COMMISSION OF THE EUROPEAN COMMUNITIES

Programme on Community action on the prevention of AIDS and
certain other communicable diseases
DG SANCO Agreement No. VS/1999/3504 (99CVF4-031)

EU-IBIS
European Union Invasive Bacterial Infections Surveillance Network

INVASIVE *NEISSERIA MENINGITIDIS* IN EUROPE – 2001

Project leaders: ***Dr Mary Ramsay and Prof Andrew Fox***

Scientific Co-ordinator: ***Sarah Handford***
Communicable Disease Surveillance Centre
Health Protection Authority
61 Colindale Ave, London, NW9 5EQ
Tel. +44-20-8200-6868 Fax. +44-20-8200-7868
Email: sarah.handford@hpa.org.uk

July 2001

SUMMARY

Introduction

The surveillance network for invasive meningococcal disease in Europe began in 1999 as part of the European Union Invasive Bacterial Infections Surveillance (EU-IBIS) project, building upon existing surveillance networks for bacterial meningitis in Europe. The aims of the network are to improve the epidemiological information on meningococcal disease in Europe, to improve the laboratory capacity to accurately characterise isolates of *N. meningitidis* and to form a focus for wider collaboration with non-EU countries.

Methods

Agreed usage of a minimum dataset and standard case definitions for *N. meningitidis* has enabled valid comparisons to be made of the disease epidemiology within Europe, and hence assist the monitoring of epidemiological changes. Information collected on the surveillance systems and the vaccination programme(s) in use by each participant country has also aided interpretation of the epidemiological analyses.

Improvements in the laboratory capacity within the EU to accurately characterise *N. meningitidis* have been achieved through gaining information on systems in use by participants, and by undertaking an External Quality Assurance Scheme (EQAS) with the participant reference laboratories. The EQAS helped identify any existing problems in correctly serotyping *N. meningitidis* isolates, and will enable corrections/assistance in laboratory methods to be made, hence improving comparability of data between countries.

Results

In 2001 the incidence of reported culture-confirmed meningococcal disease varied between 0.2 and 6.5 per 100,000 across collaborating countries. This is likely to reflect both genuine differences in disease epidemiology and in ascertainment. In three countries, ascertainment of laboratory confirmed infection has been increased by around 100% following the introduction of PCR and it is likely that similar increases will be achieved in other countries when access to and awareness of PCR diagnosis improves.

The burden of meningococcal disease is highest in young children, although in most countries a smaller, secondary peak in incidence is observed in teenagers. Serogroup B is the most common cause of invasive meningococcal disease in Europe, followed by serogroup C. The proportion of cases attributable to serogroup C disease is highly variable. Austria, Belgium and the Netherlands have experienced increases in the proportion of serogroup C disease between 1999 and 2001, whereas the proportion in England & Wales, Greece and Ireland has decreased following the implementation of serogroup C conjugate vaccine campaigns.

Disease presentation is also highly variable throughout Europe and it is unclear whether this is due to reporting differences, or if there are genuine differences in presentation. The case-fatality rate is 6-7% on average, although this varies by age and serogroup. The range of CFR estimates are between 0 and 13%, suggesting that ascertainment of outcome is also an issue.

Conclusions

This project has demonstrated the successful development of existing networks towards the objective of providing high quality surveillance information on meningococcal infection in the European Union and neighbouring countries. The importance of the reference and diagnostic microbiology under-pinning this data cannot be over-emphasised. The laboratory questionnaire and the quality assurance scheme suggest that standards in reference laboratories in the EU are high.

CONTENTS

1. INTRODUCTION

The European Commission Decision No. 2119/98/EC for setting up a network for the epidemiological surveillance and control of communicable diseases in the European Community stated that 'bacterial meningitis' was a priority. Invasive disease due to *Neisseria meningitidis* comes within this priority and this project has built on two surveillance networks that already exist within Europe. The European Monitoring Group on Meningococci (EMGM) is a consortium of reference microbiologists and epidemiologists working in Europe to exchange information on meningococcal infection. Secondly, a network for surveillance of bacterial meningitis in Europe was established in 1988 and is supported by commercial funding. This project aims to build on these networks, avoiding any duplication of activity, and to be in line with the Charter Group's priorities of the EU Communicable Disease Network.

Using the frameworks already established, a DG SANCO surveillance network for *N. meningitidis* disease was established in all 15 EU countries and 4 non-EU countries (2000-2001) to improve epidemiological information and laboratory capacity to characterise isolates of this invasive bacterial infection. The number of countries, either EU Accession countries or countries outside the EU, contributing to the network is gradually increasing. In early 2004, approximately 10 Accession Countries will be formally admitted to the EU, and hence a sizeable increase will be seen in the number of countries participating in the network

1.1 Project aims

1. To improve the epidemiological information on invasive meningococcal disease within the European Union.
2. To improve the laboratory capacity to accurately characterise the isolates of *N. meningitidis* using standardised methods.
3. To form a focus for future wider collaboration with non European Union and candidate European Union countries in Europe.

As meningococcal disease is relatively uncommon, this project will allow pooling of such data to increase the power of any epidemiological analysis. European wide analysis should be able to detect changes in serogroup and serotype distribution, which is important in formulation of vaccination strategies. In addition, by pooling data from all countries, the populations under surveillance will be composed of a wider variety of ethnic groups.

This project will set standards for the epidemiological surveillance of infections and for methods used in reference laboratories. Countries will be able to learn from models of good practice in other member states, and these standards can also be applied in other countries, especially Candidate EU and non-European Union countries. In addition, establishment of this network may facilitate the early dissemination of advances in therapy and in public health control measures and lead to the harmonisation of guidance on the control of meningococcal disease. This project will also provide a model and a focus for future research and public health collaborations, for example the evaluation of other new vaccines such as conjugate pneumococcal vaccines.

This project will provide substantial and up-to-date epidemiological information from which meningococcal disease vaccination policy can be developed within individual countries. It may also facilitate the eventual harmonisation of vaccine schedules in the European Union. The project provides an established network for the rapid dissemination of changes in the epidemiology of an infection that may have public health significance. In addition, it facilitates the rapid exchange of information on imported strains of *N. meningitidis* infections.

2. METHODS

Questionnaires on the surveillance system(s) and the laboratory diagnostic methods were sent to all the participating countries at the start of the network in 2000. Countries joining the network later were also requested to complete the two questionnaires. The information gained from both these questionnaires is important in the correct interpretation of the data that was provided by each individual country.

The agreed minimum data set is used by each contributing partner. This data set includes age, sex, date of onset, method of confirmation, site of identification, grouping, typing and subtyping results (as appropriate). (Appendix 2) Analysis of age-specific incidence rates, temporal trends and diversity of *N. meningitidis* infections will be compared. In countries with vaccination programmes, coverage data will also be requested and comparison of rates of infection in both vaccinated and unvaccinated cohorts will be interpreted in conjunction with coverage, schedule and vaccine used, years since implementation and method of introduction.

Standard case definitions developed as part of the previous collaborations are used in this project. Where surveillance is performed using other definitions, datasets are re-coded to provide comparable data for all participating countries.

The descriptive epidemiology were analysed using standard statistical packages on the minimum data set provided for *N. meningitidis* infection. Currently, because of the small number of countries yet using routine PCR confirmation, most data analyses and comparisons were performed on culture-confirmed cases only.

A rapid reporting surveillance scheme for the W135 Hajj strain (W135;P2.2a; P1.5, P1.2 or compatible phenotype) was established in September 2000 in six sentinel EU reference laboratories. Throughout 2001 the reference laboratories reported case details weekly to CDSC Colindale. Information on whether the case was a pilgrim, a contact of a pilgrim or had no known link to the Hajj, has helped monitor the disease and its spread within Europe.

In 2001 an external quality assurance scheme (EQAS) was undertaken using standard micro reagents. A panel of well-characterised strains were freeze-dried and an annual selection was sent to each national or regional reference laboratory. These laboratories characterised the strains according to their routine practice and returned the results to the coordinating laboratory. The results of testing were compared with known identity of the organism and returned to each centre. Aggregate results were anonymised for use in this report and for sharing with the group as a whole. Discussion of problems with identification will occur.

Dissemination of results from the surveillance of invasive *N. meningitidis* disease in the EU occurred through project reports to the network participants of the epidemiological analyses, and presentation of results at meetings and scientific conferences. Monthly reports on the *N. meningitidis* W135 Rapid Reporting Scheme were placed in the Eurosurveillance Weekly. Feedback reports were given to the microbiologist network participants on the External Quality Assurance Scheme (EQAS). Posters were presented at the 13th International Pathogen Neisseriae Conference (IPNC). With the completion of this report information will be placed on the shared website, and regular updates made.

No funding was available for a meeting of the collaborators within this project in 2001, but a good percentage of the partners were able to meet at the 2001 EMGM meeting in Orebro, Sweden. Also, a meeting of EU-IBIS/meningococci partners was held within the time of the 13th International Pathogen Neisseriae Conference (IPNC) in Oslo, Norway, 1-6 September 2002.

3. RESULTS

3.1 Summary of surveillance systems

Every participating country submitted a surveillance questionnaire. Information on the methods of surveillance were presented in the previous report.

3.1.1 Conjugate Meningococcal C vaccination programmes

Within the surveillance systems questionnaire, countries also provided information about conjugate meningococcal group C vaccination programmes. Routine vaccination programmes are now in place in Ireland, Iceland, Luxembourg, Netherlands, Spain, the United Kingdom and part of Belgium, and catch-up programmes of varying structures have been undertaken in each of these countries. (Table i)

Table i: Conjugate meningococcal group C vaccination programmes in the EU, as at January 2002.

Country	Routine	Year	Catch-up	Year	Voluntary	Year
Belgium 1. Wallonie 2. Flanders	 Yes Yes	 2002 2002	 <6 years 1-3 yrs 1-6 yrs & 14-17 yrs	 2002 2001 2002		
Greece	No		0-6 yrs		Yes	2001
Iceland	Yes	2002				
Ireland	Yes	2000	<23 yrs	2000		
Luxembourg	No		12 mths-19 yrs	2001-2002		
Netherlands	Yes	2002	1-19 yrs	Jun-Oct 2002		
Portugal (Madeira only)	No	2002				
Spain	Yes	2000	< 6 yrs	Oct 2000		
UK	Yes	1999	< 18 yrs 19-25 yrs	Nov 1999-2000 Dec 2001-2002		

Before the introduction of the conjugate MenC vaccination programmes, the only mass campaign using polysaccharide vaccine that was reported in the EU occurred in Spain in the period Sept-Nov 1997. Polysaccharide vaccine A+C was administered to the population aged 18 months to 19 years in 16 of the 19 autonomous Spanish regions.

3.2 Laboratory Diagnostic Methods Questionnaire

Laboratory diagnostic questionnaires were received from fourteen laboratories. The description of methods used was published in the previous report.

3.3 Summary of case data received for 2001

Seventeen countries have supplied disaggregated case data for 2001 to the co-ordinating centre in CDSC, Colindale, London. Information on 6,829 cases was supplied by the collaborators for 2001. No case data was provided by Luxembourg or Sweden for 2001. Data is fairly complete for age, serogroup, serotype and serosubtype, and method of confirmation. Source(s) of data influence the completeness of case ascertainment, and the completeness of typing information. The differing degree of completeness of data received from the collaborating countries reflects the differences in both the referral of isolates to reference laboratories, and in the reconciliation of data sources/surveillance systems within the countries. For example, Portugal was only able to provide data on cases referred to the reference laboratory. As the referral rate is known to be less than 80% of all culture confirmed cases, the numbers given for Portugal in the following tables will be lower than an expected national total. Similar issues may be relevant to data supplied from other countries, and countries are encouraged to let the centre know of any similar caveats to the data supplied.

