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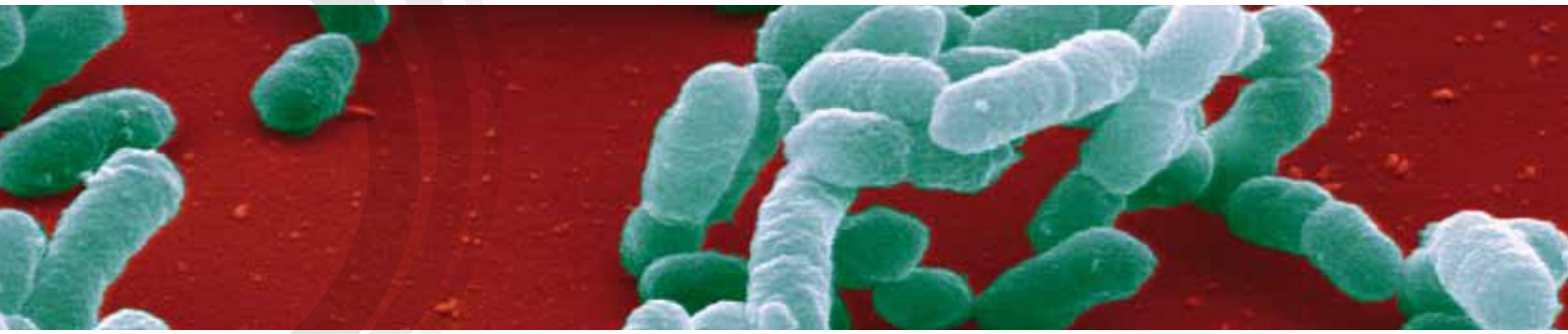

Surveillance of invasive bacterial diseases in Europe

2007

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Executive summary

This report describes the epidemiology of invasive bacterial diseases due to *Haemophilus influenzae* and *Neisseria meningitidis* in the European Union (EU) Member States (MS) in 2007. Designated national contact points were asked to submit data using the revised version of the dataset for invasive bacterial infections (IBI) developed in 2008, on the basis of the former EU-IBIS database. This dataset contains case-based information on epidemiological and laboratory variables, and is divided into a core set of variables applicable to all notifiable diseases in the EU and an enhanced dataset of variables specifically for invasive *Haemophilus influenzae* disease and invasive meningococcal disease. To facilitate data submission, the MS received online training in June 2008, and supplementary training videos and other materials were made available prior to the data call.

Of the 30 EU/EEA Member States, 27 submitted data on invasive *Haemophilus influenzae* disease and 29 submitted data on invasive meningococcal disease.

Invasive *Haemophilus influenzae* disease

- A total of 2058 cases of invasive *Haemophilus influenzae* disease were reported in 2007. The notification rates varied across the MS and the rates in the Nordic countries were higher compared to the rest of Europe, with a continued increasing trend. However, the majority of the countries stayed below 1 case per 100 000 population. The highest overall notification rates have been reported among infants younger than one year of age (3 per 100 000, 118 cases). While trends among infants decreased substantially for serotype b from 1999 to 2007 (from 3 per 100 000 to 1 per 100 000), they increased for non-capsulated strains, moving from 1.5 per 100 000 up to 2.5 per 100 000 in the same period.
- Sixty-seven per cent of all invasive *H. influenzae* cases reported in 2007 were due to non-capsulated strains. The increase in the number of non-capsulated strains reported over the years may be partially attributable to an enhanced case ascertainment and an improvement in the sensitivity of the surveillance systems, which have also been documented in several MS. However, a real increase in the number of notified serotypes not covered by the vaccine (non-b and non-capsulated strains) has also been observed in EU over the last several years. The introduction of the *H. influenzae* type b (Hib) conjugate vaccine has led to a higher proportion of invasive *H. influenzae* infection attributable to non-serotype-b strains because of the reduction in Hib disease. However, unlike the pneumococcal conjugate vaccination programme, there is no consistent or robust evidence to suggest that mass Hib vaccination in infancy has led to serotype replacement in either carriage or disease [1]. A recent World Health Organization (WHO) position paper on Hib conjugate vaccines [2] concluded that 'so far, bacterial strain replacement has not been a prominent feature of large-scale Hib immunisation'.
- In terms of absolute numbers reported, there appears to be a shift towards older age groups. Forty-six per cent of all cases reported in 2007 were among adults older than 65 years of age; this finding is consistent with a study from USA highlighting the increased incidence of invasive *H. influenzae* disease from 1996 to 2004. The epidemiological characteristics of *H. influenzae* also changed from a disease predominantly found in children and dominated by serotype b to a disease predominantly found in adults and dominated by non-typeable strains.
- In 2007, up to 60% of cases occurred in vaccinated individuals, as is usually observed in populations with high vaccination coverage. Among those fully vaccinated, the majority were children aged 1–4 years while those younger than one year accounted for 27% of cases. With the data available, it is not possible to assess whether the cases observed can be classified as true vaccine failures and more information is needed to further explore this finding. Some additional background on this topic has been provided by a study conducted by EU-IBIS that analysed Hib vaccine failure identified through national surveillance between 1996 and 2001 in Europe, Israel and Australia and described the clinical and laboratory features in a large and diverse population with different immunisation schedules [3].

A re-emergence of the disease from Hib due to vaccine failure has also been extensively reported by the UK [4].

Invasive meningococcal disease

- In 2007, 5583 cases of invasive bacterial disease due to *N. meningitidis* were notified in the EU/EEA, with an overall notification rate of 1.12 cases per 100 000. Notification rates varied across MS and were higher in Ireland and the United Kingdom (UK) compared to the rest of Europe, although in both countries there is a sustained declining trend. Apart from these two countries, another six MS have notification rates above 1 per 100 000 (Belgium, Denmark, the Netherlands, Spain, Lithuania and Malta). Infants and children still experienced the highest number of invasive meningococcal disease cases, with 50% of cases reported in

children younger than 10 years old. The highest rates observed in infants younger than one year were reported from Ireland and the UK, with rates of 74.5/100 000 and 46.6/100 000, respectively.

- As with *H. influenzae*, the heterogeneity in case reporting may be attributable to a number of possible causes: an improvement of the sensitivity of the surveillance systems; variation in the types of clinical presentations under surveillance (i.e., sepsis or meningitis or both) in each MS; differences in the applied case definitions; differences in the laboratory capacities; or differences in the healthcare practices for ensuring early blood culture sampling. At this stage, the European Centre for Disease Prevention and Control (ECDC) does not yet have a good overview of the main reasons behind these differences and therefore advises caution when comparing inter-country notification rates by serogroup and age.
- The proportion of cases with missing information on serogroup remains high, especially in the eastern European countries. However, serogroup identification has improved over the years, with the number of unknowns decreasing substantially over the last five years from 1448 in 2003 to 559 cases in 2007. In 2007, serogroup B was the most frequently reported serogroup causing invasive meningococcal disease in Europe, representing about 90% of all serogroups notified among children younger than four years of age. In countries with meningococcal C vaccination (MCC), there is a large predominance of B cases in all age groups and, in particular, in the age groups younger than one and between one and four years old (73 and 81% of cases, respectively), the usual targeted groups for vaccination against serogroup C.
- In countries with MCC vaccination, the proportion of cases due to serogroup C has decreased dramatically in the few years after the introduction of the vaccine in the national schedule, especially in the target groups of vaccination programs. The proportion of serogroup C cases appears to increase with age, which is likely due to the low vaccine coverage in the older age groups as well as decreasing effectiveness of the vaccine following the year of the primary immunisation schedule [5].
- Information on serotyping and subtyping of strains is increasing due to the adoption of molecular technologies in more and more countries. However, the number of samples serotyped and serosubtyped remains low and the interpretation of these results must be done with care. The highest number of samples serosubtyped was reported by France, the United Kingdom and Belgium.

Main conclusions

Overall, the incidence of both diseases continues to decline, especially in young children who are the target of vaccination campaigns. However, at the European level, the number of cases due to serotypes and serogroups not covered by the vaccines is increasing, affecting young children as well and this trend has to be monitored with attention.

As vaccination coverage is high for both vaccines, cases also occur in vaccinated individuals. Unfortunately, there were not sufficient data collected to make an in-depth analysis of vaccine failures possible or to make any inference on the proportion of cases occurring among vaccinated individuals in countries with or without vaccination. This is because the overall proportion of missing values for vaccination status was very high and information on date of birth, number of doses received and date of the last dose were not available. In addition, all information required for stating there is vaccine failure is not yet included in the set of variables (such as time of birth, and number and dates of doses given).

In order to improve data comparability between the participating countries, more standardised laboratory methods for identifying a case and the local adoption of a common case definition for surveillance purposes are needed. Genotyping methods will become more and more feasible in European countries and this will improve the understanding the surveillance data; still, this requires closer collaboration between laboratories and epidemiological centres at national as well as at European levels. In this respect, a call for tender named 'Laboratory surveillance and external quality assurance (EQA) of invasive bacterial diseases in EU' has been awarded in 2008 by a consortium of European institutions coordinated by the University of Würzburg, Germany, and the project now is in the second year of activity. It is focused not only on EQAs and training but particularly on strengthening and harmonising laboratory capacity in MS and reinforcing the collaboration between laboratories and public health institutes in EU. One of the key activities of the group is to promote the use of molecular typing methods in routine surveillance.

1 Introduction

Invasive bacterial infections caused by *Neisseria meningitidis* and *Haemophilus influenzae* pathogens represent a significant public health problem across Europe and can cause meningitis, sepsis, permanent disabilities—including neurological sequelae—and death. Children younger than five years are the most affected age group. Early diagnosis and treatment play an essential role in the control of invasive bacterial disease caused by these pathogens. Introduction of mass vaccination against the meningococcal C strain in several European countries has resulted in a dramatic decrease in the number of reported cases in the last decade. Similarly, the incidence of *Haemophilus influenzae* type b (Hib) disease has decreased substantially after the introduction of the vaccine on a national scale, and has contributed immensely to changing the epidemiology of the disease.

The surveillance of these diseases is important to study epidemiological trends and to monitor the circulating strains. Since the number of cases is decreasing because of the availability of effective vaccines, pooling European data together increases the power of the epidemiological analysis.

The European Union Invasive bacterial Infections Surveillance network (EU-IBIS) was established in 1999 and is funded by the European Commission's DG SANCO. Since the year of its establishment, EU-IBIS has collected data on invasive meningococcal and *H. influenzae* disease between 1999 and 2007 in European Union and European Economic Area (EU and EEA) countries and was successful in providing relevant epidemiological information to help guide the decision-making process on vaccine policies.

In October 2007, the coordination of the network was transferred to the European Centre for Disease Prevention and Control (ECDC) and data collection of IBI has been carried out through The European Surveillance System (TESSy). Coordination of laboratory surveillance activities, such as External Quality Assurance Schemes (EQAs) and training, have been outsourced and a consortium of European laboratory experts, mainly coming from national reference laboratories, has been set up to work together on these topics.

Thirty countries now participate in the network, including 27 Member States (MS) of the EU and three EEA countries (Iceland, Liechtenstein and Norway).

2 Methods

2.1 Case definitions

2.1.1 Invasive *Haemophilus influenzae* disease

The application of case definitions differed between MS, with the majority either applying the 2002 or 2008 versions of the EU case definitions:

- 10 countries applied 2002 EU case definition;
- 11 countries applied 2008 EU case definition;
- 1 country applied another case definition;
- 1 country reported using no case definition;
- 4 countries did not provide any information; and
- 3 countries did not report at all.

As displayed in Table 1, a key difference between the 2008 version of the case definition and the previous version from 2002 is that the possible and probable category of cases are no longer applicable in the 2008 edition. Moreover, clinical criteria are no longer relevant which previously, in combination with laboratory criteria, would fit a probable case. Another divergence is the isolation of the pathogen from a normally sterile site that only applied to serotype b according to the 2002 case definition, while other serotypes required a detection of nucleic acid for fitting the criteria for a confirmed case. There is no distinction between serotypes in the 2008 case definition.

Table 1: EU case definitions from 2002 and 2008 for invasive *H. influenzae* disease

EU case definition confirmed 2002 (Decision 2002/253/EC)	**EU case definition confirmed 2008 (EC Decision of 28/IV/2008)**
Confirmed case A clinically compatible case diagnosed by one of the following laboratory criteria: • Isolation of *Haemophilus influenzae* type b from a normally sterile site. • Detection of *H. influenzae* nucleic acid from a normally sterile site. **Probable case** A clinically compatible case diagnosed by the following laboratory criteria: • Detection of *H. influenzae* antigen from normally sterile site. **Possible case** A case with clinical epiglottitis without any laboratory confirmation or with identification only from non-sterile site.	**Clinical Criteria** Not relevant for surveillance purposes. **Laboratory Criteria** Laboratory criteria for case definition. At least one of the following two: • Isolation of *H. influenzae* from a normally sterile site. • Detection of *H. influenzae* nucleic acid from a normally sterile site. Typing of the isolates should be performed, if possible. **Epidemiological link**: N/A **Case Classification** • Possible case: N/A • Probable case: N/A • Confirmed case: Any person meeting the laboratory criteria for case confirmation.

In this analysis, there is no distinction made between the case classifications, and all probable cases (reported according to the 2002 case definition) combined with all confirmed cases are included, regardless of the version of case definition used. In total, six probable cases were reported.

In Table 2, the number and proportion of cases reported according to the case definition and classification are listed.

Table 2: Case classification reported according to the applied case definition

Classification	Case definition used	n cases	% of total confirmed
Confirmed	EU case definition 2002	866	42.1
	EU case definition 2008	1018	49.5
	Other Case Definition	108	5.2
	None	1	0.0
	Not reported	59	2. 9
	Total Confirmed	2052	99.7
Probable	EU case definition 2002	6	0.3
	Total Probable	6	0.30
Total		2058	100%

An epidemiological link is not applicable in any of the two EU case definitions, yet 58% of the cases that were reported according to these cases definitions provided information on the epidemiological link (yes or no). Moreover, and as stated above, clinical criteria are not relevant according to the 2008 case definition, and should therefore be reported as non-applicable, which was not done in 84% of the cases reported according to the 2008 version.

2.1.2 Invasive meningococcal disease

The case definitions referring to meningococcal disease applied by the MS differed, with the majority either applying the 2002 or 2008 versions of the EU case definitions:

- 11countries applied 2002 version of the EU case definition;
- 11 countries applied 2008 version of the EU case definition;
- 1 country did not specified the year of the version of the EU case definition applied;
- 5 countries applied other case definitions;
- 1 country reported using no international case definition; and
- 1 country did not report.

As displayed in Table 3, a major difference between the 2008 version of the case definition and the previous version (2002) is that in the 2008 definition the probable case has changed. The epidemiological link for probable cases was introduced and now cases are defined as probable according to epidemiological criteria only; this is different from the previous definition as no laboratory methods are included in the definition of a probable case. In addition, the category of a possible case has been introduced.

Table 3: EU case definitions from 2002 and 2008 for invasive meningococcal disease

EU case definition confirmed 2002 (Decision 2002/253/EC)	EU case definition confirmed 2008 (EC Decision of 28/IV/2008)
Confirmed case A clinically compatible case diagnosed by one or more of the following laboratory criteria: • Isolation of *Neisseria meningitidis* from a normally sterile site; • Detection of *N. meningitidis* nucleic acid from normally sterile site; • Detection of *N. meningitidis* antigen from normally sterile site; and/or • Demonstration of gram-negative diplococci from normally sterile site by microscopy. **Probable case** A clinically compatible case that is diagnosed by one or more of the following laboratory criteria: • *N. meningitidis* identification from a non-sterile site; • High levels of meningococcal antibody in convalescent serum; • and/or • Clinical picture compatible with meningococcal disease (e.g. meningitis and/or meningococcemia that may progress rapidly to purpura fulminans, shock and death; other manifestations are possible) without any laboratory confirmation.	**Clinical Criteria** Any person with at least one of the following five: • Fever; • Meningeal signs; • Petechial rash; • Septic shock; or • Septic arthritis. **Laboratory Criteria** At least one of the following four: • Isolation of *Neisseria meningitidis* from normally sterile site, including purpuric skin lesions; • Detection of *Neisseria meningitidis* nucleic acid from a normally sterile site, including purpuric skin lesions; • Detection of *Neisseria meningitidis* antigen in cerebrospinal fluid (CSF); or • Detection of gram negative stained diplococcus in CSF. **Epidemiological criteria** • An epidemiological link by human to human transmission. **Case Classification** *Possible case* • Any person meeting the clinical criteria. *Probable case* • Any person meeting the clinical criteria and with an epidemiological link. *Confirmed case* • Any person meeting the laboratory.

To overcome the discrepancies observed in the two case definitions, data have been analysed considering two main variables: 'classification' (separated into confirmed, probable and possible) applies mainly to cases reported according the 2008 case definition. The second, 'laboratory result' (separated into confirmed and probable) applies mainly to cases reported according the 2002 case definition.

Table 4 shows the categorisation of cases according to these two different criteria used in the analysis.

Table 4: Cases reported according to the variable selected ('classification' versus 'laboratory results')

Laboratory result	Classification			
	Confirmed	Probable	Possible	Total
Confirmed	4246	3	0	4249
Not Applicable	74	16	49	139
Probable	0	28	0	28
Unknown	839	285	5	1129
Total	**5159**	**332**	**54**	**5545**

As shown in Table 4, according to the variable 'case classification', there were 5159 cases reported as confirmed, 332 reported as probable and 54 reported as possible. According to the variable 'laboratory result', there were 4249 cases reported as confirmed, 139 as not applicable and 28 as probable laboratory. A sizable proportion of cases (1129) were reported as unknown. However, these cases were included in the analysis using the outcome under 'case classification'.

According to the 2008 case definition, the variable 'laboratory result' was not relevant for the notification of a probable case and should therefore have been reported as 'not applicable', which was done correctly only in 3% of the reported cases.

According to the 2002 case definition, the variable 'epidemiological link' was not relevant and should therefore have been reported as 'not applicable', which was done correctly in 39% of the reported cases.

2.2 Data sources

2.2.1 Invasive *Haemophilus influenzae* disease

This report includes data on *H. influenzae* disease cases submitted by the National Public Health Institutes from the Member States. Historical data (1999-2006) were retrieved from the EU IBIS database now housed at ECDC, and have been updated by the countries if needed.

Invasive *H. influenzae* disease surveillance varies between the MS in terms of strain (serotype), clinical presentation, age, and geographical coverage. In addition, the completeness of the submitted surveillance data varies quite substantially. Therefore, comparisons of data in specific analyses of certain variables and over time should be interpreted with caution.

Caution must also be taken when analysing trends, as various changes in the surveillance methods were done within the countries (e.g., expansion of age groups or serotypes, new laboratory methods available, etc) over the period in question.

All the variables included in the TESSy *H. influenzae* metadataset were expected to be reported on if the MS had them available. However, in 2007, some MS did not report certain variables even if they had been submitted data on these to EU-IBIS in the past.

At this stage, ECDC does not yet have a comprehensive overview of what variables are collected and available in the countries, partly because the information on data sources were not fully reported by MS. In Figure 42 in the Appendix, which shows the country profiles of invasive *H. influenzae* surveillance, the main characteristics of each data source are listed. This figure is essentially based upon the EU-IBIS transition document and upon variables reported in 2007.

Of the 27 reporting countries:

- 25 reported case-based data (with an enhanced set of variables);
- Two countries reported aggregated data (common set of variables);
- 25 reported data coming from national geographical coverage; and
- 24 reported they were using comprehensive surveillance systems.

2.2.2 Invasive meningococcal disease

This report includes data on invasive meningococcal disease cases submitted by the National Public Health Institutes from the MS. Historical data (1999–2006) were retrieved from the EU-IBIS database now housed at ECDC.

The surveillance of invasive meningococcal disease still varies widely between MS in terms of clinical criteria, clinical presentation, geographical coverage, and laboratory methods used at the country level. In addition, the completeness of the submitted surveillance data varies quite substantially. Therefore, comparisons of data in specific analyses of certain variables and over time should be interpreted with caution.

Laboratory capacities have improved over the years and the majority of countries are currently able to perform serotyping and serosubtyping. However, only a few of them provided this information.

All the variables included in the TESSy metadataset were expected to be reported on if the MS had them available. However, in 2007, some MS did not to report certain variables even if they had submitted data on these to EU-IBIS in the past.

All of the 29 reporting countries have a comprehensive and passive reporting system; all but one have compulsory reporting. Twenty-eight countries reported case-based data, and one (Bulgaria) reported aggregated data.

At this stage, ECDC does not yet have a comprehensive overview of what variables are collected and available in the reporting countries, partly because the information on data sources were not fully reported by MS.

2.2.3 Population data

All of the population denominator data used in this 2007 report were from the Eurostat demographic data. These data have been extracted from the Eurostat database under 'Population by sex and age on 1 January of each year'[1]. Totals per year and per country are available for all countries.

Historical notification rates from 2006 and earlier (EU-IBIS) were not recalculated if the rates were readily available in a table. If not available, as in the trend graphs, the rates from 1999 to 2006 were also recalculated using Eurostat population data from the respective years as the denominator.

2.3 Data submission and validation

The ECDC request for submission of the 2007 EU/EEA data on invasive *H. influenzae* and meningococcal disease took place in January 2009.

Designated national contact points were requested to submit data using the revised version of the dataset for invasive bacterial infections developed in 2008, on the basis of the former EU-IBIS database. It incorporates case-based information on epidemiological and laboratory variables, a core set of variables applicable to all notifiable diseases in EU and an enhanced dataset of variables specifically for these two diseases.

To facilitate the data submission, MS received online training in June 2008. Online supplementary training videos and other materials were made available prior to the data call.

Of the 30 EU and EEA MS:

- 27 submitted data on invasive *H. influenzae* disease (Liechtenstein, Netherlands and Romania did not report).
- 29 submitted data on meningococcal disease (Liechtenstein did not report).

Following the submission, the ECDC data manager assisted the MS in validating their uploaded data. This was followed by an epidemiological validation exercise, carried out by the vaccine preventable disease surveillance team at the ECDC, which included comparing the data with previous years and studying variable per variable lists and frequencies. In case of questions, the MS were approached in February with requests for clarifications of the submitted data. Around 50% of the MS responded, and data continued to be resubmitted until the second half of March 2009.

In some cases, MS did not report any data on one disease, or a particular variable, even if past epidemiological reports had quoted some data for that disease in that particular country.

Once a first draft of the annual report was prepared, it was shared with all the MS for final verification and comments.

2.4 Data analysis

Notification rates were calculated as the ratio between the number of probable and confirmed cases and the total population per 100 000 inhabitants. Overall annual, age-specific and strain-specific rates were calculated.

For the analyses of invasive *H. influenzae* disease data, no distinction was made between the case classifications, thus all confirmed and probable cases were included in all analyses.

With regard to invasive meningococcal disease cases, epidemiological data were analysed using the variable 'case classification', while laboratory data were analysed using the variable 'laboratory results'.

The notification data and the Eurostat age-specific population data were aggregated into the following age groups used in the analysis:

- *Haemophilus influenzae* disease: <1, 1–4, 5–14, 15–64 and ≥ 65 years.
- Meningococcal disease:<1, 1–4, 5–9,10–14, 15–19, 20–24, 25–44, 45–64, ≥ 65.

In the calculation of the case fatality ratios, all cases, including those with an unknown outcome status reported by countries that reported ≥ 1 case with a known outcome (acting as proxy for verifying that the outcome variable is included in the MS surveillance system), were included in the denominator.

Vaccination failures were not estimated due to the lack of sufficient information provided by the current variables in the IBI-metadataset. The vaccination status 'fully vaccinated' and 'partly vaccinated' were defined by the reporting country according to the child's age and the country's immunisation schedule.

[1] http://epp.eurostat.ec.europa.eu

In the analyses of strains of invasive *H. influenzae*, the serotypes were in most analyses and, if not stated otherwise, categorised into three major groups: serotype b; non-type b (unspecified non-b, a, c, d, e, f); and non-capsulated (non-typeable). In strain analysis of *N. meningitidis*, the strains were categorised mainly into two major groups: serogroups B and C or including serogroups A, Y, W135, NGA, or others (X, Z, Z/29E, 29E); in serotypes description analysis, the serotypes were categorised in eleven main serotypes (P2.2a, P2.2b, P2.2.c, P3.1, P3.4, P3.14, P3.15, P3.16, P3.21, P3.22, P3.23,) and non-typeable.

In the analysis, the most common serotype and serosubtype association with serogroup B and C isolates were described.

For analyses of invasive *H. influenzae* disease cases, the trends in notification rates by serotype (expressed as numbers of confirmed cases of either serotype b, non-b or non-capsulated (non-typeable) per population of 100 000) were analysed. Only the countries that have had a consistent surveillance system with consistent reporting to EU-IBIS and TESSy between 1999 and 2007 were included in these trend analyses. The trends were analysed using three different tests including chi-square for trend, linear regression, and Poisson regression. The overall trend was reported as significant if it was found to be statistically significant using all three tests ($p<0.05$). Trend analyses and chi-square for testing associations were conducted using StataSE 10.

Unless otherwise stated, all unknown responses were excluded from the epidemiological analysis, while the number and proportion of these unknown responses (perceived as missing data) were presented in the section of data quality (see Table 6).

The number of countries that reported a variable as 100% unknown is illustrated in Table 5, and was assumed to mean that it is a variable that is not under collection in the specific country.

3 Results: Invasive *Haemophilus influenzae* disease

3.1 Disease description

Haemophilus influenzae are Gram-negative coccobacilli, exclusively carried by humans. The species are divided into capsulated and non-capsulated (non-typeable) strains, and six antigenically distinct capsular types of *H. influenzae* (types a–f) have been identified. The presence or absence of a capsule, the main component of which is the polysaccharide polyribosylribitol phosphate (PRP), is a major determinant of the disease.

Haemophilus influenzae is transmitted via droplets and discharges from the nose and throat. The bacteria are present asymptomatically in the nasopharynx where they may persist and keep the host infectious for months. The incubation period is normally 2–4 days.

Typical clinical presentations of invasive *H. influenzae* diseases include meningitis, septicaemia, epiglottitis, pneumonia, septic arthritis, osteomyelitis, pericarditis, and cellulitis. In contrast, syndromes of mucosal infections, such as bronchitis, sinusitis, and otitis media, are considered non-invasive disease and are excluded from the surveillance of invasive bacterial infection surveillance.

The inclusion of the Hib vaccine in national child immunisation programmes has been the most important primary presentation intervention of *H. influenzae* across age groups due to a combination of direct and indirect protection. Prior to the introduction of effective vaccines, Hib was the cause of more than 95% of invasive *H. influenzae* diseases among children younger than five years of age. In this age group, Hib was also the most common cause of bacterial meningitis, practically the sole cause of epiglottitis, and responsible for many cases of cellulitis and joint infections.

Surveillance of invasive *H. influenzae* disease is important in order to monitor the epidemiology of these infections and to help evaluate the impact of any vaccination programmes. Since invasive *H. influenzae* disease is relatively uncommon, particularly after the introduction of the Hib-vaccine, pooling data across Europe increases the power of any epidemiological analysis.

3.1.1 Laboratory methods used for strain identification

Identifying a case of invasive disease caused by *H. influenzae* requires isolating the bacterium from a normally sterile body site—CSF, blood or joint fluid—and a positive culture to establish the diagnosis. In addition to culture, latex agglutination or antigen testing can be used, particularly in diagnosing Hib infections in patients who have been partially treated with an antibiotic, which may result in the organism not being viable on culture. A negative result from latex agglutination or antigen testing is however not definitive and false positives can occur, particularly when testing serum or urine; Hib meningitis is therefore the form of invasive *H. influenzae* disease most easily diagnosed in the laboratory. Typing of the strain is generally performed by using serological techniques. Polymerase chain reaction (PCR) and DNA sequencing strategies can also be effective for further *H. influenzae* classification. In a situation where there is a vaccine preventable disease with a vaccine available for just one serotype, one of the most important features in invasive *H. influenzae* surveillance is the monitoring of serotype distribution and trends.

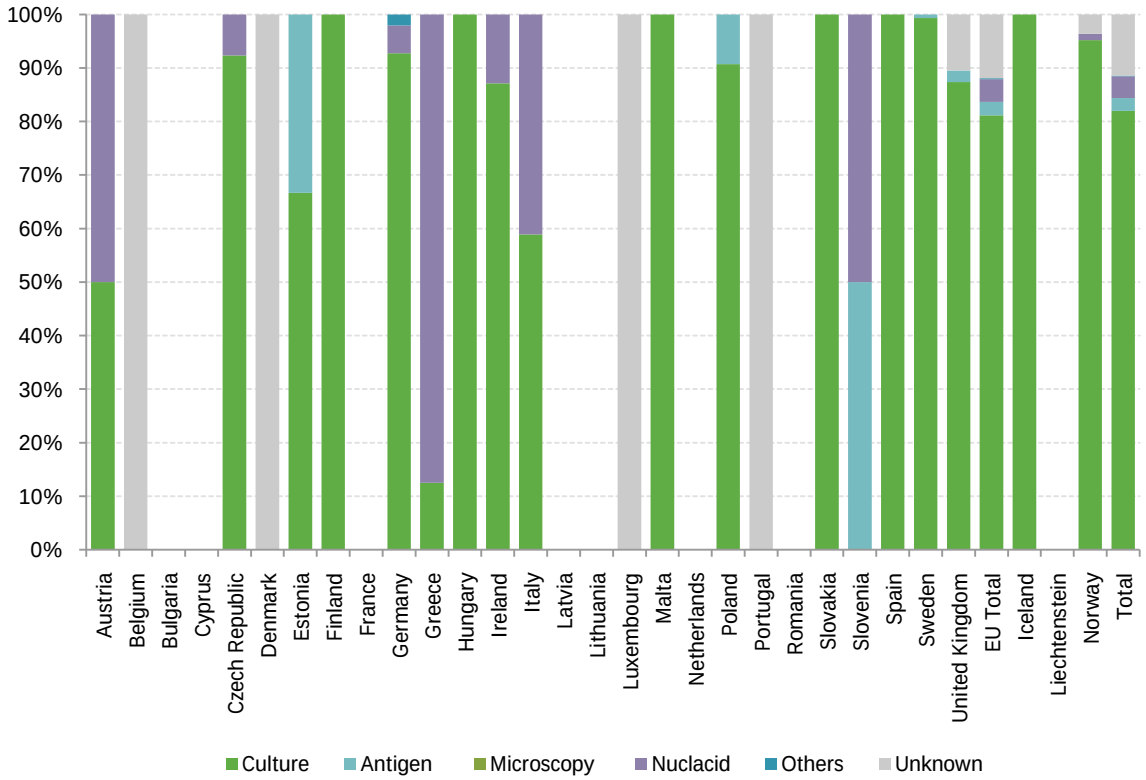
The need to correctly identify the serotype of *H. influenzae* isolate from any invasive disease has also increased since Hib has become a rare cause of invasive disease. Accurate serotype data on all *H. influenzae* isolates from children younger than five years of age is especially critical for monitoring Hib vaccine effectiveness. Serotyping is performed in the majority of the MS. However, within an individual country, the proportion of laboratories that perform serotyping and the proportion that send specimens to the reference laboratory differ widely. The serotype was specified in 39.6% of the reported cases in 2007 including the aggregated reported cases (59% if only including the case-based (Table 6)).

According to the EU-IBIS transition document and standard operating procedure 2007, Austria, Czech Republic, Denmark and Spain test over 80% of all strains for the presence of serotype b, though only Czech Republic and France test over 50% of received strains for the presence of the other serotypes. Italy and Spain test between 20 and 50% for other serotypes, and all other countries do so for less than 20% of received strains. In the Czech Republic, Finland, Germany, Ireland, Netherlands, Slovenia and Spain, over 80% of hospital laboratories send samples to the reference laboratory. Since 2007, all strains in Sweden should be sent to the national reference laboratory.

Figure 1 provides the distribution of test methods applied among the reported cases per country. All the test methods reported were combined and 'unknown test method' was only included if there were no specified test methods reported for a case (i.e., if specified once, the unknown in the other variables have been excluded).

Culture was overall the most frequently reported method with 82% in grand total, while the notifications provided little information about the typing methods (see Table 29 in Annex).

Figure 1: Proportion (%) of all reported test methods used among cases reported as invasive *H. influenzae* disease per country, 2007



No invasive H. influenzae *data were reported from Romania, Liechtenstein, and Netherlands in 2007. France and Bulgaria reported aggregated data with only a common set of variables (i.e., no enhanced variables, such as test methods), zero cases were reported from Cyprus, Latvia and Lithuania.*

3.2 Data quality

In Table 5, the numbers of countries that have reported 100% of their cases as unknown for each variable are summarised. As stated earlier, ECDC does not yet have sufficient information about the data sources to be able to distinguish if these variables are available in the country or not.

Among the 24 countries reporting cases (three countries reported zero cases):

- 20 specified the serotype ≥ 1 case;
- 18 reported the clinical presentation ≥ 1 case;
- 15 reported the vaccination status ≥ 1 case;
- 18 reported the outcome ≥ 1 case.

Table 5: Number of countries with variables reported as 100% unknown

Variable name	Number of countries	Variable name	Number of countries
Outcome	4	Serotype	4
ClinicalCriteria	5	Specimen1	2
LaboratoryResult	4	TestMeth1	4
EpiLinked	10	SpecLinkLab1	8
Imported	8	Specimen2	14
ProbableCountryOfInfection	8	ClinicalPresentation	4

In addition to these countries with only unknown notifications of certain variables, the proportions of reported common or enhanced set of variables varied greatly.

In Table 6, the proportion of reported cases as known and unknown for each variable in 2007 are listed from all countries that reported case-based data combined, meaning that all cases reported as aggregated with only a common set of variables were excluded from this analysis (Bulgaria and France, n=678, had 33% of the total number of reported cases).

The completeness of reporting varied widely between the variables. Date of onset was given in 79% of the notifications. Information on serotype and outcome (death or alive) were both completed in 59% of the notifications. Vaccination status among children younger than 15 years of age notified with serotype b had a completeness of 83%.

In the TESSy metadataset for the 2007 data there are two variables for test methods (TestMeth1 and TestMeth2), with each linked to the same order of specimen (Specimen1 and Specimen2). However, for each notified case, the test method can be repeated if several methods are performed on the first specimen (Specimen1). This was done in 30 of the 1380 case-based notified cases.

Table 6: Summary of the completeness of surveillance data: Distribution of known, unknown and blank responses per variable among all case-based reported invasive *H. influenzae* cases, 2007

Variable	Known (n)	Unknown (n)	N/A (n)	Blank (n)	Total (n)	Known (%)	Unknown (%)	N/A (%)
Age[C]	1 378	0	0	2	1380	100%	0%	-
Gender[C]	1 363	17	0	0	1380	99%	1%	-
Classification[C¤]	1 380	0	0	0	1380	100%	0%	-
ClinicalCriteria[C¤]	1 063	245	72	0	1380	77%	18%	5%
EpiLinked[C¤]	108	520	752	0	1380	8%	38%	54%
LaboratoryResult[C¤]	1 324	56	0	0	1380	96%	4%	-
ClinicalPresentation[C]	684	696	0	0	1380	50%	50%	-
DateOfDiagnosis[C]	1 024	0	0	356	1380	74%	0%	-
DateOfNotification[C]	1 021	0	0	359	1380	74%	0%	-
DateOfOnset[C]	1 086	0	0	294	1380	79%	0%	-
Outcome[C]	814	566	0	0	1380	59%	41%	-
Imported[E]	387	993	0	0	1380	28%	72%	-
ProbableCountryOfInfection1[E, I]	2	0	0	56	58	3%	0%	-
Serotype[E]	814	566	0	0	1380	59%	41%	-
Specimen1[E]	1 298	82	0	0	1380	94%	6%	-
Specimen2[E]	85	1295	0	0	1380	6%	94%	-
SpecLinkLab1[E]	951	429	0	0	1380	69%	31%	-
testMethod1HAEINF1[E]	1217	163	0	0	1380	88%	12%	-
testMethod1HAEINF2	17	6	0	1357	1380	1%	0%	-
testMethod1HAEINF3[E]	13	0	0	1367	1380	1%	0%	-
testMethod2HAEINF[E]	49	1331	0	0	1380	4%	96%	-
VaccStatus [E] *	81	17	0	0	98	83%	17%	-

C = Common set of variables
E = Enhanced set of variables
** = As this variable is only applicable for Hib, only children between 0-14 years of age reported as serotype b are included.*
¤ = These variables are linked to the case definition and the reported value is expected to correspond to the applied case definition (see previous section about case definitions)
I = Only the cases reported as imported are included as probable country of infection is only reported if the case is reported as imported.

3.3 Epidemiological analysis

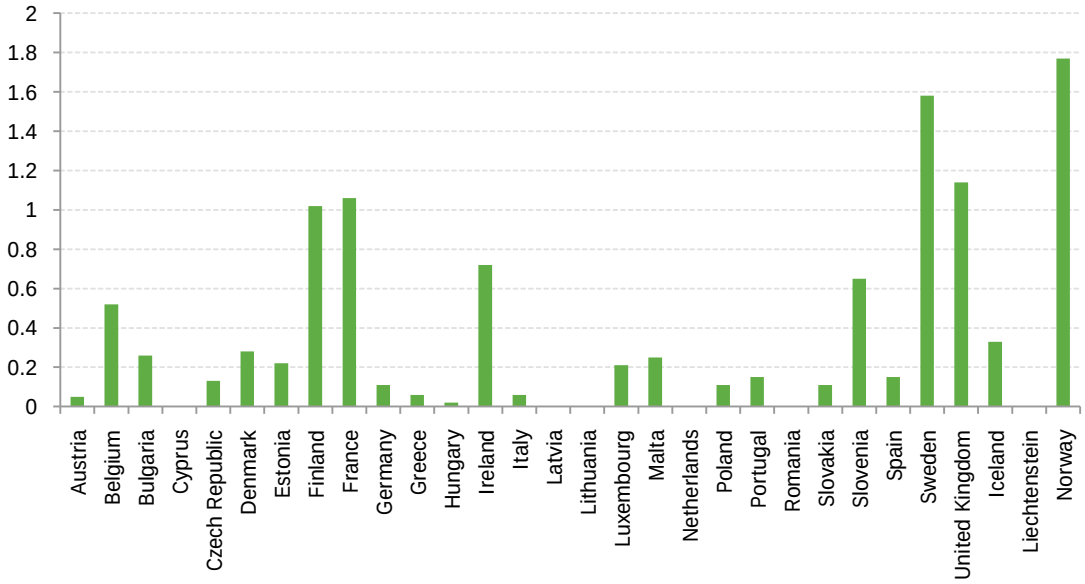
In 2007, 2058 cases of invasive *H. influenzae* disease were reported from 27 countries, with Cyprus, Latvia and Lithuania reporting zero cases. No invasive *H. influenzae* data were reported from Romania, Liechtenstein, and the Netherlands. France and Bulgaria reported aggregated data with only a common set of variables (i.e., no enhanced variables). Table 30 in the Annex displays the classification of the cases, with numbers of reported confirmed and probable cases, and the applied case definition.

3.3.1 Overall notification rates

The overall notification rates (per 100 000 population) of invasive *H. influenzae* disease by country in 2007 are presented in Figure 2.

The overall crude European notification rate in 2007 was 0.41 per 100 000. These data are further illustrated in Table 7 which also presents the number of reported cases and notification rates from 1999 to 2007 (EU-IBIS data for 1999 to 2006).

Figure 2: Overall notification rates of invasive *H. influenzae* disease by country, 2007 (n=2 056)



Zero cases reported from Cyprus, Latvia and Lithuania. No data available from Netherlands, Romania and Liechtenstein. Population source: Eurostat 2007

Not all countries report all cases of invasive *H. influenzae* disease, and great care must be taken when comparing notification rates and trends across countries and over time. Moreover, the surveillance systems within countries may also change over time; e.g., inclusion of all age groups and serotypes.

Since the disease is relatively rare, a notable change in rates may in fact represent a small change in absolute numbers and needs to be monitored over a number of years. More detailed information of the overall notification rates from 1999 to 2007 and country profiles (information of data sources) are given in the country profiles in Figure 44 in the Annex.

Table 7: Notification rates (per 100 000 population) and total number of cases of invasive *H. influenzae* disease by country, 1999–2007

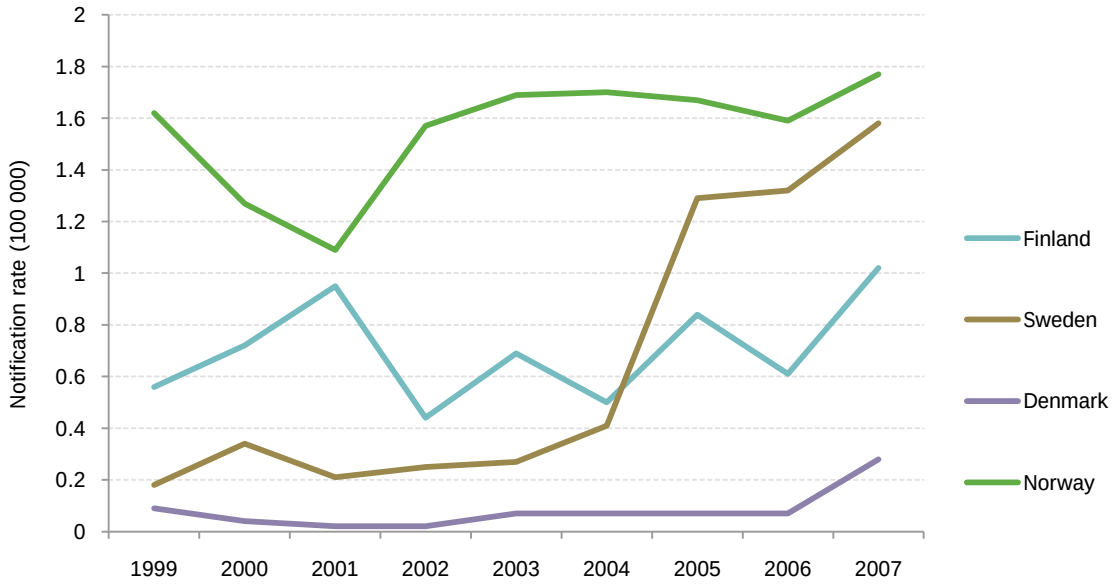
Country	Note[I]	1999	2000	2001	2002	2003	2004	2005	2006	2007
Austria		-	-	-	0.05 (4)	0.05 (4)	0.13 (11)	0.18 (15)	0.09 (7)	0.05 (4)
Belgium		-	0.61 (63)	0.52 (54)	0.63 (65)	0.53 (55)	0.56 (58)	-	-	0.52 (55)
Bulgaria		-	-	-	-	-	-	-	-	0.26 (20)
Cyprus		-	-	-	-	-	-	-	-	0 (0)
Czech Republic	*II*	1.00 (103)	1.02 (105)	0.90 (92)	0.55 (56)	0.49 (50)	0.16 (16)	0.18 (18)	0.11 (11)	0.13 (13)
Denmark	*III*	0.09 (5)	0.04 (2)	0.02 (1)	0.02 (1)	0.07 (4)	0.07 (4)	0.07 (4)	0.07 (4)	0.28 (15)
Estonia	*IV*	0.22 (3)	0.07 (1)	0.22 (3)	0.22 (3)	0.07 (1)	1.33 (18)	1.49 (20)	0.60 (8)	0.22 (3)
Finland		0.56 (29)	0.72 (37)	0.95 (49)	0.44 (23)	0.69 (36)	0.50 (26)	0.84 (44)	0.61 (32)	1.02 (54)
France	*V*	0.89 (521)	0.96 (565)	1.01 (598)	0.81 (479)	0.91 (546	1.01 (608)	1.06 (646)	0.98 (605)	1.06 (658)
Germany	*VI*	0.33 (42)	0.57 (73)	0.45 (57)	0.38 (47)	0.37 (46)	0.26 (32)	0.29 (34)	0.49 (57)	0.11 (93)
Greece	*VII*	0.35 (2)	0.52 (3)	0.34 (2)	1.39 (8)	0.50 (8)	0.56 (9)	0.13 (2)	0.19 (3)	0.06 (7)
Hungary	*VIII*	-	-	-	-	0.07 (7)	0.12 (12)	0.01 (1)	0.00 (0)	0.02 (2)
Ireland		0.78 (27)	0.55 (21)	0.70 (27)	0.54 (21)	0.56 (22)	0.94 (38)	0.82 (34)	0.90 (38)	0.72 (31)
Italy		0.19 (109)	0.11 (64)	0.05 (31)	0.03 (19)	0.04 (24)	0.02 (9)	0.03 (15)	0.04 (23)	0.06 (33)
Latvia		-	-	-	-	0.13 (3)	0.04 (1)	0.00 (0)	0.00 (0)	0 (0)
Lithuania	*VIII*	-	-	-	-	0.03 (1)	0.23 (8)	0.09 (3)	0.06 (2)	0 (0)
Luxembourg		-	-	-	-	-	-	-	-	0.21 (1)
Malta		0.00 (0)	0.26 (1)	0.00 (0)	0.00 (0)	0.00 (0)	0.77 (3)	0.00 (0)	0.00 (0)	0.25 (1)
Netherlands		0.43 (68)	0.49 (77)	0.57 (91)	0.67 (108)	0.82 (132)	0.78 (127)	0.85 (139)	0.75 (122)	-
Poland	*IX*	0.06 (25)	0.08 (31)	0.09 (35)	0.09 (33)	0.09 (36)	0.08 (32)	0.05 (19)	0.05 (20)	0.11 (43)
Portugal		0.09 (9)	0.10 (10)	0.15 (16)	0.12 (12)	0.12 (13)	0.11 (12)	0.13 (14)	0.22 (23)	0.15 (16)
Romania		-	-	-	-	-	-	-	-	-
Slovakia		0.35 (19)	0.28 (15)	0.20 (11)	0.13 (7)	0.17 (9)	0.07 (4)	0.13 (7)	0.06 (3)	0.11 (6)
Slovenia		-	0.65 (13)	0.85 (17)	0.40 (8)	0.65 (13)	0.70 (14)	0.40 (8)	0.65 (13)	0.65 (13)
Spain	*X*	-	-	-	-	-	-	-	-	0.15 (66)
Sweden	*XI*	0.18 (16)	0.34 (30)	0.21 (19)	0.25 (22)	0.27 (24)	0.41 (37)	1.29 (117)	1.32 (120)	1.58 (144)
United Kingdom		0.68 (400)	0.85 (498)	1.03 (605)	1.28 (757)	1.26 (750)	0.92 (550)	1.10 (661)	1.08 (650)	1.14 (696)
Iceland	*XII*	1.44 (4)	0.36 (1)	0.70 (2)	0.00 (0)	0.00 (0)	0.34 (1)	0.00 (0)	0.00 (0)	0.33 (1)
Liechtenstein		-	-	-	-	-	-	-	-	-
Norway		1.62 (72)	1.27 (57)	1.09 (49)	1.57 (71)	1.69 (77)	1.70 (78)	1.67 (77)	1.59 (74)	1.77 (83)

I. 1999-2006 From EU-IBIS 2006 report, 2007 using Eurostat as population source
II. (CZ): Serotype b only 1999-2004
III. (DK): Meningitis only/mostly meningitis 1999-2006, thereafter all.
IV. (EE): Serotype b only; all rates from 1999-2006 are recalculated from EU-IBIS 2006 report for including the total population number (Eurostat) as denominator. denominator (<15 only previously)
V. (FR): Aggregated data corrected for under-reporting and under-coverage. In 2007 reported with common set of variables
VI. (DE): <15 years 1999-2006 (rates based on <15 population). From 2007, all age groups/total population.
VII. (GR): Mainly serotype b & non-b; meningitis and meningitis/septicaemia only<15 years 1999-2006 (rates based on <15 population). From 2007, all age groups/total population.
VIII. (HU, LT): Meningitis and septicaemia only
IX. (PL): Mainly serotype b, also non-caps 2004-; Meningitis only 1999-2006
X. (SE): Serotype b only 1999-2004; aggregated data 2000-2001
XI. (IS): Mainly serotype b

A noteworthy change in notification rate in 2007 compared to previous years was reported from Estonia. In 2005, the Estonian notification rate peaked at 1.49 per 100 000 and decreased to 0.22 per 100 000 in 2007. A possible explanation of the increase was improved case ascertainment. In fact, until 2003, only septicaemia caused by serotype b was under Estonian national surveillance. Since then, all clinical presentations caused by serotype b have been collected. The decrease in notification rates, on the other hand, has mainly been explained by the introduction of the Hib vaccine into the immunisation schedule in September 2005.

