

Geographic variation in incidence of coronary heart disease in Britain: the contribution of established risk factors

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Abstract

Objective—To determine the extent to which geographic variation in the incidence of major coronary heart disease (CHD) in Great Britain may be explained by established risk factors.

Design—Prospective study.

Setting—24 British towns with widely differing CHD mortality.

Subjects—7735 men followed up from screening in 1978–80 for 15 years.

Main outcome measures—Percentage of variance between the towns in major CHD incidence that can be explained by individual characteristics of men in the towns.

Results—Age standardised incidence rates over a 15 year period varied from 0.52% per annum in Maidstone to 1.07% per annum in Dewsbury and tended to follow the known pattern of higher rates in Scottish and northern English towns and lower rates in southern English towns (“north-south gradient”). Higher town incidence rates were related to prevalence of current cigarette smoking, low physical activity, and low alcohol consumption, and to mean body mass index, mean systolic blood pressure, low mean height, and prevalence of manual social class, but not to mean serum total cholesterol. The 95% range for true age adjusted CHD incidence (over 15 years) was estimated as 0.58–1.03% per annum among British towns. After adjustment for baseline smoking status, physical activity, body mass index, alcohol consumption, systolic blood pressure, serum total cholesterol, occupational social class, and height, this variation was reduced by 50%. A model based on these eight variables accounted for the major part of the north-south gradient.

Conclusions—Much of the variation in CHD incidence among British towns was accounted for by established risk variables. The remaining unexplained variation may be related to measurement error in the established risk variables, to environmental factors such as climate, or to the combined effect of a wide range of minor risk factors.

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Keywords: geographic variation; established risk factors; coronary heart disease; multilevel modelling

Geographic variations in death rates from coronary heart disease (CHD) have been observed in Britain for many years¹; mortality has been observed to be lower in the south of England and higher in the north of England and Scotland. Possible explanations in earlier reports included climatic factors such as rainfall and temperature,^{2,3} and water hardness.⁴ More recent studies have implicated social deprivation^{5,6} while others have attributed variations to risk factor levels.^{7,8}

The first phase of the BRHS (British regional heart study) examined standardised mortality ratios for CHD in 253 British towns and found relations with water hardness, annual rainfall, average maximum temperature, percentage of manual workers, and average car ownership.⁹ All these studies, however, have investigated relations between area based measures of risk and CHD mortality rates. Such ecological studies are inclined to overestimate the relation between suspected risk variables and mortality. They rarely include information on important confounding measures such as cigarette smoking or physical activity. Measurements at an individual level are required to explain adequately the geographic variations observed.

The second phase of the BRHS offers an unusual opportunity to examine the variation among 24 British towns in the incidence of

CHD over 15 years of follow up. Availability of data on individual subjects within the towns allows estimation of the extent to which the variation may be explained by differing risk profiles within the towns.

Methods

The design of the BRHS has been described in detail.¹⁰ The first phase consisted of aggregated data on 253 towns whose population at the 1971 census varied between 50 000 and 100 000. In the second phase of the BRHS, 24 of the 253 towns were selected to represent the range of CHD mortality rates. A random sample of about 400 men aged 40–59 years, drawn from a single general practice in each town, were invited for screening. The general practice was chosen to be representative of the town's socioeconomic composition. A 78% response rate was obtained and 7735 men were screened between 1978 and 1980.

PHYSICAL MEASUREMENTS

Three trained observers visited all towns in succession. Towns in close proximity were visited at different times of year. The London School of Hygiene and Tropical Medicine sphygmomanometer was used to measure blood pressure twice in succession, with the subject seated and the arm supported on a cushion. The mean of the two readings was

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used in analysis. All blood pressure readings were adjusted for observer variation within each town.¹¹ Height without shoes and weight in trousers and socks were measured to the nearest millimetre and 0.1 kg, respectively. Body mass index was calculated in kg/m². Serum total cholesterol was measured by a modified Liebermann-Burchard method on a Technicon SMA 12/60 analyser in the Wolfson Research Laboratories, Birmingham.¹²

QUESTIONNAIRE DATA

The research nurses administered a standard questionnaire that included questions on smoking habits, alcohol intake, physical activity, and social class based on the longest held occupation. Smoking was defined as one of five categories: never smokers, former smokers, and smokers of 1–19, 20, or 21+ cigarettes a day. Alcohol consumption was classified on the basis of weekly intake¹³; three categories only were used for this paper: none/occasional (less than one drink a week), light/moderate (1–42 drinks a week), and heavy (more than 42 drinks a week). For physical activity, an established six category classification was used¹⁴ but was reduced to four categories for this analysis: none, occasional, light, moderate, or more (“active”). Social class (longest held occupation) involved seven categories: I, II, III non-manual, III manual, IV, V, and Armed Forces.

