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Decline in ischaemic heart disease in Iceland and change in risk factor levels

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Abstract

Objective—To monitor trends in mortality and morbidity due to ischaemic heart disease and compare these with observed levels of risk factors from population surveys.

Design—Analysis of trends in death rates from ischaemic heart disease in Iceland compared with expected rates computed from population surveys. Risk factor levels together with β factors obtained from Cox's regression analysis were used to compute expected death rates. Trends in morbidity due to acute myocardial infarction were assessed and secular trends in dietary consumption compared with trends in cholesterol concentrations.

Setting—Reykjavik, Iceland (total population 250 000; over half the population live in Reykjavik).

Subjects—12 814 randomly selected residents in the Reykjavik area aged 45-64 (6623 men, 6191 women; 72% and 80% of those invited).

Main outcome measures—Age adjusted rates of myocardial infarction and deaths from ischaemic heart disease. Expected risk from risk factor levels (smoking, total serum cholesterol concentration, systolic blood pressure) at each unique survey visit.

Results—Mortality from ischaemic heart disease has decreased by 17-18% since 1970. During 1981-6 the myocardial infarction attack rate in men under 75 decreased by 23%. A decrease occurred in the level of all three major risk factors after 1968. The fall in the serum cholesterol concentration coincided with a reduction in consumption of dairy fat and margarine. The calculated reduction in risk for the age group 45-64 was about 35%, which was closely similar to the observed decrease in mortality due to ischaemic heart disease in that age group.

Conclusion—The reduction in mortality from ischaemic heart disease was substantially due to a decreased incidence of myocardial infarction and could be attributed largely to the reduction in risk factors.

Introduction

The mortality from ischaemic heart disease has been declining in some countries and holding steady in others, but in a few countries it continues to rise.¹ Time trends or secular trends in ischaemic heart disease

mortality have been difficult to analyse because they are usually based on mortality statistics with little or no information about the individual changes in the pattern of risk factors.

Mortality from ischaemic heart disease in Iceland is similar to that in other Scandinavian countries.¹ We have analysed the trends in mortality and morbidity due to ischaemic heart disease in Iceland in relation to changes in (a) the three major risk factors for the disease as documented in population surveys from 1968 to 1988—namely, smoking, total serum cholesterol concentration, and systolic blood pressure—and (b) the consumption of saturated fats.

Subjects and methods

ASCERTAINMENT OF MORTALITY FIGURES

Information was obtained from all death certificates from 1951 to 1988 on file in the Statistical Bureau of Iceland by using the following codes of the International Classification of Diseases: 1951-60, ICD (sixth revision) code 420; 1961-70, ICD (seventh revision) code 420; 1971-80, ICD (eighth revision) codes 410-413; 1981-8, ICD (ninth revision) codes 410-414. These codes have been suggested to be the most equivalent for ischaemic heart disease in the different editions.² All death certificates were reviewed and coded by an official pathologist. Necropsy had been carried out in 30-40% of cases.

REGISTER OF MYOCARDIAL INFARCTION 1981-6

During 1981-6 all episodes of acute myocardial infarction in people aged 25-74 anywhere in Iceland were registered by the Icelandic study group of the World Health Organisation's MONICA project (multinational monitoring of trends and determinants of cardiovascular disease).^{3,5} Diagnostic criteria included symptoms, electrocardiograms, enzyme activities, and necropsy findings compatible with definite or possible myocardial infarction (category I or II).^{4,5} External quality control of event registration was performed by the WHO's reference centre in Dundee. Registrations included all occurrences of acute myocardial infarction (and sudden ischaemic cardiac death), but also, as separate categories, first and recurrent infarctions (more than 28 days apart). The proportion of cases excluded because of inade-

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quate data was 2%. Only data for men were used in this analysis because of the small number of coronary episodes among women.