In contrast to the decrease in Estonia, the overall notification rates continued to increase in most of the northern European countries in 2007. A number of these countries reported their highest rates since 1999 (Denmark 0.28, Finland 1.02, Norway 1.77, and Sweden 1.58 per 100 000), as is illustrated in Figure 3 (more detailed information is available the Annex of country profiles). The most plausible explanation for the continued increase of reported cases is enhanced surveillance systems, with inclusion of all serotypes and/or clinical presentations, increased awareness among the clinicians to notify, and an improved high case ascertainment in general (i.e., enhanced sensitivity).

Figure 3: Overall notification rates (per 100 000) of invasive *H. influenzae* disease in Denmark, Finland, Norway and Sweden, 1999–2007 (n=1487)



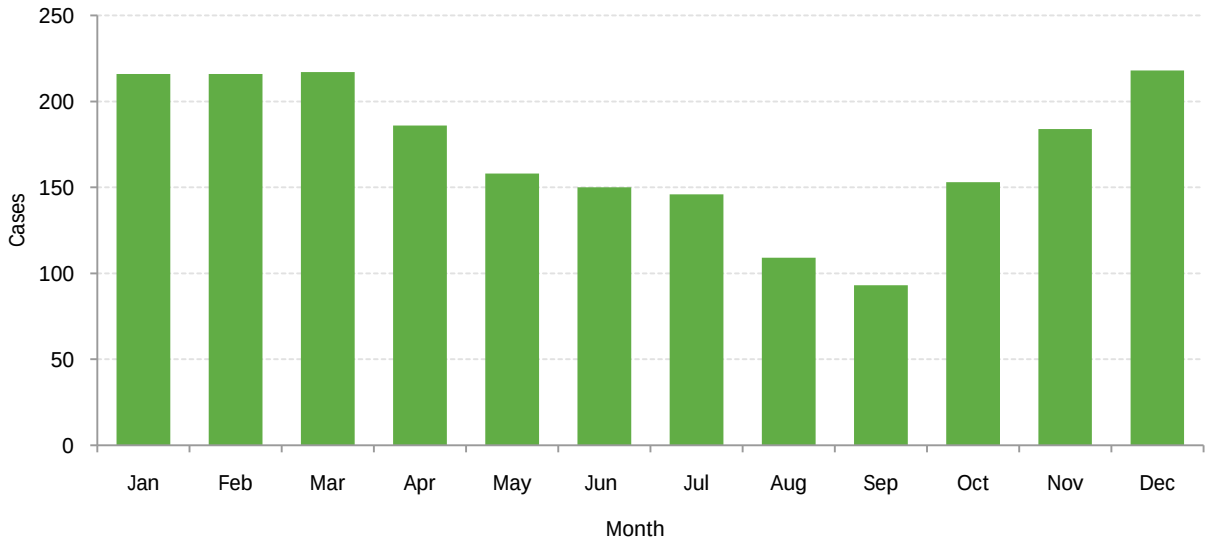
Population source: Eurostat 1999-2007

In addition, in 2007 the United Kingdom and France reported notification rates above 1.0 (1.14 and 1.06 per 100 000 respectively), while the rates in all the other countries stayed below 1.0 per 100 000 population.

3.3.2 Seasonal trend

As shown in Figure 4, the highest numbers of observed invasive *H. influenzae* infections occurred during the winter months. This was followed by a steady decrease until September when the numbers increased again to a peak in December. This annual trend was similar across the serotypes. See Table 31 in the Appendix for the number of cases reported per month and country.

Figure 4: Number of reported invasive *H. influenzae* cases per month in 2007 (n=2058)



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

3.3.3 Gender distribution

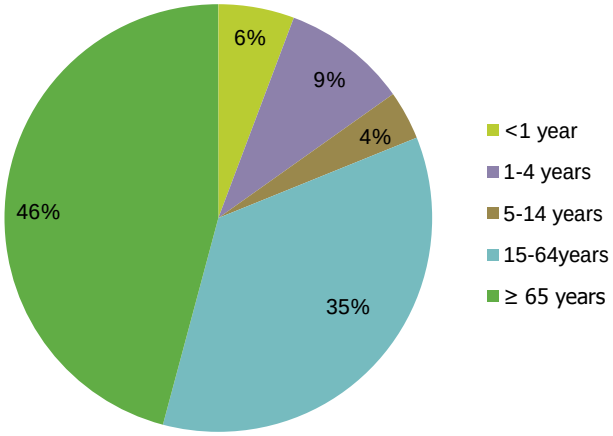
The overall male-to-female ratio was 1.03 in 2007, and remained relatively constant across age groups (see Table 32 in Annex).

3.3.4 Age distribution

In 2007, the mean age of reported invasive *H. influenzae* disease was 51.3 years 95% (CI: 49.7-52.9), and median age 61 years (range 0–99; only case based reported cases included 1378 with known age). Forty-six per cent of reported cases were above 65 years of age, and 35% between 15–64 years, as illustrated in Figure 5. The age distribution in 2007 was relatively similar to previous years, although a trend of an increasing proportion in adults older than 65 years (31.2% in 2004, 33.8% in 2005, 41.2% in 2006).

One explanation for this is the increase of reported cases with non-capsulated strains in the oldest age group (see Figure 14), and probably also an ageing population. Another factor influencing the increase from 2006 is that, in 2007, Germany included all age groups in the invasive *H. influenzae* disease reporting (previously <15 years of age only).

Figure 5: Age distribution of reported cases of invasive *H. influenzae* disease, all countries combined in 2007 (n=2056, case-based and aggregated)



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

The most affected groups in 2007 were the youngest and oldest age groups (Table 8):

- Infants below one year of age had an overall notification rate of 3 per 100 000. Highest rates were reported from Ireland, Norway and the United Kingdom, all above 7.5 per 100 000.
- Adults above 65 years had an overall notification rate of 1.19 per 100 000. Highest rates were reported from Norway and Sweden, both above 5.0 per100 000.

The highest rates are marked in italics in Table 8.

Table 8: Total number and notification rates (per 100 000 population) of invasive *H. influenzae* disease by country and age group in 2007

Age group	<1 year		1-4 years		5-14 years		15-64years		≥ 65 years	
Country	**n**	**Not. rate 100 000**	**n**	**Not. rate 100 000**	**n**	**Not. rate 100 000**	**n**	**Not. rate 100 000**	**n**	**Not. rate 100 000**
Austria	0	0.00	0	0.00	0	0.00	3	0.05	1	0.07
Belgium	3	2.46	3	0.64	3	0.25	16	0.23	30	1.66
Bulgaria*	-	-	18	*6.60*	0	0.00	1	0.02	1	0.08
Cyprus	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Czech Republic	0	0.00	4	1.03	2	0.2	6	0.08	1	0.07
Denmark	0	0.00	3	1.16	0	0.00	5	0.14	7	0.84
Estonia	1	*6.75*	0	0.00	1	*0.76*	1	0.11	0	0
Finland	1	1.70	0	0.00	2	0.33	26	*0.74*	25	*2.88*
France*	37	4.72	33	1.07	16	0.21	250	0.6	322	*3.13*
Germany	9	1.34	7	0.25	6	0.08	28	0.05	43	0.26
Greece	3	2.68	0	0.00	2	0.19	1	0.01	1	0.05
Hungary	0	0.00	0	0.00	0	0.00	2	0.03	0	0.00
Ireland	5	*7.76*	4	1.63	1	0.18	8	0.27	13	*2.77*
Italy	1	0.18	2	0.09	0	0.00	13	0.03	17	0.14
Latvia	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Lithuania	0	0.00	0	0.00	0	0.00	0	0	0	0.00
Luxembourg	0	0.00	0	0.00	0	0.00	0	0	1	1.50
Malta	0	0.00	0	0.00	0	0.00	1	0.35	0	0.00
Netherlands	-	-	-	-	-	-	-	-	-	-
Poland	12	3.22	15	1.06	11	0.26	5	0.02	0	0.00
Portugal	3	2.85	1	0.23	2	0.18	6	0.08	4	0.22
Romania	-	-	-	-	-	-	-	-	-	-
Slovakia	3	5.59	1	0.48	0	0	2	0.05	0	0.00
Slovenia	1	5.23	0	0.00	3	*1.58*	3	0.21	6	1.88
Spain	8	1.72	3	0.16	3	0.07	19	0.06	31	0.42
Sweden	3	2.82	1	0.25	3	0.29	54	*0.9*	83	*5.25*
United Kingdom	60	*8.03*	59	*2.11*	16	0.22	253	0.63	308	*3.17*
EU Total	**113**	**2.92**	**191**	**1.02**	**71**	**0.15**	**703**	**0.23**	**894**	**1.14**
Iceland	0	0.00	0	0.00	0	0.00	1	0.48	0	0.00
Liechtenstein	-	-	-	-	-	-	-	-	-	-
Norway	5	*8.51*	3	1.30	5	*0.81*	22	*0.71*	48	*7.00*
Total	**118**	**3.00**	**194**	**1.02**	**76**	**0.16**	**726**	**0.23**	**942**	**1.19**

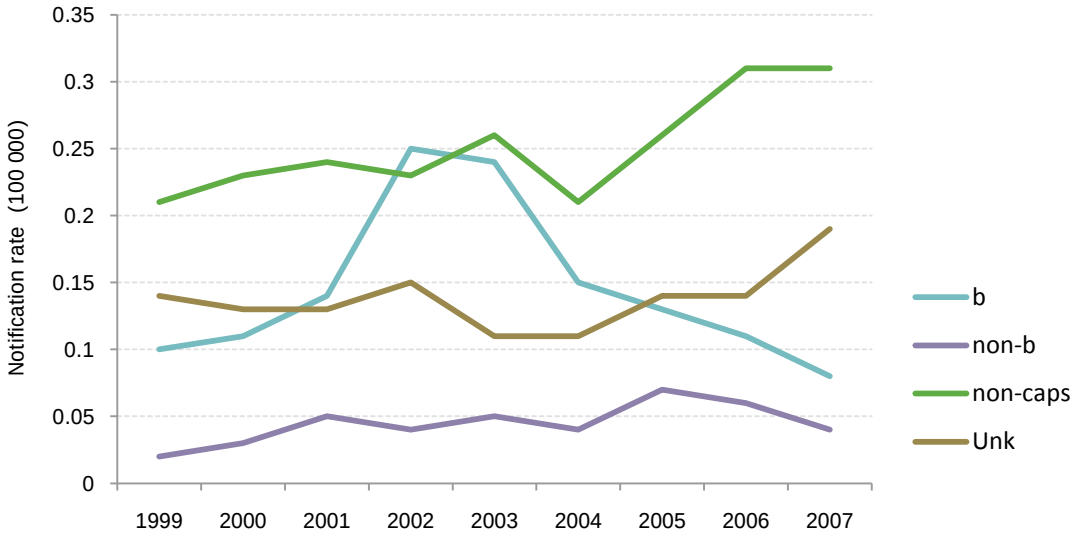
Population source: Eurostat 2007
**Countries that report using different systems*

3.3.5 Serotypes

Figure 6 illustrates the notification rates by serotype from 1999 to 2007 in selected countries (Finland, Ireland, Italy, Norway, Portugal, and the United Kingdom) with consistent reporting of all strains. In previous years' EU-IBIS reports other countries were included, but in 2007 several of these were not able to provide the data required for analysis. As illustrated in Table 7, the overall notification rates from these six countries varied over the years under observation, but have tended to be higher during the most recent years. Non-capsulated strains have been the most frequently reported serotype among these selected countries, with a statistically significant increasing trend ($p < 0.001$). This continued increase of non-capsulated strains has to be followed up in the following years.

After the peak in 2002–2003, the decrease in notification rates of serotype b was statistically significant (<0.001). While the notification rates of non-b strains remained relatively constant, there are no indications of a serotype replacement from type b to non-type b strains.

Figure 6: Notification rates (100 000) of invasive *H. influenzae* disease by serotype in selected countries, 1999—2007 (n=7323).

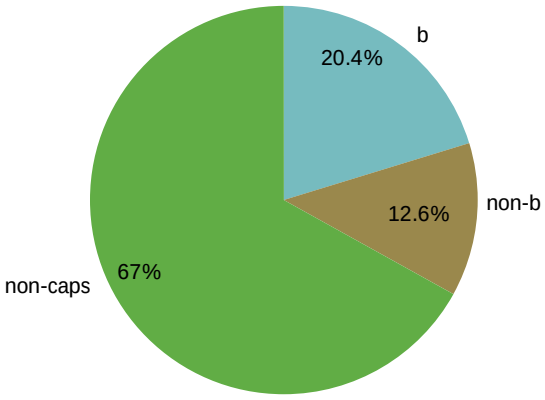


Contributing countries: Finland, Ireland, Italy, Norway, Portugal, United Kingdom
Population source: Eurostat 1999-2007

The case ascertainment and the extent of serotyping have also varied during the years observed, and therefore the notification rates of serotypes reported as unknown were also included for comparison. The trend of unknown serotype follows roughly that of the non-capsulated trends, and there appears to be no clear explanation for this trend.

Figure 7 illustrates the reported serotype distribution in 2007, and includes those countries that record all serotypes and ages. Information on serotype was available in 40% of the total number of cases reported (including the aggregated data, 59% of the case based reporting). After exclusion of the unknown serotypes, 67% were reported as non-capsulated and 20.4% as serotype b.

Figure 7: Serotype distribution of invasive *H. influenzae* disease in 2007 among countries that report all serotypes (n=786, excluding the 418 cases reported as unknown serotype).



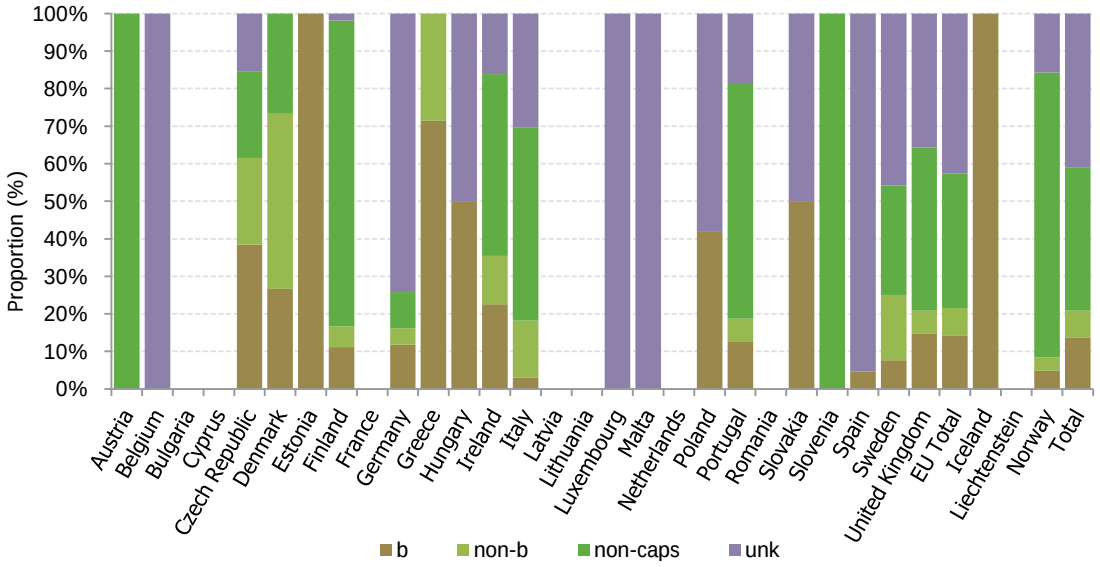
Contributing countries: Austria, Czech Republic, Denmark, Finland, Germany, Greece, Ireland, Iceland, Italy, Malta, Norway, Portugal, Slovenia, Sweden, United Kingdom.

Figure 8 illustrates the proportion of reported serotypes per country (aggregate reporting countries excluded as they reported only a common set of variables). The proportion of reported serotype as unknown was high overall, and a number of countries reported 100% of the notified cases as unknown serotype, while other countries reported a larger fraction of the cases as unknown serotype. This complicates a comparative analysis of the serotype occurrence and distribution in Europe and needs to be taken in account in all the analyses of serotypes below.

Based on the available data, it is notable that all cases from Austria (n=4) and Slovenia (n=13) were reported as non-capsulated. Also Finland (81%, n=44), Norway (76%, n=63), Portugal (63%, n=10) and Italy (52%, n=17) reported more than the half of their cases as non-capsulated strains.

In Figure 8, Estonia and Iceland reported all their notified cases as serotype b; Estonia includes serotype b only in their national surveillance system, while Iceland reported only one case. (For more information, see Table 33 in Annex.)

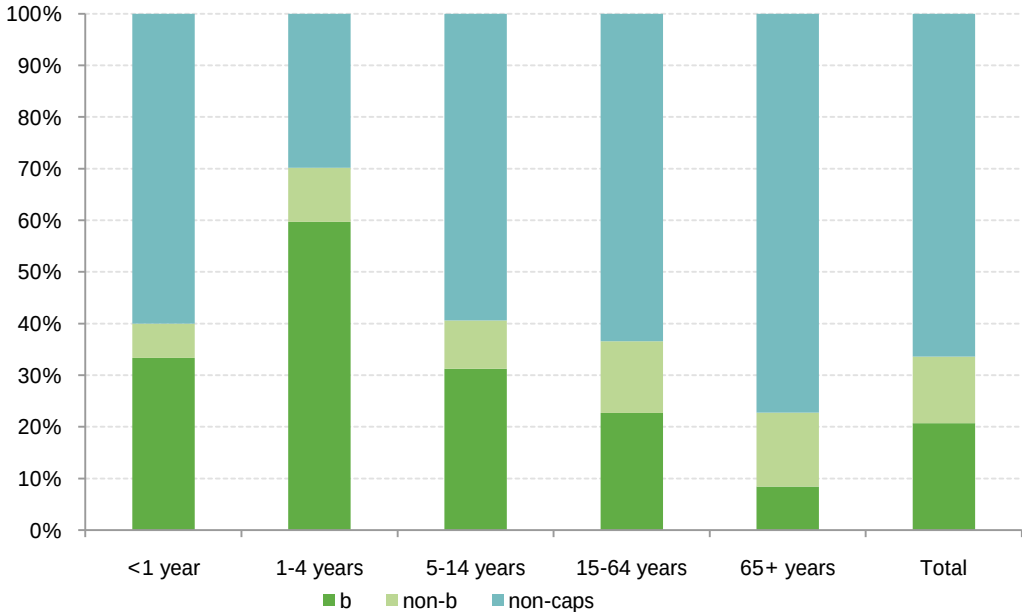
Figure 8: Reported serotype distribution of reported invasive *H. influenzae* disease by country in 2007 (n=1378).



Contributing countries: All countries that reported case-base data with enhanced dataset

In Figure 9, the distribution of serotypes by age group is illustrated (same contributing countries as in Figure 7). Cases reported as unknown serotype are excluded from the analysis (34.7% of the total numbers of reported cases in the contributing countries). Figure 9 shows an association between type of strain and age group ($p < 0.001$). Non-capsulated strains were the most commonly reported across all age groups except in the 1–4 year olds, whereas serotype b had the highest proportion of reported cases.

Figure 9: Serotype distribution of invasive *H. influenzae* cases by age group, of countries collecting all serotypes in 2007. (n=786, excluding the 418 cases reported as unknown serotype)

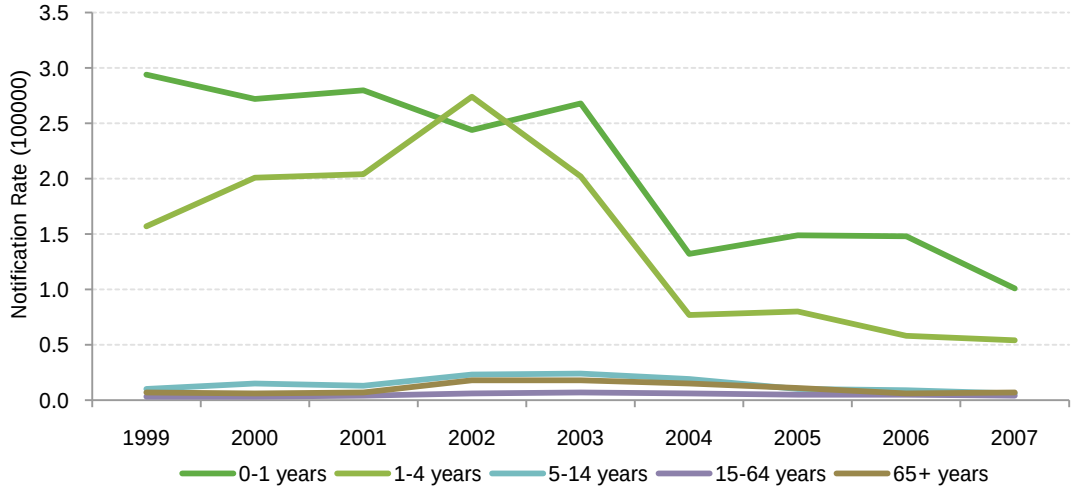


Contributing countries: Austria, Czech Republic, Denmark, Finland, Germany, Greece, Ireland, Iceland, Italy, Malta, Norway, Portugal, Slovenia, Sweden, United Kingdom

3.3.5.1 Serotype b strains

The notification rates of serotype b by age group from 1999 to 2007 in those countries with consistent reporting are illustrated in Figure 10. The rates appear to be decreasing across all age groups. In 2007, the highest rates remained in the youngest age groups.

Figure 10: Notification rate (per 100 000 population) of invasive Hib disease by age group, in selected countries, 1999–2007 (n=2538)



Contributing countries: Czech Republic, Finland, Iceland, Ireland, Italy, Malta, Norway, Poland, Portugal, United Kingdom.
Population source: Eurostat 1999-2007

In general, the number of cases reported with serotype b in 2007 was low with the consequence that single cases in small countries result in larger differences in notification rates. In total, 188 cases of serotype b were reported in 2007 with a crude Hib notification rate of 0.04 per 100 000 population as displayed in Table 9. Although with low overall numbers of reported cases, Iceland (0.33, n=1), and Estonia (0.22, n=3) reported the highest Hib notification rates, followed by United Kingdom (0.17, n= 103), Ireland (0.16, n=7), Sweden 0.12, n= 11), and Finland (0.11, n=6).

In the 1–4 year age group, it was observed that serotype b was the most frequently reported strain. In total, 71.7% (n=33) of the total number of reported Hib cases in the age of 1–4 years were reported by the United Kingdom, with the highest notification rate of 1.18 per 100 000. Denmark reported the second highest rates of 0.77 per 100 000 (n=2). Zero cases were reported by Norway, Finland and Sweden in this age group.

Table 9: Notification rate (per 100 000 population) of invasive Hib disease by age group and country, 2007

	<1 year		1-4 years		5-14 years		>15 years		Total	
Country	**n**	**NR (100 000)**	**n**	**NR (100 000)**	**n**	**NR (100 000)**	**n**	**NR (100 000)**	**n**	**NR (100 000)**
Austria	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Belgium[1]	-	-	-	-	-	-	-	-	-	-
Bulgaria[2]	-	-	-	-	-	-	-	-	-	-
Cyprus	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Czech Republic	0	0.00	2	0.52	2	0.20	1	0.01	5	0.05
Denmark	0	0.00	2	0.77	0	0.00	2	0.05	4	0.07
Estonia	1	*6.75*	0	0.00	1	*0.76*	1	0.09	3	0.22
Finland	1	1.70	0	0.00	1	0.16	4	0.09	6	0.11
France[2]	-	-	-	-	-	-	-	-	-	-
Germany	5	0.74	1	0.04	1	0.01	4	0.01	11	0.01
Greece	3	2.68	0	0.00	1	0.09	1	0.01	5	0.04
Hungary	0	0.00	0	0.00	0	0.00	1	0.01	1	0.01
Ireland	2	*3.11*	1	0.41	1	0.18	3	0.09	7	0.16
Italy	0	0.00	1	0.05	0	0.00	0	0.00	1	0.00
Latvia	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00

	<1 year		1-4 years		5-14 years		>15 years		Total	
Country	**n**	**NR (100 000)**	**n**	**NR (100 000)**	**n**	**NR (100 000)**	**n**	**NR (100 000)**	**n**	**NR (100 000)**
Lithuania	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Luxembourg[1]	-	-	-	-	-	-	-	-	-	-
Malta[1]	-	-	-	-	-	-	-	-	-	-
Netherlands[3]	-	-	-	-	-	-	-	-	-	-
Poland	5	1.34	6	0.42	6	0.14	1	0.00	18	0.05
Portugal	1	0.95	0	0.00	0	0.00	1	0.01	2	0.02
Romania[3]	-	-	-	-	-	-	-	-	-	-
Slovakia	3	*5.59*	0	0.00	0	0.00	0	0.00	3	0.06
Slovenia	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Spain	1	0.21	0	0.00	0	0.00	2	0.01	3	0.01
Sweden	1	0.94	0	0.00	1	0.10	9	0.12	11	0.12
United Kingdom	11	1.47	33	*1.18*	3	0.04	56	0.11	103	0.17
EU Total	**34**	**1.23**	**46**	**0.45**	**17**	**0.07**	**86**	**0.03**	**183**	**0.04**
Iceland	0	0.00	0	0.00	0	0.00	1	0.41	1	*0.33*
Liechtenstein[3]	-	-	-	-	-	-	-	-	-	-
Norway	1	1.70	0	0.00			3	0.08	4	0.09
Total	**35**	**1.24**	**46**	**0.45**	**17**	**0.07**	**90**	**0.04**	**188**	**0.04**

1) No data on serotypes (case based reporting with enhanced set of variables)
2) No data on serotypes (aggregating reporting with common set of variables)
3) No invasive H. influenzae *data available*
Population source: Eurostat 2007

The rate of invasive Hib disease in the younger than five year age group is often used as the main indicator of the burden of disease and it is the most reliable notification rate for comparisons between countries. Figure 11 illustrates the notification rates of Hib in Europe amongst the younger than five year age population in 2007. This pattern differs from the overall notification rates as the northern European countries reported high overall notification rates, but reported lower rates for the serotype b. For example, the notification rate from Sweden was 0.20, while Finland and Norway had 0.35 (per 100 000). The highest younger than five year age group notification rate of Hib was reported by the United Kingdom and Slovakia, both above 1.0 per 100 000. In practice, the highest rate was observed in Estonia (1.45), but this is based on only one case.

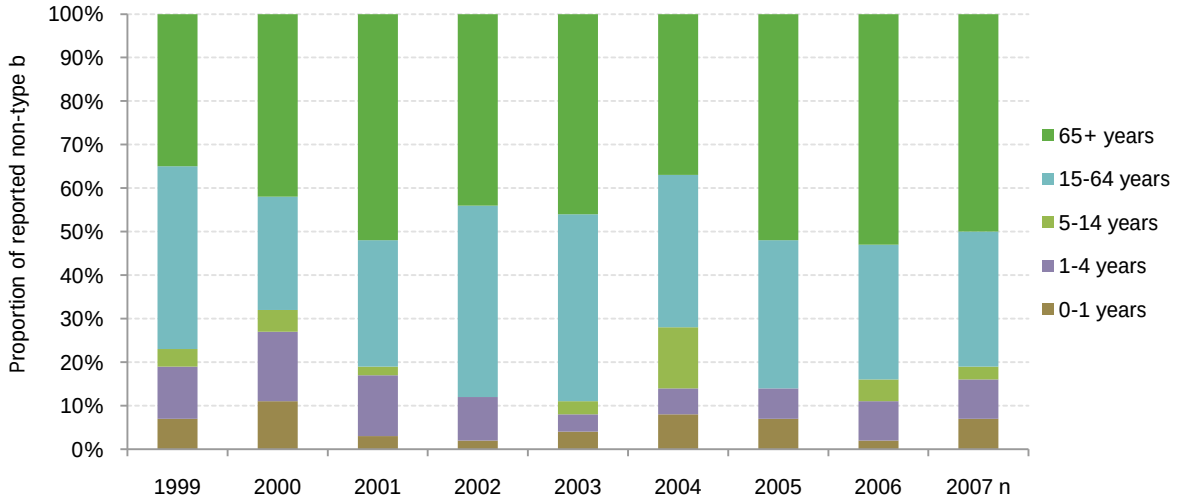
Examining the age group younger than five years of age, the infants younger than one year of age had the highest notification rate of 1.24 per100 000, with a total of 34 infants reported in 2007.

3.3.5.2 Non-type b strains

Due to the small number of reported non-type b strains, only the proportions are illustrated. Figure 11 shows the proportion of reported cases with non-type b strains across age groups from 1999–2007 in countries with consistent reporting.

As shown in Table 10 the overall rate, based on data from the countries that reported ≥1 case of non-type b in 2007 combined, was 0.04 per 100 000 population (n=99). The notification rate was highest in the age group <1 year of age (0.19, n=5).

Figure 11: Proportion of reported invasive *H. influenzae* non-type b cases by age groups in selected countries, 1999–2007 (n=547)



Contributing countries: Finland, Ireland, Italy, Norway, Portugal, United Kingdom. Included strains: a, c, d, e, f, and non-b.

The oldest age groups remained, in absolute number, the most affected proportionally. In total, 44% of the reported non-type b cases in 2007 occurred among >65 years (see total numbers and notification rates in Table 10).

In Table 10, the absolute numbers of reported cases and notification rates in 2007 of non-type b strains by age group and by country are presented. The numbers of reported cases with identified non-b strains are dependent upon the case ascertainment in each country. In total, Ireland reported the highest overall notification rate of 0.43 per 100 000 (n=19) with the number among infants younger than one year (3.1, but n=2), and in the oldest age group older than sixty-five (4.05, n=9).

Table 10: Total number of cases and notification rates (per 100 000 population) of invasive *H. influenzae* non-type b disease by age group and reporting country, 2007

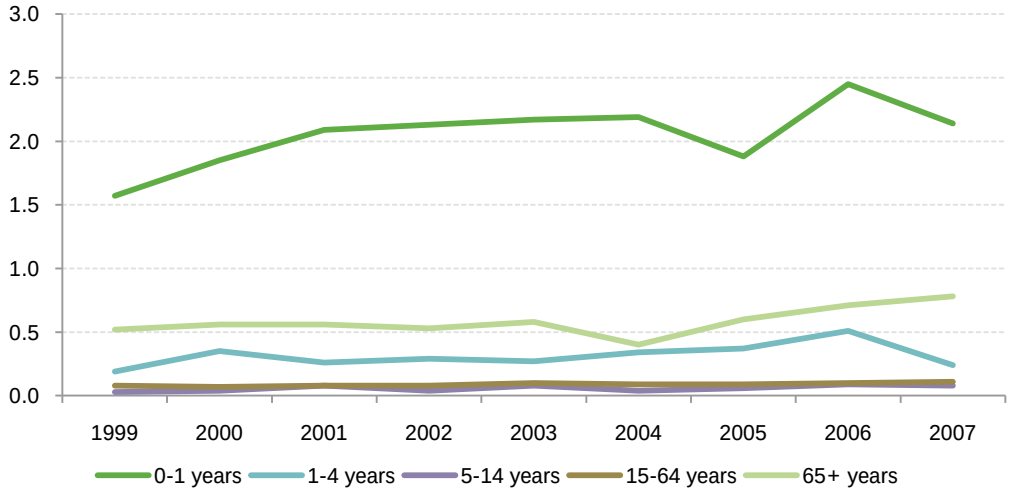
Age group	<1 year		1-4 years		5-14 years		15-64 years		>65 years		Total	
Country	n	NR (100 000)	n	NR (100 000)	n	NR (100 000)	n	NR (100 000)	n	NR (100 000)	n	NR (100 000)
Czech Republic	0	0.00	1	0.26	0	0.00	1	0.01	1	0.07	3	0.03
Denmark	0	0.00	1	0.39	0	0.00	3	0.08	3	0.36	7	0.13
Finland	0	0.00	0	0.00	0	0.00	2	0.06	1	0.12	3	0.06
Germany	0	0.00	0	0.00	0	0.00	1	0.00	3	0.02	4	0.00
Greece	0	0.00	0	0.00	1	0.09	0	0.00	1	0.05	2	0.02
Ireland	2	3.1	3	0.97	0	0.00	5	0.17	9	4.05	19	0.43
Italy	0	0.00	0	0.00	0	0.00	1	0.00	4	0.03	5	0.01
Portugal	0	0.00	1	0.23	0	0.00	0	0.00	0	0.00	1	0.01
Sweden	1	0.94	0	0.00	0	0.00	10	0.17	14	0.89	25	0.27
United Kingdom	4	0.54	3	0.11	1	0.01	14	0.03	20	0.21	42	0.07
Norway	0	0.00	0	0.00	1	0.16	0	0.00	2	0.29	3	0.06
Total	**5**	**0.19**	**7**	**0.07**	**3**	**0.01**	**33**	**0.02**	**51**	**0.11**	**99**	**0.04**

Inclusion criteria: Countries reporting ≥1case(s) of non-type b in 2007. Included strains: a, c, d, e, f, and non-b. Population source: Eurostat 2007

3.3.5.3 Non-capsulated strains

Figure 12 shows the notification rates of non-capsulated (non-typeable) strains across age groups from 1999–2007, for countries with consistent reporting during the time period. In these countries combined, the highest rates continued to occur in the youngest age group (<1 year of age), although a decline was observed in 2007. A decline from the previous year was also observed in the 1–4 year-old age group of. On the other hand the age group with the second highest notification rates (the >65 years age group) showed a steady but slight increasing trend, the highest rates were reported from Norway (5.69 per 100 000), as shown in Table 11.

Figure 12: Notification rate (per 100 000 population) of invasive *H. influenzae* non-capsulated disease in different age groups, all countries combined, 1999–2007 (n=3172)



Contributing countries: Finland, Ireland, Italy, Norway, Portugal, United Kingdom. Population source: Eurostat 1999-2007

When combining all the countries that reported ≥1 case(s) of non-capsulated strains in 2007, as illustrated in Table 11, the notification rate in infants below 1 year of age was 1.76 per 100 000 population (n=46), the >65 years 0.60 (n=282), while the overall rate was 0.20 (n=527).

Norway reported the highest rate overall rate of 1.35 (n=63), with the highest notification rates occurring among infants <1 year (6.81, n=4) and the elderly >65 years (5.69, n=63). Germany (0.01), Czech Republic (0.03), and Italy (0.03) reported the lowest rates per 100 000 population.

Table 11: Total number of cases and notification rate (per 100 000 population) of invasive *H. influenzae* non-capsulated disease by age group and reporting country, 2007

Age group	<1 year		1-4 years		5-14 years		15-64 years		>65 years		Total	
Country	n	NR (100 000)	n	NR (100 000)	n	NR (100 000)	n	NR (100 000)	n	NR (100 000)	n	NR (100 000)
Austria	0	0.00	0	0.00	0	0.00	3	0.05	1	0.07	4	0.05
Czech Republic	0	0.00	1	0.26	0	0.00	2	0.03	0	0	3	0.03
Denmark	0	0.00	0	0.00	0	0.00	1	0.03	3	0.36	4	0.07
Finland	0	0.00	0	0.00	1	0.16	21	0.60	22	2.53	44	0.83
Germany	2	0.30	1	0.04	2	0.03	2	0.00	2	0.01	9	0.01
Ireland	2	3.11	2	0.81	0	0.00	4	0.13	7	1.49	15	0.35
Italy	1	0.18	1	0.05	0	0.00	5	0.01	10	0.08	17	0.03
Portugal	2	1.90	0	0.00	2	0.18	3	0.04	3	0.16	10	0.09
Slovenia	1	5.23	0	0.00	3	1.58	3	0.21	6	1.88	13	0.65
Sweden	1	0.94	0	0.00	2	0.19	8	0.13	31	1.96	42	0.46
United Kingdom	33	4.42	14	0.5	8	0.11	90	0.22	158	1.63	303	0.50
Norway	4	6.81	1	0.43	4	0.65	15	0.49	39	5.69	63	1.35
Total	**46**	**1.76**	**20**	**0.19**	**22**	**0.08**	**157**	**0.09**	**282**	**0.60**	**527**	**0.20**

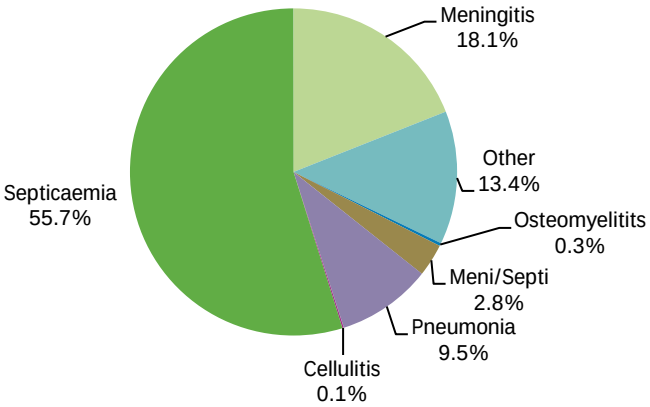
Inclusion criteria: Countries reporting ≥1case(s) of non-type b in 2007
A total of 53.5% of the reported non-capsulated strains were attributed to the oldest age group of >65 years. Population source: Eurostat 2007

3.3.6 Clinical presentation

Information on clinical presentation was available in 32.3% of the total number of reported cases (including the aggregated reported cases).

The distribution of clinical presentation of invasive *H. influenzae* disease is shown in Figure 13 with data from a total of 16 countries collecting all clinical presentation for all ages and serotypes combined. Septicaemia was the most common presentation, accounting for 55.7% of the cases. Of all cases reported with septicaemia and a known serotype, 73.3% (n=253) were reported with a non-capsulated strain and 54.5% (n=138) were in the age group of ≥65 years combined with non-caps. Meningitis was reported in 18.1% of the cases and of these, 44.7% (n=34) were non-capsulated and 38.2% (n=29) were serotype b.

Figure 13: Reported distribution of clinical presentation of invasive *H. influenzae* disease among reporting countries in 2007 (n=673, excluding the 482 cases reported as unknown, 41.7% of the total number of cases)

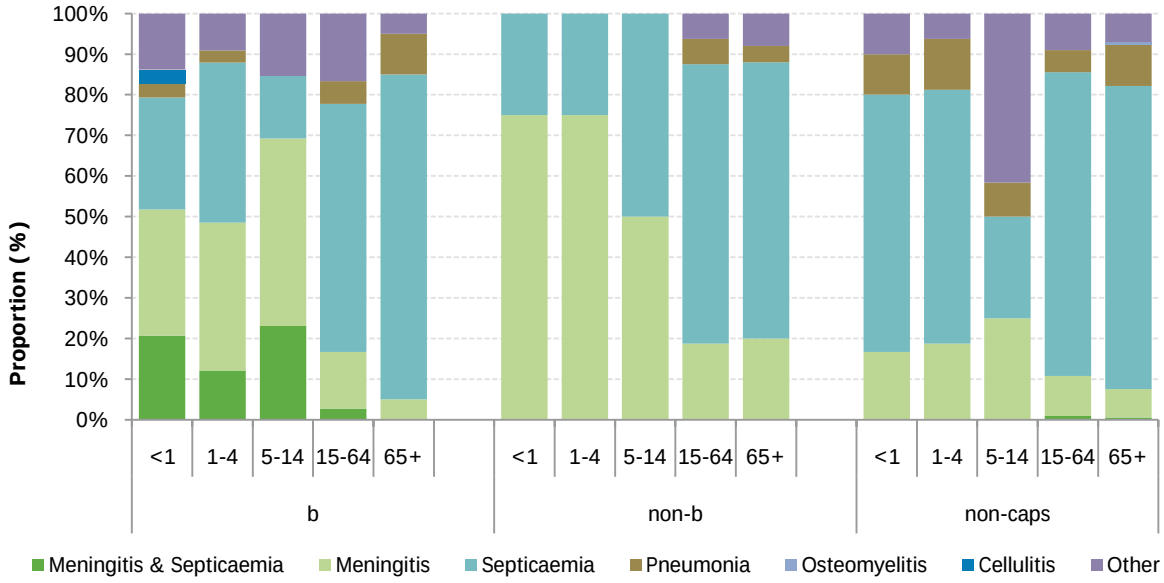


Contributing countries: Austria, Czech Republic, Denmark, Estonia, Finland, Germany, Iceland, Ireland, Italy, Norway, Poland, Portugal, Slovakia, Slovenia, Spain, United Kingdom

Certain clinical presentations tend to be associated with different kinds of serotypes. Moreover, since the serotype distribution is strongly associated with age, it is important to take this into account when further analysing the clinical presentation of invasive *H. influenzae* disease by serotype.

In Figure 14, the relationship between clinical presentation, serotype and age is illustrated.