3.4 The epidemiology of invasive meningococcal disease in Europe

3.4.1 Incidence of culture-confirmed cases

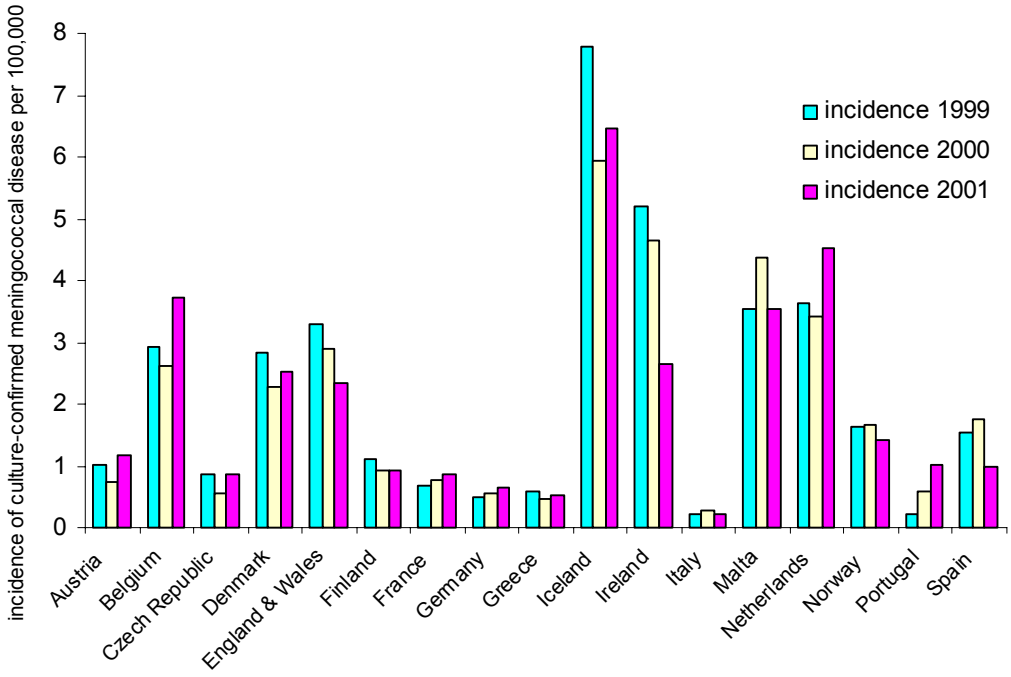
The incidence of culture confirmed invasive meningococcal disease varied widely between the participating network countries over 2001. (Table ii) Six countries exhibited rates of under 1.0 per 100,000 population, four countries were between 1-2/100,000, five between 2-4/100,000, while Iceland and Netherlands were both above 4/100,000 population. England and Wales, Greece, Ireland and Spain have all shown decreases in the overall incidence of meningococcal disease over the three years 1999-2001. (Table 1) Meanwhile, notable increases over these three years were seen in Austria, Belgium, France, Germany, and the Netherlands.(figure 1)

Table ii: Incidence of culture-confirmed cases of invasive meningococcal disease by country, 2001.

Country	No. of cases	Population	Incidence (per 100,000)
Austria	91	7,795,788	1.17
Belgium	380	10,263,414	3.70
Czech Republic	89	10,272,503	0.87
Denmark	134	5,349,212	2.52
E & W	1237	52,943,284	2.34
Finland	48	5,116,826	0.94
France	523	60,254,277	0.87
Germany	521	82,163,475	0.63
Greece	54	10,521,670	0.51
Iceland	18	278,702	6.46
Ireland	101	3,839,000	2.63
Italy	133	57,844,017	0.23
Malta	13	366,431	3.55
Netherlands	723	15,987,075	4.52
Norway	64	4,503,436	1.42
Portugal-lab*	106	10,365,117	1.02
Spain	394	39,513,630	1.00
Total	4,629	377,353,528	1.23

* Portugal's reference laboratory dataset is only a subset of the national meningococcal case

Figure 1: Incidence of culture-confirmed meningococcal disease per 100,000 population



3.4.2 Incidence of PCR-confirmed cases

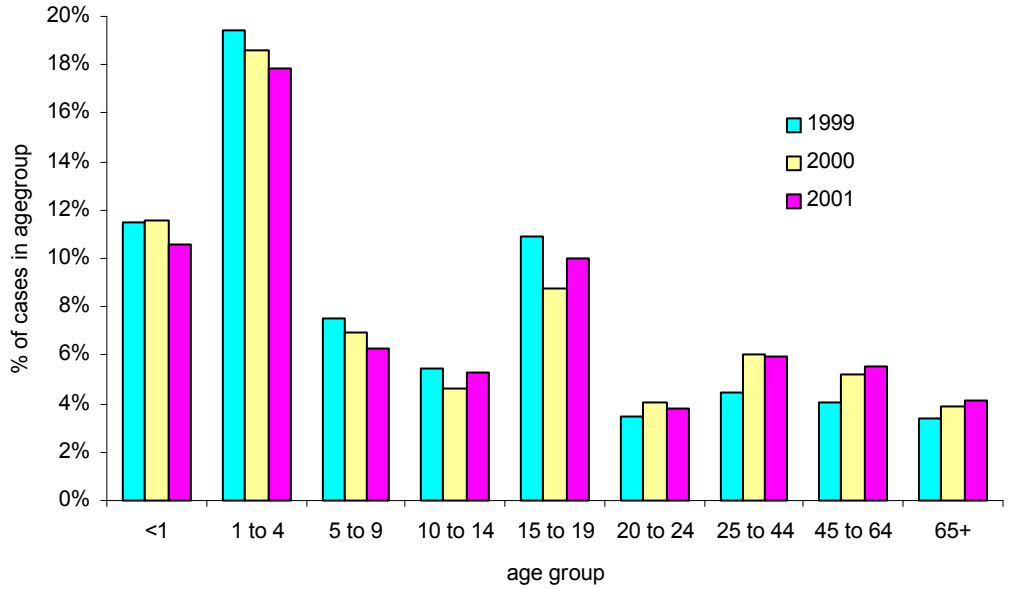
PCR-confirmed cases now account for a sizeable proportion of the total number of cases in Austria, Czech Republic, England and Wales, Greece, Iceland, Ireland, Malta and Norway. The overall incidence of disease is increased markedly by including cases confirmed only by PCR. (Table 2) In three countries the number of cases confirmed only by PCR exceeded the number culture-confirmed. Increasing use of PCR confirmation in the coming years therefore has potential to increase the number of cases being detected, and hence to inflate the incidence relative to years when PCR confirmation was not in use.

Currently, because only a small number of countries are yet using routine PCR confirmation, most data analyses and comparison will be performed on culture-confirmed cases only. To give a fairer representation of the incidence rate of meningococcal disease in those countries using PCR as a major confirmation method alongside culture, this data is looked at separately. (Table 2) Incidence rates are calculated for those cases confirmed by PCR and/or culture. These more representative values show England and Wales to have a rate of 5/100,000 population, and Ireland to have a rate of 7/100,000 population in 2001, instead of the values of 2/100,000 and 3/100,000, respectively, for culture confirmed cases. Greece shows a rate of 1.76/100,000 when culture and PCR confirmed cases are combined, rather than 0.51 when only culture confirmed cases are considered.

3.4.3 Age distribution of culture confirmed cases of invasive meningococcal disease

The age distribution of cases of invasive meningococcal disease follows the expected pattern, with the majority of cases being in the children under five years of age.(figure 2, table 3) The combined age-specific incidence rates of invasive meningococcal disease in the contributing countries over 2000 and 2001 show the highest rate in infants (18 per 100,000), followed by the 1-4 year age group and the 15-19 year age group. (Table 4) A continuing decrease is, however, seen in all age groups under 10 years of age over the years 1999-2001. Small increases were seen in the 10-14 and 15-19 year age groups between 2000 and 2001, whereas a decline was noted between 1999 and 2000. (Table 5 and earlier reports) For all age groups over 20 years, the incidence rate either decreased slightly or stayed the same over 2000-2001. The decrease observed in children under 10 years is likely to reflect the impact of the group C vaccination programme, firstly in the UK (one of the large countries in the network) and later in Ireland and Spain. The increase in incidence in the most recent year in older children is in contrast to the decreases observed in countries using MenC vaccine.

Figure 2: Age distribution of culture-confirmed meningococcal disease in Austria, Belgium, Czech Republic, Denmark, England & Wales, Finland, France, Germany, Greece, Malta, Netherlands, Norway, Portugal and Spain: 1999, 2000, 2001



Austria, Czech Republic, England & Wales, Greece, Iceland, Ireland and Norway confirmed a proportion of their invasive meningococcal disease cases by PCR-only. The age distribution of the PCR-only confirmed cases shows a very similar pattern to that of the culture-confirmed cases. (Tables 5) Data on the age distribution of PCR confirmed cases from Greece, Czech Republic and Iceland only became available for 2001. It is expected that other countries will add PCR data as the methods become more readily available.

3.4.4 Incidence of meningococcal disease serogroup B, by year and agegroup

The incidence of serogroup B meningococcal disease in the European Union was highest in the children under one year of age. (Table 6). A smaller secondary peak in the incidence of serogroup B was seen in the 15-19 year old age group, but remains low in all older age groups. Between 2000 and 2001 a decrease was seen in under ones (16.69 to 13.24). Apart from the 10-14 year age group, the incidence in all other age groups decreased between 2000 and 2001. These decreases were smallest in the age groups over 25 years.

3.4.5 Incidence of meningococcal disease serogroup C, by year and agegroup

Similar to the incidence of serogroup B, the incidence of serogroup C in the EU is greatest in the infant population (2.10), but is also high in the 1-4 years age group (1.65) A secondary peak is seen in the 15-19 year olds (0.95). (Table 7) In nearly all age groups, except the 15-19 years age group, a decrease in incidence rate was observed between 2000 and 2001. The largest decreases were shown in the under ones and in the 1-4 year olds : 2.63 to 2.10 and 2.24 to 1.65, respectively. These decreases are likely to be influenced by the impact of MenC conjugate vaccination programme.

3.4.6 Age-specific incidence of group B and C infection by country

The incidence of culture-confirmed meningococcal disease serogroups B and C by age group varied widely amongst the participating countries. However, all showed a similar pattern in the age groups with the highest and the lowest incidence rates.

For the incidence of serogroup B, all countries had the highest rate in the under ones year olds, and the vast majority had a second peak in incidence in the 15-19 year olds. This held true for 1999, 2000 and 2001. (table 27 & previous report) The variation in rates between countries in 2001 was very wide, but this may reflect small numbers in some countries. In the under one year old age group it varied from 0.0 (Malta) to 45.5 (Ireland).

The pattern was less consistent for the age-specific serogroup C incidence rate amongst participant countries. In 2001, ten of the 17 contributing EU countries displayed the highest incidence rate of serogroup C disease in the under one year olds, with a secondary increase in incidence in the 15-19 year olds (or in the nearest age group to this). (tables 28 & previous report) Countries not displaying this in were Denmark, Finland, Germany, Italy, Malta, Netherlands and Norway. Of these countries, Denmark, Netherlands and Norway had a higher rate in the 15-19 year olds than in the under ones. Caution must be taken with countries such as Finland and Malta, as case numbers are very small in comparison to other participant countries.

3.4.7 Proportion of meningitis to septicaemia in culture-confirmed cases of invasive meningococcal disease,

The proportion of culture confirmed cases reported with meningitis varied widely by country and also varied within each country over the three years. The reasons for these differences are unclear but seem to be consistent within each country.

Overall, the proportion of culture-confirmed meningococcal disease cases presenting with meningitis was 59%, 61% and 64% in 1999, 2000 and 2001, respectively.(tables 8,9&10) In 2001, nine of the sixteen countries contributing this data exhibited proportions of greater than 60% for meningitis to septicaemia.(table 8)

Cultured confirmed group B cases displayed, overall, the proportion of cases with meningitis to be in the range 63%-65% over year 1999-2001. The majority of countries had greater than 60% of reported cases diagnosed with meningitis. (tables 15&16)

The proportion of cases with meningitis in the culture-confirmed Group C cases was lower than for group B, 50% in 1999, 53% in 2000 and 49% in 2001. (tables 17&18) Once again, the majority of countries had greater than 60% of their Group C cases presenting with meningitis, whilst England and Wales, Ireland and Malta displayed the opposite pattern.

3.4.8 Distribution of serogroups in invasive meningococcal disease, 1999-2001

Group B is the major cause of invasive meningococcal disease in Europe, causing the majority of infections in all countries except Iceland. (table 12 & previous report) The second most common serogroup is group C, but the proportion of cases caused by group C infection is quite variable between countries, ranging from 8% to 78% in 2001. A number of countries have shown an increase in the proportion of cases caused by Group C over 1999, 2000 and 2001: Austria, Belgium, and Netherlands showing big increases. But it is notable that the proportion of group C infections in England and Wales, Greece, and Ireland have all declined over 1999-2001, reflecting the impact of conjugate meningococcal group C vaccine. (Table iii).

Table iii: Proportion of cases due to serogroup C by country, 1999-2001

% Group C	**1999**	**2000**	**2001**
<10%	-	Malta	Malta
10-19%	Austria Denmark Finland Netherlands Norway	Austria Denmark Netherlands Norway	England & Wales* Finland Ireland*
20-29%	Belgium France Germany Italy Malta	Czech Republic England & Wales* Finland France Germany Greece Italy	Denmark Germany Greece Italy Norway Spain*
30-39%	England & Wales* Greece Ireland* Spain*	Belgium Ireland* Spain*	Czech Republic France Netherlands
40+%	Czech Republic Iceland Portugal-lab	Iceland Portugal-lab	Austria Belgium Iceland Portugal-lab

* countries implementing MenC vaccination during this period

The serogroup distribution of the PCR-only confirmed cases is difficult to interpret, as the distribution will be affected by the serogroups each particular country is testing for and by the sensitivity of the grouping PCRs (Tables 14) The latter explanation probably accounts for the high proportion of cases that were PCR-confirmed but not grouped.

