Effect of socioeconomic group on incidence of, management of, and survival after myocardial infarction and coronary death: analysis of community coronary event register

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Abstract

Objective: To investigate the effect of socioeconomic group (with reference to age and sex) on the rate of, course of, and survival after coronary events.
Design: Community coronary event register from 1985 to 1991.
Setting: City of Glasgow north of the River Clyde, population 196 000.
Subjects: 3991 men and 1551 women aged 25-64 years on the Glasgow MONICA coronary event register with definite or fatal possible or unclassifiable events according to the criteria of the World Health Organisation's MONICA project (monitoring trends and determinants in cardiovascular disease).
Main outcome measures: Rate of coronary events; proportion of subjects reaching hospital alive; case fatality in admitted patients and in community overall.
Results: Event rates increased with age for both sexes and were greater in men than women at all ages. The rate increased 1.7-fold in men and 2.4-fold in women from the least (Q1) to the most (Q4) deprived socioeconomic quarter. The socioeconomic gradient decreased with age and was steeper for women than men. The proportion treated in hospital (66%) decreased with age, was greater in women than men, and decreased in both sexes with increasing deprivation (age standardised odds ratio 0.82 for Q4 *v* Q1) Case fatality in hospital (20%) increased with age, was greater for women than men when age was standardised, and showed no strong socioeconomic pattern. Overall case fatality in the community (50%) increased with age, was similar between the sexes, and increased from Q1 to Q4 (age standardised odds ratio 1.12 in men, 1.18 in women).
Conclusions: Socioeconomic group affects not only death rates from myocardial infarction but also event rates and chance of admission. This should be taken into account when different groups of patients are compared. Because social deprivation is associated with so many more deaths outside hospital, primary and secondary prevention are more likely than acute hospital care to reduce the socioeconomic variation in mortality.

Introduction

Age, sex, and socioeconomic group all affect a population's mortality from coronary heart disease.[1-3] Population registers have been used to document the effect of age and sex on event rates and case fatality in a community.[4-6] Studies limited to patients admitted to coronary care units or hospital wards [7-10] or to those in drug trials related to myocardial infarction[11 12] have reported the relation between case fatality in hospital, age, and sex. Social class may be related to event rates,[13-17] delay in seeking medical care during myocardial infarction,[18 19] and case fatality in hospital.[20] We investigated the relation of socioeconomic group to four things—event rates, the proportion of people reaching hospital alive, mortality in hospital, and overall case fatality—in men and women who had fatal and non-fatal consecutive events over a period of seven years in a defined geographical population. Wilhelmsen and Rosengren recently showed the surprising lack of data on these things.[21]

Subjects and methods

The Glasgow MONICA coronary event register comprises all cases of myocardial infarction and coronary death occurring in men and women aged 25-64 years resident in north Glasgow. The methods of ascertainment and investigation have been described previously.[5] Ascertainment derives from hospital discharge data, the registrar general, and other, minor, sources. We validated the events ascertained using the criteria of the World Health Organisation's MONICA (monitoring trends and determinants in cardiovascular disease) project,[6] and these depend on symptoms, electrocardiographic evidence, cardiac enzyme concentrations, and necropsy reports. Diagnostic information was gathered from many sources, including hospital case notes, general practitioners, and police reports to the procurators fiscal (the medicolegal authority in Scotland). Survival was determined at 28 days from the onset of the event. For this analysis we used all events classified as definite and all fatal events classified as possible and unclassifiable.[6] This definition excludes

