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EU-IBIS
European Union Invasive Bacterial Infections Surveillance Network

INVASIVE *NEISSERIA MENINGITIDIS* IN EUROPE – 2002

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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 2002 the incidence of reported culture-confirmed meningococcal disease varied between 0.3 and 4.7 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. Belgium and the Netherlands have experienced increases in the proportion of serogroup C disease between 1999 and 2001, and then seen decreases since serogroup C conjugate vaccination programmes were introduced in 2002. The proportion in England & Wales, Greece, Ireland and Spain has decreased following the implementation of serogroup C conjugate vaccine campaigns at different times between 1999 and 2001.

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 7-8% on average, although this varies by age and serogroup. The range of CFR estimates in 2002 are between 4 and 20%, 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 a number of non-EU countries (2000-2002) 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, and continued through 2001 and 2002. 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 followed.

A Quality Assurance Study for non-culture confirmation of meningococcal infection using nucleic acid amplification was completed during 2003. A total of twenty samples of which eighteen were cerebrospinal fluid samples were distributed to thirteen reference centres in thirteen participant countries by the Institut Pasteur. All the samples were extracted by boiling prior to distribution. The participating laboratories were requested to perform their standard non-culture approach. Each laboratory performed its in-house polymerase chain reaction assays covering a range of meningococcal gene targets. The majority of laboratories also performed genogrouping assays on the samples. In addition seven laboratories performed non-culture detection for *S. pneumoniae* and *H. influenzae*.

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). Data on the EU-IBIS network and on meningococcal infection in Europe is now presented on the EU-IBIS web-site (http://www.euibs.org/). Future developments include a web-enabled database for

performing live queries and the eventual availability of web-based reporting from participant countries.

Insufficient funding was available for a stand-alone meeting of the collaborators within this project for 2001-2003, but a meeting of EU-IBIS/meningococci partners was held within the time of the 13th International Pathogen *Neisseria* 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 was presented in the 1999& 2000 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
Austria					Yes	2002
Belgium 1. Wallonie 2. Flanders	 Yes Yes	 2002 2002	 1-6 years 1-3 yrs 1-6 yrs & 14-17 yrs	 2002 2001 2002		
Greece	No		0-6 yrs 3-12 mths	2001 2002	Yes	2001
Iceland	Yes	2002				
Ireland	Yes	2000	<23 yrs	2000-2002		
Luxembourg	No		12 mths-19 yrs	2001-2002		
Netherlands	Yes	2002	1-19 yrs	Jun-Oct 2002		
Portugal	No (Except for Madeira)	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

3.2.1 Laboratory Diagnostic Methods Questionnaire

Laboratory diagnostic questionnaires were received from fourteen laboratories. The description of methods used was published in the 1999 & 2000 report.

3.2.2 External quality assurance scheme (EQAS) for non-culture confirmation of meningococcal infection

The reference laboratories compared reasonably well in 2003 for the non-culture detection of meningococcal infection by nucleic acid amplification versus conventional diagnostic methods, but the performance of geno-grouping was more variable between laboratories. In conclusion, after analysis of all the returned data (results were returned from eleven laboratories) it appeared that the various gene targets used for meningococcal non-culture detection were equivalent in sensitivity and specificity for the confirmation of meningococcal infection. Although genogrouping for serogroup B gave the best correlation between participants, the performance of genogrouping was variable between laboratories and, in particular, serogroups A and W135.

Recommendations were made to carry out future QA distributions for non-culture confirmation of meningococcal infection, to include a greater diversity of sample types, and to address variations in sensitivity and/or specificity, which may occur due to variations in extraction methods.

3.3 Summary of case data received for 2002

Nineteen countries supplied disaggregated case data for 2002 to the co-ordinating centre in CDSC, Colindale, London. Information on 6,229 invasive meningococcal disease cases was supplied by the collaborators for 2002**.** No case data was provided by Luxembourg for 2002. 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 invasive meningococcal disease

The incidence of overall invasive meningococcal disease varied widely within Europe over 2002: 0.39 – 7.41 per 100,000 population. (Table ii) The overall incidence is higher than that calculated for laboratory- or culture-confirmed cases alone: four countries had incidence rates below 1 per 100,000 population, 7 countries between 1-2/100,000, 4 between 2-4/100,000, and 4 above 4/100,000 population. These figures were calculated using the total number of cases reported by each country. Surveillance systems supplying the data to the EU-IBIS project differ between countries. Some countries report only laboratory confirmed cases, while others include clinical cases as well. In England and Wales, Ireland and Spain, a large percentage of the cases are clinical cases. Considerable differences are subsequently seen between the incidence rates of total reported cases and laboratory-confirmed cases in these three countries. (Table ii)

The incidence of culture confirmed invasive meningococcal disease also varied widely between the participating network countries over 2002. (Table ii) Eight countries exhibited rates of less than 1.0 per 100,000 population, 6 countries were between 1-2/100,000, 4 between 2-4/100,000, while Iceland and Netherlands were both above 4/100,000 population.

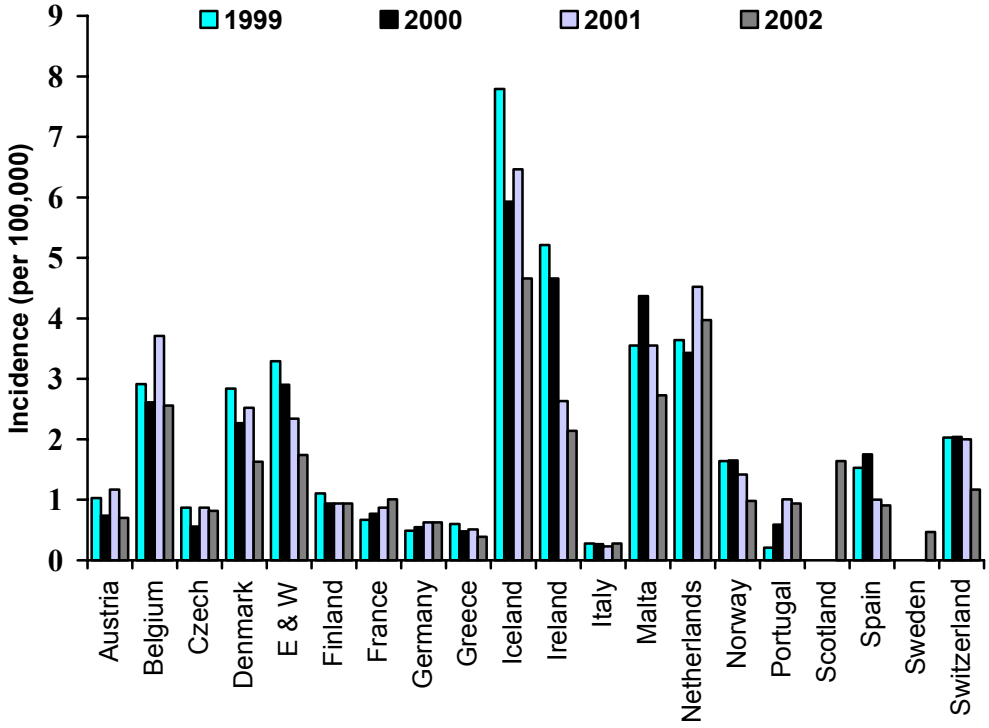
A decrease in the overall incidence of culture-confirmed meningococcal disease has been seen in England and Wales, Greece, Ireland and Spain over the four years 1999-2002. (Table 1) Meanwhile, notable increases have been observed within this time in Belgium, France, Germany, and the Netherlands (Figure i). Belgium and the Netherlands, however, introduced a conjugate meningococcal disease group C vaccination programme in 2002, and impact from this is seen in the 2002 data for each of these countries. France has seen a steady increase over the four years in the incidence of meningococcal disease.