Figure 14: Clinical presentation of invasive *H. influenzae* disease by serotype and age group, 2007 (n=526)



Contributing countries: Austria, Czech Republic, Estonia, Finland, Germany, Greece, Iceland, Ireland, Italy, Norway, Poland, Portugal, Slovakia, Slovenia, United Kingdom

3.3.6.1 Serotype b (Hib) and clinical presentation

Large variations were observed across age groups and clinical presentations among the cases reported with serotype b strains. In this group, the broadest spectrum of clinical presentations was observed, especially in infants younger than one year of age. Meningitis alone occurred mainly in the age group of 5–14 years.

Among infants younger than one year, meningitis and septicaemia accounted for 30.8% each, whereas 15.4% were diagnosed with both meningitis and septicaemia. Fifteen per cent of the cases were reported as clinical presentation 'other'. The only reported case of cellulitis occurred in this youngest age group.

Septicaemia accounted for 64.7% of all reported serotype b cases in the age group >65 years, while there were no cases reported with meningitis in this group.

3.3.6.2 Serotype Non-type b and clinical presentation

Overall numbers of non-type b infections were small (49 in total), particularly in the children younger than 15 years old (four in <1, four in 0–4, and one in the 5–14 age group). Meningitis was the most common presentation in the two age groups younger than five years, while septicaemia was the most common presentation in the age groups older than five years. Meningitis also occurred in the older age groups and accounted for 18.8% and 16.7% in the age groups of 15–64 and >65, respectively. There were no cases reported with both meningitis and septicaemia combined among the non-type b strains. Other clinical presentations accounted in total for 6.1%.

3.3.6.3 Serotype non-capsulated and clinical presentation

Large variations were observed across age groups and clinical presentation among the cases reported with non-capsulated strains. Septicaemia was the most dominant clinical presentation reported across nearly all age groups, in total 71.7%. These results do not show any large divergence from the previous years' results.

3.3.7 Case fatality ratio

In 2007, the crude overall case fatality ratio (CFR) of invasive *H. Influenzae* among the European countries was 9.65% (assuming all cases reported with unknown outcome were alive). This may be compared with an average annual CFR from 1999–2007 of 7.58%.

The CFR was varied markedly across age groups in 2007. The highest CFR was observed in the youngest age group (10.28% younger than one year) and in the oldest (14.72% older than 65 years). The CFR was also strongly associated with serotype ($p < 0.01$ in 2007).

Table 12 shows the relationship between CFR and serotype, stratified by age group, where the distribution of case fatality ratio by serotypes differs by age groups. The highest overall CFRs were observed in non-capsulated strains (15.7%, n=82).

- Among serotype b, the highest CFR was observed in the age group 5–14 years (17.6%, n=3) and older than 65 years (16.7%, n=5).
- Among non-type b, there were no (zero) deaths reported in the age groups younger than 15 years.
- Among the non-capsulated strains, CFR was high in the older than 65 years age group (21.4%, n 60), followed by <1 year (17.4%, n 8) and 1—4 years (15.0%, n 3) age groups.

Table 12: Case fatality ratio of invasive H. influenzae disease, by age group and serotype, all countries combined, 2007

Serotype	b		Non-type b		Non-caps		Unknown		Total (age)	
Age group	**n deaths**	**CFR**	**n deaths**	**CFR**	**n deaths**	**CFR**	**n deaths**	**CFR**	**n deaths**	**CFR**
<1 years	2	5.9%	0	0.0%	8	17.4%	1	4.5%	11	10.3%
1–4 years	2	4.3%	0	0.0%	3	15.0%	1	3.7%	6	6.0%
5–14 years	3	17.6%	0	0.0%	0	0.0%	0	0.0%	3	5.6%
15–64 years	4	7.0%	2	6.1%	11	7.1%	2	1.0%	19	4.4%
>65 years	5	16.7%	5	9.8%	60	21.4%	12	6.2%	82	14.7%
Total (serotype)	16	8.7%	7	7.1%	82	15.7%	16	3.6%	121	9.6%

Contributing countries: Czech Republic, Denmark, Estonia, Finland, Germany, Greece, Hungary, Ireland, Italy, Luxembourg, Malta, Norway, Poland, Portugal, Slovakia, Slovenia, Sweden, United Kingdom (n cases = 1254)

As expected, the CFR varied widely across clinical presentations. The overall highest CFR among clinical presentations was observed in septicaemia at 17.1% (n=64) followed by pneumonia at 9.7% (n=6).

As discussed previously, the CFR also varied with serotype. Table 13 shows the CFR by serotype, stratified by clinical presentation, where the distribution of case fatality ratio by serotypes differs widely by clinical presentation.

As expected, 'septicaemia' caused the highest CFR in nearly all serotypes (17.1%, n=64), and with the highest rate seen among the non-capsulated cases (20.6%, n=52). 'Meningitis' caused the second highest CFR (9.1%, n=3)

among serotype b, while 'unknown' clinical presentation had the highest proportion of reported deaths among non-type b strains. Notable, and perhaps warranting further investigation, is that both 'other' and 'unknown' reported clinical presentations had a total CFR of 6.7%.

Table 13: Case fatality ratio of invasive *H. influenzae* by serotype and clinical presentation, all countries combined, 2007

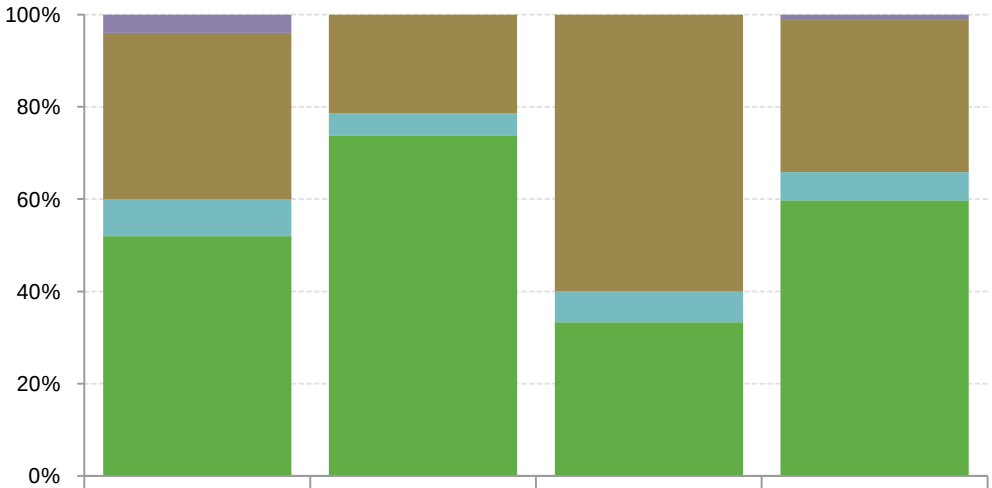
Serotype	b		Non-type b		Non-caps		Unknown		Total (CP)	
Clinical presentation	**n deaths**	**CFR**	**n deaths**	**CFR**	**n deaths**	**CFR**	**n deaths**	**CFR**	**n deaths**	**CFR**
Cellulitis	0	0.0%	0	0.0%	0	0.0%	0	0.0%	**0**	**0.0%**
Meni/Septi	1	7.7%	0	0.0%	0	0.0%	0	0.0%	**1**	**4.8%**
Meningitis	3	9.1%	0	0.0%	2	6.3%	0	0.0%	**5**	**4.2%**
Osteomyelitits	0	0.0%	0	0.0%	0	0.0%	0	0.0%	**0**	**0.0%**
Other	1	6.3%	0	0.0%	3	9.4%	2	5.3%	**6**	**6.7%**
Pneumonia	0	0.0%	0	0.0%	4	12.9%	2	8.7%	**6**	**9.7%**
Septicaemia	7	11.5%	2	6.5%	52	20.6%	3	10%	**64**	**17.1%**
Unknown	4	7.4%	5	10.4%	21	12.1%	9	2.9%	**39**	**6.7%**
Total (serotype)	**16**	**8.7%**	**7**	**7.1%**	**82**	**15.7%**	**16**	**3.6%**	**121**	**9.6%**

Contributing countries: Czech Republic, Denmark, Estonia, Finland, Germany, Greece, Hungary, Ireland, Italy, Luxembourg, Malta, Norway, Poland, Portugal, Slovakia, Slovenia, Sweden, United Kingdom (n cases = 1 254)

3.3.8 Vaccination status

As described in the methods section, there are not yet enough variables describing the vaccination status included in the TESSy metadataset for invasive *H. influenzae* disease for enabling the determination of true vaccination failures. Therefore, only the numbers and proportions of reported vaccination status are described here. Figure 15 displays the distribution of the reported vaccination status by age groups among children younger than 15 years in cases with serotype b. As illustrated, the overall highest proportion (59.8%) of notified cases occurred among those reported as fully vaccinated, with the highest proportion observed in those aged 1–4 years old (73.8%). The largest proportion of non-vaccinated cases occurred in those aged 5–14 old (60%).

Figure 15: Distribution of vaccination status and number of cases reported with invasive Hib disease of among children <15 year of age, all countries combined, 2007 (n=82)



	<1 year	1-4 years	5-14 years	Total
Unknown	1	0	0	1
Not vaccinated	9	9	9	27
Partly vaccinated	2	2	1	5
Fully Vaccinated	13	31	5	49

Contributing countries: Czech Republic, Estonia, Finland, Ireland, Poland, Portugal, Slovakia, Sweden, United Kingdom
Fully vaccinated = according to age and the recommended schedule in the reporting country.
Partly vaccinated, = according to age and the recommended schedule in the reporting country.
Not vaccinated = not vaccinated at all
Unknown = Vaccination status unknown

In Table 14, the total numbers of reported Hib cases by country and vaccination status are listed. Noteworthy in the age group of 1–4 year-olds are the 29 out of 33 cases (87.9%) that were reported as fully vaccinated from the UK. As described earlier, the UK represents 71.7% of all cases reported in this age group.

Table 14: Total numbers of invasive Hib disease among cases <15 year of age with reported vaccination status, by country, 2007

Age group	Country	Not vaccinated		Partly vaccinated		Fully vaccinated		Unknown		Total
		n	%	n	%	n	%	n	%	n
<1 year	Estonia	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1
	Finland	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1
	Ireland	1	50.0%	0	0.0%	1	50.0%	0	0.0%	2
	Poland	3	60.0%	1	20.0%	1	20.0%	0	0.0%	5
	Portugal	0	0.0%	0	0.0%	1	100.0%	0	0.0%	1
	Slovakia	1	33.3%	1	33.3%	1	33.3%	0	0.0%	3
	Sweden	0	0.0%	0	0.0%	0	0.0%	1	100.0%	1
	United Kingdom	2	18.2%	0	0.0%	9	81.8%	0	0.0%	11
1-4 years	Czech Republic	0	0.0%	0	0.0%	2	100.0%	0	0.0%	2
	Ireland	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1
	Poland	6	100.0%	0	0.0%	0	0.0%	0	0.0%	6
	United Kingdom	2	6.1%	2	6.1%	29	87.9%	0	0.0%	33
5-14 years	Czech Republic	2	100.0%	0	0.0%	0	0.0%	0	0.0%	2
	Estonia	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1
	Finland	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1
	Ireland	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0
	Poland	5	71.4%	1	14.3%	1	14.3%	0	0.0%	7
	Sweden	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0
	United Kingdom	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0

3.3.9 Vaccination schedules

In 1992, the conjugate Hib vaccine was introduced into the national immunisation program in several EU/EEA countries. By 2007 nearly all MS had included the vaccine into their programs. However, the actual vaccine in use varies widely across Europe in terms of combined products used, vaccination schedule and population covered, as shown in Table 15.

Table 15: Year of introduction of conjugate Hib vaccination and childhood immunisation schedules in 2007

Country	Year of Hib introduction	Vaccine given	Combined with	Immunisation schedule	Source date
Austria	1994	Hib-PRP-T	DTaP, IPV, HBV	2, 4, 6 months, AND 2nd year of life	14-Jan-08
Belgium	1993	Hib-PRP-T	DTaP, IPV, HBV	2, 3, 4, AND 15 months	06-Aug-08
Bulgaria	Not introduced	-	-	-	23-Jan-07
Cyprus	2001	Hib-PRP-T	not combined	2-3, 4-5, 6-8, AND 12-18 months	08-Dec-06
Czech Republic	2001	Hib-PRP-T	DTaP, IPV, HBV	13 weeks, 17 weeks-1 year, 21 weeks-1 year, 11 months 1 week-18 months	18-Sep-07
Denmark	1993	Hib-PRP-T	DTaP, IPV	3 , 5 AND 12 months	01-Oct-08
Estonia	2005	Hib-PRP-T	DTwP	3, 4 1/2, 6 months AND 2 years	01-Jan-08
Finland	1986	Hib-PRP-T		3, 5 AND 12 months	01-Sep-08
France	1992	Hib-PRP-T	DTaP, IPV, HBV	2, 3, 4, AND 16-18 months	15-Nov-07
Germany	1990	Hib-PRP-T	DTaP, IPV, HBV	2, 3, 4 months, AND 11-14 months	12-Nov-07
Greece	1999	Hib-PRP-T	(DTaP, IPV/OPV, HBV also given)	2, 4, 6, AND 12-15 months	10-Apr-07
Hungary	1999	Hib-PRP-T	DTaP, IPV	2, 3, 4, AND 18 months	15-Jan-07
Iceland	1989	Hib-PRP-T	DTaP, IPV	3, 5, AND 12 months	19-Oct-07
Ireland	1992	Hib-PRP-T	DTaP, IPV	2, 4, 6, AND 13 months	10-Jan-09

Country	Year of Hib introduction	Vaccine given	Combined with	Immunisation schedule	Source date
Italy	1995 (1999 included in routine schedule)	Hib PRP-T	DTaP, IPV, HBV	2-3, 4-5, AND 10-12 months	21-Oct-08
Latvia	1994	Hib-PRP-T	Dose 1-2: DTaP, IPV; Dose 3: DTaP, IPV, HBV	3, 4 1/2, AND 6 months	23-May-08
Lichtenstein	?	?	?	?	
Lithuania	2004	Hib-PRP-T	Dose 1-2: DTaP, IPV; Dose 3: DTaP, IPV, HBV	2, 4, 6, AND 18 months	03-Jan-08
Luxembourg	?	?	1st, 2nd, AND 4th: DTaP, IPV, HBV 3rd: DTaP, IPV	2, 3, 4, AND 12 months	01-Apr-08
Malta	1996	Hib-PRP-T	DTwP(OPV also given)	Public: 6-8 weeks, 3 AND 4 months Private: 2, 3, 4, AND 12-18 months	26-Nov-07
Netherlands	1993	Hib-PRP-T	DTwP, IPV	2, 3, 4, AND 11 months	16-Dec-06
Norway	1992		DTaP, IPV	3, 5, 11-12 months	27-Sep-06
Poland	2005	Hib		2, 3-4, 5-6, AND 16-18 months	22-Apr-07
Portugal	2000	Hib		2, 4, 6, AND 18 months	13-Sep-06
Romania	Not introduced	-	-	-	06-May-08
Slovak Republic	2000	Hib	DTaP-IPV-HBV	3, 5, AND 10 months	15-Jul-07
Slovenia	2000	Hib-PRP-T	DTaP, IPV	3, 4-5, 6, AND 12-24 months	04-Oct-07
Spain	1998	Hib-PRP-T	DTaP, IPV, IPV	2, 4, 6, AND 15-18 months	01-Jun-08
Sweden	1993	Hib-PRP-T	DTaP, IPV	3, 5, AND 12 months	18-Jun-08
United Kingdom	1992	Hib-PRP-T	Dose 1-3: DTaP, IPV Dose 4: MenC	2, 3, 4 AND 12 months	10-Jan-07

Source: EUVAC.NET (January 22nd 2009) http://www.euvac.net/graphics/euvac/vaccination/vaccination.html
Cyprus, Estonia, Sweden: comments received from the country

4 Results: Invasive meningococcal disease

4.1 Disease description

Meningococcal disease is a broad term used to describe the different clinical syndromes caused by *Neisseria meningitidis* infection. Meningococcal disease is a global problem. In Europe, cases occur sporadically, but occasionally outbreaks happen and can be an important cause of illness and death.

There is a clear seasonal variation and the notification rate of the disease is higher during the winter and early spring.

Infants are at the highest risk of acquiring the disease, followed by adolescents. In addition to age, another individual risk factor includes underlying immune deficiencies; the deficiency of complement components are known to determine infection. Crowding and concurrent upper respiratory tract infections might also contribute to acquiring the disease.

Meningococcal disease usually manifests itself as meningitis, with or without septicaemia, though a considerable number of cases manifest septicaemia without any other symptoms; these are at a higher risk of death. A significant proportion of meningococcal patients who survive can have permanent sequelae, including neurologic disability, limb loss and hearing loss.

Treatment of meningococcal disease requires prompt administration of antibiotics including penicillins, third generation cephalosporins or chloramphenicol. Rifampicin, ciprofloxacin and ceftriaxone have been demonstrated to eradicate *N. meningitidis* colonisation and these agents are recommended for chemoprophylaxis of close contacts in order to reduce the number of subsequent cases.

4.1.1 Laboratory methods used for strain identification

Neisseria meningitidis is a Gram-negative, aerobic diplococcus. *Neisseria* are divided into serogroups according to the immunological reactivity of their capsular polysaccharide.

Worldwide, serogroups A, B and C are responsible for at least 90% of the cases, although the proportion of disease caused by serogroups Y and W135 is increasing in some areas. In Europe, North and South America, serogroups B and C cause the majority of the reported cases, while serogroup A causes the majority of disease in Africa and Asia.

The organism can be defined by variations in the biochemistry of the capsule, determining its serogroup and its outer membrane protein (OMP). The porB gene (2 or 3 OPM) determines the serotype and porA gene (1 OMP) determines the serosubtype. Both proteins have a number of variable regions which are surfaced exposed and this contributes to antigenic variability between strains. In the case of porA proteins, the variants for two of the variable regions (VR1 and VR2) are frequently quoted, with a third region (VR3) used less often.

Of the 12 different serogroups identified so far, the major ones associated with disease are A, B, C, W135, and Y, and to a much lesser extent X and Z/29E.

However, some disease strains have been isolated for which the serogroup cannot be identified (designated as NGA, or non-groupable), and are thus assumed to have no capsule.

Serogroups A, B, C, Y, W135 and X are all capable of causing outbreaks, but serogroup A is mainly responsible for large epidemics. However, the outbreaks of meningococcal disease caused by serogroup A have been restricted to Africa particularly in the so called 'African meningitis belt'. In the early 2000s in several countries, epidemics of serogroup W135 occurred among pilgrims and their close contacts returned from the Hajj in Saudi Arabia.

Only a few serotypes and serosubtypes are associated with invasive meningococcal disease. Identification of serotypes and serosubtypes is important as this information determines the components of the vaccine during the vaccine development process.

The laboratory methods used in the routine strain characterisation in the majority of MS include phenotyping (serogroup, serotype and serosubtype), genotyping (*porA*/fetA) and multilocus sequence typing (MLST), techniques from culture specimens and, when available, detection and strain characterisation from non-culture specimens as well as antibiotic sensitivity testing for the pathogen.

The methods used range from basic microbiology for meningococcal speciation to immunoassays for phenotyping, to nucleic acid amplification (including real-time PCR) and nucleic acid sequencing for genotyping with attendant bioinformatic software.

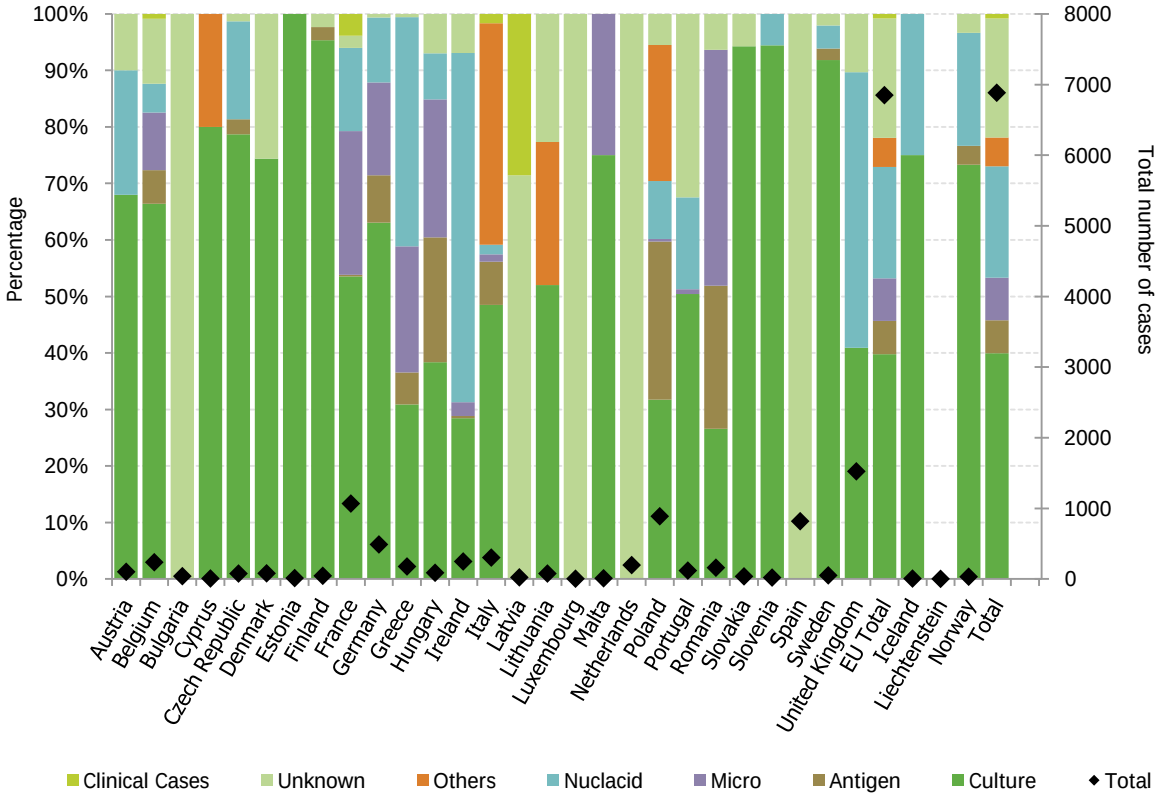
Molecular subtyping (multilocus enzyme electrophoresis, pulsed–field gel electrophoresis or pulsed field electrophoresis of enzyme-restricted DNA fragments) may also allow recognition of outbreak strains and permit a better demarcation of outbreaks from endemic diseases.

Figure 16 shows the distribution of test methods used on the reported cases by country. There is a high variability of the methods used for confirming a case.

Identifying the disease by culture represents the most common method for the majority of the countries. In Estonia, Finland, Slovakia, Slovenia and Sweden, cultures represent the main method for case confirmation. In Ireland, the UK and Greece, a sizable proportion of cases are identified by PCR. There were no cases confirmed by clinical criteria only.

The methods used for case confirmation were reported as unknown by Austria, Bulgaria, Luxembourg, the Netherlands, and Spain.

Figure 16: Percentage distribution (%) of all reported test methods used for confirming an invasive meningococcal disease case by country, 2007 (n=5583)



**For Austria, only the first test method was considered for each case. For all other countries, all test methods for each case were considered.*

4.2 Data quality

Table 16 shows the number of countries that have reported 100% of their cases as unknown by each main variable. As stated earlier, ECDC does not yet have sufficient information about the data source to clearly distinguish if any of these variables are currently available in the countries.

Table 16: Number of countries with variable s reported as 100% unknown

Variable name	n of countries	Variable name	n of countries
Outcome	2	Serogroup	2
ClinicalCriteria	5	Serotype	12
LaboratoryResult	3	Specimen1	4
EpiLinked	11	TestMeth1	6
Imported	8	SpecLinkLab1	15
ProbableCountryOfInfection	9	Specimen2	11
ClinicalPresentation	5	TestMeth2	14

Table 17 shows the proportion of reported cases in 2007 with known and unknown information per variable from all countries that reported case based data. Aggregated data are not included in the table. The completeness of reporting varied substantially between variables.

Information on basic laboratory characterisation was available in the majority of cases but information on advanced laboratory methods for the diagnosis of *N. meningitidis* was generally unknown. Looking into this in more detail, the serogroup was available for 79% of cases and the reporting of this variable has improved over the years. However, in 63% of cases information on serotype was missing; information on serosubtype identification using genotyping techniques (Por A1, Por A2 and Por A3) was reported in about 10% of cases.

The information on minimum inhibitory concentration (MIC) for different kind of antibiotics was reported for a mean of 66% of the total number of cases, but sensitive intermediate resistance (SIR) was reported as known in only 12% of cases, on average.

In the TESSy metadataset for 2007 data, there are two variables for test methods (TestMeth1 and TestMeth2), each linked to the same order of specimen (Specimen1 and Specimen2). However, for each notified case the test method can be repeated if several methods are performed on the first specimen (Specimen1). Information on more than one test method and on more than one specimen collected was reported as unknown in 87% and 86% of cases, respectively.

Vaccination status was reported as known in 23% of cases. The epidemiological link of the cases was reported as known in 26% and the information on imported cases was known in 33% of cases. The 'age', 'gender' and 'outcome' variables have been reported as known in more than 90% of cases and clinical presentation in more than half of cases.

Table 17: Distribution of known, unknown, not applicable and blank responses per variable among all case based reporting invasive meningococcal disease, 2007

Variable	Known (n)	UNK (n)	NA (n)	Blank (n)	Total (n)	Known (%)	UNK (%)	NA (%)	Blank (%)
Age[C]	5384	0	0	161	5545	97%	0%	0%	3%
AgeMonth	1504	0	0	4041	5545	27%	0%	0%	73%
Classification[C] ¤	5545	0	0	0	5545	100%	0%	0%	0%
ClinicalCriteria [C]¤	3950	1595	0	0	5545	71%	29%	0%	0%
ClinicalPresentation	3184	2361	0	0	5545	57%	43%	0%	0%
DateOfDiagnosis	3400	0	0	2145	5545	61%	0%	0%	39%
DateOfNotification	3758	0	0	1787	5545	68%	0%	0%	32%
DateOfOnset	4240	0	0	1305	5545	76%	0%	0%	24%
Plinked ¤	1423	1960	2162	0	5545	26%	35%	39%	0%
Gender[C]	5519	26	0	0	5545	100%	0%	0%	0%
Imported [E]	1817	3728	0	0	5545	33%	67%	0%	0%
LaboratoryResult [C]¤	4330	1076	139	0	5545	78%	19%	3%	0%
MIC_CHL	1269	4276	0	0	5545	23%	77%	0%	0%
MIC_CIP	2733	2812	0	0	5545	49%	51%	0%	0%
MIC_CTX	1363	4182	0	0	5545	25%	75%	0%	0%
MIC_PEN	2736	2809	0	0	5545	49%	51%	0%	0%
MIC_RIF	2739	2806	0	0	5545	49%	51%	0%	0%
MIC_SSS	2497	3048	0	0	5545	45%	55%	0%	0%
Outcome	5046	499	0	0	5545	91%	9%	0%	0%

Variable	Known (n)	UNK (n)	NA (n)	Blank (n)	Total (n)	Known (%)	UNK (%)	NA (%)	Blank (%)
Pathogen	5545	0	0	0	5545	100%	0%	0%	0%
probableCountryOfInfection1 [E, I]	68	2745	22	2710	5545	1%	50%	0%	49%
probableCountryOfInfection2 [E, I]	2835	0	0	2710	5545	51%	0%	0%	49%
resultMLSTMENI2	230	5315	0	0	5545	4%	96%	0%	0%
ResultPorA1	550	4995	0	0	5545	10%	90%	0%	0%
ResultPorA2	550	4995	0	0	5545	10%	90%	0%	0%
ResultPorA3	92	5453	0	0	5545	2%	98%	0%	0%
ResultSeqType	34	0	0	5511	5545	1%	0%	0%	99%
ResultVr1	1739	3806	0	0	5545	31%	69%	0%	0%
ResultVr2	1760	3785	0	0	5545	32%	68%	0%	0%
ResultVr3	0	0	0	0	5545	0%	0%	0%	0%
Serogroup [E]	4394	1151	0	0	5545	79%	21%	0%	0%
Serotype [E]	2074	3471	0	0	5545	37%	63%	0%	0%
SIR_CHL	442	5103	0	0	5545	8%	92%	0%	0%
SIR_CIP	697	4848	0	0	5545	13%	87%	0%	0%
SIR_CTX	566	4979	0	0	5545	10%	90%	0%	0%
SIR_PEN	713	4832	0	0	5545	13%	87%	0%	0%
SIR_RIF	643	4902	0	0	5545	12%	88%	0%	0%
SIR_SSS	902	4643	0	0	5545	16%	84%	0%	0%
Specimen1 [E]	4057	1488	0	0	5545	73%	27%	0%	0%
Specimen2 [E]	714	4831	0	0	5545	13%	87%	0%	0%
SpecLinkLab1 [E]	1767	3778	0	0	5545	32%	68%	0%	0%
testMethod1MENI1 [E]	4022	1523	0	0	5545	73%	27%	0%	0%
testMethod1MENI2 [E]	458	451	0	4636	5545	8%	8%	0%	84%
testMethod1MENI3 [E]	268	287	0	4990	5545	5%	5%	0%	90%
testMethod1MENI4 [E]	428	481	0	4636	5545	8%	9%	0%	84%
testMethod2MENI1 [E]	789	4756	0	0	5545	14%	86%	0%	0%
testMethod2MENI2 [E]	26	262	0	5257	5545	0%	5%	0%	95%
VaccStatus	1284	4261	0	0	5545	23%	77%	0%	0%

C = Common set of variables

E= enhanced set of variables

[¤] = These variables are linked to the case definition and the reported value is expected to correspond to the applied case definition (se previous section about case definitions)

I = probable country of infection is only reported if the case is reported as imported.

All cases reported as aggregated with only a common set of variables are excluded from this analysis (Bulgaria)

4.3 Epidemiological analysis

4.3.1 Overall notification rates

In 2007, 5583 cases of invasive meningococcal disease were reported by 29 countries with an overall notification rate of 1.1 per 100 000 population. This was a substantial decline compared to the rate in 1999 (1.9 per 100 000). Almost all cases were laboratory confirmed (93%). Only 347 (6%) were classified as probable and 54 (1%) possible according the EU case definition. There was wide variability in the overall notification rates across Europe, as shown in Figure 17 and Table 18.

Meningococcal disease appears to be rare in the majority of MS, although Ireland and the UK reported a relatively higher notification rate than the rest, at 3.76 and 2.50 per 100 000 respectively. The lowest notification rate was reported by Italy (0.3 per 100 000). These figures may reflect real differences in incidences, but might also reflect the difference in the sensitivity of the surveillance systems and in the case definition used; caution is advised when comparing these notification rates across countries.

Figure 17: Overall notification rate (per 100 000 population) of invasive meningococcal disease by case classification and country, 2007(n=5583)

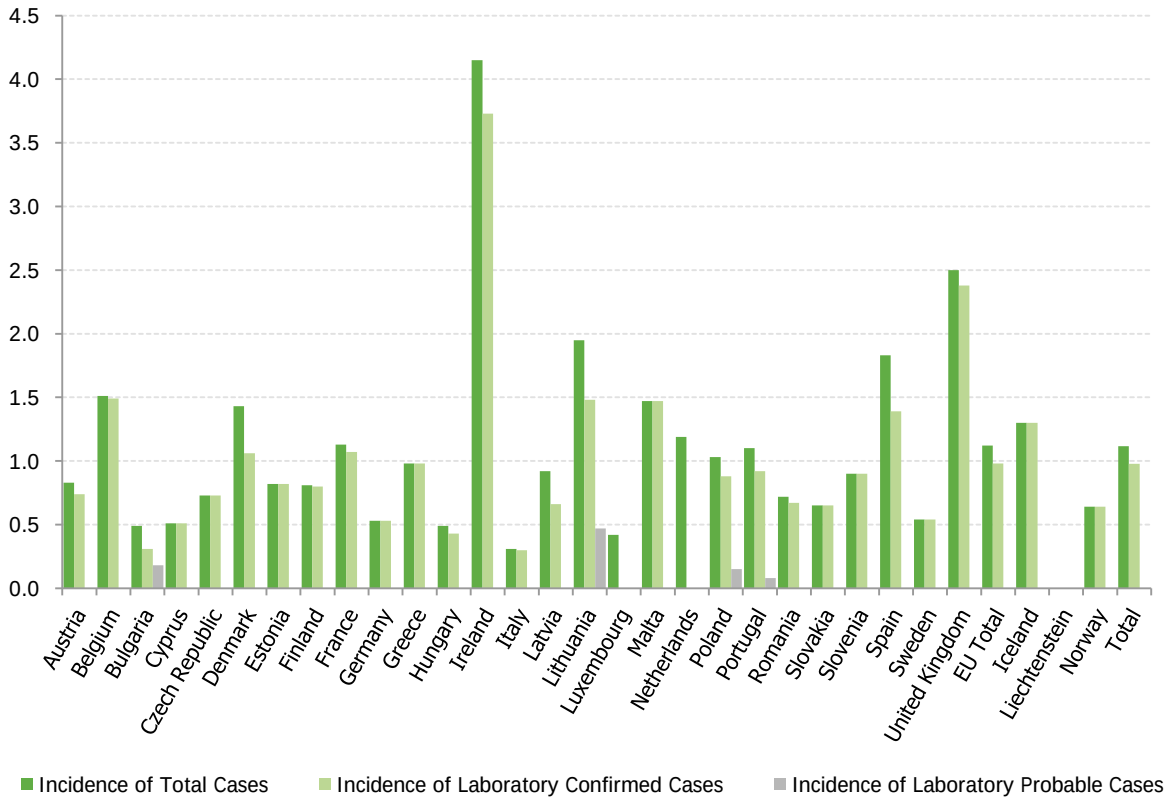


Table 18 shows the notification rates by country between 1999 and 2007. For the majority of countries consistently reporting data during this period, the notification rate peaked between 1999 and 2003. Belgium, Denmark, Ireland, Netherlands, Spain and the UK reported relatively higher notification rates. On average, however, the table show a steady decline over that period in the EU.

It is known that meningococcal disease incidence varies naturally with time but vaccination policies, the introduction of routine conjugate vaccinations and implementation of catch-up campaigns have to be taken into account when interpreting this table.

Table 18: Notification rates per 100 000 and total number cases of invasive meningococcal disease (in brackets) by country, 1999-2007**

Country	1999	2000	2001	2002	2003	2004	2005	2006	2007*
Austria	1.20 (97)	1.05 (85)	1.32 (107)	1.06 (86)	1.00 (82)	1.08 (88)	1.30 (106)	0.93 (76)	0.74 (69)
Belgium	2.90 (297)	2.60 (267)	3.69 (380)	2.54 (262)	2.20 (228)	1.51 (157)	1.63 (171)	1.32 (138)	1.49 (158)
Bulgaria	-	-	-	-	-	-	-	-	0.31 (24)
Cyprus	-	-	-	-	-	-	-	-	0.51 (4)
Czech Republic	1.00 (103)	0.72 (74)	1.06 (108)	1.20 (122)	0.98 (100)	1.03 (105)	0.95 (97)	0.77 (79)	0.73 (75)
Denmark	3.50 (186)	3.00 (160)	3.08 (165)	1.86 (100)	1.95 (105)	1.85 (100)	1.64 (89)	1.45 (79)	1.43 (78)
Estonia	0.44 (6)	0.80 (11)	1.61 (22)	0.73 (10)	0.74 (10)	0.81 (11)	0.96 (13)	0.82 (11)	0.82 (11)
Finland	1.11 (57)	0.93 (48)	0.98 (51)	0.94 (49)	0.81 (42)	0.86 (45)	0.77 (40)	0.86 (45)	0.81 (43)
France	0.74 (448)	0.81 (489)	0.92 (559)	1.11 (678)	1.31 (803)	1.13 (699)	1.19 (748)	1.13 (714)	1.07 (680)
Germany	0.49 (402)	0.55 (452)	0.95 (782)	0.89 (736)	0.94 (774)	0.73 (601)	0.76 (629)	0.67 (555)	0.53 (439)
Greece	1.94 (211)	2.39 (261)	2.14 (234)	2.12 (233)	1.19 (131)	0.65 (72)	0.88 (98)	1.02 (114)	0.95 (106)
Hungary	-	-	-	-	0.42 (43)	0.43 (43)	0.32 (32)	0.35 (35)	0.43 (43)
Ireland	14.33 (536)	13.59 (515)	8.58 (330)	6.49 (253)	5.96 (237)	4.92 (198)	4.91 (203)	4.97 (209)	3.76 (162)
Italy	0.48 (275)	0.44 (250)	0.36 (203)	0.39 (223)	0.48 (278)	0.55 (321)	0.56 (327)	0.30 (176)	0.30 (178)
Latvia	-	-	-	-	1.03 (24)	1.03 (24)	0.78 (18)	0.52 (12)	0.66 (15)
Lithuania	-	-	2.18 (76)	1.90 (66)	1.27 (44)	2.67 (92)	2.36 (81)	2.26 (77)	1.48 (50)
Luxembourg	4.15 (18)	0.23 (1)	0.23 (1)	0.23 (1)	0.45 (2)	0.00	0.22 (1)	-	0.42 (2)
Malta	5.88 (23)	7.92 (31)	5.32 (21)	3.52 (14)	4.25 (17)	3.33 (13)	2.47 (10)	8.90 (36)	1.47 (6)
Netherlands	3.65 (576)	3.42 (542)	4.51 (721)	3.82 (616)	2.19 (354)	1.75 (284)	1.51 (246)	1.09 (178)	1.19 (195)
Poland	0.17 (67)	0.11 (43)	0.10 (37)	0.09 (35)	0.15 (58)	0.31 (117)	0.52 (198)	0.43 (165)	0.88 (335)
Portugal	-	0.57 (59)	1.03 (106)	2.08 (216)	1.99 (208)	1.73 (182)	1.60 (169)	1.25 (132)	0.92 (98)
Romania	-	-	-	-	-	-	-	-	0.67 (145)
Slovakia	-	-	-	-	0.91 (49)	0.59 (32)	0.82 (44)	0.67 (36)	0.65 (35)
Slovenia	0.30 (6)	0.40 (8)	0.50 (10)	0.40 (8)	0.80 (16)	0.45 (9)	0.80 (16)	0.40 (8)	0.90 (18)
Spain	3.52 (1403)	3.74 (1499)	2.23 (904)	2.71 (1109)	2.45 (1019)	2.11 (892)	2.15 (923)	1.84 (800)	1.39 (620)
Sweden	0.37 (33)	0.46 (41)	0.64 (57)	0.53 (47)	0.63 (56)	0.65 (59)	0.63 (57)	0.57 (52)	0.54(49)
United Kingdom	5.39 (3150)	5.23 (3067)	4.51 (2655)	3.38 (2004)	3.10 (1848)	2.59 (1549)	2.78 (1672)	2.33 (1401)	2.50 (1522)
Iceland	7.58 (21)	6.40 (18)	6.67 (19)	5.22 (15)	2.77 (8)	3.42 (10)	1.69 (5)	1.31 (4)	1.30 (4)
Liechtenstein	-	-	-	-	-	-	-	-	-
Norway	1.80 (80)	1.94 (87)	1.71 (77)	1.13 (51)	1.12 (51)	0.74 (34)	0.85 (39)	0.75 (35)	0.64 (30)

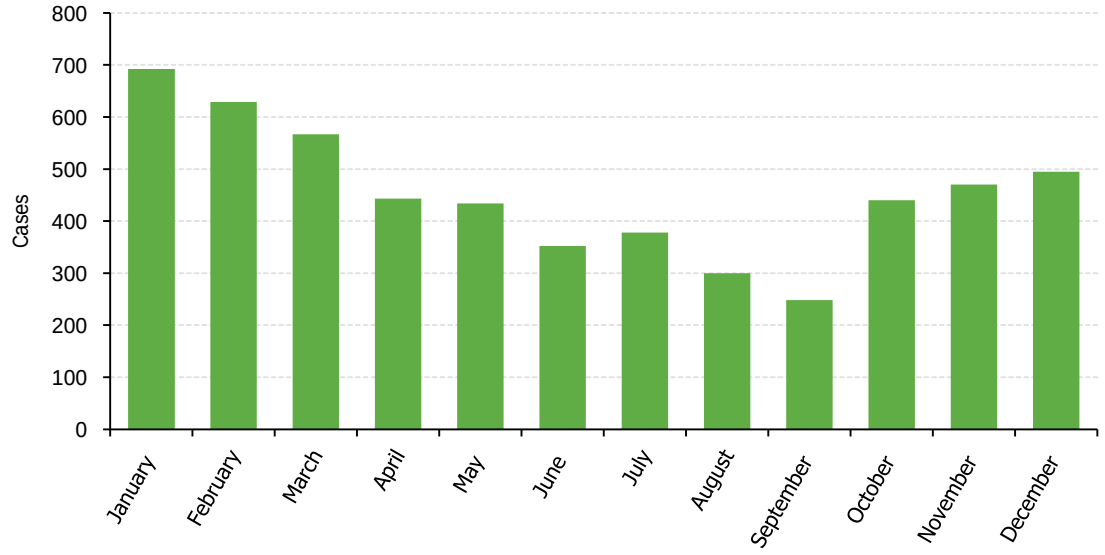
**Contributing countries all (n=5583); population data source: EUROSTAT*
***1999-2006 contains confirmed and probable cases according to the 2002 case definition; 2007 contains only confirmed cases*

4.3.2 Seasonal trend

Information on seasonal distribution was available for 5511 cases. There was a marked seasonal variation with peak levels in the winter months declining to low levels by late summer.

The highest number of reported cases were observed in January (n=692) and the lowest in September (n=248).

Figure 18: Number of reported invasive meningococcal disease cases per month, 2007(n=5511)



Contributing countries 2007: Austria, Bulgaria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, Sweden, United Kingdom

4.3.3 Gender distribution

Information on gender was available for 5519 cases, with the percentage of unknown only 0.4%. As expected, males and females were almost equally affected, with a male-to-female ratio of 1.08, and remained relatively constant across countries. Belgium, Greece and Sweden experienced a slightly higher level of the disease rate among females (see Table 54 in Annex).

4.3.4 Age distribution

Of the 5564 cases with a known age, 50% were reported in children younger than 10 years-old.

The most affected age group was the 1–4 year olds (26%) followed by the infants younger than one year (16%) and teenagers 15–19 years old (13%). Among the older age groups, the disease was reported only rarely.

The total number of reported cases younger than one year of age was higher in the first month of age (n=265) which represents 17% of the total number of reported cases younger than one year age.

Table 19: Age distribution of invasive meningococcal disease cases, all countries combined, 2007(n=5564)

Age group	Number of cases	Percentage
<1 year	886	16.46
01–04 years	1457	27.07
05–09 years	487	9.05
10–14 years	307	5.70
15–19 years	702	13.04
20–24 years	316	5.87
25–44 years	483	8.97
45–64 years	409	7.60
65+	335	6.22
Total	**5382**	**100**

Contributing countries 2007: Austria, Bulgaria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, Sweden, United Kingdom

Table 20 shows the notification rate and total number of invasive meningococcal disease cases by country in 2007. In all MS, the highest rates ware observed in children younger than five years of age. In infants younger than one year, the highest rates were reported by Ireland (74. 5) and the UK (46.6) followed by Luxembourg (36.4), Latvia (35.8) and Estonia (33.7).