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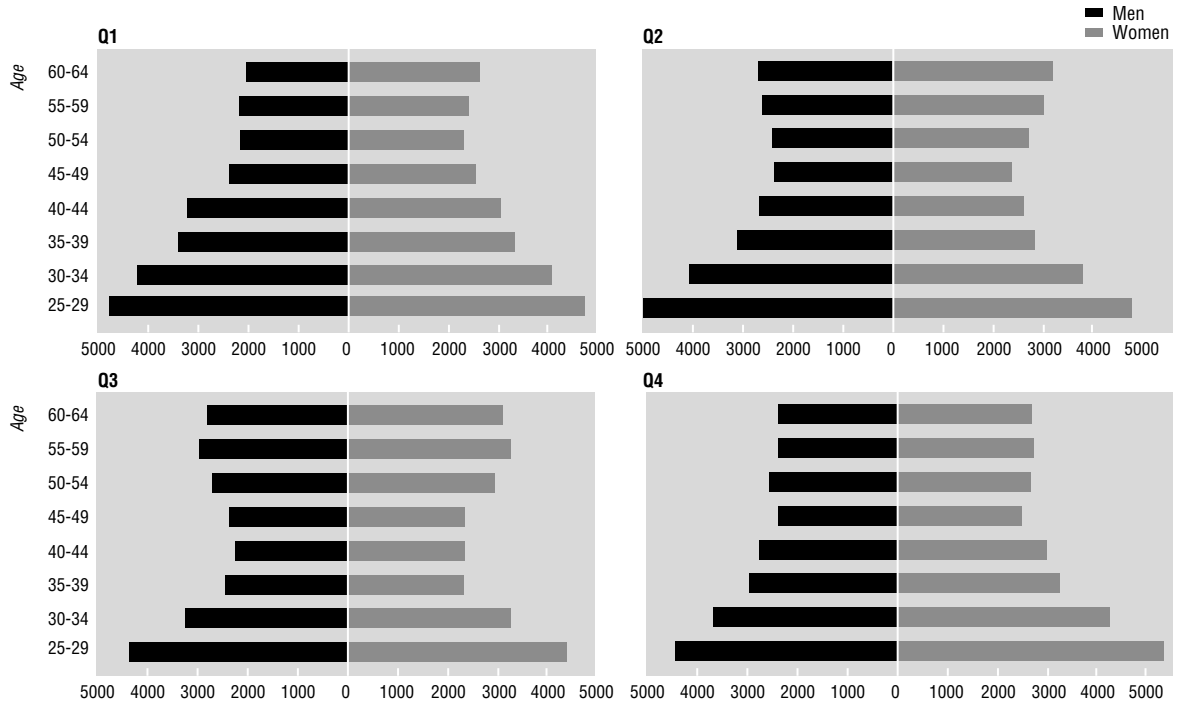

Fig 1 Distribution of Glasgow MONICA population by age, sex, and socioeconomic quarter (Q1 is least deprived)

non-fatal admissions without categorical evidence of infarction.

Socioeconomic group was derived for the postcode of residence at the time of the illness using the Carstairs and Morris deprivation score[2] as updated by McLoone using 1991 census data.[22] In this study we ranked postcodes in the order of the score. The population aged 25-64 for each postcode sector was obtained from the small area statistics from the 1991 census, and the total study population was divided into quarters (socioeconomic quarters) according to the updated Carstairs and Morris score rankings (Q1 is the least deprived quarter and Q4 the most deprived). We used the populations of the Carstairs and Morris quarters at the 1991 census as the denominators for calculation of age standardised rates. The specific populations in each socioeconomic quarter for each year were not available. The denominator for case fatality in hospital was all those who reached hospital alive. It did not include those transported to hospital but found to be dead on arrival.

Age standardised event rates were calculated as weighted sums of Poisson variables using the world standard population as the reference population.[23] Age adjusted relative risks by socioeconomic quarter were calculated from Poisson regression models. Age standardised percentages of people with events who reached hospital alive, of those who died after reaching hospital alive, and of those dying overall were calculated as weighted means of binomial variables using the Glasgow male population of all events in this study as the reference population. Age adjusted odds ratios by socioeconomic quarter were calculated from logistic regression models. Age standardisation and age adjustment of relative risks were carried out using 10 year age bands. Age adjustment of odds ratios used one year age bands.