Table ii Incidence per 100,000 population of invasive meningococcal disease by country, 2002

Country	Total reported cases (laboratory-confirmed + clinical)			Laboratory-confirmed cases		Culture-confirmed cases		Population
	No.	Incidence	Data source for Total cases	No.	Incidence	No.	Incidence	
Austria	86	1.10	Not specified	81	1.04	60	0.77	7,795,788
Belgium			Ref lab only	262	2.54	262	2.54	10,309,725
Czech Republic	122	1.19	Not specified	113	1.10	84	0.82	10,272,503
Denmark	100	1.87	Enhanced surveillance	98	1.79	87	1.63	5,349,212
E & W	2818	5.32	Enhanced Surveillance	1772	3.35	923	1.74	52,943,284
Finland	49	0.96	Not specified	49	0.96	48	0.94	5,116,826
France	678	1.13	Not specified	648	1.08	610	1.01	60,254,277
Germany			Ref lab only	518	0.63	518	0.63	82,163,475
Greece	233	2.21	Not specified	175	1.66	41	0.39	10,521,670
Iceland	15	5.38	Not specified	15	5.38	13	4.66	278,702
Ireland	251	7.41	Enhanced surveillance	224	6.61	82	2.14	3,839,000
Italy	225	0.39	National surveillance of bacterial meningitis	216	0.37	163	0.28	57,844,017
Luxembourg	N/A	N/A		N/A	N/A	N/A	N/A	
Malta	14	3.82	Not specified	14	3.82	10	2.73	366,431
Netherlands	680	4.25	Not specified	636	3.98	634	3.97	15,987,075
Norway	51	1.13	Not specified	51	1.13	44	0.98	4,503,436
Portugal-lab*			Ref lab only	93	0.90	93	0.90	10,365,117
Scotland	178	3.51	Not specified	122	2.41	83	1.64	5,064,200
Spain	737	1.87	Plus notifications??	544	1.38	544	1.38	39,513,630
Sweden	47	0.53	Enhanced surveillance	44	0.50	39	0.44	8,846,625
Switzerland	114	1.58	Not specified	91	1.26	84	1.17	7,204,055
Total	**7271**	**1.82**		**5766**	**1.45**	**4422**	**1.11**	**398,539,048**

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

Figure i **Incidence of culture-confirmed meningococcal disease per 100,000 population 1999-2002**



3.4.2 Incidence of PCR-confirmed cases

PCR-confirmed cases now account for a proportion of the total number of cases in Austria, Czech Republic, England and Wales, France, Greece, Iceland, Ireland, Malta, Norway, Scotland, Sweden and Switzerland. 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.

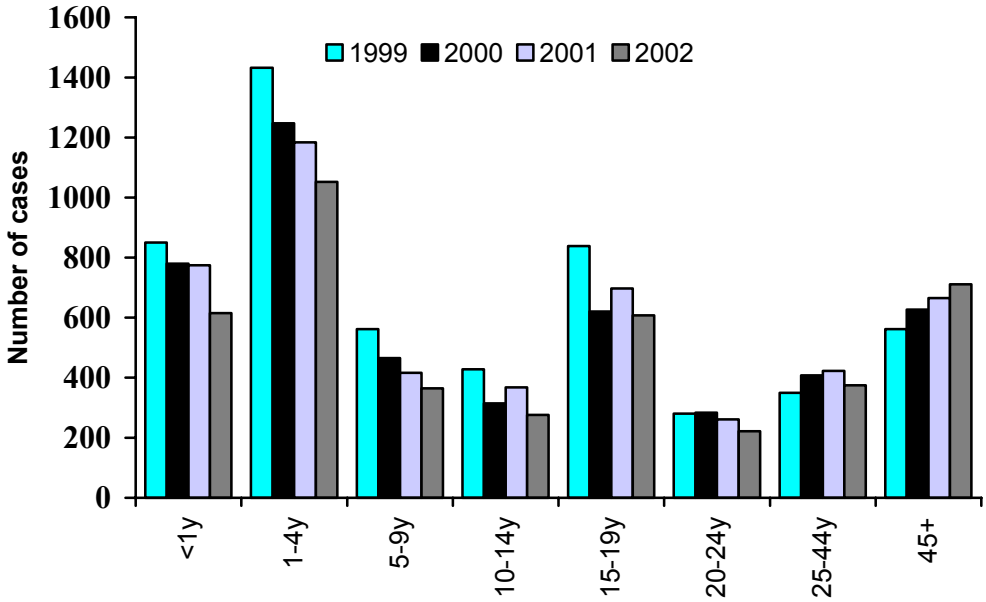
Currently, because only a small number of countries are yet using routine PCR confirmation, most data analyses and comparison will be performed on culture-confirmed cases only. To give a fairer representation of the incidence rate of meningococcal disease in those countries using PCR as a major confirmation 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 for 2002 show England and Wales to have a rate of 3/100,000 population, and Ireland to have a rate of 6/100,000 population in 2001, compared to 2/100,000 for culture confirmed cases. Greece shows a rate of 1.6/100,000 when culture and PCR confirmed cases are combined, rather than 0.4/100,000 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 (ii), Table 3). The combined age-specific incidence rates of invasive meningococcal disease in the contributing countries over 2001 and 2002 show the highest rate in infants (17 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 1999-2002. Small fluctuations were seen in the annual incidence rates for the 10-14 and 15-19 year age groups over the 1999-2002 period (Table 4 and earlier reports). For all age groups over 20 years, the incidence rate was relatively stable over 2000-2002. The decrease observed in children under 10 years is likely to reflect the impact of the group C vaccination programmes, firstly in the UK (one of the larger countries in the network) and later in Ireland and Spain. The Netherlands introduced a routine vaccination programme and a catch-up programme for 1-19 year olds in 2002, and these are likely to have contributed to the decrease seen in disease incidence in the overall 10-14 and 15-19 age groups in 2002.

Figure ii **Age distribution of culture-confirmed invasive meningococcal disease in contributing partner countries : 1999-2002**



In 2002, Austria, Czech Republic, England & Wales, France, Greece, Ireland, Norway, Scotland, Sweden and Switzerland confirmed a proportion of their invasive meningococcal disease cases by PCR-only**.** The age distribution of the PCR-only confirmed cases shows a similar pattern to that of the culture-confirmed cases. (Tables 3a) Data on the age distribution of PCR confirmed cases from Greece, Czech Republic, Iceland and Scotland have only been available for 2001 onwards. 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 5). 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 2001 and 2002 a decrease was seen in under ones (15 to 13 per 100,000). Apart from the elderly population (65+ years), the incidence in all other age groups decreased between 2001 and 2002. 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 (2.23 per 100,000), with a secondary peak seen in the 15-19 year olds (0.94 per 100,000) (Table 6). All age groups under 20 years have seen a steady decrease in the incidence rate of serogroup C meningococcal disease over the four years, 1999-2002. These decreases are likely to be influenced by the impact of MenC conjugate vaccination programmes into a number of the participant countries over the study period.

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 one year olds, and most had a second peak in incidence in the 15-19 year olds. This held true for 1999-2002 (Table 15 & previous report). The variation in rates between countries in 2002 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 32.4 (Netherlands) per 100,000.

The pattern was less consistent for the age-specific serogroup C incidence rate amongst participant countries. In 2002, the incidence rate of serogroup C disease was highest in the under one year olds rate in only five of the 19 contributing countries, with a secondary increase in incidence in the 15-19 year olds (or in the nearest age group to this) (Table 16 & previous report). Nine countries had a higher rate in the 15-19 year olds than in the under ones: Austria, Czech Republic, Denmark, Finland, Iceland, Norway, Scotland, Sweden and Spain. Caution must be taken interpreting data from 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 four years (table iii). 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%, 64% and 66% in 1999, 2000, 2001 and 2002, respectively. In 2002, seven of the seventeen countries contributing this data exhibited proportions of greater than 70% for meningitis to septicaemia.

Table iii Proportion of meningitis in culture confirmed cases of invasive meningococcal disease, 1999-2002

% meningitis	**1999**	**2000**	**2001**	**2002**
<50%	England & Wales Ireland Malta	England & Wales Ireland	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	Austria Denmark Greece Malta Norway Scotland Spain-lab Sweden Switzerland
> 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	Belgium Czech Republic Germany Iceland Italy Netherlands Portugal-lab

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 7 & 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 6% to 92% in 2002. A number of countries displayed large increases in the proportion of cases caused by Group C over 1999, 2000 and 2001(Austria, Belgium, and Netherlands), but a reduction was seen in 2002. It is notable that the proportion of group C infection in England and Wales, Greece, and Ireland has all declined over 1999-2001, and has declined in Belgium and the Netherlands over 2001-2002, suggesting the impact of conjugate meningococcal group C vaccine (Table iv). The proportion of serogroup C cases in France has shown a steady increase over the four years (22% - 34%).

