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Invasive meningococcal disease among university undergraduates: association with universities providing relatively large amounts of catered hall accommodation

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SUMMARY

The incidence of invasive meningococcal disease (IMD) among UK university students and non-students of similar age was investigated. In addition, we sought to identify structural risk factors associated with high rates of IMD in individual universities. Cases were ascertained via Consultants in Communicable Disease Control (or equivalent officers) between September 1994 and March 1997. Data on individual universities were obtained from university accommodation officers.

University students had an increased annual rate of invasive meningococcal disease ($13{\cdot}2/10^5$, 95% CI 11·2–15·2) compared with non-students of similar age in the same health districts ($5{\cdot}5/10^5$, CI 4·7–6·4) and in those health districts without universities ($3{\cdot}7/10^5$, CI 2·9–4·4). This trend was highly significant. Regression analysis demonstrated catered hall accommodation to be the main structural risk factor. Higher rates of disease were observed at universities providing catered hall places for $> 10\%$ of their student population ($15{\cdot}3/10^5$, CI 11·8–18·8) compared with those providing places for $< 10\%$ of students ($5{\cdot}9/10^5$, CI 4·1–7·7). The majority of IMD amongst students was caused by serogroup B organisms.

University students in the UK are at increased risk of IMD compared with non-students of a similar age. The incidence of IMD tends to be greatest at universities with a high provision of catered hall accommodation.

INTRODUCTION

In many developed countries the incidence of invasive meningococcal disease has increased during the 1990s [1, 2]; in particular there has been an increase in serogroup C disease which has been most marked among teenagers and young adults [3]. In the UK, a number of health districts have observed higher than expected levels of invasive meningococcal disease (IMD) among university students, along with several clusters. In November 1996 a large outbreak occurred at University of Wales, Cardiff [4], with another at University of Southampton (England) in October 1997 [5].

No studies on the epidemiology of meningococcal disease among university students in non-outbreak situations have been published [6]. We therefore

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performed a survey to determine if UK university students were at increased risk of IMD compared with non-students of the same age.

METHODS

Collection of data on cases

A questionnaire was sent to each health administrative district in England, Scotland, Wales and Northern Ireland, addressed to the Consultant in Communicable Disease Control (CCDC) or equivalent officer requesting information on cases of IMD in persons aged 18–22 years (17–21 in Scotland in order to correspond with the usual age of entry to university), for the period 1 September 94 to 31 March 97, covering three IMD seasons. All non-responders received one reminder message. The questionnaire covered basic demography; local government and health administrative district; educational or occupational status; residence; diagnostic tests and clinical features. For students in higher education at the time of their illness, details on institution, academic year, and term-time residence were also requested.

Cases were classified as 'definite', 'probable' or 'possible' using national guidelines (Table 1) [7], but only definite and probable cases were included in the analysis. Where the academic year of an individual student was not stated, it was assumed that they became 19 years of age (18 in Scotland) during their first year at university. In addition, cases aged 18 years of age (17 in Scotland) who became ill before they could reasonably have attended university (i.e. prior to October) were counted as non-students. Local microbiological data were augmented by data from the national Meningococcal Reference Laboratories. Mature students were those aged 21 years, or older, when starting university. Non-mature students were those below this age when starting university.

Classification, structure and layout of universities.

Detailed information on each institution (1996/7 data) was obtained by means of a postal questionnaire and telephone follow-up of university accommodation officers. This included data on campus layout, number and capacity of catered and self-catered halls/complexes, and the number of first year undergraduates living in each unit. Institutions holding university status prior to 1992 were defined as 'old' universities. 'New' universities were defined as those institutions granted university status after 1992, and included former polytechnics and some colleges of higher education.

Table 1. *Case definitions for invasive meningococcal disease (IMD)*

Degree of certainty	Description
Definite	Clinical diagnosis of meningitis or septicaemia confirmed microbiologically as due to *Neisseria meningitidis*
Probable	Clinical diagnosis of meningitis or septicaemia without microbiological confirmation where meningococcal disease is the likeliest diagnosis
Possible	Clinical diagnosis of meningitis or septicaemia without microbiological confirmation where other diagnoses are as likely as meningococcal disease

Data analysis, calculation of rates and statistical testing

For the calculation of disease rates, denominator data on student numbers in 1995/6 (middle year of study period) were obtained from the worldwide website of the Universities and Colleges Admissions Service [8]. Mean annual rates of IMD were calculated on the basis that the study had covered three complete meningococcal seasons. The rates in universities were calculated using total student numbers, less the number of mature students in 1995/6, as the denominator.

