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National enhanced surveillance of meningococcal disease in England, Wales and Northern Ireland, January 1999–June 2001

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SUMMARY

Enhanced surveillance of meningococcal disease (ESMD) was implemented nationally across ten regions of England, Wales and Northern Ireland from 1 January 1999. It aims to deliver more sensitive surveillance than laboratory reporting by including clinically diagnosed but laboratory unconfirmed cases. Consultants in Communicable Disease Control (CsCDC) report all clinically diagnosed cases of meningococcal disease (MD) to the Regional Epidemiologist in the relevant regional unit of the Public Health Laboratory Service (PHLS) Communicable Disease Surveillance Centre (CDSC). These reports are reconciled with laboratory data from the PHLS Meningococcal Reference Unit and then forwarded to the national CDSC where further reconciliation with laboratory data takes place. In addition, CsCDC are asked to report any clusters of MD that occur. Between 1 January 1999 and 30 June 2001, 12074 cases of MD were ascertained through ESMD. The majority (57%) were laboratory confirmed. The estimated incidence of MD fell between 1999 and 2001 from 9·2 to 8·0 per 100000 population. Of laboratory confirmed cases, the number of cases of serogroups B and W135 increased and of serogroup C and of ungrouped meningococcal infection decreased. Variation between regions was considerable and deserves further investigation. Of 11522 cases with a reported clinical diagnosis, 53·6% were diagnosed as septicaemia, 32·6% as meningitis, 12·5% as both septicaemia and meningitis, and 1·3% had other invasive MD. Between 1 January 1999 and 30 June 2001 698 deaths were reported, an overall case fatality rate (CFR) of 5·8%; 567 deaths were in confirmed cases and 131 probable (CFR 8·2% and 2·5%, respectively). CFR was higher in serogroup C (13·5%) than B (5·8%). No peak in serogroup C meningococcal infection occurred in the winter of 2000/1 and no clusters of serogroup C meningococcal infection were reported in the first half of 2001. ESMD provides information about the epidemiology of MD that is more complete than statutory notification and laboratory surveillance and is useful for evaluating the impact of the meningococcal serogroup C vaccination programme and of the other non-vaccine preventable serogroups.

INTRODUCTION

In January 1999, enhanced surveillance of invasive meningococcal diseases (ESMD) began in England, Wales and Northern Ireland [1], following the success of regional enhanced surveillance and a pilot scheme in five regions of England carried out during 1998 [2–5]. The active surveillance scheme aimed to increase completeness of the national surveillance data. Routine passive surveillance of Meningococcal disease (MD) for England and Wales includes statutory

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notification of meningococcal meningitis and septicaemia to the Office for National Statistics (ONS) through the Public Health Laboratory Service (PHLS) Communicable Disease Surveillance Centre (CDSC), laboratory reports of *Neisseria meningitidis* from the PHLS Meningococcal Reference Unit (MRU) in Manchester, and certified deaths coded as meningococcal disease reported to ONS. Several recent changes including those in notifications, clinical diagnostic procedures, laboratory techniques (e.g. PCR) and the introduction of a new conjugate vaccine for serogroup C meningococcal disease (MenC) mandated development of an appropriate enhanced surveillance system to estimate the MD burden more accurately [6–10].

The new conjugate vaccine providing long-term protection against MenC was licensed in the United Kingdom and introduced into the routine vaccination schedule of infants on 29 November 1999 [11–14], alongside a catch-up programme for older children [15–17]. Since supplies of vaccine were initially limited, the programme was implemented in phases, giving priority to those at higher risk [6, 16–18]. These were infants (aged under 1 year) with the highest burden of MD and teenagers aged 15–17 years old with the highest case fatality rate. From January 2000, the catch-up programme was extended to include all children aged between 2 and 14 years [16–17, 19]. In addition, a single dose of meningococcal A/C polysaccharide (MACP) vaccine had been offered upon entry to higher education to all those aged 18–19 years from October 1999 [16, 17]. MD may progress rapidly and causes high morbidity and mortality especially in children under 5 years of age despite appropriate early antibiotic therapy [20]. Prevention of MD is a public health priority and ESMD became important for monitoring the effectiveness of these major public health interventions.

In this report, we describe the epidemiology of MD between January 1999 and June 2001 and evaluate the impact of the MenC vaccination campaign using the data collected through ESMD.

METHODS

Enhanced surveillance of invasive meningococcal disease (ESMD)

National ESMD began in all regions of England, Wales and Northern Ireland in 1999 following a protocol modified from the regional ESMD including a pilot in five regions in 1998 [1–3, 5, 21]. The main objectives were to ascertain all sporadic cases of invasive meningococcal disease and all clusters in educational institutions, to identify those cases with fatal outcome and to monitor the impact of the serogroup C conjugate vaccine. Consultants in Communicable Disease Control (CsCDC) in each participating health authority were asked to report all cases of probable and confirmed MD (Table 1) on a weekly or monthly basis. The minimum dataset included demographic details, date of onset or admission to hospital, laboratory confirmatory data, clinical diagnosis, outcome (including death) and details of serogroup C conjugate vaccination. This information was sent weekly or monthly using a proforma via email, facsimile or post to the relevant regional unit of PHLS CDSC. Zero returns were sent when no cases were ascertained. Regional units also followed up confirmed cases of MD identified by MRU that had not been reported via the CCDC returns. Additionally, CsCDC identified clusters on the reporting proforma and assisted regional units in completing a cluster surveillance report describing the characteristics of clusters and their management.