Other than groups B and C, serogroups W135, Y, X, Z/29E and A were the major groups identified. Group W135 is the most common of these and the number of W135 cases increased from 1999 to 2001 in Belgium, England and Wales, and Norway.(table 20) These countries and a number of others, particularly France, observed an increase in the number of W135 cases from 1999 to 2000 in association with the Hajj in 2000. In 2001, the total number of W135 cases remained similar to that of 2000.(table 19 & previous report) Greece experienced a sizeable increase in the number of Group A cases between 1999 to 2001. This is believed to be due to importation from Russia (personal communication).

3.4.9 Distribution of serotypes of group C and B meningococcal disease

The leading serotype of group C was C2a, with C2b as the second most common. Overall, serotype C2a increased steadily from 1999 to 2001. This increase was seen in 8 individual countries who supplied data for all three years.(Tables 21, 22 & 23) In 1999, serotype 2a was the leading type associated with group C disease in nine of the 15 countries who contributed data but by 2001, serotype 2a had become the most common type in 12 countries (Table 25).

Group B infections appear to be more diverse, with more than 50% of cases in the "other" category. (Tables 24 & previous reports)) There are considerable differences between countries in strain composition. Of the two major group B sero-subtypes identified (B:15:1.7,1.16 and B:4:1.4), the leading strain in most countries was consistent between years 1999-2001. Spain displays a very different pattern from other contributing countries over these three years. The B:4:1.15 strain was dominant; comprising approximately one quarter of the serotyped B strains in each year. In 2001, 6% of the serotyped group B strains were not-typable, and in Austria, France and Spain this was in the range of 12-16%.

3.4.10 Overall case fatality rates

The overall case fatality rates (CFR) for all cases of laboratory confirmed meningococcal disease in 1999, 2000 and 2001 were 6-7%. (Table 29) Between 2000 and 2001 case fatality rates in Belgium and Czech Republic showed an increase of 2% or greater, and Norway has had a decrease of 8% from 1999 to 2001. Because of differences in method of coding deaths, and to allow comparison of CFR between countries, the denominator included all cases and therefore cases with unknown outcome were assumed to have survived. Using this method, the CFR ranged from 0% to 13% in 2001, although it is recognised that reporting of outcome was likely to vary in completeness between countries. Variation between countries is present, and care must be taken when making comparisons purely on CFRs, as the case numbers vary greatly within our study partners.

The exclusion of PCR confirmed cases made minimal difference to the case fatality rates observed for the majority of individual countries, suggesting that CFR did not vary between cases confirmed by culture and by PCR.(table 30) However, England and Wales saw an increase from 2000-2001 of 3%, and small increases were observed in a few countries. The resulting overall CFR for laboratory confirmed cases excluding those cases confirmed only by PCR confirmed cases increased from 6% in 2000 to 8% in 2001.

3.4.11 Case fatality ratio by serogroup

The highest case fatality ratio in the EU countries in 2001 was seen amongst cases with serogroup W135 infection (15%) followed by serogroup C infection (11.0%). (Table 31) France was the only country with recorded deaths due to infection with serogroup A meningococcal disease. Overall, the CFR for serogroup C cases is approximately double that of serogroup B cases. Detailed analysis of CFR in relation to the phenotypic characteristics of the strain is being conducted.

3.4.12 Case fatality ratio by age for serogroup B and C infections by age

Age specific case fatality rates for serogroup B infection (Table 32) decreases from the under one year old age group to 15-19 year age group, and then increases steadily to its highest value in the population over 65 years of age. The overall pattern of CFR by age for serogroup C infection is for it to decrease from under ones to 10-14 year olds, from where it steadily increases with age.

3.4.13 Antibiotics resistance

Twelve countries (Austria, Belgium, Czech Republic, Denmark, England & Wales, Germany, Greece, Iceland, Italy, Malta, Netherlands, Portugal and Spain) contributed antibiotic minimum inhibitory concentration (MIC) data for isolates tested for antibiotic susceptibility. The proportion of such strains in each country varies widely in 2001. (table iv) This difference probably, in part, reflects differences in methods used. The overall percentage of isolates with MICs between 0.06-1.99 for penicillin was 53% in 1999, 61% in 2000 and 54% in 2001.(tables 34 & 35) However, collection of additional years of data, and further analysis of this data, will be necessary before conclusions can be drawn. As part of the DGXII funded EU-MENNET project, Spain is be leading a work package to look at standardisation of assays of penicillin sensitivity.

Table iv: Susceptibility of *N. meningitidis* to penicillin, by country: 2001

Country	2001		
	MIC <= 0.06	MIC >0.06 and <2.00	Total
Austria	66 (80%)	16 (20%)	82
Belgium	328 (92%)	30 (8%)	358
Czech Republic	56 (97%)	2 (3%)	58
Denmark	67 (54%)	57 (46%)	124
E&W	439 (35%)	823 (65%)	1262
Germany	31 (6%)	490 (94%)	521
Greece-lab	35 (83%)	7 (17%)	42
Iceland	14 (78%)	4 (22%)	18
Italy	60 (98%)	1 (2%)	61
Malta	2 (15%)	11 (85%)	13
Netherlands	1 (6%)	16 (94%)	17
Portugal-lab*	82 (77%)	24 (23%)	106
Spain-lab*	212 (54%)	182 (46%)	394
Total	1393 (46%)	1663 (54%)	3056

* Greek and Spanish reference laboratory data was used here as it was the only dataset with antibiotic resistance

* Portugal's reference laboratory data only is used here, and in 1999 includes only a small number of reporting labs/hospitals

3.5 Impact of conjugate group C meningoccal disease vaccination programmes on the epidemiology of the disease

The introduction of MenC vaccination programmes into England and Wales, Ireland and Spain has seen a notable decrease in the number of culture confirmed group C meningococcal disease cases in all the age groups that have received routine vaccination or been within the catch-up programmes run at the beginning of each countries campaign. (figure 3) Looking at the combined data of countries that did not have MenC vaccination programmes established in the 1999-2001 period, the reverse pattern can be seen: a increase in the number of group C cases in all age groups over the three year period. (figure 4) This has been paralleled by an overall increase in these countries of the proportion of serogroup C cases that are serotype P2.2a, the hypervirulent strain of this serogroup. (figure 5). In 2002, other countries introduced MenC vaccination programmes (table (i)), and the impact of these will be seen in future reports.

Figure 3: No. of culture-confirmed cases of invasive meningococcal disease serogroup C cases in countries with established conjugate group C meningococcal vaccine programmes (England & Wales, Ireland and Spain combined), by age group and year, 1999-2001

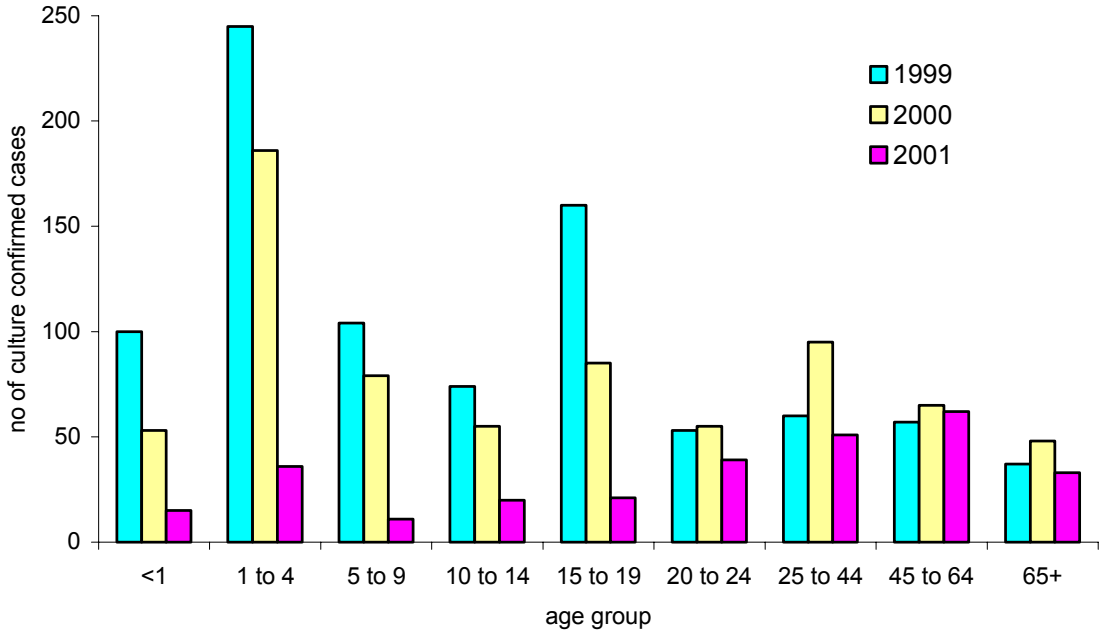


Figure 4: No. of culture-confirmed invasive meningococcal disease serogroup C cases in EU-IBIS countries without established nationwide conjugate group C meningococcal vaccination programmes, by age group and year, 1999-2001.

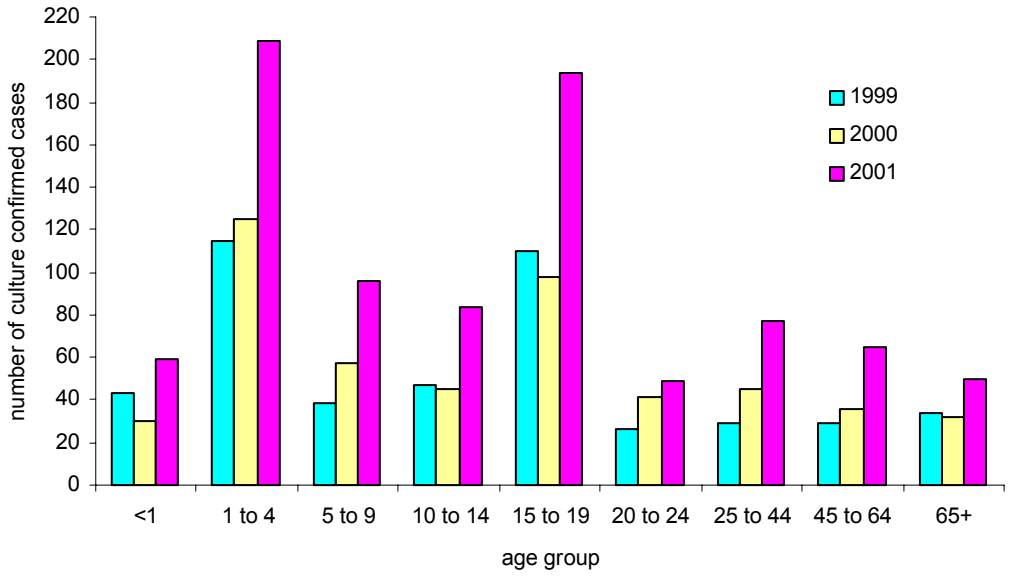
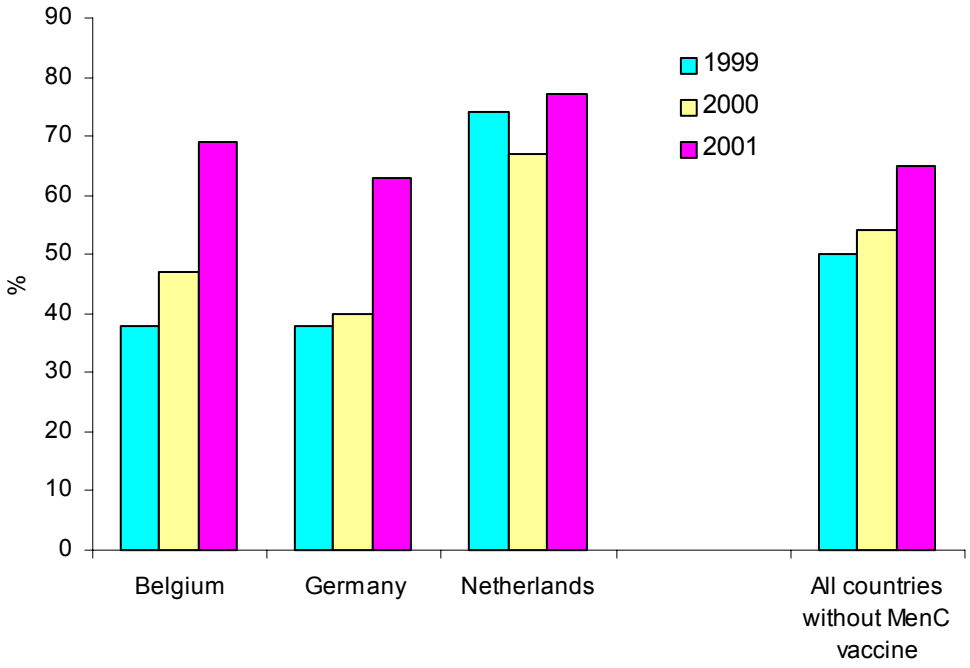


Figure 5: Proportion of culture-confirmed meningococcal disease serogroup C cases that are serotype P2.2a – 1999-2001



3.6 Rapid sentinel surveillance of W135 infection

In 2000, outbreaks of W135 meningococcal disease were observed in a number of European countries amongst people returning from the Muslim pilgrimage to Mecca in Saudi Arabia (The Hajj) and their contacts. Prior to Hajj 2000, different vaccines had been recommended for pilgrims in each country, some using AC polysaccharide vaccine with others using quadrivalent (A/C/Y/W135) vaccine. In 2001, many countries recommended quadrivalent vaccine, but sufficient quantity was not available for all pilgrims. In 2002 the Saudi Arabian authorities required all pilgrims to be vaccinated with QV before Hajj visas were issued.