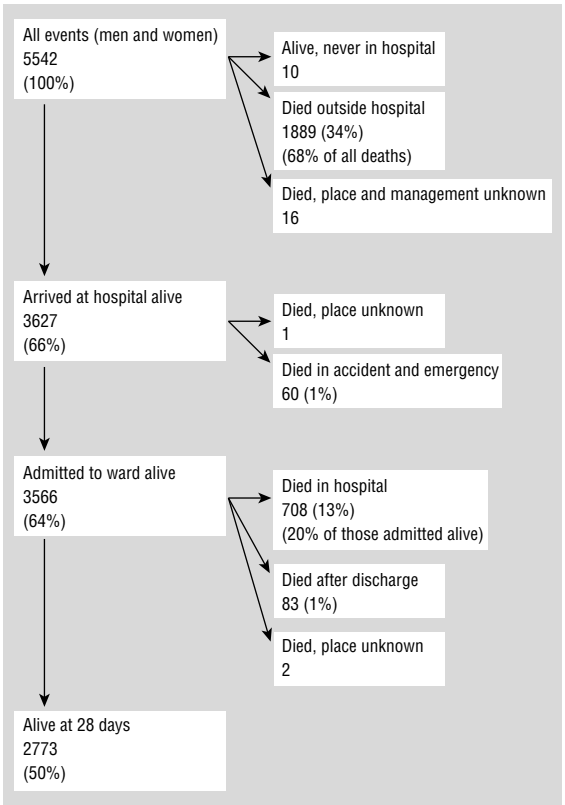

Fig 2 Pathway through myocardial infarction and coronary death in Glasgow MONICA project, 1985-91

Results

Population distribution

The estimated study population for 1991 was 96 063 men and 99 768 women. The total population in the age group 25-64 years declined each year from 1985 until a small upturn in 1991.

Table 1 Numbers of events (MONICA definition) by age, sex, and socioeconomic quarter. Values in parentheses are age specific relative risks unless stated otherwise

Quarter (1=least deprived)	Age group (years)					Age standardised rate (SE)†	Age adjusted relative risk (95% CI)
	25-34	35-44	45-54	55-64	Total*		
Men							
Q1	3 (1)	42 (1)	163 (1)	421 (1)	629	4.0 (0.16)	1
Q2	6 (2.0)	56 (1.5)	268 (1.6)	641 (1.2)	971	5.5 (0.18)	1.35 (1.22 to 1.49)
Q3	12 (4.8)	85 (2.9)	365 (2.0)	739 (1.3)	1201	6.5 (0.19)	1.57 (1.42 to 1.73)
Q4	19 (7.1)	115 (3.2)	338 (1.9)	714 (1.5)	1186	7.1 (0.21)	1.74 (1.58 to 1.91)
Total‡	40 (0.20)	298 (2.0)	1134 (7.9)	2519 (16.7)	3991	5.5 (0.09)	1.19 (1.15 to 1.22)¶
Women							
Q1	0	8 (1)	32 (1)	157 (1)	197	1.1 (0.08)	1
Q2	1 (1)	14 (2.0)	87 (2.6)	285 (1.5)	387	1.9 (0.10)	1.67 (1.41 to 1.98)
Q3	1 (1.1)	25 (2.6)	107 (3.1)	339 (1.7)	472	2.3 (0.11)	2.00 (1.70 to 2.36)
Q4	4 (3.5)	14 (1.8)	144 (4.2)	331 (2.0)	493	2.6 (0.12)	2.34 (1.98 to 2.76)
Total‡	6 (0.03)	61 (0.4)	371 (2.4)	1113 (6.5)	1551	1.9 (0.05)	1.28 (1.22 to 1.34)¶

*Includes some people whose socioeconomic quarter was not known.
†Per 1000 population per year.
‡Numbers in parentheses are age specific event rates per 1000 population per year.
¶Constant multiplicative increase with increasing quarter.