Cases were reported by regions and collated at the national CDSC in Colindale where the data were validated through reconciliation with laboratory reports of MD to MRU. ESMD cases were reconciled with MRU reports by name or soundex (a non-unique code derived from a surname), gender and date of birth, allowing a difference between date of onset and specimen date of up to 14 days. Any additional confirmatory data for cases in ESMD identified in MRU were updated and any additional cases not included in ESMD were followed up. Data reconciliation was also carried out with deaths due to MD certified to ONS and updated in ESMD. Quarterly reports have been published in the Communicable Disease Report CDR Weekly [21, 22].

Analysis

Cases of MD with date of onset where available, or date of admission between 1 January 1999 and 30 June 2001 were analysed. Annual rates were calculated by age group, gender and region of residence using 1999 and 2000 mid year population estimates from ONS. The rates for the first half of 2001 were estimated by halving the denominator for 2000. The number of cases was compared to cases ascertained by routine surveillance to estimate under reporting. EPI INFO™

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Table 1. *Case definition for invasive MD used in the enhanced surveillance of MD scheme (ESMD)*

Confirmed case	Clinically diagnosed meningitis, septicaemia or other invasive disease (e.g. orbital cellulitis, septic arthritis) and at least **one** of the following: 1. Isolation of *N. meningitidis* from blood, cerebrospinal fluid (CSF) or skin rash aspirate 2. Isolation of a Gram negative diplococci in blood or CSF 3. Identification of *N. meningitidis* DNA in blood, CSF or rash aspirate by PCR 4. Serological identification of *N. meningitidis* antigen in blood, CSF or urine 5. Over fourfold rise of IgG antibody to *N. meningitidis* serogroup C polysaccharide
Probable case	Clinically diagnosed meningitis, septicaemia or other invasive disease in the absence of laboratory confirmation where *Neisseria meningitidis* infection is thought to be the most likely diagnosis by the clinician managing the case and/or CCDC.
Cluster	Two or more cases of confirmed or probable MD with dates of onset within 4 weeks and attending the same educational establishment (i.e. pre-school group, school, sixth form college or hall of residence at university). Includes cases occurring within 4 weeks of last attendance at institution and clusters with cases due to different strains.

6.04d and STATA™ version 7.0 were used for further statistical analysis.

RESULTS

ESMD identified cases and incidence

There was a total of 12074 cases of invasive MD identified between 1 January 1999 and 30 June 2001 in the ten participating regions (Table 2). The estimated annual incidence per 10^5 population did not change between 1999 and 2000, but declined in 2001 [$P <$ 0·001, incidence rate ratio (IRR) 0·87, 95% CI: 0·83, 0·92]. Data from the first 6 months of each year also showed a decline in 2001 ($P < 0·001$, IRR 0·76, 95% CI: 0·71, 0·80), with estimated incidence falling from 10·9 (95% CI: 10·5, 11·3) per 10^5 population in 2000 to 8·0 (95% CI: 7·7, 8·3) in 2001.

The majority of cases were laboratory confirmed (57·1%), with the remainder classified as probable. The proportion confirmed remained similar during 1999 and 2000, but increased in 2001 [Pearson $\chi^2 =$ 22·0 (2 D.F.), $P < 0·0001$, Table 2]. The proportion of reported serogroups changed from year to year [Pearson $\chi^2 = 319·1$ (6 D.F.), $P < 0·0001$]. The number of cases due to serogroup B increased [Pearson $\chi^2 =$ 191·3 (2 D.F.), $P < 0·001$] each year, while cases of serogroup C fell [Pearson $\chi^2 = 248·1$ (2 D.F.), $P <$ 0·001]. The proportion of cases classified as 'other serogroups' remained constant at around 10% each year. Within this group, cases without identified serogroup (e.g. ungrouped) decreased, but those of serogroup W135 increased from 44 cases in 1999 to 78 in the first 6 months of 2001 [Pearson $\chi^2 = 57·3$ (1 D.F.), $P < 0·001$].

The clinical diagnosis was reported as septicaemia, meningitis, both septicaemia and meningitis, other invasive MD (e.g. septic arthritis) and not known. Of 11522 cases with a reported clinical diagnosis, 53·6% were diagnosed as septicaemia, 32·6% as meningitis, 12·5% as both septicaemia and meningitis, and 1·3% had other invasive MD. The proportion of cases with septicaemia alone declined each year, 58·0% in 1999, 51·5% in 2000 to 48·5% in 2001 [Pearson $\chi^2 = 67·8$ (2 D.F.), $P < 0·001$], but septicaemia remained the most common diagnosis. Cases diagnosed with symptoms of both septicaemia and meningitis increased from 11·3% in 1999 by approximately 1·5 times to 16·3% in 2001 [Pearson $\chi^2 = 34·9$ (2 D.F.), $P < 0·001$], while cases with only meningitis remained unchanged at approximately 30%. A similar trend was observed among confirmed cases, where the proportion with septicaemia fell from 57·4% in 1999 to 50·3% in 2001 [Pearson $\chi^2 = 17·5$ (2 D.F.), $P < 0·001$].

