.6	1	4.5					3	13.6							22
Slovakia	7	22.6	1	3.2	7	22.6							2	6.5	1	3.2					31
Slovenia	38	16.0	5	2.0	8	3.3	14	5.7	5	2.0			42	17.1	1	0.4	3	1.2	1	0.4	237
Spain	286	12.8	157	6.9	215	9.5	146	6.5	111	4.9	106	4.7	132	5.8	96	4.2	98	4.3	54	2.4	2 241
Sweden	159	13.7	99	8.3	80	6.7	23	1.9	144	12.1	29	2.4	25	2.1	8	0.7	37	3.1	9	0.8	1 158
United Kingdom	297	7.6	474	12.2	367	9.4	213	5.5	337	8.7	447	11.5	23	0.6	112	2.9	131	3.4	192	4.9	3 884
EU total	**1 324**	**10.7**	**1 093**	**8.8**	**1 063**	**8.6**	**985**	**7.9**	**874**	**7.0**	**863**	**7.0**	**469**	**3.8**	**439**	**3.5**	**350**	**2.8**	**338**	**2.7**	**12 413**
Iceland	2	13.3					3	11.5					3	11.5							15
Norway	48	7.9	96	15.8	53	8.7	30	4.9	89	14.7	22	3.6	5	0.8	5	0.8	25	4.1	8	1.3	606
Total	**1 374**	**10.5**	**1 189**	**9.1**	**1 116**	**8.6**	**1 018**	**7.8**	**963**	**7.4**	**885**	**6.8**	**477**	**3.7**	**444**	**3.4**	**375**	**2.9**	**346**	**2.7**	**13 034**

** Covered by 10- and 13-valent vaccines and PPV23*

~ Covered by the 13-valent vaccine and PPV23

 # Covered by the 7-, 10- and 13-valent vaccines and PPV23

^ Covered by the PPV23

*** Total refers to all cases for which serotype is known*

Table A12. Distribution of ten most frequent IPD serotypes by age group, EU/EEA countries, 2012 (n=12992*)

Serotype	< 1 year		1–4 years		5–14 years		15–24 years		25–44 years		45–64 years		≥ 65 years	
	N	%	N	%	N	%					N	%	N	%
3	15	5.0	28	4.3	20	5.8	10	4.2	97	6.4	395	11.1	805	12.6
7F	27	8.9	27	4.1	39	11.4	56	23.5	251	16.7	363	10.2	425	6.7
19A	28	9.2	81	12.3	11	3.2	14	5.9	91	6.1	279	7.8	607	9.5
1	6	2.0	111	16.9	127	37.0	39	16.4	222	14.8	266	7.5	237	3.7
22F	10	3.3	23	3.5	8	2.3	14	5.9	88	5.9	265	7.5	552	8.6
8	12	4.0	4	0.6	4	1.2	17	7.1	143	9.5	334	9.4	367	5.7
14	15	5.0	52	7.9	12	3.5	11	4.6	52	3.5	97	2.7	238	3.7
12F	15	5.0	29	4.4	7	2.0	7	2.9	72	4.8	147	4.1	163	2.6
6C	6	2.0	5	0.8	2	0.6	6	2.5	23	1.5	67	1.9	266	4.2
15A	8	2.6	16	2.4	6	1.7	3	1.3	20	1.3	71	2.0	221	3.5
Total*		**303**		**658**		**343**		**238**		**1 504**		**3 557**		**6 389**

** Total = total number of cases for which serotype information is available by age group*

Table A13. Distribution of clinical specimens from confirmed IPD cases by country, EU/EEA countries, 2012 (n=20 626)

Country	Blood		CSF*		Joint		Other		Peritoneal liquid		Pleural liquid		Total
	N	%	N	%	N	%	N	%	N	%	N	%	N
Austria	167	83.5	27	13.5		0.0	5	2.5		0.0	1	0.5	200
Belgium	1 657	95.3	81	4.7		0.0		0.0		0.0		0.0	1 738
Cyprus	8	100.0		0.0		0.0		0.0		0.0		0.0	8

Country	Blood		CSF*		Joint		Other		Peritoneal liquid		Pleural liquid		Total
	N	%	N	%	N	%	N	%	N	%	N	%	N
Czech Republic	262	78.4	70	21.0		0.0		0.0		0.0	2	0.6	334
Denmark	837	94.9	43	4.9		0.0	1	0.1		0.0	1	0.1	882
Estonia	8	50.0	8	50.0		0.0		0.0		0.0		0.0	16
Finland	728	96.8	24	3.2		0.0		0.0		0.0		0.0	752
France	4 011	90.5	419	9.5		0.0		0.0		0.0		0.0	4 430
Greece		0.0	18	100.0		0.0		0.0		0.0		0.0	18
Hungary	106	63.5	61	36.5		0.0		0.0		0.0		0.0	167
Iceland	23	85.2	4	14.8		0.0		0.0		0.0		0.0	27
Ireland	306	87.7	28	8.0		0.0		0.0	1	0.3	14	4.0	349
Italy	584	74.5	200	25.5		0.0		0.0		0.0		0.0	784
Latvia	38	67.9	17	30.4		0.0		0.0		0.0	1	1.8	56
Lithuania	6	85.7	1	14.3		0.0		0.0		0.0		0.0	7
Luxembourg		0.0	1	100.0		0.0		0.0		0.0		0.0	1
Malta	13	86.7	2	13.3		0.0		0.0		0.0		0.0	15
Netherlands	592	93.2	43	6.8		0.0		0.0		0.0		0.0	635
Norway	591	94.4	32	5.1	1	0.2	2	0.3		0.0		0.0	626
Poland	231	62.3	117	31.5		0.0	23	6.2		0.0		0.0	371
Romania	39	49.4	36	45.6		0.0	4	5.1		0.0		0.0	79
Slovakia	32	65.3	12	24.5		0.0	5	10.2		0.0		0.0	49
Slovenia	233	95.1	8	3.3		0.0	4	1.6		0.0		0.0	245
Spain	1 979	87.6	153	6.8	9	0.4	17	0.8	21	0.9	81	3.6	2 260
Sweden	1 322	95.7	36	2.6	9	0.7	8	0.6		0.0	7	0.5	1 382
United Kingdom	4 286	82.5	149	2.9	18	0.3	674	13.0	10	0.2	58	1.1	5 195
Total	**18 059**	**87.6**	**1590**	**7.7**	**37**	**0.2**	**743**	**3.6**	**32**	**0.2**	**165**	**0.8**	**20 626**

** CSF = cerebrospinal fluid*

Table A14. Distribution of clinical specimens from confirmed IPD cases by age group, EU/EEA countries, 2012 (n=10 135)

Specimen	< 1 year		1–4 years		5–14 years		15–24 years		25–44 years		45–64 years		≥ 65 years	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Blood	359	71.9	817	80.4	398	72.1	307	85.0	2 022	84.9	4 838	86.2	9 253	91.3
CSF*	120	24.0	92	9.1	82	14.9	32	8.9	253	10.6	497	8.9	508	5.0
Joint	1	0.2	3	0.3		0.0		0.0	2	0.1	9	0.2	22	0.2
Other	17	3.4	75	7.4	48	8.7	18	5.0	84	3.5	211	3.8	289	2.9
Peritoneal liquid	0	0.0	1	0.1		0.0		0.0	3	0.1	17	0.3	11	0.1
Pleural liquid	2	0.4	28	2.8	24	4.3	4	1.1	17	0.7	38	0.7	52	0.5
Total	**499**		**1 016**		**552**		**361**		**2381**		**5 610**		**10 135**	

** CSF = cerebrospinal fluid*

Table A15. Quality of 2012 data; distribution of known, unknown, not applicable and blank responses per variable for all confirmed cases of IPD in EU/EEA countries

Variable	Known		NA/NT^		Unknown		Blank		Overall missing		Total confirmed cases
	N	%	N	%	N	%	N	%	N	%	N
Month used for statistics	20 778	99.97					7	0.03	7	0.03	20 785
Age*	20 694	99.6					91	0.4	91	0.4	20 785
Age in months**	744	88.3			10	1.2	89	10.6	99	11.7	843
Gender*	20 726	99.7			59	0.3			59	0.3	20 785
Clinical presentation	10 383	50.0			10 383	50.0	19	0.1	10 402	50.0	20 785
Outcome	6 328	30.4			13 686	65.8	771	3.7	14 457	69.6	20 785
Vaccination status	3 750	18.0			12 586	60.6	4 449	21.4	17 035	82.0	20 785
Vaccine type***	153	40.7			94	25.0	129	34.3	223	59.3	376
Place of notification	15 037	72.3			2 260	10.9	3 488	16.8	5 748	27.7	20 785
Place of residence	11 219	54.0			7 793	37.5	1 773	8.5	9 566	46.0	20 785
Specimen	20 626	99.2			129	0.6	30	0.1	159	0.8	20 785
Serotype	13 837	66.6	119	0.6	1 995	9.6	4 834	23.3	6 948	33.4	20 785
First test method for typing	12 592	60.6	1 937	9.3	897	4.3	5 359	25.8	8 193	39.4	20 785
Second test method for typing	392	1.9	6			0.00	20 387	98.1	20 393	98.1	20 785
Test method for MIC	5 658	27.2			1 244	6.0	13 883	66.8	15 127	72.7	20 785
MIC sign for cefotaxime/ceftriaxone	4 659	22.4					16 126	77.6	16 126	77.6	20 785
MIC value for cefotaxime/ceftriaxone	4 864	23.4					15 921	76.6	15 921	76.6	20 785
SIR for cefotaxime/ceftriaxone	5 443	26.2			1 931	9.3	13 411	64.5	15 342	73.8	20 785
MIC sign for erythromicin	4 752	22.9					16 033	77.1	16 033	77.1	20 785
MIC value for erythromicin	4 776	23.0					16 009	77.0	16 009	77.0	20 785

Variable	Known		NA/NT^		Unknown		Blank		Overall missing		Total confirmed cases
	N	%	N	%	N	%	N	%	N	%	N
SIR for erythromicin	8 682	41.8			1 034	5.0	11 069	53.3	12 103	58.2	20 785
MIC sign for penicillin	4 754	22.9					16 031	77.1	16 031	77.1	20 785
MIC value for penicillin	4 959	23.9					15 826	76.1	15 826	76.1	20 785
SIR for penicillin	11 222	54.0			1 028	4.9	8 535	41.1	9 563	46.0	20 785

** Includes case-based and aggregated data*

*** Age in months is required only for cases with age < 2 years.*
A total of 843 cases under two years of age were reported in 2012 by 22 countries. Only Belgium did not report 'age in months'.