In response the outbreaks seen in 2000 amongst returning pilgrims and contacts, EU-IBIS established, in September 2000, a sentinel reporting system for the Hajj 2000 outbreak strain in six EU member states. National reference laboratories in France, Germany, Ireland, Netherlands, Spain, and England and Wales reported weekly all cases of W135:2a:1.2,5 or compatible strains.

The aims of this surveillance system were:

1. to rapidly monitor the spread of W135 outbreak strain in Europe, and
2. to inform future interventions within Europe and in relation to travel.

Between week 36 in 2000 and week 30 in 2002, a total of 159 cases of W135:2a:1.2,5 (or compatible strains) were reported from the six sentinel reference laboratories in the EU. Of the total number of cases, 7 were pilgrims, 31 were contacts of pilgrims and 121 were cases

with no known link to a Hajj pilgrimage. (table v) The number of cases in all three categories was lower in 2002 compared to the number in the same period in 2001. (table vi)

Table v: Distribution of meningococcal disease caused by W135:2a:1.2,5 (or strains phenotypically compatible) in the 6 sentinel surveillance countries, by case status, from week 36 in 2000 to week 30 in 2002 inclusive.

Country	Total cases	Case status		
		Pilgrim	Contact	No known link
France	55	-	3	52
Germany	18	-	1	17
Ireland	-	-	-	-
The Netherlands	12	-	3	9
Spain	1	-	-	1
United Kingdom	73	7	24	42
Total	159	7	31	121

Table vi: Distribution of cases of meningococcal disease caused by W135 strains compatible with W135:2a:1.2,5 in the six sentinel surveillance countries, by case status, in compatible periods in 2001 and 2002 (the 23 weeks following the Hajj)

Year	Total cases	Case status		
		Pilgrim	Contact	No known link
2001	65	6	25	34
2002	20	0	2	18
Total	85	6	27	52

The age distribution of cases infected with the outbreak strain (excluding pilgrims) differs from cases infected with other W135 strains, with relatively more cases infected in the younger age groups, and less infectious in those over 45 years of age.

The case fatality rate (CFR) observed in cases infected with the outbreak strain, in the period week 36 in 2000 to week 30 in 2002, is 15.7%, a CFR higher than any other serogroup across all EU countries. From the EU-IBIS complete database, the CFR among cases infected by W135 strains other than the outbreak strain is comparable to that shown by serogroups C and Y.

A marked reduction was seen in the number of cases in Hajj pilgrims and contacts following Hajj 2002, the year when vaccination with quadrivalent vaccine became a requirement by Saudi Arabian authorities. The large number of cases in England and Wales after Hajj 2001 pilgrimage may, in part, result from insufficient quadrivalent vaccine supplies to cover all pilgrims that year. Cases of meningococcal disease caused by the outbreak strain are still being recognised in individuals with no link to the hajj, suggesting that transmission is sustained. In France, in contrast to the UK, the number of cases of W135 meningococcal strain increased in the second half of 2001 and in 2002, most of which is not related to the Hajj. This increase appears to be due to cases of genetic lineages different from those in the UK.

4. CONCLUSIONS

This project has demonstrated the successful development of existing networks towards the objective of providing high quality surveillance information on meningococcal infection in the European Union and neighbouring countries. The improved quality of the data is demonstrated by the inclusion of cases confirmed by PCR in more countries and by the improved completeness of data provided (eg. data on age is now supplied by Greece).

The data provided on meningococcal disease shows marked variations in overall incidence. Excluding very small countries, a twenty-fold variation in the incidence of culture confirmed infection was seen in 2001. This is likely to reflect both genuine differences in the epidemiology and in ascertainment. The contribution of each of these is difficult to quantify, but secular trends within countries and between age-groups and serogroups are likely to be valid in most instances. Countries should be aware, however, of the major influence that changes in clinical and laboratory practice can exert on ascertainment. For example, reduced used of lumbar puncture for the diagnosis of meningitis, the use of pre-admission antibiotics and the introduction of new laboratory tests. The potential for ascertainment to change because of new technological advances is illustrated by the data provided on PCR diagnosis for those countries where the test is being used routinely. In three countries, ascertainment of laboratory confirmed infection has been increased by around 100% and it is likely that similar increases will be achieved in other countries when access to and awareness of PCR diagnosis improves. The ability to confirm and group a larger number of meningococcal infections, however, is clearly a major advance that will improve the data available and help to better establish the burden of disease with a view to vaccine introduction. We hope that countries without a routine service can learn from other countries in the project about the development and provision of such services.

The age-specific incidence and age-distribution of meningococcal disease follows the pattern previously described, with the majority of cases in children under five. Minor differences were noted in the age distribution between countries. Group B is still the commonest cause of infection in Europe, although the proportion of disease due to group C varies quite considerably. The proportion of group C infection did change within countries over the years 1999-2001. In some instances this was due to the introduction of a group C vaccine, in others it may reflect changes in epidemiology such as the introduction of a hyper-virulent strain. Identification of such changes at a European level is important, as it may predict changes that will subsequently take place in neighbouring countries.

For groups other than B and C, there was also variation in the predominant strains between countries and between years. In 2000, a dramatic increase in cases due to W135 infection had been observed in several countries in association with the Hajj, and another epidemic of the Hajj strain disease was seen following Hajj 2001. In many countries, small numbers of cases prevent valid interpretation of such changes but this phenomenon illustrates the strength of the European project in pooling data from many countries. In late 2000 a rapid reporting system was established by EU-IBIS in sentinel EU countries for the W135 Hajj strain. This scheme monitored the spread of this strain in Europe and was able to monitor the impact of the Saudi Arabian government's vaccination requirement for entry to Hajj 2002. A dramatic decrease in the number of Hajj-linked cases was seen in 2002, and this has continued after the Hajj 2003, also.

As well as changes in serogroup, there are differences in major serotypes of group C and group B within Europe. Changes were noted in the predominant group C serotype in two countries and may be associated with a future shift in incidence or case-fatality rates. The major group C serotype was P2.2a in 12 countries. Six countries have shown an increase in the proportion of group C cases of serotype P2.2a over 1999-2001, and four of these have

shown a steady increase in the overall, and group C, case fatality rates. The increase in serogroup C serotype 2a infection in many countries without MenC programmes is of concern in view of the association between this serotype and strains of the ST-11 complex. The introduction of strains from the latter complex has been associated with increases in incidence and high case fatality rates in many developed countries (including Canada, UK, Czech Republic). Group B strain variation is seen across Europe, and phenotypic data displayed in this study, and from previous records, shows marked variation in the prevalent strains across Europe. Observation over more years will allow the early recognition of emerging strains that might be missed within any one country. Consideration needs to be given to the substantial proportion of group B strains that are non-typable for serotype and serosubtype. Differences in the proportions may reflect different methods or reagents in use and should be established via the EQAS scheme. Molecular analysis of meningococcal strains is part of the DGXII funded EU-MENNET project and may shed light on this area in future years.

Analysis of case fatality ratio is prone to difficulties for a variety of reasons. We suspect that the figures presented here are an underestimate of true fatality ratios, as there is likely to be under-ascertainment of outcome in some countries. Comparison between countries is unlikely to be valid as it may be explained by differences in ascertainment, in age distribution or serogroup/serotype distribution between countries. Comparison between serogroups and age-groups however is likely to reflect genuine differences. Analysis indicates that fatality is higher in older individuals. Case fatality ratios for group B infections are low overall, and in most countries lower than that observed for group C or for other serogroups. Case fatality for group Y and W135, however, is high, and the CFR for W135 increased in 2000 and 2001. This occurred at the same time as the incidence increased in association with the Hajj and is probably due to the main Hajj-associated strain belonging to a hyper-virulent lineage (ST-11 complex).

The impact of vaccination on the epidemiology of meningococcal disease in Europe is small so far. As the UK is one of the largest countries, the impact of conjugate group C vaccine (introduced in late 1999 for those under 18 years) has had a small impact on the overall incidence and a larger impact on the incidence of group C infection. Ireland and Spain have also recently introduced vaccine and other countries are likely to implement vaccination over the next year or so. In future, therefore, data may need to be presented separately for those countries with vaccination programmes. Demonstration of a change in the epidemiology is likely to encourage neighbouring countries to consider vaccination, particularly if the incidence of group C infection increases or case-fatality becomes higher than previously observed.

The flexible rapid reporting system that was established in September 2000 for the meninogocccal W135 strain associated with the Hajj 2000 outbreak has shown to be an important asset in informing intervention policies. Circulation of the outbreak strain in Europe continued throughout 2001 and 2002. However, rates of disease in Western Europe have remained low, substantially lower than for group B or C infections.

Although true penicillin resistance has not been observed, a substantial proportion of strains have MICs in the range of 0.06-1.99. In general, the proportion is fairly constant between years. In 2001, 54% of cases tested for antibiotic sensitivity were in this range. There were dramatic differences in the proportion of isolates with reduced penicillin sensitivity between countries. This difference probably reflects differences in methods used. In general, the proportion is fairly constant between years. The clinical significance of this finding is not fully established but resistance patterns are being investigated further as part of EU-MENNET.

Data on EU-IBIS and on meningococcal infection in Europe is now presented on the EU-IBIS web-site. Future developments include a web-enabled database for performing live queries and the eventual availability of web-based reporting from participant countries.

5. PROJECT ACHIEVEMENTS

This project has made considerable contributions to:

1. improving epidemiological information on *Neisseria meningitidis*;
2. improving the laboratory capacity of countries within the EU to accurately identify isolates of *N. meningitidis;*
3. forming a focus for wider collaboration with non European Union countries and candidate European Union countries

5.1 Improvements in the epidemiological information on *N. meningitidis* within the EU

A combination of tools has been used to improve the epidemiological information on *N. meningitidis* within the EU. The surveillance system questionnaires from participant countries have allowed greater understanding of the data supplied by each country and have helped to explain any limitations in the data supplied. Use of a minimum dataset and analysis by standard case definitions for meningococcal infection has enabled valid comparisons to be made of the disease epidemiology between member countries, and hence to assist the monitoring of epidemiological changes within Europe. Information collected on the vaccination programme(s) being introduced in various participant countries has also aided interpretation of the epidemiological analyses. The availability of data on laboratory methods used in identification of *N. meningitidis* and on the characterisation of isolates also contributes significantly to the understanding comparability of the epidemiological information between EU countries.

A rapid reporting surveillance system for meningococcal disease W135; P2.2a. P1.2,5 was established in sentinel reference laboratories in the EU in late 2000 and continued through 2001 and 2002. The aims were to rapidly monitor the spread of the W135 outbreak strain in Europe, and to inform future interventions in Europe, and in relation to travel.

5.2 Improvements in the laboratory capacity within the EU to accurately identify *N. meningitidis* isolates

These improvements will be achieved through gaining information on systems in use by participant countries, and by feedback of information from the External Quality Assurance Scheme (EQAS) with the participant reference laboratories. Questionnaires completed by network members on the laboratory methods used in the identification of *N. meningitidis* gave information that, and, as with the surveillance system questionnaire results, allowed greater understanding of any limitations that could impact on the data individual countries supplied. The EQAS helped identify any existing problems in correctly serotyping *N. meningitidis* isolates, and enabled corrections/assistance in laboratory methods to be made, hence improving comparability of data between countries. In collaboration with EU-MENNET improvements may also be made in the methods used for assessing and comparing data on penicillin sensitivity.

5.3 Forming a focus for wider collaboration with non European Union countries and candidate European Union countries

Through establishment of this *N. meningitidis* disease surveillance network in the European Union, with standard case definitions, minimum dataset, and laboratory quality assurance scheme, and a website, a focus for wider collaboration with non-EU and candidate EU countries is provided. Involvement of the Czech Republic and Malta in this collaboration has increased the population under surveillance. It is hoped that other non-EU countries will join the collaboration later.