FIFTH YEAR QUESTIONNAIRE

A self administered postal questionnaire sent five years after initial assessment (1983–5) provided further information on current smoking status, car ownership, and housing tenure. The response rate for this questionnaire was 98% among surviving men. Car ownership and housing tenure have shown relations with mortality independent of occupational social class.¹⁵ Car ownership was classed as none, one, or two or more cars, while housing tenure was defined as owner, renting privately, renting from council, or other. Smoking status at screening and five years later allowed us to define a “change in smoking status” variable: never smokers, former smokers before screening, smokers at screening who quit during the five years following screening, and smokers who smoked both at screening and five years later.

TOWN LEVEL MEASURES

Town level measures were water hardness (measured between 1969 and 1973) together with four climatic measures (maximum temperature, minimum temperature, daily rainfall, and sunshine hours), which were averaged over the years 1978–94 (corresponding to the follow up period) from data provided by meteorological stations in or just outside the towns.⁹

FOLLOW UP

All men were followed up for major non-fatal and fatal CHD events (myocardial infarction and including sudden cardiac death).¹⁶ Deaths were flagged through the National Health Service (NHS) central registers in Southport for England and Wales and in Edinburgh for Scotland. Fatal events caused by CHD were

recorded if the *International classification of diseases*, ninth revision (ICD-9) classification was coded 410 to 414. Sudden death for which no other cause was apparent was included if certified to be the result of CHD.¹⁷ Regular reviews of general practice records were carried out biennially throughout the follow up period. Non-fatal myocardial infarctions were defined according to standard World Health Organization criteria in which at least two of the following three conditions were present: severe chest pain lasting at least half an hour, electrocardiographic evidence of a myocardial infarction, and raised cardiac enzyme concentrations.¹⁶ Follow up rates were over 99%. A cross check between medical records and the subjects’ recall of diagnoses confirmed that 97% of diagnoses were correctly identified by the medical records.¹⁸ We therefore believe that the ascertainment rate for this type of non-fatal event was very high in the study.

A record review carried out in 1996 completed at least 15 years of follow up for every subject. We have therefore been able to calculate rates of fatal or non-fatal CHD events as a percentage per annum (% pa) for all 24 towns over a 15 year follow up period.

STATISTICAL METHODS

Explanatory variables at the subject level were selected on the basis of established strong relations with CHD.¹⁹

Simple correlations of age standardised CHD incidence with mean systolic blood pressure, serum total cholesterol concentration, body mass index, height, and prevalence of any cigarette smoking, “active” physical activity, heavy drinking, and manual social class were calculated for the 24 towns. These ecological correlations provided some indication of which variables might be important in explaining town variation in CHD incidence.

MULTILEVEL MODELLING

Because a sample of 24 towns was chosen from a larger number of possible towns and because subjects were chosen from each of the towns, the data formed a multilevel structure.²⁰ Variation in observed incidence of CHD among the 24 towns is an inadequate measure of true variation among British towns because estimated incidence for a town would be influenced by sampling error. A logistic regression model for binary outcome data was used to estimate the “true” variance among the populations of possible towns on the log(odds) scale. The statistical package MLwiN was used (Institute of Education, London, UK). All models were adjusted for subjects’ age as a continuous variable. The other eight subject level variables (smoking status, physical activity, alcohol consumption, systolic blood pressure, height, body mass index, serum total cholesterol, and social class) were entered one at a time and then cumulatively according to their ability to explain between-town variance. Effects of the five town level variables (water hardness and four climatic variables) were entered before adjustment for any subject level variables and then after adjustment for all of