**** Indicates which IPD vaccine was administered. Calculation is based on the total of vaccinated confirmed cases (n=376; vaccination status known for 3750 confirmed cases, of which 3374 were not vaccinated)*

^ Not applicable/non-typable

Annex 2. Invasive *H. influenzae* disease

Table B1. Description of the data sources for surveillance of invasive *H. influenzae* disease, 2012

Country	Data source	Legal character	Comprehensive	Active/passive	Case-based/aggregated	Data reported by				Case definition
						Labs	Physicians	Hosp.	Other	
Austria	AT-Epidemiegesetz	Cp	Co	P	C	Y	Y	Y	Y	EU 2008
Belgium	BE-LABNET	V	Se	A	C	Y	N	U	U	
Bulgaria	BG-NATIONAL_SURVEILLANCE	Cp	Co	P	A	Y	Y	Y	Y	EU 2008
Cyprus	CY-NOTIFIED_DISEASES	Cp	Co	P	C	N	Y	N	N	EU 2008
Cyprus	CY-LABNET									
Czech Republic	CZ-EPIDAT	Cp	Co	A	C	N	Y	Y	N	EU 2008
Denmark	DK-LAB	Cp	Co	P	C	Y	N	N	N	Unk
Estonia	EE-HIB	Cp	Co	P	C	Y	Y	Y	Y	EU 2008
Finland	FI-NIDR	Cp	Co	P	C	Y	N	N	N	EU 2008
France	FR-EPIBAC	V	Se	A	C	Y	N	Y	N	EU 2008
Germany	DE-SURVNET@RKI-7.1/6	Cp	Co	P	C	Y	Y	Y	Y	Other
Greece	GR-NOTIFIABLE_DISEASES	Cp	Co	P	C	Y	Y	Y	N	Other
Hungary	HU-EFRIR	Cp	Co	P	C	Y	Y	Y	N	EU 2008
Ireland	IE-CIDR	Cp	Co	P	C	Y	Y	Y	N	EU 2008
Italy	IT-MENINGITIS	V	Co	P	C	N	Y	Y	N	EU 2012
Latvia	LV-BSN	Cp	Co	P	C	Y	Y	Y	Y	EU 2012
Lithuania	LT-COMMUNICABLE_DISEASES	Cp	Co	P	C	Y	Y	N	N	EU 2008
Malta	MT-DISEASE_SURVEILLANCE	Cp	Co	P	C	Y	Y	Y	Y	EU 2008
Netherlands	NL-NRBM	V	Co	P	C	Y	N	N	N	EU 2008
Norway	NO-MSIS_A	Cp	Co	P	C	Y	Y	Y	N	EU 2012
Poland	PL-NATIONAL_SURVEILLANCE	Cp	Co	P	C	N	Y	Y	N	EU 2008
Portugal	PT-HAEMOPHILUS_INFLUENZAE	Cp	Co	P	C	Y	Y	N	N	EU 2002
Romania	RO-RNSSy	Cp	Co	P	C	N	N	Y	N	EU 2008
Slovakia	SK-EPIS	Cp	Co	A	C	Y	Y	Y	N	EU 2012
Slovenia	SI-SURVIVAL	Cp	Co	P	C	Y	Y	Y	N	EU 2008
Spain	ES-MICROBIOLOGICAL	V	Se	P	C	Y	N	N	N	EU 2008
Sweden	SE-SMINET	Cp	Co	P	C	Y	Y	N	N	EU 2012
United Kingdom	UK-HIB	O	Co	P	C	Y	N	Y	Y	EU 2002

Cp: compulsory, V: voluntary, Co: comprehensive, O: other, Se: sentinel, P: passive, A: active, C: case-based, A: aggregated, Y: yes, N: no, Unk: unknown

Table B2. Population coverage of the FR-EPIBAC data source from France, 2010–12

Age group (years)	2010			2011			2012		
	Female	Male	Both	Female	Male	Both	Female	Male	Both
< 1	292 337	304 734	597 071	289 992	303 065	593 057	283 924	298 083	582 007
1 to 4	1 149 157	1 196 485	2 345 642	1 139 941	1 189 930	2 329 871	1 157 326	1 205 333	2 362 659
5 to 14	2 818 916	2 960 405	5 779 321	2 818 951	2 957 650	5 776 601	2 899 630	3 033 769	5 933 399
15 to 24	2 888 589	2 977 796	5 866 385	2 851 593	2 945 889	5 797 482	2 864 892	2 956 651	5 821 543
25 to 44	6 215 743	6 138 592	12 354 335	6 168 748	6 082 890	12 251 724	6 203 150	6 103 685	12 306 835
45 to 64	6 433 081	6 127 310	12 560 391	6 384 443	6 071 711	12 456 068	6 472 125	6 160 645	12 632 769
≥ 65	4 731 817	3 321 250	8 053 067	4 790 599	3 421 240	8 211 839	4 943 947	3 586 926	8 530 873

Table B3. Distribution of confirmed invasive *H. influenzae* disease cases by country and month, EU/EEA countries, 2012 (n=2 542)

Country	Jan	Feb	Mar	Apr	May	June	July	Aug	Sept	Oct	Nov	Dec
Austria	1	0	0	1	0	1	0	1	0	0	0	2
Belgium	6	5	8	12	8	8	5	3	4	3	7	9
Bulgaria*	0	0	0	0	0	0	0	0	0	0	0	0
Cyprus	1	0	3	4	0	0	0	0	0	0	0	0
Czech Republic	1	2	1	0	1	0	0	0	0	0	4	2
Denmark	8	6	8	2	4	4	4	3	5	7	6	8
Estonia	0	0	1	0	0	0	0	0	0	0	2	0
Finland	7	7	6	3	3	8	10	6	7	14	5	5
France	59	47	55	49	35	29	28	28	15	48	40	58
Germany	27	35	26	29	26	20	19	16	14	40	30	37
Greece	1	0	0	1	0	1	0	1	1	0	1	0
Hungary	1	0	1	0	0	0	1	0	1	0	0	0
Ireland	4	3	9	4	0	1	5	2	3	6	3	1
Italy	7	5	6	6	4	7	6	2	1	2	8	5
Latvia	0	0	0	0	0	1	0	0	0	0	0	0
Lithuania	0	0	0	0	1	1	0	0	0	1	0	0
Netherlands	12	12	19	13	15	10	9	8	6	10	15	10
Poland	4	5	1	2	3	2	0	2	2	5	6	3
Portugal	4	10	8	5	6	4	0	2	1	1	2	2

Country	Jan	Feb	Mar	Apr	May	June	July	Aug	Sept	Oct	Nov	Dec
Romania	0	0	2	0	0	0	0	0	2	1	2	2
Slovakia	0	1	0	0	0	0	0	0	0	1	0	1
Slovenia	3	1	1	3	0	2	2	1	0	2	1	2
Spain	14	12	12	9	3	6	9	3	1	5	4	12
Sweden	17	24	13	12	20	18	22	18	16	15	18	21
United Kingdom	75	73	81	59	60	57	43	39	37	54	60	97
EU total	**252**	**248**	**261**	**214**	**189**	**180**	**163**	**135**	**116**	**215**	**214**	**277**
Norway	3	6	12	6	10	5	5	5	2	4	6	14
Total	**255**	**254**	**273**	**220**	**199**	**185**	**168**	**140**	**118**	**219**	**220**	**291**

** Aggregated data*

Table B4. Distribution of confirmed invasive *H. influenzae* disease by country and age group, EU/EEA countries, 2012 (n=2 536*)

Country	< 1 year		1–4 years		5–14 years		15–24 years		25–44 years		45–64 years		≥ 65 years		Total
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N
Austria	0	0.0	0	0.0	0	0.0	1	16.7	0	0.0	2	33.3	3	50.0	6
Belgium	4	5.4	4	5.4	3	4.1	0	0.0	9	12.2	13	17.6	41	55.4	74
Bulgaria	0	0.0	1	33.3	1	33.3	0	0.0	0	0.0	1	33.3	0	0.0	3
Cyprus	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	12.5	7	87.5	8
Czech Republic	2	18.2	2	18.2	0	0.0	0	0.0	0	0.0	2	18.2	5	45.5	11
Denmark	3	4.6	0	0.0	0	0.0	3	4.6	2	3.1	22	33.8	35	53.8	65
Estonia	0	0.0	2	66.7	0	0.0	0	0.0	1	33.3	0	0.0	0	0.0	3
Finland	4	4.9	0	0.0	0	0.0	4	4.9	6	7.4	16	19.8	51	63.0	81
France	17	3.5	18	3.7	15	3.1	14	2.9	70	14.3	98	20.0	259	52.7	491
Germany	5	1.6	14	4.4	9	2.8	7	2.2	24	7.5	58	18.2	202	63.3	319
Greece	1	16.7	2	33.3	0	0.0	0	0.0	1	16.7	0	0.0	2	33.3	6
Hungary	0	0.0	1	25.0	0	0.0	0	0.0	0	0.0	2	50.0	1	25.0	4
Ireland	3	7.3	3	7.3	3	7.3	5	12.2	5	12.2	5	12.2	17	41.5	41
Italy	5	8.5	1	1.7	2	3.4	0	0.0	4	6.8	17	28.8	30	50.8	59
Latvia	1	100	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1
Lithuania	0	0.0	2	66.7	0	0.0	0	0.0	1	33.3	0	0.0	0	0.0	3
Netherlands	12	8.6	10	7.2	5	3.6	1	0.7	22	15.8	24	17.3	65	46.8	139
Poland	3	8.6	4	11.4	2	5.7	1	2.9	6	17.1	8	22.9	11	31.4	35
Portugal	6	13.3	3	6.7	2	4.4	0	0.0	8	17.8	5	11.1	21	46.7	45
Romania	0	0.0	6	66.7	3	33.3	0	0.0	0	0.0	0	0.0	0	0.0	9
Slovakia	1	33.3	0	0.0	0	0.0	0	0.0	1	33.3	0	0.0	1	33.3	3
Slovenia	1	5.6	1	5.6	0	0.0	0	0.0	1	5.6	7	38.9	8	44.4	18
Spain	6	7.0	3	3.5	3	3.5	1	1.2	6	7.0	20	23.3	47	54.7	86
Sweden	7	3.3	6	2.8	4	1.9	4	1.9	12	5.6	48	22.4	133	62.1	214
United Kingdom	67	9.1	32	4.4	12	1.6	20	2.7	68	9.3	136	18.5	399	54.4	734
EU total	**148**	**0.06**	**114**	**0.05**	**63**	**0.10**	**61**	**0.02**	**247**	**0.10**	**484**	**0.20**	**1 338**	**0.55**	**2 458**
Norway	0	0.0	2	0.0	2	0.0	1	0.0	9	0.1	17	0.2	47	0.6	78
Total	**148**	**0.06**	**116**	**0.05**	**65**	**0.10**	**62**	**0.02**	**256**	**0.10**	**501**	**0.20**	**1 385**	**0.55**	**2 536**

Table B5. Notification rates of confirmed invasive *H. influenzae* disease by age group and gender, EU/EEA countries, 2012 (n=2 456*)

Age group (years)	Male		Female		Total	
	N	NR	N	NR	N	NR
< 1	73	4.4	69	4.0	142	4.2
1–4	68	1.0	42	0.5	110	0.8
5–14	33	0.2	30	0.2	63	0.2
15–24	28	0.2	34	0.2	62	0.2
25–44	82	0.2	164	0.3	246	0.2
45–64	247	0.5	242	0.5	489	0.5
≥ 65	659	2.2	685	1.7	1 344	1.9
Total	**1 190**		**1 266**		**2 456**	