5.4 Establishment of web-site

Data on EU-IBIS and on meningococcal infection in Europe is now presented on the EU-IBIS web-site. Future developments include a web-enabled database for performing live queries and the eventual availability of web-based reporting from participant countries.

APPENDIX 1: DATA TABLES

INDEX OF TABLES

Table 1: Incidence of culture-confirmed cases of invasive meningococcal disease, by country and year.

	1999			2000			2001		
Country	No. of cases	Population	Incidence	No. of cases	Population	Incidence	No. of cases	Population	Incidence
Austria	80	7,795,788	1.03	58	7,795,788	0.74	91	7,795,788	1.17
Belgium	297	10,213,752	2.91	267	10,239,085	2.61	380	10,263,414	3.70
Czech Republic	89	10,282,784	0.87	57	10,272,503	0.56	89	10,272,503	0.87
Denmark	151	5,313,577	2.84	121	5,330,020	2.27	134	5,349,212	2.51
E & W	1704	51,820,200	3.29	1534	52,943,284	2.90	1237	52,943,284	2.34
Finland	57	5,116,826	1.11	48	5,116,826	0.94	48	5,116,826	0.94
France	394	59,146,337	0.67	464	60,254,277	0.77	523	60,254,277	0.87
Germany	402	82,163,475	0.49	452	82,163,475	0.55	521	82,163,475	0.63
Greece	63	10,516,366	0.60	50	10,516,366	0.48	54	10,521,670	0.51
Iceland	21	269,735	7.79	16	269,735	5.93	18	278,702	6.46
Ireland	189	3,626,087	5.21	169	3,626,087	4.66	101	3,839,000	2.63
Italy	129	57,679,895	0.28	153	57,844,017	0.27	133	57,844,017	0.23
Malta	13	366,431	3.60	16	366,431	4.37	13	366,431	3.55
Netherlands	574	15,760,225	3.64	544	15,863,950	3.43	723	15,987,075	4.52
Norway	73	4,445,329	1.64	74	4,478,497	1.65	64	4,503,436	1.42
Portugal-lab*	21	9,920,760	0.21	59	9,920,760	0.59	106	10,365,117	1.02
Spain-lab**	602	39,418,017	1.53	692	39,465,702	1.75	394	39,513,630	1.00
Total	**4859**	**373,855,584**	**1.30**	**4774**	**376,466,803**	**1.27**	**4,629**	**377,377,857**	**1.23**

* Portugal's reference laboratory dataset is only a subset of the national meningococcal case data and in 1999 includes only a small number of reporting labs/hospitals

** Spain's reference laboratory data only is used here

Table 2: Incidence of Culture confirmed cases and/or PCR confirmed cases – 1999-2001

Country	1999			2000			2001		
	No. of cases	Population	Incidence	No. of cases	Population	Incidence	No. of cases	Population	Incidence
Austria	89	7,795,788	1.14	68	7,795,788	0.87	109	7,795,788	1.40
Czech Republic	89	10,282,784	0.87	57	10,272,503	0.55	100	10,272,503	0.97
E & W	2784	51,820,200	5.37	2651	52,943,284	5.01	2832	52,943,284	5.35
Greece	123	10,516,366	1.17	160	10,516,366	1.52	185	10,521,670	1.76
Iceland	-			-			20	278,702	7.18
Ireland	429	3,626,087	11.83	390	3,626,087	10.76	273	3,839,000	7.11
Malta	-			-			14	366,431	3.82
Norway	76	4,445,329	1.71	83	4,478,497	1.85	71	4,503,436	1.58
Total	3,590	88,486,554	4.06	3,409	89,632,525	3.80	3,604	90,520,814	3.98 (3.97)*

* minus Iceland & Malta figures

Table 3: **Age distribution of culture-confirmed meningococcal disease in Austria, Belgium, Czech Republic, Denmark, England & Wales, Finland, France, Germany, Greece**, Iceland, Ireland, Italy, Malta, Netherlands, Norway, Portugal* and Spain: 1999, 2000 & 2001**

Year	Age group (years)																		
	<1		1-4		5-9		10-14		15-19		20-24		25-44		45-64		65+		Total known
	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%	No
1999	771	16.4	1305	27.7	503	10.7	368	7.8	730	15.5	235	5.0	302	6.4	271	5.8	228	4.8	4713
2000	765	16.6	1225	26.7	457	9.9	304	6.6	580	12.6	265	5.8	397	8.6	345	7.5	258	5.6	4596
2001	691	15.2	1170	25.7	413	9.1	345	7.6	656	14.4	248	5.5	392	8.6	365	8.0	269	5.9	4549
Total	2227	16.1	3700	26.7	1373	9.9	1017	7.3	1966	14.2	748	5.4	1091	7.9	981	7.1	755	5.4	13,858

**Greece only included for 2001

Table 4: Age specific incidence of culture-confirmed meningococcal disease in the reporting countries (Austria, Belgium, Czech Republic, Denmark, E&W, Finland, France, Germany, Greece*, Iceland, Ireland, Italy, Malta, Netherlands, Norway, Portugal and Spain): 2000 & 2001

	Age group (years)									
Year	*<1*	*1-4*	*5-9*	*10-14*	*15-19*	*20-24*	*25-44*	*45-64*	*65+*	*NK*
2000	765	1225	457	304	580	265	397	345	258	127
2001	691	1170	413	345	656	248	392	365	269	75
Population 2000	4,068,596	16,221,278	20,938,532	21,384,693	22,713,060	24,530,704	109,916,949	86,016,761	58,304,391	
Population 2001	4,039,842	16,252,691	21,209,972	22,074,859	22,786,182	24,040,500	113,240,326	91,703,215	60,791,627	
Incidence 2000	18.80	7.55	2.18	1.45	2.55	1.08	0.36	0.40	0.44	
Incidence 2001*	17.10	7.20	1.95	1.56	2.88	1.03	0.35	0.40	0.44	
Average annual incidence 00/01	17.96	7.38	2.06	1.49	2.72	1.06	0.35	0.40	0.44	

*includes Greece 2001

Table 5: Age distribution of culture and/or PCR confirmed cases of invasive meningococcal disease in Austria, Czech Republic*, England & Wales, Greece*, Iceland*, Ireland and Norway : 1999, 2000 & 2001

Year	Age group																		
	<1 year		*1-4 years*		*5-9 years*		*10-14 years*		*15-20 years*		*20-24 years*		*25-44 years*		*45-64 years*		*65+ years*		*Total known*
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
1999	616	18%	965	29%	351	10%	247	7%	474	14%	149	4%	231	7%	188	6%	123	4%	3344
2000	574	18%	922	29%	291	9%	199	6%	349	11%	175	6%	292	9%	243	8%	133	4%	3178
2001*	602	20%	798	26%	290	10%	214	7%	353	12%	151	5%	273	9%	221	7%	133	4%	3035
Total	1792	19%	2685	28%	932	10%	660	7%	1176	12%	475	5%	796	8%	652	7%	389	4%	9557

*only 2001 data for Czech Republic, Greece & Iceland

Table 6: Age specific incidence rate (per 100,000 population) of culture-confirmed meningococcal disease serogroup B in the EU reporting countries: 1999, 2000 and 2001

Year	Total	*< 1 year*		*1-4 years*		*5-9 year*		*10-14 years*		*15-19 years*		*20-24 years*		*25-44 years*		*45-64 years*		*65 years plus*	
		No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
1999	3315	568	13.96	950	5.86	415	1.98	258	1.21	468	2.06	155	0.66	193	0.18	173	0.20	135	0.23
2000	3196	679	16.69	893	5.51	322	1.54	189	0.88	381	1.68	157	0.64	227	0.21	217	0.25	131	0.22
2001*	2877	535	13.24	817	5.02	277	1.31	210	0.95	377	1.65	135	0.56	200	0.18	194	0.21	111	0.18

* includes Greece

Table 7: Age specific incidence rate (per 100,000 population) of culture-confirmed meningococcal disease serogroup C in the EU reporting countries: 1999, 2000 and 2001

Year	Total	*< 1 year*		*1-4 years*		*5-9 year*		*10-14 years*		*15-19 years*		*20-24 years*		*25-44 years*		*45-64 years*		*65 years plus*	
		No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
1999	1518	132	3.24	391	2.41	167	0.80	152	0.71	293	1.29	106	0.43	97	0.09	99	0.12	80	0.14
2000	1389	107	2.63	363	2.24	156	0.75	110	0.51	200	0.88	102	0.42	149	0.14	108	0.13	94	0.16
2001*	1221	85	2.10	268	1.65	115	0.54	106	0.48	216	0.95	87	0.36	133	0.12	128	0.14	83	0.14

* includes Greece

Table 8: Proportion of meningitis and septicaemia in culture-confirmed cases of meningococcal disease by country, 1999

Country	Meningitis alone	Meningitis or Meningitis & Septicaemia combined		Septicaemia alone		Total
Austria	31	56	74%	20	26%	76
Belgium	107	202	75%	68	25%	270
Czech	42	63	71%	26	29%	89
Denmark	33	112	74%	39	26%	151
E&W	367	560	39%	860	61%	1420
Finland	33	33	66%	17	34%	50
France	270	314	80%	80	20%	394
Germany	167	237	77%	70	23%	307
Iceland	7	14	70%	6	30%	20
Ireland	25	46	24%	143	76%	189
Italy	69	88	68%	41	32%	129
Malta	0	0	0%	12	100%	12
Netherlands	195	341	80%	83	20%	424
Norway	18	42	64%	24	36%	66
Spain-lab*	156	276	63%	162	37%	438
Total	1520	2384	59%	1651	41%	4035

*Spanish reference laboratory data only is used here

Table 9: Proportion of meningitis and septicaemia in culture-confirmed cases of meningococcal disease by country, 2000

Country	Meningitis alone	Meningitis or Meningitis & Septicaemia combined		Septicaemia alone		Total
Austria	27	43	74%	15	26%	58
Belgium	90	167	67%	81	33%	248
Czech	38	46	82%	10	18%	56
Denmark	28	88	73%	33	27%	121
E&W	235	365	38%	608	63%	973
Finland	26	26	65%	14	35%	40
France	300	353	76%	111	24%	464
Germany	197	281	77%	84	23%	365
Iceland	6	10	71%	4	29%	14
Ireland	20	41	24%	128	76%	169
Italy	87	119	78%	34	22%	153
Malta	3	8	50%	8	50%	16
Netherlands	179	332	80%	81	20%	413
Norway	19	46	67%	23	33%	69
Spain-lab*	173	308	63%	181	37%	489
Total	1428	2233	61%	1415	39%	3648

* Spanish reference laboratory data only is used here

Table 10: Proportion of meningitis and septicaemia in culture-confirmed cases of meningococcal disease by country, 2001

Country	Meningitis alone	Meningitis or Meningitis & Septicaemia combined		Septicaemia alone		Total
Austria	84	84	92%	7		91
Belgium	119	253	71%	101		354
Czech	50	68	82%	15		83
Denmark	14	98	73%	36		134
E&W	263	404	48%	436		840
Finland	23	23	59%	16		39
France	N/A			N/A		
Germany	215	310	76%	100		410
Greece	22	30	56%	24		54
Iceland	5	10	59%	7		17
Ireland	16	32	32%	69		101
Italy	78	97	73%	36		133
Malta	2	10	77%	3		13
Netherlands	207	381	74%	135		516
Norway	16	35	59%	24		59
Spain-lab*	79	160	61%	103		263
Total	1194	1995	64%	1112		3107

*Spanish reference laboratory data only is used here

Table 11: Proportion of meningitis in culture confirmed cases of invasive meningococcal disease, 1999, 2000 and 2001

% meningitis	1999	2000	2001
<50%	England & Wales Ireland Malta	England & Wales Ireland	England & Wales Ireland
50-70%	Finland Iceland Italy Malta Norway Spain	Belgium Finland Malta Norway Spain	Finland Greece Iceland Norway Spain-lab
> 70%	Austria Belgium Czech Republic Denmark France Germany Netherlands	Austria Czech Republic Denmark France Germany Italy Netherlands	Austria Belgium Czech Republic Denmark Germany Italy Malta Netherlands

Table 12: Proportion of invasive meningococcal disease in culture-confirmed cases by serogroup and country – 2001