Table 1 Risk profile of men in the 24 towns

Town (ordered by latitude)	Number of subjects	15 year incidence of CHD (age standardised % pa)	Mean SBP	Mean serum total cholesterol (mmol/l)	Current smokers (%)	Manual social class (%)	Physically "active" (%)	Mean height (cm)	Mean BMI (kg/m ²)	Heavy drinkers (%)
Exeter	332	0.81	139	6.5	38	45	40	173.6	25.8	25
Guildford	335	0.54	136	6.3	24	23	45	175.8	24.8	25
Maidstone	318	0.52	146	6.3	43	55	34	174.2	25.5	32
Merthyr Tydfil	283	0.91	149	6.2	48	72	27	170.9	25.6	51
Gloucester	311	0.82	145	6.0	45	70	39	172.2	25.9	34
Bedford	298	0.64	148	6.1	28	46	38	174.1	25.4	25
Ipswich	362	0.81	143	6.3	32	42	47	174.5	25.5	20
Shrewsbury	311	1.05	136	6.5	34	39	45	174.0	25.3	30
Lowestoft	324	0.54	142	6.5	37	63	43	174.3	25.2	23
Mansfield	321	0.74	144	6.4	41	58	37	173.0	25.7	31
Newcastle-u-Lyme	293	1.00	149	6.3	48	68	34	173.6	25.7	50
Scunthorpe	332	0.89	140	6.0	49	77	42	172.2	25.8	35
Grimsby	318	1.04	148	6.2	60	81	28	172.8	25.6	48
Wigan	337	0.99	148	6.2	40	65	30	172.8	25.4	55
Southport	322	0.94	147	6.2	36	43	45	173.8	25.3	34
Dewsbury	325	1.07	151	6.4	50	64	29	172.7	25.5	44
Burnley	287	0.82	146	6.4	46	69	22	171.7	25.1	43
Harrogate	280	0.84	139	6.4	32	33	44	174.5	25.8	36
Darlington	382	0.60	147	6.5	34	41	42	174.1	25.3	36
Hartlepool	313	0.96	148	6.1	42	73	30	173.2	25.6	60
Carlisle	389	1.01	150	6.6	41	58	32	173.2	25.3	44
Ayr	301	0.90	143	6.3	51	63	35	171.2	25.1	44
Falkirk	309	1.02	148	6.2	49	74	37	172.1	26.1	43
Dunfermline	352	1.02	152	6.3	46	61	43	172.8	25.4	30
Correlation with CHD incidence			0.37	-0.07	0.56	0.45	-0.32	-0.54	0.34	0.59

% pa, percentage per annum; BMI, body mass index; CHD, coronary heart disease; SBP, systolic blood pressure.

them. The degree to which the estimated variance decreased after entering explanatory variables indicated how well the model explained between-town variance.

A further analysis was carried out for men who responded to the fifth year questionnaire; this allowed inclusion of the redefined smoking status variable, as well as car ownership and housing tenure. Incidence rates after the fifth year questionnaire were analysed.

For each model fitted, the square root of the estimated between-town variance was taken, then multiplied by 1.96, then added and subtracted from the estimated log(odds) of CHD adjusted to age 50. Taking the inverse of the logistic transformation allowed us to estimate a 95% range of CHD incidence in the population of such towns. The odds ratio for a town at the upper end of the range, compared with a town at the lower end, was also calculated.

For each model fitted, a set of 24 "town level" residuals was calculated, representing the difference between the observed rate of CHD for each town and the rate predicted by the model (on the log(odds) scale). Scatter plots were produced for these residuals against latitude of the town. Lack of a relation between residuals and latitude would indicate that the model had succeeded in explaining the north-south gradient in CHD incidence.

Variation among towns in risk factors was also estimated using multilevel modelling. For continuous variables (systolic blood pressure, serum total cholesterol, body mass index, and height), the intratown correlation was calculated. This was the between town variance divided by the sum of the between town and within town variance. For categorical variables, between town variance was calculated for the percentage of current smokers, the percentage of drinkers, the percentage of physically active men, and the percentage of men of manual social class. This analysis was carried out in the same way as for the incidence of CHD.

Results

Over 15 years of follow up, major CHD events occurred in 984 of 7731 men (12.7%) with follow up data, equivalent to 0.85 first events per cent per annum (% pa). Of the 984 events, 406 (41%) were fatal within 28 days.