** Excludes aggregated data where different age groups were reported. Data from Belgium were excluded since population coverage was unknown.*

Contributing countries: Austria, Bulgaria, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom

Table B6. Notification rate of confirmed invasive *H. influenzae* disease by age group, EU/EEA countries, 2008–12 (n=10 706)

Age group (years)	2008		2009		2010		2011		2012	
	N	NR	N	NR	N	NR	N	NR	N	NR
< 1	138	4.0	156	4.0	138	3.5	140	3.7	142	4.2
1–4	109	0.7	143	0.8	105	0.7	119	0.8	109	0.7
5–14	80	0.2	70	0.2	52	0.1	61	0.2	62	0.2
15–24	55	0.2	70	0.2	60	0.2	72	0.2	62	0.2
25–44	216	0.2	207	0.2	201	0.2	262	0.3	246	0.2
45–64	444	0.4	425	0.4	420	0.4	500	0.5	487	0.5
≥ 65	938	1.5	939	1.4	1 006	1.5	1 135	1.7	1 337	1.9
Total	**1 980**		**2 010**		**1 982**		**2 289**		**2 445**	

Contributing countries: Austria, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom

Table B7. Distribution of confirmed invasive *H. influenzae* disease by clinical presentation and country, EU/EEA countries, 2012 (n=1 019*)

Country	Septicaemia		Meningitis		Pneumonia		Other**		Meningitis and septicaemia		Cellulitis		Osteo-myelitis/ septic arthritis		Total
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N
Austria	2	33.3	0	0.0	2	33.3	2	33.3	0	0.0	0	0.0	0	0.0	6
Czech Republic	5	45.5	5	45.5	1	9.1	0	0.0	0	0.0	0	0.0	0	0.0	11
Estonia	0	0.0	3	100.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	3
France	47	39.8	30	25.4	31	26.3	6	5.1	0	0.0	4	3.4	0	0.0	118
Germany	37	13.8	17	6.3	153	57.1	53	19.8	3	1.1	0	0.0	5	1.9	268
Greece	0	0.0	5	83.3	0	0.0	0	0.0	1	16.7	0	0.0	0	0.0	6
Hungary	0	0.0	4	100	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	4
Ireland	11	36.7	2	6.7	12	40.0	4	13.3	1	3.3	0	0.0	0	0.0	30
Italy	27	45.8	15	25.4	14	23.7	1	1.7	2	3.4	0	0.0	0	0.0	59
Latvia	0	0.0	0	0.0	0	0.0	0	0.0	1	100	0	0.0	0	0.0	1
Lithuania	0	0.0	0	0.0	1	33.3	2	66.7	0	0.0	0	0.0	0	0.0	3
Poland	11	31.4	8	22.9	0	0.0	12	34.3	4	11.4	0	0.0	0	0.0	35
Portugal	7	31.8	4	18.2	10	45.5	1	4.5	0	0.0	0	0.0	0	0.0	22
Romania	0	0.0	8	88.9	0	0.0	1	11.1	0	0.0	0	0.0	0	0.0	9
Slovakia	0	0.0	3	100	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	3
Slovenia	1	100	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1
United Kingdom	345	89.6	14	3.6	10	2.6	16	4.2	0	0.0	0	0.0	0	0.0	385
EU total	**493**	**51.1**	**118**	**12.2**	**234**	**24.3**	**98**	**10.1**	**12**	**1.2**	**4**	**0.4**	**5**	**0.5**	**964**
Norway	16	29.1	2	3.6	20	36.4	16	29.1	1	1.8		0.0		0.0	55
EU/EEA total	**509**	**50.0**	**120**	**11.8**	**254**	**24.9**	**114**	**11.2**	**13**	**1.3**	**4**	**0.4**	**5**	**0.5**	**1 019**

** Excludes cases reported as 'not under surveillance'*

*** 'Other' includes cases where clinical presentation was recorded as 'other', and one case with epiglottitis reported by France.*

Table B8. Case fatality rate due to invasive *H. influenzae* disease in EU/EEA countries*, 2012 (n=1 422)

Country	Cases (N)	Cases with known outcome (N)	Deaths (N)	CFR (%)	95% confidence interval (%)
Austria	6	6	0	0.0	0–45.9
Cyprus	8	8	0	0.0	0–36.9
Czech Republic	11	11	1	9.1	0.2–41.3
Estonia	3	3	0	0.0	0–70.8
Germany	319	319	27	8.5	5.7–12.1
Greece	6	2	1	50	1.3–98.7
Hungary	4	4	0	0.0	0–60.2
Ireland	41	20	1	5.0	0.1–24.9
Italy	59	39	7	18	7.5–33.5
Latvia	1	1	1	100	2.5–100
Lithuania	3	2	0	0.0	0–84.2
Norway	78	41	3	7.3	1.5–19.9
Poland	35	35	6	17	6.6–33.7
Portugal	45	23	0	0.0	0–14.8
Romania	9	9	0	0.0	0–33.6
Slovakia	3	2	0	0.0	0–84.2
Slovenia	18	18	1	5.6	0.1–27.3
Sweden	214	214	38	18	12.9–23.6
United Kingdom	735	665	51	7.7	5.8–10
Total	**1 598**	**1 422**	**137**	**9.6**	**8.2–11.3**

** Only 'unknown' outcomes reported by Belgium, Bulgaria, Denmark, Finland, France, the Netherlands and Spain.*

Table B9. Number of cases, number of deaths and case fatality rate due to invasive *H. influenzae* disease by age group in EU/EEA countries, 2012 (n=1 422)

Age group (years)	Cases (N)	Cases with known outcome (N)	Deaths (N)	CFR (%)
< 1	148	94	10	10.6
1–4	116	69	5	7.2
5–14	65	31	1	3.2
15–24	62	33		0.0
25–44	256	122	2	1.6
45–64	501	270	20	7.4
≥ 65	1 385	803	99	12.3
Total	**2 533**	**1 422**	**137**	**9.6**

Table B10. Number of cases, number of deaths and case fatality rate due to invasive *H. influenzae* disease by clinical presentation in EU/EEA countries*, 2012

Clinical presentation	Cases (N)	Cases with known outcome (N)	Deaths (N)	CFR (%)
Septicaemia	509	443	40	9.0
Meningitis	120	78	2	2.6
Meningitis and septicaemia	13	12	3	25.0
Pneumonia	254	207	27	13.0
Osteomyelitis/septic arthritis	5	5	0	0.0
Other	113	96	3	3.1
Unknown	1 442	581	62	10.7
Total	**2 456**	**1 422**	**137**	**8.9**

** Excludes cases reported as 'not under surveillance'.*

Table B11. Distribution of confirmed invasive *H. influenzae* disease by serotype and country, EU/EEA countries, 2012 (n=1 352)

Country	b strain		Non-capsulated strains		Non-b strains*		Total
	N	%	N	%	N	%	N
Czech Republic	1	10.0	7	70.0	2	20.0	10
Denmark	7	10.8	49	75.4	9	13.8	65
Estonia	3	100.0	0	0.0	0	0.0	3
Finland	4	4.9	73	90.1	4	4.9	81
France	13	9.0	104	72.2	27	18.8	144
Germany	0	0.0	0	0.0	2	100.0	2
Greece	2	33.3	4	66.7	0	0.0	6
Hungary	0	0.0	0	0.0	2	100.0	2
Ireland	3	8.6	26	74.3	6	17.1	35
Italy	5	15.6	22	68.8	5	15.6	32
Latvia	1	100.0	0	0.0	0	0.0	1
Netherlands	28	20.1	100	71.9	11	7.9	139
Poland	2	5.7	33	94.3	0	0.0	35

Portugal	4	14.8	19	70.4	4	14.8	27
Romania	4	100.0	0	0.0	0	0.0	4
Slovakia	0	0.0	0	0.0	1	100.0	1
Slovenia	2	11.1	14	77.8	2	11.1	18
Sweden	6	3.8	120	76.9	30	19.2	156
United Kingdom	17	3.3	410	79.5	89	17.2	516
EU total	**102**	**8.0**	**981**	**76.8**	**194**	**15.2**	**1 277**
Norway	6	8.0	57	76.0	12	16.0	75
Total	**108**	**8.0**	**1 038**	**76.8**	**206**	**15.2**	**1 352**

** Non-b includes serotypes a (n=4), e (n=53), f (n=127) and isolates classified as 'non-b' (n=22)*

Table B12. Notification rates of invasive *H. influenzae* disease by serotype and year, EU and EEA countries, 2008–12 (n=6 933)

Serotype	2008	2009	2010	2011	2012
b strain	0.06	0.05	0.05	0.03	0.03
Non-b strains*	0.07	0.06	0.06	0.06	0.07
Non-capsulated strains	0.19	0.21	0.20	0.28	0.35
Unknown	0.20	0.19	0.19	0.19	0.12

** Non-b strain includes serotypes a, c, d, e, f and isolates classified as 'non-b'*

Contributing countries: Czech Republic, Denmark, Estonia, Finland, Greece, Hungary, Ireland, Italy, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovenia, Sweden and the United Kingdom

Table B13. Distribution of invasive *H. influenzae* disease serotypes by age group, EU/EEA countries, 2012 (n=1 348*)

Age groups (years)	b strain		Non-b strain^		Non-caps strain		Total
	N	%	N	%	N	%	N
< 1	16	15.7	11	10.8	75	73.5	102
1–4	17	26.2	10	15.4	38	58.5	65
5–14	8	22.2	9	25.0	19	52.8	36
15–24	2	5.9	3	8.8	29	85.3	34
25–44	12	9.0	17	12.8	104	78.2	133
45–64	30	11.2	52	19.3	187	69.5	269
≥ 65	23	3.2	104	14.7	582	82.1	709
Total	**108**		**206**		**1 034**		**1 348**

Total cases = total number of cases for which serotype information was available by age group.