The rates of IMD among non-students in the same district and in other non-university districts were calculated using 1996 Office for National Statistics population estimates for individual single year bands.

To estimate the number of non-students within university districts, the non-mature student numbers were subtracted from the estimated 1996 population of 18- to 22-year-olds in each district. In districts without universities the entire age-specific population was taken directly from 1996 population estimates.

Epi-Info version 6.04 and Confidence Interval Analysis [9] were used to determine relative risks and 95% confidence intervals. Multiple linear regression (SPSS for Windows version 6.1.3) was employed to assess the influence of university layouts and type of accommodation using the combined rate of 'definite' and 'probable' IMD in individual institutions as the dependent variable. Independent variables were con-

structed for both catered and self-catered halls to represent: number of halls; total number of places available (absolute and as a percentage of total student roll); number of first years in hall; mean hall size; campus configuration (single, multiple or non-campus); 'new' or 'old' university status; and percentages of first-year and postgraduate students.

RESULTS

Of 123 health districts contacted, responses were received from 103. Five of these provided insufficient data and were excluded from further analysis. In addition, all data from the eight London districts which responded were excluded because of the amount of missing information caused by the recent merging of several health authorities and large numbers of students attending university in one district, whilst residing in another and falling into a hospital catchment area covered by a third. Of the remaining 90 districts (73% of total), 43 contained one or more universities (total = 64 universities) and 47 were classified as 'non-university districts'. Of the 64 universities, 43 (66%) provided detailed information on accommodation layout.

Mean annual rates of IMD for university students and the two comparison non-student populations are shown in Table 2. The mean annual rates in individual universities ranged from 0 to $58{\cdot}6/10^5$ for all IMD, 0–$23{\cdot}2/10^{-5}$ for serogroup B disease and 0–$29{\cdot}3/10^5$ for serogroup C disease. Over the study period the rate of serogroup C disease among students increased from $1{\cdot}9/10^5$ in 1994/5 and 1995/6 to $6{\cdot}9/10^5$ in 1996/7. These differences were not statistically significant. No excess risks were detected for medical, dental or nursing students.

After adjustment for disease clusters (i.e. by counting only the first of any probably linked cases), the overall rate of definite and probable cases amongst university students was $12{\cdot}6/10^5$ (95% CI 10·7–14·6) for serogroup B cases and $2{\cdot}9/10^5$ (95% CI 2·0–3·9) for serogroup C. Amongst non-students in university districts there were 7 cases in 3 linked clusters (4 serogroup B and 3 not grouped) and in non-university districts there were 2 linked cases, both serogroup C. The differences between students and non-students remained statistically significant. The peak incidence of IMD in students occurred in November, 6 weeks earlier than the usual mid-winter peak observed nationally [3].

The results of univariate modelling are shown in

Table 2. *Numbers of cases and mean annual rates of invasive meningococcal disease among undergraduate students attending 64 UK universities, and non-students of similar age (18–22 years in England, Wales, and Northern Ireland and 17–21 years in Scotland): 1994/5 to 1996/7*

	Population at risk per year	Definite and probable cases	Serogroup B disease	Serogroup C disease	Annual rates per 100000 population: Definite and probable cases (95% CI)	Serogroup B cases (95% CI)	Serogroup C cases (95% CI)
Students (non-mature) in 64 universities (in 43 health districts)	420000	166	66	44	13·2 (11·2–15·2)	5·2 (4·0–6·5)	3·5 (2·5–4·5)
Non-students (18- to 22-year-olds*) in 43 health districts with universities	1003000	168	61	49	5·5 (4·7–6·4)	2·0 (1·5–2·5)	1·6 (1·2–2·1)
18- to 22-year-olds* in 47 health districts without universities	797000	88	30	36	3·7 (2·9–4·4)	1·3 (0·8–1·7)	1·5 (1·0–2·0)

Based on 1995/6 student population and 1996 population estimates. * 17–21 in Scotland.
Definite and probable disease in students at universities compared to non-students in the same districts: relative risk = 2·4 (95% CI 1·9–2·9), $P < 10^{-8}$.
Serogroup B in universities compared to non-students in the same districts: relative risk = 2·6 (95% CI 1·8–3·7), $P = < 10^{-8}$.
Serogroup C in universities compared to non-students in the same districts: relative risk = 2·1 (95% CI 1·4–3·2), $P = 0{\cdot}0002$.
Definite and probable disease in students at universities compared to non-university districts: relative risk = 3·6 (95% CI 2·8–4·6), $P < 10^{-8}$.
Serogroup B in universities compared to non-university districts: relative risk = 4·2 (95% CI 2·7–6·4), $P = < 10^{-8}$.
Serogroup C in universities compared to non-university districts: relative risk = 2·3 (95% CI 1·5–3·6), $P = 0{\cdot}0002$.