Table 2 Numbers (percentages) of people with coronary events who were alive on arrival at hospital by age, sex, and socioeconomic quarter

Quarter (1=least deprived)	Men					Women				
	Age group (years)				Age adjusted odds ratio (95% CI)	Age group (years)				Age adjusted odds ratio (95% CI)
	25-34	35-44	45-54	55-64		25-34	35-44	45-54	55-64	
Q1	3 (100)	33 (79)	104 (64)	275 (65)	1	No event	6 (75)	22 (69)	111 (71)	1
Q2	3 (50)	42 (75)	193 (72)	396 (62)	0.97 (0.78 to 1.37)	1 (100)	9 (64)	59 (68)	197 (69)	0.90 (0.62 to 1.31)
Q3	8 (67)	60 (71)	264 (72)	450 (61)	0.94 (0.76 to 1.15)	0	17 (68)	77 (72)	233 (69)	0.92 (0.64 to 1.33)
Q4	10 (53)	71 (62)	220 (65)	432 (60)	0.81 (0.66 to 0.99)	2 (50)	10 (71)	98 (68)	217 (66)	0.81 (0.56 to 1.16)
Total*	24 (60)	206 (69)	782 (69)	1556 (62)	0.93 (0.87 to 0.99)†	3 (50)	42 (69)	256 (69)	758 (68)	0.94 (0.85 to 1.05)†
Age standardised percentage (SE)					64.3 (0.76)					68.2 (1.22)

*Includes some people whose socioeconomic quarter was not known. Zero means numerator of cell percentage is zero.
†Constant multiplicative increase with increasing quarter.

The socioeconomic distribution of the population of north Glasgow is skewed towards greater deprivation compared with Scotland overall. In north Glasgow 68% of the population live in postcode sectors with scores below a cut off point that defines 18% of the Scottish population when applied nationally. The populations of each deprivation quarter of the population showed different age structures both between the sexes and between quarters for each sex (fig 1), although there was no systematic pattern from Q1 to Q4.

Event rates

Figure 2 shows the aggregate numbers of events at various points in the pathway through myocardial infarction and coronary death in the Glasgow MONICA register from 1985-91. Deaths outside hospital accounted for 68% of all deaths. The community case fatality at 28 days (all deaths, both in and out of hospital, related to all events) was 50%.

More men than women had events (3991 *v* 1551). The age distribution of events for men and women is shown in table 1. Event rates were much greater for men than women for each 10 year age band. Both sexes showed an increase with age. The distribution of the events by deprivation quarter is also shown in table 1. For both men and women the risk of myocardial infarction increased with increasing deprivation. The socioeconomic gradient was steeper in women ($P = 0.01$). The effect of deprivation was highly consistent across all age groups in both sexes. The socioeconomic gradient decreased with age for men and women, although men in the youngest age group and women in the two youngest age groups were too few to provide meaningful comparisons.

Arrival at hospital

A total of 3627 (65%) subjects arrived at hospital alive. Table 2 shows the variation by age and sex. For both men and women there was no obvious pattern with age except that the oldest group of men had less chance than the younger men of being admitted. Only older women were more likely to reach hospital alive than men. The variation by socioeconomic quarter showed a decreasing proportion reaching hospital alive (Q1 to Q4) for men and women, with no obvious difference in the socioeconomic gradient between the sexes.

Fatality in admitted patients

In all, 854 of the 3627 (22%) of patients who reached hospital alive died within 28 days. The case fatality in hospital of all those reaching hospital alive—including those who died in an accident and emergency department—was 21% (769/3627); it was 20% (708/3566) of all those reaching a hospital ward alive (fig 2). Two per cent (83/3566) of those admitted to hospital were discharged alive but they died within 28 days from the onset of the illness; 2%(70/3566) were alive at 28 days, although they were still in hospital.

Table 3 shows the case fatality in hospital for each age group and for both sexes. It increased with age and

Table 3 Numbers (percentages) of patients dying of coronary event within 28 days among those reaching hospital alive by age, sex, and socioeconomic quarter

Quarter (1=least deprived)	Men					Women				
	Age group (years)				Age adjusted odds ratio (95% CI)	Age group (years)				Age adjusted odds ratio (95% CI)
	25-34	35-44	45-54	55-64		25-34	35-44	45-54	55-64	
Q1	0	2 (12)	15 (14)	81 (30)	1	No event	1 (17)	6 (27)	32 (29)	1
Q2	0	5 (12)	31 (16)	108 (27)	0.98 (0.72 to 1.32)	0	1 (11)	13 (22)	60 (31)	1.03 (0.65 to 1.65)
Q3	0	4 (7)	44 (17)	124 (28)	0.97 (0.73 to 1.30)	No event	1 (6)	11 (14)	70 (30)	0.96 (0.61 to 1.51)
Q4	1 (10)	7 (10)	32 (15)	115 (27)	0.94 (0.70 to 1.26)	0	1 (10)	12 (12)	74 (34)	1.07 (0.68 to 1.68)
Total*	1 (4)	18 (9)	122 (16)	431 (28)	0.98 (0.90 to 1.07)†	0	4 (10)	42 (16)	236 (31)	1.01 (0.89 to 1.16)†
Age standardised percentage (SE)					22.6 (0.82)					25.0 (1.29)