Table iv Proportion of cases due to serogroup C by country, 1999-2002

% Group C	**1999**	**2000**	**2001**	**2002**
<10%	-	Malta	Malta	Ireland
10-19%	Austria Denmark Finland Netherlands Norway	Austria Denmark Netherlands Norway	England & Wales Finland Ireland	Denmark England & Wales Finland Greece Malta Scotland
20-29%	Belgium France Germany Italy Malta	Czech Republic England & Wales Finland France Germany Greece Italy	Denmark Germany Greece Italy Norway Spain Scotland	Austria Norway Spain Sweden
30-39%	England & Wales* Greece Ireland* Spain* Switzerland	Belgium Ireland Spain	Czech Republic France Netherlands Switzerland	Belgium* France Germany Netherlands* Italy
40+%	Czech Republic Iceland Portugal-lab	Iceland Portugal-lab Switzerland	Austria Belgium Iceland Portugal-lab	Czech Republic Iceland Portugal-lab Switzerland

*countries implementing MenC vaccination duting 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 . The latter explanation probably accounts for the high proportion of cases that were PCR-confirmed but not grouped.

Other than groups B and C, cases caused by serogroups W135, Y, X, Z/29E and A were also identified (Table v). Overall, serogroup W135 is the most common of these,

but the total number of W135 cases decreased between 2001 and 2002 (Table 10). The total number of cases of serogroup Y infection increased from 2001 to 2002, and in ten countries serogroup Y is the dominant serogroup amongst serogroups W135, Y, X, Z/29E and A, in 2001. In England and Wales, and France, W135 remains most common after serogroups B and C. These two countries observed an increase in the number of W135 cases from 1999 to 2000 in association with the Hajj in 2000. England and Wales has seen a large decrease in the number of W135 cases from 2001 to 2002, but France has seen a continued increase over 1999-2002 (Table 10 & earlier reports).

Table v **Serogroup of invasive meningococcal disease cases other than groups B and C amongst the contributing countries: 1999-2002**

Major serogroup	**1999**	**2000**	**2001**	**2002**
W135	England & Wales Ireland Malta Netherlands Portugal-lab	Austria Belgium Czech Republic (+ A) Denmark England & Wales Finland France Greece-lab Netherlands Norway Portugal-lab Spain-lab	Belgium Denmark (+ A) England & Wales France Ireland Netherlands Norway Portugal-lab	Austria (+ Y) Denmark Portugal-lab England & Wales France Ireland Norway Scotland (+ Y)
X	Denmark (+ Y)	-	-	-
Y	Austria Belgium Czech Republic Denmark (+ X) Finland France Germany Norway Spain-lab	Germany Iceland Ireland Italy	Austria Finland Germany Spain-lab	Austria (+ W135) Spain Czech Republic Belgium Finland Netherlands Germany Switzerland Italy Scotland (+W135)
29E	-	-	Malta	-
A	Greece Italy	Czech Republic (+W135)	Czech Republic Denmark (+W135) Greece	

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 decreased from 2001 to 2002 (Table 11). However, serotype C2a has become the dominant C serotype in an increasing number of the participant countries. In 2002, C2a was dominant C serotype in 13 of the 18 countries (Table 12).

Group B infections appear to be more diverse, with 50%, or more, of cases in the "other" category (Tables 13 & previous reports). There are considerable differences between

countries in strain composition. Overall, the major B sero-subtype was B:4:1.4. A number of major group B sero-subtypes were identified (Table 14), and the leading strain in most countries was consistent between years 1999-2002. In 2002, 6% of the serotyped group B strains were not-typable, and in Italy, Netherlands and Norway this was in the range of 13-32%.

3.4.10 Overall case fatality rates

The overall case fatality rates (CFR) for all cases of laboratory confirmed meningococcal disease over 1999-2002 increased from 7% to 8% (Table 17). Between 2001 and 2002, case fatality rates increased in Czech Republic, France, Italy, Malta, Norway, Scotland, Spain and Switzerland. 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 4% to 16% in 2002, 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.

3.4.11 Case fatality rates by serogroup

The highest case fatality rates in the EU countries in 2002 was seen amongst cases with serogroup C infection (12%) followed by serogroup W135 (10%) and Y (10%) (Table 18). 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.

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

Age specific case fatality rates for serogroup B infection (Table 19) decrease from the under one year old age group to 10-14 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 its lowest level in the 5-9 year olds, from where it steadily increases with age.

3.4.13 Antibiotics resistance

Sixteen countries (Austria, Belgium, Czech Republic, Denmark, England & Wales, Germany, Greece, Iceland, Italy, Malta, Netherlands, Portugal, Scotland, Spain, Sweden and Switzerland) contributed antibiotic minimum inhibitory concentration (MIC) data for isolates tested for antibiotic susceptibility. The proportion of such strains in each country varies widely in 2002 (table vi). 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, 54% in 2001, and 44% in 2002 (table vi & previous reports). 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 vi Susceptibility of *N. meningitidis* to penicillin, by country: 2002

Country	2002		
	MIC <= 0.06	MIC >0.06 and <2.00	Total
Austria	42 (70%)	18 (30%)	60
Belgium	216 (88%)	29 (12%)	245
Czech Republic	59 (91%)	6 (9%)	65
Denmark	56 (65%)	30 (35%)	86
E&W	568 (62%)	355 (38%)	923
Germany	45 (9%)	467 (91%)	512
Greece-lab	21 (91%)	2 (9%)	23
Iceland	13 (100%)	0	13
Italy	68 (87%)	10 (13%)	78
Malta	1 (13%)	7 (88%)	8
Netherlands	0	1 (100%)	1
Portugal-lab*	69 (74%)	24 (26%)	93
Scotland	77 (95%)	4 (5%)	81
Spain-lab*	175 (49%)	183 (51%)	358
Sweden	36 (84%)	7 (16%)	43
Switzerland	41 (53%)	36 (47%)	77
Total	1487 (56%)	1179 (44%)	2666

* 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 during 1999/2000 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 iii). 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 iv). This was 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 v). However, in 2002 Belgium and the Netherlands introduced MenC vaccination programmes (table (i)), and the impact of these is seen in the decrease of both the number of culture confirmed group C meningococcal disease cases, and in the proportion of serogroup C cases that are P2.2a serotype in 2002.

Figure iii: **Cases of culture-confirmed serogroup C in countries with established MenC programmes, England & Wales, Ireland and Spain, (combined) by age group and year, 1999-2002**

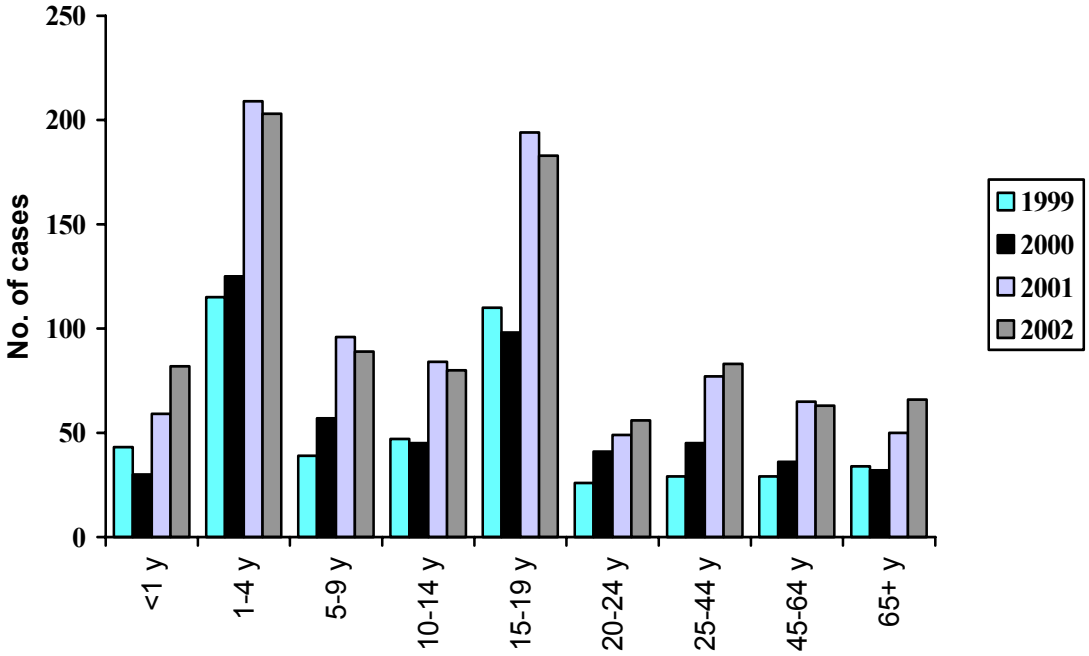


Figure viv: **Cases of culture-confirmed serogroup C in countries without Men C programmes (Netherlands & Belgium included in all years) by age group and year, 1999-2002**