SECULAR TRENDS IN RISK FACTORS 1968-88

The Icelandic Heart Association Research Centre has been conducting a prospective population survey in Reykjavik since 1968 (Reykjavik study). Over half of the quarter of a million population of Iceland live in the Reykjavik area. Icelanders, however, are almost homogeneous ethnically (of Nordic origin) and have closely similar living habits (and risk factor levels; unpublished results). The standard of living in Iceland has been increasing steadily during the observation period and is comparable with that in other Scandinavian countries. This study examines the three main factors found to be associated with increased risk of ischaemic heart disease death in the Icelandic population⁶ (unpublished results)—namely, total serum cholesterol concentrations, smoking, and systolic blood pressure.

Data were obtained at baseline in stages I-IV of the Reykjavik study on a random sample of the general population in the area. The participation rate was 72% and 80% of the men and women invited. In addition, data from the MONICA risk factor surveys in Iceland during 1983 (survey I) and 1988 (survey II), also conducted by the Icelandic Heart Association Research Centre, were used (table I). Each survey sample comprised a unique group of participants. The age group 45-64 years was chosen as it was common to all these surveys. Age adjustment was performed by using the mean of the age specific values for the four five year age groups. Each of the four age groups was examined and the trends found to be similar.

Total serum cholesterol concentration was measured after overnight fasting. In stages of I-IV at the Reyk-

javik study and in MONICA I cholesterol was determined by a chemical colorimetric method (Technicon autoanalyser method N-24a).⁷ In MONICA II an automated enzymatic method was used (Roche MA 30; Cobas, Mira). In 250 serum samples subjected to both methods of measurement results showed close agreement, the mean total cholesterol concentration being 6.37 mmol/l by the chemical method and 6.33 mmol/l by the enzymatic method ($r=0.93$). Internal and external laboratory quality controls were used.

Systolic blood pressure was measured by a mercury sphygmomanometer (Erka) after five minutes' rest. Information on smoking habits and use of antihypertensive agents was obtained from a health questionnaire.⁸

The predicted risk associated with each risk factor was calculated from (a) β coefficients (see table II) derived from multivariate analysis using Cox's proportional hazard model⁹ of survival in an Icelandic prospective population survey (1968-85; comprising 15 000 men and 16 000 women, of whom 493 and 104 respectively died of ischaemic heart disease) and (b) the level of these risk factors for each person in the first examination at the Icelandic Heart Association Research Centre⁶ (unpublished results).

SECULAR TRENDS IN DIETARY FAT CONSUMPTION

A national survey showed that milk, butter, other dairy products, margarine, meat, and meat products together contribute 90% of saturated fat in the Icelandic diet.¹⁰ In this study changes in the consumption of these foods were assessed on the basis of annual sales and production records from the Agricultural Production Board (dairy and meat products)¹¹ and annual production records from the Statistical Bureau of Iceland (margarine).¹² These data reflect actual consumption as Iceland is totally self sufficient in these products and prohibits all import of meat and dairy products. Furthermore, all food exports and reserves were excluded from these data. No imports or exports of margarine occurred during the years covered by the study. Finally, dietary fat from these products was calculated by using Icelandic food composition tables.

STATISTICS

Secular trends during a defined period were determined by linear regression. Levels of significance were computed with two tailed *t* tests. In establishing

TABLE I—Numbers of men and women aged 45-64 who participated in population surveys in Iceland during 1968-88

Survey	Men		Women	
	Year of examination	No	Year of examination	No
Reykjavik study stage I	1968	1416	1969	1535
Reykjavik study stage II	1970-1	1599	1971-2	1756
Reykjavik study stage III	1974-6	1646	1976-8	739
Reykjavik study stage IV	1979-81	1089	1982-3	1228
MONICA I	1983	444	1983	468
MONICA II	1988	429	1988	465

TABLE II—Major risk factors for ischaemic heart disease deaths in Icelandic men and women aged 45-64 examined during 1968-88 (men) and 1969-88 (women)