Table 1 shows the age standardised 15 year incidences of major CHD in the 24 towns, ordered by latitude. These varied from 0.52% pa in Maidstone to 1.07% pa in Dewsbury. Table 1 also shows risk factor distributions for each town. Strong correlations were observed between CHD incidence and the prevalence of current smoking and heavy alcohol consumption (positively), and mean height (negatively). Moderate correlations existed with mean systolic blood pressure, mean body mass index, and prevalence of manual social class (positively), and with prevalence of "active" physical activity (negatively). There was a slight negative correlation with mean serum total cholesterol.

Relations between town level variables and age standardised CHD incidence were also examined. The strongest correlation was found with average maximum temperature ($r = -0.51$). There was a modest negative correlation with water hardness ($r = -0.34$).

CHD incidence was modelled for 7543 subjects with complete data for the variables listed in table 1. The first model included age only, and average CHD incidence standardised to age 50 was estimated as 0.78% pa. The between town variance of log(odds of CHD) was 0.0284 (table 2); back transformation of this quantity gave a 95% range for between town incidence of 0.58–1.03% pa. The odds ratio for the opposite ends of this range was 1.94, suggesting that a typical town of high incidence would have almost double the odds of CHD compared with a typical town of low incidence.

Further models were adjusted for other variables (table 2). The variable that most

Table 2 The variance of the log(odds of CHD) between towns after adjustments for individual level variables (n = 7543)

Model	Analysis A*			Analysis B*		
	Town variance	% of town variance explained	Odds ratio for high incidence to low incidence town	Town variance	% of town variance explained	Odds ratio for high incidence to low incidence town
None	0.0284	0	1.94	0.0284	0	1.94
Smoking	0.0155	45	1.63	0.0155	45	1.63
Social class	0.0202	29	1.75	0.0128	55	1.56
SBP	0.0206	27	1.76	0.0087	69	1.44
Physical activity	0.0208	27	1.76	0.0076	73	1.41
Height	0.0222	22	1.79	0.0064	77	1.37
BMI	0.0266	6	1.89	0.0061	79	1.36
Alcohol	0.0267	6	1.90	0.0095	67	1.47
Cholesterol	0.0375	-32	2.14	0.0141	50	1.59

*In analysis A, each variable is adjusted for age alone. Variables are listed in order of their ability to explain town variance. In analysis B, each variable is adjusted successively for all variables above it in the table. The percentage of town variance explained is the percentage reduction in the variance for a particular model to that given for a model only including age.

explained the between town variance was smoking (45%), followed by social class, systolic blood pressure, physical activity, and height (20–30% each). Body mass index and alcohol intake explained very little and serum total cholesterol increased the variance. A model that included all eight physiological, behavioural, and social status variables gave an estimated between town variance of 0.0141, a 50% reduction from the model that adjusted only for age. A model that included smoking, physical activity, systolic blood pressure, social class, and height reduced between town variance to 0.0064, a 77% reduction from the model that adjusted only for age. From the model with all eight variables, an adjusted 95% range of town incidences was estimated as 0.63–0.95% pa, equivalent to an odds ratio of 1.59.

Analysis was repeated on 10 year CHD incidence after the fifth year questionnaire for 7271 subjects who responded. Compared with a model that adjusted for age alone, the estimated variance between towns was reduced by 60% when the redefined smoking variable was included. The reductions in variance associated with housing status, car ownership, and occupational social class were 65%, 33%, and 47%, respectively. Including all three social status measures together reduced the variance by 90%.

Fifteen year CHD incidence was also analysed after omission of 292 men who had reported recalling a doctor's diagnosis of "heart attack", "coronary thrombosis", or "myocardial infarction" before the initial assessment. After adjustment for age alone, the between town variance was 0.0226. After adjustment for age and the eight risk variables

listed in table 2, the between town variance was 0.0067, a 70% reduction.

Table 3 shows the effect of town level variables. When each of these variables was included in turn to a model that adjusted only for age, reductions in town variance were particularly pronounced for average maximum temperature (59%) and average daily sunshine (45%). However, when each was added to the model that included the eight behavioural, physiological, and social class variables, the percentage reductions in variance were much less impressive (30% and 21% for average maximum temperature and average daily sunshine, respectively). Moreover, confidence intervals for odds ratios of effects of these town level variables included 1.0, and evidence for their association with CHD after adjustment for subject based variables was therefore weak.

Residual plots of the difference between observed and expected town CHD incidences against the latitude of the town showed that the north-south gradient was pronounced in a model that allowed only for age. However, the gradient became much shallower in a model that allowed for the eight individual level variables (fig 1). The gradient disappeared when average maximum temperature was included in addition to the individual level variables.