** Overall, four non-capsulated cases had missing data for missing of for age group*

^ Non-b includes serotypes a, e, f and isolates classified as 'non-b'

Table B14. Distribution of invasive *H. influenzae* disease serotypes by gender, EU/EEA countries, 2012 (n=1 348*)

Serotype	Male		Female		Total
	N	%	N	%	N
b strain	55	8.5	53	7.5	108
Non-b strain^	93	14.4	113	16.1	206
Non-caps strain	497	77.1	537	76.4	1 034
Total	**645**		**703**		**1 348**

** Overall 4 non-capsulated cases had missing data for missing of for age group*

^ Non-b includes serotypes a, e, f and isolates classified as 'non-b'

Table B15. Notification rate of invasive *H. influenzae* serotype b disease, by age group and year of reporting, EU/EEA, 2008–12 (n=555)

Age group (years)	2008		2009		2010		2011		2012		Total
	N	NR	N	NR	N	NR	N	NR	N	NR	N
< 1	22	0.78	19	0.65	17	0.58	12	0.41	13	0.46	83
1–4	26	0.24	16	0.14	16	0.14	7	0.06	14	0.12	79
5–14	20	0.07	5	0.02	4	0.01	6	0.02	7	0.03	42
15-44	21	0.02	22	0.02	22	0.02	10	0.01	11	0.01	86
≥ 45	72	0.07	53	0.05	62	0.06	33	0.03	45	0.04	265
Total	**161**		**115**		**121**		**68**		**90**		**555**

Contributing countries: Czech Republic, Denmark, Estonia, Finland, Greece, Hungary, Ireland, Italy, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovenia, Sweden and the United Kingdom

Table B16. Notification rate of invasive *H. influenzae* non-b strains, by age group and year of reporting, EU/EEA, 2008–12 (n=832)

Age group (years)	2008		2009		2010		2011		2012		Total
	N	NR	N	NR	N	NR	N	NR	N	NR	N
< 1	16	0.57	14	0.48	9	0.31	4	0.14	9	0.32	52
1–4	12	0.11	10	0.09	10	0.09	9	0.08	7	0.06	48
5–14	7	0.03	10	0.04	1	0.004	5	0.02	7	0.03	30
15-44	21	0.02	16	0.01	19	0.02	17	0.02	18	0.02	91
≥ 45	118	0.11	118	0.11	121	0.11	123	0.11	131	0.11	611
Total	**174**		**168**		**160**		**158**		**172**		**832**

Contributing countries: Czech Republic, Denmark, Estonia, Finland, Greece, Hungary, Ireland, Italy, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovenia, Sweden and the United Kingdom

Table B17. Notification rate of invasive *H. influenzae* non-capsulated strains, by age group and year of reporting, EU/EEA, 2008–12 (n=3 211)

Age group (years)	2008		2009		2010		2011		2012		Total
	N	NR	N	NR	N	NR	N	NR	N	NR	N
< 1	51	1.80	59	2.02	44	1.51	59	2.04	64	2.27	277
1–4	27	0.25	45	0.40	28	0.25	35	0.30	34	0.29	169
5–14	11	0.04	13	0.05	20	0.07	18	0.07	14	0.05	76
15-44	69	0.06	76	0.07	74	0.07	119	0.11	110	0.10	448
≥ 45	327	0.30	364	0.33	357	0.32	500	0.44	693	0.60	2 241
Total	**485**		**557**		**523**		**731**		**915**		**3 211**

Contributing countries: Czech Republic, Denmark, Estonia, Finland, Greece, Hungary, Ireland, Italy, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovenia, Sweden and the United Kingdom

Table B18. Distribution of confirmed invasive *H. influenzae* disease by specimen type and country, EU/EEA countries, 2012 (n=2 772)

Country	Blood		CSF		LAV		Other sterile site		Total known	Total confirmed cases
	N	%	N	%	N	%	N	%		
Austria	3	75.0		0.0		0.0	1	25.0	4	6
Czech Republic	6	54.5	5	45.5		0.0		0.0	11	11
Denmark	62	95.4	3	4.6		0.0		0.0	65	65
Estonia		0.0	3	100.0		0.0		0.0	3	3
Finland	80	98.8	1	1.2		0.0		0.0	81	81
France	439	90.1	48	9.9		0.0		0.0	487	491
Germany	287	91.4	27	8.6		0.0		0.0	314	319
Greece	1	16.7	5	83.3		0.0		0.0	6	6
Hungary		0.0	4	100.0		0.0		0.0	4	4
Ireland	37	90.2	2	4.9		0.0	2	4.9	41	41
Italy	42	71.2	15	25.4		0.0	2	3.4	59	59
Latvia		0.0	1	100.0		0.0		0.0	1	1
Lithuania		0.0	3	100.0		0.0		0.0	3	3
Netherlands	123	88.5	16	11.5		0.0		0.0	139	139
Poland	15	62.5	9	37.5		0.0		0.0	24	35
Portugal	15	62.5	5	20.8	2	8.3	2	8.3	24	45
Romania	9	100.0		0.0		0.0		0.0	9	9
Slovakia		0.0	3	100.0		0.0		0.0	3	3
Slovenia	13	72.2	5	27.8		0.0		0.0	18	18
Spain	82	91.1	5	5.6		0.0	3	3.3	90	90
Sweden	201	95.3	9	4.3		0.0	1	0.5	211	214
United Kingdom	657	89.4	11	1.5		0.0	67	9.1	735	735
EU total	**2 072**	**88.9**	**180**	**7.7**	**2**	**0.1**	**78**	**3.3**	**2 332**	**2 378**
Norway	76	97.4	1	1.3		0.0	1	1.3	78	78
Total	**2 148**	**89.1**	**181**	**7.5**	**2**	**0.1**	**79**	**3.3**	**2 410**	**2 456**

** CSF = cerebrospinal fluid*

*** LAV = bronchoalveloar lavage*

Table B19. Distribution of confirmed invasive *H. influenzae* disease by specimen type and age group, EU/EEA countries, 2012 (n=2 405)

Specimen	< 1 year		1–4 years		5–14 years		15–24 years		25–44 years		45–64 years		≥ 65 years		Total
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	
Blood	113	81.3	76	68.5	50	82.0	55	90.2	204	86.4	410	85.1	1 235	93.9	2 143
CSF*	20	14.4	27	24.3	10	16.4	5	8.2	21	8.9	51	10.6	47	3.6	181
LAV**		0.0		0.0		0.0		0.0	1	0.4		0.0	1	0.1	2

Other sterile site	6	4.3	8	7.2	1	1.6	1	1.6	10	4.2	21	4.4	32	2.4	79
Total	**139**		**111**		**61**		**61**		**236**		**482**		**1 315**		**2 405**

** CSF = cerebrospinal fluid*

*** LAV = bronchoalveolar lavage*

Table B20. Quality of 2012 data: distribution of known, unknown, not applicable and blank responses per variable for all confirmed cases of invasive *H. influenzae* disease by country, EU/EEA countries (n=2 545*)

Variable	Known		Unknown		Blank		NUS/NT/NA^^		Missing	Total reported
	N	%	N	%	N	%	N	%	%	
Age**	2 533	99.5		0.0	12	0.5		0.0	0.5	2 545
Age in months***	195	88.2	1	0.5	25	11.3		0.0	11.8	221
Clinical presentation	1 019	40.0	1 442	56.7	3	0.1	81	3.2	60.0	2 545
Gender**	2 334	99.5	11	0.5		0.0		0.0	0.5	2 345
Month of notification	2 542	99.9		0.0	3	0.1		0.0	0.1	2 545
Outcome	1 422	55.9	1 120	44.0	3	0.1		0.0	44.1	2 545
Place of notification	1 887	74.1	90	3.5	568	22.3		0.0	25.9	2 545
Place of residence	1 384	54.4	670	26.3	491	19.3		0.0	45.6	2 545
Serotype	1 352	53.1	1 190	46.8	3	0.1		0.0	46.9	2 545
Specimen n1	2 410	94.7	132	5.2	3	0.1		0.0	5.3	2 545
Specimen n2	373	13.0	2 169	75.8	3	0.1	315	11.0	87.0	2 860
First test for specimen n1^	2 162	85.0	380	14.9	3	0.1		0.0	15.0	2 545
Second test for specimen n1^	17	0.7	1	0.0	2 527	99.3		0.0	99.3	2 545
First test for specimen n2^	15	0.6	850	33.4	3	0.1	1 677	65.9	99.4	2 545
Vaccination status	293	11.5	2 249	88.4	3	0.1		0.0	88.5	2 545

** N includes aggregated data that are only considered in the variables age, classification and gender.*

*** Includes case-based and aggregated data*

**** 'Age in months' is required only for cases under two years of age; the completeness of this variable is calculated on the total number of cases younger than two years of age.*

^ Refers to the laboratory methods used to detect the pathogen

^^ Not applicable/not under surveillance/non-typable

Annex 3. Invasive meningococcal disease

Table C1. Description of data sources for surveillance of IMD, 2012

Country	Data source	Legal character	Comprehensive	Active/passive	Case-based/aggregated	Data reported by				Case definition
						Labs	Physicians	Hosp.	Other	
Austria	AT-Epidemiegesetz	Cp	Co	P	C	Y	Y	Y	Y	EU 08
Belgium	BE-REFLAB	V	Se	A	C	Y	N	N	N	Unk
Bulgaria	BG-NATIONAL_SURVEILLANCE	Cp	Co	P	A	Y	Y	Y	Y	EU 08
Croatia	HR-CNIPH	Cp	Co	P	C	Y	Y	Y	Y	EU 2012
Cyprus	CY-LABNET	V	Se	A	C	Y	N	N	N	none
Czech Republic	CZ-EPIDAT	Cp	Co	A	C	Y	Y	Y	Y	EU 08
Denmark	DK-LAB	V	Co	P	C	Y	N	N	N	Unk
Estonia	EE-MENINGOCOCC	Cp	Co	P	C	Y	Y	Y	Y	EU 08
Finland	FI-NIDR	Cp	Co	P	C	Y	Y	N	N	Other
France	FR-MANDATORY_INFECTIOUS_DISEASES	Cp	Co	P	C	Y	Y	Y	Y	EU 08
Germany	DE-SURVNET@RKI-7.1/6	Cp	Co	P	C	Y	Y	Y	Y	Other
Greece	GR-NOTIFIABLE_DISEASES	Cp	Co	P	C	Y	Y	Y	N	EU 08
Hungary	HU-EFRIR	Cp	Co	P	C	Y	Y	Y	N	EU 08
Ireland	IE-CIDR	Cp	Co	P	C	Y	Y	Y	N	EU 08
Italy	IT-MENINGITIS	V	Co	P	C	N	Y	Y	N	EU 12
Latvia	LV-BSN	Cp	Co	P	C	Y	Y	Y	Y	EU 2012
Lithuania	LT-COMMUNICABLE_DISEASES	Cp	Co	P	C	Y	Y	N	N	EU 08
Luxembourg	LU-SYSTEM1	Cp	Co	P	C	N	Y	N	N	EU 02
Malta	MT-DISEASE_SURVEILLANCE	Cp	Co	P	C	Y	Y	Y	Y	EU 08
Netherlands	NL-OSIRIS	Cp	Co	P	C	Y	Y	N	N	EU 08
Norway	NO-MSIS_A	Cp	Co	P	C	Y	Y	Y	N	EU 2012
Poland	PL-NATIONAL_SURVEILLANCE	Cp	Co	P	C	Y	Y	Y	N	EU 08
Portugal	PT-MENINGOCOCAL	Cp	Co	P	C	Y	Y	N	N	EU 02
Romania	RO-RNSSy	Cp	Co	P	C	N	N	Y	N	EU 08
Slovakia	SK-EPIS	Cp	Co	A	C	Y	Y	Y	N	EU 2012
Slovenia	SI-SURVIVAL	Cp	Co	P	C	Y	Y	Y	N	EU 08
Spain	ES-STATUTORY_DISEASES	Cp	Co	P	C	N	Y	Y	N	EU 08
Sweden	SE-SMINET	Cp	Co	P	C	Y	Y	N	N	EU 2012
United Kingdom	UK-MENINGOCOCCAL	O	Co	P	C	Y	N	Y	Y	EU 2012