Compared with 1999, the odds of septicaemia remained similar in 2000 [odds ratio (OR) 0·97, 95% CI: 0·87, 1·08], but the odds declined in 2001 (OR = 0·82, 95% CI: 0·71, 0·94). The majority of confirmed serogroup C cases presented as septicaemia [62·9% in 1999, 62·7% in 2000 and 55·1% in 2001, Pearson $\chi^2 = 4·1$ (2 D.F.), $P = 0·13$] whereas around half of serogroup B infected cases were diagnosed as septicaemia (53%). The odds of septicaemia were higher in serogroup C infection (OR = 1·43, 95% CI: 1·28, 1·60).

Seasonality

Confirmed cases peaked during the winter months each year, reflecting the typical seasonality of MD,

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Table 2. *Summary of the cases of MD reported through ESMD in England, Wales and Northern Ireland from 1999 to mid 2001*

	1999	2000	First half 2001†	Total
Cases per year	4980	4912	2182	12074
Incidence rate (per 10^5)	9·2	9·0	8·0	8·9
Confirmed cases (%)	2810 (56·4)	2744 (55·9)	1344 (61·6)	6898 (57·1)
Confirmed case				
Serogroup B (%)	1463 (52·1)	1709 (62·3)	996 (74·1)	4168 (60·4)
Serogroup C (%)	1037 (36·9)	729 (26·6)	184 (13·7)	1950 (28·3)
Serogroup W135 (%)	44 (1·6)	98 (3·6)	78 (5·8)	220 (3·2)
Other serogroups (%)	266 (9·5)	208 (7·6)	86 (6·4)	780 (11·3)
Male : female				
All cases	1·1 : 1·0	1·2 : 1·0	1·1 : 1·0	1·2 : 1·0
Confirmed cases	1·1 : 1·0	1·1 : 1·0	1·1 : 1·0	1·1 : 1·0
Confirmed case				
Age < 1 yr (%)	511 (18·2)	506 (18·4)	240 (17·9)	1257 (18·2)
Age 1–4 yr (%)	802 (28·5)	792 (28·9)	380 (28·3)	1974 (28·6)
Age 5–14 yr (%)	471 (16·8)	417 (15·2)	211 (15·7)	1099 (15·9)
Age 15–17 yr (%)	250 (8·9)	153 (5·6)	87 (6·5)	490 (7·1)
Age 18 yr+ (%)	770 (27·4)	874 (31·9)	423 (31·5)	2067 (30·0)
Deaths	295	267	136	698
CFR* (%)				
All cases	5·9	5·4	6·2	5·8
Confirmed cases	8·2	8·2	8·4	8·2
Probable cases	3·0	2·0	2·7	2·5
Serogroup B	5·9	5·4	6·5	5·8
Serogroup C	12·5	14·4	18·5	13·8
Serogroup W135	15·9	14·3	15·4	15·0

* CFR (deaths/cases).
† First half of year: 1 Jan–30 June.