Country	Group B		Group C		Other		Not known	Total known
	No.	*%*	*No.*	*%*	*No.*	*%*	*No.*	
Austria	46	55%	35	42%	3	4%	7	84
Belgium	172	47%	179	49%	13	4%	16	364
Czech Republic	54	61%	27	30%	8	9%	0	89
Denmark	98	75%	27	21%	5	4%	4	130
E & W	901	73%	197	16%	139	11%	0	1237
Finland	34	71%	9	19%	5	10%	0	48
France	259	55%	163	34%	53	11%	48	475
Germany	355	68%	115	22%	51	10%	0	521
Greece	40	78%	10	20%	1	2%	3	51
Iceland	4	22%	14	78%	0	0%	0	18
Ireland	84	83%	12	12%	5	5%	0	101
Italy	57	71%	19	24%	4	5%	53	80
Malta	9	69%	1	8%	3	23%	0	13
Netherlands	422	58%	279	39%	22	3%	0	723
Norway	37	58%	14	22%	13	20%	0	64
Portugal-lab*	53	50%	50	47%	3	3%	0	106
Spain-lab*	270	69%	103	26%	21	5%	0	394
Total	2895	64%	1254	28%	349	8%	131	4498

* Reference laboratory data only is used here

Table 13: Proportion of cases due to serogroup C by country, 1999-2001

% Group C	1999	2000	2001
<10%	-	Malta	Malta
10-19%	Austria Denmark Finland Netherlands Norway	Austria Denmark Netherlands Norway	England & Wales Finland Ireland
20-29%	Belgium France Germany Italy Malta	Czech Republic England & Wales Finland France Germany Greece Italy	Denmark Germany Greece Italy Norway Spain
30-39%	England & Wales Greece Ireland Spain	Belgium Ireland Spain	Czech Republic France Netherlands
40+%	Czech Republic Iceland Portugal-lab	Iceland Portugal-lab	Austria Belgium Iceland Portugal-lab

Table 14: Proportion of invasive meningococcal disease in Culture- or PCR-confirmed cases by serogroup and country – 2001

Country	Group B		Group C		Other		Not grouped		Total known
	No	*%*	*No*	*%*	*No*	*%*	*No*	*%*	*No*
Austria	55	57%	39	40%	3	3%	0	0%	97
Czech Republic	55	61%	27	30%	8	9%	0	0%	90
E & W	1688	73%	319	14%	184	8%	136	6%	2327
Greece	72	46%	14	9%	39	25%	32	20%	157
Ireland	228	84%	34	12%	6	2%	5	2%	273
Malta	9	64%	1	7%	3	21%	1	7%	14
Norway	43	61%	14	20%	13	18%	1	1%	71
Total	2150	71%	448	15%	256	8%	175	6%	3029

Table 15: Proportion of cases presenting with meningitis in the Group B culture confirmed cases, by country: 1999 & 2000

Country	Year	Meningitis alone	Meningitis OR (Meningitis & Septicaemia)		Septicaemia alone	Total	Year	Meningitis alone	Meningitis OR (Meningitis & Septicaemia)		Septicaemia alone	Total
Austria	**1999**	23	42	72%	16	58	**2000**	23	36	77%	11	47
Belgium	**1999**	67	132	75%	44	176	**2000**	54	101	67%	49	150
Czech Republic	**1999**	25	36	75%	12	48	**2000**	26	31	79%	8	39
Denmark	**1999**	28	97	76%	30	127	**2000**	21	75	76%	24	99
E&W	**1999**	249	347	43%	452	799	**2000**	166	252	42%.	353	605
Finland	**1999**	24	24	77%	7	31	**2000**	17	17	71%	7	24
France	**1999**	191	215	79%	55	270	**2000**	200	229	80%	57	286
Germany	**1999**	129	183	81%	42	225	**2000**	143	206	80%	52	258
Iceland	**1999**	2	5	50%	5	10	**2000**	3	4	80%	1	5
Ireland	**1999**	16	34	28%	88	122	**2000**	14	29	29%	70	99
Italy	**1999**	50	68	78%	19	87	**2000**	52	70	85%	12	82
Malta	**1999**	0	0	0%	6	6	**2000**	3	8	53%	7	15
Netherlands	**1999**	173	289	80%	72	361	**2000**	146	265	82%	60	325
Norway	**1999**	14	34	62%	21	55	**2000**	14	35	69%	16	51
Spain-lab*	**1999**	75	154	63%	89	243	**2000**	107	180	64%	102	282
TOTAL	**1999**	**1066**	**1660**	**63%**	**958**	**2618**	**2000**	**989**	**1538**	**65%**	**829**	**2367**

*Spanish reference laboratory data only is used here.

Table 16: Proportion of cases presenting with meningitis in the Group B culture confirmed cases, by country: 2001

Country	Year	Meningitis alone	Meningitis OR (Meningitis & Septicaemia)		Septicaemia alone	Total
Austria	**2001**	42	42	91%	4	46
Belgium	**2001**	58	119	75%	39	158
Czech Republic	**2001**	30	41	84%	8	49
Denmark	**2001**	9	73	74%	25	98
E&W	**2001**	205	315	51%	306	621
Finland	**2001**	21	21	72%	8	29
France	**2001**					
Germany	**2001**	159	223	79%	59	282
Greece	**2001**	15	22	55%	18	40
Iceland	**2001**	0	3	75%	1	4
Ireland	**2001**	13	26	31%	58	84
Italy	**2001**	23	36	63%	21	57
Malta	**2001**	1	6	67%	3	9
Netherlands	**2001**	136	237	76%	75	312
Norway	**2001**	10	21	58%	15	36
Portugal-lab	**2001**	28	35	68%	18	53
Spain-lab*	**2001**	60	111	59%	78	189
TOTAL	**2001**	**810**	**1331**	**65%**	**736**	**2067**

*Spanish reference laboratory data only is used here.

Table 17: Proportion of cases presenting with meningitis in the Group C culture-confirmed cases, by country: 1999& 2000

Country	Year	Meningitis alone	Meningitis OR (Meningitis & Septicaemia		Septicaemia alone	Total	Year	Meningitis alone	Meningitis OR (Meningitis & Septicaemia)		Septicaemia alone	Total
Austria	**1999**	6	10	77%	3	13	**2000**	4	7	70%	3	10
Belgium	**1999**	31	54	72%	21	75	**2000**	30	53	65%	29	82
Czech Republic	**1999**	15	25	68%	12	37	**2000**	6	9	82%	2	11
Denmark	**1999**	4	13	62%	8	21	**2000**	6	11	61%	7	18
E&W	**1999**	97	183	33%	368	551	**2000**	48	86	29%	209	295
Finland	**1999**	5	5	56%	4	9	**2000**	6	6	60%	4	10
France	**1999**	50	67	80%	17	84	**2000**	56	70	71%	28	98
Germany	**1999**	30	44	65%	24	68	**2000**	42	57	70%	24	81
Iceland	**1999**	5	9	90%	1	10	**2000**	3	6	75%	2	8
Ireland	**1999**	9	12	20%	49	61	**2000**	5	11	18%	51	62
Italy	**1999**	15	17	65%	9	26	**2000**	11	18	55%	15	33
Malta	**1999**	0	0	0%	3	3	**2000**	0	0	0%	1	1
Netherlands	**1999**	18	45	85%	8	53	**2000**	30	61	77%	18	79
Norway	**1999**	4	7	78%	2	9	**2000**	4	10	91%	1	11
Spain-lab*	**1999**	74	111	61%	70	181	**2000**	63	122	62%	76	198
TOTAL	**1999**	**363**	**602**	**50%**	**599**	**1201**	**2000**	**314**	**527**	**53%**	**470**	**997**

*Spanish reference laboratory data only is used here

Table 18: Proportion of cases presenting with meningitis in the Group C culture-confirmed cases, by country: 2001

Country	Year	Meningitis alone	Meningitis OR (Meningitis & Septicaemia		Septicaemia alone	Total
Austria	**2001**	33	33	94%	2	35
Belgium	**2001**	50	117	69%	52	169
Czech Republic	**2001**	14	20	77%	6	26
Denmark	**2001**	2	17	63%	10	27
E&W	**2001**	25	48	34%	92	140
Finland	**2001**	2	2	29%	5	7
France	**2001**					
Germany	**2001**	41	61	67%	30	91
Greece	**2001**	4	5	50%	5	10
Iceland	**2001**	5	7	54%	6	13
Ireland	**2001**	2	5	42%	7	12
Italy	**2001**	9	10	53%	9	19
Malta	**2001**	0	1	100%	0	1
Netherlands	**2001**	68	137	71%	57	194
Norway	**2001**	5	8	57%	6	14
Portugal-lab*	**2001**	23	34	69%	15	49
Spain-lab*	**2001**	14	44	65%	24	68
TOTAL	**2001**	**297**	**549**	**63%**	**326**	**875**

*Portuguese and Spanish reference laboratory data only is used here

Table 19: No. (Proportion) of invasive meningococcal disease in culture-confirmed cases other than serogroup B and C, by country – 2001 (NGA's left out of this table, but incl. In total known)

Country	Group A		Group W135		Group X		Group Y		Group Z/29E		Not known of total	Total known
	No	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*No.*
Austria	0		1	1.2%	0		2	2.4%	0		7	84
Belgium	0		10	2.7%	1	0.3%	0		0		16	364
Czech Republic	4	4.5%	1	1.1%	0		3	3.4%	0		0	89
Denmark	2	1.5%	2	1.5%	0		1	0.8%	0		4	130
E & W	2	0.2%	97	7.8%	7	0.6%	24	1.9%	4	0.3%	0	1237
Finland	0		1	2.1%	0		4	8.3%	0		0	48
France	7	1.5%	31	6.5%	12	2.5%	13	2.7%	0		48	475
Germany	1	0.2%	17	3.2%	0		22	4.2%	1	0.2%	0	521
Greece	1	2.0%	0		0		0		0		3	51
Iceland	0		0		0		0		0		0	18
Ireland	0		2	2.0%	0		1	9.9%	0		0	101
Italy	2	2.5%	2	2.5%	0		0		0		53	80
Malta	0		0		0		0		1	7.7%	0	13
Netherlands	0		14	1.9%	0		4	0.6%	2		0	723
Norway	0		8	12.5	0		4	6.3%	0		0	64
Portugal-lab*	0		2	1.9%	0		1	0.9%	0		0	106
Spain-lab*	3	0.8%	4	1.0%	0		10	2.5%	4	1.0%	0	394
Total	22	0.5%	192	4.3%	20	0.5%	89	2.0%	12	0.3%	131	4498

* Portugal's reference laboratory data only is used here

* Spanish reference laboratory data only is used here

Table 20: Major serogroup of invasive meningococcal disease cases other than groups B and C amongst the contributing countries: 1999-2001

Major serogroup	1999	2000	2001
W135	England & Wales Ireland Malta Netherlands Portugal-lab	Austria Belgium Czech Republic (with A) Denmark England & Wales Finland France Greece-lab Netherlands Norway Portugal-lab Spain-lab	Belgium Denmark (with A) England & Wales France Ireland Netherlands Norway Portugal-lab
X	Denmark (with Y)		
Y	Austria Belgium Czech Republic Denmark (with X) Finland France Germany Norway Spain-lab	Germany Iceland Ireland Italy	Austria Finland Germany Spain-lab
29E	-	-	Malta
A	Greece Italy	Czech Republic (with W135)	Czech Republic Denmark (with W135) Greece

Table 21: No. of cases (%) of group C serotypes by country : 1999 (cases where serotype known/given)

Country	P2.2a		P2.2b		NT		Other		Total
	No	*%*	*No*	*%*	*No*	*%*	*No*	*%*	
Austria	1	7%	6	43%	5	36%	2	14%	14
Belgium	29	38%	34	44%	10	13%	4	5%	77
Czech Republic	20	83%	3	13%	1	4%	0	0%	24
Denmark	8	38%	1	5%	2	10%	10	48%	21
E & W	429	67%	65	10%	123	19%	23	4%	640
Finland	1	11%	2	22%	6	67%	0	0%	9
France	31	31%	38	38%	24	24%	7	7%	100
Germany	33	38%	24	27%	20	23%	11	13%	88
Greece	14	78%	0	0%	4	22%	0	0%	18
Ireland	34	81%	4	10%	1	2%	3	7%	42
Italy	15	75%	0	0%	3	15%	2	10%	20
Malta	1	100%	0	0%	0	0%	0	0%	1
Netherlands	61	74%	14	17%	4	5%	3	4%	82
Norway	4	40%	1	10%	1	10%	4	40%	10
Spain	40	17%	175	76%	8	3%	7	3%	230
Total	721	52%	367	27%	212	15%	76	6%	1376

Table 22: No. of cases (%) of group C serotypes by country : 2000 (in cases where serotype known/given)