Cp: compulsory, V: voluntary, Co: comprehensive, O: other, Se: sentinel, P: passive, A: active, C: case-based, A: aggregated, Y: yes, N: no, Unk: unknown

Table C2. Distribution of confirmed IMD cases by country and month, EU/EEA countries, 2012 (n=3 452*)

Country	Jan	Feb	March	April	May	June	July	Aug	Sept	Oct	Nov	Dec
Austria	5	5	9	7	2	2	2	2	4	5	5	8
Belgium	13	6	14	11	13	6	5	11	7	10	6	13
Bulgaria												
Cyprus	0	1	0	0	0	0	1	4	0	0	0	0
Czech Republic	9	5	5	3	3	7	3	1	1	8	4	10
Denmark	8	8	6	4	4	3	4	1	2	6	5	5
Estonia	0	1	1	0	1	1	0	0	0	0	0	2
Finland	3	5	6	2	3	2	0	3	4	4	0	1
France	58	61	73	39	44	37	31	26	27	60	40	54
Germany	44	43	28	23	32	24	17	19	26	38	35	25
Greece	4	5	20	5	2	2	2	2	0	3	5	9
Hungary	7	7	14	4	3	1	4	0	0	4	1	6
Ireland	13	7	3	2	6	5	2	4	1	4	10	3
Italy	17	20	19	15	10	7	3	7	5	16	11	6
Latvia	0	0	1	0	1	0	0	1	0	0	1	0
Lithuania	5	5	2	10	3	8	2	5	0	3	7	3
Luxembourg												
Malta	0	0	0	0	0	0	0	2	0	0	0	1
Netherlands	13	9	10	11	11	9	6	4	10	8	7	11
Poland	29	21	20	24	25	27	13	13	8	16	20	22
Portugal	4	10	18	5	4	4	4	6	1	5	3	5
Romania	9	6	12	6	7	7	4	1	3	6	6	4
Slovakia	4	5	9	3	2	1	2	3	0	0	2	0
Slovenia	1	2	4	0	0	1	0	1	0	0	0	0
Spain	61	46	39	32	28	18	17	15	17	15	21	26

Country	Jan	Feb	March	April	May	June	July	Aug	Sept	Oct	Nov	Dec
Sweden	12	6	11	11	10	6	5	6	5	12	9	10
United Kingdom	119	82	79	83	68	60	55	58	31	58	65	104
EU total	**438**	**366**	**403**	**300**	**282**	**238**	**182**	**195**	**152**	**281**	**263**	**328**
Norway	4	2	3	0	1	3	4	1	0	2	3	1
Total	**442**	**368**	**406**	**300**	**283**	**241**	**186**	**196**	**152**	**283**	**266**	**329**

** Number of cases by month was not reported by Luxembourg (three cases) and Bulgaria (eight cases).*

Table C3. Distribution of confirmed IMD cases by country and age group, EU/EEA countries, 2012 (n=3 450)

Country	< 1 year		1–4 years		5–14 years		15–24 years		25–44 years		45–64 years		≥ 65 years		Tot
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N
Austria	7	12.5	11	19.6	8	14.3	20	35.7	3	5.4	4	7.1	3	5.4	56
Belgium	17	15.2	26	23.2	14	12.5	26	23.2	11	9.8	8	7.1	10	8.9	112
Bulgaria	1	12.5	3	37.5	1	12.5	2	25.0	0	0.0	1	12.5	0	0.0	8
Cyprus	1	16.7		0.0	2	33.3	3	50.0		0.0		0.0		0.0	6
Czech Republic	12	20.3	18	30.5	6	10.2	11	18.6	5	8.5	5	8.5	2	3.4	59
Denmark	9	16.1	13	23.2	2	3.6	6	10.7	3	5.4	13	23.2	10	17.9	56
Estonia	1	16.7	1	16.7		0.0	2	33.3	1	16.7		0.0	1	16.7	6
Finland	3	9.1	2	6.1	2	6.1	10	30.3	2	6.1	8	24.2	6	18.2	33
France	70	12.7	95	17.3	53	9.6	148	26.9	62	11.3	64	11.6	58	10.5	550
Germany	47	13.3	57	16.1	27	7.6	86	24.3	50	14.1	44	12.4	43	12.1	354
Greece	3	5.1	16	27.1	9	15.3	21	35.6	5	8.5	3	5.1	2	3.4	59
Hungary	8	15.7	11	21.6	5	9.8	12	23.5	11	21.6	2	3.9	2	3.9	51
Ireland	17	28.3	20	33.3	6	10.0	8	13.3	1	1.7	5	8.3	3	5.0	60
Italy	16	11.8	25	18.4	20	14.7	22	16.2	15	11.0	19	14.0	19	14.0	136
Latvia		0.0		0.0	1	25.0	1	25.0	2	50.0		0.0		0.0	4
Lithuania	9	17.0	13	24.5	8	15.1	13	24.5	6	11.3	2	3.8	2	3.8	53
Luxembourg		0.0	1	50.0		0.0		0.0		0.0	1	50.0		0.0	2
Malta		0.0		0.0		0.0	2	66.7		0.0	1	33.3		0.0	3
Netherlands	19	17.4	31	28.4	10	9.2	18	16.5	12	11.0	7	6.4	12	11.0	109
Poland	52	21.8	58	24.4	28	11.8	37	15.5	34	14.3	20	8.4	9	3.8	238
Portugal	16	23.5	24	35.3	4	5.9	9	13.2	10	14.7	3	4.4	2	2.9	68
Romania	14	19.7	22	31.0	11	15.5	11	15.5	7	9.9	2	2.8	4	5.6	71
Slovakia	7	22.6	6	19.4	2	6.5	8	25.8	6	19.4	1	3.2	1	3.2	31
Slovenia	3	33.3		0.0		0.0	4	44.4		0.0	1	11.1	1	11.1	9
Spain	58	17.5	77	23.3	38	11.5	41	12.4	37	11.2	43	13.0	37	11.2	331
Sweden	1	1.0	8	7.8	6	5.8	21	20.4	11	10.7	21	20.4	35	34.0	103
United Kingdom	195	22.7	253	29.5	76	8.9	117	13.6	51	5.9	84	9.8	82	9.6	858
EU total	**586**	**17.1**	**791**	**23.1**	**339**	**9.9**	**659**	**19.2**	**345**	**10.1**	**362**	**10.6**	**344**	**10.0**	**3 426**
Norway	3	12.5	1	4.2%		0.0%	13	54.2	3	12.5	1	4.2	3	12.5	24
Total	**589**	**17.1**	**792**	**23.0**	**339**	**9.8**	**672**	**19.5**	**348**	**10.1**	**363**	**10.5**	**347**	**10.1**	**3 450**

Table C4. Notification rate of confirmed IMD cases by age group and year, EU/EEA countries, 2008–12 (n=20 055*)

Age group (years)	2008		2009		2010		2011		2012	
	N	NR	N	NR	N	NR	N	NR	N	NR
< 1	1 107	21.7	984	18.9	687	13.4	657	12.4	587	11.4
1–4	966	4.7	924	4.5	882	4.2	880	4.2	789	3.7
5–14	585	1.1	610	1.2	412	0.8	439	0.9	336	0.7
15–24	915	1.5	875	1.5	736	1.2	773	1.3	667	1.1
25–44	401	0.3	352	0.2	326	0.2	342	0.2	348	0.3
45–64	406	0.3	381	0.3	341	0.3	352	0.3	362	0.3
≥ 65	321	0.4	315	0.4	286	0.4	364	0.4	347	0.4
Total	**4 701**		**4 441**		**3 670**		**3 807**		**3 436**	

Contributing countries: Austria, Belgium, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom

** Excludes aggregated data if different age groups were reported.*

Table C5. Notification rate of confirmed IMD cases by age group and gender, EU/EEA countries, 2012 (n=3 439*)

Age group (years)	Male		Female		Total	
	N	NR	N	NR	N	NR
< 1	324	12.3	261	10.6	585	11.5
1–4	425	3.9	366	3.5	791	3.7
5–14	193	0.7	144	0.6	337	0.7
15–24	373	1.2	294	1.0	667	1.1
25–44	188	0.3	160	0.2	348	0.3
45–64	171	0.3	193	0.3	364	0.3
≥ 65	110	0.3	237	0.5	347	0.4

** Excludes 19 cases for which data for age and/or gender were unknown and data from Cyprus for which rates of population coverage were unknown*

Table C6. Distribution of confirmed IMD cases by clinical presentation and country, EU/EEA countries, 2012 (n=1 674*)

Country	Septicaemia		Meningitis		Meningitis and septicaemia		Pneumonia		Other		Total
	N	%	N	%	N	%	N	%	N	%	N
Austria	4	7.7	28	53.8	9	17.3		0.0	11	21.2	52
Belgium	25	26.3	32	33.7	35	36.8		0.0	3	3.2	95
Bulgaria											
Cyprus	1	16.7	4	66.7	1	16.7		0.0		0.0	6
Czech Republic											
Denmark											
Estonia	2	33.3	4	66.7		0.0		0.0		0.0	6
Finland											
France											
Germany	114	32.3	141	39.9	38	10.8		0.0	60	17.0	353
Greece	9	15.3	24	40.7	26	44.1		0.0		0.0	59
Hungary	7	13.7	26	51.0	18	35.3		0.0		0.0	51
Ireland	20	39.2	6	11.8	25	49.0		0.0		0.0	51
Italy	38	27.9	69	50.7	29	21.3		0.0		0.0	136
Latvia		0.0	2	50.0	2	50.0		0.0		0.0	4
Lithuania	18	34.0	17	32.1		0.0		0.0	18	34.0	53
Luxembourg		0.0	3	100.0		0.0		0.0		0.0	3
Malta	2	66.7	1	33.3		0.0		0.0		0.0	3
Netherlands											NUS
Poland	73	30.7	92	38.7	70	29.4		0.0	3	1.3	238
Portugal	4	7.7	31	59.6	16	30.8	1	1.9		0.0	52
Romania	3	4.2	55	77.5	13	18.3		0.0		0.0	71
Slovakia	6	19.4	19	61.3		0.0		0.0	6	19.4	31
Slovenia		0.0	1	100.0		0.0		0.0		0.0	1
Spain	134	40.2	138	41.4	54	16.2		0.0	7	2.1	333
Sweden											NUS
United Kingdom	17	32.1	23	43.4	11	20.8	1	1.9	1	1.9	53
EU total	**477**	**28.9**	**716**	**43.4**	**347**	**21.0**	**2**	**0.1**	**109**	**6.6**	**1 651**
Norway	8	34.8	6	26.1	6	26.1		0.0	3	13.0	23
Total	**485**	**29.0**	**722**	**43.1**	**353**	**21.1**	**2**	**0.1**	**112**	**6.7**	**1 674**