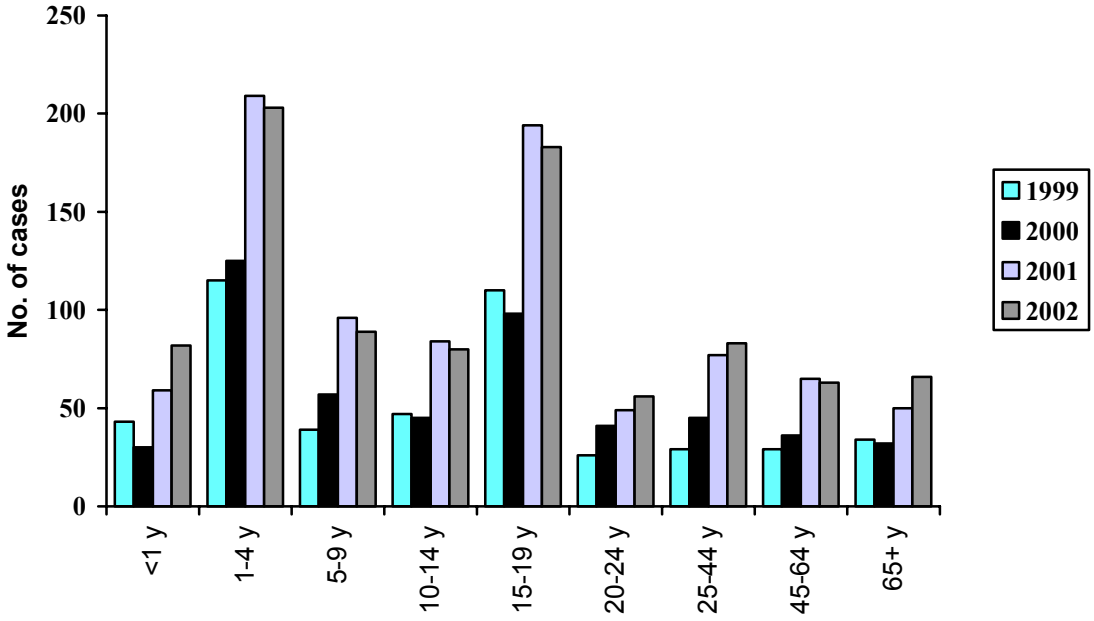
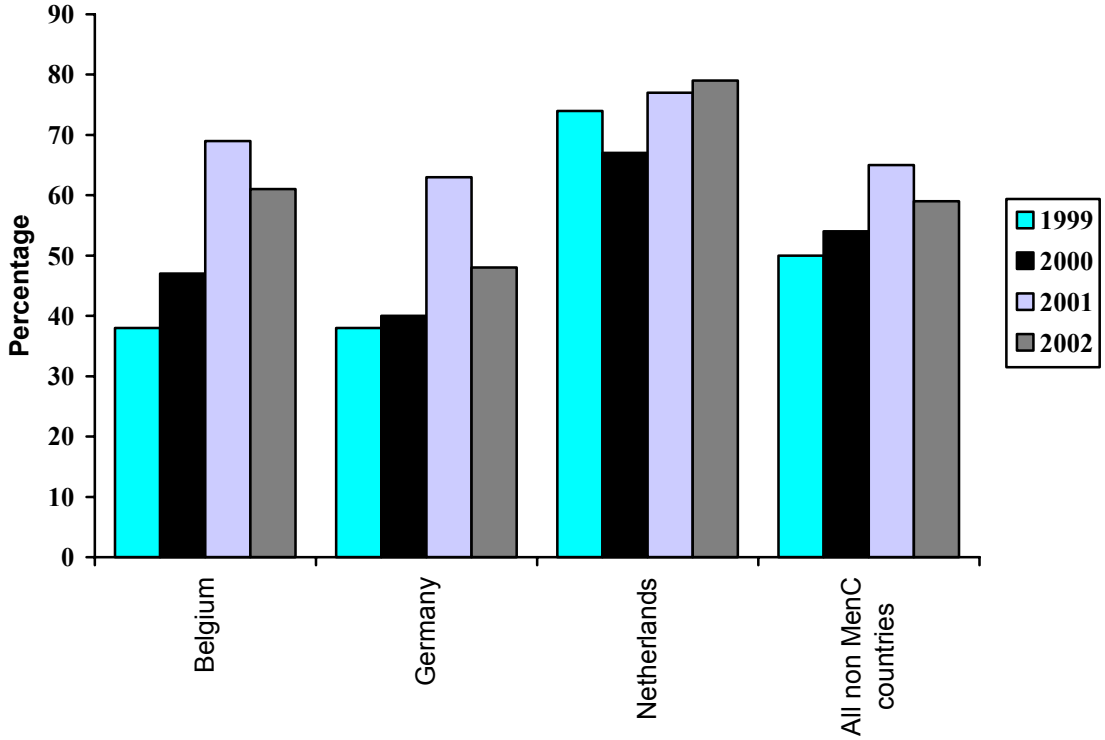


Figure v: Proportion of culture-confirmed meningococcal disease serogroup C cases that are serotype P2.2a – 1999-2002



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 vii) The number of cases in all three categories was lower in 2002 compared to the number in the same period in 2001. (table viii)

Table vii 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 viii 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 (e.g. data on age is now supplied by Greece). Expansion of the network into other countries within Europe has also occurred.

The data provided on meningococcal disease shows marked variations in overall incidence by country. Excluding very small countries, a twenty-fold variation in the incidence of culture confirmed infection was seen in 2002. 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 1999-2002. 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. In 2002, the highest proportion of meningococcal disease cases in serogroups other than B and C was seen in serogroup Y infection cases

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 three countries and may be associated with a future shift in incidence or case-fatality rates. The

major group C serotype was P2.2a in 13 countries. 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 rates 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 rates for group B infections are low overall, and in most countries lower than that observed for group C or for other serogroups. Serogroup C infection cases exhibited the highest CFR in 2002 (12%), but serogroup Y(10%) and W135(10%) were also high. A decrease has, however, been seen in the overall CFR for W135. In 2001 the CFR for W135 had increased to 15%. 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 now being seen. 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 introduced vaccine in 2000,Belgium and the Netherlands established routine programmes in 2002, 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 2002, 44% 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. Development of a web-enabled database has enabled easy access to current data (via set queries) and the capacity for performing live queries. Preparatory work has begun on establishing web-based reporting for 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 (www.euibis.org). Future developments include a web-enabled database for performing live queries and the eventual availability of web-based reporting from participant countries.