*Includes some people whose socioeconomic quarter was not known. Zero means numerator of cell percentage is zero.
†Constant multiplicative increase with increasing quarter.

more steeply in women than men. Age standardised case fatality rose consistently with increasing deprivation for men. In women the pattern was not consistent but a contrast was seen between the most deprived and least deprived quarter.

Community case fatality (in and out of hospital)
The case fatality in the community overall was 50% (2769/5542) We previously showed the remarkable similarity in case fatality in men and women at 28 day even when age was standardised[5]; table 4 shows other variations. Case fatality increased with age in both men and women. Age standardised case fatality rose consistently with increasing deprivation in men; the pattern was not consistent in women but showed an increase between the least deprived and most deprived quarter.

Discussion

The population of north Glasgow is skewed to the lower end of the socioeconomic scale, but we still found socioeconomic gradients in myocardial infarction among people who overall are least advantaged. This socioeconomic variation is seen in event rate and most obviously in the proportion of people reaching hospital alive. No variation is seen in case fatality in hospital. These findings are reflected in the socioeconomic variation in the proportion of people dying outside hospital and the case fatality in the community overall. Socioeconomic disadvantage thus increases the chance of a person having a myocardial infarction, decreases the chance of reaching hospital alive, and increases the chance of dying during the attack. This gradient is found in both women and men.

Event rates
We found a large socioeconomic variation in the event rate in men and women. This agrees with studies using various markers of socioeconomic group which show that deprivation, a shorthand for poorer education, poorer housing, increasing poverty, and lack of employment, relates to increasing event rates.[14-16] Furthermore, socioeconomic variations in the extent of coronary risk factors in a population are associated with socioeconomic variation in disease prevalence.[24] This supports the idea of reducing the unequal distribution of risk as a prime objective for local and national health promotion activities.

Arrival at hospital
The socioeconomic differences we and others have found may reflect poorer awareness of the importance of symptoms such as crushing chest pain or arm pain among those who are less well educated.[18 19] Alternatively, the proportion of sudden deaths may rise by association with cigarette smoking.[25]

Seventy one per cent of all deaths in men but only 63% of deaths in women occurred outside hospital, reflecting the greater proportion of women arriving alive at hospital. A similar socioeconomic gradient was seen in men and women. We have already shown that women are more likely to reach hospital after a call to the family doctor, whereas men are more likely to go directly.[5] Perhaps referral patterns also vary subtly according to patients' backgrounds.

Only two thirds of patients were admitted to hospital. The remaining third died outside hospital, limiting the impact of treatments in hospital.

Table 4 Numbers (percentages) of patients dying of coronary event within 28 days among all those who had events by age, sex and socioeconomic quarter

Quarter (1=least deprived)	Men					Women				
	Age group (years)				Age adjusted odds ratio (95% CI)	Age group (years)				Age adjusted odds ratio (95% CI)
	25-34	35-44	45-54	55-64		25-34	35-44	45-54	55-64	
Q1	0	11 (26)	73 (45)	227 (54)	1	No event	2 (25)	16 (50)	78 (50)	1
Q2	3 (50)	19 (34)	105 (39)	353 (55)	1.01 (0.82 to 1.23)	0	6 (43)	41 (47)	146 (51)	1.08 (0.76 to 1.53)
Q3	4 (33)	29 (34)	144 (39)	412 (56)	1.02 (0.84 to 1.23)	1 (100)	9 (36)	40 (37)	176 (52)	1.02 (0.73 to 1.43)
Q4	10 (53)	51 (44)	150 (44)	395 (55)	1.14 (0.93 to 1.38)	2 (50)	5 (36)	58 (40)	118 (52)	1.19 (0.85 to 1.67)
Total*	17 (42)	110 (37)	472 (42)	1390 (55)	1.04 (0.98 to 1.11)†	3 (50)	22 (36)	156 (42)	589 (53)	1.05 (0.95 to 1.16)†
Age standarised percentage (SE)					49.8 (0.78)					48.5 (1.29)