Survey	Years of examination	Smoking				Mean systolic blood pressure (mm Hg)	% Taking antihypertensive drugs	Mean serum cholesterol (mmol/l)	Relative risk explained by risk factors* (95% confidence interval)
		% Never smokers	% Former smokers	% Smoking 1/24 cigarettes daily or cigars or pipe	% Smoking ≥ 25 cigarettes daily				
<i>Men</i>									
Reykjavik study stage I	1968	19.0	22.9	53.5	4.6	139.2	5.9	6.65	1.00
Reykjavik study stage II	1970-1	22.1	22.7	51.0	4.3	149.4	4.3	6.47	1.01 (0.94 to 1.08)
Reykjavik study stage III	1974-6	22.4	23.0	49.0	5.5	143.8	6.7	6.46	0.94 (0.88 to 1.00)
Reykjavik study stage IV	1979-81	16.4	26.6	44.0	13.0	135.3	8.5	6.17	0.80 (0.72 to 0.88)
MONICA I	1983	26.9	37.5	30.4	5.2	130.1	10.8	6.38	0.72 (0.67 to 0.79)
MONICA II	1988	34.5	32.9	25.4	7.2	131.3	12.6	6.18	0.67 (0.62 to 0.73)
Change in risk factor over 20 years†		12.0	13.7	-29.3	3.6	-15.5	7.4	-0.42	
β Coefficient from Cox's regression		0	0.34	0.79	1.07	0.012	0.64	0.366	
% Change in explained risk				-13		-17	7	-14	-34
<i>Women</i>									
Reykjavik study stage I	1969	43.4	13.0	41.5	2.0	141.9	7.9	7.16	1.00
Reykjavik study stage II	1971-2	46.9	11.9	39.7	1.5	149.6	10.3	6.94	1.09 (0.97 to 1.22)
Reykjavik study stage III	1976-8	44.1	14.9	38.2	2.7	130.1	10.1	6.61	0.72 (0.66 to 0.79)
Reykjavik study stage IV	1982-3	40.0	16.4	38.6	4.9	129.8	11.3	6.28	0.69 (0.62 to 0.77)
MONICA I	1983	46.0	21.1	31.7	1.2	129.3	18.8	6.74	0.70 (0.63 to 0.78)
MONICA II	1988	52.5	17.0	28.6	2.2	128.9	17.2	6.38	0.64 (0.56 to 0.73)
Change in risk factor over 19 years†		4.5	6.7	-11.8	0.8	-19.3	9.5	-0.75	
β Coefficient from Cox's regression		0	0.19	1.06	1.98	0.014	0.64	0.25	
% Change in explained risk				-8		-24	8	-17	-37

*Relative risk compared with group examined in 1968 (men) and 1969 (women).

†Computed by linear regression.

confidence intervals for rates and ratios between rates their logarithm was assumed to follow the normal distribution and its variance estimated as the sum of reciprocals of the underlying number of individuals.^{13 14} Variance of the estimates of risk explained by the risk factors was computed directly from the risk in the individuals in each survey. The risk in each individual was computed relative to the risk in a person having never smoked, not taking antihypertensive drugs, having a total serum concentration cholesterol of 6.5 mmol/l, and having a systolic blood pressure of 140 mm Hg.

Results

MORTALITY FIGURES

Figure 1 shows the secular trends from 1951 to 1988 of death rates in Iceland due to ischaemic heart disease age standardised to the world population.¹⁵ The maximum rate was reached after 1965 for both sexes and rates then remained steady until after 1985. A significant reduction occurred during 1986-8 compared with 1981-5—namely, a 17% reduction among men and a 12% reduction among women. The death rate during 1986-8 was similar to that in the early 1960s. In women mortality fell by 18% between 1970 and 1986-8. Analysis of age specific mortality showed that this reduction had already occurred during 1980-5 in age groups under 75 but no decrease occurred in the oldest age groups (data not shown).