6. APPENDIX 1: DATA TABLES

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Table 1: Incidence of culture confirmed cases of invasive meningococcal disease per 100,000 population, by country and year, 1999-2002

Country		1999			2000			2001			2002		
		No. of cases	Population	Incidence	No. of cases	Population	Incidence	No. of cases	Population	Incidence	No. of cases	Population	Incidence
Austria	289	80	7,795,788	1.03	58	7,795,788	0.74	91	7,795,788	1.17	60	7,795,788	0.77
Belgium	1206	297	10,213,752	2.91	267	10,239,085	2.61	380	10,263,414	3.70	262	10,309,725	2.54
Czech Republic	319	89	10,282,784	0.87	57	10,272,503	0.55	89	10,272,503	0.87	84	10,272,503	0.82
Denmark	496	151	5,313,577	2.84	121	5,330,020	2.27	135	5,349,212	2.52	87	5,349,212	1.63
E&W	5398	1704	51,820,200	3.29	1534	52,943,284	2.90	1237	52,943,284	2.34	923	52,943,284	1.74
Finland	201	57	5,116,826	1.11	48	5,116,826	0.94	48	5,116,826	0.94	48	5,116,826	0.94
France	1991	394	59,146,337	0.67	464	60,254,277	0.77	523	60,254,277	0.87	610	60,254,277	1.01
Germany	1893	402	82,163,475	0.49	452	82,163,475	0.55	521	82,163,475	0.63	518	82,163,475	0.63
Greece	95	63	10,516,366	0.60	50	10,516,366	0.48	54	10,521,670	0.51	41	10,521,670	0.39
Iceland	68	21	269,735	7.79	16	269,735	5.93	18	278,702	6.46	13	278,702	4.66
Ireland	541	189	3,626,087	5.21	169	3,626,087	4.66	101	3,839,000	2.63	82	3,839,000	2.14
Italy	607	158	57,679,895	0.27	153	57,844,017	0.26	133	57,844,017	0.23	163	57,844,017	0.28
Malta	52	13	366,431	3.55	16	366,431	4.37	13	366,431	3.55	10	366,431	2.73
Netherlands	2477	574	15,760,225	3.64	544	15,863,950	3.43	723	15,987,075	4.52	634	15,987,075	3.97
Norway	255	73	4,445,329	1.64	74	4,478,497	1.65	64	4,503,436	1.42	44	4,503,436	0.98
Portugal-lab	279	21	9,920,760	0.21	59	9,920,760	0.59	106	10,365,117	1.02	93	10,365,117	0.90
Scotland	170	N/A	N/A	N/A	N/A	N/A	N/A	87	5,064,200	1.72	83	5,064,200	1.64
Spain-notifs	3105	947	39,418,017	2.40	971	39,418,017	2.46	643	39,513,630	1.63	544	39,513,630	1.38
Spain-lab*	2046	602	39,418,017	1.53	692	39,418,017	1.75	394	39,513,630	1.00	358	39,513,630	0.91
Sweden	N/A	N/A		N/A	N/A		N/A	N/A		N/A	39	8,846,625	0.44
Switzerland	521	146	7,204,055	2.03	147	7,204,055	2.04	144	7,204,055	2.00	84	7,204,055	1.17
TOTAL	19,963	5,379	381059639	1.41	5,200	383670858	1.36	4861	389646112	1.31	4,422	398539048	1.11

* Spain-lab not included in Total

Table 2: Incidence of PCR and/or culture confirmed cases of invasive meningococcal disease in countries using both methods, by country : 2002

Country	No. of cases	Population	Incidence
Austria	76	7,795,788	0.97
Czech Republic	100	0,272,503	0.97
England & Wales	1772	52,943,284	3.35
France	619	60,254,277	1.03
Greece	173	10,521,670	1.64
Iceland	15	278,702	5.38
Ireland	212	3,839,000	5.52
Norway	48	4,503,436	1.07
Scotland	97	5,064,200	1.92
Sweden	44	8,846,625	0.50
Switzerland	91	7,204,055	1.26
TOTAL	3203	162676915	1.97

Table 3: Age distribution of culture-confirmed invasive meningococcal disease in contributing partner countries : 1999-2002

Year	Total	< 1 yr		1-4 yrs		5-9 yrs		10-14 yrs		15-19 yrs		20-24 yrs		25-44 yrs		45-64 yrs		65+ yrs	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
1999	5301	850	16.03	1432	27.01	561	10.58	428	8.07	838	15.81	280	5.28	350	6.60	304	5.73	258	4.87
2000	4743	780	16.45	1247	26.29	465	9.80	314	6.62	620	13.07	283	5.97	407	8.58	354	7.46	273	5.76
2001	4787	774	16.17	1184	24.73	416	8.69	368	7.69	697	14.56	261	5.45	422	8.82	374	7.81	291	6.08
2002	4222	615	14.56	1052	24.92	365	8.65	276	6.54	608	14.40	221	5.23	374	8.86	312	7.39	399	9.45

Table 3(a) PCR-only confirmed meningococcal disease in Austria, Czech Republic, England and Wales, France, Greece, Iceland, Ireland, Norway, Scotland, Sweden and Switzerland, 1999-2002

Year	Total	< 1 yr		1-4 yrs		5-9 yrs		10-14 yrs		15-19 yrs		20-24 yrs		25-44 yrs		45-64 yrs		65+ yrs		NK
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.
1999	1334	227	17.02%	391	29.31%	144	10.79%	109	8.17%	189	14.17%	51	3.82%	103	7.72%	77	5.77%	25	1.87%	18
2000	1359	235	17.29%	427	31.42%	128	9.42%	95	6.99%	159	11.70%	72	5.30	125	9.20%	93	6.84%	22	1.62%	3
2001	1429	258	18.05%	408	28.55%	172	12.04%	115	8.05%	165	11.55%	69	4.83%	129	8.96%	78	5.46%	25	1.75%	10
2002	1176	221	18.79	391	33.25	142	12.07	84	7.14	126	10.71	45	3.83	78	6.63	68	5.78	22	1.87	1

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, Scotland, Spain, Sweden and Switzerland): 2001 & 2002

	Age group (years)									
Year	*<1*	*1-4*	*5-9*	*10-14*	*15-19*	*20-24*	*25-44*	*45-64*	*65+*	*NK*
2001	774	1184	416	368	697	261	422	374	291	75
2002	615	1052	365	276	608	221	374	312	399	17
Population 2001	4,178,263	16,982,685	21,945,751	22,649,858	23,327,302	25,097,424	116,293,793	93,984,711	62,629,707	
Population 2002	4,268,443	17,411,037	22,559,255	23,172,274	23,829,927	25,646,886	118,725,642	96,154,574	64,168,081	
Incidence 2001*	18.52	6.97	1.90	1.62	2.99	1.04	0.36	0.40	0.46	
Incidence 2002*	14.41	6.04	1.62	1.19	2.55	0.86	0.32	0.32	0.62	
Average annual incidence 2001/2002	16.44	6.57	1.77	1.41	2.79	0.96	0.34	0.36	0.55	

Table 5: Age specific incidence rate (per 100,000 population) of culture-confirmed meningococcal disease serogroup B in the EU reporting countries: 1999-2002

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	3379	574	14.26	960	5.87	419	1.98	265	1.22	482	2.16	162	0.68	198	0.18	180	0.20	139	0.23
2000	3245	689	17.12	898	5.49	325	1.54	192	0.88	389	1.75	166	0.69	229	0.20	220	0.24	137	0.29
2001	3142	630	15.08	881	5.19	297	1.35	228	1.01	406	1.74	149	0.59	215	0.18	210	0.22	126	0.20
2002	2712	537	12.58	756	4.34	252	1.12	177	0.76	340	1.43	121	0.47	196	0.17	180	0.19	153	0.24

Table 6:Age specific incidence rate (per 100,000 population) of culture-confirmed meningococcal disease serogroup C in the EU reporting countries: 1999-2002

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	1576	140	3.39	405	2.48	172	0.81	159	0.73	300	1.35	110	0.46	104	0.09	102	0.11	84	0.14
2000	1474	112	2.71	376	2.30	161	0.76	117	0.54	230	1.03	110	0.46	154	0.14	112	0.12	102	0.17
2001*	1380	104	2.49	282	1.66	128	0.58	116	0.51	254	1.09	100	0.40	161	0.14	139	0.15	96	0.15
2002*	1244	95	2.23	234	1.34	110	0.49	100	0.43	223	0.94	95	0.37	153	0.13	112	0.12	122	0.19

* includes Greece & Scotland

Table 7: Proportion of invasive meningococcal disease in culture-confirmed cases by country – 2002