*Includes some people whose socioeconomic quarter was not known. Zero means numerator of cell percentage is zero.
†Constant multiplicative increase with increasing quarter.

Death rate in admitted patients

We found no social class variation in case fatality in hospital. This is consistent with the Scottish Office's data on mortality in hospital 30 days after a myocardial infarction, which show little variation when standardised for social class.[26] A greater case fatality in hospital has been reported among people who are less well educated[20] and among African-American women (with higher unemployment rates) compared with white women,[27] and this was only partly explained by differences in case mix. Our findings may reflect a lack of bias in the care given to different socioeconomic groups. The case mix of hospital admissions may vary by socioeconomic quarter.[20] Severely ill people from deprived background might be more likely to die outside hospital because of delays in admission. If care shows a socioeconomic bias against deprived people this might cancel out a better case mix.

Cardiologists and general physicians differ in their management of patients during myocardial infarction[28] and unstable angina.[29] Do they differ in how they care for patients with myocardial infarction of different socioeconomic groups? Socioeconomic bias applies to angiography for men in Glasgow[30] and elsewhere[31] but not to invitation to rehabilitation after myocardial infarction.[32] Furthermore, men and women are treated similarly once they are receiving care for myocardial infarction.[5]

Community case fatality

The increase in overall case fatality with deprivation may have several explanations. Non-fatal events in deprived people may be less frequently recognised—that is, the denominator for case fatality in the more deprived groups may be comparatively more incomplete. Death, however, is enumerated similarly for all social groups. Any undercount in the denominator would imply an underestimate of the socioeconomic gradient.

Several factors could explain the variation in the numerator between socioeconomic groups. Firstly, the number of concomitant illnesses, particularly respiratory disease, increases with increasing deprivation.[33]

Secondly, coronary disease itself may be different in different socioeconomic groups, perhaps manifesting more often among deprived people as sudden death through the mediation of factors such as higher rates of cigarette smoking.[25]

Thirdly, there may be a social class gradient in the ability to heal or to ward off insults to various organs. In Glasgow recovery from various surgical procedures for cancer is worse among people who are deprived after adjustment for stage of disease and treatment.[34]

Finally, the potential for resuscitation, available for 38% of people who died outside hospital in north Glasgow, was fulfilled in less than a third of that number.[35] This proportion is much greater elsewhere.[34] The advent of Heartstart Scotland—the equipping of all emergency ambulances with semiautomatic defibrillators—has had little effect on successful resuscitation outside hospital in north Glasgow[35] in contrast to other places.[36] Exploration of the possible reasons for these differences is required to maximise the benefit of available services such as Heartstart Scotland.

The quality of Glasgow MONICA registration data in terms of completeness, accuracy, and consistency over time has been documented.[5 6] Carstairs and Morris deprivation scores are better than occupational classification in discriminating between deprived socioeconomic groups as many of those on the register are unemployed.[5] Postcode of residence, but not occupation, is routinely coded on both death certificates and hospital discharge data. The Carstairs and Morris score has been criticised for its complexity and for not relating to people but to geographical areas. However, it remains useful in describing variation over a wide range of morbidity, mortality, and other health related population measurements.[2 38 39] Calculation of rates for deprivation quarters of the population using the 1991 census population as denominator for all of the data from 1985-91 might be criticised. However, there are no intercensal estimates made at that population level. As our data refer to 1985-91 we used the closest census population, that of 1991.

Implications and conclusions

Tackling inequalities in health has only recently received government emphasis.[40] Reductions in mortality from coronary heart disease principally reflect reduction in risk factors in a population.[41] Socioeconomic variation in health and disease has been recognised for hundreds of years.[42] Action to reduce the variation has many years of inaction at all levels to redress.