Table 4 shows the components of variance (between and within towns) for the eight risk variables. Systolic blood pressure showed the highest intratown correlation of 0.042, while the lowest intratown correlation was obtained for body mass index. Serum total cholesterol also showed a small intraclass correlation (0.019, or 1.9%), indicating that only 1.9% of the variance in cholesterol was explained by the similarities of men within towns. For the

Table 3 The effects of town level variables before and after adjustment for individual level variables

Town level variable	Analysis A*			Analysis B*		
	Town variance, after fitting each variable on its own (plus age)	% of town variance explained, after age adjustment	Odds ratio for effect of town level variable, per SD increase (95% CI)	Town variance, after fitting each variable plus all subject level variables	% of town variance explained, after adjustment for all subject level variables	Odds ratio for effect of town level variable (95% CI)
Water hardness	0.0200	30	0.91 (0.83 to 1.00)	0.0128	9	0.96 (0.88 to 1.05)
Average maximum temperature	0.0116	59	0.88 (0.81 to 0.95)	0.0098	30	0.93 (0.86 to 1.02)
Average minimum temperature	0.0243	14	0.94 (0.85 to 1.03)	0.0114	19	0.95 (0.87 to 1.03)
Average daily sunshine	0.0157	45	0.89 (0.82 to 0.98)	0.0112	21	0.95 (0.87 to 1.03)
Annual rainfall	0.0192	32	1.10 (1.01 to 1.21)	0.0125	11	1.04 (0.96 to 1.14)

*In analysis A, each variable is adjusted for age alone. In analysis B, each variable is adjusted for all eight subject level variables: age, smoking, physical activity, BMI, alcohol intake, systolic blood pressure, cholesterol, social class, and height. The percentage of town variance explained is the percentage reduction in the variance for a model that includes the particular town level variable from that given for a model not including that town level variable.

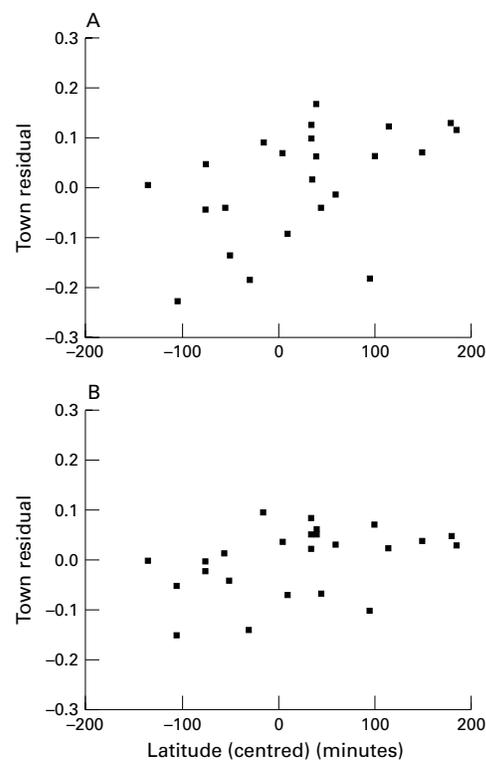


Figure 1 Scatter plot of residuals on log (odds) scale when model is fitted against latitude of town (units are minutes, compared with average latitude of 24 towns). Each point represents a town. Residuals are the difference between CHD incidence observed and that expected based on the model. Negative residuals imply that a town's CHD incidence was lower than expected. (A) Only age is fitted in the model. (B) Age, smoking, physical activity, body mass index, alcohol intake, systolic blood pressure, cholesterol, social class, and height are fitted

categorical variables, the proportion of men of manual social class varied most between towns, while the proportions of current smokers, heavy drinkers, and physically inactive men varied somewhat less.