Country	Total known*	Group B		Group C		Other		NK
	No.	No.	%	No.	%	No.	%	No.
Austria	60	39	65.00	17	28.33	4	6.67	0
Belgium	253	161	63.64	89	35.18	3	1.19	9
Czech Republic	82	42	51.22	35	42.68	5	6.10	2
Denmark	86	65	75.58	16	18.60	5	5.81	1
E&W	923	722	78.22	118	12.78	83	8.99	0
Finland	48	36	75.00	6	12.50	6	12.50	0
France	572	279	48.78	233	40.73	60	10.49	38
Germany	517	316	61.12	162	31.33	39	7.54	1
Greece	39	33	84.62	6	15.38	0	0.00	2
Iceland	13	1	7.69	12	92.31	0	0.00	0
Ireland	82	72	87.80	5	6.10	5	6.10	0
Italy	92	55	59.78	36	39.13	1	1.09	71
Malta	7	6	85.71	1	14.29	0	30.00	3
Netherlands	632	383	60.41	227	35.80	22	3.47	2
Norway	45	27	60.00	12	26.67	6	13.33	0
Portugal-lab	93	36	38.71	52	55.91	5	5.38	0
Scotland	83	63	75.90	10	12.05	10	12.05	0
Spain-lab	358	229	63.97	104	29.05	25	6.98	0
Sweden	39	21	53.85%	11	28.21%	7	17.95%	0
Switzerland	82	34	41.46	39	47.56	9	10.98	2
TOTAL	4106	2620	63.81	1191	29.01	295	7.18	131

* Total known serogrouped cases. The 'NK' (Not known) total not included

Table 8: Proportion of culture-confirmed cases due to serogroup C by country, 1999-2002

% Group C	1999	2000	2001	2002
<10%	-	Malta	Malta	Ireland
10-19%	Austria Denmark Finland Netherlands Norway	Austria Denmark Netherlands Norway	England & Wales Finland Ireland	Denmark England & Wales Finland Greece Malta Scotland
20-29%	Belgium France Germany Italy Malta	Czech Republic England & Wales Finland France Germany Greece Italy	Denmark Germany Greece Italy Norway Spain Scotland	Austria Norway Spain Sweden
0-39%	England & Wales Greece Ireland Spain Switzerland	Belgium Ireland Spain	Czech Republic France Netherlands Switzerland	Belgium France Germany Netherlands Italy
40+%	Czech Republic Iceland Portugal-lab	Iceland Portugal-lab Switzerland	Austria Belgium Iceland Portugal-lab	Czech Republic Iceland Portugal-lab Switzerland

Table 9: No. (Proportion) of invasive meningococcal disease in culture-confirmed cases other than serogroup B and C, by country – 2002 (Not groupable [NGA] cases are included in the Total known)

Country	Total known	A	%	W135	%	X	%	Y	%	Z/29E	%	Not known of total
Austria	60	0	0.00	1	1.67	0	0.00	1	1.67	0	0.00	0
Belgium	253	0	0.00	1	0.40	0	0.00	2	0.79	0	0.00	9
Czech Republic	82	0	0.00	2	2.44	0	0.00	3	3.66	0	0.00	2
Denmark	86	0	0.00	3	3.49	1	1.16	1	1.16	0	0.00	1
E&W	923	1	0.11	56	6.07	3	0.33	21	2.28	0	0.00	0
Finland	48	0	0.00	1	2.08	0	0.00	4	8.33	0	0.00	0
France	572	2	0.35	40	6.99	1	0.17	15	2.62	0	0.00	38
Germany	517	0	0.00	11	2.13	0	0.00	14	2.71	2	0.39	1
Greece	39	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	2
Iceland	13	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0
Italy	92	0	0.00	0	0.00	0	0.00	1	1.09	0	0.00	71
Ireland	82	0	0.00	3	3.66	0	0.00	2	2.44	0	0.00	0
Malta	7	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	3
Netherlands	632	1	0.16	7	1.11	0	0.00	8	1.27	1	0.16	0
Norway	45	0	0.00	3	6.67	0	0.00	1	2.22	0	0.00	0
Portugal-lab	93	0	0.00	3	3.23	0	0.00	2	2.15	0	0.00	0
Scotland	83	0	0.00	3	3.61	1	1.20	3	3.61	1	1.20	0
Spain-lab	358	0	0.00	8	2.23	1	0.28	12	3.35	1	0.28	0
Sweden	39	0	0.00	1	2.56	0	0.00	5	12.82	0	0.00	0
Switzerland	82	0	0.00	3	3.66	0	0.00	4	4.88	0	0.00	3
TOTAL	4106	4	0.10	146	3.56	7	0.17	99	2.41	5	0.12	130

Table 10: Major serogroup of invasive meningococcal disease cases other than groups B and C amongst the contributing countries: 1999-2002

Major serogroup	1999	2000	2001	2002
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	Scotland (with Y) Austria (with Y) Denmark Portugal-lab England & Wales France Ireland Norway
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	Austria (with W135) Spain Czech Republic Belgium Finland Netherlands Germany Italy Sweden Switzerland (with W135)
29E	-	-	Malta	-
A	Greece Italy	Czech Republic (with W135)	Czech Republic Denmark (with W135) Greece	

Table 11: No. of cases (%) of group C serotypes by country : 2002 (cases where serotype known/given)

Country	P2.2a		P2.2b		NT		Other		Total
	No	*%*	*No*	*%*	*No*	*%*	*No*	*%*	*No.*
Austria	9	52.94	6	35.29	1	5.88	1	5.88	17
Belgium	54	60.67	25	28.09	9	10.11	1	1.12	89
Czech Republic	20	71.43	0	0.00	7	25.00	1	3.57	28
Denmark	7	43.75	4	25.00	0	0.00	5	31.25	16
E&W	88	74.58	5	4.24	24	20.34	1	0.85	118
Finland	4	66.67	0	0.00	0	0.00	2	33.33	6
France	106	62.35	29	17.06	32	18.82	3	1.76	170
Germany	42	47.73	26	29.55	15	17.05	5	5.68	88
Greece	0	0.00	0	0.00	2	33.33	4	66.67	6
Ireland	4	100.00	0	0.00	0	0.00	0	0.00	4
Italy	10	31.25	13	40.63	7	21.88	2	6.25	32
Netherlands	180	79.30	25	11.01	15	6.61	7	3.08	227
Norway	0	0.00	0	0.00	1	8.33	11	91.67	12
Portugal-lab	9	17.31	39	75.00	3	5.77	1	1.92	52
Scotland	5	83.33	0	0.00	1	16.67	0	0.00	6
Spain-lab	61	58.65	28	26.92	13	12.50	2	1.92	104
Sweden	1	9.09	0	0.00	4	36.36	6	54.55	11
Switzerland	17	43.59	15	38.46	4	10.26	3	7.69	39
TOTAL	617	60.20	215	20.98	138	13.07	55	5.37	1025

Table 12: Major serotype of group C invasive meningococcal disease amongst the contributing countries 1999-2002

Major serotype	1999	2000	2001	2002
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	Austria Belgium Czech Republic Denmark England & Wales Finland France Germany Ireland Netherlands Scotland Spain-lab Switzerland
2b	Austria Belgium France Spain	Norway Spain		Italy Portugal-lab
NT	Finland	Finland	Finland Malta Norway	Greece Norway Sweden

Table 13: No. of cases (%) of selected group B phenotypes by country : 2002 (cases where serotype known/given)