Table 20: Notification rates per 100 000 and total number of invasive meningococcal disease cases (in brackets) by age group and country in 2007

Country	<1 year	1-4 years	5-9 years	10-14 years	15-19 years	20-24 years	25-44 years	45-64 years	65+ years
Austria	10.36 (6)	6.23 (20)	0.96 (4)	1.68 (8)	3.02 (15)	0.96 (5)	0.04 (1)	0.33 (7)	0.21 (3)
Belgium	25.47 (31)	8.11 (38)	3.21 (19)	1.14 (7)	3.73 (24)	0.78 (5)	0.34 (10)	0.47 (13)	0.72 (13)
Bulgaria	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0.09 (2)	0.14 (3)	0.08 (1)
Cyprus	-	3.06 (1)	-	-	1.78 (1)	1.54 (1)	0.43 (1)	-	-
Czech Republic	12.29 (13)	4.13 (16)	0.89 (4)	0.37 (2)	1.84 (12)	0.86 (6)	0.41 (13)	0.25 (7)	0.13 (2)
Denmark	12.27 (8)	5.01 (13)	0.89 (3)	1.7 (6)	8.05 (26)	1.35 (4)	0.4 (6)	0.27 (4)	0.96 (8)
Estonia	33.73 (5)	7.41 (4)	-	-	-	-	0.54 (2)	-	-
Finland	5.09 (3)	1.31 (3)	0.35 (1)	0.62 (2)	4.3 (14)	0.6 (2)	0.29 (4)	0.8 (12)	0.23 (2)
France	12.46 (103)	4.05 (129)	1.57 (62)	1.05 (40)	3.07 (125)	1.65 (67)	0.49 (84)	0.31 (49)	0.6 (62)
Germany	9.66 (65)	3.18 (90)	0.69 (27)	0.79 (32)	1.62 (77)	0.7 (34)	0.19 (45)	0.16 (35)	0.19 (31)
Greece	17.87 (20)	4.49 (19)	3.71 (19)	1.09 (6)	2.38 (14)	1.14 (8)	0.38 (13)	0.29 (8)	0.1 (2)
Hungary	11.13 (11)	3.39 (13)	0.62 (3)	0.71 (4)	0.96 (6)	0.3 (2)	0.14 (4)	0.15 (4)	0.12 (2)
Ireland	74.54 (48)	23.63 (58)	4.76 (14)	4.72 (13)	6.96 (20)	1.44 (5)	0.87 (12)	0.53 (5)	0.85 (4)
Italy	3.24 (18)	1.71 (38)	0.55 (15)	0.21 (6)	0.88 (26)	0.61 (19)	0.15 (26)	0.14 (21)	0.08 (10)
Latvia	35.81 (8)	3.62 (3)	3.17 (3)	-	2.28 (4)	-	-	0.52 (3)	-
Lithuania	28.96 (9)	19.13 (23)	4.08 (7)	2.79 (6)	3.01 (8)	1.5 (4)	0.62 (6)	0.24 (2)	0.19 (1)
Luxembourg	36.35 (2)	-	-	-	-	-	-	-	-
Malta	-	6.29 (1)	4.5 (1)	3.82 (1)	-	-	0.9 (1)	0.87 (1)	1.78 (1)
Netherlands	13.56 (25)	6.9 (54)	2.49 (25)	1.01 (10)	2.3 (23)	1.04 (10)	0.32 (15)	0.3 (13)	0.84 (20)
Poland	19.06 (71)	5.86 (83)	1.93 (37)	1.99 (46)	2.01 (56)	0.7 (23)	0.3 (32)	0.35 (35)	0.18 (9)
Portugal	25.66 (27)	10.17 (45)	2.75 (15)	1.47 (8)	0.17 (1)	0.44 (3)	0.16 (5)	0.26 (7)	0.33 (6)
Romania	15.67 (34)	3.08 (26)	2.18 (24)	1.04 (12)	0.82 (13)	0.37 (6)	0.27 (18)	0.25 (13)	0.28 (9)
Slovakia	22.37 (12)	3.34 (7)	1.46 (4)	0.3 (1)	0.5 (2)	0.68 (3)	0.12 (2)	0.22 (3)	0.16 (1)
Slovenia	15.68 (3)	4.17 (3)	4.38 (4)	1.01 (1)	4.18 (5)	-	0.17 (1)	0.18 (1)	-
Spain	1.29 (6)	19.2 (350)	4.2 (88)	1.93 (40)	2.89 (66)	1.31 (37)	0.55 (81)	0.62 (66)	1.11 (82)
Sweden	5.65 (6)	0.98 (4)	0.43 (2)	0.88 (5)	1.61 (10)	0.74 (4)	0.25 (6)	0.17 (4)	0.51 (8)
United Kingdom	46.57 (348)	14.56 (407)	3.04 (105)	1.34 (50)	3.66 (147)	1.55 (64)	0.55 (94)	0.62 (93)	0.59 (57)
EU Total	**17.07 (882)**	**7.12 (1448)**	**1.89 (486)**	**1.13 (306)**	**2.3 (695)**	**0.97 (312)**	**0.34 (484)**	**0.32 (409)**	**0.4 (334)**
Iceland	-	17.64 (3)	-	-	4.34 (1)	-	-	-	-
Liechtenstein	-	-	-	-	-	-	-	-	-
Norway	10.22 (6)	2.6 (6)	0.33 (1)	0.32 (1)	1.95 (6)	1.44 (4)	0.08 (1)	0.25 (3)	0.29 (2)
Overall	**16.98 (888)**	**7.07 (1457)**	**1.87 (487)**	**1.12 (307)**	**2.29 (702)**	**0.98 (316)**	**0.33 (485)**	**0.32 (412)**	**0.4 (336)**

4.3.5 Probable country of infection

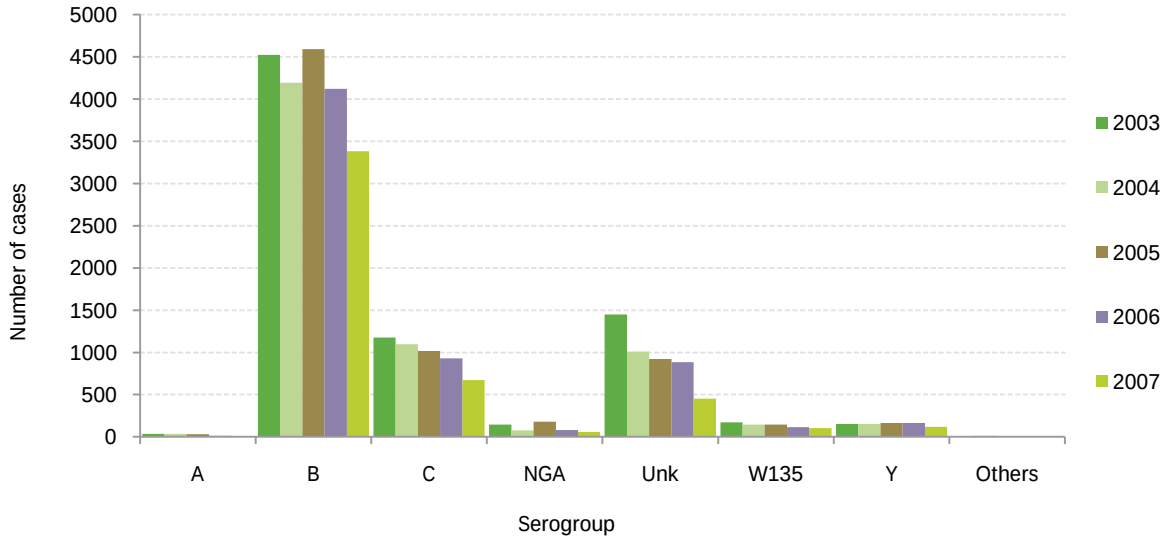
According to the cases reported in 2007, only four cases were reported as acquired out of Europe: two cases in Turkey (serogroups B and Y) and one case in USA (C) and one case in Namibia (B). However, this variable had information missing in 90% of the case reports.

4.3.6 Serogroups

Phenotypic identification of *N. meningitidis* strains is usually described in terms of serogroup, serotype and three serosubtype (PorA) variants. The distribution of serogroups among laboratory diagnosed cases reported between 2003 and 2007 is shown in Figure 19. There was a decreasing trend over time in all serogroups, especially in serogroups B and C, dropping from 4819 to 3406 and from 1221 to 684, respectively. Data quality has been

improving over the years and the number of cases with unknown serogroups has decreased from 1448 (19% of reported cases) in 2003 to 453 (9% of reported cases) in 2007.

Figure 19: Distribution of serogroups among laboratory diagnosed invasive meningococcal disease cases in EU and EEA countries with consistent reporting, 2003–2007 (n=32 566)



Population source: 2003-2007: EUROSTAT
Contributing countries 2003-2006: Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Norway, Poland, Portugal, Slovak Republic, Slovenia, Spain, Sweden, United Kindom

The distribution of serogroups in laboratory diagnosed cases in all participant countries in 2007 is shown in Figure 20. Serogroup B was the most frequently reported in all MS (74%), followed by serogroup C (14%).

Serogroup Y was more frequently reported by Scandinavian countries; the highest proportion of cases was reported by Sweden (20%) followed by Finland (12%) and Norway (7%). In the rest of the countries, serogroup Y was present in a range lying between 0 and 4%.

The highest proportion of serogroup W135 was notified by Malta (17%) followed by Lithuania (9%) and Slovenia (6%). However, the total number of cases due to serogroup Y and W135 was relatively small: 119 and 105 cases respectively for 2007.

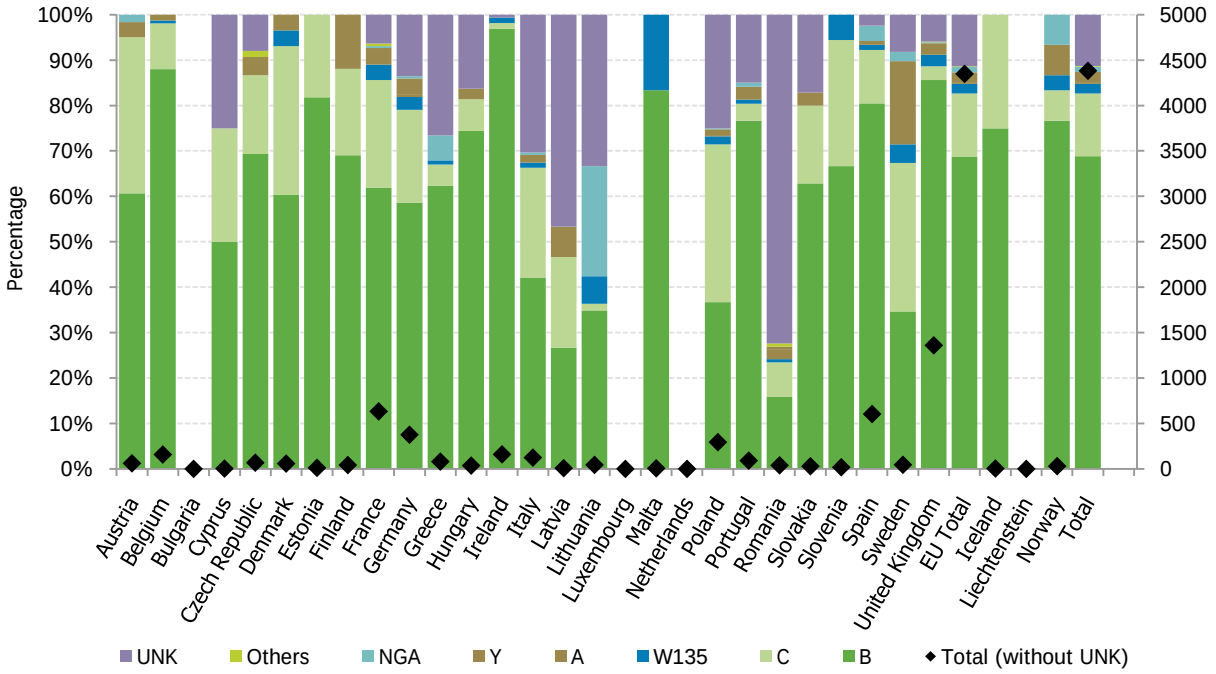
We have no evidence of outbreaks among travellers outside Europe due to serogroup W135, according to reported epidemiological link variable.

Serogroup A caused very few cases (10) in Europe in 2007 and this finding is consistent with the observation in the previous years.

The proportion of cases with missing information on serogroup remains high, especially in the countries towards the east of Europe.

Cases in which a serogroup could not be identified were designated as non-groupable (n=58), and assumed that they were no capsulated strains.

Figure 20: Percentage distribution of serogroups of invasive meningococcal disease cases by country, 2007 (n=4 382)

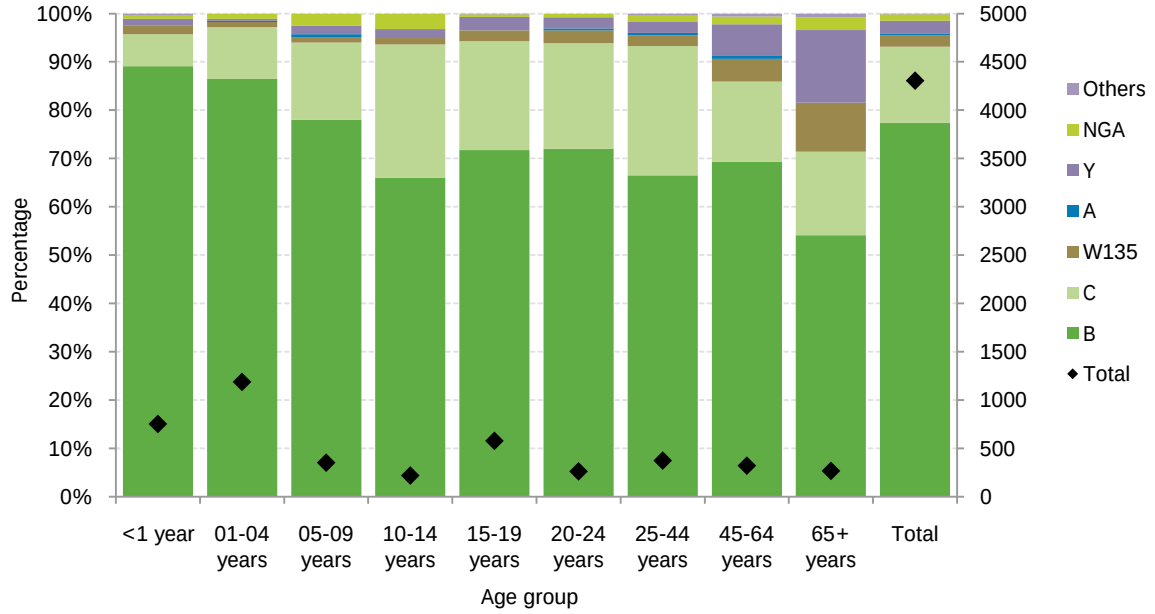


The distribution of serogroups by age group is illustrated in Figure 21. Among the infants younger than one year, 89% of cases were due to serogroup B and only 7% to serogroup C. Among the infants 1–4 years of age, 86 % of cases were due to serogoup B and only 11 % due to serogroup C.

This finding could be explained by the impact of the vaccination against serogroup C in age groups targeted by vaccination. The proportion of serogroup C cases increased with age and it was quite high in adolescents, ranging from 23 to 28% in those aged 10–19 years.

The highest proportion of non-B and non-C serogroup cases was reported among elderly people older than 65 years.

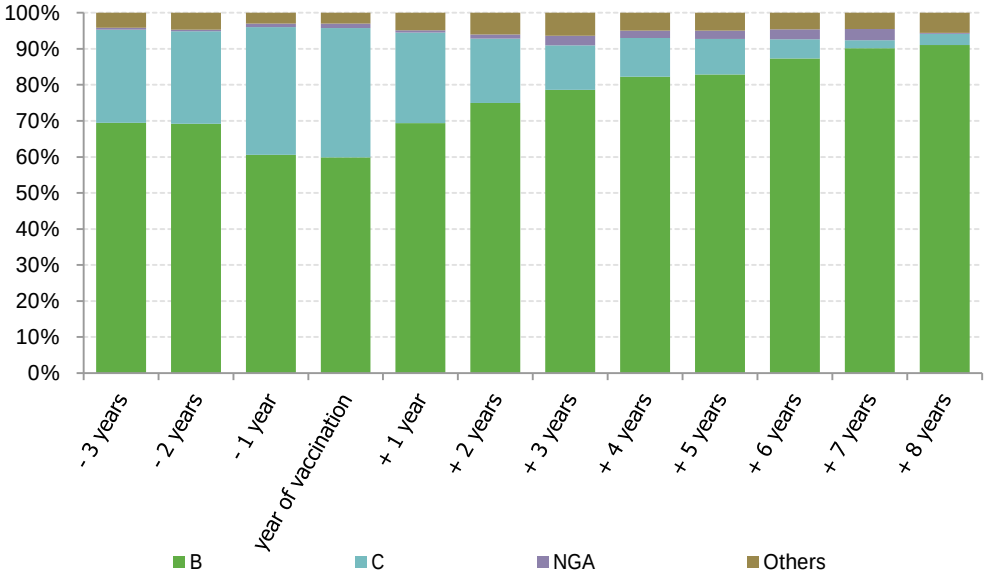
Figure 21: Distribution of invasive meningococcal disease serogroups by age group, 2007 (n=4305)



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

The percentage distribution of serogroups over time, before and after the year of introduction of MCC into the country's routine vaccination schedule, is shown in Figure 22. The figure highlights the noteworthy impact of MCC vaccination as the proportion of cases due to serogroup C dramatically decreased by increasing the number of years post vaccination.

Figure 22: Percentage distribution of invasive meningococcal disease serogroups in MCC countries* in the years before and after the introduction of MCC vaccination into the routine vaccination schedule (n=50 329)



**Countries included in figure as MCC countries: Belgium, Germany, Greece, Iceland, Italy, Ireland, Netherlands, Portugal, Spain, and UK.*
Source: EVAC.NET

Table 21 shows the percentage distribution of serogroup B cases by age group in countries with and without MCC vaccination in 2007.

Almost half of the total number of B cases was reported to have occurred in children younger than five years old. Comparing the proportion of cases in countries with or without generalised vaccination programmes shows that serogroup B was predominant in countries with MCC vaccination in all age groups, but in particular in small children aged 0–4 years.

Table 21: Percentage distribution of serogroup B invasive meningococcal disease cases by age group in countries with and without MCC vaccination, 2007

Age group	2007		
	with MCC	without MCC	total
<1 year	486 (19%)	184 (21%)	670 (20%)
01-04 years	836 (33%)	190 (21%)	1026 (30%)
05-09 years	212 (8%)	62 (7%)	274 (8%)
10-14 years	98 (4%)	46 (5%)	144 (4%)
15-19 years	270 (11%)	144 (16%)	414 (12%)
20-24 years	116 (5%)	72 (8%)	188 (6%)
25-44 years	168 (7%)	80 (9%)	248 (7%)
45-64 years	146 (6%)	76 (9%)	222 (7%)
65+ years	108 (4%)	36 (4%)	144 (4%)
Unknown	76 (3%)	0 (0%)	76 (2%)
Total	**2 516**	**890**	**3 406**

** Countries with MCC: 'Belgium,'Iceland,'Ireland,'Netherland,'Spain',United Kingdom,'Germany','Greece','Italy','Portugal'*
***Countries without MCC: Austria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Hungary, Latvia, Lithuania, Luxembourg, Malta, Norway, Romania, Slovak Republic, Slovenia, Sweden.*

Table 22 shows the percentage distribution of serogroup C cases by age group in countries with and without MCC vaccination in 2007.

Teenagers aged 10–19 years were the most affected by serogroup C disease, with 28% of the total cases notified. In contrast with serogroup B, cases due to serogroup C were much less among those younger than five years of age, accounting for only 26% of cases. In particular, infants younger than one year old accounted for only 7% of cases. Comparing the proportion of cases in countries with and without vaccination, we can see that cases due to serogroup C in countries with MCC vaccination were less than those in countries without MCC vaccination, especially in children and adolescents aged between 0 and 19 years. Among infants younger than one year in countries with MCC vaccination, serogroup C cases accounted for 4% of cases; children between one and four years old accounted for 17% of cases.

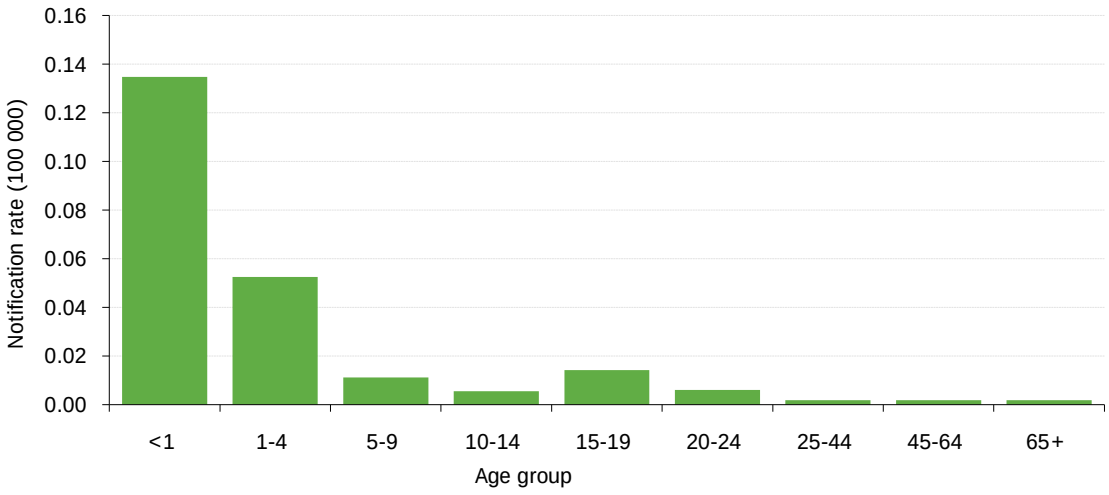
Table 22: Percentage distribution of serogroup C invasive meningococcal disease cases by age group in countries with and without MCC vaccination, 2007

Age Group	2007		
	with MCC	without MCC	Total % of C cases
<1 year	12 (4%)	38 (9%)	50 (7%)
01–04 years	46(17%)	82 (20%)	128 (19%)
05–09 years	19 (7%)	37 (9%)	56 (8%)
10–14 years	16 (6%)	44 (11%)	60 (9%)
15–19 years	40 (14%)	90 (22%)	130 (19%)
20–24 years	28 (10%)	29 (7%)	57 (8%)
25–44 years	53 (19%)	47 (12%)	100 (15%)
45–64 years	28 (10%)	25 (6%)	53 (8%)
65+ years	30 (11%)	16 (4%)	46 (7%)
Unknown	4 (1%)	0 (0%)	4 (1%)
Total	**276**	**408**	**684**

** Countries with MCC: 'Belgium,'Island,'Ireland,'Netherland,'Spain',United Kingdom,'Germany','Greece','Italy','Portugal'*
***Countries without MCC: Austria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Hungary, Latvia, Lithuania, Luxembourg, Malta, Norway, Romania, Slovak Republic, Slovenia, Sweden.*

Age group specific rates of serogroup B cases for 2007 are shown in Figure 23. Although rates were very low in all age groups (below 0.15 per 100 000), the highest were observed in infants younger than one year.

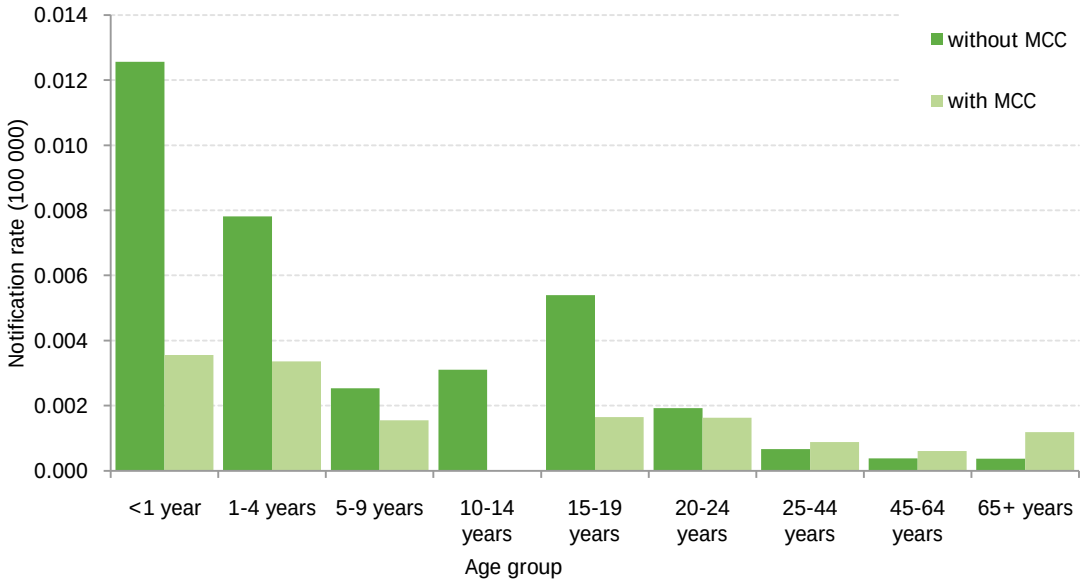
Figure 23: Age group specific notification rates (per 100 000) of serogroup B invasive meningococcal disease cases, 2007 (n=5020)



Population data: EUROSTAT
Contributing countries: Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, Sweden, United Kingdom

The age specific rates for serogroup C in 2007, divided by countries with and without MCC vaccination, is shown in Figure 24. In cases coming from countries without MCC vaccination, the pattern was quite similar to the one observed among the serogroup B cases, although the rate in those with serogroup B was 10 times higher. In countries with MCC vaccination, the effect of the vaccine was evident as notification rates were extremely low in all age groups (below 0.004) and no cases coming from MCC countries have been observed in children aged 10–14 years.

Figure 24: Age group specific notification rates (per 100 000) of serogroup C invasive meningococcal disease cases, in countries with MCC and without MCC vaccination, 2007 (n=830)

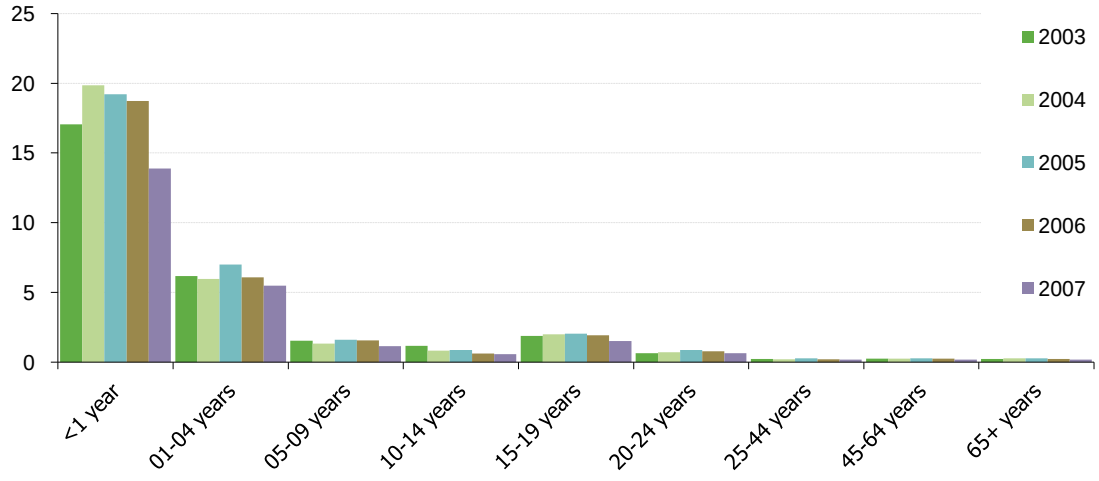


Population data: EUROSTAT
**Countries included in figure as MCC countries: Belgium, Iceland, Ireland, Netherlands, Spain, and UK*
***Countries included in figure as non-MCC countries: Austria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Italy, Latvia, Lithuania, Luxembourg, Malta, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Sweden, .*

The notification rate of serogroup B cases by age group in countries with consistent reporting between 2003 and 2007 is illustrated in Figure 25. The distribution by age group and from 2003 to 2007 was generally similar between cases due to serogroups C and B, but the rate was much higher in the B cases.

Notification rates among B cases were quite consistent over time for all age groups and the highest rate was always observed among infants younger than one year, followed by the rate among children aged 1–4 years.

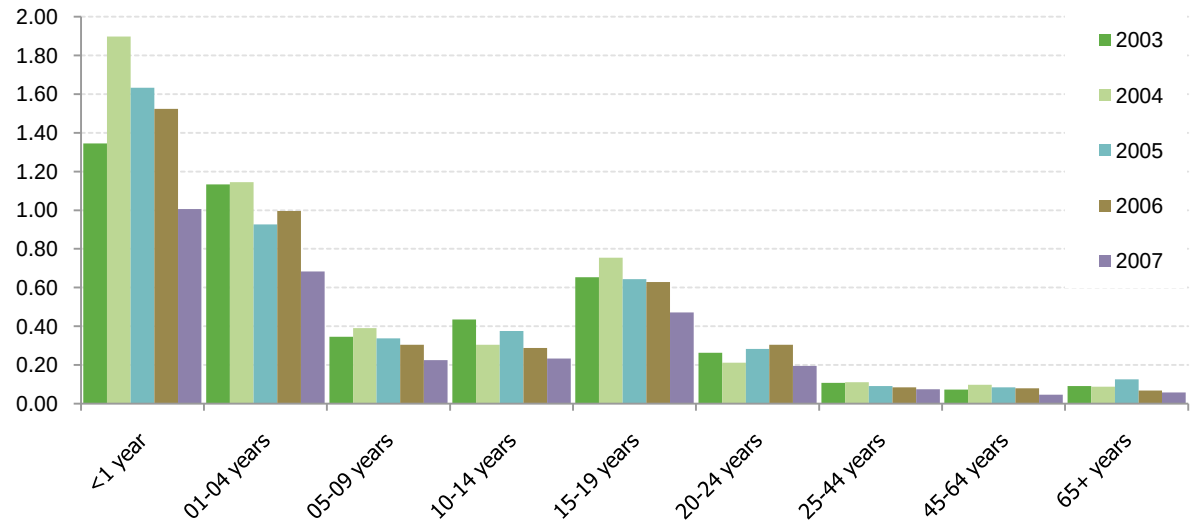
Figure 25: Notification rate (per 100 000) of serogroup B invasive meningococcal disease cases by year and age group in countries with consistent reporting between 2003 and 2007 (n=21 672)



Population source: 2003-2007: EUROSTAT
Contributing countries 2003-2006: Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Norway, Poland, Portugal, Slovak Republic, Slovenia, Spain, Sweden, United Kingdom
Contributing countries 2007: Austria, Belgium, , Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Norway, Poland, Portugal, Slovak Republic, Slovenia, Spain, Sweden, United Kingdom

The notification rate of serogroup C cases by age group in countries with consistent reporting between 2003 and 2007 is illustrated in Figure 26. The notification rate among C cases declined quite steadily over time, especially in those aged 0–4 years.

Figure 26: Notification rate (per 100 000) of serogroup C invasive meningococcal disease cases by year and age group in countries with consistent reporting between 2003 and 2007 (n=4970)



Population source: 2003-2007: EUROSTAT
Contributing countries 2003-2006: Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Norway, Poland, Portugal, Slovak Republic, Slovenia, Spain, Sweden, United Kingdom
Contributing countries 2007: Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Norway, Poland, Portugal, Slovak Republic, Slovenia, Spain, Sweden, United Kingdom

4.3.7 Serotypes

Table 23 shows the distribution of serotypes associated with all serogroups. Also in brackets in the first column, the number of strains reported for each serogroup is listed.

There was a clear association between certain serogroups and serotypes: serotype A carried P3_a in all the cases, serotype W135 carried non-typeable serotypes (NT) in 80% of cases and P2_2a in 14 % of cases; serotype Y carried P3_14 in 42% of cases while the most frequently reported serotype among serogroup B cases was P3_4 (25%) and among serogroup C cases was P2_2a (45%). A very large number of serogroup B strains carried a non-typeable serotype, representing 42% of all serogroup B strains. However, these figures must be interpreted with caution, as only half (n=15) countries are reporting serotypes identification and most of these with a low proportion of serotyped samples. In addition, number of strains belonging to each serogroup varied widely.

Table 23: Distribution of serotypes associated with serogroups of invasive meningococcal disease cases, all participating countries, 2007 (n=2071)

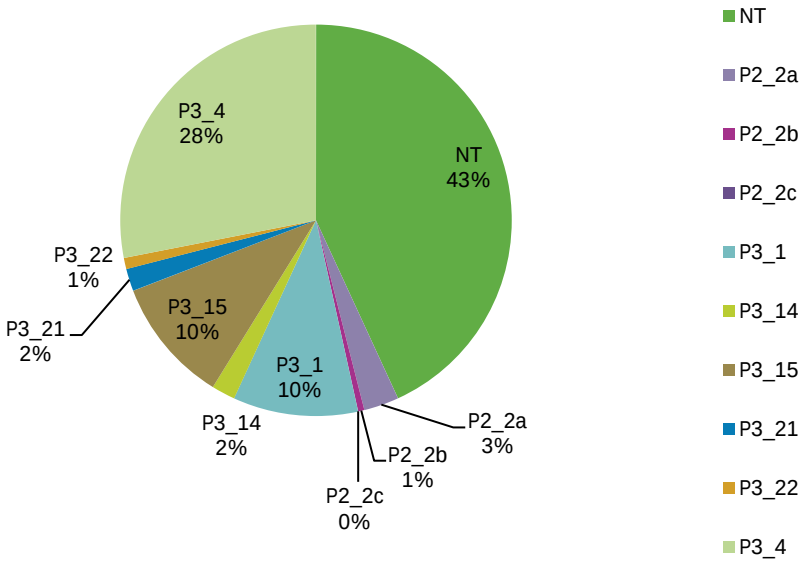
Serogroup	NT	P2_2a	P2_2b	P2_2c	P3_1	P3_14	P3_15	P3_21	P3_22	P3_23	P3_4
A (1)	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	100%
W135 (63)	80%	14%	2%	0%	0%	3%	2%	0%	0%	0%	0%
X (6)	33%	0%	0%	0%	17%	0%	0%	17%	0%	0%	33%
NGA (25)	88%	0%	0%	0%	0%	0%	8%	0%	0%	0%	4%
Unk (9)	89%	0%	0%	0%	0%	0%	11%	0%	0%	0%	0%
C (373)	30%	45%	10%	0%	1%	5%	5%	0%	1%	0%	3%
Z (18)	100%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Y (82)	40%	1%	0%	1%	0%	42%	14%	0%	0%	0%	1%
B (1511)	42%	2%	1%	0%	9%	6%	12%	1%	2%	0%	25%

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

Figures 27 and 28 illustrate the distribution of serotypes associated with serogroup B in participating countries, divided into those with and without MCC vaccination in 2007, respectively.

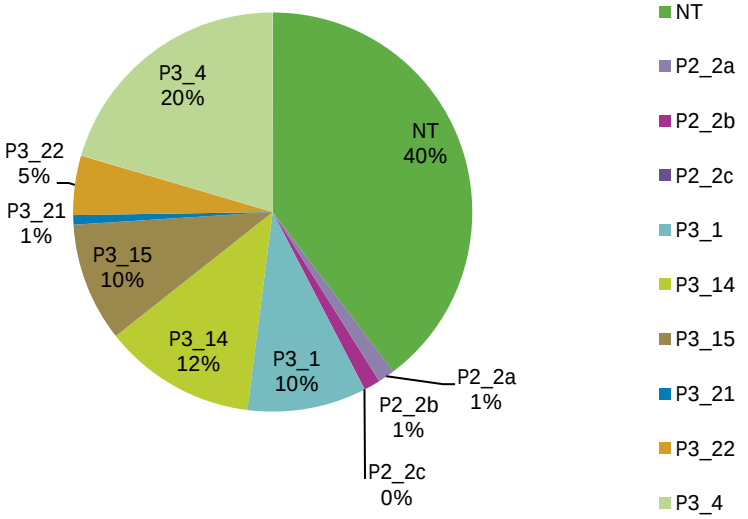
The serotypes most frequently reported in association with serogroup B were P3_4, P3_14, P3_15 and P3_1 in both those countries with MCC vaccination and those without. However, the proportion of P3_4 was slightly higher in MCC countries. Conversely non-MCC countries experienced higher proportions of P3_14 and P3_22 serotypes.

Figure 27: Distribution of serotypes associated with serogroup B invasive meningococcal disease cases in countries with MCC vaccination, 2007 (n=969)



Countries with MCC and with reported serotypes : Belgium, Ireland, Italy, Spain, United Kingdom

Figure 28: Distribution of serotypes associated with serogroup B of invasive meningococcal disease cases in countries without MCC vaccination, 2007 (n=519)

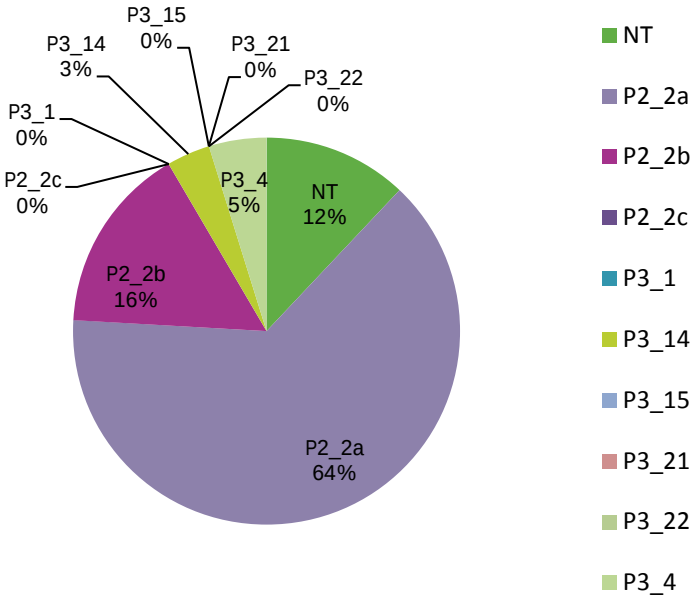


Countries without MCC and reported serotypes: Austria, Czech Republic, Denmark, Finland, France, Lithuania, Poland, Slovakia, Slovenia, Sweden

Figures 29 and 30 illustrate the distribution of serotypes associated with serogroup C in participating countries divided in those with and without MCC vaccination in 2007.

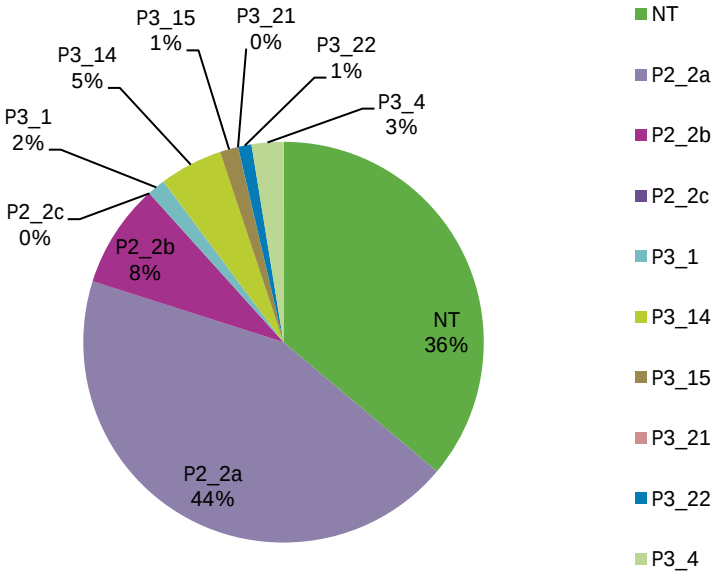
Serotypes P2_2a and P2_2b were the two mainly associated with serogroup C strains, as opposed to several commonly associated with serogroup B strains (P3_1, P3_14, P3_15, P3_22 and P3_4). The difference in distribution of serotypes was quite evident between MCC and non-MCC countries; in fact, the proportion of P2_2b (16%) and P2_2a (64%) strains were appreciably higher in countries with MCC vaccination. On the contrary, in non-MCC countries, several serotypes were notified and a much higher proportion of strains were reported as non-typeable.

Figure 29: Distribution of serotypes associated with serogroup C of invasive meningococcal disease cases in countries with MCC vaccination, 2007 (n=83)



Countries with MCC and with reported serotypes: Belgium, Ireland, Italy, Spain, United Kingdom

Figure 30: Distribution of serotypes associated with serogroup C invasive meningococcal disease cases in countries without MCC vaccination, 2007 (n=274)



Countries without MCC and reported serotypes: Austria, Czech Republic, Denmark, Finland, France, Lithuania, Poland, Slovakia, Slovenia, Sweden

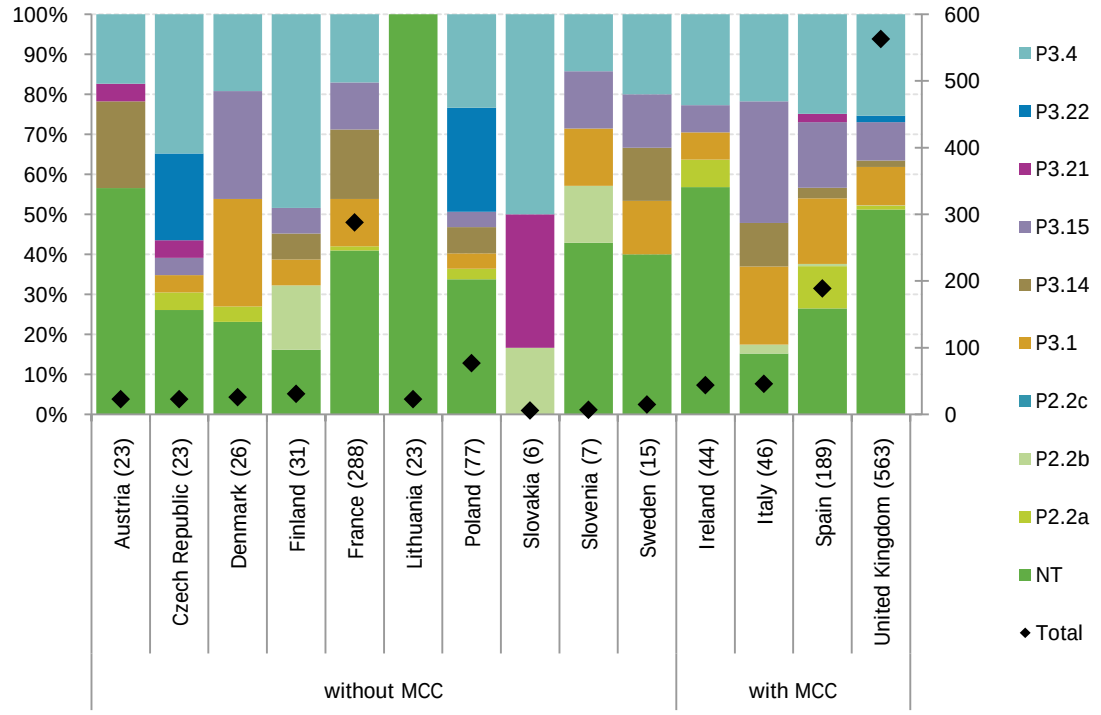
Figure 31 shows the distribution of serotypes associated with serogroup B in 2007 in countries with and without MCC vaccination. An obvious characteristic pattern can not be described in either MCC or non-MCC countries.

Some of the differences seen among countries could also be related to random variation, due to the low number of strains reported by the majority of them.

A non-typeable serogroup was prevalent in almost all countries apart from Italy; P3_4 (25%) was the serotype most frequently reported in many countries, followed by P3_15 (9.6%), P3_1 (9.6%) and P3_14 (1.6%). In the Czech Republic and Poland, there was a high proportion of P3_22 reported while in Slovakia there was a high percentage of P3_21 reported.

There were no major differences in the serotype distribution in countries with and without MCC vaccination.

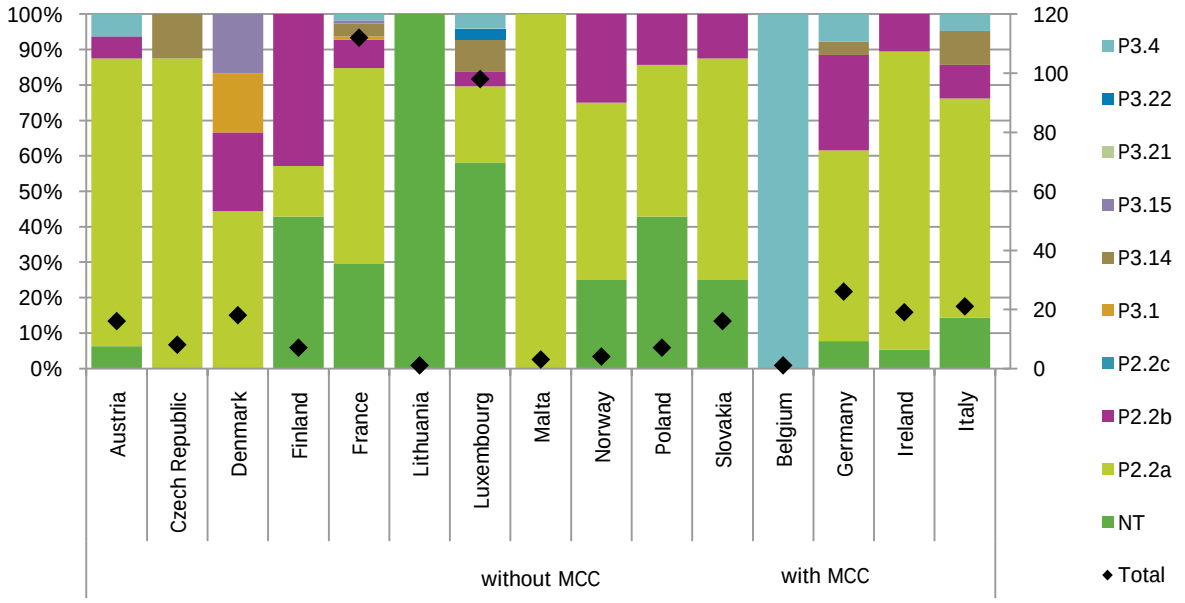
Figure 31: Distribution of serotypes associated with serogroup B of invasive meningococcal disease cases, by country, 2007 (Non-MCC n=519; MCC n=837)



Countries with MCC and reported serotypes: Belgium, Ireland, Italy, Spain, United Kingdom
Countries without MCC and reported serotypes: Austria, Czech Republic, Denmark, Finland, France, Lithuania, Poland, Slovakia, Slovenia, Sweden

Figure 32 shows the distribution of serotypes associated with serogroup C in countries with and without MCC vaccination in 2007. The most prevalent serotype in these countries was P2_2a (62%). However, in Finland, P2_2b was the most frequently reported, and in Ireland P3_4 was the only reported serotype. The proportion of non-typeable cases was lower than among serogroup B and much lower in countries with MCC vaccination.