Discussion

MAIN FINDINGS

True between town variance was estimated in this national prospective study. The odds of a major CHD event for towns at either end of a 95% range of incidence was 1.94. Up to three quarters of the town variance could be attributed to the combined effects of smoking, physical activity, systolic blood pressure, occupational social class, and height. Smoking status was the single most important factor for

Table 4 Between town and within town components of variance for the individual risk variables

Risk variable	Between town variance	Within town variance	Intra-town correlation
Continuous variables			
Systolic blood pressure	17.7	403.4	0.042
Serum total cholesterol	0.0203	1.07	0.019
Body mass index	0.0473	10.32	0.005
Height	1.06	42.1	0.025
Categorical variables			
Current smoking*	0.109	1.0	
Heavy drinking	0.204	1.0	
Physical inactivity	0.108	1.0	
Manual social class	0.412	1.0	

*Within town variance is set at 1 for categorical binary variables.

explaining town variance, and this effect has been shown elsewhere.⁸ The individual variables were able to account for most of the north-south gradient and left town level variables with a marginal role.

To explain town variance, a risk variable had to hold a strong relation to incidence of CHD at an individual level and to be more prevalent in towns with high incidence. Despite the extremely strong positive relation between serum total cholesterol and CHD at an individual level, mean serum total cholesterol concentration was slightly lower in towns with a higher incidence of CHD. However, mean total cholesterol was uniformly high in all towns (range 6.0–6.6 mmol/l, intratown correlation of only 0.019), thus conferring high susceptibility to atherosclerosis and other CHD risk factors.¹⁹ The variation in CHD incidence was therefore explained by those risk factors that differed between towns.

STRENGTHS AND WEAKNESSES OF THE STUDY

The BRHS provides data from towns in all major British regions. Despite it excluding major conurbations, the pattern of CHD incidence followed the well established north-south gradient. It was possible to investigate variations in CHD incidence among the towns by taking into account data at the individual level, rather than at the level of the town. Multilevel modelling allowed simultaneous examination of individual level and town level covariates and permitted estimation of between town variance, both before and after adjustment for these covariates.

As only 24 towns were included in the study, the analysis relating the between town variance to town level variables such as water hardness lacked statistical power. However, the association with average maximum temperature and lack of association with water hardness are similar to findings of phase 1 of the study.⁹

The analysis of variation among towns considers only the residence of the men at the start of the study. It might be expected that inclusion of subsequent migrants would have diluted the between town variance. However, exclusion of men who migrated from the town within five years scarcely altered the estimates of variance (results not shown).

Imprecise measurement of individual covariates would almost certainly have resulted in a failure to account for some of the between town variance. Systolic blood pressure alone explained 26% of the variance, and this figure might have been higher had a true average blood pressure for each man over the follow up period been obtainable. Conversely a true serum total cholesterol reading would have inflated the between town variance, given the negative between town correlation of serum total cholesterol and CHD incidence in this study. Smoking was the individual variable that most effectively reduced between town variance. Smoking history based on questionnaire reports both at screening and after five years appeared to explain an even greater percentage of the town variance than the history taken only at screening.

Although this study concerns incidence of CHD, it was considered appropriate in our primary analysis to include men who reported recalling a doctor diagnosis of myocardial infarction before the initial assessment. To have excluded such men would have under represented the true variation in CHD across Britain. When an analysis that omitted these men was carried out, the between town variance predictably decreased to a small extent, but the extent of the remaining variance that was explained by the eight risk variables was 70%, even greater than before.

Strenuous efforts were made to ensure that the general practice selected in each town was representative of that town.¹⁰ However, it is possible that by chance the practices were not always representative, and small amounts of sampling error may have been introduced. The between town variance from this study would thus have been overestimated. However, assuming the sampling error was random and uncorrelated with characteristics of the towns, the absolute amount of overestimation would apply equally to between town variance calculated before and after adjustments for subject level variables. If anything, therefore, the percentage of between town variance explained by subject level variables would have been underestimated and our conclusions would be conservative.

SOCIAL DEPRIVATION

The classification of the men's longest held occupation, which explained only a little of the town variance after adjustment for the physical and behavioural variables, may have been incapable of capturing the deprivation experienced by men in the varying town environments.²¹ Measures of car ownership and housing status were applied to men who survived and responded to the fifth year questionnaire. In this analysis, housing status explained more town variance than either longest held occupation or car ownership. Measures of deprivation of areas where men lived, linked with census data associated with their postcodes, may also be worthy of future investigation.