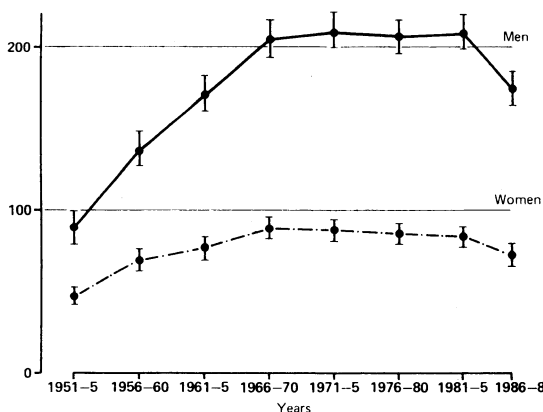


FIG 1—Ischaemic heart disease mortality in Iceland during 1951-88 standardised to world population and expressed per 100 000 population yearly. Bars are 95% confidence intervals

MYOCARDIAL INFARCTION 1981-6

Time trends in rates for myocardial infarction during 1981-6 were calculated from the regression lines shown in figure 2. The attack rate of myocardial infarction in men aged 25-74 decreased by 23% ($p=0.02$), the incidence rate of myocardial infarction by 19% ($p=0.015$), and the total death rate from ischaemic heart disease (myocardial infarction plus sudden ischaemic cardiac death) by 34% ($p=0.04$) (fig 2). The case fatality rate for men was 45% (194/432) in 1981 and 36% (125/343) in 1986, but this difference was not significant ($p=0.14$). Episodes of recurrent myocardial infarction did not decrease significantly more than the incidence of myocardial infarction (30% v 19%; $p=0.35$).

SECULAR TRENDS IN RISK FACTOR LEVELS 1968-88

Table II shows that there was a gradual improvement in all three risk factors over time for both sexes. Thus the mean serum cholesterol concentration decreased by 0.42 mmol/l (6.3%) for men and 0.75 mmol/l (10.5%) for women according to the regression line. The prediction values of the main risk factors were estimated by using Cox's proportional hazard model on survival from the Reykjavik study

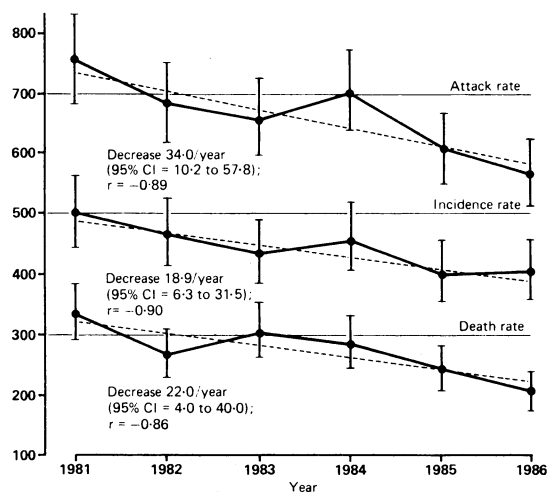


FIG 2—Myocardial infarction registration during 1981-6 among Icelandic men aged 25-74. Rates expressed per 100 000 yearly. Bars are 95% confidence intervals. Dotted lines are fitted regression lines. CI=Confidence interval

1968-85⁶ (unpublished results). According to that model the observed reduction in cholesterol concentration should reduce the risk of death from ischaemic heart disease by 14% in men and 17% in women.

Mean systolic blood pressure decreased by 15.5 and 19.3 mm Hg in men and women, respectively, the risk of death from ischaemic heart disease decreasing by 17% and 24% according to the model. The proportion of subjects taking antihypertensive medication increased considerably. This treatment, however, seems to have offset the beneficial effects of lowering high blood pressure by one third, as has been reported in other prospective studies. (This finding is largely unexplained but might be related to more severe and longstanding hypertension in the treated cases.)¹⁶

There was an overall decrease in smoking (though no fall at all in the proportion of heavy smokers), and this reduction decreased the risk of death from ischaemic heart disease by 8% in women and 13% in men.