Table 3. *Results of univariate analyses showing structural factors significantly associated with annual rates of invasive meningococcal disease in 43 UK universities*

Factor		*B*	*P*	r^2
Number of first-year students in catered halls	0–499	—		
	⩾ 500	8·98	0·03	0·11
Number of places available in catered halls	0–499	—		
	⩾ 500	8·10	0·04	0·10
Total number of catered halls	0–2	—		
	⩾ 3	8·84	0·03	0·11
Mean catered hall size	0–199	—		
	⩾ 200	8·23	0·04	0·10
Percentage of total students in catered halls	0–9·9	—		
	⩾ 10	10·7	0·008	0·16

Table 3 (significant variables only). All five structural factors significantly associated with the rate of IMD related in some way to the provision of catered hall accommodation, with the highest rates of IMD occurring at institutions with relatively large numbers of catered hall places. Using stepwise or forwards multiple regression (based on 43 institutions) only the proportion of students accommodated in catered halls (percentage of total roll size) was significantly associated with the rate of IMD ($B = 0{\cdot}33$, $P = 0{\cdot}02$, $r^2 = 0{\cdot}16$); using backwards regression, the total number of catered hall places at each institution featured as the only significant factor ($B = 0{\cdot}006$, $P = 0{\cdot}003$, $r^2 = 0{\cdot}24$). Using a restricted model containing only those variables identified as significant during univariate analyses, the total number of catered hall places was the only significant factor ($B = 0{\cdot}004$, $P = 0{\cdot}01$, $r^2 = 0{\cdot}15$). Table 4 clarifies the significance of these results by illustrating the rates of IMD at universities according to the levels of provision of catered hall accommodation.

DISCUSSION

Our study is the first of its kind to attempt to define the rates of IMD among university students over a sustained period of time and to attempt to define structural factors that might contribute to overall risk. By calculating age-specific rates among non-students of similar age in both university and non-university districts we believe we have drawn robust comparisons which take into account any possible differences in ascertainment between university and non-university districts.

The results show increased rates of IMD for both serogroups B and C, among students attending universities compared with non-students of the same age. Given the way the data were collected, the rates of IMD among students are, if anything, underestimates because some students, particularly those living off-campus, may have been misclassified as non-students. The slightly higher rates among non-students in university districts may be explained by this misclassification bias and/or different patterns of social behaviour among young people in university towns and cities. The extensive opportunities for social mixing and the closer confines of university life share many of the features associated with the increased risk of IMD in military environments [10, 11]. The finding of an earlier peak of IMD in students suggests that these factors exert their effects early in the academic year.

The most important structural risk factor we demonstrated among individual universities was the provision of catered hall accommodation both in absolute terms and in relation to total student roll size. All five factors shown to be significantly associated with higher rates of IMD related in some way to the availability of catered hall places; these findings were confirmed by multiple linear regression. Catered halls provide significant opportunities for sustained close social mixing on a large scale. The majority of universities now offer hall places almost exclusively to first year students who need to form new social relationships after leaving home. These two factors are undoubtedly strongly inter-related.

Most cases of known serogroup in university students were caused by serogroup B strains. Since such cases are not currently vaccine-preventable this is

Table 4. *Numbers of cases and mean annual rates of invasive meningococcal disease by catered hall provision at 43 universities according to provision of catered hall accommodation: 1994/5 to 1996/7*

	Population at risk per year*	Definite and probable cases	Serogroup B disease	Serogroup C disease	Annual rate per 100000 population		
					Definite and probable cases (95% CI)	Serogroup B cases (95% CI)	Serogroup C cases (95% CI)
Students in universities ($n = 17$) with high provision of catered halls†	159000	73	29	18	15·3 11·8–18·8	6·1 3·9–8·3	3·8 2·0–5·5
Students in universities ($n = 26$) with low provision of catered halls†	238000	42	19	9	5·9 4·1–7·7	2·7 1·4–3·9	1·3 0·4–2·1