It is of additional interest that height explained some of the geographic variation, even after adjustment for the other seven subject level variables. A strong relation between height and CHD was shown in this cohort of men²² and geographic variation in height may indicate differences in risk factors acting in early childhood.²³

ECOLOGICAL VERSUS INDIVIDUAL DATA

A lack of difference in mean serum cholesterol among 22 local government districts was found in the Scottish heart health study, in which mean serum cholesterol was as high as in our own study, averaging 6.4 mmol/l for men whose age range was also 40–59 years.²⁴ This was despite the wide range in standardised mortality ratios among the districts (61–136). Variation in CHD incidence has been studied for whole countries in the seven countries study and in the MONICA (monitoring trends and determinants in cardiovascular disease) project. Each of these studies reported some

paradoxical findings from ecological data. The former noted an inverse ecological relation between mean systolic blood pressure and stroke death rates in 25 years of follow up among 16 cohorts of subjects, while there was a strong positive relation within 14 of the 16 cohorts.²⁵ The latter noted that ecological relations of national death rates from ischaemic heart disease with smoking prevalence and mean cholesterol were rather weak.²⁶ The multilevel modelling analysis reported in this paper allows us to quantify the percentage of variance explained in disease rates by adjusting for relations observed at the individual level.

IMPLICATIONS OF FINDINGS

A considerable proportion of the between town variance in CHD, and in particular the north-south nature of this variation, was explained by individual risk factors. Our analysis of incidence subsequent to the fifth year questionnaire suggests that the estimate of 50% of variance explained may be conservative. Other measures of social deprivation and a measure of smoking status that separated recent quitters from those who quit a long time ago and those who continued to smoke would have explained a greater proportion of variance. Remaining variation may be explained either by measurement error of other known risk factors or by measures of social deprivation that operate at an area level rather than an individual level. There was weak evidence that the remaining north-south gradient was associated (negatively) with average maximum temperature. However, this variable might be acting as a surrogate for other measures related either to climate or to social environment. In addition a wide range of other risk factors have been identified in recent years,¹⁹ and the aggregated effect of these may well explain further between town variance.

If behavioural risk factors such as smoking and physical activity explain much of the geographic variation in CHD incidence, attention should shift to reasons why men in certain regions continue to adopt and maintain less healthy behaviour patterns in terms of smoking and exercise. Less healthy patterns are probably related to socioeconomic and cultural characteristics of towns. Research is needed to explore whether treatment patterns for those at high risk of CHD vary geographically; if so, interventions to redress this should be implemented.

CONCLUSION

Much of the variation in CHD incidence among British towns was accounted for by variables known to be related to individual risk. The variation remaining to be explained may be related simply to measurement error in the known risk variables, to environmental factors such as climate, or to the aggregated effects of a wide range of other less critical risk factors.

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Electronic pages

eHEART: www.heartjnl.com

The following electronic only articles are published in conjunction with this issue of *Heart* (see also p 261).

Left internal mammary graft stenosis and restenosis following angioplasty and stenting

C G C Spencer, G Y H Lip

Coronary bypass grafts using the internal mammary artery usually have an excellent record of success and long term patency. We report a 42 year old man who initially presented with a history of atypical left sided chest pain, who had coronary artery bypass surgery for a severe stenosis in his proximal left anterior descending coronary artery (LAD) and moderate stenosis of his proximal circumflex artery, with his LIMA being grafted to his mid-LAD and a saphenous venous graft to the proximal LAD. He subsequently developed multiple stenoses in the LIMA graft which required coronary angioplasty and stenting, on more than one occasion, in view of rapid restenosis within the LIMA graft.

(*Heart* 2001;**86**:e9) www.heartjnl.com/cgi/content/full/86/3/e9

Long term inhalation of iloprost in a child with primary pulmonary hypertension: an alternative to continuous infusion

M Beghetti, M Berner, P C Rimensberger

Primary pulmonary hypertension is a rare disease in childhood associated with a poor prognosis. However, during the past 10 years, pulmonary vasodilator treatment has somewhat improved its prognosis. Long term continuous infusion of prostacyclin (epoprostenol) has been shown to improve physical capacity and to reduce mortality in primary and secondary pulmonary hypertension. It has been reported in adults that daily repetitive inhalation of iloprost, a prostacyclin analogue, seems also suitable for long term therapy of pulmonary hypertension. Repetitive inhalation of iloprost was administered to a 5 year old boy with severe primary pulmonary hypertension. He showed continuous clinical improvement without any side effects over the three years of treatment. This treatment may offer an alternative to continuous intravenous prostacyclin infusion and obviates the need for a permanent central venous catheter.

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