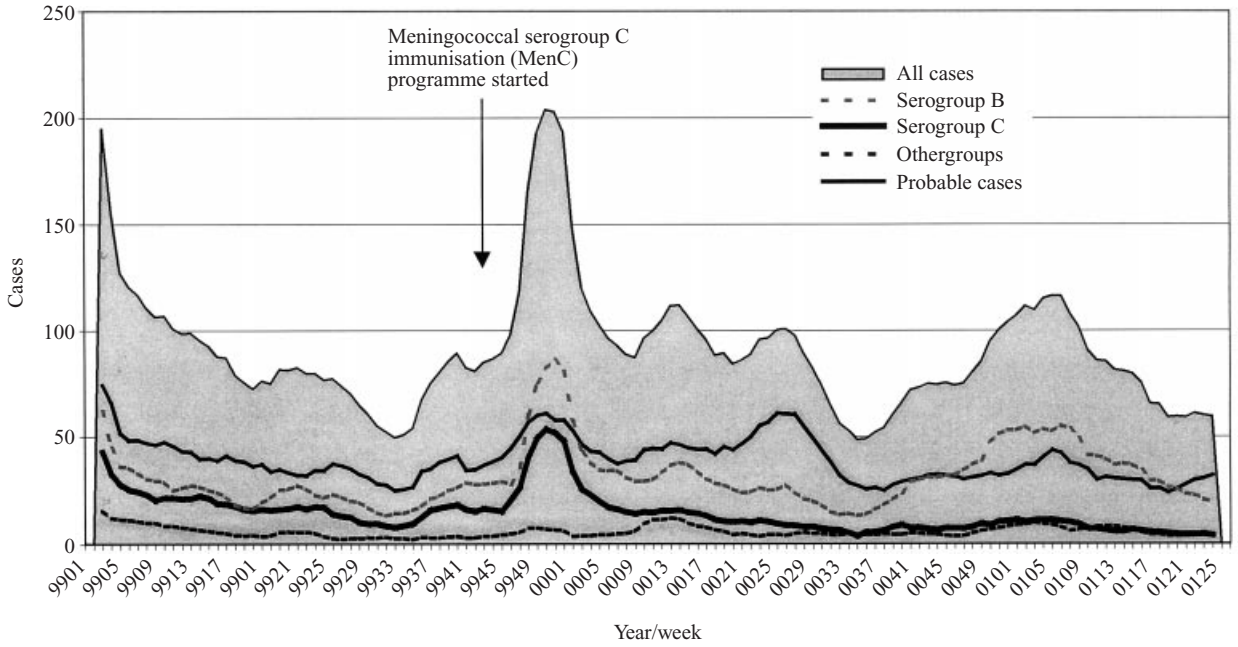

Fig. 1. Cases of meningococcal disease in England, Wales and Northern Ireland: 5 week moving average, 1999 to June 2001.

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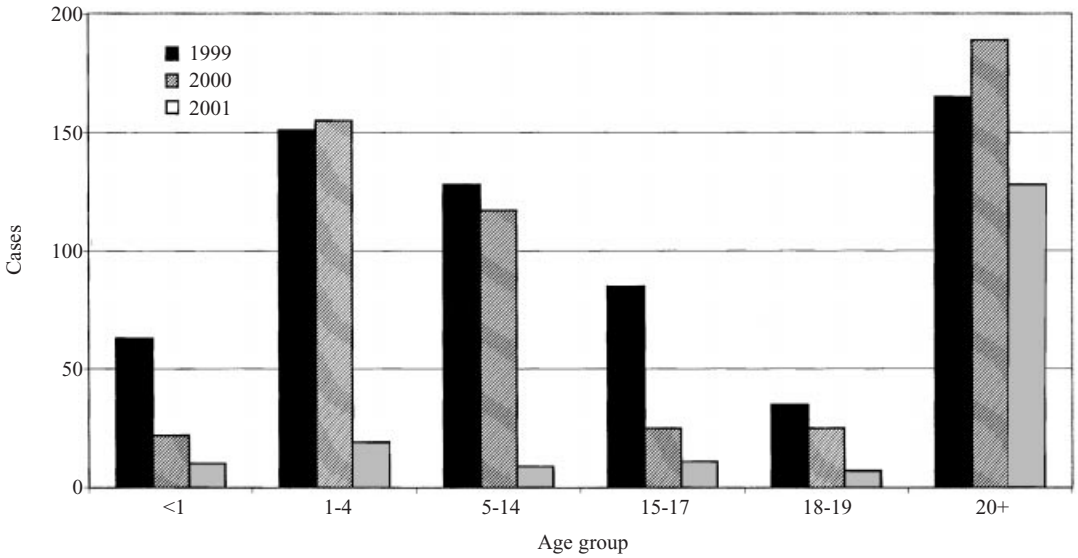

Fig. 2. Comparison of serogroup C cases of MD for the half year from January to June (Week 01 to 26) by age group, 1999, 2000 and 2001.

although the winter peak in 2000/2001 was lower but wider than previous years (Fig. 1). A smaller second peak was seen in both 1999 and 2000 during April (weeks 14–17). In the year 2000 this peak was attributable to a rise in serogroup B and other serogroups. Cases of serogroup C began to decline following the winter of 1999/2000 when fewer than 10 cases per week were identified and there was no winter peak of serogroup C in 2000/2001. Probable cases generally reflected the seasonal pattern of confirmed cases with the exception of July 2000 (weeks 27–30), when a peak in probable cases occurred that was unlikely to have been accounted for by unconfirmed MD.

Gender and age

Overall there were marginally more cases of MD in males (53·6%) than females. However, in those aged 18 years and over there were slightly more female cases (52·8%).

Overall, approximately half of the cases occurred in children less than 5 years of age (49·0%, 95% CI: 0·48, 0·50). This proportion did not change throughout the period of study either in all MD cases or in confirmed cases (Table 2).

Cases of serogroup C declined each year (Table 2). Cases in infants and those aged 15–17 years decreased markedly between the first 6 months of 1999 and the comparable period of 2000 (Fig. 2). The decline in other groups was not so obvious until 2001, although reports in adults aged over 20 years still remained high. Hence, the median age of the cases rose from 15 years in 1999 to 27 in 2001. Cases of serogroup B MD increased in children aged 1–4 years but remained steady in all other age groups. The median age (4 years) of the cases was lower than seen for serogroup C, and did not change during the period of this report. The winter peak of reporting was similarly observed by all age groups throughout the period. The age distribution of W135 showed two peaks, one in infants and the other in those aged 18 years and over.

Region

The more northern regions of England, Wales and Northern Ireland had higher rates of MD (confirmed and probable) per 10^5 population than the south (Table 3). The winter peak and seasonal pattern observed in overall ESMD cases were seen in all regions.