* Based on 1995/6 student population (data from UCAS).
† High provision, 10% or more of total student roll; low provision, < 10% of total student roll.
Definite and probable disease in high compared to low provision of catered accommodation: relative risk = 2·6 (95% CI 1·8–3·8), $P = 10^{-6}$.
Serogroup B disease in high compared to low provision of catered accommodation: relative risk = 2·3 (95% CI 1·3–4·1), $P = 0{\cdot}006$.
Serogroup C disease in high compared to low provision of catered accommodation: relative risk = 3·0 (95% CI 1·3–6·7), $P = 0{\cdot}008$.

important when considering any changes to current vaccination policy. Serogroup B disease is classically endemic [12], suggesting that increased rates in university students reflect a 'hyper-endemic' (rather than 'epidemic') situation which is more likely to reflect structural and environmental factors such as the ones we identified. In the late 1980s studies in Norwegian Army recruits during an epidemic of serogroup B disease showed rates of IMD four times higher than the comparable age-specific rate [11]. This increased risk is similar to the one we have demonstrated for serogroup B disease among students compared with young people in non-university districts. The predominance of serogroup B disease partially explains why adjusting for linked cases (usually serogroup C) did not alter our assessment of the increased risk of IMD posed to students.

It is possible that there may have been inter-district differences in microbiological investigation as many cases from universities will have been admitted to teaching, or other large hospitals where polymerase chain reaction (PCR) and other confirmatory tests might have been more readily available, thus increasing the likelihood of 'probable' diagnoses becoming 'definite'. This is unlikely as PCR is a national service and the inclusion of probable cases in our calculation of incidence rates will have allowed all patients with a typical clinical picture to be included and is likely to have produced greater consistency across districts. The significant difference between students and non-students within the same districts also makes differential case ascertainment a highly unlikely explanation of the results.

As the census is taken midweek, early on in the spring term nearly all students attending university at that time are likely to have been resident on that night; thus they will have been included in the census as residents at their university address and not their parents' address. Students who reside with their parents whilst at university are likely to live reasonably close to the university and hence be residents within the same health district. Most universities included in this study are centrally placed within the district. In the case of one university in this study where many students live in a neighbouring district, this district also had a university. Therefore we believe the errors introduced into the study by use of census derived population estimates are likely to have been small.

As we excluded London health districts we are unable to comment on whether the same increased risk would also apply in London. Importantly the

structures of universities in London are different from many of those included in our study. There is also unlikely to be any significant non-response bias because only 11 non-London districts did not respond, of the 90 included in the study.

The subject of meningitis among university students attracts considerable media attention; cases and their contacts are portrayed as young and successful, yet vulnerable through living away from home and being isolated from immediate family support during times of illness. Some universities have requested universal immunization of students against IMD, representing a change from current UK policy [13]. Our study is the first to quantify the rate of IMD in the UK student population and that this risk varies by institution and correlates well with the provision of catered hall places. We were unable to take this further as our data were not sufficiently detailed at all universities to calculate a rate for students in catered accommodation.

Although the rate of vaccine-preventable serogroup C disease was two to three times higher among students attending universities with high levels of catered hall provision compared with other universities and the non-student population, this was similar to the rate of serogroup C disease seen generally in 16- to 17-year-olds in England and Wales (Public Health Laboratory Service: unpublished data 1994–7). Much of the overall higher rate of IMD among students was attributable to serogroup B disease which is not currently vaccine preventable. This suggests that the impact of any national vaccination programme aimed at students, using currently available vaccines, would be limited. Notwithstanding, we acknowledge that there was considerable variation in the average annual rates of IMD observed at individual institutions which ranged from 0 to $58{\cdot}6/10^5$. In addition, rates of vaccine preventable serogroup C disease also varied markedly between institutions from 0 to $29{\cdot}3/10^5$.

During the study period, most UK universities did not have a substantial problem related to serogroup C disease and a policy of universal vaccination would have produced few benefits in the majority of universities. A few institutions have persistently raised rates of IMD among their student populations which, for the most part, are due more to hyperendemic activity than to outbreaks. In these circumstances it would be appropriate to determine the case for vaccination on the basis of local epidemiology and the existence of structural factors we have identified. Given the benefit of early antibiotic treatment for IMD [13], policies to raise awareness amongst students, especially those in halls of residence, should be emphasized in all universities at the beginning of the academic year.

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