** Excludes cases with clinical presentation reported as not under surveillance*

NUS = not under surveillance

Table C7. Case fatality rate due to IMD by country, EU/EEA countries*, 2012 (n=3 185)

Country	No. confirmed cases	No. confirmed cases with known outcome	Number of deaths	CFR (%)	95% confidence interval (%)
Austria	56	56	4	7.1	2–17.3
Belgium	115	52	6	11.5	4.4–23.4
Bulgaria	8				
Cyprus	6	5	0	0.0	0–52.2
Czech Republic	59	59	3	5.1	1.1–14.2
Denmark	56				
Estonia	6	6	0	0.0	0–45.9
Finland	33				
France	550	550	43	7.8	5.7–10.4
Germany	354	353	33	9.3	6.5–12.9
Greece	59	59	6	10.2	3.8–20.8

Country	No. confirmed cases	No. confirmed cases with known outcome	Number of deaths	CFR (%)	95% confidence interval (%)
Hungary	51	51	6	11.8	4.4–23.9
Ireland	60	44	2	4.6	0.6–15.5
Italy	136	98	24	24.5	16.4–34.2
Latvia	4	4	1	25.0	0.6–80.6
Lithuania	53	52	6	11.5	4.4–23.4
Luxembourg	3	3	0	0.0	0–70.8
Malta	3	3	0	0.0	0–70.8
Netherlands	109	109	6	5.5	2.1–11.6
Poland	238	238	21	8.8	5.5–13.2
Portugal	69	50	2	4.0	0.5–13.7
Romania	71	71	9	12.7	6–22.7
Slovakia	31	29	4	13.8	3.9–31.7
Slovenia	9	9	0	0.0	0–33.6
Spain	335	328	28	8.5	5.8–12.1
Sweden	103	103	10	9.7	4.8–17.1
United Kingdom	862	829	35	4.2	3–5.8
EU total	**3 439**	**3 161**	**249**	**7.9**	**7–8.9**
Norway	24	24	3	12.5	2.7–32.4
Total	**3 463**	**3 185**	**252**	**7.9**	**7–8.9**

** Only 'unknown' outcomes reported by Bulgaria, Denmark and Finland*

Table C8. Number of confirmed cases, number of deaths and case fatality rate due to IMD, by clinical presentation, EU/EEA countries*, 2012 (n=1 563)

Clinical presentation	No. of confirmed cases	No. confirmed cases with known outcome	No. of deaths	CFR (%)
Meningitis	722	675	25	3.7
Meningitis and septicaemia	353	323	36	11.1
Other	112	110	9	8.2
Pneumonia	2	2	1	50.0
Septicaemia	485	453	85	18.8
Total	**1 674**	**1 563**	**156**	**10.0**

** Excludes cases with clinical presentation reported as not under surveillance*

Table C9. Number of confirmed cases, number of deaths and case fatality rate due to IMD, by age group, EU/EEA countries, 2012 (n=3 175)

Age group (years)	No. of confirmed cases	No. of confirmed cases with known outcome	No. of deaths	CFR (%)
< 1	588	541	29	5.4
1–4	789	728	48	6.6
5–14	338	307	16	5.2
15–24	670	629	47	7.5
25–44	348	325	29	8.9
45–64	362	325	37	11.4
≥ 65	347	320	45	14.1
Total	**3 442**	**3 175**	**251**	**7.9**

Table C10. Total number of confirmed IMD cases by serogroup and country, EU/EEA, 2012

Country	Serogroup										Total
	B	C	Y	W	A	29E	Z	Other	NGA	Unknown	
Austria	26	12	2	1					1	14	56
Belgium	82	19	9	2					3		115
Bulgaria										8	8
Cyprus	3	2	1								6
Czech Republic	45	8	1	1	1					3	59
Denmark	19	30	6	1							56
Estonia	4				1					1	6
Finland	17	3	8	1					1	3	33
France	366	99	30	40		1			3	11	550
Germany	199	77	14	13	4			4		43	354
Greece	43		3	1	1				1	10	59
Hungary	20	21							10	0	51
Ireland	58		2							0	60
Italy	54	32	18	1	1	1		1		28	136
Latvia	3	1								0	4

Country	Serogroup										Total
	B	C	Y	W	A	29E	Z	Other	NGA	Unknown	
Lithuania	35	2		1					15	0	53
Luxembourg										3	3
Malta	1		0						1	1	3
Netherlands	76	4	15	2			1			11	109
Poland	129	90	2	4						13	238
Portugal	44	4	4	1					2	14	69
Romania	21	7			2				2	39	71
Slovakia	23	5		1						2	31
Slovenia	7	2									9
Spain	211	54	5	13	2			10	25	15	335
Sweden	23	26	45	5						4	103
United Kingdom	674	32	89	50		1			10	6	862
EU total	**2 183**	**530**	**254**	**138**	**12**	**3**	**1**	**15**	**74**	**229**	**3 439**
Norway	9	9	6								24
Total	**2 192**	**539**	**260**	**138**	**12**	**3**	**1**	**15**	**74**	**229**	**3 463**

NGA = not groupable

Table C11. Number and notification rates of IMD cases, by serogroup and year, EU/EEA countries, 2008–12 (n=20 161)

Serogroup	2008		2009		2010		2011		2012	
	N	NR	N	NR	N	NR	N	NR	N	NR
A	17	0.003	24	0.005	13	0.003	9	0.002	12	0.002
B	3 368	0.684	3166	0.641	2 551	0.515	2 569	0.517	2 189	0.438
C	678	0.138	582	0.118	499	0.101	503	0.101	537	0.108
Y	141	0.029	192	0.039	206	0.042	286	0.058	259	0.052
W	81	0.016	85	0.017	83	0.017	80	0.016	138	0.028
Other	9	0.002	16	0.003	16	0.003	13	0.003	19	0.004
NGA	50	0.010	57	0.012	40	0.008	28	0.006	74	0.015
Unknown	383	0.078	343	0.069	292	0.059	332	0.067	221	0.044
Total	**4 727**	**0.96**	**4 465**	**0.90**	**3 700**	**0.75**	**3 820**	**0.77**	**3 449**	**0.69**

NGA = not groupable. Unk = unknown. In addition to serogroups reported as 'other' (n=42), 'other' includes cases of serogroup 29E (13), serogroup X (n=13) and serogroup Z (n=5) reported during 2008–12.

Contributing countries: Austria, Belgium, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom

Table C12. Distribution of IMD cases by age and serogroup, EU/EEA countries, 2012 (n=3 223)

Serogroup	< 1 year		1–4 years		5–14 years		15–24 years		25–44 years		45–64 years		≥ 65 years		Total
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	
B	459	82.9	608	82.9	226	72.2	400	63.4	171	52.8	195	57.2	126	38.5	2 185
C	58	10.5	65	8.9	48	15.3	131	20.8	110	34.0	72	21.1	54	16.5	538
Y	8	1.4	9	1.2	21	6.7	56	8.9	22	6.8	45	13.2	96	29.4	257
W	12	2.2	24	3.3	5	1.6	27	4.3	13	4.0	22	6.5	35	10.7	138
NGA	14	2.5	19	2.6	10	3.2	14	2.2	7	2.2	1	0.3	9	2.8	74
Other		0.0	5	0.7	1	0.3	3	0.5	1	0.3	2	0.6	3	0.9	15
A	3	0.5	3	0.4	1	0.3		0.0		0.0	2	0.6	3	0.9	12
29E		0.0		0.0		0.0		0.0		0.0	2	0.6	1	0.3	3
Z		0.0		0.0	1	0.3		0.0		0.0		0.0		0.0	1
Total		**554**		**733**		**313**		**631**		**324**		**341**		**327**	**3 223**

NGA = not groupable

Table C13. Number and notification rate of serogroup B, C and Y IMD by age group, EU/EEA countries, 2012 (n=2 974)

Age group (years)	B		C		Y	
	N	NR	N	NR	N	NR
< 1	459	8.91	57	1.11	8	0.16
1–4	608	2.88	65	0.31	9	0.04
5–14	225	0.44	48	0.09	20	0.04
15–24	398	0.68	130	0.22	56	0.10
25–44	171	0.12	110	0.08	22	0.02
45–64	195	0.15	72	0.05	45	0.03
≥ 65	126	0.14	54	0.06	96	0.11

Contributing countries: Austria, Belgium, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom

Table C14. Number and notification rate of confirmed serogroup B IMD cases by age group and country, 2012 (n=2 182)

Country	< 1 year		1–4 years		5–14 years		15–24 years		25–44 years		45–64 years		≥ 65 years	
	N	NR	N	NR	N	NR	N	NR	N	NR	N	NR	N	NR
Austria	3	3.87	7	2.21	2	0.24	10	0.98	0	0.00	2	0.09	2	0.13
Belgium	15	11.63	21	4.01	12	0.97	18	1.34	7	0.24	4	0.13	3	0.16
Czech Republic	10	9.20	12	2.49	4	0.42	9	0.74	4	0.12	5	0.18	1	0.06
Denmark	4	6.74	7	2.69	0	0.00	2	0.28	0	0.00	3	0.20	3	0.31
Estonia	1	6.73	0	0.00			2	1.20	0	0.00			1	0.43
Finland	3	4.99	1	0.41	0	0.00	7	1.06	1	0.07	3	0.20	2	0.20
France	52	6.51	74	2.29	38	0.47	98	1.23	42	0.25	37	0.22	25	0.22
Germany	33	4.98	39	1.42	19	0.26	48	0.53	25	0.12	17	0.07	18	0.11
Greece	1	0.94	11	2.44	7	0.65	16	1.34	4	0.12	3	0.11	1	0.05
Hungary	4	4.56	6	1.56	1	0.10	4	0.33	3	0.10	1	0.04	1	0.06
Ireland	17	22.88	20	6.82	6	0.96	7	1.25	1	0.07	5	0.48	2	0.37
Italy	9	1.66	11	0.48	9	0.16	8	0.13	4	0.02	5	0.03	8	0.06
Latvia	0	0.00	0	0.00	1	0.53	0	0.00	2	0.36	0	0.00	0	0.00
Lithuania	4	13.25	6	5.05	5	1.69	11	2.64	5	0.64	2	0.25	2	0.37
Malta	0	0.00	0	0.00	0	0.00	1	1.80	0	0.00	0	0.00	0	0.00
Netherlands	16	8.91	25	3.38	6	0.30	12	0.59	7	0.16	4	0.09	6	0.22
Norway	2	3.31	1	0.40			4	0.61	1	0.07	1	0.08	0	0.00
Poland	33	8.50	33	1.96	13	0.35	20	0.39	15	0.13	10	0.09	5	0.09
Portugal	11	11.49	21	5.33	4	0.37	2	0.18	3	0.10	2	0.07	0	0.00
Romania	6	3.11	7	0.83	2	0.10	3	0.12	1	0.02	1	0.02	1	0.03
Slovakia	6	9.90	6	2.62	1	0.18	5	0.69	3	0.18	1	0.07	1	0.14
Slovenia	3	13.63					3	1.34			1	0.17	0	0.00
Spain	49	10.30	58	2.90	28	0.61	16	0.34	11	0.07	28	0.23	18	0.22
Sweden	1	0.89	3	0.66	4	0.39	6	0.48	4	0.16	3	0.12	2	0.11
United Kingdom	176	21.77	239	7.58	63	0.87	86	1.04	28	0.16	57	0.35	24	0.24