	B:NT:NT/P1.15/NT		B:3.4/P1.15		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/NT/NT		Other		Total
Country	*No.*	*%*			*No.*	*%*	*No.*	*%*	*No.*	*%*	*No*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	
Austria	0	0%	0	0%	1	3%	5	13%	0	0%	1	3%	4	10%	0	0%	1	3%	27	69%	39
Belgium	0	0%	4	3%	1	1%	3	2%	74	46%	6	4%	5	3%	3	2%	2	1%	63	39%	161
Czech Republic	0	0%	12	32%	0	0%	3	8%	0	0%	1	3%	0	0%	0	0%	0	0%	21	57%	37
Denmark	1	2%	3	5%	3	5%	25	38%	2	3%	0	0%	2	3%	0	0%	3	5%	26	40%	65
E&W	41	6%	25	4%	75	10%	21	3%	150	20%	9	1%	21	3%	46	6%	30	4%	304	42%	722
Finland	1	3%	12	3%	0	0%	0	0%	1	3%	0	0%	0	0%	1	3%	0	0%	20	57%	35
France	2	1%	5	2%	5	2%	2	1%	38	17%	0	0%	18	8%	12	5%	15	7%	125	56%	222
Germany	0	0%			3	2%	1	1%	27	16%	2	1%	8	5%	0	0%	4	2%	124	73%	169
Greece	0	0%			0	0%		0%	4	12%	1	3%	0	0%	0	0%	2	6%	26	79%	33
Ireland	3	6%	2	4%	5	10%	1	2%	13	26%	2	4%	3	6%	1	2%	0	0%	21	41%	51
Italy	0	0%	0	0%	0	0%	1	2%	4	8%	2	4%	0	0%	0	0%	4	8%	38	78%	49
Malta	0	0%	5	83%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%	1	16%	6
Netherlands	5	1%	8	2%	2	1%	2	1%	95	25%	2	1%	9	3%	6	2%	25	13%	206	54%	360
Norway	0	0%			0	0%	5	20%	3	12%	0	0%	0	0%	0	0%	8	32%	9	36%	25
Portugal-lab	4	11%	2	6%	0	0%	2	6%	2	6%	0	0%	1	3%	3	8%	0	0%	22	61%	36
Scotland	2	5%	3	7%	4	10%	1	2%	2	5%	0	0%	0	0%	4	10%	2	5%	24	57%	42
Spain-lab	20	9%	33	14%	15	7%	3	1%	7	3%	19	8%	9	4%	12	5%	3	1%	108	47%	229
Sweden	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Switzerland	1	3%	0	0%	0	0%	2	6%	4	12%	0	0%	4	2%	2	6%	1	2%	20	59%	34
Total*	80	3%	114	5%	114	5%	77	3%	426	18%	45	2%	84	4%	90	4%	100	6%	1185	51%	231540

*TOTAL = all culture confirmed serotyped/serosubtyped B's

Table 14: Major serotype of group B invasive meningococcal disease amongst the contributing countries 1999-2002

Major serotype	1999	2000	2001	2002
B:15:P1.7, P.16	Austria Denmark France (with B4: P1.4) Germany Norway	Austria Denmark Germany Italy Norway	Austria Denmark Germany Italy	Austria Denmark
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	Belgium England & Wales France Germany Greece Ireland Netherlands Switzerland
B:4:1.15	Malta Spain	Malta Spain	Malta Spain	Czech Republic Finland Malta Spain

Table 15: Age specific incidence (per 100,000) of culture-confirmed Group B meningococcal disease by country : 2002

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	39	9	9.9	7	1.9	5	1.1	3	0.7	5	1.0	2	0.3	5	0.2	2	0.1	1	0.1	0
Belgium	161	26	23.0	56	12.1	20	3.2	12	2.0	21	3.4	5	0.8	7	0.2	12	0.5	2	0.1	0
Czech Republic	42	7	7.8	9	2.5	1	0.2	4	0.6	11	1.6	2	0.2	7	0.3	1	0.0		0.0	0
Denmark	65	8	11.9	14	5.1	6	1.7	6	1.9	14	5.0	3	0.9	3	0.2	6	0.4	5	0.6	0
E&W	722	195	30.8	219	8.6	57	1.7	43	1.3	58	1.8	32	1.0	40	0.3	40	0.3	38	0.5	0
Finland	36	3	4.8	8	3.1	2	0.6	2	0.6	5	1.5	2	0.7	5	0.3	6	0.5	3	0.4	0
France	279	50	6.8	69	2.3	24	0.6	15	0.4	43	1.1	20	0.5	28	0.2	21	0.1	9	0.1	0
Germany	316	47	6.1	88	2.8	12	0.3	20	0.4	76	1.6	22	0.5	19	0.1	16	0.1	16	0.1	0
Greece	33	4	4.0	9	2.2	7	1.3	2	0.3	3	0.4	1	0.1	2	0.1	3	0.1	2	0.1	0
Iceland	1	1	26.3	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
Ireland	72	15	27.3	24	11.1	5	1.9	6	2.1	8	2.5	4	1.2	4	0.4	3	0.4	2	0.5	1
Italy	55	8	1.5	14	0.7	7	0.3	2	0.1	8	0.3	0	0.0	8	0.04	4	0.02	4	0.04	0
Malta	6	0	0.0	0	0.0	1	4.0	2	7.1	0	0.0	0	0.0	0	0.0	3	3.1	0	0	0
Netherlands	383	65	31.4	118	14.9	54	5.4	31	3.2	42	4.5	9	0.9	22	0.4	20	0.5	21	1.0	1
Norway	27	6	10.1	6	2.5	1	0.3	2	0.7	2	0.8	1	0.4	3	0.2	4	0.4	2	0.3	0
Portugal-lab*	36	5	4.7	17	3.8	6	1.1		0.0	1	0.1	1	0.1	1	0.03	1	0.04	4	0.3	0
Scotland	63	6	11.5	20	8.9	8	2.6	2	0.6	4	1.3	1	0.3	5	0.3	0	0.0	2	0.2	15
Spain-lab**	229	31	7.8	52	3.4	19	0.8	8	0.4	18	0.7	1	0.03	17	0.1	22	0.2	61	0.9	0
Sweden	21	2	2.2	1	0.23	1	0.2	2	0.4	3	0.60	2	0.4	4	0.2	5	0.2	1	0.01	0
Switzerland	34	3	3.9	9	2.8	1	0.2	1	0.2	5	1.2	5	1.2	4	0.2	4	.2	2	0.2	0
Total	2620	491	11.5	740	4.25	237	1.1	163	0.7	327	1.4	113	0.4	184	0.15	173	0.18	175	0.27	17

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

Table 16: Age specific incidence (per 100,000) of culture-confirmed Group C meningococcal disease by country : 2002

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	17	2	2.2	4	1.1	4	0.9	0	0.9	5	9.9	0	0.0	2	0.1	0	0.0	0	0.0	2
Belgium	89	10	8.9	17	3.7	8	1.3	5	0.8	19	3.1	8	1.3	9	0.3	7	0.3	6	0.3	10
Czech Republic	35	0	0.0	1	0.3	7	1.2	6	0.9	10	1.4	2	0.2	3	0.1	4	0.1	2	0.1	0
Denmark	16	0	0.0	2	0.7	1	0.3	2	0.6	5	1.8	0	0.0	3	0.2	1	0.1	2	0.3	0
E&W	118	3	0.5	6	0.2	3	0.1	2	0.1	13	0.4	20	0.6	29	0.2	24	0.2	18	0.2	3
Finland	6	0	0.0	0	0.0	0	0.0	0	0.0	3	0.9	0	0.0	2	0.1	1	0.1	0	0.0	0
France	233	33	4.5	51	1.7	16	0.4	11	0.4	39	1.0	18	0.5	23	0.1	18	0.1	24	0.3	33
Germany	162	14	1.0	47	1.5	14	0.3	17	0.4	31	0.7	7	0.2	11	0.04	10	0.05	11	0.1	14
Greece	6	1	1.0	2	0.5	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0	1	0.04	0	0.0	1
Iceland	12	0	0.0	2	11.6	1	4.4	2	9.6	3	14.1	1	4.7	3	3.7	0	0.0	0	0.0	0
Ireland	5	0	0.0	2	0.9	0	0.0	1	0.3	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0	0
Italy	36	1	0.2	15	0.7	3	0.1	2	0.1	6	0.2	1	0.03	7	0.04	0	0.0	1	0.1	1
Malta	1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	1.0	0	0.0	0
Netherlands	227	13	6.3	41	5.2	30	3.0	27	2.8	49	5.3	17	1.8	18	0.4	17	0.4	15	0.7	0
Norway	12	1	1.7	0	0.0	0	0.0	1	0.3	6	2.3	1	0.4	1	0.1	2	0.2	0	0.0	1
Portugal-lab*	52	7	6.6	20	4.5	5	0.9	6	0.	6	0.8	1	0.12	1	0.04	1	0.04	5	0.3	7
Scotland	10	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3	1	0.3	3	0.2	2	0.2	3	0.4	0
Spain-lab**	104	1	0.3	7	0.5	8	0.4	7	0.3	16	0.7	8	0.3	17	0.1	9	0.1	31	0.5	1
Sweden	11	0	0.0	2	0.5	2	0.3	2	0.4	1	0.2	0	0.0	1	0.04	1	0.05	2	0.1	0
Switzerland	39	2	2.6	13	4.1	1	0.2	2	0.5	5	1.2	3	0.7	5	0.2	2	0.1	6	0.5	2
Total	1266	88	2.06	232	1.3	103	0.5	94	0.4	219	0.9	88	0.3	139	0.1	102	0.1	126	0.2	75