Disease registers are valuable datasets for exploring variation in diseases in a population. Examination of subgroups, such as patients admitted to a coronary care unit or a trial, will always give a biased picture when 34% of people never reach hospital alive and two thirds of deaths occur before hospital admission. Those allocating scarce healthcare resources should therefore consider socioeconomic variation not only in community death rates but also at other points in the disease process such as the chance of dying outside hospital and therefore of reaching hospital care alive.

We have shown that the greatest socioeconomic variation in death is during the prehospital phase of myocardial infarction and coronary death. Thus treatments applied equitably in hospitals across socioeconomic groups during acute myocardial infarction will have little impact on socioeconomic variation in death rates. If the deaths outside hospital were not inevitable and patients reached hospital and received hospital treatment then acute care could have an impact on the socioeconomic variation in coronary mortality.

Further investigation is required to understand the reasons for the differences in prehospital mortality in terms of different patterns of accessing care, differences between socioeconomic groups in treatment before the attack, and socioeconomic gradients in disease severity before strategies can be devised to address this aspect of socioeconomic variation in myocardial infarction and coronary death.

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Key messages

- Socioeconomic variation in rates of coronary events was greater for women than men
- The largest social class gradient was in the proportion of deaths occurring outside hospital
- Overall, 68% of all people who died of coronary events did so before admission
- Acute hospital care applied to only 66% of all cases and therefore could affect only 32% of all deaths
- Reduction in socioeconomic variation in mortality from coronary disease is best addressed by reducing the variation of event rates—that is, by primary and secondary prevention
- Allocation of resources for reduction of coronary mortality should take account of social class differences and the relative potential effect of hospital care and primary and secondary prevention

managing, and checking and verifying the data. We would be unable to maintain the register without the unfailing goodwill of the general practitioners of north Glasgow. We are also grateful for the support of ISD, the Information and Statistics Division of the Common Services Agency; hospital records officers and their staff in Glasgow Royal Infirmary and University NHS Trust, West Glasgow Hospitals and University NHS Trust, and Stobhill Hospital Trust; and other records departments throughout the United Kingdom. We thank the staff of the deaths unit of the Office of the Procurator Fiscal, Glasgow, the staff of offices of other procurators fiscal throughout Scotland, and staff of coroner's offices in England for their willing cooperation. Although we are unable to acknowledge them individually, many other people and agencies have generously supported the work of the Glasgow MONICA project register. The views expressed in this paper are ours alone and do not necessarily reflect those of the funding body or of those acknowledged above as previous or current members of staff.

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Lifetime socioeconomic position and mortality: prospective observational study

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Abstract

Objectives: To assess the influence of socioeconomic position over a lifetime on risk factors for cardiovascular disease, on morbidity, and on mortality from various causes.

Design: Prospective observational study with 21 years of follow up. Social class was determined as manual or non-manual at three stages of participants' lives: from the social class of their father's job, the social class of their first job, and the social class of their job at the time of screening. A cumulative social class indicator was constructed, ranging from non-manual social class at all three stages of life to manual social class at all three stages.

Setting: 27 workplaces in the west of Scotland.

Participants: 5766 men aged 35-64 at the time of examination.

Main outcome measures: Prevalence and level of risk factors for cardiovascular disease; morbidity; and mortality from broad causes of death.

Results: From non-manual social class locations at all three life stages to manual at all stages there were strong positive trends for blood pressure, body mass index, current cigarette smoking, angina, and bronchitis. Inverse trends were seen for height, cholesterol concentration, lung function, and being an ex-smoker. 1580 men died during follow up. Age adjusted relative death rates in comparison with the men of non-manual social class locations at all three stages of life were 1.29 (95% confidence interval 1.08 to 1.56) in men of two non-manual and one manual social class; 1.45 (1.21 to 1.73) in men of two manual and one non-manual social class; and 1.71 (1.46 to 2.01) in men of manual social class at all three stages. Mortality from cardiovascular disease showed a similar graded association with cumulative social class. Mortality from cancer was mainly raised among men of manual social class at all three stages. Adjustment for a wide range of risk factors caused little attenuation in the association of cumulative social class with mortality from all causes and from cardiovascular disease; greater attenuation was seen in the association with mortality from non-cardiovascular, non-cancer disease. Fathers having a non-manual occupation was strongly associated with mortality from cardiovascular disease: relative rate 1.41 (1.15 to 1.72). Participants' social class at the time of screening was more strongly associated than the other social class indicators with mortality from cancer and from non-cardiovascular, non-cancer causes.