The proportion of confirmed cases of MD reported from Trent increased (approximately 37%, $P = 0{\cdot}04$, IRR 1·37, 95% CI: 1·02, 1·84) in 2001, when it became the region with the highest incidence rate (6·71 per 100 000 population, 95% CI: 5·75, 7·79). The incidence in London and South West also increased steadily up to 5·0 per 10^5 in 1999 to 4·6 in 2001 ($P < 0{\cdot}001$, IRR 0·66, 95% CI: 0·55, 0·80), and the rate in the South East region also decreased to the lowest level of 3·62 (95% CI: 3·07, 4·22) in 2001. The incidence in Northern Ireland also declined significantly (6·3 to 3·9,

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Table 3. *MD reported through the EMSD scheme by region of England, Wales and Northern Ireland, 1999 to June 2001*

	MD reported cases		Confirmed cases		Probable cases	
Region	No.	Rate*	No.	Rate*	No.	Rate*
Eastern	965	7·1	566	4·2	399	2·9
London	1517	8·3	765	4·2	752	4·1
North West	1691	10·2	1020	6·2	671	4·1
Northern and Yorkshire	1589	10·0	1022	6·5	567	3·6
South East	1533	7·0	851	3·9	682	3·1
South West	917	7·4	573	4·6	344	2·8
Trent	1283	10·0	700	5·4	583	4·5
Wales	861	11·7	467	6·4	394	5·4
West Midlands	1288	9·7	670	5·0	618	4·6
England & Wales	11644	8·8	6634	5·0	5010	3·8
Northern Ireland	430	10·2	264	6·2	166	3·9
Total	12074	8·9	6898	5·1	5176	3·8

* Rate per 10^5 population.

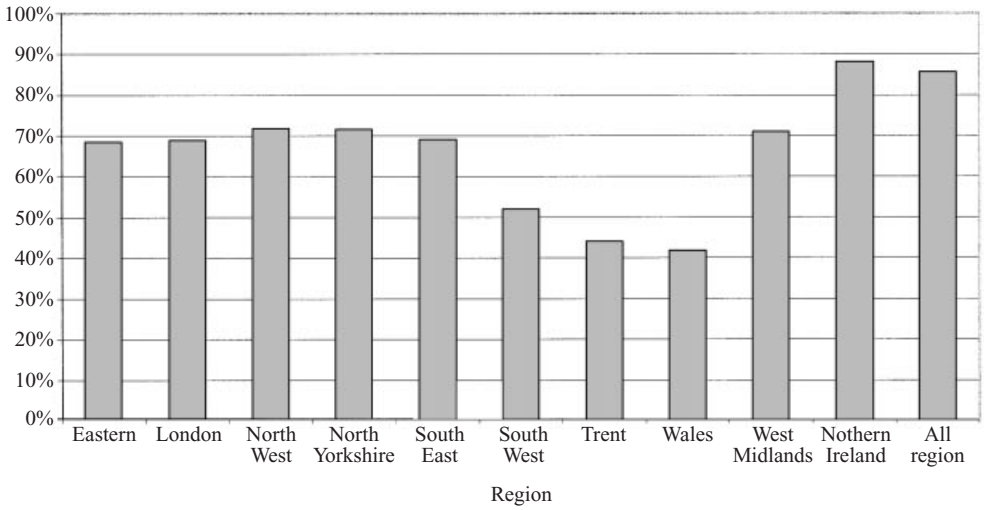

Fig. 3. Percentage reduction in cases of serogroup C meningococcal disease identified in ESMD by region between the epidemiological years 1999/2000 and 2000/2001.

$P = 0{\cdot}016$, IRR 0·62, 95 % CI: 0·42, 0·92). Rates in all other regions did not change greatly between 1999 and 2001 (data not shown).

The estimated incidence of serogroup B increased over time in every region except for Northern Ireland, whereas that of serogroup C decreased in all ten regions (Fig. 3).

Deaths

There were 698 deaths reported between 1 January 1999 and 30 June 2001, an overall case fatality rate (CFR) of 5·8 % (Table 2). Of those, 567 were confirmed cases (CFR 8·2 %) and 131 were probable (CFR 2·5 %). Among those targeted in the MenC vaccination programme, infants aged under 1 year had the highest number of deaths per 10^5 population in 1999 (5·2 per 10^5) but this dropped by 21 % (4·1 per 10^5) in 2001 with no death from serogroup C reported (data not shown). A fall in death rate per 10^5 was first apparent in the age group 15–17 years in 2000, followed by infants under 1 year and these aged 1–4 years in 2001 (data not shown). The death rate for two age groups 5–14 years and over 18 years remained approximately 0·3 per 100000 population during the surveillance period, although the serogroup proportion changed. There were 567 deaths among confirmed MD cases during the period and approximately a quarter (161 deaths)

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Table 4. *Annual deaths and CFR by age groups in confirmed cases of MD identified by ESMD, January 1999–June 2001*

	1999		2000		2001*		Total	
Age group (years)	Death	CFR† (%)	Death	CFR† (%)	Death	CFR† (%)	Death	CFR† (%)
Under 1	34	6·7	30	5·9	13	5·4	77	6·1
1–4	36	4·5	31	3·6	17	4·5	84	4·3
5–14	18	3·8	22	5·3	13	6·2	53	4·8
15–17	25	10·0	8	5·2	4	4·6	37	7·6
18+	117	15·2	133	15·2	66	15·6	316	15·3
All age groups	230	8·2	224	8·2	113	8·4	567	8·2

* 1 January 2001 to 30 June 2001.
† CFR, deaths/cases.