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

Table 17: Case fatality rate in laboratory confirmed cases of meningococcal disease, by country and year: 1999-2002

Country	Year	Total cases	Died	CFR	Year	Total cases	Died	CFR	Year	Total cases	Died	CFR	Year	Total	Died	CFR
Austria	**1999**	97	7	7%	**2000**	83	5	6%	**2001**	106	7	7%	**2002**	81	6	7%
Belgium	**1999**	297	16	5%	**2000**	267	13	5%	**2001**	380	27	7%	**2002**	262	15	6%
Czech Republic	**1999**	93	7	8%	**2000**	61	5	8%	**2001**	93	10	11%	**2002**	113	18	16%
Denmark	**1999**	177	14	8%	**2000**	151	12	8%	**2001**	161	10	6%	**2002**	98	7	7%
E&W	**1999**	2784	201	7%	**2000**	2651	199	8%	**2001**	2327	189	8%	**2002**	1772	115	6%
Finland	**1999**	57	10	18%	**2000**	N/A	N/A	N/A	**2001**	N/A	N/A	N/A	**2002**	N/A	N/A	N/A
France	**1999**	411	35	8%	**2000**	489	59	12%	**2001**	559	73	13%	**2002**	648	94	15%
Germany**	**1999**	402	21	5%	**2000**	452	28	6%	**2001**	521	34	7%	**2002**	517	38	7%
Greece	**1999**	108	7	7%	**2000**	133	9	7%	**2001**	160	7	4%	**2002**	175	7	4%
Iceland	**1999**	21	2	10%	**2000**	18	2	11%	**2001**	20	2	10%	**2002**	15	1	7%
Ireland	**1999**	445	17	4%	**2000**	410	25	6%	**2001**	301	12	4%	**2002**	224	8	4%
Italy	**1999**	246	16	7%	**2000**	217	19	9%	**2001**	194	14	7%	**2002**	216	25	12%
Malta	**1999**	18	5	28%	**2000**	21	3	14%	**2001**	14	0	0%	**2002**	14	2	14%
Netherlands	**1999**	583	23	4%	**2000**	546	30	5%	**2001**	725	41	6%	**2002**	636	25	4%
Norway	**1999**	77	9	12%	**2000**	85	7	8%	**2001**	77	3	4%	**2002**	51	5	10%
Portugal-lab*	**1999**	N/A	N/A	N/A	**2000**	N/A	N/A	N/A	**2001**	N/A	N/A	N/A	**2002**	N/A	N/A	N/A
Scotland	**1999**	N/A	N/A	N/A	**2000**	N/A	N/A	N/A	**2001**	170	11	6%	**2002**	122	11	9%
Spain-notifs	**1999**	947	74	8%	**2000**	N/A	N/A	N/A	**2001**	643	59	9%	**2002**	544	75	14%
Sweden	**1999**	N/A	N/A	N/A	**2000**	N/A	N/A	N/A	**2001**	N/A	N/A	N/A	**2002**	44	9	20%
Switzerland	**1999**	146	11	8%	**2000**	152	10	7%	**2001**	147	11	7%	**2002**	91	15	16%
Total	**1999**	6909	475	7%	**2000**	5736	426	7%	**2001**	6590	510	8%	**2002**	5623	476	8%

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

Table 18: Case Fatality Rate in laboratory confirmed cases of invasive meningococcal disease, by country and serogroup: 2002

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%	57	5	9%	19	0	0%	1	0	0%	1	1	100%
Belgium	0	0	0%	161	7	4%	89	8	9%	1	0	0%	2	0	0%
Czech Republic	0	0	0%	53	6	1%	42	8	19%	2	1	50%	4	0	0%
Denmark	0	0	0%	65	5	8%	16	1	6%	3	0	0%	1	0	0%
E&W	1	0	0%	1385	70	5%	166	30	18%	82	9	11%	26	4	15%
Finland	0	N/A	N/A	36	N/A	N/A	6	N/A	N/A	1	N/A	N/A	4	N/A	N/A
France	3	1	33%	290	35	12%	250	44	18%	41	7	17%	15	2	13%
Germany	0	0	0%	316	24	8%	162	13	8%	11	0	0%	14	0	0%
Greece	0	0	0%	72	5	9%	11	1	9%	17	0	0%	2	0	0%
Iceland	0	0	0%	1	0	0%	12	1	8%	0	0	0%	0	0	0%
Ireland	0	0	0%	198	8	4%	14	0	0%	6	0	0%	2	0	0%
Italy	0	0	0%	68	8	12%	46	7	15%	0	0	0%	1	0	0%
Malta	1	0	0%	6	2	33%	2	0	0%	0	0	0%	0	0	0%
Netherlands	0	0	0%	368	16	4%	227	8	4%	7	1	14%	8	0	0%
Norway	0	0	0%	30	4	13%	13	1	8%	3	0	0%	1	0	0%
Portugal-lab*	0	0	0%	36	N/A	N/A	52	N/A	N/A	3	N/A	N/A	2	N/A	N/A
Scotland	0	0	0%	72	7	10%	14	2	14%	3	0	0%	3	0	0%
Spain-lab*	0	0	0%		N/A	N/A	?	N/A	N/A	8	0	N/A	12	0	N/A
Spain-notifs	0	0	0%	335	39	12%	157	32	20%	N/A	N/A	N/A	N/A	N/A	N/A
Sweden	0	0	0%	23	4	17%	11	4	36%	1	0	0%	5	1	20%
Switzerland	0	0	0%	34	244	7%	39	7	1%	3	0	0%	4	2	50%
Total**	5	1	20%	3606	248	7%	1348	167	12%	184	18	10%**	89	10	11%**

* 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

** EXCL. Finland, Spain lab, Spain notifs & Portugal-lab

Table 19: Case Fatality Rate in laboratory confirmed cases of group B and group C meningococcal disease, by age group: 1999 –2002 (where age group given)

Age group		1999		2000		2001		2002	
		Group B	*Group C*	*Group B*	*Group C*	*Group B*	*Group C*	*Group B*	*Group C*
Under 1	Cases	732	191	799	105	777	98	704	97
	Deaths	43	11	61	10	60	6	45	15
	CFR	5.9%	5.8%	7.6%	9.5%	7.7%	6.1%	6.4%	15.5%
1-4yrs	Cases	1110	479	1133	409	1206	300	1045	235
	Deaths	44	30	48	24	60	22	65	19
	CFR	4.0%	6.3%	4.2%	5.9%	5.0%	7.3%	6.2%	8.1%
5-9yrs	Cases	419	203	384	178	414	131	340	110
	Deaths	14	11	9	7	14	5	????5	7
	CFR	3.3%	5.4%	2.3%	3.9%	3.4%	3.8%	????4.1%	6.4%
10-14yrs	Cases	285	167	230	139	293	115	230	103
	Deaths	2	14	7	15	14	9	7	11
	CFR	0.7%	8.4%	3.0%	10.8%	4.8%	7.2%	3.0	10.7
15-19yrs	Cases	524	347	483	220	512	256	445	225
	Deaths	22	44	19	31	25	30	32	22
	CFR	4.2%	12.7%	3.9%	14.1%	4.9%	11.7%	7.2%	9.8%
20-24yrs	Cases	167	98	196	124	187	116	149	114
	Deaths	16	7	15	18	9	28	7	19
	CFR	9.6%	7.1%	7.7%	14.5%	4.8%	24.1%	4.7%	16.7%
25-44yrs	Cases	237	123	298	186	283	182	250	158
	Deaths	12	17	16	25	14	34	18	20
	CFR	5.1%	13.8%	5.4%	13.5%	4.9%	18.7%	7.2%	12.7%
45-64 yrs	Cases	193	121	276	118	249	163	214	112
	Deaths	19	24	19	17	22	29	27	9
	CFR	9.8%	19.8%	6.9%	14.4%	8.8%	17.8%	12.6	8.0%
65+yrs	Cases	178	107	209	114	131	92	158	121
	Deaths	26	18	25	19	23	19	30	39
	CFR	14.6%	17.3%	12%	16.7%	17.6%	20.7%	19.0%	32.2%

APPENDIX 2 : *N. meningitidis* surveillance network collaborators

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