Country	P2.2a		P2.2b		NT		Other		Total
	No	*%*	*No*	*%*	*No*	*%*	*No*	*%*	
Austria	6	60%	4	40%	0	0%	0	0%	10
Belgium	40	47%	31	36%	10	12%	4	5%	85
Czech Republic	9	90%	0	0%	1	10%	0	0%	10
Denmark	12	67%	1	6%	1	6%	4	22%	18
E & W	332	74%	31	7%	76	17%	12	3%	451
Finland	3	30%	0	0%	6	60%	1	10%	10
Germany	38	40%	17	18%	35	36%	6	6%	96
Greece	8	80%	1	10%	1	10%	0	0%	10
Ireland	47	92%	3	6%	1	2%	0	0%	51
Italy	12	50%	6	25%	5	21%	1	4%	24
Malta	0	0%	1	100%	0	0%	0	0%	1
Netherlands	71	67%	21	20%	10	9%	4	4%	106
Norway	8	67%	3	25%	0	0%	1	8%	12
Spain	56	24%	147	63%	31	13%	1	0%	235
Total	642	57%	266	24%	177	16%	34	3%	1119

Table 23: No. of cases (%) of group C serotypes by country : 2001 (in cases where serotype known/given)

Country	P2.2a		P2.2b		NT		Other		Total
	No	%	No	%	No	%	No	%	
Austria	17	50%	11	32%	5	15%	1	3%	34
Belgium	122	69%	47	26%	7	4%	2	1%	178
Czech Republic	13	59%	0	0%	9	41%	0	0%	22
Denmark	9	36%	5	20%	6	24%	5	20%	25
E & W	164	83%	6	3%	21	11%	6	3%	197
Finland	3	33%	0	0%	5	56%	1	11%	9
France	65	53%	36	30%	16	13%	5	4%	122
Germany	73	63%	19	17%	17	15%	6	5%	115
Greece	3	38%	2	25%	1	13%	2	25%	8
Ireland	6	100%	0	0%	0	0%	0	0%	6
Italy	8	53%	6	40%	1	7%	0	0%	15
Malta	0	0%	0	0%	1	100%	0	0%	1
Netherlands	216	77%	37	13%	15	5%	11	4%	279
Norway	4	33%	1	8%	5	42%	2	17%	12
Spain-lab	53	51%	38	37%	8	8%	4	4%	103
Total	756	67%	208	18%	117	10%	45	4%	1126

Table 24: No. of cases (%) of selected group B phenotypes by country : 2001 (cases where serotype known/given)

	B:NT:NT/ P1.15/NT		**B:NT:1.9**		**B:15:1.7,1.16**		**B:4:1.4**		**B:2a subtypes**		**B:NT:P1.5 and/or P1.2**		**B:P3.1:NT /NT/NT**		**B:NT:NT/N T/NT**		**Other**		**Total**
	No.	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*
Austria	2	4%	0	0%	12	26%	1	2%	0	0%	3	7%	0	0%	6	13%	22	48%	46
Belgium	0	0%	0	0%	9	5%	79	47%	7	4%	9	5%	1	1%	6	4%	58	34%	169
Czech Rep.	1	3%	0	0%	3	9%	2	6%	1	3%	5	15%	0	0%	2	6%	20	59%	34
Denmark	1	1%	2	2%	45	49%	1	1%	1	1%	0	0%	4	4%	4	4%	34	37%	92
E&W	112	12 %	71	8%	31	3%	201	22%	14	2%	28	3%	26	3%	35	4%	383	43%	901
Finland	1	3%	1	3%	2	6%	5	15%	0	0%	1	3%	1	3%	2	6%	21	62%	34
France	5	3%	2	1%	1	1%	33	17%	2	1%	7	4%	8	4%	23	12%	111	58%	192
Greece	0	0%	0	0%	0	0%	6	17%	5	14%	0	0%	0	0%	0	0%	25	69%	36
Germany	6	2%	3	1%	49	14%	34	10%	5	1%	17	5%	4	1%	16	5%	221	62%	355
Ireland	0	0%	6	12%	1	2%	18	35%	0	0%	1	2%	0	0%	0	0%	26	50%	52
Italy	0	0%	1	2%	5	11%	2	4%	1	2%	1	2%	0	0%	3	7%	33	72%	46
Malta	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	9	100%	9
Netherlands	2	1%	5	1%	15	4%	115	27%	3	1%	3	1%	6	1%	15	4%	258	61%	422
Norway	3	10 %	0	0%	7	23%	2	6%	0	0%	0	0%	2	6%	2	6%	15	48%	31
Spain	19	7%	10	4%	3	1%	7	3%	8	3%	10	4%	5	2%	42	16%	166	61%	270
Total	152	6%	101	4%	183	7%	506	19%	47	2%	85	3%	57	2%	156	6%	1402	52%	2689

TOTAL = all culture confirmed serotyped/serosubtyped B's incl. B; NT; NT/NT/NT

Table 25: Major serotype of group C invasive meningococcal disease amongst the contributing countries 1999-2001

Major serotype	1999	2000	2001
2a	Czech Republic Denmark England and Wales Germany Greece Italy Ireland Netherlands Norway	Austria Belgium Czech Republic Denmark England and Wales Germany Greece Ireland Italy Netherlands	Austria Belgium Czech Republic Denmark England & Wales France Germany Greece Ireland Italy Netherlands Spain
2b	Austria Belgium France Spain	Norway Spain	
NT	Finland	Finland	Finland Malta Norway

Table 26: Major serotype of group B invasive meningococcal disease amongst the contributing countries 1999-2001

Major serotype	1999	2000	2001
B:15:P1.7, P.16	Austria Denmark France (with B4: P1.4) Germany Norway	Austria Denmark Germany Italy Norway	Austria Denmark Germany Italy
B:4: P1.4	Belgium England & Wales Finland France (with B:15:P1.7, P.16) Greece Ireland Italy Netherlands	Belgium England & Wales Finland Greece Ireland Netherlands	Belgium England & Wales Finland France Greece Ireland Netherlands Norway

Note: The major Group B serotype over 1999-2001 in both Spain and Malta was B:4:1.15

Table 27: Age specific incidence (per 100,000) of culture-confirmed Group B meningococcal disease by country : 2001

Country	Total cases	<1 yr		1-4yrs		5-9yrs		10-14yrs		15-19yrs		20-24yrs		25-44yrs		45-64yrs		65+yrs		NK
		No	*Inc*	*No*	*Inc*	*No*	*Inc*	*No*	*Inc*	*No*	*Inc*	*No*	*Inc*	*No*	*Inc*	*No*	*Inc*	*No*	*Inc*	*No*
Austria	46	9	9.93	9	2.48	5	1.08	4	0.91	8	1.59	1	0.15	3	0.13	3	0.17	4	0.34	0
Belgium	172	29	25.68	57	12.28	12	1.93	16	2.64	27	4.39	8	1.27	8	0.26	11	0.45	4	0.23	0
Czech Republic	54	10	11.12	8	2.20	4	0.68	1	0.15	17	2.46	2	0.23	5	0.23	6	0.22	1	0.07	0
Denmark	98	15	23.85	24	8.75	15	4.31	12	3.89	14	5.02	2	0.61	4	0.25	9	0.65	3	0.38	0
E&W	901	238	37.56	255	10.06	73	2.14	51	1.49	92	2.85	35	1.12	66	0.42	59	0.48	30	0.36	2
Finland	34	5	7.96	6	2.29	3	0.95	0	0.00	5	1.53	5	1.64	3	0.20	7	0.55	0	0.00	0
France	259	57	7.75	48	1.61	22	0.58	19	0.49	41	1.03	20	0.53	24	0.14	13	0.09	10	0.11	5
Germany	355	29	3.76	107	3.37	25	0.59	30	0.64	73	1.58	22	0.49	25	0.10	26	0.12	9	0.07	9
Greece	40	7	6.94	12	2.96	10	1.89	7	1.16	1	0.14	1	0.13	2	0.07	0	0.00	0	0.00	0
Iceland	4	1	24.89	1	5.62	0	0.00	1	4.92	1	4.69	0	0.00	0	0.00	0	0.00	0	0.00	0
Ireland	84	25	45.45	25	11.58	7	2.67	7	2.42	10	3.07	5	1.49	2	0.18	1	0.12	2	0.47	0
Italy	57	6	1.11	17	0.79	4	1.44	5	0.18	7	0.23	5	0.14	7	0.04	4	0.03	2	0.02	0
Malta	9	0	0.00	4	18.54	1	3.72	2	6.99	1	3.57	0	0.00	1	0.91	0	0.00	0	0.00	0
Netherlands	422	67	32.35	142	17.88	53	5.32	35	3.57	54	5.80	12	1.25	22	0.44	23	0.58	14	0.64	0
Norway	37	2	3.38	7	2.90	3	0.97	3	1.02	7	2.63	2	0.73	5	0.38	2	0.19	6	0.88	0
Portugal-lab*	53	18	16.9	20	4.45	4	0.74	4	0.62	0	0.00	1	0.12	2	0.07	1	0.04	3	0.00	0
Spain-lab**	270	48	12.11	58	3.76	25	1.29	14	0.69	18	0.75	10	0.33	21	0.17	26	0.29	26	0.39	24
Total	2895	566	13.98	800	4.87	266	1.25	211	0.96	376	1.66	139	0.57	200	0.18	191	0.21	114	0.19	40

* Portugal's reference laboratory data only is used here, and includes only a proportion of reporting labs/hospitals

Table 28: Age specific incidence (per 100,000) of culture-confirmed Group C meningococcal disease by country : 2001

Country	Total cases	<1 yr		1-4yrs		5-9yrs		10-14yrs		15-19yrs		20-24yrs		25-44yrs		45-64yrs		65+yrs		NK
		No	*Inc*	*No*	*Inc*	*No*	*Inc*	*No*	*Inc*	*No*	*Inc*	*No*	*Inc*	*No*	*Inc*	*No*	*Inc*	*No*	*Inc*	*No*
Austria	35	5	5.52	6	1.65	2	0.43	7	1.58	8	1.59	1	0.15	3	0.13	3	0.17	0	0.00	0
Belgium	179	15	13.28	40	8.62	29	4.67	3	0.49	36	5.85	11	1.75	26	0.85	8	0.33	10	0.58	1
Czech Republic	27	1	1.11	3	0.83	2	0.34	3	0.46	14	2.03	1	0.11	2	0.09	1	0.04	0	0.00	0
Denmark	27	0	0.00	6	2.19	2	0.57	3	0.97	8	2.87	1	0.31	1	0.06	4	0.29	2	0.25	0
E&W	197	8	1.26	24	0.95	3	0.09	6	0.18	11	0.34	26	0.83	42	0.26	52	0.42	25	0.30	0
Finland	9	0	0.00	0	0.00	1	0.32	1	0.30	0	0.00	0	0.00	4	0.26	3	0.24	0	0.00	0
France	163	16	2.17	44	1.48	16	0.42	12	0.31	24	0.60	9	0.24	10	0.06	10	0.07	17	0.18	5
Germany	115	6	0.78	43	1.35	9	0.21	14	0.30	20	0.43	4	0.09	9	0.04	7	0.03	3	0.02	0
Greece	10	3	2.97	0	0.00	1	0.19	2	0.33	2	0.27	0	0.00	1	0.03	1	0.04	0	0.00	0
Iceland	14	2	49.78	2	11.23	1	4.48	1	4.92	1	4.69	5	23.71	0	0.00	1	1.97	1	3.22	0
Ireland	12	2	3.64	3	1.39	0	0.00	1	0.35	1	0.31	1	0.30	1	0.09	2	0.25	1	0.23	0
Italy	19	1	0.18	2	0.09	4	1.44	1	0.04	3	0.10	1	0.03	3	0.02	1	0.01	3	0.03	0
Malta	1	0	0.00	1	4.63	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0
Netherlands	279	20	9.66	53	6.68	27	2.71	39	3.98	67	7.20	15	1.56	19	0.38	26	0.66	13	0.60	0
Norway	14	1	1.69	4	1.65	1	0.32	0	0.00	6	2.26	0	0.00	0	0.00	1	0.10	1	0.15	0
Portugal-lab*	50	12	11.28	24	5.34	7	1.29	2	0.31	1	0.13	0	0.00	3	0.11	1	0.04	0	0.00	0
Spain-lab**	103	5	1.26	9	0.58	8	0.41	13	0.64	9	0.37	12	0.40	8	0.06	8	0.09	7	0.10	24
Total	1254	86	2.12	269	1.64	115	0.54	106	0.48	216	0.96	87	0.36	133	0.12	129	0.14	83	0.14	30

- Portugal's reference laboratory data only is used here
- Spain's reference laboratory data only is used here

Table 29: Case fatality rate in laboratory confirmed cases of meningococcal disease, by country: 1999-2001