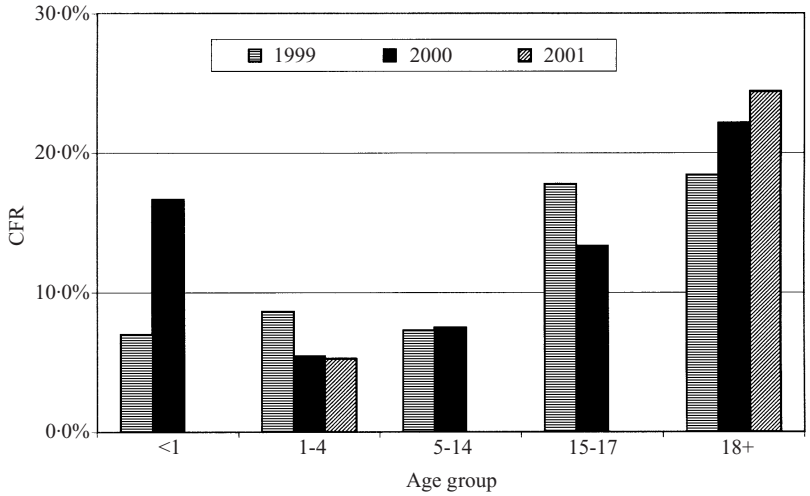

Fig. 4. Estimated annual case fatality rate of cases of serogroup C meningococcal disease reported through the enhanced surveillance of meningococcal disease by age groups, 1999 to June 2001.

were in those aged under 5 years (Table 4). The proportions of deaths documented in infants and in those aged 15–17 years declined (14·8% to 11·5% and 10·9% to 3·5%, respectively).

The CFR was higher in serogroup C (13·8%) than B (5·8%) infection [Pearson $\chi^2 = 109{\cdot}9$ (1 D.F.), $P < 0{\cdot}001$]. Overall CFR and CFR by serogroup did not vary significantly over the period, except for serogroup C where CFR rose from 12·5% in 1999 to 18·5% in 2001 [Pearson $\chi^2 = 5$ (2 D.F.), $P = 0{\cdot}082$]. CFR of MenC disease cases by age groups (Fig. 4) changed dramatically from 1999 to 2001. The two age groups initially targeted in the meningococcal serogroup C conjugate (MCC) vaccination programme showed opposite results in the first year. However, numbers were small in these two years (13 deaths in infants and 28 in the 15–17 year age group) and were followed by no deaths from serogroup C in the first half of 2001 in these two groups as well as no deaths in the 5–14 year age group. CFR of serogroup C infection in the 1–4 year age group remained at 5·3%. In those aged over 18 years it increased to 24·4% from 18·4% in 1999 (OR = 1·13, 95% CI: 0·71, 1·18, $P = 0{\cdot}6$). This latter increase accounted for the rise in overall CFR from serogroup C MD during the period. The interactions between age group, year and serogroup were not significant.

Small differences in CFR of confirmed cases were observed between the genders [male 7·6%, female 9·0%, Pearson $\chi^2 = 4{\cdot}8$ (1 D.F.), $P = 0{\cdot}028$] and between regions [Pearson $\chi^2 = 12{\cdot}19$ (9 D.F.), $P = 0{\cdot}2$, range 4·9% (Northern Ireland) 9·7% (Trent)]. Forty-five deaths were reported in MenC vaccinated individuals from 2000 to 2001 (10·1% and 36·0% vaccinated, respectively), but only one case in 2000 was a serogroup C infection. Vaccination status appeared to be under-reported in ESMD compared with surveillance of vaccine failures carried out by CDSC [15].

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Table 5. *Clusters of MD by serogroup occurring in educational institutions in England, Wales and Northern Ireland identified through the ESMD scheme, 1 January 1999–30 June 2001*

	Not Confirmed	Serogroup B	Serogroup C	Mixed serogroup	Serogroup not known*
1999	14	6	13	3	2
2000	4	7	1	0	0
2001	3	4	0	0	0
Total	21	17	14	3	2

* Known serogroup for only one case in the cluster.