Table C15. Number and notification rate of serogroup B IMD by year and age group, EU/EEA countries, 2008–12 (n=13 765)

Age group (years)	2008		2009		2010		2011		2012	
	N	NR	N	NR	N	NR	N	NR	N	NR
< 1	944	18.55	835	16.08	573	11.16	535	10.14	459	8.91
1–4	766	3.75	724	3.50	685	3.28	699	3.30	608	2.88
5–14	396	0.76	412	0.80	294	0.58	304	0.59	225	0.44
15–24	594	0.98	599	1.00	464	0.78	478	0.81	398	0.68
≥ 25	646	0.18	579	0.16	511	0.15	545	0.15	492	0.14

Contributing countries: Austria, Belgium, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Lithuania, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom

Table C16. Number and notification rate of confirmed serogroup C IMD cases by age group and country, 2012 (n=538)

Country	< 1 year		1–4 years		5–14 years		15–24 years		25–44 years		45–64 years		≥ 65 years		MCC
	N	NR	N	NR	N	NR	N		N	NR	N	NR	N	NR	
Austria	2	2.58	2	0.63	2	0.24	4	0.39	1	0.04	1	0.04	0	0.00	Y
Belgium	2	1.55	3	0.57	0		4	0.30	3	0.10	3	0.10	3	0.16	Y
Cyprus	1		0		0		1		0		0		0		Y
Czech Republic	1	0.92	4	0.83	1	0.11	1	0.08	1	0.03	0		0		N

Country	< 1 year		1–4 years		5–14 years		15–24 years		25–44 years		45–64 years		≥ 65 years		MCC
	N	NR	N	NR	N	NR	N		N	NR	N	NR	N	NR	
Denmark	4	6.74	6	2.31	2	0.30	3	0.42	3	0.21	8	0.54	4	0.41	N
Estonia	0		0		0		0		0		0		0		N
Finland	0		0		1	0.17	0		0		1	0.07	1	0.10	N
France	12	1.50	8	0.25	10	0.12	30	0.38	13	0.08	12	0.07	14	0.13	Y
Germany	11	1.66	4	0.15	3	0.04	21	0.23	17	0.08	12	0.05	9	0.05	Y
Greece	0		0		0		0		0		0		0		Y
Hungary	3	3.42	3	0.78	2	0.21	7	0.58	5	0.17	1	0.04	0		N
Ireland	0		0		0		0		0		0		0		Y
Italy	1	0.18	4	0.18	3	0.05	7	0.12	9	0.05	5	0.03	3	0.02	Y
Latvia	0		0		0		1	0.38	0		0		0		N
Lithuania	1	3.31	1	0.84	0		0		0		0		0		N
Malta	0		0		0		0		0		0		0		N
Netherlands	2	1.11	1	0.14	0		0		1	0.02	0		0		Y
Norway	1	1.65	0				4	0.61	2	0.15	0		2	0.26	N
Poland	15	3.86	20	1.19	14	0.37	14	0.28	15	0.13	9	0.08	3	0.06	N
Portugal	0		0		0		2	0.18	2	0.07	0		0		Y
Romania	0		2	0.24	0		5	0.21	0		0		0		N
Slovakia	0		0		1	0.18	1	0.14	3	0.18	0		0		N
Slovenia	0		0		0		1	0.45			0		1	0.29	N
Spain	1	0.21	0		2	0.04	14	0.30	21	0.14	11	0.09	5	0.06	Y
Sweden	0		5	1.10	1	0.10	5	0.40	3	0.12	7	0.29	5	0.28	N
United Kingdom	1	0.12	2	0.06	6	0.08	6	0.07	11	0.06	2	0.01	4	0.04	Y

Table C17. Number and notification rates of confirmed serogroup C IMD cases, by age group and meningococcal C conjugate (MCC) immunisation schedule, EU/EEA countries, 2012 (n=536)

Age group (years)	Countries without MCC		Countries with MCC	
	N	NR	N	NR
< 1	25	2.08	32	0.81
1–4	41	0.82	24	0.15
5–14	22	0.20	26	0.07
15–24	42	0.28	88	0.20
25–44	32	0.09	78	0.07
45–64	26	0.08	46	0.04
≥ 65	16	0.09	38	0.05

Contributing countries with MCC: Austria, Belgium, France, Germany, Greece, Ireland, Italy, the Netherlands, Portugal, Spain and the United Kingdom

Contributing countries without MCC: Czech Republic, Denmark, Estonia, Finland, Hungary, Latvia, Lithuania, Malta, Norway, Poland, Romania, Slovakia, Slovenia and Sweden

Table C18. Notification rate of serogroup C IMD by year and meningococcal C conjugate (MCC) immunisation schedule, EU/EEA countries, 2008–12 (n=2 792)

MCC vaccination	2008	2009	2010	2011	2012
Countries without MCC	0.19	0.17	0.17	0.18	0.18
Countries with MCC	0.09	0.08	0.07	0.07	0.07
Countries with MCC after 2008	0.23	0.22	0.15	0.13	0.15

Contributing countries with MCC: Belgium, Germany, Greece, Ireland, Italy, the Netherlands, Portugal, Spain and the United Kingdom

Contributing countries with MCC after 2008: Austria, France

Contributing countries without MCC: Czech Republic, Denmark, Estonia, Finland, Hungary, Latvia, Lithuania, Malta, Norway, Poland, Romania, Slovakia, Slovenia and Sweden

Table C19. Notification rates of serogroup C IMD by age group and meningococcal C conjugate (MCC) immunisation schedule, EU/EEA countries, 2008–12 (n=2 792)

Age group	MCC vaccination	2008		2009		2010		2011		2012	
		N	NR	N	NR	N	NR	N	NR	N	NR
< 5 years	Countries without MCC	56	0.94	77	1.26	74	1.20	68	1.06	66	1.06
	Countries with MCC	45	0.30	44	0.29	41	0.27	36	0.23	32	0.20
	Countries with MCC after 2008	54	1.24	30	0.68	30	0.68	20	0.45	24	0.54
5–14 years	Countries without MCC	90	0.10	70	0.08	62	0.07	87	0.09	96	0.10
	Countries with MCC	163	0.06	132	0.05	118	0.05	116	0.05	135	0.05
	Countries with MCC after 2008	70	0.12	85	0.14	44	0.07	38	0.06	53	0.09

Age group	MCC vaccination	2008		2009		2010		2011		2012	
		N	NR	N	NR	N	NR	N	NR	N	NR
> 14 years	Countries without MCC	79	0.49	44	0.28	56	0.36	54	0.36	42	0.28
	Countries with MCC	74	0.21	52	0.15	38	0.11	50	0.14	54	0.16
	Countries with MCC after 2008	45	0.49	45	0.49	35	0.39	34	0.38	34	0.38

Contributing countries with MCC: Belgium, Germany, Greece, Ireland, Italy, the Netherlands, Portugal, Spain and the United Kingdom

Contributing countries with MCC after 2008: Austria, France

Contributing countries without MCC: Czech Republic, Denmark, Estonia, Finland, Hungary, Latvia, Lithuania, Malta, Norway, Poland, Romania, Slovakia, Slovenia and Sweden

Table C20. Number and notification rate of confirmed serogroup Y IMD cases by age group and country, EU/EEA, 2012 (n=256)

Country	< 1 year		1–4 years		5–14 years		15–24 years		25–44 years		45–64 years		≥ 65 years	
	N	NR	N	NR	N	NR	N	NR	N	NR	N	NR	N	NR
Austria	0	0.00	0	0.00	1	0.12	1	0.10	0	0.00	0	0.00	0	0.00
Belgium	0	0.00	1	0.19	2	0.16	2	0.15	1	0.03	1	0.03	2	0.10
Czech Republic	0	0.00	0	0.00	0	0.00	1	0.08	0	0.00	0	0.00	0	0.00
Denmark	1	1.69	0	0.00	0	0.00	1	0.14	0	0.00	2	0.13	2	0.21
Finland	0	0.00	0	0.00	1	0.17	2	0.30	1	0.07	2	0.13	2	0.20
France	1	0.13	0	0.00	1	0.01	10	0.13	1	0.01	6	0.03	11	0.10
Germany	0	0.00	0	0.00	1	0.01	2	0.02	1	0.00	2	0.01	8	0.05
Greece	0	0.00	1	0.22	1	0.09	1	0.08	0	0.00	0	0.00	0	0.00
Ireland	0	0.00	0	0.00	0	0.00	1	0.18	0	0.00	0	0.00	1	0.18
Italy	1	0.18	1	0.04	4	0.07	3	0.05	1	0.01	4	0.02	4	0.03
Netherlands	0	0.00	3	0.41	3	0.15	1	0.05	1	0.02	3	0.06	4	0.15
Norway	0	0.00	0	0.00	0	0.00	5	0.76	0	0.00	0	0.00	1	0.13
Poland	0	0.00	0	0.00	1	0.03	1	0.02	0	0.00	0	0.00	0	0.00
Portugal	0	0.00	0	0.00	0	0.00	1	0.09	3	0.10	0	0.00	0	0.00
Spain	0	0.00	2	0.10	0	0.00	1	0.02	0	0.00	1	0.01	1	0.01
Sweden	0	0.00	0	0.00	1	0.10	7	0.56	4	0.16	10	0.41	23	1.29
United Kingdom	5	0.62	1	0.03	4	0.06	16	0.19	9	0.05	14	0.09	37	0.36

Table C21. Number and notification rate of serogroup Y IMD by year and age group, EU/EEA countries, 2008–12 (n=1 080)

Age group (years)	2008		2009		2010		2011		2012	
	N	NR	N	NR	N	NR	N	NR	N	NR
< 1	9	0.18	9	0.17	11	0.21	11	0.21	8	0.16
1–4	4	0.02	6	0.03	10	0.05	15	0.07	9	0.04
5–14	16	0.03	15	0.03	13	0.03	29	0.06	20	0.04
15–24	29	0.05	52	0.09	61	0.10	62	0.11	56	0.10
≥ 25	83	0.02	110	0.03	111	0.03	168	0.05	163	0.05

Contributing countries: Austria, Belgium, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Ireland, Italy, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom

Table C22. Number of FetVR variants isolated from confirmed IMD cases, by serogroup, EU/EEA, 2012 (n=1 367)