Country	Year	Total cases	Died	CFR	Year	Total cases	Died	CFR	Year	Total cases	Died	CFR
Austria	**1999**	97	7	7%	**2000**	83	5	6%	**2001**	106	7	7%
Belgium	**1999**	297	16	5%	**2000**	267	13	5%	**2001**	380	27	7%
Czech Republic	**1999**	93	7	8%	**2000**	61	5	8%	**2001**	93	10	11%
Denmark	**1999**	177	14	8%	**2000**	151	12	8%	**2001**	161	10	6%
E&W	**1999**	2784	201	7%	**2000**	2651	199	8%	**2001**	2327	189	8%
Finland	**1999**	57	10	18%	**2000**	N/A	N/A	N/A	**2001**	51	N/A	N/A
France	**1999**	411	35	8%	**2000**	489	59	12%	**2001**	559	73	13%
Germany	**1999**	402	21	5%	**2000**	452	28	6%	**2001**	521	34	7%
Greece	**1999**	108	7	7%	**2000**	133	9	7%	**2001**	160	7	4%
Iceland	**1999**	21	2	10%	**2000**	18	2	11%	**2001**	20	2	10%
Ireland	**1999**	445	17	4%	**2000**	410	25	6%	**2001**	301	12	4%
Italy	**1999**	246	13	5%	**2000**	217	20	9%	**2001**	194	14	7%
Malta	**1999**	18	5	28%	**2000**	21	3	14%	**2001**	14	0	0%
Netherlands	**1999**	583	23	4%	**2000**	546	30	5%	**2001**	725	41	6%
Norway	**1999**	77	9	12%	**2000**	85	7	8%	**2001**	77	3	4%
Portugal-lab*	**1999**	N/A	N/A	N/A	**2000**	N/A	N/A	N/A	**2001**	100	N/A	N/A
Spain-lab*	**1999**	602	9	1%	**2000**	692	5	1%	**2001**	394	1	0%
Total	**1999**	6418	396	6%	**2000**	6276	424	7%	**2001**	6183	430	7%

* Spanish reference laboratory data only is used here

* Portugal's reference laboratory data only is used here, and in 1999 includes a small number of reporting labs/hospitals

Table 30: Case fatality rate in laboratory confirmed cases (minus PCR) of meningococcal disease, by country: 1999-2001

Country	Year	Total cases	Died	CFR	Year	Total cases	Died	CFR	Year	Total cases	Died	CFR
Austria	**1999**	85	4	5%	**2000**	68	3	4%	**2001**	88	7	8%
Belgium	**1999**	297	16	5%	**2000**	264	13	5%	**2001**	380	27	7%
Czech Republic	**1999**	92	6	7%	**2000**	61	4	7%	**2001**	82	8	10%
Denmark	**1999**	177	14	8%	**2000**	151	12	8%	**2001**	161	10	6%
E&W	**1999**	952	59	6%	**2000**	912	77	8%	**2001**	732	79	11%
Finland	**1999**	57	10	18%	**2000**	N/A	N/A	N/A	**2001**	N/A	N/A	N/A
France	**1999**	411	35	8%	**2000**	489	59	12%	**2001**	559	73	13%
Germany	**1999**	402	21	5%	**2000**	452	28	6%	**2001**	521	34	7%
Greece	**1999**	108	7	7%	**2000**	133	9	7%	**2001**	29	1	3%
Iceland	**1999**	21	2	10%	**2000**	18	2	11%	**2001**	18	2	11%
Ireland	**1999**	205	10	5%	**2000**	189	8	4%	**2001**	129	5	4%
Italy	**1999**	246	13	5%	**2000**	217	20	9%	**2001**	194	14	7%
Malta	**1999**	18	5	28%	**2000**	21	3	14%	**2001**	14	0	0%
Netherlands	**1999**	583	23	4%	**2000**	546	30	5%	**2001**	725	41	6%
Norway	**1999**	73	9	12%	**2000**	76	5	7%	**2001**	70	3	4%
Portugal-lab*	**1999**	N/A	N/A	N/A	**2000**	N/A	N/A	N/A	**2001**	N/A	N/A	N/A
Spain-lab*	**1999**	602	9	1%	**2000**	692	5	1%	**2001**	643	59	9%
Total	**1999**	**4329**	**243**	**6%**	**2000**	**4289**	**278**	**6%**	**2001**	**4344**	**363**	**8%**

*Spanish reference laboratory data only is used here for 1999 & 2000, and reconciled dataset used for 2001
* Portugal's reference laboratory data only is used here, and in 1999 includes a small number of reporting labs/hospitals

Table 31: Case Fatality Rate in laboratory confirmed cases of invasive meningococcal disease, by serogroup: 2001

Country	A			B			C			W135			Y		
	No	*Deaths*	*CFR*	*No.*	*Deaths*	*CFR*	*No.*	*Deaths*	*CFR*	*No.*	*Deaths*	*CFR*	*No.*	*Deaths*	*CFR*
Austria	0	0	0%	55	4	7%	39	2	5%	1	0	0%	2	0	0%
Belgium	0	0	0%	172	3	2%	179	22	12%	10	2	20%	0	0	0%
Czech Republic	4	0	0%	55	3	5%	28	6	21%	1	0	0%	3	1	33%
Denmark	2	0	0%	99	5	5%	27	4	15%	2	0	0%	1	1	100%
E&W	2	0	0%	1688	105	6%	319	57	18%	135	21	16%	31	4	13%
Finland	0	N/A		34	N/A	%	9	N/A		0	N/A		0	N/A	
France	11	2	18%	270	29	11%	172	26	15%	31	6	19%	13	2	15%
Germany	1	0	0%	355	16	5%	115	12	10%	17	5	29%	22	4	5%
Greece	28	0	0%	72	5	7%	14	2	14%	9	0	0%	2	0	0%
Iceland	0	0	0%	4	1	25%	14	1	7%	0	0	0%	0	0	0%
Ireland	0	0	0%	249	8	3%	35	3	9%	3	1	33%	1	0	0%
Italy	3	0	0%	64	7	11%	21	5	24%	2	0	0%	0	0	0%
Malta	0	0	0%	9	0	0%	1	0	0%	0	0	0%	0	0	0%
Netherlands	0	0	0%	424	30	7%	279	11	4%	14	0	0%	4	0	0%
Norway	0	0	0%	47	1	2%	15	2	13%	8	0	0%	0	0	0%
Portugal-lab*	0	N/A		50	N/A		47	N/A		0	N/A		0	N/A	
Spain-lab*	3	0	0%	270	1	0.4%	103	0	0%	4	0	0%	10	0	0%
Spain-notifs	6	0	0%	428	25	6%	147	31	21%						
Total	+57	2	4%	+3833	218	6%	1361	153	11%	237	35	15%	89	12	13%

* Spanish reference laboratory data only is used here

* Portugal's reference laboratory data only is used here, and in 1999 includes a small number of reporting labs/hospitals

+ using Spain-lab

Table 32: Case Fatality Rate in laboratory confirmed cases of group B and group C meningococcal disease, by age group: 1999 –2001 (where age group given)

Age group		1999		2000		2001	
		Group B	*Group C*	*Group B*	*Group C*	*Group B*	*Group C*
Under 1	Cases	732	191	799	105	777	98
	Deaths	43	11	61	10	60	6
	CFR	5.9%	5.8%	7.6%	9.5%	7.7%	6.1%
1-4yrs	Cases	1110	479	1133	409	1206	300
	Deaths	44	30	48	24	60	22
	CFR	4.0%	6.3%	4.2%	5.9%	5.0%	7.3%
5-9yrs	Cases	419	203	384	178	414	131
	Deaths	14	11	9	7	14	5
	CFR	3.3%	5.4%	2.3%	3.9%	3.4%	3.8%
10-14yrs	Cases	285	167	230	139	293	115
	Deaths	2	14	7	15	14	9
	CFR	0.7%	8.4%	3.0%	10.8%	4.8%	7.2%
15-19yrs	Cases	524	347	483	220	512	256
	Deaths	22	44	19	31	25	30
	CFR	4.2%	12.7%	3.9%	14.1%	4.9%	11.7%
20-24yrs	Cases	167	98	196	124	187	116
	Deaths	16	7	15	18	9	28
	CFR	9.6%	7.1%	7.7%	14.5%	4.8%	24.1%
25-44yrs	Cases	237	123	298	186	283	182
	Deaths	12	17	16	25	14	34
	CFR	5.1%	13.8%	5.4%	13.5%	4.9%	18.7%
45-64 yrs	Cases	193	121	276	118	249	163
	Deaths	19	24	19	17	22	29
	CFR	9.8%	19.8%	6.9%	14.4%	8.8%	17.8%
65+yrs	Cases	178	107	209	114	131	92
	Deaths	26	18	25	19	23	19
	CFR	14.6%	17.3%	12%	16.7%	17.6%	20.7%

Table 33: Case fatality rate amongst culture-confirmed cases of meningococcal disease presenting with meningitis, by country: 1999, 2000 & 2001 (*i.e. meningitis plus men/sept combined)*

Country	1999			2000			2001		
	Total Meningitis cases	*Died*	*CFR*	*Total Meningitis cases*	*Died*	*CFR*	*Total meningitis cases*	*Died*	*CFR*
Austria	56	2	3.57%	43	2	4.65%	84	0	0%
Belgium	202	13	6.44%	167	10	5.99%	253	19	7.5%
Czech Republic	63	2	3.17%	46	3	6.52%	68	6	8.8%
Denmark	112	11	9.82%	88	7	7.959.09%	99	7	7.1%
E&W	560	34	6.07	365	27	7.40%	404	24	5.9%
Finland	33	4	12.12%	26	N/A	N/A	N/A	N/A	N/A
France	314	22	7.01%	353	31	8.78%	N/A	N/A	N/A
Germany	237	8	3.38%	281	7	2.49%	310	11	3.5%
Greece							30	0	0%
Iceland	14	1	7.14%	10	1	10.00%	10	2	20%
Ireland	46	4	8.70%	41	2	4.88%	32	1	3.1%
Italy	88	5	5.68	87	4	4.60%	96	6	6.3%
Malta	0	0	0%	8	0	0%	10	0	0%
Netherlands	341	9	2.64%	332	16	4.82%	381	23	6.0%
Norway	42	5	11.90%	46	1	2.17%	35	0	0%
Portugal-lab*	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Spain-lab*	276	5	1.81%	308	2	0.65%	160	0	0%
Total	2384	125	5.24	2201	113	5.13	1972	99	5.0%

* Spanish reference laboratory data only is used here

* Portugal's reference laboratory data only is used here, and in 1999 includes only a small number of reporting labs/hospitals

Table 34: Susceptibility of *N. meningitidis* to penicillin, by country: 1999 & 2000

Country	1999			2000		
	MIC <= 0.06	MIC >0.06 and <2.00	Total	MIC <= 0.06	MIC >0.06 and <2.00	Total
Austria	76 (96%)	3 (4%)	79	48 (86%)	8 (14%)	56
Belgium	267 (96%)	12 (4%)	279	237 (94%)	14 (6%)	251
Czech Republic	56 (97%)	2 (3%)	58	46 (98%)	1 (2%)	47
Denmark	95 (65%)	51 (35%)	146	74 (63%)	44 (37%)	118
E&W	517 (31%)	1128 (69%)	1645	418 (28%)	1068 (72%)	1486
Germany	51 (13%)	351 (87%)	402	22 (5%)	430 (95%)	452
Greece-lab*	41 (84%)	8 (16%)	49	38 (86%)	6 (14%)	44
Iceland	20 (95%)	1 (5%)	21	12 (75%)	4 (25%)	16
Italy	80(92%)	7(8%)	87	84(94%)	5(6%)	89
Malta	0(0%)	9(100%)	9	0(0%)	14(100%)	14
Portugal-lab*	5(24%)	16(76%)	21	20(43%)	27(57%)	47
Spain-lab*	381 (63%)	221 (37%)	602	301 (43%)	391 (57%)	692
Total	1589 (47%)	1809 (53%)	3398	1300 (39%)	2012 (61%)	3312

*_Greek and Spanish reference laboratory data was used here as it was the only dataset with antibiotic resistance

* Portugal's reference laboratory data only is used here, and in 1999 includes only a small number of reporting labs/hospitals

Table 35: Susceptibility of *N. meningitidis* to penicillin, by country: 2001

Country	2001		
	MIC <= 0.06	MIC >0.06 and <2.00	Total
Austria	66 (80%)	16 (20%)	82
Belgium	328 (92%)	30 (8%)	358
Czech Republic	56 (97%)	2 (3%)	58
Denmark	67 (54%)	57 (46%)	124
E&W	439 (35%)	823 (65%)	1262
Germany	31 (6%)	490 (94%)	521
Greece-lab	35 (83%)	7 (17%)	42
Iceland	14 (78%)	4 (22%)	18
Italy	60 (98%)	1 (2%)	61
Malta	2 (15%)	11 (85%)	13
Netherlands	1 (6%)	16 (94%)	17
Portugal-lab*	82 (77%)	24 (23%)	106
Spain-lab*	212 (54%)	182 (46%)	394
Total	1393 (46%)	1663 (54%)	3056

*_Greek, Portuguese and Spanish reference laboratory data was used here