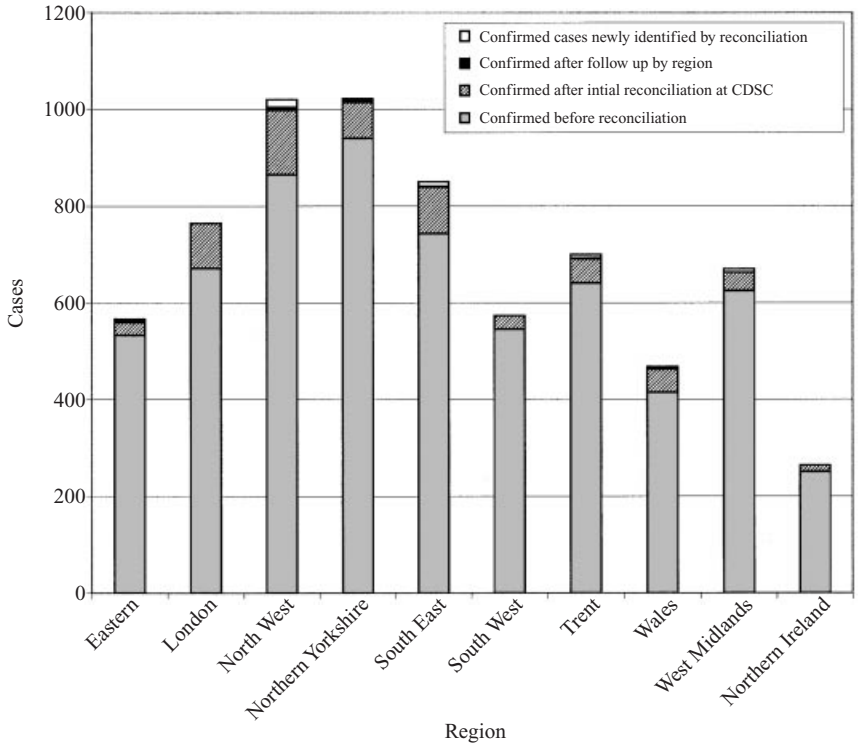

Fig. 5. Reconciliation of cases of meningococcal disease identified in the enhanced surveillance of meningococcal disease (ESMD) scheme and reported to the Meningococcal Reference Unit (MRU) by regions of England, Wales and Northern Ireland, 1999 to June 2001.

CFR of confirmed cases was highest in those diagnosed as septicaemia (11·0%, 95% CI: 10·0, 12·1), followed by cases diagnosed as both septicaemia and meningitis (7·9%, 95% CI: 6·3, 9·8), other invasive MD and the lowest was for meningitis (3·8%, 95% CI: 3·0, 4·8).

Clusters

Fifty-seven clusters occurred in educational institutions in England, Wales and Northern Ireland between 1 January 1999 and 30 June 2001; 15 occurred in pre-school groups, 32 in primary or secondary schools, 5 in sixth form or further educational colleges and 5 in universities. Most of the clusters were confirmed clusters of serogroup B, C, unknown serogroups or mixed serogroups B and C (Table 5). Overall there was no statistically significant reduction in cluster incidence stratified by serogroups during the period. However, no clusters of serogroup C were reported in the first 6 months of 2001. Annual incidence of clusters decreased from 38 in 1999, 12 in 2000 and 7 in the first half of 2001.

Reconciliation and comparison

Ascertainment of confirmed cases was improved by 9·0% on average by reconciliation of reports with

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MRU data at the CDSC, Colindale (Fig. 5). Further reconciliation by contacting original regions only raised this by 1%. As contacting regions for reconciliation introduced significant delay on analysis but added little to data completeness, this process was discontinued from mid 2001. Comparison between confirmed cases reported through the ESMD system and MRU revealed that the majority (6265 cases, 90·8%, 95% CI: 90·1, 91·5) of confirmed cases from ESMD were matched with MRU reported cases but there were 522 cases (excluding 111 cases from Northern Ireland) with no matched report from MRU.

In the same period 7099 cases (incidence rate 5·4, 95% CI: 5·3, 5·5) of MD were notified from England and Wales, approximately 60% of the cases ascertained by ESMD (58·8%, 95% CI: 57·9, 59·7). This proportion varied slightly between 57% and 62% during the surveillance period. Comparison by clinical diagnosis (septicaemia and meningitis) was difficult as notifications had to be coded either as septicaemia or meningitis and no double diagnosis was allowed.

DISCUSSION

This the first report since the ESMD was modified and extended to the whole of England as well as Wales and Northern Ireland in 1999 after the pilot in 1998 [1, 5]. During this period of surveillance, the new public health intervention of MCC vaccination was introduced in the United Kingdom, the first country to include these vaccines in the national immunization programme [17]. ESMD is providing important information on the impact of the programme.

The routine MCC vaccination programme, complemented by vaccination of first-year students in higher education, has brought about a dramatic reduction in serogroup C meningococcal infection (Table 2). However, the vaccination programme has not yet successfully delivered herd immunity in the population aged over 20 years (Fig. 2). Because supplies of the vaccine were initially limited, these were made available to high risk age groups first – those aged under 1 year and those aged 15–17 years. Different reductions in rate are seen in each target vaccination age group supporting the fact that the decrease of cases in 2001 was due to the direct protective effect of vaccination. Those over 20 years are not included in the current vaccination programme and have not yet shown a significant reduction in incidence. However, the majority of the cases that occurred in this group during the surveillance period were serogroup B, against which MCC vaccine is ineffective. MenC infection in older age groups is known to have a poor prognosis. Although there was no statistical significance in changes of CFR during the surveillance period among those aged over 18 years, the steady increase of CFR may require close monitoring for a longer period in view of the extension of the vaccination programme from January 2002 to those aged up to 24 years [23]. Studies from expert centres have indicated that CFRs in children have fallen with improved intensive management of critically ill cases [24, 25]. In our report, the rise in CFR in 2001 for serogroup C reflected elevation of the median age of cases. The probable cases had a lower CFR than those confirmed. This may be a true effect because cases with milder disease may be less likely to have complete microbiological investigations. Alternatively, some of these cases may not be true MD and may be caused by less virulent infections such as enteroviruses; if so, estimates of CFR would be expected to be lower [5].