Figure 32: Distribution of serotypes associated with serogroup C of invasive meningococcal disease cases, by country, 2007 (MCC n=67; non-MCC n=274)



Countries with MCC and with reported serotypes: Belgium, Ireland, Italy, Spain, United Kingdom
Countries without MCC and reported serotypes: Austria, Czech Republic, Denmark, Finland, France, Lithuania, Poland, Slovakia, Slovenia, Sweden

Table 24a shows the proportion of serogroup C strains which carried the P2_2a serotype, by country and year between 2003 and 2007. This proportion varied within countries and with time. A clear pattern cannot be described in either MCC or non-MCC countries. Meningococcal C vaccination countries did appear to experience a higher proportion of P2_2a strains than did non-MCC strains between 2003 and 2006. Then, in 2007, the proportion of P2_2a strains among countries with MCC vaccination become much lower comparing to the previous years and comparing to non-MCC countries. However, the number of reporting countries with and without MCC vaccination differs and the vaccination schedules in the countries has been modified over the years. In 2003 and 2007 in MCC countries, the range varied between 79% and 29%. The range in non-MCC countries for the same time period was between 70% in 2004 and to 31 % in 2007.

Table 24a: Proportion of serogroup C invasive meningococcal disease cases (number of all serotyped cases) that belong to serotype P2_2a in countries with consistent reporting, with MCC vaccination, 2003–2007

Countries with consistent MCC vaccination					
Country	**Y2003**	**Y2004**	**Y2005**	**Y2006**	**Y2007**
Belgium	67% (46)	60% (20)	56% (18)	82% (11)	63% (10)
Ireland	100% (2)	100% (1)	100% (4)	100% (3)	0% (0)
Spain*	71% (98)	60% (104)	69% (81)	70% (46)	22% (16)
United Kingdom	78% (65)	59% (34)	65% (17)	65% (17)	30% (13)
Mean	79% (211)	67% (159)	73% (120)	79% (77)	29% (39)

Table 24b: Proportion of serogroup C invasive meningococcal disease cases (number of all serotyped cases) that belong to serotype P2_2a in countries with consistent reporting without MCC vaccination, 2003–2007

Countries without consistent MCC vaccination					
Country	**Y2003**	**Y2004**	**Y2005**	**Y2006**	**Y2007**
Austria	33% (12)	40%(15)	75% (16)	91% (22)	62% (13)
Czech Republic	78% (23)	84% (25)	56% (18)	27% (11)	54% (7)
Denmark	26% (19)	21% (14)	29% (21)	32% (19)	42% (8)
Finland	0% (5)	0% (5)	0% (1)	20% (5)	13% (1)
France	53% (115)	55% (130)	48% (120)	50% (135)	39% (62)
Greece	100% (2)	0% (0)	0% (5)	0% (1)	0% (0)
Italy	18% (55)	7% (83)	16% (92)	22% (27)	33% (14)
Poland	10% (21)	5% (40)	11% (62)	22% (67)	15% (21)
Slovenia	0% (3)	0% (0)	25% (4)	0% (0)	40% (2)
Sweden	8% (12)	18% (11)	13% (15)	27% (15)	19% (3)
Norway	44% (9)	100% (1)	33% (3)	0% (1)	0% (0)
Overall	**39% (276)**	**70% (324)**	**54% (357)**	**46% (303)**	**31% (131)**

Source: National Reference Laboratory (years 2003 to 2006) and the ES-Statutory-Diseases source (year 2007).

4.3.8 Distribution of serosubtypes

Table 25 shows the distribution of invasive meningococcal disease cases by serosubtype and by country in 2007. The percentage of serosubtypes belonging to serogroup C that are reported out of the total number of serotype C cases (this was used as a proxy measure of the proportion of samples for which the serosubtyping was carried out) is also listed in brackets. The serosubtype most frequently reported in serogroup C cases was P1.5:NST:NST (n=86) followed by NST:NST:NST (n=62) and then NST:P1.13:NST and P1.5:P1.1:NST, which have been detected in the United Kingdom and in Belgium.

The highest number of samples were serosubtyped in France at 114 (71%) and in Poland at 96 (71%).

Table 25: Frequency of serosubtypes present in serogroup C isolates of invasive meningococcal disease cases, by country in 2007

Country	C:NST:NST:NST	C:NST:NST:P1_6	C:NST:P1.13:NST	C:NST:P1.14:NST	C:NST:P1.15:NST	C:NST:P1.16:NST	C:NST:P1.2:NST	C:NST:P1.3:NST	C:NST:P1.3:P1.6	C:NST:P1.9:NST	C:P1.19:NST:NST	C:P1.5:NST:NST	C:P1.5:P1.1:NST	C:P1.5:P1.2:NST	C:P1.7:NST:NST	C:P1.7:P1.1:NST	C:P1.7:P1.16:NST	Listed Total (%) serotyped total
Austria	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**2 (10%)**
Belgium	2	0	0	0	0	0	1	0	0	0	1	9	1	2	0	0	0	**16 (100%)**
Denmark	5	0	0	0	0	3	1	0	0	0	0	2	0	5	2	0	1	**19 (100%)**
Finland	3	0	0	0	0	0	0	1	2	0	0	1	0	0	1	0	0	**8 (100%)**
France	19	2	0	0	1	2	5	0	0	0	0	26	0	31	0	26	2	**114 (71%)**
United Kingdom	3	0	1	0	0	0	0	0	0	0	1	12	0	3	1	1	0	**22 (51%)**
Ireland	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	**1 (50%)**
Italy	5	0	0	0	0	0	0	0	1	0	0	13	0	5	0	0	0	**24 (56%)**
Poland	22	0	0	2	2	3	0	14	20	2	0	23	0	7	0	1	0	**96 (71%)**
Slovenia	1	0	0	1	0	0	0	0	0	0	0	0	0	2	0	0	0	**4 (80%)**
Total	**62**	**2**	**1**	**3**	**3**	**8**	**7**	**15**	**23**	**3**	**2**	**86**	**1**	**55**	**4**	**28**	**3**	**306 (67%)**

Table 26 shows the distribution by serosubtype and by country and the percentage of serosubtypes belonging to serogroup B that are reported out of the total number of serotype b invasive meningococcal disease cases. The most frequently reported serosubtypes were B:1.4 (n=283) followed by B:1.14 (n=166) and B:1.9 (n=105). The highest number of samples were serosubtyped in the UK at 544(44%) in France at 290(69%) and in Belgium at 135(96%).

Table 26: Frequencies of serosubtypes present in serogroup B isolates of invasive meningococcal disease cases, by country in 2007*

Country	NST:NST:NST:B	1.6P:NST:NST:B	NST:1.1P:NST:B	NST:1.10P:NST:B	NST:1.13P:NST:B	NST:1.14P:NST:B	1.14:1.6P:NST:B	NST:1.15P:NST:B	NST:1.16P:NST:B	NST:1.2P:NST:B	NST:1.3P:NST:B	1.69:1.3P:NST:B	NST:1.4P:NST:B	NST1.9P:NST:B	NST:NST:1.12P:B	NST:1.13P:1.12P:B	NST:1.16P:1.12P:B	NST:1.4P:1.12P:B	NST:1.9P:1.12P:B	NST:NST:1.19P:B	NST:1.9P:1.19P:B	NST:1.13P:1.19P:B	NST:1.14P:1.19P:B	NST:1.15P:1.19P:B	NST:1.16P:1.19P:B	NST:NST:1.5P:B	NST:1.2P:1.5P:B	NST:1.4P:1.5P:B	NST:NST:1.7P:B	NST:1.1P:1.7P:B	NST:1.13P:1.7P:B	NST:1.15P:1.7P:B	NST:1.16P:1.7P:B	NST:1.3P:1.7P:B	NST:1.4P:1.7P:B	NST:1.9P:1.7P:B	Listed total (serotyped total %)
UK	40	3	0	4	7	90	1	2	24	1	3	5	122	86	2	1	1	0	2	7	1	3	2	78	3	16	10	1	10	3	0	0	15	0	0	1	**544 (44%)**
BE	6	3	0	1	1	29	0	3	3	1	0	0	51	0	0	1	0	2	0	0	0	1	0	5	0	3	3	0	3	6	0	0	2	1	10	0	**135 (96%)**
AU	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**6 (16%)**
SI	6	0	0	0	0	1	0	0	0	0	0	0	2	0	1	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	**12 (100%)**
IT	5	3	0	0	7	4	0	4	7	0	0	1	9	3	0	0	0	0	0	0	0	0	0	0	0	3	1	0	1	1	0	0	0	0	0	0	**49 (65%)**
DK	4	0	0	0	1	5	0	2	1	0	0	1	3	0	0	0	0	0	0	0	0	0	0	0	0	2	3	0	4	0	0	0	9	0	0	0	**35 (100%)**
IE	6	0	1	0	1	3	0	0	1	0	0	1	7	4	0	0	0	0	0	3	0	1	0	7	0	4	1	0	0	0	0	1	3	0	0	0	**44 (28%)**
PL	18	0	0	7	0	10	0	2	6	1	2	2	7	1	1	0	0	1	0	0	0	0	0	0	0	9	10	0	1	3	0	0	21	0	0	0	**102 (71%)**
FR	52	6	3	0	13	21	0	25	13	1	0	0	72	11	5	6	0	0	0	0	0	0	0	0	0	10	9	0	10	1	1	0	29	0	2	0	**290 (69%)**
FI	7	0	0	0	1	3	0	0	0	1	0	0	10	0	0	0	0	0	0	0	0	0	0	1	0	5	0	0	1	0	0	0	0	0	0	0	**29 (100%)**
To	**150**	**15**	**4**	**12**	**31**	**166**	**1**	**38**	**55**	**5**	**5**	**10**	**283**	**105**	**9**	**8**	**1**	**3**	**2**	**10**	**1**	**5**	**2**	**91**	**3**	**53**	**38**	**1**	**30**	**14**	**1**	**1**	**79**	**1**	**12**	**1**	**1246 (54%)**

4.3.9 Clinical presentation

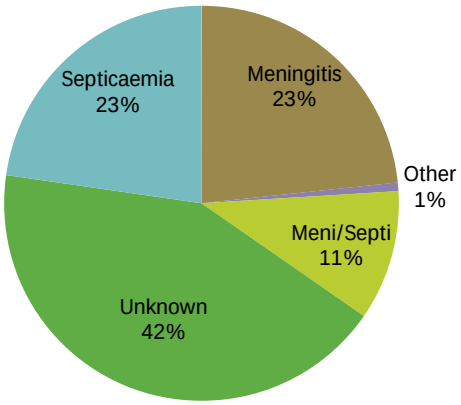
There are two main meningococcal clinical presentations: meningitis and septicaemia.

The distribution of these clinical presentations in selected EU and EEA countries in 2007 is shown in Figure 33. According to the reported data in countries with known clinical presentations, meningitis and septicaemia contribute in the same proportion to the clinical picture of the disease.

However, these data have to be interpreted with caution as information on the data sources were not fully available and it was not known if countries were reporting only one specific clinical form or more. There were some countries where the disease was entirely represented by a single clinical form (in Cyprus, Iceland and Denmark) where all cases were reported as meningitis, while in France all cases were reported as septicaemia.

This figure is therefore heavily influenced by what is routinely reported to the surveillance systems in MS and may not reflect the real distribution of the clinical forms. Unfortunately there was a high proportion of data with the clinical presentation reported as unknown (more than 40%).

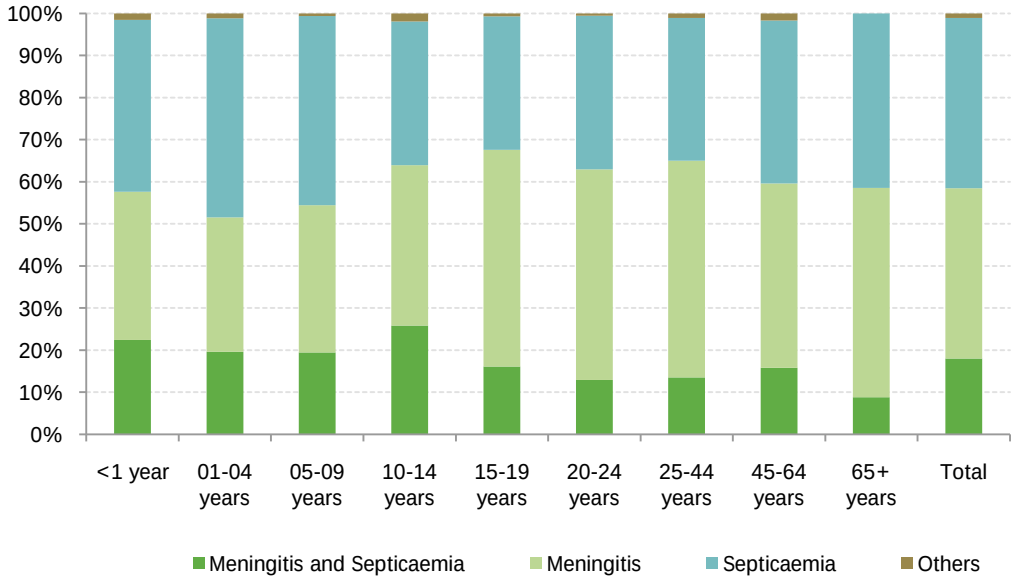
Figure 33: Percentage distribution of clinical presentation of invasive meningococcal disease cases, 2007 (n=5491)



Contributing countries: Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, United Kingdom

The association between clinical presentation and age is shown in Figure 34. The clinical presentations were equally distributed among the age groups, with only some minor differences. The proportion of meningitis cases was higher (30%) in those aged 15–19 years, while the proportion of meningitis with septicaemia was higher (17%) in young teenagers aged 10–14 years. This figure also requires caution in the interpretation, as countries collect information on clinical presentation differently.

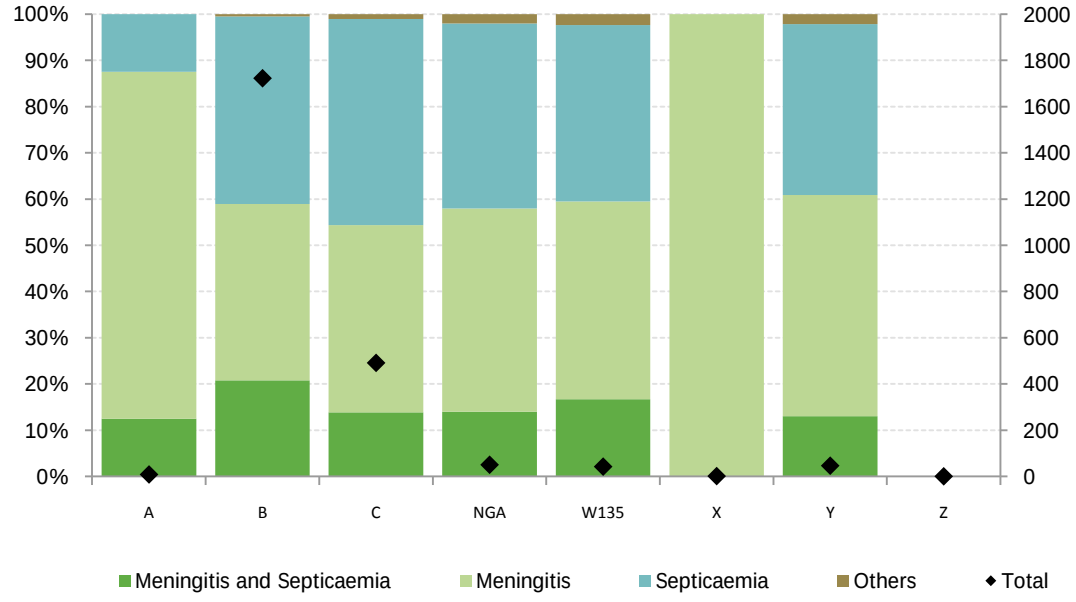
Figure 34: Clinical presentation of invasive meningococcal disease cases by age group, 2007 (n=3031)



Contributing countries: Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, United Kingdom

Figure 35 shows the association between clinical presentation and serogroup. It seems that meningitis is predominant in serogroups A and X. However, this could be a spurious association as the total number of cases reported for these serogroups was very low. Among serogroups B and C, meningitis and septicaemia were reported in almost equal proportions.

Figure 35: Clinical presentation of invasive meningococcal disease cases by serogroup, 2007 (n=2361)



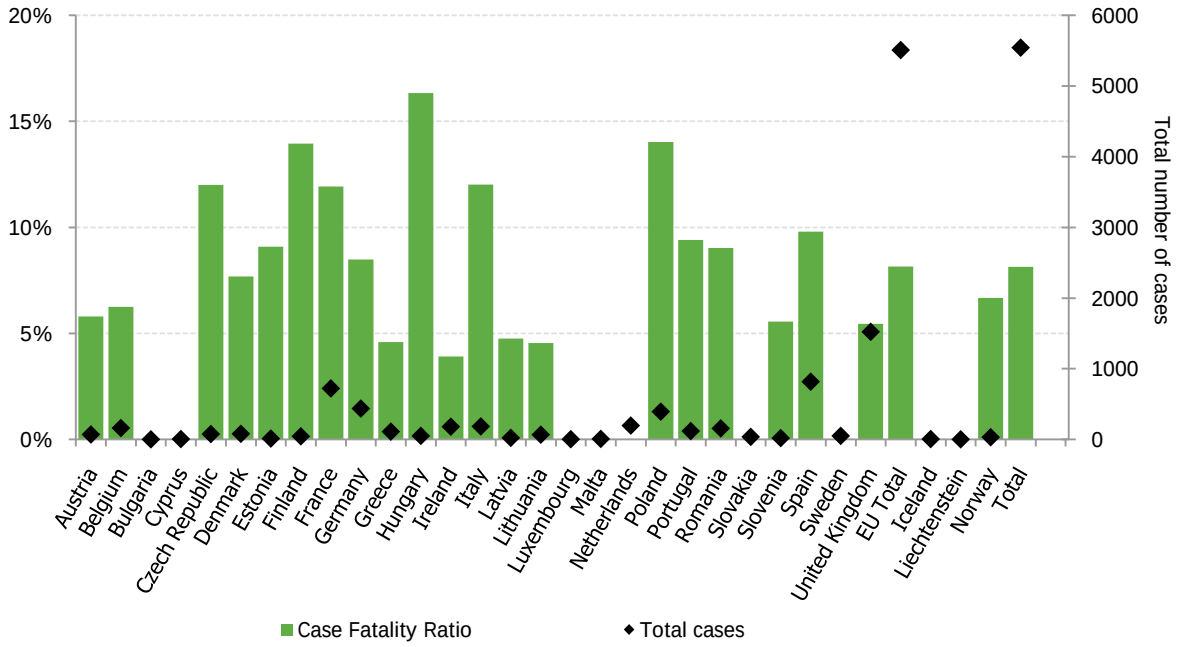
Contributing countries: Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, United Kingdom

4.3.10 Case fatality ratio

The CFR for the total number of cases reported in 2007 is shown in Figure 36.

The overall CFR in Europe was 8.1% in 2007, slightly higher than that reported in 2006 (7.7%). Outcome data were lacking from three countries, while one country did not submit any data. However, the highest CFRs were found in Hungary (16.3%) and Poland (14%) and the lowest reported in Ireland (3.9%). There were no deaths reported by Cyprus, Malta, Iceland, Slovakia and Luxembourg. When interpreting this table it is important to bear in mind that countries with a very low notification rate of disease but high fatality ratio might indicate a bias in their reporting systems towards focussing on the more severe cases, while the opposite may indicate a situation where deaths were occurring after the disease was notified. In this analysis, it was assumed that those cases whose outcome was unknown did in fact survive since it is more likely to be informed of a patients' death than of their survival.

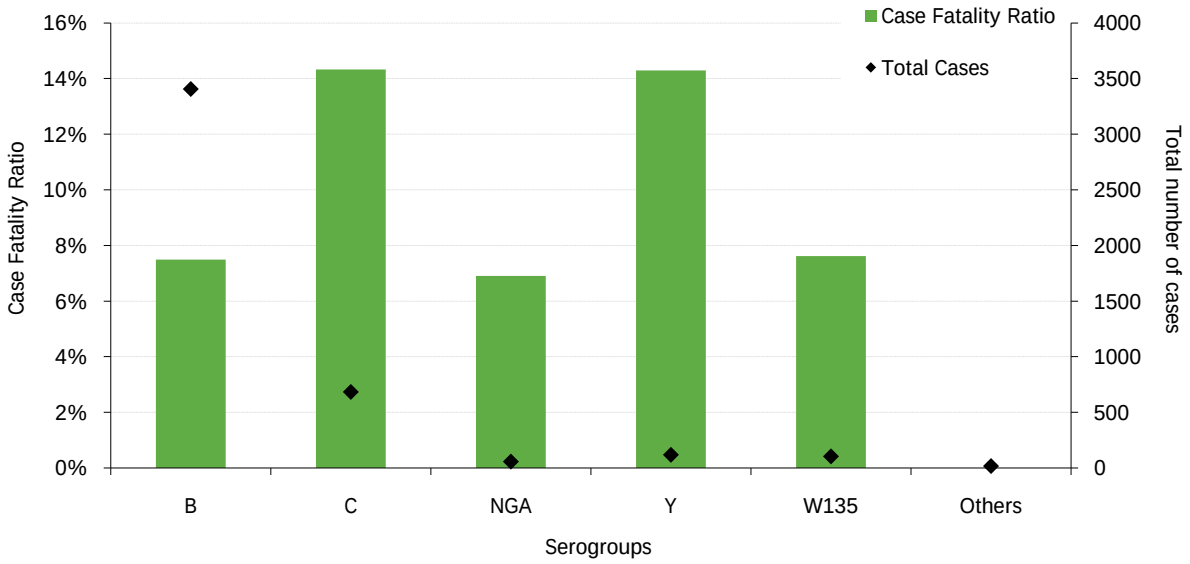
Figure 36: Case fatality ratio and total number of invasive meningococcal disease cases, by country, 2007* (n=5545)



**Case fatality ratio using all reported cases as denominator; No cases reported: Liechtenstein: No outcome reported: Bulgaria, the Netherlands, Sweden. No death reported: Cyprus, Luxembourg, Malta, Slovakia, Iceland*

Figure 37 shows the CFR by serogroup in 2007. While the highest number of deaths were reported among serogroup B, the case fatality ratio was twice as high for cases due to serogroup Y (CFR= 14.3%) and due to serogroup C (CFR= 14.3%) than that of serogroup B (CFR= 7.5%).

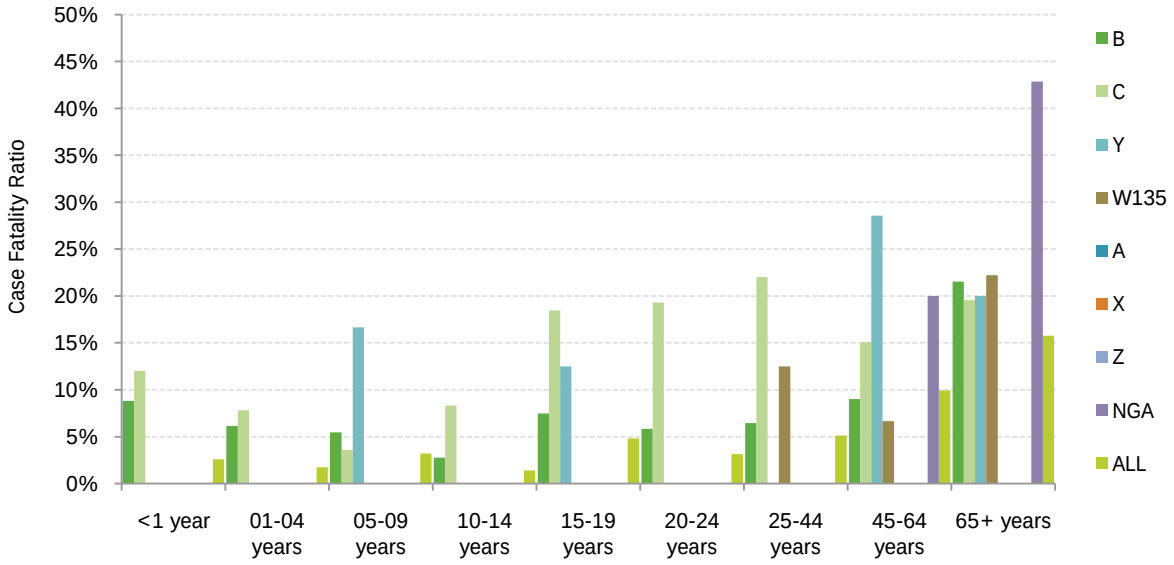
Figure 37: Serogroup specific case fatality ratio of invasive meningococcal disease cases in all countries for which outcome data is available, 2007* (n=4390)



Contributing countries: Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, United Kingdom.
**Serogroup specific case fatality ratio using all reported cases with data on serogroup as denominator.*

The effect of age and serogroup on CFR is illustrated in Figure 38. Overall, CFR increased with age, with the over 65 year age group suffering an overall CFR of 15.7%, and the lowest overall CFR of 1.3% being in the 10–14 year-old age group. In the age groups younger than 45, the highest CFR was reported in disease caused by the serogroup C for the 4–9 year old age group. Outcome was reported as unknown in 9% of cases.

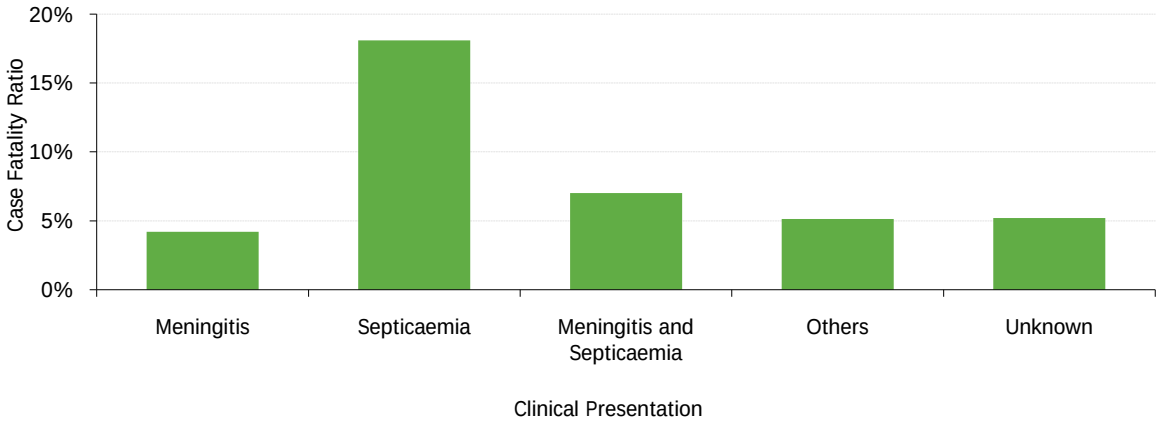
Figure 38: Age and serogroup specific case fatality ratios of invasive meningococcal disease cases* in all countries for which outcome data is available, 2007 (n=4 305)



Contributing countries: Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, United Kingdom.
**Age and Serogroup specific case fatality ratio using all reported cases with data on serogroup and age as denominator.*

Figure 39 shows the percentage distribution of CFR by clinical presentation in 2007. The highest CFR was reported among cases reported as septicaemia (18%). Those who presented with meningitis had a much lower CFR (4.2%).

Figure 39: Case fatality ratio by clinical presentation of invasive meningococcal disease cases all countries, 2007 (N=5545)



Contributing countries: Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, United Kingdom

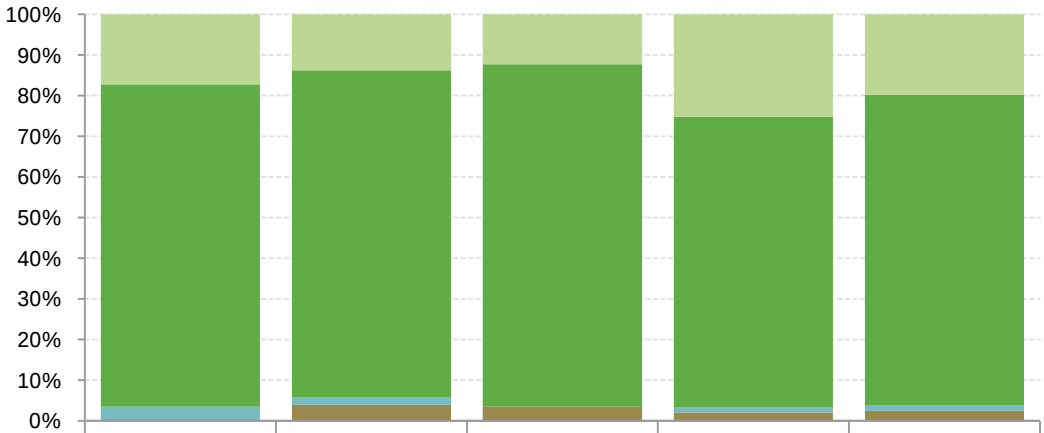
4.3.11 Vaccination status

As described in the method section, the currently available dataset does not allow estimates of true vaccination failure. Therefore, only the number and proportion of reported vaccination status are summarised here.

Figure 40 shows the vaccination status by age group among serogroup C cases in 2007, including all meningococcal, conjugate and polysaccharide vaccines. The total percentage of vaccination status reported as unknown was significantly high (77%), with the largest proportion in age groups over 15 years old.

Not surprisingly, the highest proportion of cases occurred among those reported as not vaccinated. The highest proportion of vaccinated cases (4%) was reported in those aged 1–4 years.

Figure 40: Vaccination status by age group among serogroup C invasive meningococcal disease cases, all countries, 2007 (N=284)



	<1 year	1-4 years	5-14 years	>=15 years	Total
Unknown	17%	14%	12%	25%	20%
Not vaccinated	79%	80%	84%	71%	76%
Partly vaccinated	3%	2%	0%	1%	1%
Fully Vaccinated	0%	4%	4%	2%	2%

Contributing countries: Belgium, Denmark, Estonia, Hungary, Ireland, Italy, Lithuania, Malta, Norway, Poland, Portugal, Romania, Slovak Republic, United Kingdom
Fully vaccinated = according to age and the recommended schedule in the reporting country.
Partly vaccinated, = according to age and the recommended schedule in the reporting country.
Not vaccinated = not vaccinated at all
Unknown = Vaccination status unknown

Table 27 shows the vaccination status by countries. Unfortunately, as already mentioned, several countries reported this variable as 100% unknown. Relatively complete information was made available by Portugal and Ireland only.

Table 27: Vaccination status of invasive meningococcal disease cases, by country, 2007

Country	Fully vaccinated	Partly vaccinated	Not vaccinated	Unknown	Total
Austria	0 (0%)	0 (0%)	0 (0%)	69 (100%)	**69**
Belgium	18 (11%)	0 (0%)	41(26%)	101(63%)	**160**
Bulgaria	-	-	-	-	**0**
Cyprus	1 (25%)	0 (0%)	0 (0%)	3 (75%)	**4**
Czech Republic	0 (0%)	0 (0%)	0 (0%)	75 (100%)	**75**
Denmark	2 (3%)	0 (0%)	36 (46%)	40 (51%)	**78**
Estonia	0 (0%)	0 (0%)	11 (100%)	0 (0%)	**11**
Finland	0 (0%)	0 (0%)	0 (0%)	43 (100%)	**43**
France	0 (0%)	0 (0%)	0 (0%)	721(100%)	**721**
Germany	0 (0%)	0 (0%)	0 (0%)	436 (100%)	**436**
Greece	0 (0%)	0 (0%)	0 (0%)	109 (100%)	**109**
Hungary	0 (0%)	0 (0%)	49 (100%)	0 (0%)	**49**
Ireland	1 (1%)	0(0%)	158 (88%)	20 (11%)	**179**
Italy	3 (2%)	0 (0%)	72 39%	108 (59%)	**183**
Latvia	0 (0%)	0 (0%)	0 (0%)	21 (100%)	**21**
Lithuania	0 (0%)	0 (0%)	56 (85%)	10 (15%)	**66**
Luxembourg	0 (0%)	0 (0%)	0 (0%)	2 (100%)	**2**
Malta	0 (0%)	0 (0%)	6 (100%)	0 (0%)	**6**
Netherlands	0 (0%)	0 (0%)	0 (0%)	195 (100%)	**195**
Poland	0 (0%)	5 (1%)	387 (99%)	0 (0%)	**392**
Portugal	74 (63%)	0 (0%)	11 (9%)	32 (27%)	**117**
Romania	0 (0%)	0 (0%)	155 (100%)	0 (0%)	**155**
Slovakia	0 (0%)	0 (0%)	29 (83%)	6 (17%)	**35**
Slovenia	0 (0%)	0 (0%)	0 (0%)	18 (100%)	**18**
Spain	0 (0%)	0 (0%)	0 (0%)	816 (100%)	**816**
Sweden	0 (0%)	0 (0%)	0 (0%)	49 (100%)	**49**
United Kingdom	69 (5%)	16 (1%)	65 (4%)	1372 (90%)_	**1522**
EU Total	**168 (3%)**	**21 (0%)**	**1076 (20%)**	**4246 (77%)**	**5511**
Iceland	0 (0%)	0 (0%)	0 (0%)	4 (100%)	**4**
Liechtenstein	-	-	-	-	**0**
Norway	0 (0%)	0 (0%)	19 (63%)	11 (37%)	**30**
Overall	**168 (3%)**	**21 (0%)**	**1095 (20%)**	**4261 (77%)**	**5545**

4.3.12 Vaccination schedules

Before the introduction of the MCC vaccine, the polysaccharide meningococcal vaccine was the only vaccine available against the disease caused by serogroup C. Vaccination with polysaccharide preparations is not recommended for the general population because of the short term protection it confers and poor immunogenicity in children younger than two years. Three different single MCC vaccines are currently available, two of which are conjugated to diphtheria and the other to tetanus toxoid.

Tetravalent conjugate vaccine against serogroup A, C, W135 and Y has recently been licensed and recommended for the use in adolescents in USA (Center for Disease Prevention and Control (CDC) 2005).

In 2007, serogroup B caused the majority of invasive meningococcal cases. At present, there are no effective vaccines with a serogroup B component suitable for routine immunisation. However, several conjugate vaccines are now in phase three trials and it is likely that some of them will be available on the EU market in the forthcoming years.

The first MCC vaccines were licensed and have been in used in Europe since 1999.

The countries that have introduced MCC vaccination to date are those that experienced the highest burden of serogroup C disease. The UK was the first country to introduce MCC vaccination followed by Ireland and Spain (both in 2000). Subsequently the Netherlands, Belgium, Iceland (all 2002), Portugal and Germany (both in 2006) included the MCC vaccination into the routine infant immunisation schedule. A further two countries, Greece and Luxembourg, incorporated the vaccination into the national vaccination calendar in 2007. Italy introduced the vaccination into the routine vaccination schedule in 2005 for selected groups only.

Meningococcal C conjugate national vaccination schedules vary quite widely across Europe and are frequently changing in keeping with new scientific evidence.

The majority of the countries offer two alternatives: the infant schedule or a single dose of vaccine in the second year of life. In some of the countries (the UK and Iceland), the infant schedule is used in order to protect infants, and in other countries (Belgium, the Netherlands, Luxembourg) only a single dose is offered in the second year of life.

Due to the secondary peak of serogroup C reports in teenagers, the majority of the countries have conducted catch-up campaigns in these age groups.

The routine vaccination schedules and details of catch-up campaigns in these countries and the use of MCC vaccine in other European countries are summarised in Tables 28a and 28b.

Table 28a: Conjugate meningococcal group C vaccination programmes in European countries. Countries with routine vaccination, 2007

Country	Routine schedule	Year introduced	Catch- up	Year undertaken
Belgium ¤	13-18 month	2002	1 years -17 years	2001 - 2004
Germany	12-13 month, one dose in the 2nd year of life	2006	General recommendation to complete all outstanding vaccinations, including MCC in older children	
Greece	2, 4, 15-18 month one dose in the 2nd year of life	2007	No info	
Iceland	6-8 month	2002	6 month -19 years	Oct 2002 - Oct 2003
Italy ¤	Between 2 month and 2 years	2005	-	-
Ireland ¤	4, 6 and 13 month one dose in the 2nd year of life	2000	< 23 years	Oct 2000 - March 2002
Luxembourg	13 month	2007	No info	
Netherlands	14 month	2002	1 year- 18 years	June 2002 – Nov 2002
Portugal	3, 5 and 15 month	2006	<10 years 10 years-18 years	Jan 2006 - Dec 2006 Jan 2007- Dec 2007
Spain ¤	2, 6 month booster dose from the age of 12 month	2000	7 month -19 years	2001-2004
UK ¤	3, 4, 12	1999	<18 years 19 years-25 years	November 1999 - 2000 December 2001- 2002

Source: EUVAC.NET (January 22nd 2009); Report EU IBIS 2006
¤ = Historical changes: BE: 2002-2006: 12 months; IR: 2000-2006: 2, 4, 6 months; UK: 1999-2006: vaccination schedule: 2, 3, 4 months; ES: 2000-2006: 2, 4, 6 months; IT: for selected groups only

Table 28b: Conjugate meningococcal group C vaccination programmes in European countries. Countries with voluntary vaccination, 2007

Country	Given to Travellers	Contacts of cases	Outbreak control	Underlying conditions	Other	Year introduced
Czeck Republic	Yes	Yes	Yes		On request	2001
Hungary	Yes		Yes	Yes	On request	2000
Norway	Yes	Yes				
Poland		Yes	Yes	Yes	Generally recommended	
Sweden			Yes		On request	

Source: EUVAC.NET (22 January 2009); Report EU IBIS 2006
Countries comment: HU:

5 Discussion

This was the first data collection after the transition of the EU surveillance activities on invasive bacterial infections from EU-IBIS to ECDC. Although the whole transition was successful due to the good collaboration between the hub coordination of EU-IBIS and the surveillance unit at ECDC, it has been a challenging first time data call with submission of data from the MS to TESSy.

5.1 Case definitions

The EU case definition changed twice over the past few years for both *N. meningitidis* and *H. influenzae*, and an equal amount of countries applied the EU case definition 2002 version and 2008 version, while there was information lacking from a few numbers of countries. The use of different case definitions did, however, not affect the data analyses of invasive *H. influenzae* disease as there was no distinction made distinguish between probable and confirmed cases in the analyses. This occurred because probable cases in the 2002 case definition are considered confirmed in the 2008 case definition.

In the interest of the best possible data comparison for invasive meningococcal disease, analyses were based on two inclusion criteria: confirmed and probable laboratory cases for the analyses of laboratory variables, and classification criteria of confirmed, probable and possible for the epidemiological analyses. These two criteria were used to overcome the difference between the 2002 and 2008 case definitions.

From the next data call, countries are supposed to report using only the 2008 EU case definition; this will increase data comparability.

5.2 Data sources

The general overview of national surveillance systems reveals a heterogeneous situation for both diseases. Of the 30 countries reporting, most data came from surveillance systems working on the general population; nevertheless, there are differences in terms of age groups under surveillance, sensitivity of the systems, laboratory methods used for case confirmation, completeness information on clinical symptoms and outcome, and reliability of information on vaccination status collected. In some countries, the system collects data for certain serotyping only with regard to *H. influenzae* cases and mainly for some clinical pictures (i.e., meningitis) with regard to *N. meningitidis* cases.

These differences between the surveillance systems in the MS complicate comparative analyses. In addition, changes in the systems over time and improvement in case ascertainment further complicated the comparability of trend data, even within countries.

At the time of the analyses, ECDC did not have a full overview of the surveillance systems in place. Therefore the inclusion criteria for different analyses followed what was stated in the EU-IBIS report from 2006 and according to its consistency with the reported data from 2007. However, only countries with consistent reporting over the years have been included for trend analyses. In 2007 some countries, such as the Netherlands and France (with regard to *H. influenzae* cases), did not provide data although they had done so previously until 2006. Therefore, the number of countries with consistent reporting during 1999–2007 was actually less in 2007; consequently the UK data contributed as majority (59.3%) of the total number of cases included in the trends, providing some bias in the interpretation of the results of the analysis.

Based upon the information above, inferences on the difference observed between MS have to be made with caution. It is expected that the data comparability will gradually improve in the coming years as MS move towards a common EU surveillance system.

5.3 Laboratory test methods

One of the objectives of IBD surveillance is to monitor circulating strains in order to detect any modification in phenotype and genotype characteristics of the more commonly observed strains. Laboratory surveillance can also serve to monitor the circulation of emerging strains and any serotype replacement due to the selective pressure of vaccines. Therefore, a high completeness of laboratory data is desirable for accurate epidemiological analyses.

The availability of the laboratory methods have been increasing over the years and more and more countries are able to perform sophisticated laboratory tests for molecular typing of *N. meningitidis* in particular; nevertheless, only a minority of countries reported this kind of information to the EU level.

Culture was the most frequently reported laboratory method for both diseases, and consisted of 82% of the total reported tests methods (n=1424) for *H. influenzae* and 39% of the total reported tests methods (n=6851) for *N. meningitidis* (missing information for methods used for case confirmation in 22% of *N. meningitidis* cases).

Information on molecular methods was reported in 19% of cases; this is a significant achievement, but their routine use for case identification in surveillance appears to be limited in the majority of MS.

However, the feedback received by many MS during the validation period of the data call indicated that the descriptions of the variables related to the test method used, and its link to a particular specimen provided a certain level of confusion and may have been interpreted differently in different MS.

Therefore, even if information on further test methods performed would have been available in MS, only information on the test methods used on the first specimen taken for case confirmation was reported.

The description about the variables related to the specimen collected and the test method used would benefit further simplifications and standardisation before the next data call in order to obtain valid and utilisable data.

5.4 Completeness of surveillance data

The completeness of reporting varied greatly between variables and across countries.

With regard to invasive *H. influenzae* disease, a total of 12 variables were reported as 100% unknown by 2–14 countries, while a total of 14 variables were reported as 100% unknown by 2–15 countries for invasive meningococcal disease.

The variables 'Laboratory Result', 'Clinical Criteria' and 'Epidemiological Link' are included in the common set of variables and linked to the case classification and the used case definition. However, in the surveillance of invasive *H. influenzae* disease, these variables are not all applicable. If using the 2008 EU case definition, both 'Clinical Criteria' and 'Epidemiological Link' are non-applicable and should therefore have been reported as such. Another example is the variable of the second laboratory specimen (Specimen2) which, as described above, is not applicable for the laboratory analyses of *H. influenzae*.

This was the first data call using the new metadata set. Several lessons were learned and a revision of the metadata set will be carried out prior to the next data call. This may include a removal or change of certain variables, changes/additions in codes of the variables, and development of further automatic validation rules when uploading the data.

With a vaccine available for just one of the *H. influenzae* serotypes and with a vaccine that does not yet cover *N. meningitidis* cases due to serogroup B, quality strain data is one the most important features in IBI surveillance, for the potential risk for strain replacement and/or capsule switching.

The large proportion of missing data for *H. influenzae* cases, covering about 60.4% of all reported cases, markedly reduced the validity of the surveillance data submitted. It is also important to note that countries reporting 100% unknown serotype were excluded in the serotype analyses, while the serotype data from countries with a large proportion of reported unknown serotype provide an important bias. Typing of strains is carried out in the majority of the MS, and this is another priority for the coming years to increase the level of completeness in serotype reporting

With regard to invasive meningococcal disease cases, information on serogroup was available (79%) in almost all MS, but further molecular typing characterisation was reported for less than 40% of cases. Information on serosubtype using serological analysis (VR1 and VR2 variables) were reported in 30% of cases while information on serosubtype using genotyping methods (PorA1, PorA2, PorA3 variables) were reported as unknown with a range lying between 90–98%. Information on MLST was reported as unknown in 96% of cases.