FetA VR	Serogroups									
	B	C	Y	W	Z	29E	NGA	Other	Unknown	Total
F3-3	129	127						1	2	259
F1-5	228	7	2				2		4	243
F4-1	34	7	63	19					2	125
F5-5	80	11	1	1			1		1	95
F3-6	23	62	5	1					1	92
F3-9	31	39	4	2						76
F5-1	68	3							1	72
F1-7	34	11		1		2	1		1	50
F5-8	18	3	18	2						41
F5-9	25	2		2						29
F1-1	1	9		14					1	25
F4-28	22									22
F5-12	16		6							22
F5-2	18	1	1					1		21
F3-4	3	3	13							19
F3-7	6	4	3	3						16

FetA VR	Serogroups									
	B	C	Y	W	Z	29E	NGA	Other	Unknown	Total
F1-15	8	1	3							12
F1-55	11									11
F4-3	8	1	2							11
F5-36	8	1			1					10
Other*	71	14	22	8	0	0	1	0	0	116
Total	**842**	**306**	**143**	**53**	**1**	**2**	**5**	**2**	**13**	**1 367**

NGA = not groupable

** 'Other' includes 59 variants*

Contributing countries: Austria, Belgium, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Italy, Lithuania, the Netherlands, Norway, Poland, Portugal, Slovakia and Sweden

Table C23. Number of clonal complexes (MLST results) isolated from confirmed IMD cases, by serogroup, EU/EEA, 2012 (n=783)

MLST	Serogroups								
	B	C	Y	W	NGA	A	29E	Unknown	Total
ST-103	3	20	1						24
ST-11	7	120	1	16				1	145
ST-1157	4								4
ST-162	30								30
ST-167			6						6
ST-174	1		1						2
ST-175				1					1
ST-18	13								13
ST-213	38								38
ST-22		1		10					11
ST-23	3	2	69	1	1	1		3	80
ST-254	2								2
ST-269	68	8							76
ST-32	141	11							152
ST-334	1	4							5
ST-35	8	1			1				10
ST-364	1							1	2
ST-37	2								2
ST-41/44	119	14			1			1	135
ST-461	19	1			1				21
ST-60	9	1					2		12
ST-8		1							1
ST-865	5	2	2	2					11
Total	**474**	**186**	**80**	**30**	**4**	**1**	**2**	**6**	**783**

Contributing countries: Czech Republic, Denmark, Estonia, France, Germany, Greece, Italy, Lithuania, Norway, Poland, Portugal and Sweden

Table C24. Number and percentage distribution of PorA gene VR1, VR2 variants in confirmed cases of IMD, EU/EEA, 2012 (n=1 496)

Subtypes PorA gene VR1, VR2	No. of isolates	%
P1.5, 2	171	11.4
P1. 7-2, 4	151	10.1
P1.22, 14	124	8.3
P1.18-1, 3	94	6.3
P1.7,16	77	5.1
P1.5-2, 10-1	65	4.3
P1.19, 15	60	4.0
P1.22, 9	56	3.7
P1.5-1, 10-8	51	3.4
P1. 19-1,15-11	47	3.1
P1.5-1, 2-2	42	2.8
P1. 7-1, 1	40	2.7
P1.5-1, 10-4	17	1.1
P1.22, 14-6	14	0.9
P1.5-2, 10	13	0.9
P1.5-2, 10-2	12	0.8

Subtypes PorA gene VR1, VR2	No. of isolates	%
P1.7, 16-29	10	0.7
P1.18-1, 30	10	0.7
P1.7-2, 13-2	9	0.6
Other	433	28.9
Total	**1 496**	**100**

Contributing countries: Austria, Belgium, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Italy, Lithuania, the Netherlands, Norway, Poland, Portugal, Spain, Sweden and the United Kingdom

Table C25. Distribution of specimens among confirmed IMD cases, by country, EU/EEA countries, 2012 (n=2 581)

Country	Blood		CSF*		Other sterile site		Skin**		Total
	N	%	N	%	N	%	N	%	
Austria	20	39.2	30	58.8		0.0	1	2.0	51
Cyprus	3	50.0	3	50.0		0.0		0.0	6
Czech Republic	28	56.0	22	44.0		0.0		0.0	50
Denmark	31	55.4	24	42.9	1	1.8		0.0	56
Estonia	4	66.7	2	33.3		0.0		0.0	6
Finland	21	63.6	12	36.4		0.0		0.0	33
France	228	42.0	291	53.6	9	1.7	15	2.8	543
Germany	198	56.4	152	43.3	1	0.3		0.0	351
Greece	11	18.6	48	81.4		0.0		0.0	59
Hungary	6	11.8	45	88.2		0.0		0.0	51
Ireland	57	95.0	2	3.3	1	1.7		0.0	60
Italy	56	41.2	80	58.8		0.0		0.0	136
Latvia	2	50.0	2	50.0		0.0		0.0	4
Lithuania	41	77.4	12	22.6		0.0		0.0	53
Luxembourg		0.0	3	100.0		0.0		0.0	3
Malta	3	100.0	0	0.0		0.0		0.0	3
Netherlands	45	41.3	62	56.9	2	1.8		0.0	109
Norway	15	62.5	8	33.3	1	4.2		0.0	24
Poland	101	42.6	136	57.4		0.0		0.0	237
Portugal	29	56.9	22	43.1		0.0		0.0	51
Romania	2	2.8	68	95.8	1	1.4		0.0	71
Slovakia	11	35.5	18	58.1	2	6.5		0.0	31
Slovenia	4	44.4	5	55.6		0.0		0.0	9
Spain	18	47.4	20	52.6		0.0		0.0	38
Sweden	57	55.9	39	38.2	6	5.9		0.0	102
United Kingdom	385	86.7	59	13.3		0.0		0.0	444
Total	**1 376**	**1 299.2**	**1 165**	**1 270.9**	**24**	**25.1**	**16**	**4.7**	**2 581**

** CSF = cerebrospinal fluid*

*** Skin = skin biopsy or aspirate of purpura/petechiae*

Table C26. Distribution of specimens among confirmed IMD cases, by age group EU/EEA countries, 2012 (n=2 578)

Specimen	< 1 year		1–4 years		5–14 years		15–24 years		25–44 years		45–64 years		≥ 65 years		Total
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	
Blood	231	55	278	54	115	48	235	43	110	40	161	57	244	82	1 374
CSF	188	45	229	44	122	51	300	55	164	59	113	40	48	16	1 164
Other sterile site	1	0	7	1	2	1	1	0	1	0	7	2	5	2	24
Skin	2	0	4	1	2	1	5	1	2	1	1	0		0	16
Total	**422**	**100**	**518**	**100**	**241**	**100**	**541**	**100**	**277**	**100**	**282**	**100**	**297**	**100**	**2 578**

Table C27. Quality of 2012 data; distribution of known, unknown, not applicable and blank responses per variable for all confirmed cases of IMD, EU/EEA countries (n=3463)

Variable	Known		NA/NT/NUS		Unknown		Blank		Overall missing		Total confirmed cases
	N	%	N	%	N	%	N	%	N	%	N
Month used for statistics	3 452	99.7		0.0		0.0	11	0.3	11	0.3	3 463
Age*	3 450	99.6		0.0	2	0.1	11	0.3	13	0.4	3 463
Age in months**	914	96.7		0.0	2	0.2	29	3.1	31	3.3	945
Gender*	3 449	99.6		0.0	14	0.4		0.0	14	0.4	3 463
Clinical presentation	1 674	48.3	212	6.1	1 569	45.3	8	0.2	1 789	51.7	3 463
Imported	1 697	49.0		0.0	1 758	50.8	8	0.2	1 766	51.0	3 463
Probable country of infection^	161	4.6		0.0	954	27.5	2 348	67.8	3 302	95.4	3 463

Variable	Known		NA/NT/NUS		Unknown		Blank		Overall missing		Total confirmed cases
	N	%	N	%	N	%	N	%	N	%	N
Place of notification	1 923	55.5		0.0	335	9.7	1 205	34.8	1 540	44.5	3 463
Place of residence	1 572	45.4		0.0	1 410	40.7	481	13.9	1 891	54.6	3 463
Outcome	3 185	92.0		0.0	270	7.8	8	0.2	278	8.0	3 463
Serogroup	3 234	93.4		0.0	221	6.4	8	0.2	229	6.6	3 463
Specimen 1	2 581	74.5		0.0	874	25.2	8	0.2	882	25.5	3 463
Specimen 2	1 036	29.9		0.0	2 419	69.9	8	0.2	2 427	70.1	3 463
First test method for specimen 1	2 789	80.5		0.0	666	19.2	8	0.2	674	19.5	3 463
Second test method for specimen 1	101	2.9		0.0	125	3.6	3 237	93.5	3 362	97.1	3 463
First test method for specimen 2	459	13.3	2 595	74.9	401	11.6	8	0.2	3 004	86.7	3 463
Second test method for specimen 2	6	0.2		0.0		0.0	3 457	99.8	3 457	99.8	3 463
FetVR gene	1 367	39.5	775	22.4	1 051	30.3	270	7.8	2 096	60.5	3 463
Multilocus sequence typing (MLST)	783	22.6	59	1.7	2 613	75.5	8	0.2	2 680	77.4	3 463
PorA1 gene	1 508	43.5	773	22.3	1 174	33.9	8	0.2	1 955	56.5	3 463
PorA2 gene	1 499	43.3	773	22.3	1 183	34.2	8	0.2	1 964	56.7	3 463
Susceptibility to ciprofloxacin	826	23.9		0.0	2 629	75.9	8	0.2	2 637	76.1	3 463
Susceptibility to cefotaxime	506	14.6		0.0	2 949	85.2	8	0.2	2 957	85.4	3 463
Susceptibility to penicillin	1 106	31.9		0.0	2 349	67.8	8	0.2	2 357	68.1	3 463
Susceptibility to rifampicin	824	23.8		0.0	2 631	76.0	8	0.2	2 639	76.2	3 463
MIC sign for ciprofloxacin	136	3.9		0.0		0.0	3 327	96.1	3 327	96.1	3 463
MIC sign for cefotaxime	136	3.9		0.0		0.0	3 327	96.1	3 327	96.1	3 463
MIC sign for penicillin	136	3.9		0.0		0.0	3 327	96.1	3 327	96.1	3 463
MIC sign for rifampicin	135	3.9		0.0		0.0	3 328	96.1	3 328	96.1	3 463
MIC value for ciprofloxacin	146	4.2		0.0		0.0	3 317	95.8	3 317	95.8	3 463
MIC value for cefotaxime	146	4.2		0.0		0.0	3 317	95.8	3 317	95.8	3 463
MIC value for penicillin	146	4.2		0.0		0.0	3 317	95.8	3 317	95.8	3 463
MIC value for rifampicin	145	4.2		0.0		0.0	3 318	95.8	3 318	95.8	3 463
Vaccination status	1 098	31.7		0.0	2 357	68.1	8	0.2	2 365	68.3	3 463

** Includes case-based and aggregated data*

*** Age in months is reported only for cases above two years of age.*

 # MIC values

^ Required only if the case was imported (imported cases: 'YES'=41, imported cases: 'NO'=1 811)