Figure 3 shows the secular patterns in total risk attributed to the three risk factors and death rates from ischaemic heart disease observed in men and women aged 45-64. The total risk attributed to the three risk factors decreased from the beginning of the 1970s and declined by 34-37% by 1988. This decrease in total risk corresponded closely to the observed decline in the death rate from ischaemic heart disease in the groups. For women the two curves coincided, but there was a lag of several years for men.

TRENDS IN FOOD CONSUMPTION

Patterns of food consumption changed considerably in Iceland during the observation period, resulting in a significant reduction in saturated fat consumption (table III). Whole milk consumption decreased from 280 to 150 kg/person/year and butter and margarine from 21.6 to 16.8 kg/person/year. Low fat milk became available in 1982 and low fat butter and margarine also became available during the study period, accounting

TABLE III—Consumption of dairy products and margarine (kg/person/year)

	Year				
	1970	1975	1980	1985	1988
Whole milk	280.0	230.0	200.0	170.0	150.0
Low fat milk				21.0	34.0
Skimmed milk	5.0	6.0	7.0	8.0	12.0
Cream	4.5	6.0	5.8	6.3	6.7
Cheese	4.2	5.4	6.0	8.8	10.5
Butter/margarine	21.6	18.4	19.8	17.6	16.8
Total fat from these products	31.4	27.9	27.6	26.0	25.3

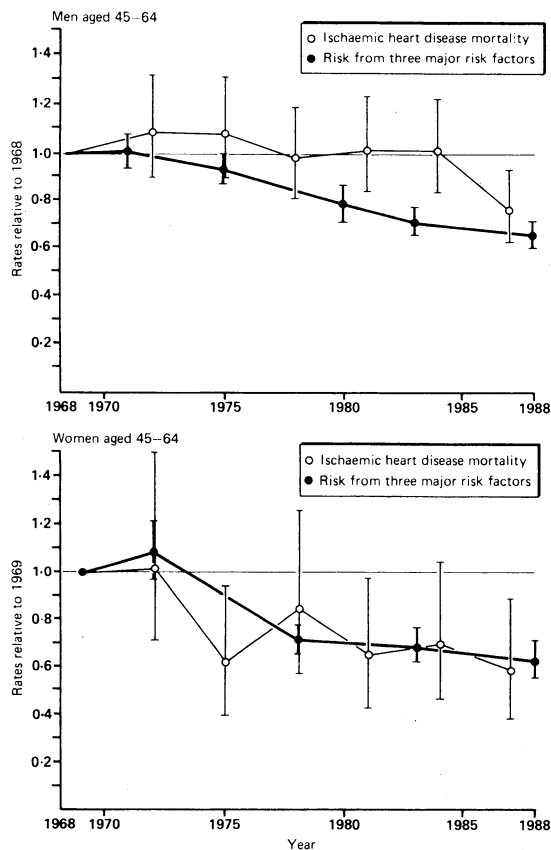


FIG 3—Observed death rates from ischaemic heart disease and calculated risks explained by major risk factors (smoking, systolic blood pressure, serum cholesterol concentration) relative to 1968 (men) and 1969 (women). Bars are 95% confidence intervals

for part of the reduction in fat from these products. Though sales of cheeses and cream increased, there was an overall reduction of 20% in dietary fat from all dairy products and margarine—that is, from a total of 86 to 69 g/person/day.

Total meat sales did not change appreciably during the period. Nevertheless, there was a trend towards purchase of leaner varieties such as chicken and lean beef and away from the traditional fatty lamb and mutton.