5.5 Epidemiology of invasive *Haemophilus influenzae* disease

5.5.1 Overall notification rates

Invasive *Haemophilus influenzae* is a rare disease, with an overall notification rate in all EU and EEA countries of 0.41 per 100 000 population. The impact of the Hib vaccine has proven to be continuously successful. Being a rare disease, small changes in numbers may cause large differences in notification rates in the smaller countries, which always need to be taken into account when examining the data. The performance of the surveillance system and its level of sensitivity and population coverage also influence greatly the country comparisons.

Higher rates were observed in the Nordic countries compared to the rest of Europe, and with a continued increasing trend. This had been observed and explained already in previous EU-IBIS reports as being most likely

due to the improved quality of the surveillance system with an enhanced case ascertainment in these countries. For example, in Sweden, only serotype b was notifiable until July 2004. Thereafter, all serotypes were made obligatory to be reported which is the main attributable factor to the observed rapid increase in 2005. The continued increase could be explained by a finding in a previous sensitivity analysis of the Swedish statutory surveillance system, which describes a delay of several years until a new notifiable disease reaches a level of acceptable sensitivity. This delay is probably attributed to the level of awareness among physicians and laboratories reporting a case. In 2007, there was also a questionnaire sent out to physicians regarding clinical information of invasive *H. influenzae*, which probably increased the awareness as well.

In addition to the inclusion of all serotypes into the system (as in Sweden), a number of additional factors could explain the changes in serotype distribution observed in these countries:

- A true increase in the non-capsulated strains;
- Increased proportion of serotyping in the laboratories/increased completeness of serotype reporting; or
- Enhanced laboratory methods with an improved detection of non-capsulated strains (combined with automatic notification system).

Unlike Sweden, both Finland and Norway have had stable surveillance of invasive *H. influenzae* disease for many years. Denmark reported a large increase in overall notification rates in 2007. However, up until 2006, only meningitis (clinical presentation) was reported, while from 2007, all invasive infections caused by *H. influenzae* are now reported. No increase was observed when comparing the number of reported meningitis cases only.

The notification rates in Estonia are continuing to decrease, mainly explained by the Hib vaccine introduced in 2005.

5.5.2 Age distribution

The overall mean age of invasive *H. influenzae* was 51.3 years with a median age 61 years, reflecting that the age group of 65 years and over is the most affected group in terms of absolute numbers. Compared to previous years an increase was observed, especially in the non-capsulated strains, which also caused the highest case fatality rates in this age group. Sweden and Norway reported the highest rates, and improved case ascertainment could well be the reason for the increase in reported cases, as already mentioned. In the USA, the incidence of invasive *H. influenzae* disease increased from 1996 to 2004, and its epidemiological characteristics changed from a disease predominantly found in children and dominated by serotype b to a disease predominantly found in adults and dominated by non-typeable strains.

This phenomenon would be interesting to investigate further in Europe.

Infants younger than one year of age had the highest observed notification rates, with the highest rates reported from Ireland, Norway and the United Kingdom.

5.5.3 Serotypes

Non-capsulated strains were the most frequently reported serotype during the period 1999–2007, with a significantly increasing trend over recent years. In 2007, it was also the most frequently reported strain across all age groups, apart from the 1–4 year-olds. These results are consistent with what was described in the previous section. There have been some concerns regarding the replacement of the *H. influenzae* serotype in populations where the conjugated Hib vaccine has been introduced, but so far there do not appear to be indications of any increase among the capsulated non-type b strains in the EU. Moreover, despite the statistically significant trends in the increase in the non-capsulated strains, there are too many influencing factors that may bias the data and do not allow any inferences to be made with confidence. One such factor is the low completeness of reported serotypes; another is the small sample of countries with stable surveillance systems and consistent reporting. The issue of serotype replacement was discussed by Ramsay et al in The Lancet in 2008, concluding that there is no evidence for *Haemophilus influenzae* serotype replacement in Europe up until 2004. However, the continued increasing trend is an important observation, and will need to be followed up.

Serotype b is continuing to decrease, but still was the most commonly reported strain in the age group of 1–4 years. However, this finding may cause some concern as it appears to imply that vaccine effectiveness declines after the primary immunisation course in the first year of life. The large proportion of cases reported were reported from the UK (71.7%, 33 out of 46 cases), and this strongly influenced the high numbers of cases in this age group. In 2003, there was a successful vaccination campaign in the UK that reduced the small but steady increase in cases of invasive Hib disease in young children, which had been observed since 1999. However, as illustrated in this report, the rates did not return to previous levels as was expected. Therefore, a booster dose of Hib vaccine for all children at 12 months of age was introduced into the British routine childhood immunisation programme in September 2006, (as a combined Hib/MenC vaccine). At the same time, a booster catch-up campaign was organised, starting from September 2007 and ending in March 2009. This campaign aimed to protect the cohort of children who were either too young to have been offered a Hib booster in the 2003 national campaign, or too old to have been offered the routine Hib booster delivered as a combined Men C/Hib conjugate vaccine at 12 months

of age since September 2006. Therefore, the Hib rates in this age group are anticipated to decrease in the next coming years.

In contrast to their overall high notification rates, the Nordic countries reported some of the lowest notification rates of serotype b, indicating achievements of their effective national immunisation programmes.

5.5.4 Clinical presentation

Exactly 50% of case-based reported cases were lacking information on clinical presentation, which somewhat reduced the validity of this analyses. As expected, septicaemia accounted for the largest proportion of the reported cases (55.7%), with the majority occurring in the oldest age group. It is well known that it is often the most severe cases of this disease that are reported, with many countries reporting only meningitis or meningitis/septicaemia, mainly based on hospital data only, and this will tend to bias this data.

The presentation of epiglottitis has nearly disappeared after the introduction of the Hib vaccine, and was so far not included as a category (code) in the variable 'clinical presentation'. However, although it is a rare presentation, it is still known to occur. Moreover, there are still two countries in EU who have not implemented vaccination, and epiglottitis may still be a relatively frequent clinical presentation in these countries. There will be some discussion on whether this needs to be included in the metadataset for future data calls.

5.5.5 Case fatality ratio

Outcome was reported as known in 59% of the invasive *H. influenzae* cases, and the calculations of case fatality ratio are most likely an underestimate of the actual CFR in EU, this due to the inclusion of cases with unknown outcome in the analyses. In addition, a number of countries expressed doubts regarding the quality of the outcome data which would weaken the estimations of CFR. This is applicable to both invasive bacterial diseases.

Based upon the available data, the overall CFR was 9.65% (121 deaths) and highest among the non-capsulated strains in the oldest age group (21.4%). In total, 16 deaths (CFR 8.7%) were reported among serotype b, with four deaths among children younger than five years of age: one was reported as fully vaccinated, one partly and the other two unknown.

5.5.6 Vaccination status

Based on the variables currently collected, it is not possible to analyse vaccination data for the determination of true vaccine failures of any of the two invasive bacterial diseases, as the following variables are missing in order to do so: birth date, number and dates of doses. There will be further discussions among national surveillance ECDC focal points on how to best follow up true vaccine failures at the EU level; this will remain a priority for the coming years in combination with higher completeness of serotype reporting.

In any population with high vaccination coverage, the majority of observed cases are expected to be vaccinated. However, in 2007, the proportion of cases in vaccinated patients was found to be highest in the age group of 1–4 years, which is mainly explained by the situation described above in the UK. Consequently, the 1–4 year old age group accounted for 63% of the total number of cases among those reported as fully vaccinated.

5.5.7 Vaccination schedule

The Hib vaccine is included in all national immunisation programmes expect for Bulgaria and Romania. Since Bulgaria reported aggregated data (with a limited set of variables), and Romania does not yet have a surveillance system in place for invasive *H. influenzae* disease, it is as yet unclear just how much of a problem invasive Hib disease is in these two countries.

The vaccination schedules continue to vary between the countries, both in number of doses and ages (see Table 15 of Hib vaccination schedules).

5.6 Epidemiology of invasive meningococcal disease

5.6.1 Overall notification rates

In 2007, 5183 cases of invasive meningococcal disease were reported in the EU with an overall incidence of 1.1 per 100 000, which indicates an important decline compared to the rates reported 8–9 years earlier.

A considerable variability in the overall notification rate across Europe has been observed.

The disease remains quite rare, with the majority of the countries reporting a notification rate of between 0.6 and 2.00/100 000 (a notification rate of less than 0.6/100 000 was registered in seven countries). However, Ireland and the UK still experience relatively high rates (4.1/100 000 and 2.1/100 000, respectively).

This variation in rates might reflect real differences, but might be also due to the sensitivity and the population coverage of the surveillance systems in place. For more explanations of these variations, a better understanding of data sources along with a better awareness of healthcare practices regarding blood culture sampling availability at the Member State level would be required.

5.6.2 Age groups

Infants and children still experienced the highest rates of invasive meningococcal disease cases. Of the 5564 cases with a known age, 50% were reported in children younger than 10 years. The highest rates in infants younger than one year were reported from Ireland and United Kingdom, with rates of 74.5/100 000 and 46.6/100 000 respectively.

The high number of cases, which is still being observed in age groups targeted by the vaccination programmes, needs to be further investigated. Cases due to serogroup C observed in countries with MCC vaccination should be especially followed up meticulously to identify any vaccine failure cases due to waning immunity after the primary immunisation, as this might be attributed to the type of the schedule and or the co-administration with other antigens.

5.6.3 Serogroups

As shown in Table 17, the proportion of cases with missing serogroup information remains high (21%). As in previous years, the most frequent serogroup causing invasive meningococcal disease in Europe in 2007 was serogroup B, which was especially prevalent in those younger than four years old (Figure 24). In countries with MCC vaccination, the proportion of cases due to serogroup C dramatically decreased by increasing the number of years post vaccination. This was not the case in countries where vaccination against serogroup C is not included in the routine vaccination schedule; for example in Sweden, Poland, Italy and Austria, the proportions of B and C cases were very similar. Similarly, the proportion of B cases in countries with MCC vaccination was high in all age groups and, in particular, in children aged 0–4 years old (Table 20) who would normally be the target group for vaccination against serogroup C.

Although the proportion of C cases remained low in infants younger than one year, the proportion of serogroup C cases was seen to increase with age. This can be explained by the lower vaccine coverage in the older age groups, as well as by the decrease in the effectiveness of vaccine following the year of the primary immunisation schedule [6].

The difference in notification rates in those younger than four years of age in countries with and without MCC vaccination is quite impressive and shows the substantial impact of the vaccination in reducing the burden of the disease in EU.

Cases due to serogroup Y were mainly observed in Scandinavian countries (Sweden, Finland and Norway) and among older age groups. This could be explained by good laboratory surveillance and good case ascertainment in these countries, past and present travel choices by the Scandinavians, or by a true circulation of this serogroup especially in this area.

Serogroup identification has improved over the years and, as a result, the number of unknowns for this variable has decreased substantially over the last five years, from 1448 to 559 cases.

5.6.4 Serotypes and serosubtypes

Despite the low number of serotype data submitted, a clear association between certain serogroups and serotypes is evident.

There was much less variability in serotypes for serogroup C than for serogroup B and certain serotypes (P3_4, P3_14, P3_1, P3_15 and P3_22) tend to cluster with serogroup B, whereas serotypes P2_2a and P2_2b are more frequently associated to the serogroup C.

Comparing the distribution of serotypes among serogroup C cases in countries with or without MCC vaccination, the diversity of serotypes and the proportion of non-typeable cases was much higher in non-MCC countries while the proportion of P2_2b and P2_2a strains was higher in countries with MCC vaccination.

Information on serotyping and subtyping of strains is increasing due to the adoption of molecular technologies in more and more countries, but the number of samples serotyped and serosubtyped reported still remains low and any interpretation of these results must be done with care.

The highest numbers of serosubtyped cases were reported by France (114) and Poland (99) with regard to serogroup C and by France (290), United Kingdom (44) and Belgium (36) with regard to serogroup B. The most prevalent serosubtype was P1.5:NST:NST (86) for serogroup C and B:1.4 (n=283) followed by the B:1.14 (n=166) for serogroup B.

5.6.5 Clinical presentation

The variable 'clinical presentation' was not always collected at the national level. A total of 43% of the cases reported lacked information on clinical presentation, which affected the validity of the analyses.

As expected, the top two clinical manifestations of invasive meningococcal disease reported in 2007 were septicaemia (23%) and meningitis (23%).

Septicaemia was the most common presentation in the younger age groups, varying between 41–47% in those younger than nine years of age. Meningitis was most frequently reported in the older age groups with a peak (52%) in those aged 25–44 years.

Meningitis and septicaemia were reported in roughly equal proportions among serogroups B and C. It is clear that these data need to be interpreted with caution as in some countries meningitis is mainly reported, while the proportion of sepsis cases notified is heavily influenced by the health practices in MS and is likely to be underreported. A better understanding of surveillance systems is required in order to explore the different practices of reporting in place in different MS.

5.6.6 Case fatality ratio

The outcome was reported in 91% of the cases and, as mentioned previously, due to the inclusion of cases with unknown outcome the CFR might be underestimated especially in countries with a high per cent of unknown outcome.

The overall CFR was 8.1% and ranged between 3.9 and 16.3%. The highest CFR in countries with low notification rates may indicate a bias in their data towards reporting the most severe cases. Similarly, the low CFR in countries with high notification rates may indicate that their system has a higher sensitivity.

As shown in Figure 40, disease caused by serogroup C (14.3%) appears to be more likely to cause death then that due to serogroup B. However these data may be biased as, in certain countries, the emphasis is on reporting deaths mainly among older age groups.

5.6.7 Vaccination status and vaccination schedule

The prevention of meningococcal disease depends greatly on effective vaccination on a large scale. Although polysaccharide vaccines have been available for serogroup A, C, Y and W135 for many years in several European countries, serogroup C polysaccharide–protein conjugate vaccines have only recently been licensed and introduced in Europe and less than half of the countries have been included this vaccination in their routine national schedule.

At the end of 2007, eleven countries had implemented routine MCC vaccination and all of these countries experienced substantial declines in the incidence of serogroup C over the years.

Unfortunately, it was not possible in this report either to analyse in depth vaccine failures or to make inferences on the proportion of cases among vaccinated individuals in countries with and without vaccination. This is because of the proportion of missing values for vaccination status was 77% and only Portugal and Ireland reported complete information. In addition, information on date of birth, number of doses received and date of the last dose were not collected.

5.7 Conclusions

- Comparisons between countries, in particular their notification rates and trends, need to be made with caution at this stage. Differences in notification rates between the MS are influenced by the diversity of their surveillance systems, to the case definition applied, variation in vaccination policies, and to the different test methods used for confirming a case.
- Encouraging MS to apply the 2008 case definition in order to facilitate data comparability is an important step.
- In order to achieve the long-term objective of good comparability of data, there is a need for deeper knowledge and insight of the different surveillance systems in the EU.
- The main purpose of the surveillance of these diseases is to monitor not only epidemiological trends but also to describe the circulation of emerging strains and any potential changes in the strains usually circulating (bearing in mind the risk for serotype replacement and capsule switching). Therefore, a high level of completeness of laboratory data is required to achieve these aims.
- The low completeness of reported serotypes of *H. influenzae* and of *N. meningitidis* in 2007 considerably affected the validity of the data and subsequently the results.
- In order to improve the data comparability between the reporting countries, better standardisation of the laboratory methods used for identifying a case is required.

- Genotyping methods will most likely become more and more feasible for routine use in European countries and they will be very helpful in providing reliable and exhaustive information on circulating strains. To best obtain these data, closer collaboration between the laboratories and the epidemiological centres at national level will be needed.
- In this light in 2009, the IBD metadataset has been modified including information on the following molecular typing data: PorA VR1, PoR A VR2, FetA VR, clonal complex (MLST). On the Neisseria.org website[2], the list of codes for each of these variables is available and daily updated. The implementation of a new metadataset has been done in collaboration with the experts in the reference national laboratories and will be used for the 2008–09 data call.
- Many of the EU countries have, over the last few years, enhanced their surveillance systems. It is expected that in the coming years they will be able to provide good quality data with a high level of completeness. This should facilitate data comparability between countries and, over years, within countries.

[2] http://neisseria.org/nm/typing/tessy/

References

1) Ladhani S, Ramsay ME, Chandra M, Slack MP, EU-IBIS. No evidence for Haemophilus influenzae serotype replacement in Europe after introduction of the Hib conjugate vaccine. Lancet Infect Dis. 2008 May;8(5):275–6

2) WHO. WHO position paper on Haemophilus influenzae type b conjugate vaccines. Wkly Epidemiol Rec 2006; 81: 445–52

3) Ladhani S, Heath PT, Slack MP, McIntyre PB, Diez-Domingo J, Campos J, Dagan R, Ramsay ME, EU-IBIS Network. Haemophilus influenzae serotype b conjugate vaccine failure in twelve countries with established national childhood immunization programmes. Clin Microbiol Infect. 2009 Nov 4

4) Aracil B, Slack M, Pérez-Vázquez M, Román F, Ramsay M, Campos J. Molecular epidemiology of Haemophilus influenzae type b causing vaccine failures in the United Kingdom. J Clin Microbiol. 2006 May;44(5):1645–9.

5) Borrow R, Miller E. Long-term protection in children with meningococcal C conjugate vaccination: lessons learned. Expert Rev Vaccines. 2006 Dec;5(6):851-7. Review

6) Heyman D. (ed.), the control of communicable diseases manual: an official publication of the American Public Health Association. 18. ed., 2004. Washington, D.C.: The Assoc.

Bibliography

Dworkin, M.S., L. Park, and S.M. Borchardt, The changing epidemiology of invasive Haemophilus influenzae disease, especially in persons > or = 65 years old. Clin Infect Dis, 2007. 44(6): p. 810-6.

EU-IBIS Network. Invasive Haemophilus influenzae in Europe 2006. Health Protection Agency, London 2006. Available from www.euibis.org

EU-IBIS Network. Invasive Neiserria Meningitides in Europe 2006. Health Protection Agency, London 2006. Available from www.euibis.org

EU-IBIS Network. Transition document and Standard Operating Procedure 2007. Health Protection Agency, London 2007.

Harrison's principals of Internal Medicine. 17th ed./editors, Anthony S. Fauci...[et al] 2008 McGrowHill

Heymann, D. (ed.), the control of communicable diseases manual: an official publication of the American Public Health Association. 18. ed., 2004. Washington, D.C.: The Assoc.

Jansson A, Arneborn M, Ekdahl K. Sensitivity of the Swedish statutory surveillance system for communicable diseases 1998-2002, assessed by the capture-recapture method. Epidemiol Infect. 2005 Jun; 133: 401-7.

Ladhani S, Ramsay ME, Chandra M, Slack MP; EU-IBIS. No evidence for Haemophilus infl uenzae serotype replacement in Europe after introduction of the Hib conjugate vaccine. Lancet Infect Dis. 2008 May;8(5):275-6

Larrauri A, Cano R, García M, de Mate S. Impact and effectiveness of meningococcal C conjugate vaccine following its introduction in Spain. Vaccine. 2005 Jul 14; 23(32): 4097-4100

Manual for the Surveillance of Vaccine-Preventable Diseases (4th Edition, 2008). Chapter 2: *Haemophilus influenzae* Type b Invasive Disease.

Mims C et al. Medical Microbiology. 3rd ed., 2004. Edinburgh; Elsevier Science, cop.

NHS, Department of Health, 23 July 2007. Haemophilus influenzae type b (hib) vaccine for young children – catch-up programme http://www.sehd.scot.nhs.uk/cmo/CMO(2007)07.pdf

Plotkin S. Vaccines (Expert consult title). 5.ed.,2008. Elsevier

Roberts R, Chandra M, Pebody R, Stuart J. Variation in incidence of pneumococcal and meningococcal disease across Europe. Eurosurveillance 2007;12(46):pii=3310 http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=3310

SMI (Swedish Institute for Infectious Disease Control). Downloaded 12 April 2009 http://www.smittskyddsinstitutet.se/statistik/haemophilus-influenzae-hib/?t=com#statistics-nav

Snape M, Kelly DF, Green B, Moxon ER, Borrow R, Pollard AJ. Lack of serum bactericidal activity in preschool children two years after a single dose of serogroup c meningococcal polysaccharide-protein conjugate vaccine. The Pediatric Infectious Disease Journal 2005 February; 24(2): 128–131

Trotter C, N. Andrews, E.Kaczmarski, E.Miller, M.Ramsay Effectiveness of meningococcal serogroup C conjugate vaccine 4 years after introduction. Lancet. 2004 July; 364(9431): 365-367

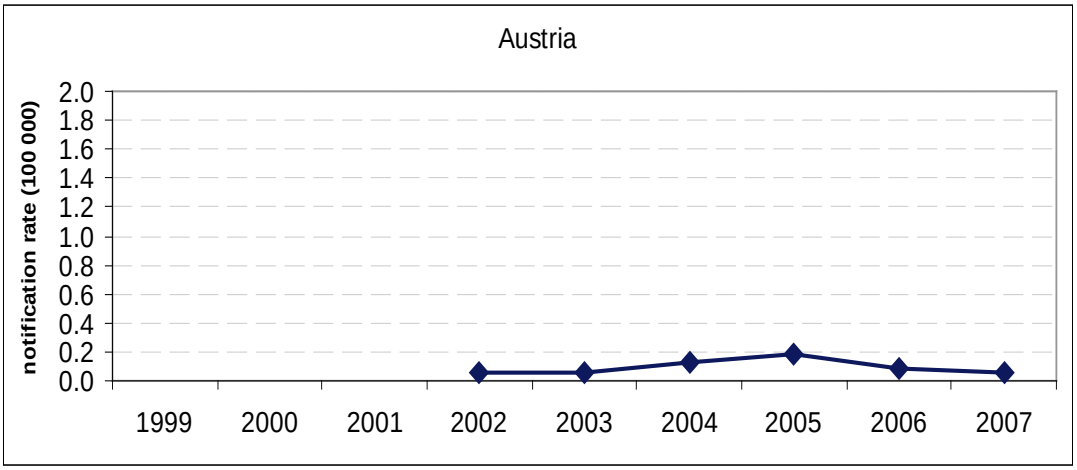
Trotter C, Samuelsson S, Perrocheau A, de Greeff S, de Melker H, Heuberger S, Ramsay M. Ascertainment of meningococcal disease in Europe. Eurosurveillance. 2005 December 01; 10(12)

Tsang R. Capsule switching and capsule replacement in vaccine-preventable bacterial diseases. Lancet Infect Dis. 2007. 7(9): 569–70.

Appendix 1: Invasive *Haemophilus influenzae* disease

Figure 42: Country profiles and overall notification rates of invasive *H. influenzae* disease and information of data sources by country, 1999–2007

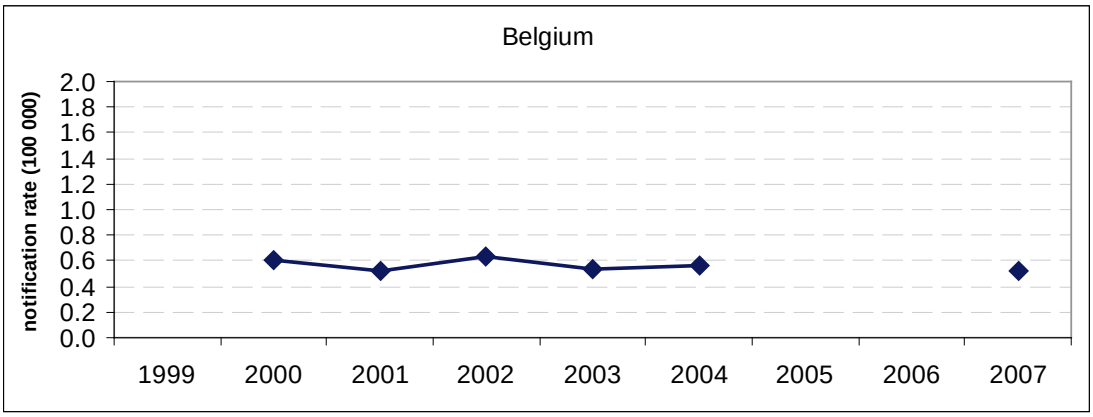
1999-2006 notification rates used directly from EU-IBIS 2006 report (based on national population data sources), 2007 using Eurostat as population source.



Data available: 2002-2007
Serotype: All
Clinical presentation: All
Reporting “outcome” in 2007: No
Compulsory
Case-based
Comments:

Age coverage: All

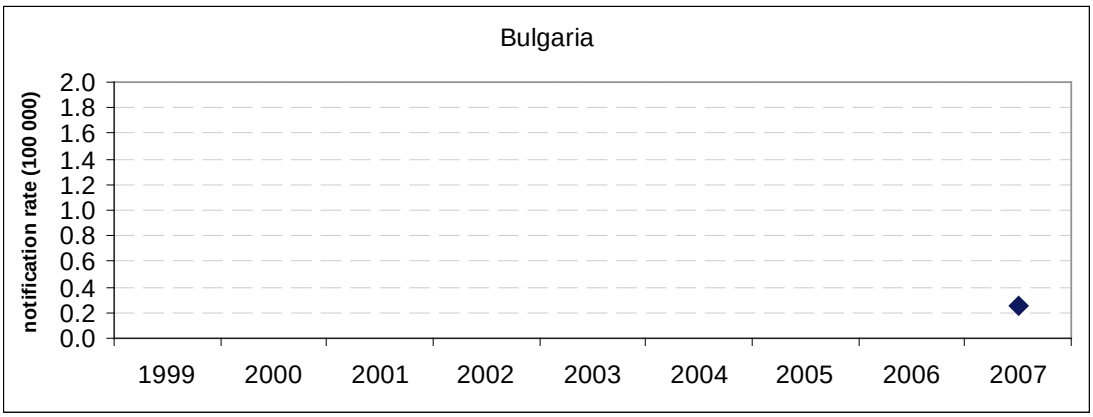
Reporting “vacc status” 2007: No
Comprehensive
Hib vaccine introduced: 1994



Data available: 2002-2007
Serotype: Not determined
Clinical presentation: All: 2000-2004, not determined: 2007
Reporting “outcome” in 2007: No
Voluntary
Case based
Comments: No reporting 2005-2006

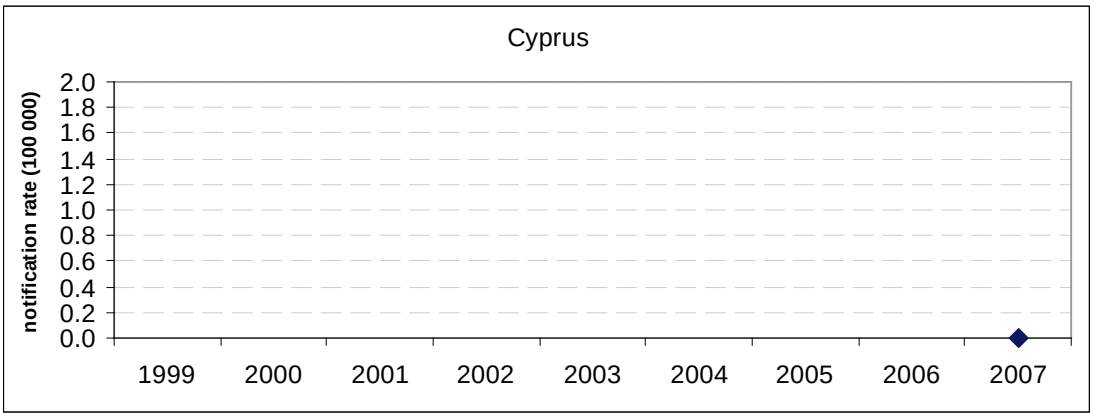
Age coverage: All

Reporting “vacc status” 2007: No
Sentinel
Hib vaccine introduced: 1993



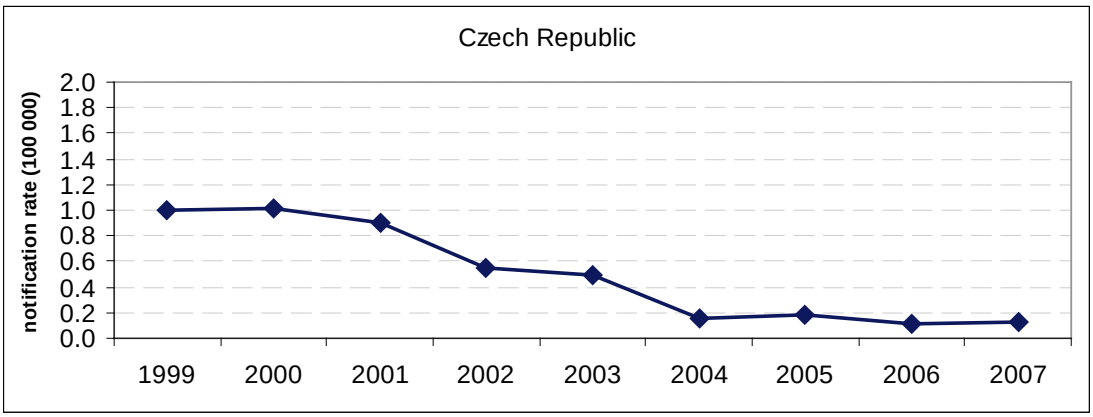
Data available: 2007
Age coverage: All
Serotype: Not determined
Clinical presentation: Not determined
Reporting "outcome" in 2007: No
Reporting "vacc status" 2007: No
Aggregated
Hib vaccine introduced: No
Comments:

- Aggregated reporting in 2007, which only enabled reporting a common set of variables.
- Information of gender not available in 2007.



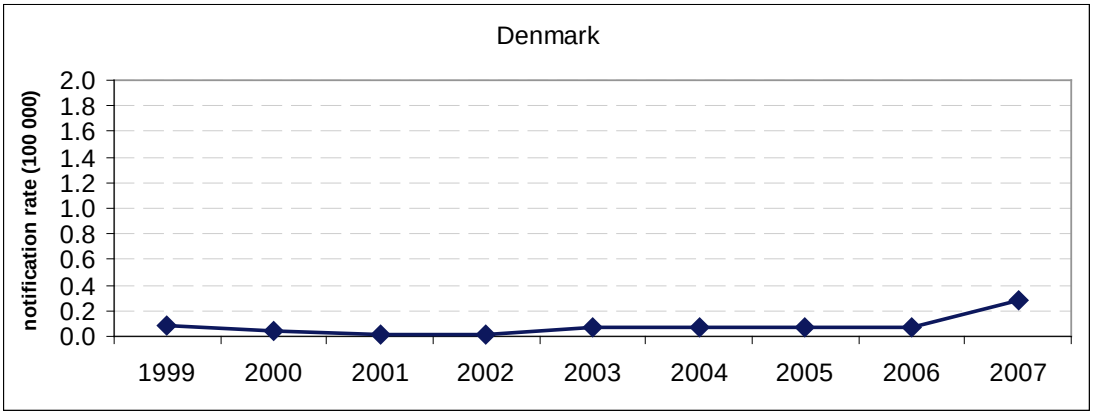
Data available: 2007
Age coverage: All
Serotype: Unknown (zero reporting in 2007)
Clinical presentation: (zero reporting in 2007)
Reporting "outcome" in 2007: zero reporting
Reporting "vacc status" 2007: zero reporting
Compulsory
Comprehensive
Case-based
Hib vaccine introduced: ?
Comments:

- Reported zero cases in 2007.



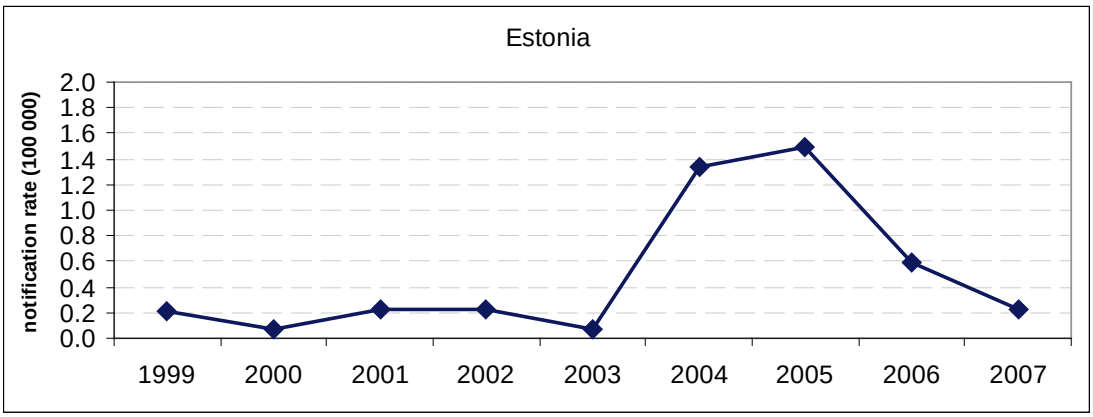
Data available: 1999 – 2007
Age coverage: All
Serotype: b 1999-2004; all 2005-
Clinical presentation:
Reporting "outcome" in 2007: Yes
Reporting "vacc status" 2007: Yes
Compulsory
Comprehensive
Case-based
Hib vaccine introduced: 2001
Comments:

- Sharp decrease in notification rates over 2001–2004 attributed mainly to the introduction of the Hib vaccine in 2001. Since 2005, all strained are typed and reported, which may explain the stabilisation in the overall notification rates.



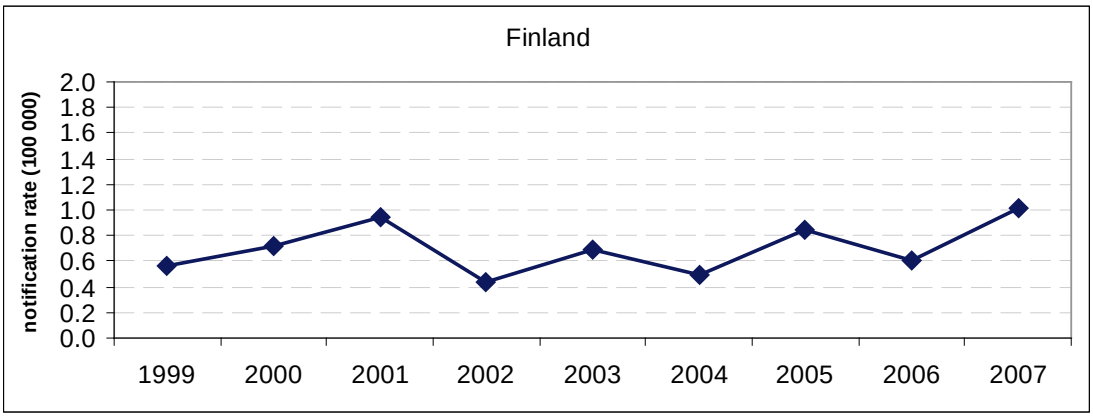
Data available: 1999-2007
Age coverage: All
Serotype: All
Clinical presentation: Meningitis only 1999-2006, All 2007-
Reporting "outcome" in 2007: Yes
Reporting "vacc status" 2007: Yes
Compulsory
Comprehensive
Case-based
Hib vaccine introduced: 1993
Comments:

- Increases in overall notification rates from 2006–2007 attributable to the inclusion of bacteraemia/septicaemia cases in the reporting from 2007: During 2003–2006, four cases per year were reported, all with "Clinical presentation" meningitis; in 2007, a total of 15 cases were reported, whereas two were reported as meningitis, the remaining 13 with "Clinical presentation" unknown (isolates from blood according to direct communication with SSI/DK).
- Reporting of invasive isolates of *H. influenzae* type b are mandatory since October 2007, thus an expected increase in notification rates the coming year. However, since non-type b and non-capsulated are not mandatory, the serotype distribution is also expected to be skewed (source: SSI/DK).



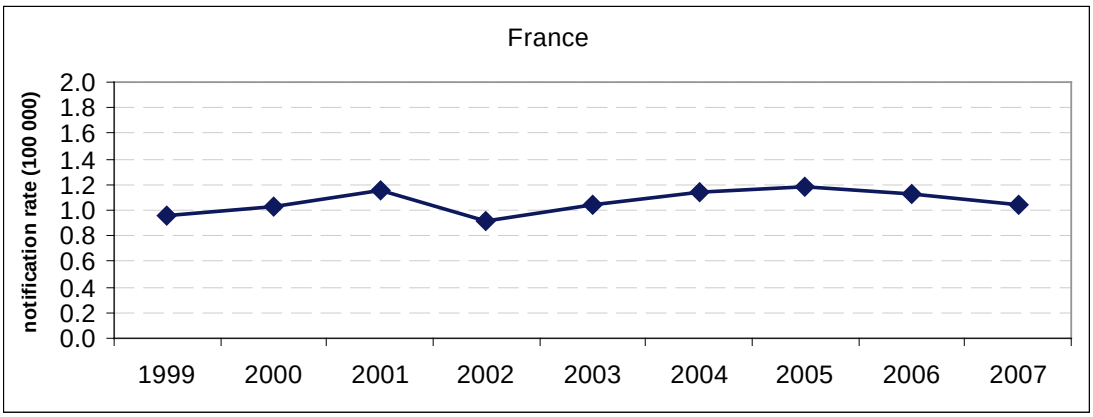
Data available: 1999 – 2007 Age coverage: All
Serotype: b
Clinical presentation: Septicaemia: 1999-2003; All: 2004
Reporting "outcome" in 2007: Yes Reporting "vacc status" 2007: Yes
Compulsory Comprehensive
Case-based Hib vaccine introduced: 2005
Comments:

- The increase partially explained by improved case ascertainment, and by inclusion of all clinical (source: NSCP/EE)
- The decrease after 2005 possibly explained by the Hib-vaccine introduction the same year (source: NSCP/EE).
- Rates 1999-2006 recalculated from EU-IBIS 2006 report using total population as denominator (Eurostat).



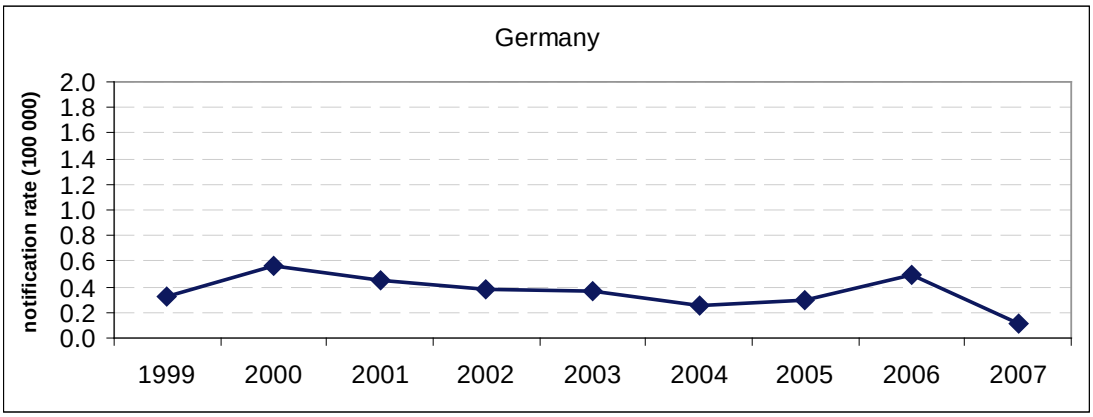
Data available: 1999 – 2007 Age coverage: All
Serotype: All
Clinical presentation: All
Reporting "outcome" in 2007: Yes Reporting "vacc status" 2007: Yes
Compulsory Comprehensive
Case-based Hib vaccine introduced: 1986
Comments:

- Consistent reporting/stable surveillance system 1999-2007, with coverage of strains typed has been very high since 1995 (Source: THL/FI)



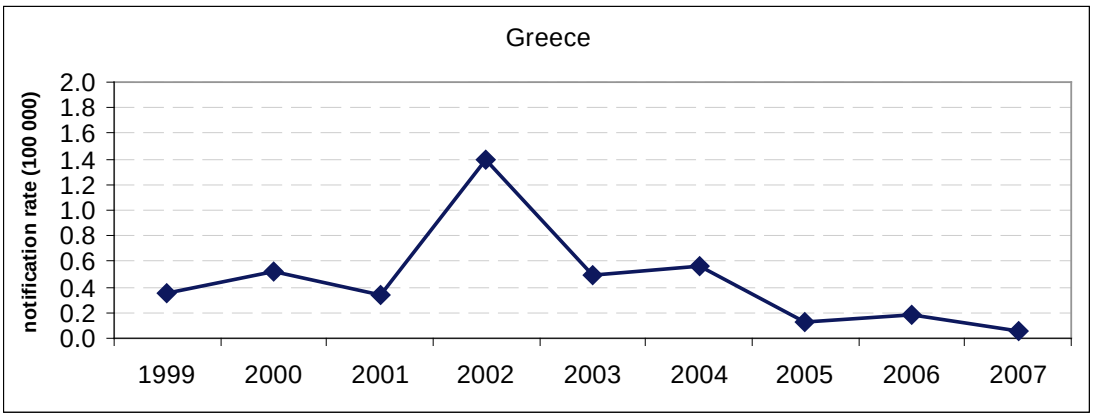
Data available: 1999–2007 Age coverage: All
Serotype: All: 1999-2006, not determined in 2007
Clinical presentation: All: 1999–2006, not determined in 2007
Reporting "outcome" in 2007: No Reporting "vacc status" 2007: No
Voluntary Sentinel
Aggregated Hib vaccine introduced: 1992
Comments:

- Aggregated data corrected for under-reporting and under-coverage.
- The aggregated reporting to TESSy in 2007 only enabled reporting a common set of variables.



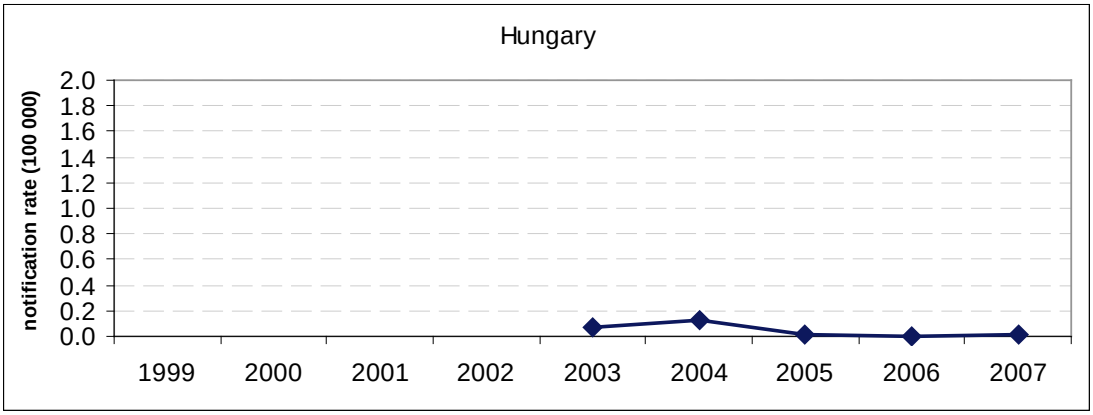
Data available: 1999–2007 Age coverage: <15 yrs: 1999–2006; All: 2007
Serotype: All
Clinical presentation: All
Reporting "outcome" in 2007: Yes Reporting "vacc status" 2007: No
Compulsory Comprehensive
Case-based Hib vaccine introduced: 1990
Comments:

- Notification rates 1999–2006 based upon <15 years of age population data only (from EU-IBIS report 2006). In 2007, all age groups were reported. Therefore, an increase of number of cases, but decrease in overall notification rate.

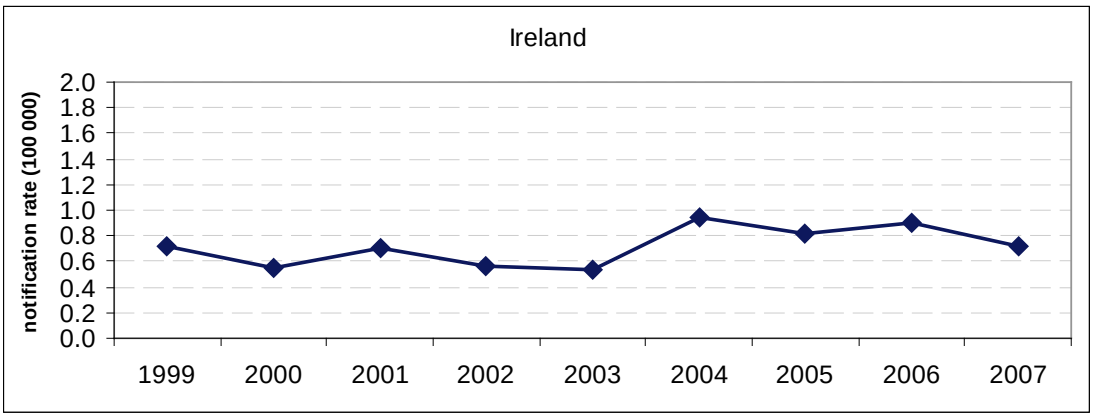


Data available: 1999–2007 Age coverage: <15 years
Serotype: Mainly b & non-b
Clinical presentation: meningitis and meningitis/septicaemia only
Reporting "outcome" in 2007: Yes Reporting "vacc status" 2007: No
Compulsory Comprehensive
Case-based Hib vaccine introduced: 1999
Comments:

- Notification rates 1999-2006 based upon <15 years of age population data only (from EU-IBIS report 2006). In 2007, all age groups were reported. Therefore, an increase of number of cases, but decrease in overall notification rate.