The reduction in incidence that occurred was in serogroup C cases and not in B which increased over the period. The winter (Dec–Jan) peak of serogroup C infection disappeared from winter 2000/2001 (Fig. 1). The impact of vaccination might have been even greater than that estimated from historical data if serogroup C cases had continued to rise in parallel with the rising incidence observed for serogroup B [10]. An increase of serogroup W135 linked to outbreaks among pilgrims to Saudi Arabia continued in 2001 [26]. Quadrivalent vaccine which includes this strain (ACWYVax™) is now recommended by the Department of Health and is a visa requirement for those travelling to Saudi Arabia for pilgrimage. ESMD will facilitate monitoring the progress of this outbreak.

More cases are now ascertained through ESMD than were detected by routine surveillance or by previous regional enhanced surveillance [2–3, 5, 17]. This illustrates that ESMD has successfully achieved the higher sensitivity in identifying MD cases and deaths than any other routine system (Fig. 4). Over-reporting, under-reporting and mis-reporting caused by a number of factors (influence of awareness of MD, trends in reporting practice among clinicians and similar clinical presentation in cases of viral meningitis etc.) have to be taken into account in interpreting these data for practical use, although these potential errors have been minimized by the reconciliation process.

The total number of MD cases reported has not changed in the first 2 years despite the vaccination programme. Increased reporting in five regions in the

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pilot study may be attributable to early implementation and increased awareness of the surveillance system [5]. For example, incidence rates increased from 7·6 in 1998 [5] to 10·2 per 10^5 population in 1999 in the North West region and 8·2 to 10·0 in the Trent region, respectively. Similar increases were observed between 1999 and 2000 in some regions. None of these regions had major outbreaks during this period. The increased case ascertainment during implementation may have masked a reduction of cases achieved by the vaccination programme.

A single peak appeared between weeks 27 and 30 in the year 2000 that mirrored a surge in probable cases. This may have been caused by misdiagnosis of viral meningitis (e.g. echovirus type 13) which has a summer seasonal peak in England and Wales [27]. Because probable cases of ESMD are based on clinical diagnoses, an increase in other causative agents of septicaemia and meningitis may create a false apparent increase in invasive MD cases. The pilot study found that 16% of cases reported by ESMD as suspected MD had later received an alternative diagnosis [5]. Validation through laboratory confirmation is important to avoid false alerts and data could be improved if more virological investigations were carried out.

The reduction observed in septicaemia is thought to be the result of the vaccination programme. Although improved notification practice mainly increased the number of septicaemia reports [5], reduction of MenC cases due to the MCC vaccination programme had a far greater impact because 63% of those cases had been diagnosed as septicaemia. As a result, the proportion of serogroup C among septicaemia cases reduced by 12% in 2001 and instead serogroup B accounted for 47·5% of this severe form of MD (data not shown).

In ESMD, an excess of cases in males was observed in most of the age groups. This confirms an observation that MD is more likely to be contracted by males [28].

A large difference exists amongst the number of reports and the incidence in each region. The proportion of confirmed cases also differs from region to region. A higher confirmation rate was more frequently observed in regions that reported lower numbers of cases, implying that regions where the surveillance system has higher specificity may have less sensitive surveillance. A greater proportion of cases was unconfirmed during the winter season. This suggests the attribution of final diagnosis is affected by the prevalence of disease, differences in reporting practices, and the accessibility and/or level of liaison between CsCDC and local laboratories.

The number of clusters during the period 1999 to June 2001 is similar to that documented in the previous study from 1993 to March 1995 [29], with 57 and 45 clusters ascertained in these respective time periods. Clusters of cases identified as serogroup C infection started to decline from 2000 and none was reported in 2001 up to the end of June. The period covered by this report was still too short to identify a statistically significant decrease in clusters.

Thirteen MenC cases were detected by ESMD among the MCC vaccinated population from January 1999 to June 2001. Miller and others have reported 14 vaccine failures up to April 2001 in their previous report on the MCC immunization campaign based on detailed follow-up of cases [17, 30]. Other missing data such as date of admission, age and other relevant information were found in approximately 1% of cases each year. Further effort has to be made to encourage reporting complete information including the vaccination status of each case.

ESMD is meeting its aims and providing information about the epidemiology of MD that is more complete than NOIDS and laboratory surveillance. ESMD also successfully identified the great impact of the MCC vaccination programme in reducing both incidence and mortality of MenC disease. Regional units of CDSC are now using the information to help evaluate the impact of the MCC vaccination programme locally and for surveillance of non-vaccine preventable serogroups.

We believe these results provide information to support the vaccination programmes of other countries such as Spain and Republic of Ireland (www.meningitis.ie), which started national vaccination programmes in 2000. This report may encourage other countries that have licensed MCC (e.g. Canada, Germany) and are considering or currently implementing a national vaccination programmes and those with a high incidence of MenC infection (e.g. The Netherlands, Greece, Belgium) to investigate the possibility of early implementation [31, 32].

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