Reliable data on fish consumption are lacking. According to a household study from 1985, however, Icelanders purchased about 119 kg of whole fish per person yearly,¹⁷ which thereby ranked them as the largest consumers of fish in Europe. Though sales of most fatty foods declined during this period, sales of carbohydrate rich foods such as bread, fruit, and vegetables rose, and so did the sales of soft drinks and fruit juices.¹⁷ Clearly, during the period studied the overall composition of the Icelandic diet changed towards more carbohydrates and fewer saturated fats.

Discussion

Ongoing population surveys in Iceland offer an opportunity to explore time trends in risk factor levels and compare them with the mortality and morbidity due to ischaemic heart disease. Total mortality from ischaemic heart disease decreased significantly after 1985 (17% in men, 12% in women). At the same time registrations of myocardial infarction in Iceland (MONICA project 1981-6) showed a significant decline in the incidence rate, suggesting that the reduction in mortality was largely due to a reduction in incidence. The case fatality rate did not decrease significantly. This study did not include analysis of changes in management of ischaemic heart disease during 1968-88, so their effect cannot be estimated.

It is possible that changes in death rates attributed to particular causes may be an artefact of changes in classification techniques and diagnostic fashions. The most likely shift would be into other categories of cardiovascular mortality (ICD codes 390-448). That the recent trend in total cardiovascular mortality was similar to the trend in mortality from ischaemic heart disease, however, suggests that the decline was real. Furthermore, after 1966-70 the life expectancy of 40 year old men and women in Iceland increased by 1.8 and 3.0 years respectively. According to official statistics the proportionate mortality due to ischaemic heart disease decreased from 35.3% to 30.5% in men and from 22.9% to 19.5% in women.

The levels of all three risk factors studied decreased over time. The Reykjavik study showed the multiplicative effects of these factors on risk. The factors themselves were nearly uncorrelated and explained about 75% of all deaths from ischaemic heart disease (see coefficients in table II)⁶ (unpublished results). According to the Cox model a decrease of 0.4 mmol/l (6%) in the cholesterol concentration in men should decrease the risk by 14% and a reduction of 0.75 mmol/l (10.5%) in the cholesterol concentration in women should decrease the risk by 17%. Most other studies have indicated that a 1% reduction in cholesterol values decreases the risk of ischaemic heart disease by 2% in men.¹⁸

Altered food habits in Iceland coincide strongly with the observed decline in serum cholesterol concentrations. Decreased consumption of dairy fat and margarine alone would be expected to lower the serum cholesterol concentration by 0.3 mmol/l according to the equation of Keys *et al.*¹⁹ In addition, consumption of meat fat has certainly decreased as more carcass fat is discarded during production and leaner meats have become available. Exact figures regarding these changes are, however, not available. Cholesterol values would accordingly be expected to have decreased more than 0.3 mmol/l as a result of changes in diet, as indeed they had (0.42 mmol/l among men, 0.75 mmol/l among women). The more dramatic fall in cholesterol concentrations among women was unexplained, but possibly women changed their diet to a greater extent.

The fall in blood pressure came somewhat later, and the decrease in smoking was not apparent until after 1980.

The multiplicative effect of relatively moderate changes in all three risk factors adds up to a 34-37% decrease in risk in the age group 45-64 years. The calculated decline in risk by 1988 coincides with the observed fall in ischaemic heart disease death rates in the same age groups. This is consistent with the hypothesis that most of the decline in ischaemic heart disease in Iceland over the period can be explained by the changes observed in the three major risk factors.

Little is known about the lag between changes in risk factors in the population and changes in the incidence of ischaemic heart disease. In this study the changes in risk factors and ischaemic heart disease incidence were coincident in women whereas in men there was a lag of several years.

Studies from Great Britain, United States, Australia, and New Zealand have estimated that 30-75% of the observed decline in death rates from ischaemic heart disease was related to changes in lifestyle resulting in a fall in the three major risk factors.²⁰⁻²³ Most of the studies were based on mortality statistics, with little or no direct information about the individual changes in risk factor pattern, which our Icelandic surveys have offered an opportunity to observe.