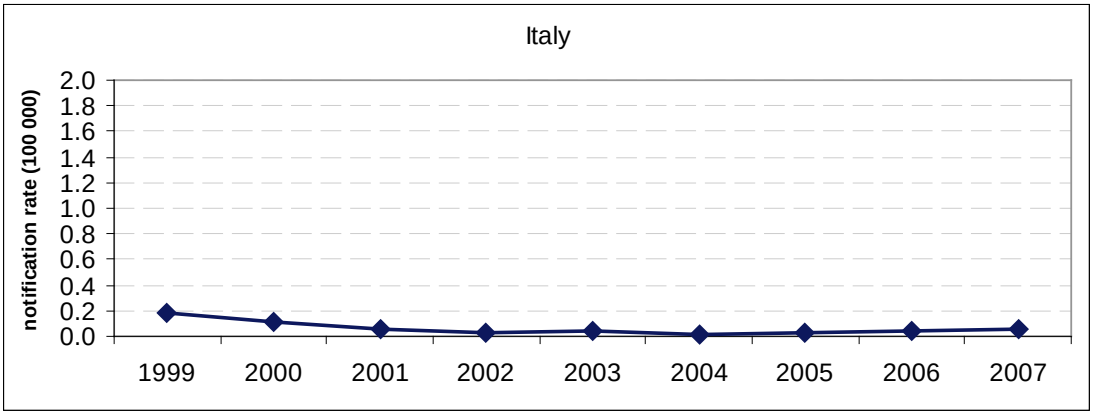


Data available: 2003-2007 Age coverage: All
Serotype: Not determined
Clinical presentation: Meningitis and septicaemia only
Reporting "outcome" in 2007: Yes Reporting "vacc status" 2007: Yes
Compulsory Comprehensive
Case-based Hib vaccine introduced: 1999
Comments:



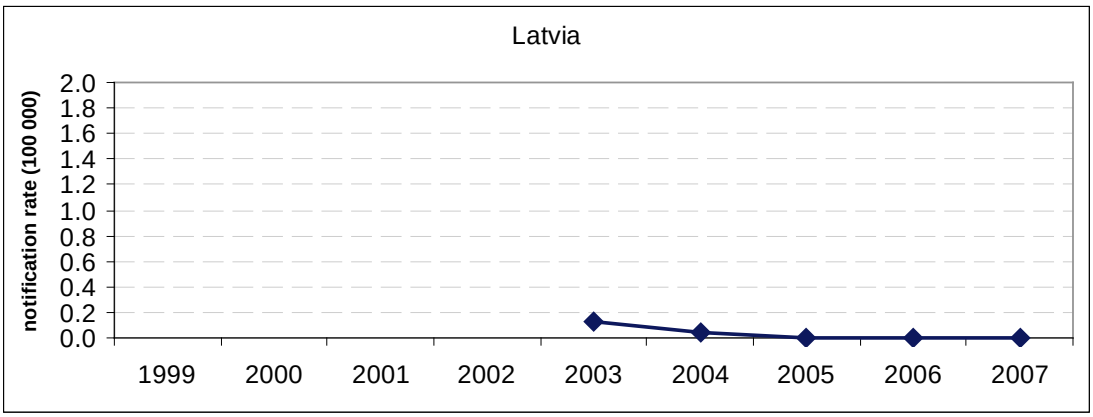
Data available: 1999-2007
Age coverage: All
Serotype: All
Clinical presentation: All
Reporting "outcome" in 2007: Yes
Reporting "vacc status" 2007: Yes
Compulsory
Comprehensive
Case-based
Hib vaccine introduced: 1992
Comments:

- Consistent reporting/stable surveillance system 1999-2007

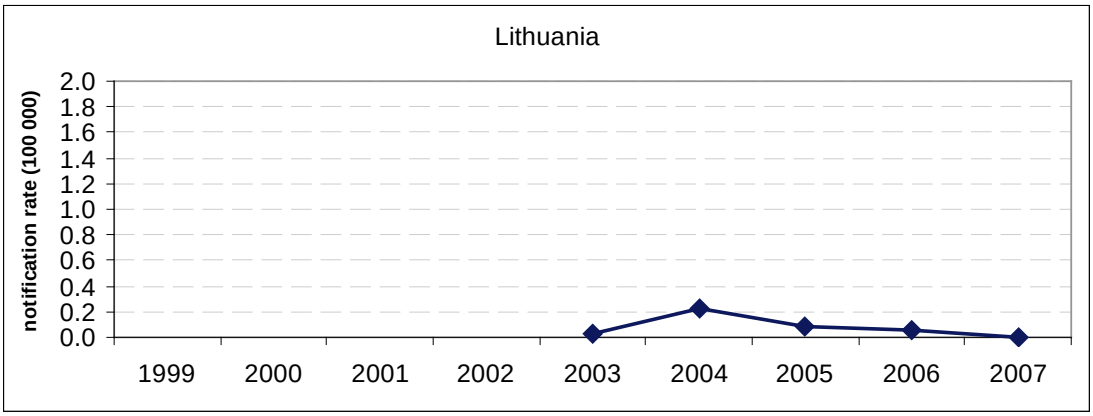


Data available: 1999-2007
Age coverage: All
Serotype: All
Clinical presentation: All
Reporting "outcome" in 2007: Yes
Reporting "vacc status" 2007: No
Compulsory
Comprehensive
Case-based
Hib vaccine introduced: 1995 (1999 in routine schedule)
Comments:

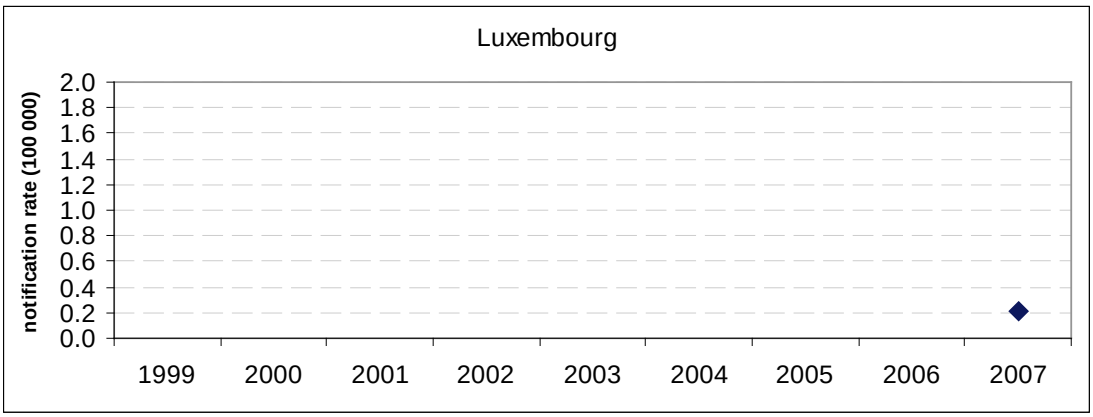
- Consistent reporting/stable surveillance system 1999-2007



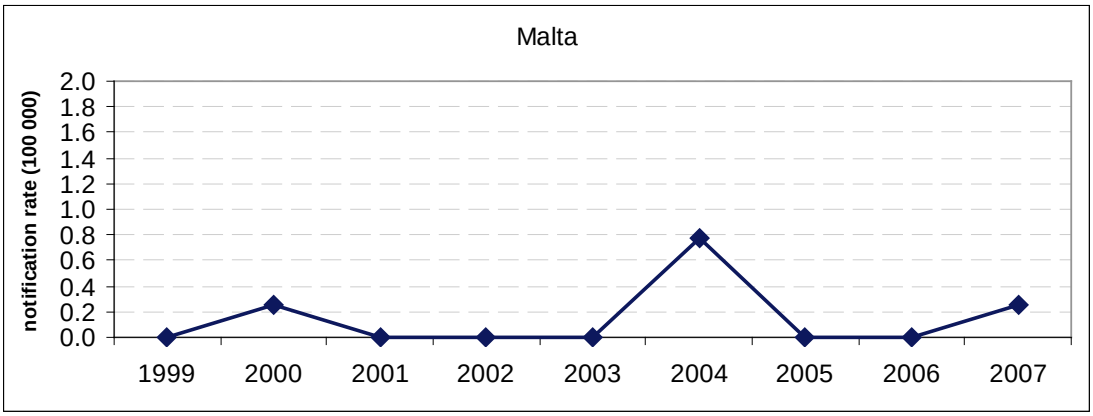
Data available: 2003-2007
Age coverage: All
Serotype: b
Clinical presentation: All
Reporting "outcome" in 2007: zero reporting
Reporting "vacc status" 2007: zero reporting
Compulsory
Comprehensive
Case-based
Hib vaccine introduced: 1994
Comments:



Data available: 2003-2007
Age coverage: All
Serotype: b
Clinical presentation: Meningitis and septicaemia only
Reporting "outcome" in 2007: zero reporting
Reporting "vacc status" 2007: zero reporting
Compulsory
Comprehensive
Case-based
Hib vaccine introduced: 2004
Comments:

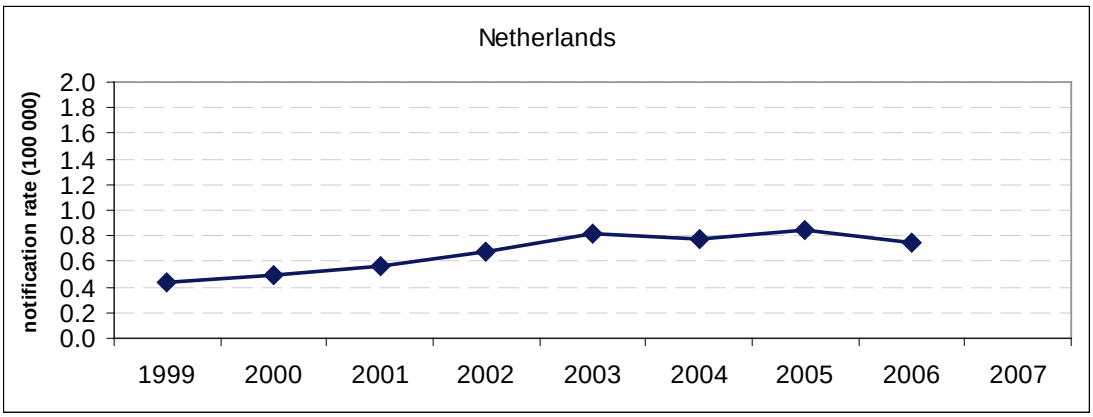


Data available: 2007
Age coverage: All
Serotype: Not determined
Clinical presentation: Meningitis
Reporting "outcome" in 2007: Yes
Reporting "vacc status" 2007: No
Compulsory
Comprehensive
Case-based
Hib vaccine introduced: ?
Comments:



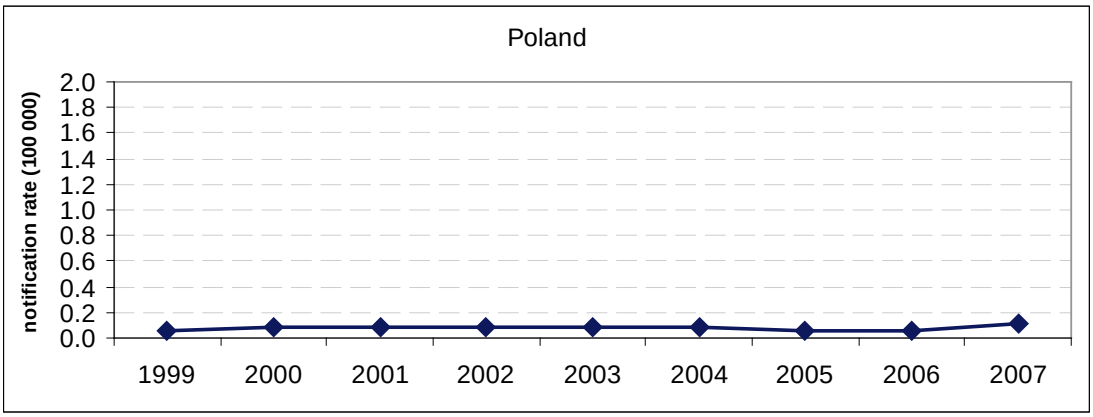
Data available: 1999-2007
Age coverage: All
Serotype: All (not determined in 2007)
Clinical presentation: Not determined
Reporting "outcome" in 2007: Yes
Reporting "vacc status" 2007: Yes
Compulsory
Comprehensive
Case-based
Hib vaccine introduced: 1996
Comments:

- Few cases in a small population, with a total of five cases reported during 1999-2007

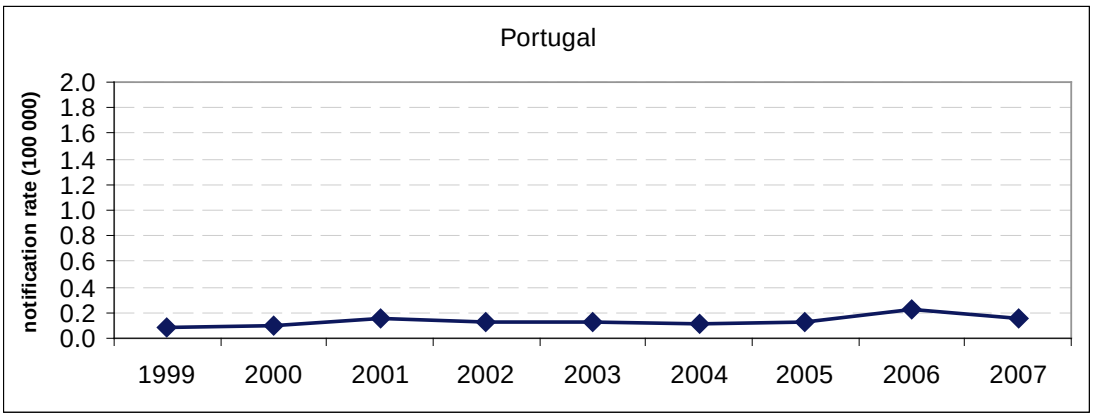


Data available: 1999-2006
Age coverage: All
Serotype: All
Clinical presentation: All
Reporting "outcome" in 2007: -
Reporting "vacc status" 2007: -
Compulsory
Comprehensive
Case-based
Hib vaccine introduced: 1993
Comments:

- Consistent reporting until 2006. No available data from 2007 due to larger changes (upgrading) in the national surveillance system.

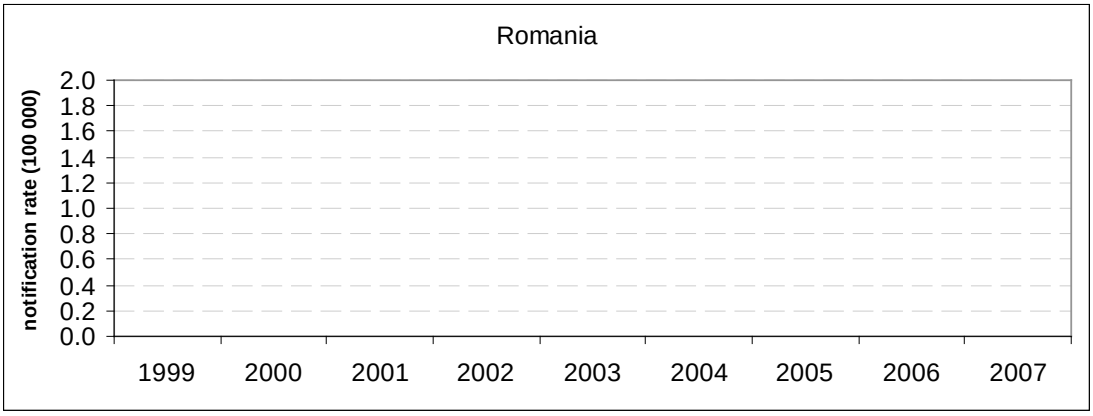


Data available: 1999-2007
Age coverage: All
Serotype: Mainly b, but also non-caps 2004-
Clinical presentation: Meningitis: 1999-2006; All: 2007
Reporting "outcome" in 2007: Yes
Reporting "vacc status" 2007: Yes
Compulsory
Comprehensive
Case-based
Hib vaccine introduced: 2005
Comments:



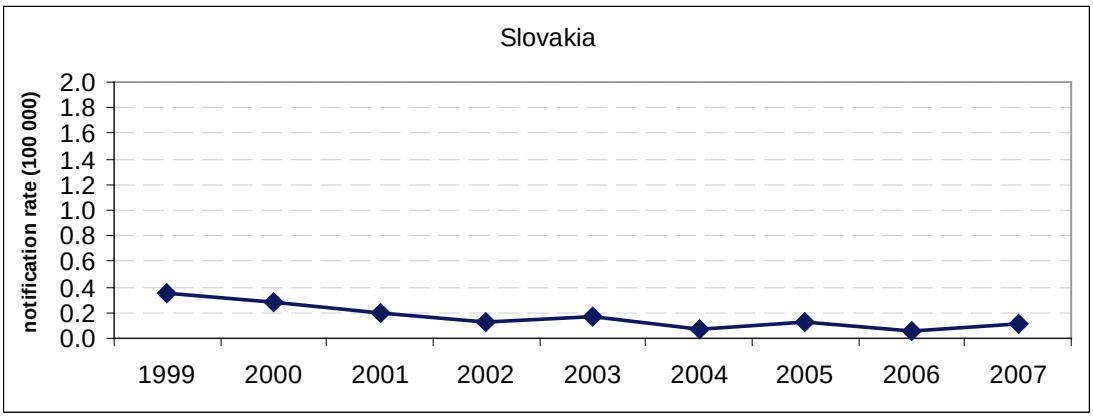
Data available: 1999-2007
Age coverage: All
Serotype: All
Clinical presentation: All
Reporting "outcome" in 2007: Yes
Reporting "vacc status" 2007: Yes
Compulsory
Comprehensive
Case-based
Hib vaccine introduced: 2000
Comments:

- Consistent reporting/stable surveillance system 1999-2007



Data available: -
Age coverage: -
Serotype: -
Clinical presentation: -
Reporting "outcome" in 2007: -
Reporting "vacc status" 2007: -
Hib vaccine introduced: No
Comments:

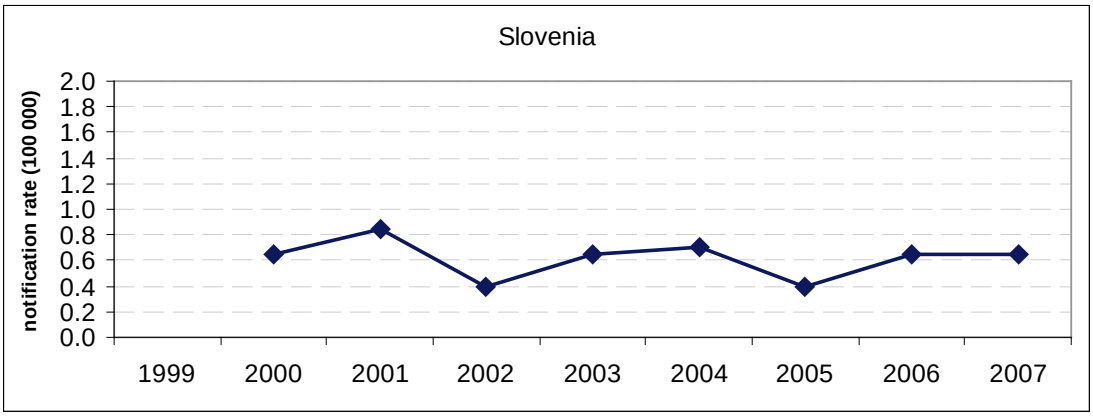
- Planning to initiate invasive Hi disease surveillance in 2009



Data available: 1999-2007
Serotype: Not determined: 1999-2006, b: 2007
Clinical presentation: All
Reporting “outcome” in 2007: Yes
Compulsory
Case-based
Comments:

Age coverage: All

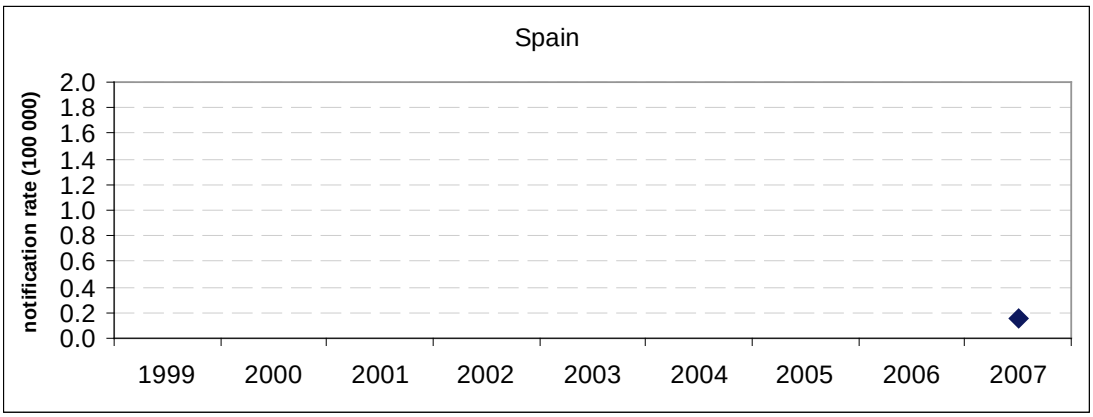
Reporting “vacc status” 2007: Yes
Comprehensive
Hib vaccine introduced: 1994



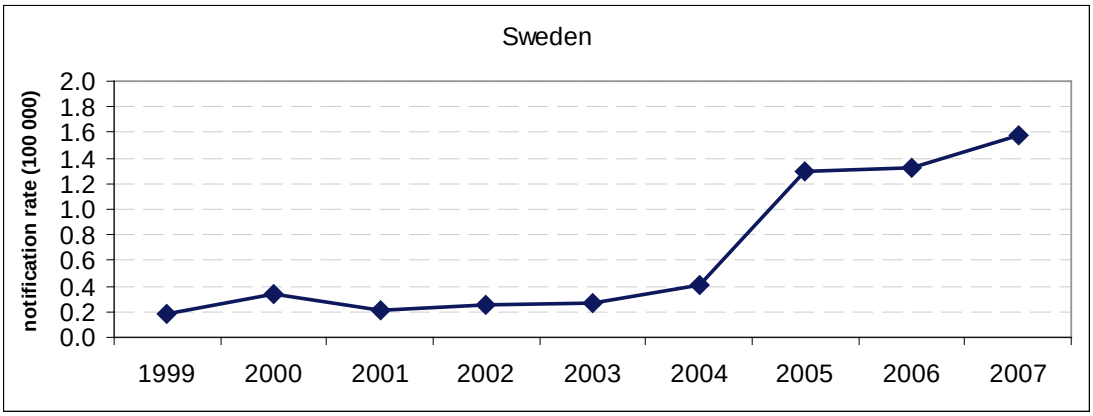
Data available: 2000-2007
Serotype: All
Clinical presentation: All
Reporting “outcome” in 2007: Yes
Compulsory
Case-based
Comments:

Age coverage: All

Reporting “vacc status” 2007: Yes
Comprehensive / Regional
Hib vaccine introduced: 1994

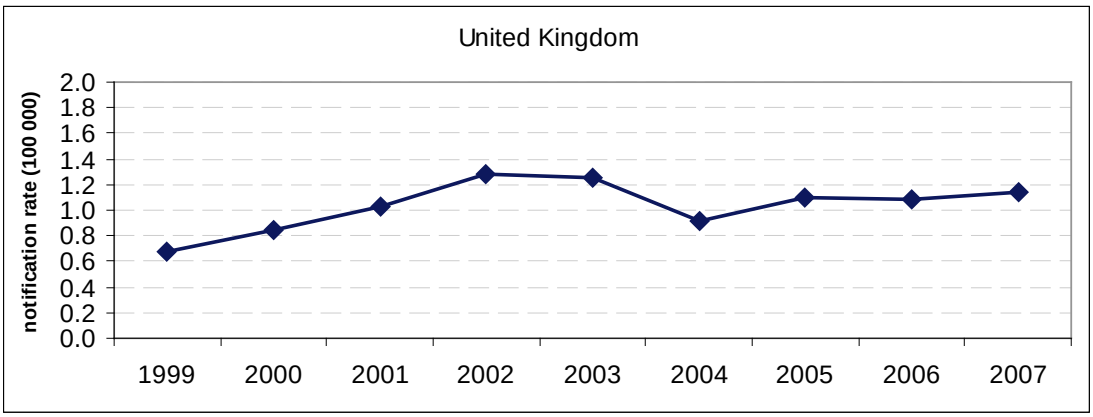


Data available: 2007
Age coverage: All
Serotype: All
Clinical presentation: All
Reporting "outcome" in 2007: No
Reporting "vacc status" 2007: No
Voluntary
Sentinel / Regional
Case-based
Hib vaccine introduced: 1998
Comments:



Data available: 1999-2007
Age coverage: All
Serotype: b: 1999-2004, All: 2005-
Clinical presentation: All: 1999-2006; Not determined: 2007
Reporting "outcome" in 2007: Yes
Reporting "vacc status" 2007: Yes
Compulsory
Comprehensive
Case-based
Hib vaccine introduced: 1994
Comments:

- Only Hib was notifiable until July 2004 when a new Communicable Disease Act came into place and all strains became mandatorily notifiable.
- Enhanced surveillance ongoing since 2006, collecting all invasive isolates in Sweden and since 2007 sending questionnaire to the physicians regarding clinical information of invasive bacterial infections, which may have increased the awareness and thus the sensitivity of the surveillance.
- Few Hib cases.

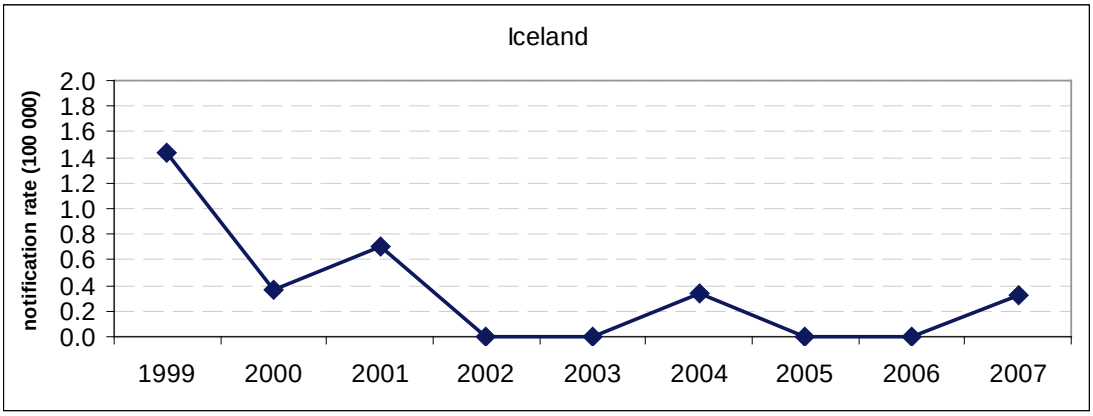


Data available: 1999-2007
Serotype: All
Clinical presentation: All
Reporting "outcome" in 2007: Yes
Compulsory
Case-based
Comments:

Age coverage: All

Reporting "vacc status" 2007: Yes
Comprehensive
Hib vaccine introduced: 1992

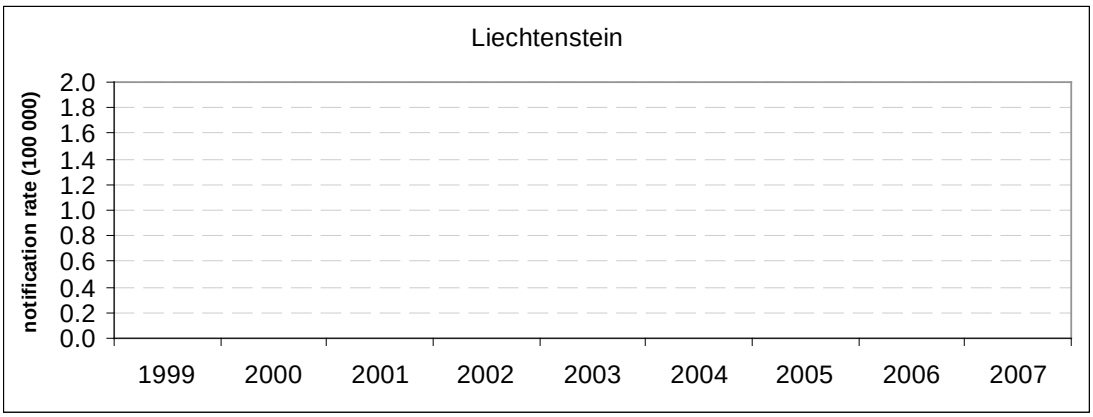
- Consistent reporting/stable surveillance system 1999-2007
- Reported the highest notification rates of Hib among children <5 in Europe 2007 (1.24/100 000, n=44). Booster introduced into the vaccination program September 2006, and a catch-up campaign organised September 2007–March 2009



Data available: 1999-2007
Serotype: Mainly b
Clinical presentation: All
Reporting "outcome" in 2007: Yes
Compulsory
Case-based
Comments:

Age coverage: All

Reporting "vacc status" 2007: Yes
Comprehensive
Hib vaccine introduced: 1989

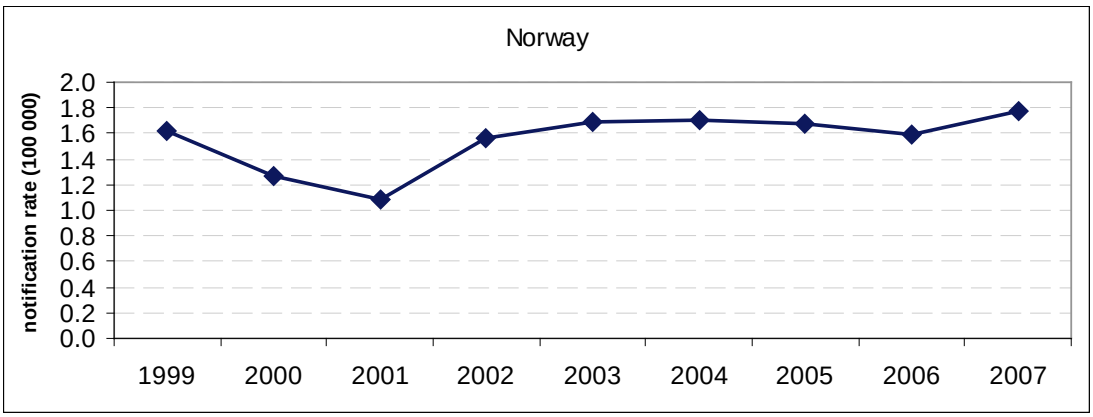


Data available: -
Serotype: -
Clinical presentation: -

Age coverage: -

Hib vaccine introduced: 1994

Comments:



Data available: 1999-2007
Serotype: All
Clinical presentation: All
Reporting “outcome” in 2007: Yes
Compulsory
Case-based

Age coverage: All

Reporting “vacc status” 2007: Yes
Comprehensive
Hib vaccine introduced: 1992

Comments:

- Consistent reporting/stable surveillance system 1999-2007
- Highest overall notification rate in Europe. The majority of the cases are hospitalised cases based upon positive culture from blood or CSF.
- Strengthening of reference laboratory in recent years, but inclusion of results into MSIS surveillance not done systematically, which may have influenced the serotype data (completeness and/or skewed distribution).
- Few Hib cases.

Table 29: Number and proportion (%) of all reported test methods used among cases of invasive *Haemophilus influenzae* disease per country, 2007

Test method	Antigen		Culture		Nuclear acid		Unknown		Total
Country	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**
Austria	0	0%	4	50%	4	50%	0	0%	8
Belgium	0	0%	0	0%	0	0%	55	100%	55
Bulgaria	-	-	-	-	-	-	-	-	-
Cyprus	0	0%	0	0%	0	0%	0	0%	0
Czech Republic	0	0%	12	92%	1	7%	0	0%	13
Denmark	0	0%	0	0%	0	0%	15	100%	15
Estonia	1	33%	2	66%	0	0%	0	0%	3
Finland	0	0%	54	100%	0	0%	0	0%	54
France	-	-	-	-	-	-	-	-	-
Germany	0	0%	89	92%	5	5%	0	0%	94
Greece	0	0%	1	12%	7	87%	0	0%	8
Hungary	0	0%	2	100%	0	0%	0	0%	2
Ireland	0	0%	27	87%	4	12%	0	0%	31
Italy	0	0%	33	58%	23	41%	0	0%	56
Latvia	0	0%	0	0%	0	0%	0	0%	0
Lithuania	0	0%	0	0%	0	0%	0	0%	0
Luxembourg	0	0%	0	0%	0	0%	1	100%	1
Malta	0	0%	1	100%	0	0%	0	0%	1
Netherlands	-	-	-	-	-	-	-	-	-
Poland	4	9%	39	90%	0	0%	0	0%	43
Portugal	0	0%	0	0%	0	0%	16	100%	16
Romania	-	-	-	-	-	-	-	-	-
Slovakia	0	0%	6	100%	0	0%	0	0%	6
Slovenia	13	50%	0	0%	13	50%	0	0%	26
Spain	0	0%	66	100%	0	0%	0	0%	66
Sweden	1	0%	143	99%	0	0%	0	0%	144
United Kingdom	15	2%	608	87%	0	0%	73	10%	696
EU Total	**34**	**3%**	**1087**	**81%**	**57**	**4%**	**160**	**12%**	**1338**
Iceland	0	0%	1	100%	0	0%	0	0%	1
Liechtenstein	-	-	-	-	-	-	-	-	-
Norway	0	0%	79	95%	1	1%	3	3%	83
Total	**34**	**2%**	**1167**	**82%**	**58**	**4%**	**163**	**11%**	**1422**

Table 30: Number and notification rates (per 100 000 population) of confirmed and probable cases of invasive Hi disease EU and EEA countries, by country, 2007

Country		Number of cases			Population	Notification rate		
	Case definition	Confirmed	Probable	Total		Confirmed	Probable	Total
Austria	Not determined	4	0	4	8298923	0.05	0.00	0.05
Belgium	Not determined	55	0	55	10584534	0.52	0.00	0.52
Bulgaria	EU 2002	19	1	20	7679290	0.25	0.01	0.26
Cyprus	EU 2002	0	0	0	778684	0.00	0.00	0.00
Czech Republic	EU 2008	13	0	13	10287189	0.13	0.00	0.13
Denmark	Other	15	0	15	5447084	0.28	0.00	0.28
Estonia	EU 2002	2	1	3	1342198	0.15	0.07	0.22
Finland	EU 2002	54	0	54	5276955	1.02	0.00	1.02
France	EU 2008	658	0	658	63392140	1.04	0.00	1.04
Germany	Other	93	0	93	82314906	0.11	0.00	0.11
Greece	EU 2002	7	0	7	11171740	0.06	0.00	0.06
Hungary	EU 2002	2	0	2	10066158	0.02	0.00	0.02
Ireland	EU 2002	31	0	31	4312526	0.72	0.00	0.72
Italy	EU 2008	33	0	33	59131287	0.06	0.00	0.06
Latvia	EU 2002	0	0	0	2281305	0.00	0.00	0.00
Lithuania	Not determined	0	0	0	3384879	0.00	0.00	0.00
Luxembourg	None	1	0	1	476187	0.21	0.00	0.21
Malta	EU 2008	1	0	1	407810	0.25	0.00	0.25
Netherlands	-	-	-	-	16357992	-	-	-
Poland	EU 2002	39	4	43	38125479	0.10	0.01	0.11
Portugal	EU 2002	16	0	16	10599095	0.15	0.00	0.15
Romania	-	-	-	-	21565119	-	-	-
Slovakia	EU 2008	6	0	6	5393637	0.11	0.00	0.11
Slovenia	EU 2008	13	0	13	2010377	0.65	0.00	0.65
Spain	EU 2008	66	0	66	44474631	0.15	0.00	0.15
Sweden	EU 2008	144	0	144	9113257	1.58	0.00	1.58
United Kingdom	EU 2002	696	0	696	60816701	1.14	0.00	1.14
EU Total		**1968**	**6**	**1974**	**495090083**	**0.40**	**0.00**	**0.40**
Iceland	EU 2008	1	0	1	307672	0.33	0.00	0.33
Liechtenstein	-	-	-	-	-	-	-	-
Norway	EU 2008	83	0	83	4681134	1.77	0.00	1.77
Overall		**2052**	**6**	**2058**	**500078889**	**0.41**	**0.00**	**0.41**

Table 31: Number of reported invasive *H. influenzae* cases per country and month in 2007

Country	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Unk	Tot
Austria	0	0	0	0	1	0	0	1	0	1	0	1	0	4
Belgium	9	9	2	8	9	2	3	2	1	2	3	5	0	55
Bulgaria	1	1	3	0	1	1	2	3	0	3	3	2	0	20
Cyprus	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Czech Republic	3	0	0	1	3	1	2	0	0	1	2	0	0	13
Denmark	1	0	2	1	1	0	1	0	1	0	3	5	0	15
Estonia	0	0	0	1	0	1	0	0	0	0	1	0	0	3
Finland	3	5	4	10	5	3	2	3	6	6	4	3	0	54
France	82	75	64	66	40	58	42	35	22	40	54	80	0	658
Germany	6	7	9	9	6	5	8	1	2	9	9	10	12	93
Greece	0	1	0	1	0	1	1	0	2	0	1	0	0	7
Hungary	0	1	0	0	0	0	0	0	0	0	0	1	0	2
Ireland	1	4	4	3	5	3	2	1	2	2	3	1	0	31
Italy	4	2	8	5	2	3	0	0	0	2	3	4	0	33
Latvia	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lithuania	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Luxembourg	0	0	1	0	0	0	0	0	0	0	0	0	0	1
Malta	0	0	0	0	0	0	1	0	0	0	0	0	0	1
Netherlands	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Poland	2	5	6	1	4	2	3	4	0	3	7	6	0	43
Portugal	1	3	1	2	0	2	0	0	1	1	3	2	0	16
Romania	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Slovakia	0	0	1	0	1	0	0	4	0	0	0	0	0	6
Slovenia	3	0	0	1	0	0	5	0	1	2	1	0	0	13
Spain	7	9	2	8	10	5	1	3	3	10	5	3	0	66
Sweden	16	9	18	12	11	6	17	9	14	10	10	12	0	144
United Kingdom	65	76	84	49	49	49	50	41	31	60	64	78	0	696
EU Total	**204**	**207**	**209**	**178**	**148**	**142**	**140**	**107**	**86**	**152**	**176**	**213**	**12**	**1974**
Iceland	0	0	0	0	0	1	0	0	0	0	0	0	0	1
Liechtenstein	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Norway	12	9	8	8	10	7	6	2	7	1	8	5	0	83
Total	**216**	**216**	**217**	**186**	**158**	**150**	**146**	**109**	**93**	**153**	**184**	**218**	**12**	**2058**

Table 32: Total number of invasive *H. influenzae* disease cases by gender and countries, 2007

Country	Females	Males	Unknown	Gender ratio
Austria	2	2	0	1.0
Belgium	33	22	0	1.5
Bulgaria	0	0	20	-
Cyprus	-	-	-	-
Czech Republic	8	5	0	1.6
Denmark	6	9	0	0.7
Estonia	1	2	0	0.5
Finland	25	29	0	0.9
France	326	330	2	1.0
Germany	46	47	0	1.0
Greece	4	3	0	1.3
Hungary	0	2	0	0.0
Ireland	6	25	0	0.2
Italy	18	15	0	1.2
Latvia	14	7	0	2.0
Lithuania	35	31	0	1.1
Luxembourg	0	1	0	0.0
Malta	1	0	0	2.0
Netherlands	-	-	-	-
Poland	19	24	0	0.8
Portugal	5	10	1	0.5
Romania	-	-	-	-
Slovakia	2	4	0	0.5
Slovenia	5	8	0	0.6
Spain	25	41	0	0.6
Sweden	77	67	0	1.1
United Kingdom	350	330	16	1.1
EU Total	**1008**	**1014**	**39**	**1.0**
Iceland	0	1	0	0.0
Liechtenstein	-	-	-	-
Norway	37	46	0	0.8
Overall	**1045**	**1061**	**39**	**1.0**

Table 33: Degree of completeness of serotype reporting of invasive *H. influenzae* cases by country in 2007

Serotype	b		non-type b		non-caps		unknown		Total
Country	n	%	n	%	n	%	n	%	n
Austria	0	0.0%	0	0.0%	4	100.0%	0	0.0%	4
Belgium	0	0.0%	0	0.0%	0	0.0%	55	100.0%	55
Bulgaria[2]	-	-	-	-	-	-	20	100.0%	20
Cyprus[1]	-	-	-	-	-	-	-	-	-
Czech Republic	5	38.5%	3	23.1%	3	23.1%	2	15.4%	13
Denmark	4	26.7%	7	46.7%	4	26.7%	0	0.0%	15
Estonia	3	100.0%	0	0.0%	0	0.0%	0	0.0%	3
Finland	6	11.1%	3	5.6%	44	81.5%	1	1.9%	54
France[2]	-	-	-	-	-	-	658	100.0%	658
Germany	11	11.8%	4	4.3%	9	9.7%	69	74.2%	93
Greece	5	71.4%	2	28.6%	0	0.0%	0	0.0%	7
Hungary	1	50.0%	0	0.0%	0	0.0%	1	50.0%	2
Ireland	7	22.6%	4	12.9%	15	48.4%	5	16.1%	31
Italy	1	3.0%	5	15.2%	17	51.5%	10	30.3%	33
Latvia[1]	-	-	-	-	-	-	-	-	-
Lithuania[1]	-	-	-	-	-	-	-	-	-
Luxembourg[1]	0	0.0%	0	0.0%	0	0.0%	1	100.0%	1
Malta	0	0.0%	0	0.0%	0	0.0%	1	100.0%	1
Netherlands[3]	-	-	-	-	-	-	-	-	-
Poland	18	41.9%	0	0.0%	0	0.0%	25	58.1%	43
Portugal	2	12.5%	1	6.3%	10	62.5%	3	18.8%	16
Romania[3]	-	-	-	-	-	-	-	-	-
Slovakia	3	50.0%	0	0.0%	0	0.0%	3	50.0%	6
Slovenia	0	0.0%	0	0.0%	13	100.0%	0	0.0%	13
Spain	3	4.7%	0	0.0%	0	0.0%	63	95.3%	66
Sweden	11	7.6%	25	17.4%	42	29.2%	66	45.8%	144
United Kingdom	103	14.8%	42	6.0%	303	43.5%	248	35.6%	696
EU Total	**183**	**9.3%**	**96**	**4.8%**	**464**	**23.5%**	**1231**	**62.4%**	**1974**
Iceland	1	100.0%	0	0.0%	0	0.0%	0	0.0%	1
Liechtenstein[3]	-	-	-	-	-	-	-	-	-
Norway	4	4.8%	3	3.6%	63	75.9%	13	15.7%	83
Total	**188**	**9.1%**	**99**	**4.8%**	**527**	**25.6.2%**	**1244**	**60.4%**	**2058**