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Excess mortality associated with the HIV epidemic in England and Wales

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Increased mortality unattributed to but probably associated with HIV infection has been reported in the United States.¹⁻³ Excess mortality has also been identified among HIV positive haemophiliac patients in the United Kingdom.⁴ A study of trends in mortality between 1984 and 1987 suggested that the increase found among single men was probably related to HIV infection.⁵ In this paper I examine the number of excess deaths in England and Wales in 1988 and 1989 and relate this to the HIV epidemic.

Patients, methods, and results

Draft death entries on which one of 95 selected conditions was stated to be the cause of death were identified at the Office of Population Censuses and Surveys (OPCS). These causes were selected because they had been mentioned on death certificates of people known to have had AIDS. They included 86 medical causes, including AIDS and HIV infection (International Classification of Diseases (ICD) code 279.1). Nine external causes were also included, covering drug dependence and poisoning due to various substances. The number of excess deaths was estimated by subtracting the number of deaths in 1984 from the number in each subsequent year after adjusting for population changes within each five year age group. The numbers of reports of people who died with AIDS and HIV positive people who died without developing an AIDS indicator disease were obtained from the Public Health Laboratory Service Communicable Disease Surveillance Centre (CDSC).

There were 2505 deaths due to one of the 95 causes among single men aged 15-54 in 1989—498 (25%) above the number expected based on rates in 1984. AIDS or HIV infection was stated as the cause of death for only 233 (47%) of the excess deaths, leaving 265 (53%) probable HIV related deaths attributed to some other cause.

Analysis of the 86 medical causes alone showed that there were 1362 deaths among single men aged 15-54 in

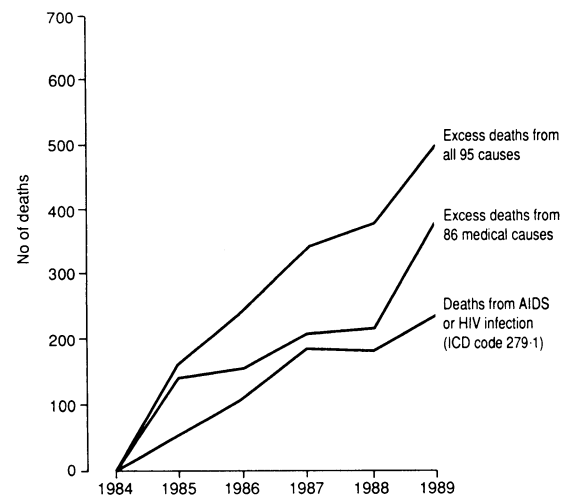
1989—379 (39%) above the number expected—233 (61%) of which were attributed to AIDS or HIV infection. There was no similar increase among men of other marital states or among women. The increase was greatest among single men aged 30-44 and in the Thames health regions.

Analysis of the nine external causes alone, however, showed a different picture. Among single men aged 15-54 there were 1143 deaths in 1989, 119 (12%) above the number expected compared with 1984. Smaller increases also occurred among men of other marital states and among women. The increase among single men was greatest among those aged 15-24 and was fairly evenly distributed across the country, suggesting that factors other than the HIV epidemic may have contributed.

In all, 376 deaths among HIV positive single men aged 15-54 were reported to CDSC in 1989, an excess of 347 compared with 1984. If the total number of deaths reported to OPCS is used as the denominator 70% were reported to CDSC in 1989. However, if deaths reported to OPCS due to the 86 medical causes alone is used 92% were reported to CDSC.

Comment

The associations with age, sex, marital state, and geographic location suggest that the continuing increase in the number of deaths due to the 86 HIV related



Number of excess deaths due to HIV related causes and of deaths from AIDS or HIV infection in single men aged 15-54 in England and Wales during 1985-9 compared with rates in 1984