Appendix 2: Invasive meningococcal disease

Table 34: Population data by country

Country	1999	2000	2001	2002	2003	2004	2005	2006	2007
AT	7982461	8002186	8020946	8065146	8102175	8140122	8206524	8265925	8298923
BE	10213752	10239085	10263414	10309725	10355844	10396421	10445852	10511382	10584534
BG	8230371	8190876	8149468	7891095	7845841	7801273	7761049	7718750	7679290
CY	682862	690497	697549	705539	715137	730367	749175	766414	778684
CZ	10289621	10278098	10266546	10206436	10203269	10211455	10220577	10251079	10287189
DK	5313577	5330020	5349291	5368354	5383507	5397640	5411405	5427459	5447084
EE	1379237	1371630	1366518	1360801	1355604	1350692	1347186	1344428	1342198
FI	5159645	5171302	5181115	5194901	5206295	5219732	5236611	5255580	5276955
FR	60158533	60537977	60963775	61399344	61831779	62251817	62637596	62998773	63392140
DE	82037011	82163475	82259540	82440309	82536680	82531671	82500849	81070169	82314906
EL	10861402	10903757	10931206	10968708	11006377	11040650	11082751	11125179	11171740
HU	10253416	10221644	10200298	10174853	10142362	10116742	10097549	10076581	10066158
IE	3732201	3777763	3832973	3899876	3963665	4027732	4109173	4208148	4312526
IT	56909109	56923524	56960692	56993742	57321070	57888245	58462375	58751711	59131287
LV	2399248	2381715	2364254	2345768	2331480	2319203	2306434	2294590	2281305
LT	3536401	3512074	3486998	3475586	3462553	3445857	3425324	3403284	3384879
LU	427350	433600	439000	444050	448300	454960	461230	469086	476187
MT	378518	380201	391415	394641	397296	399867	402668	405006	407810
NL	15760225	15863950	15987075	16105285	16192572	16258032	16305526	16334210	16357992
PL	38666983	38653559	38253955	38242197	38218531	38190608	38173835	38157055	38125479
PT	10148883	10195014	10256658	10329340	10407465	10474685	10529255	10569592	10599095
RO	22488595	22455485	22430457	21833483	21772774	21711252	21658528	21610213	21565119
SK	5393382	5398657	5378783	5378951	5379161	5380053	5384822	5389180	5393637
SI	1978334	1987755	1990094	1994026	1995033	1996433	1997590	2003358	2010377
ES	39802827	40049708	40476723	40964244	41663702	42345342	43038035	43758250	44474631
SE	8854322	8861426	8882792	8909128	8940788	8975670	9011392	9047752	9113257
UK	58579685	58785246	58999781	59217592	59437723	59699828	60060000	60425786	60816701
EU Total	**481617951**	**482760224**	**483781316**	**484613120**	**486616983**	**488756349**	**491023311**	**491638940**	**495090083**
IS	275712	279049	283361	286575	288471	290570	293577	299891	307672
LI	32015	32426	32863	33525	33863	34294	34597	34905	35165
NO	4445329	4478497	4503436	4524066	4552252	4577457	4606363	4640219	4681134
Overall	**486371007**	**487550196**	**488600976**	**489457286**	**491491569**	**493658670**	**495957848**	**496613955**	**500114054**

Table 35: Number and notification rate (per 100 000 population) of confirmed, probable and possible cases of invasive meningococcal disease EU and EEA countries, by country, 2007

Country	Number of cases				Population	Notification rate			
	Confirmed	Probable	Possible	Total		Confirmed	Probable	Possible	Total
Austria	61	8	0	69	8298923	0.74	0.10	0.00	0.83
Belgium	158	0	2	160	10584534	1.49	0.00	0.02	1.51
Bulgaria	24	14	0	38	7679290	0.31	0.18	0.00	0.49
Cyprus	4	0	0	4	778684	0.51	0.00	0.00	0.51
Czech Republic	75	0	0	75	10287189	0.73	0.00	0.00	0.73
Denmark	78	0	0	78	5447084	1.43	0.00	0.00	1.43
Estonia	11	0	0	11	1342198	0.82	0.00	0.00	0.82
Finland	43	0	0	43	5276955	0.81	0.00	0.00	0.81
France	680	0	41	721	63392140	1.07	0.00	0.06	1.14
Germany	436	0	0	436	82314906	0.53	0.00	0.00	0.53
Greece	106	3	0	109	11171740	0.95	0.03	0.00	0.98
Hungary	43	6	0	49	10066158	0.43	0.06	0.00	0.49
Ireland	162	17	0	179	4312526	3.76	0.39	0.00	4.15
Italy	178	0	5	183	59131287	0.30	0.00	0.01	0.31
Latvia	15	0	6	21	2281305	0.66	0.00	0.26	0.92
Lithuania	50	16	0	66	3384879	1.48	0.47	0.00	1.95
Luxembourg	2	0	0	2	476187	0.42	0.00	0.00	0.42
Malta	6	0	0	6	407810	1.47	0.00	0.00	1.47
Netherlands	195	0	0	195	16357992	1.19	0.00	0.00	1.19
Poland	335	57	0	392	38125479	0.88	0.15	0.00	1.03
Portugal	98	19	0	117	10599095	0.92	0.18	0.00	1.10
Romania	145	10	0	155	21565119	0.67	0.05	0.00	0.72
Slovakia	35	0	0	35	5393637	0.65	0.00	0.00	0.65
Slovenia	18	0	0	18	2010377	0.90	0.00	0.00	0.90
Spain	620	197	0	816	44474631	1.39	0.44	0.00	1.83
Sweden	49	0	0	49	9113257	0.54	0.00	0.00	0.54
United Kingdom	1522	0	0	1522	60816701	2.50	0.00	0.00	2.50
EU Total	**5149**	**347**	**54**	**5549**	**495090083**	**1.04**	**0.07**	**0.01**	**1.12**
Iceland	4	0	0	4	307672	1.30	0.00	0.00	1.30
Liechtenstein	-	-	-	-	-	-	-	-	-
Norway	30	0	0	30	4681134	0.64	0.00	0.00	0.64
Overall	**5183**	**347**	**54**	**5583**	**500078889**	**1.04**	**0.07**	**0.01**	**1.12**

Table 36: Age distribution (number and % distribution) of all laboratory confirmed invasive meningococcal disease cases, in EU and EEA countries, 1999–2007

Age Group	1999	2000	2001	2002	2003	2004	2005	2006	2007
Numbers of cases									
<1 year	1155	1384	1208	1096	1068	990	1009	916	888
01-04 years	2170	2167	1826	1662	1559	1299	1412	1241	1457
05-09 years	997	904	767	649	546	443	481	437	487
10-14 years	718	605	583	468	506	310	353	240	307
15-19 years	1181	1012	1008	869	803	740	687	675	702
20-24 years	444	441	397	361	331	270	330	298	316
25-44 years	543	673	666	619	532	476	525	409	485
45-64 years	477	556	516	470	424	422	438	391	412
65+ years	359	359	354	402	310	334	369	299	336
Unknown	102	22	33	12	20	13	23	24	174
Total	**8146**	**8123**	**7358**	**6608**	**6099**	**5297**	**5627**	**4930**	**5564**
% distribution									
<1 year	14%	17%	16%	17%	18%	19%	18%	19%	16%
01-04 years	27%	27%	25%	25%	26%	25%	25%	25%	26%
05-09 years	12%	11%	10%	10%	9%	8%	9%	9%	9%
10-14 years	9%	7%	8%	7%	8%	6%	6%	5%	6%
15-19 years	14%	12%	14%	13%	13%	14%	12%	14%	13%
20-24 years	5%	5%	5%	5%	5%	5%	6%	6%	6%
25-44 years	7%	8%	9%	9%	9%	9%	9%	8%	9%
45-64 years	6%	7%	7%	7%	7%	8%	8%	8%	7%
65+ years	4%	4%	5%	6%	5%	6%	7%	6%	6%
Unknown	1%	0%	0%	0%	0%	0%	0%	0%	3%

Table 37: Age distribution of confirmed and probable laboratory diagnosed serogroup B invasive meningococcal disease cases, in EU and EEA countries, 1999–2007

Age Group	1999	2000	2001	2002	2003	2004	2005	2006	2007
Numbers of cases									
<1 year	775	976	890	807	801	780	819	747	670
01-04 years	1201	1218	1202	1105	1065	935	1063	937	1026
05-09 years	519	427	417	364	333	267	320	311	274
10-14 years	343	254	320	256	295	173	201	132	144
15-19 years	604	537	552	473	475	451	450	440	414
20-24 years	202	215	195	179	159	173	218	190	188
25-44 years	259	311	314	286	273	223	298	215	248
45-64 years	235	304	258	251	239	235	251	215	222
65+ years	174	157	144	166	140	168	163	147	144
Unknown	48	13	16	8	7	12	16	16	76
Total	**4360**	**4412**	**4308**	**3895**	**3787**	**3417**	**3799**	**3350**	**3406**
% distribution									
<1 year	18%	22%	21%	21%	21%	23%	22%	22%	20%
01-04 years	28%	28%	28%	28%	28%	27%	28%	28%	30%
05-09 years	12%	10%	10%	9%	9%	8%	8%	9%	8%
10-14 years	8%	6%	7%	7%	8%	5%	5%	4%	4%
15-19 years	14%	12%	13%	12%	13%	13%	12%	13%	12%
20-24 years	5%	5%	5%	5%	4%	5%	6%	6%	6%
25-44 years	6%	7%	7%	7%	7%	7%	8%	6%	7%
45-64 years	5%	7%	6%	6%	6%	7%	7%	6%	7%
65+ years	4%	4%	3%	4%	4%	5%	4%	4%	4%
Unknown	1%	0%	0%	0%	0%	0%	0%	0%	2%

Table 38: Age distribution of confirmed and probable laboratory diagnosed serogroup C invasive meningococcal disease cases, in EU and EEA countries, 1999—2007

Age Group	1999	2000	2001	2002	2003	2004	2005	2006	2007
Numbers of cases									
<1 year	200	148	116	113	67	68	56	53	50
01-04 years	550	503	276	232	168	154	123	124	128
05-09 years	231	212	131	120	62	70	55	47	56
10-14 years	224	168	124	116	97	63	68	52	60
15-19 years	404	288	286	242	151	158	126	124	130
20-24 years	141	146	126	110	76	48	70	60	57
25-44 years	150	210	197	189	118	117	96	82	100
45-64 years	150	136	168	133	77	86	80	71	53
65+ years	95	120	102	125	63	56	72	44	46
Unknown	17	6	9	1	4	1	3	3	4
Total	**2162**	**1937**	**1535**	**1381**	**883**	**821**	**749**	**660**	**684**
% distribution									
<1 year	9%	8%	8%	8%	8%	8%	7%	8%	7%
01-04 years	25%	26%	18%	17%	19%	19%	16%	19%	19%
05-09 years	11%	11%	9%	9%	7%	9%	7%	7%	8%
10-14 years	10%	9%	8%	8%	11%	8%	9%	8%	9%
15-19 years	19%	15%	19%	18%	17%	19%	17%	19%	19%
20-24 years	7%	8%	8%	8%	9%	6%	9%	9%	8%
25-44 years	7%	11%	13%	14%	13%	14%	13%	12%	15%
45-64 years	7%	7%	11%	10%	9%	10%	11%	11%	8%
65+ years	4%	6%	7%	9%	7%	7%	10%	7%	7%
Unknown	1%	0%	1%	0%	0%	0%	0%	0%	1%

Table 39: Serogroup distribution of confirmed and probable laboratory diagnosed invasive meningococcal disease cases, by country, 2007

Country	Serogroup							Non group-able	Not known	Serogroup C vaccination introduced (year of introduction)
	B	C	W135	A	X	Y	Z			
Austria	37	21	0	0	0	2	0	1	0	
Belgium	139	16	1	0	0	2	0	0	0	Yes (2002)
Bulgaria	-	-	-	-	-	-	-	-	-	
Cyprus	2	1	0	0	0	0	0	0	1	
Czech Republic	52	13	0	0	1	3	0	0	6	
Denmark	35	19	2	0	0	2	0	0	0	
Estonia	9	2	0	0	0	0	0	0	0	
Finland	29	8	0	0	0	5	0	0	0	
France	421	161	23	1	4	24	0	3	43	Yes (2010)
Germany	255	89	12	3	0	15	0	2	59	
Greece	68	5	1	0	0	0	0	6	29	Yes (2007)
Hungary	32	3	0	1	0	0	0	0	7	
Ireland	156	2	2	0	0	0	0	0	1	Yes (2000)
Italy	75	43	2	0	0	3	0	1	54	Yes (2005)
Latvia	4	3	0	1	0	0	0	0	7	
Lithuania	23	1	4	0	0	0	0	16	22	
Luxembourg	-	-	-	-	-	-	-	-	-	
Malta	5	0	1	0	0	0	0	0	0	
Netherlands	-	-	-	-	-	-	-	-	-	Yes (2002)
Poland	144	136	7	1	0	5	0	1	98	
Portugal	82	4	1	0	0	3	0	1	16	Yes (2006)
Romania	23	11	1	3	1	1	0	0	105	
Slovakia	22	6	0	0	0	1	0	0	6	
Slovenia	12	5	1	0	0	0	0	0	0	
Spain	498	73	7	0	0	5	0	21	15	Yes (2000)
Sweden	17	16	2	0	0	9	0	1	4	
United Kingdom	1240	43	37	0	1	37	1	3	86	Yes (1999)
EU Total	**3380**	**681**	**104**	**10**	**7**	**117**	**1**	**56**	**559**	
Iceland	3	1	0	0	0	0	0	0	0	Yes (2002)
Liechtenstein	-	-	-	-	-	-	-	-	-	
Norway	23	2	1	0	0	2	0	2	0	
Overall	**3406**	**684**	**105**	**10**	**7**	**119**	**1**	**58**	**559**	

Table 40: Notification rate (per 100 000) of confirmed and probable laboratory diagnosed invasive meningococcal disease cases, by serogroup and by country, 2007

Country	Serogroup							Non-groupable	Not Known	Serogroup C vaccination introduced (year of introduction)
	B	C	W135	A	X	Y	Z			
Austria	0.45	0.25	0.00	0.00	0.00	0.02	0.00	0.01	0.00	
Belgium	1.31	0.15	0.01	0.00	0.00	0.02	0.00	0.00	0.00	Yes (2002)
Bulgaria	-	-	-	-	-	-	-	-	-	
Cyprus	0.26	0.13	0.00	0.00	0.00	0.00	0.00	0.00	0.13	
Czech Republic	0.51	0.13	0.00	0.00	0.01	0.03	0.00	0.00	0.06	
Denmark	0.64	0.35	0.04	0.00	0.00	0.04	0.00	0.00	0.00	
Estonia	0.67	0.15	0.00	0.00	0.00	0.00	0.00	0.00	0.00	
Finland	0.55	0.15	0.00	0.00	0.00	0.09	0.00	0.00	0.00	
France	0.66	0.25	0.04	0.00	0.01	0.04	0.00	0.00	0.07	
Germany	0.31	0.11	0.01	0.00	0.00	0.02	0.00	0.00	0.07	
Greece	0.61	0.04	0.01	0.00	0.00	0.00	0.00	0.05	0.26	
Hungary	0.32	0.03	0.00	0.01	0.00	0.00	0.00	0.00	0.07	
Ireland	3.62	0.05	0.05	0.00	0.00	0.00	0.00	0.00	0.02	Yes (2000)
Italy	0.13	0.07	0.00	0.00	0.00	0.01	0.00	0.00	0.09	
Latvia	0.18	0.13	0.00	0.04	0.00	0.00	0.00	0.00	0.31	
Lithuania	0.68	0.03	0.12	0.00	0.00	0.00	0.00	0.47	0.65	
Luxembourg	-	-	-	-	-	-	-	-	-	
Malta	1.23	0.00	0.25	0.00	0.00	0.00	0.00	0.00	0.00	
Netherlands	-	-	-	-	-	-	-	-	-	
Poland	0.38	0.36	0.02	0.00	0.00	0.01	0.00	0.00	0.26	
Portugal	0.77	0.04	0.01	0.00	0.00	0.03	0.00	0.01	0.15	
Romania	0.11	0.05	0.00	0.01	0.00	0.00	0.00	0.00	0.49	
Slovakia	0.41	0.11	0.00	0.00	0.00	0.02	0.00	0.00	0.11	
Slovenia	0.60	0.25	0.05	0.00	0.00	0.00	0.00	0.00	0.00	
Spain	1.12	0.16	0.02	0.00	0.00	0.01	0.00	0.05	0.03	
Sweden	0.19	0.18	0.02	0.00	0.00	0.10	0.00	0.01	0.04	
United Kingdom	2.04	0.07	0.06	0.00	0.00	0.06	0.00	0.00	0.14	Yes (1999)
EU Total	**0.74**	**0.14**	**0.03**	**0.00**	**0.00**	**0.02**	**0.00**	**0.03**	**0.12**	
Iceland	0.98	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	Yes (2002)
Liechtenstein	-	-	-	-	-	-	-	-	-	
Norway	0.49	0.04	0.02	0.00	0.00	0.04	0.00	0.04	0.00	
Overall	**0.74**	**0.14**	**0.03**	**0.00**	**0.00**	**0.02**	**0.00**	**0.02**	**0.11**	

Table 41: Dominant serotype of confirmed and probable laboratory diagnosed serogroup C invasive meningococcal disease cases (total number of serotyped C cases), by country, 1999—2007

Country	1999	2000	2001	2002	2003	2004	2005	2006	2007
Austria	P2.2b (14)	P2.2a (10)	P2.2a (34)	P2.2a (17)	P2.2b (12)	NT (15)	P2.2a (16)	P2.2a (22)	P2.2a (13)
Belgium	P2.2b (77)	P2.2a (85)	P2.2a (178)	P2.2a (89)	P2.2a (46)	P2.2a (20)	P2.2a (18)	P2.2a (11)	P2.2a (10)
Bulgaria	-	-	-	-	-	-	-	-	-
Cyprus	-	-	-	-	-	-	-	-	-
Czech Republic	P2.2a (26)	P2.2a (10)	P2.2a (23)	P2.2a (28)	P2.2a (23)	P2.2a (25)	P2.2a (18)	NT (11)	P2.2a (7)
Denmark	P2.2a (21)	P2.2a (16)	P2.2a (24)	P2.2a (16)	P3.15 (19)	P3.15 (14)	P2.2b (21)	P2.2b (19)	P2.2a (8)
Estonia	-	-	-	-	-	-	-	-	-
Finland	NT (9)	NT (10)	NT (9)	P2.2a (6)	NT (5)	NT (5)	P2.2b (1)	P2.2b (5)	NT, P2,2b(8)
France	P2.2b (100)	-	P2.2a (126)	P2.2a (172)	P2.2a (115)	P2.2a (130)	P2.2a (120)	P2.2a (135)	P2.2a (62)
Germany	P2.2a (86)	P2.2a (96)	P2.2a (118)	P2.2a (140)	P2.2a (116)	P2.2a (75)	P2.2a (71)	P2.2a (74)	-
Greece	P2.2a (17)	P2.2a (9)	P2.2a (8)	NT, P2.2a (6)	P2.2a (2)	-	P2.2a (2)	P2.2a, P3.4 (2)	-
Hungary	-	-	-	-	-	-	-	-	-
Ireland	P2.2a (42)	P2.2a (54)	P2.2a (6)	P2.2a (4)	P2.2a (2)	P2.2a (1)	P2.2a (4)	P2.2a (3)	P3.4 (1)
Italy	P2.2a (16)	P2.2a (24)	P2.2a (15)	P2.2b (32)	P2.2b (55)	P2.2b (83)	P2.2b (92)	P2.2b (27)	P2.2a (14)
Latvia	-	-	-	-	-	-	-	-	-
Lithuania	-	-	-	-	-	-	-	-	NT (1)
Luxembourg	-	-	-	-	-	-	-	-	-
Malta	P2.2a (1)	P2.2b (1)	NT (1)	-	P2.2a (1)	-	NT (3)	P2.2a (1)	-
Netherlands	P2.2a (81)	P2.2a (106)	P2.2a (277)	P2.2a (222)	P2.2a (44)	P2.2a (17)	NT, P2.2a (4)	No serotyping	-
Poland	NT, P3.22 (8)	NT (7)	P3.4 (4)	NT (11)	NT (21)	NT (40)	NT (62)	NT (67)	NT (57)
Portugal	-	-	-	-	-	-	-	-	-
Romania	-	-	-	-	-	-	-	-	-
Slovakia	-	-	-	-	-	-	-	-	P2.2a (3)
Slovenia	-	P2.2a (1)	P2.2a (1)	P2.2a (1)	NT (3)	-	P2.2b (4)	-	P2.2a (2)
Spain	P2.2b (230)	P2.2b (235)	P2.2a (102)	P2.2a (140)	P2.2a (98)	P2.2a (104)	P2.2a (81)	P2.2a (46)	P2.2a (16)
Sweden	NT (11)	NT (14)	P2.2a (14)	NT, P3.15 (11)	P3.15 (12)	NT, P3.15 (11)	P3.15 (15)	P3.15 (15)	P3.15 (8)
United Kingdom	P2.2a (713)	P2.2a (514)	P2.2a (220)	P2.2a (128)	P2.2a (65)	P2.2a (34)	P2.2a (17)	P2.2a (17)	P2.2a (13)
Iceland	-	-	-	-	-	-	-	-	-
Liechtenstein	-	-	-	-	-	-	-	-	-
Norway	P2.2a (10)	P2.2a (12)	NT, P2.2a (13)	NT, P3.15, P3.4 (3)	P2.2a (9)	P2.2a (1)	NT (3)	P3.1 (1)	-

Table 42: Dominant serotype of confirmed and probable laboratory diagnosed serogroup B invasive meningococcal disease cases (total number of serotyped B cases), by country, 1999–2007

Country	1999	2000	2001	2002	2003	2004	2005	2006	2007
Austria	P3.15 (60)	NT, P3.15 (45)	NT (46)	NT (39)	NT (37)	P3.15 (32)	P3.15 (36)	NT (26)	NT (13)
Belgium	P3.4 (198)	P3.4 (165)	P3.4 (169)	P3.4 (161)	P3.4 (164)	P3.4 (122)	P3.4 (141)	P3.4 (109)	P3.4 (62)
Bulgaria	-	-	-	-	-	-	-	-	-
Cyprus	-	-	-	-	-	-	-	-	-
Czech Republic	NT (36)	NT (34)	NT (34)	P3.4 (37)	P3.15 (20)	P3.4 (40)	P3.4 (35)	P3.4 (27)	P3.4 (8)
Denmark	P3.15 (126)	P3.15 (98)	P3.15 (92)	P3.15 (65)	P3.15 (57)	P3.15 (56)	P3.15 (39)	NT (34)	P3.15 (16)
Estonia	-	-	-	-	-	-	-	-	-
Finland	P3.4 (33)	P3.4 (29)	P3.4 (34)	NT (35)	NT, P3.4 (28)	P3.4 (29)	P3.4 (28)	P3.4 (37)	P3.4 (29)
France	NT (302)	-	NT (194)	NT (224)	NT (213)	NT (239)	NT (292)	NT (293)	NT (118)
Germany	P3.15 (292)	NT (319)	P3.15 (359)	P3.4 (154)	P2.2a (4)	P2.2b (2)	P2.2b (2)	-	-
Greece	NT (30)	P3.4 (20)	P3.4 (35)	P3.4 (37)	P3.4 (28)	P3.4 (29)	P3.4 (37)	P3.4 (33)	-
Hungary	-	-	-	-	-	-	-	-	-
Ireland	P3.4 (86)	P3.4 (86)	P3.4 (55)	NT (51)	NT (49)	NT, P3.4 (45)	P3.4 (40)	NT (46)	NT (25)
Italy	P3.14 (60)	P3.4 (61)	P3.15 (46)	P3.4 (47)	P3.15 (66)	P3.15 (48)	P3.4 (67)	P3.15 (51)	P3.15 (14)
Latvia	-	-	-	-	-	-	-	-	-
Lithuania	-	-	-	-	-	-	-	-	NT (23)
Luxembourg	-	-	-	-	-	-	-	-	-
Malta	P3.4 (6)	P3.4 (13)	P3.4 (9)	P3.4 (6)	P3.4 (3)	NT (4)	P3.1, P3.4, P3.15 (3)	P3.4 (5)	-
Netherlands	P3.4 (466)	P3.4 (413)	P3.4 (417)	P3.4 (371)	P3.4 (293)	P3.4 (232)	P3.4 (211)	-	-
Poland	NT (55)	NT (33)	P3.22 (29)	NT (23)	NT (31)	NT (71)	NT (113)	NT (63)	P3.15 (30)
Portugal	-	-	-	-	-	-	-	-	-
Romania	-	-	-	-	-	-	-	-	-
Slovakia	-	-	-	-	-	-	-	-	P3.15 (7)
Slovenia	NT (6)	P3.15 (4)	NT, P3.15 (8)	NT (5)	NT, P3.22 (6)	NT (5)	NT (9)	-	P3.15 (6)
Spain	P3.4 (345)	P3.4 (431)	NT (268)	NT (375)	NT (479)	NT (442)	NT (362)	NT (379)	NT (50)
Sweden	P3.15 (15)	NT (22)	NT (32)	NT (24)	NT (27)	NT (25)	P3.15 (22)	NT (20)	NT (6)
United Kingdom	P3.4 (1020)	NT (1018)	NT (964)	NT (796)	NT (779)	NT (639)	NT (659)	NT (574)	NT (288)
Iceland	-	-	-	-	-	-	-	-	-
Liechtenstein	-	-	-	-	-	-	-	-	-
Norway	P3.15 (57)	P3.15 (49)	P3.15 (32)	P3.4 (24)	P3.4 (31)	P3.4, P3.15 (19)	P3.4 (24)	P3.4 (24)	-

Table 43: Serogroup-specific case fatality ratio (CFR) in confirmed and probable laboratory diagnosed invasive meningococcal disease cases, by country, 2007

Country	Serogroup B			Serogroup C			Other serogroups / non-groupable		
	Deaths	Cases	CFR	Deaths	Cases	CFR	Deaths	Cases	CFR
Austria	1	37	3%	2	21	10%	1	3	33%
Belgium	8	139	6%	1	16	6%	1	3	33%
Bulgaria	-	-	-	-	-	-	-	-	-
Cyprus	0	2	0%	0	1	0%	0	1	0%
Czech Republic	6	52	12%	1	13	8%	2	10	20%
Denmark	3	35	9%	2	19	11%	0	4	0%
Estonia	0	9	0%	1	2	50%	0	0	0%
Finland	2	29	7%	3	8	38%	1	5	20%
France	42	421	10%	27	161	17%	11	98	11%
Germany	19	255	7%	13	89	15%	5	91	5%
Greece	4	68	6%	0	5	0%	1	36	3%
Hungary	4	32	13%	1	3	33%	2	8	25%
Ireland	6	156	4%	0	2	0%	0	3	0%
Italy	11	75	15%	8	43	19%	3	60	5%
Latvia	1	4	25%	0	3	0%	0	8	0%
Lithuania	0	23	0%	0	1	0%	3	42	7%
Luxembourg	0	0	0%	0	0	0%	0	0	0%
Malta	0	5	0%	0	0	0%	0	1	0%
Netherlands	-	-	-	-	-	-	-	-	-
Poland	29	144	20%	14	136	10%	12	112	11%
Portugal	5	82	6%	0	4	0%	2	21	10%
Romania	2	23	9%	0	11	0%	8	111	7%
Slovakia	0	22	0%	0	6	0%	0	7	0%
Slovenia	0	12	0%	1	5	20%	0	1	0%
Spain	42	498	8%	17	73	23%	7	48	15%
Sweden	-	17	-	-	16	-	-	16	-
United Kingdom	68	1240	5%	7	43	16%	5	165	3%
EU Total	**253**	**3380**	**7%**	**98**	**681**	**14%**	**64**	**854**	**7%**
Iceland	0	3	0%	0	1	0%	0	0	0%
Liechtenstein	0	0	0%	0	0	0%	0	0	0%
Norway	2	23	9%	0	2	0%	0	5	0%
Overall	**255**	**3406**	**7%**	**98**	**684**	**14%**	**64**	**859**	**7%**

Table 44: Proportion of meningitis in confirmed and probable laboratory diagnosed cases of invasive meningococcal disease, 1999–2007

Meningitis	1999	2000	2001	2002	2003	2004	2005	2006	2007
<50%	Germany	Germany	Germany	Germany	Lithuania	Iceland	Iceland	Ireland	Austria
	Greece	Hungary	Hungary	Hungary	Spain	Ireland	Ireland	Spain	Belgium
	Hungary	Ireland	Ireland	Ireland	Sweden	Malta	Spain	Sweden	Czech Republic
	Ireland	Latvia	Latvia	Latvia		Spain			Estonia
	Latvia	Lithuania	Slovak Republic	Slovak Republic					Finland
	Lithuania	Slovak Republic	Sweden	Spain					France
	Malta	Sweden	United Kingdom	Sweden					Greece
	Slovak Republic	United Kingdom		United Kingdom					Iceland
	Sweden								Ireland
	United Kingdom								Latvia
									Lithuania
									Luxembourg
									Malta
									Netherlands
									Norway
									Poland
									Portugal
									Slovenia
									Spain
									Sweden
									United Kingdom
50-70%	Belgium	Belgium	Belgium	Belgium	Austria	Austria	Austria	Belgium	Germany
	Estonia	Finland	Finland	Denmark	Belgium	Belgium	Belgium	Denmark	Hungary
	Iceland	Greece	Iceland	Finland	Denmark	Czech Republic	Denmark	Estonia	Italy
	Netherlands	Iceland	Lithuania	France	Finland	Finland	Finland	Finland	Romania
	Norway	Malta	Norway	Malta	Germany	Greece	Greece	Italy	
	Slovenia	Portugal	Spain	Netherlands	Iceland	Latvia	Latvia	Latvia	
	Spain			Norway	Ireland	Lithuania	Lithuania	Lithuania	
				Portugal	Latvia	Netherlands	Norway	Norway	
				Slovenia	Malta	Norway	Portugal	Poland	
				Switzerland	Netherlands	Slovenia	Slovenia	Portugal	
					United Kingdom	Sweden	Sweden	Switzerland	
						United Kingdom	Switzerland	United Kingdom	
							United Kingdom		
>70%	Austria	Austria	Austria	Austria	Czech Republic	Denmark	Czech Republic	Austria	Cyprus
	Czech Republic	Czech Republic	Czech Republic	Czech Republic	Estonia	Estonia	Estonia	Czech Republic	Denmark
	Denmark	Denmark	Denmark	Estonia	France	France	France	France	Slovakia
	Finland	Estonia	Estonia	Greece	Greece	Germany	Germany	Germany	
	France	France	France	Iceland	Hungary	Hungary	Hungary	Greece	

Meningitis	1999	2000	2001	2002	2003	2004	2005	2006	2007
	Italy	Italy	Greece	Italy	Italy	Italy	Italy	Hungary	
	Poland	Netherlands	Italy	Lithuania	Norway	Poland	Malta	Iceland	
	Portugal	Norway	Malta	Poland	Poland	Portugal	Netherlands	Malta	
	Switzerland	Poland	Netherlands		Portugal	Slovak Republic	Poland	Netherlands	
		Slovenia	Poland		Slovak Republic	Switzerland	Slovak Republic	Slovak Republic	
		Spain	Portugal		Slovenia			Slovenia	
		Switzerland	Slovenia		Switzerland				
			Switzerland						

Table 45: Total number of invasive meningococcal disease cases and notification rate, by gender and by country, 2007

Country	Cases of Males	Cases of Females	Cases of Unknowns	Population of Males	Population of Females	Incidence of Males	Incidence of Females
Austria	34	35	0	4037171	4261752	0.84	0.82
Belgium	73	87	0	5181408	5403126	1.41	1.61
Bulgaria							
Cyprus	3	1	0	383360	395324	0.78	0.25
Czech Republic	45	30	0	5026184	5261005	0.90	0.57
Denmark	40	38	0	2696662	2750422	1.48	1.38
Estonia	7	4	0	618145	724053	1.13	0.55
Finland	25	18	0	2583742	2693213	0.97	0.67
France	368	352	1	30804152	32587988	1.19	1.08
Germany	231	205	0	40301166	42013740	0.57	0.49
Greece	51	58	0	5532047	5639693	0.92	1.03
Hungary	27	22	0	4779078	5287080	0.56	0.42
Ireland	97	82	0	2157681	2154845	4.50	3.81
Italy	91	92	0	28718441	30412846	0.32	0.30
Latvia	14	7	0	1051034	1230271	1.33	0.57
Lithuania	35	31	0	1576963	1807916	2.22	1.71
Luxembourg	1	1	0	235792	240395	0.42	0.42
Malta	4	2	0	202613	205197	1.97	0.97
Netherlands	100	95	0	8088514	8269478	1.24	1.15
Poland	201	191	0	18426775	19698704	1.09	0.97
Portugal	67	50	0	5129937	5469158	1.31	0.91
Romania	89	66	0	10511076	11054043	0.85	0.60
Slovakia	17	18	0	2618284	2775353	0.65	0.65
Slovenia	10	8	0	986982	1023395	1.01	0.78
Spain	409	405	2	21942724	22531907	1.86	1.80
Sweden	20	29	0	4523523	4589734	0.44	0.63
United Kingdom	791	708	23	29817947	30998754	2.65	2.28
EU Total	**2850**	**2635**	**26**	**237931401**	**249479392**	**1.20**	**1.06**
Iceland	3	1	0	156576	151096	1.92	0.66
Liechtenstein							
Norway	19	11	0	2325788	2355346	0.82	0.47
Overall	**2872**	**2647**	**26**	**240413765**	**251985834**	**1.19**	**1.05**

Table 46: Seasonal distribution of total number of invasive meningococcal disease cases, by country, 2007*

Country	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7	Month 8	Month 9	Month 10	Month 11	Month 12	Un-known	Total
Austria	11	8	10	2	3	3	1	6	3	7	6	9	0	69
Belgium	19	14	17	15	9	11	14	6	13	14	20	8	0	160
Bulgaria	-	-	-	-	-	-	-	-	-	-	-	-	-	0
Cyprus	0	1	0	1	0	0	1	0	0	0	0	1	0	4
Czech Republic	12	8	7	4	5	8	4	3	5	8	8	3	0	75
Denmark	4	12	13	3	7	7	6	5	3	8	4	6	0	78
Estonia	1	2	2	0	2	1	0	0	0	1	0	2	0	11
Finland	4	3	8	4	3	2	2	1	6	7	1	2	0	43
France	77	99	57	65	61	58	44	42	30	59	66	63	0	721
Germany	46	40	46	34	15	13	24	25	27	32	29	28	77	436
Greece	18	23	9	15	9	4	0	3	2	12	2	12	0	109
Hungary	5	1	6	7	6	3	3	0	3	5	6	4	0	49
Ireland	22	18	17	23	14	7	20	10	11	11	13	13	0	179
Italy	18	23	20	14	17	8	6	5	7	20	14	31	0	183
Latvia	3	1	1	1	4	2	0	1	0	2	1	5	0	21
Lithuania	8	5	12	6	7	5	5	1	1	3	9	4	0	66
Luxembourg	1	0	0	0	1	0	0	0	0	0	0	0	0	2
Malta	0	1	1	0	2	2	0	0	0	0	0	0	0	6
Netherlands	11	32	15	21	20	10	20	11	2	35	6	12	0	195
Poland	51	29	50	20	37	25	28	18	22	31	34	47	0	392
Portugal	19	10	17	7	11	12	12	6	4	6	8	5	0	117
Romania	19	11	16	10	10	7	22	20	7	9	14	10	0	155
Slovakia	5	5	1	3	1	3	3	3	2	3	5	1	0	35
Slovenia	2	1	3	0	2	2	1	1	0	2	2	2	0	18
Spain	129	104	75	63	68	58	48	35	26	52	79	59	20	816
Sweden	5	2	4	2	5	5	5	5	2	7	4	3	0	49
United Kingdom	201	168	158	119	111	95	107	92	70	104	136	161	0	1522
EU Total	691	621	565	439	430	351	376	299	246	438	467	491	97	5511
Iceland	0	0	0	1	0	0	0	0	1	0	1	1	0	4
Liechtenstein	-	-	-	-	-	-	-	-	-	-	-	-	-	0
Norway	1	8	2	3	4	1	2	1	1	2	2	3	0	30
Overall	692	629	567	443	434	352	378	300	248	440	470	495	97	5545

***** *For seasonal distribution the date used is DateUsedForStatistics".*

Table 47: Vaccination status of reported invasive meningococcal disease cases, by country, 2007

Country	Fully vaccinated *	Partly vaccinated **	Not vaccinated ***	Unknown ****	Total	Fully vaccinated (%)	Partly vaccinated (%)	Not vaccinated (%)	Unknown (%)
Austria	0	0	0	69	69	0%	0%	0%	100%
Belgium	18	0	41	101	160	11%	0%	26%	63%
Bulgaria	-	-	-	-	0	-	-	-	-
Cyprus	1	0	0	3	4	25%	0%	0%	75%
Czech Republic	0	0	0	75	75	0%	0%	0%	100%
Denmark	2	0	36	40	78	3%	0%	46%	51%
Estonia	0	0	11	0	11	0%	0%	100%	0%
Finland	0	0	0	43	43	0%	0%	0%	100%
France	0	0	0	721	721	0%	0%	0%	100%
Germany	0	0	0	436	436	0%	0%	0%	100%
Greece	0	0	0	109	109	0%	0%	0%	100%
Hungary	0	0	49	0	49	0%	0%	100%	0%
Ireland	1	0	158	20	179	1%	0%	88%	11%
Italy	3	0	72	108	183	2%	0%	39%	59%
Latvia	0	0	0	21	21	0%	0%	0%	100%
Lithuania	0	0	56	10	66	0%	0%	85%	15%
Luxembourg	0	0	0	2	2	0%	0%	0%	100%
Malta	0	0	6	0	6	0%	0%	100%	0%
Netherlands	-	-	-	-	-	-	-	-	-
Poland	0	5	387	0	392	0%	1%	99%	0%
Portugal	74	0	11	32	117	63%	0%	9%	27%
Romania	0	0	155	0	155	0%	0%	100%	0%
Slovakia	0	0	29	6	35	0%	0%	83%	17%
Slovenia	0	0	0	18	18	0%	0%	0%	100%
Spain	0	0	0	816	816	0%	0%	0%	100%
Sweden	0	0	0	49	49	0%	0%	0%	100%
United Kingdom	69	16	65	1372	1522	5%	1%	4%	90%
EU Total	**168**	**21**	**1076**	**4246**	**5511**	**3%**	**0%**	**20%**	**77%**
Iceland	0	0	0	4	4	0%	0%	0%	100%
Liechtenstein	-	-	-	-	0	-	-	-	-
Norway	0	0	19	11	30	0%	0%	63%	37%
Overall	**168**	**21**	**1095**	**4261**	**5545**	**3%**	**0%**	**20%**	**77%**

**Fully vaccinated = according to age and the recommended schedule in the reporting country.*
***Partly vaccinated, = according to age and the recommended schedule in the reporting country.*
****Not vaccinated = not vaccinated at all*
*****Unknown = Vaccination status unknown*

Table 48: Total number of invasive meningococcal disease cases and percentage distribution (%), by clinical presentation, by country, 2007

Country	Meningitis		Meningitis and Septicaemia		Septicaemia		Unknown	
	Cases	%	Cases	%	Cases	%	Cases	%
Austria	30	43%	13	19%	17	25%	3	4%
Belgium	49	31%	47	29%	48	30%	3	2%
Bulgaria	-	-	-	-	-	-	-	-
Cyprus	4	100%	0	0%	0	0%	0	0%
Czech Republic	-	-	-	-	-	-	-	-
Denmark	58	74%	0	0%	0	0%	0	0%
Estonia	4	36%	5	45%	2	18%	0	0%
Finland	13	30%	18	42%	11	26%	0	0%
France	0	0%	197	27%	0	0%	0	0%
Germany	237	54%	147	34%	33	8%	0	0%
Greece	24	22%	13	12%	72	66%	0	0%
Hungary	27	63%	6	14%	10	23%	0	0%
Ireland	32	18%	69	39%	74	41%	0	0%
Italy	115	63%	49	27%	17	9%	2	1%
Latvia	-	-	-	-	-	-	-	-
Lithuania	22	33%	20	30%	21	32%	3	5%
Luxembourg	-	-	-	-	-	-	-	-
Malta	2	33%	3	50%	1	17%	0	0%
Netherlands	-	-	-	-	-	-	-	-
Poland	127	32%	165	42%	97	25%	3	1%
Portugal	52	44%	48	41%	16	14%	1	1%
Romania	103	66%	18	12%	23	15%	11	7%
Slovakia	29	83%	5	14%	0	0%	1	3%
Slovenia	4	22%	0	0%	1	6%	1	6%
Spain	285	35%	380	47%	101	12%	3	0%
Sweden	-	-	-	-	-	-	-	-
United Kingdom	56	4%	51	3%	36	2%	6	0%
EU Total	**1273**	**23%**	**1254**	**23%**	**580**	**11%**	**37**	**1%**
Iceland	0	0%	0	0%	4	100%	0	0%
Liechtenstein	-	-	-	-	-	-	-	-
Norway	11	37%	12	40%	5	17%	2	7%
Overall	**1284**	**23%**	**1266**	**23%**	**589**	**11%**	**39**	**1%**

Table 49: Data quality of the variables reported on invasive meningococcal disease, all countries, 2007

Variable	Known	Unknown	Not Applicable	Blank	Total	Known (%)	Unk. (%)	Not Appl. (%)	Blank (%)	Number countries
Age	5384	0	0	161	5545	97%	0%	0%	3%	28
AgeMonth	1504	0	0	4041	5545	27%	0%	0%	73%	21
Classification	5545	0	0	0	5545	100%	0%	0%	0%	28
ClinicalCriteria	3950	1595	0	0	5545	71%	29%	0%	0%	23
ClinicalPresentation	3184	2361	0	0	5545	57%	43%	0%	0%	23
DateOfDiagnosis	3400	0	0	2145	5545	61%	0%	0%	39%	18
DateOfNotification	3758	0	0	1787	5545	68%	0%	0%	32%	20
DateOfOnset	4240	0	0	1305	5545	76%	0%	0%	24%	24
EpiLinked	1423	1960	2162	0	5545	26%	35%	39%	0%	12
Gender	5519	26	0	0	5545	100%	0%	0%	0%	28
Imported	1817	3728	0	0	5545	33%	67%	0%	0%	20
LaboratoryResult	4330	1076	139	0	5545	78%	19%	3%	0%	25
MIC_CHL	1269	4276	0	0	5545	23%	77%	0%	0%	9
MIC_CIP	2733	2812	0	0	5545	49%	51%	0%	0%	12
MIC_CTX	1363	4182	0	0	5545	25%	75%	0%	0%	11
MIC_PEN	2736	2809	0	0	5545	49%	51%	0%	0%	12
MIC_RIF	2739	2806	0	0	5545	49%	51%	0%	0%	12
MIC_SSS	2497	3048	0	0	5545	45%	55%	0%	0%	10
Outcome	5046	499	0	0	5545	91%	9%	0%	0%	26
Pathogen	5545	0	0	0	5545	100%	0%	0%	0%	28
probableCountryOfInfection1	68	2745	22	2710	5545	1%	50%	0%	49%	8
probableCountryOfInfection2	2835	0	0	2710	5545	51%	0%	0%	49%	19
resultMLSTMENI2	230	5315	0	0	5545	4%	96%	0%	0%	4
ResultPorA1	550	4995	0	0	5545	10%	90%	0%	0%	6
ResultPorA2	550	4995	0	0	5545	10%	90%	0%	0%	6
ResultPorA3	92	5453	0	0	5545	2%	98%	0%	0%	2
ResultSeqType	34	0	0	5511	5545	1%	0%	0%	99%	2
ResultVr1	1739	3806	0	0	5545	31%	69%	0%	0%	13
ResultVr2	1760	3785	0	0	5545	32%	68%	0%	0%	14
ResultVr3	0	0	0	0	5545	0%	0%	0%	0%	-
Serogroup	4394	1151	0	0	5545	79%	21%	0%	0%	26
Serotype	2074	3471	0	0	5545	37%	63%	0%	0%	16
SIR_CHL	442	5103	0	0	5545	8%	92%	0%	0%	5
SIR_CIP	697	4848	0	0	5545	13%	87%	0%	0%	10
SIR_CTX	566	4979	0	0	5545	10%	90%	0%	0%	9
SIR_PEN	713	4832	0	0	5545	13%	87%	0%	0%	12
SIR_RIF	643	4902	0	0	5545	12%	88%	0%	0%	10
SIR_SSS	902	4643	0	0	5545	16%	84%	0%	0%	10
Specimen1	4057	1488	0	0	5545	73%	27%	0%	0%	24
Specimen2	714	4831	0	0	5545	13%	87%	0%	0%	17
SpecLinkLab1	1767	3778	0	0	5545	32%	68%	0%	0%	13
testMethod1MENI1	4022	1523	0	0	5545	73%	27%	0%	0%	23
testMethod1MENI2	458	451	0	4636	5545	8%	8%	0%	84%	6
testMethod1MENI3	268	287	0	4990	5545	5%	5%	0%	90%	5
testMethod1MENI4	428	481	0	4636	5545	8%	9%	0%	84%	6
testMethod2MENI1	789	4756	0	0	5545	14%	86%	0%	0%	14
testMethod2MENI2	26	262	0	5257	5545	0%	5%	0%	95%	2
VaccStatus	1284	4261	0	0	5545	23%	77%	0%	0%	15
Overall	**100084**	**118319**	**2323**	**39889**	**266160**	**38%**	**44%**	**1%**	**15%**	**-**