Conclusions: Socioeconomic factors acting over the lifetime affect health and risk of premature death. The relative importance of influences at different stages varies for the cause of death. Studies with data on socioeconomic circumstances at only one stage of life are inadequate for fully elucidating the contribution of socioeconomic factors to health and mortality risk.

See editorial by Haines and Smith and pp 541, 553, 558, 591

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Introduction

The ubiquitous nature of the association between unfavourable socioeconomic circumstances in adulthood and premature death has been shown in many studies, with various socioeconomic indicators being related to morbidity and mortality.[1-6] It has long been recognised that the effects of poor social circumstances in early life can have lasting influences,[7 8] and studies relating childhood socioeconomic position to later risk of illness and premature death have been performed.[9-12] These studies have generally been inspired by suggestions that the early environment has specific influences which alter later susceptibility to disease. They have yielded somewhat equivocal findings, well illustrated by two reports from the same study coming to opposite conclusions about the relative importance of childhood and adulthood socioeconomic environment in relation to the risk of coronary heart disease.[10 13]

Recently the importance of considering the cumulative effect of socioenvironmental exposures over a life time has been recognised.[14-16] The Department of Health's report *Variations in Health* concluded that "it is likely that cumulative differential lifetime exposure to health damaging or health promoting physical and social environments is the main explanation for observed variations in health and life expectancy."[17] Few empirical data exist on such cumulative effects, however. In the national longitudinal survey of older men in the United States education, first occupation, occupation in middle age, and family assets contributed independently to the risk of premature death,[18] but other data on risk factors were not available and patterns for different causes of death have not been examined. We investigated the contributions of indicators of socioeconomic position over the course of a lifetime to the risk of premature death in a large cohort of men in the west of Scotland who had detailed examinations in middle age and for whom 21 years of subsequent mortality follow up data were available.

Subjects and methods

This analysis is based on a cohort of men recruited from 27 workplaces in Glasgow, Grangemouth, and Clydebank between 1970 and 1973. The workplaces included engineering, manufacturing, and petrochemical plants; a publishing house; civil service departments; administrative and professional divisions from British Rail; architectural institutes; legal and dental offices; and banks. Response rates were available for the workplaces from which 87% of the sample was recruited. For these sites 70% of those invited completed the questionnaire and attended for examination. The achieved sample was 6022 men and 1006

women, from which the 5766 men aged 35-64 at the time of examination are the basis for the present report. The mortality data in the women were not analysed as only 176 women had died.

The examinations used similar procedures to those used and previously described for the Renfrew-Paisley study population.[19] An extensive questionnaire, completed by the subject, was checked at the screening examination. These examinations were conducted at clinics established for this purpose at or near the workplaces.

The information collected at baseline examination included:

- Sociodemographic data—age, father's occupational social class, the social class of the participant's first regular job, excluding temporary work, and his occupational social class at the time of screening, and whether he drove a car regularly
- Medical history—angina, previous heart attack and intermittent claudication from the Rose questionnaire,[20] respiratory symptoms from the Medical Research Council questionnaire[21]
- Health related behaviours—detailed smoking history
- Physical examination—height, weight, blood pressure while seated (taken with a London School of Hygiene and Tropical Medicine sphygmomanometer, diastolic pressure being recorded at the disappearance of the fifth Korotkoff sound), lung function measured with the Garthur Vitalograph, serum cholesterol concentration, and six lead electrocardiogram (leads I, II, III, aVR, aVL, and aVF).
- Persistent phlegm was defined as usually bringing up phlegm from the chest first thing in the morning on most days for three months during winter each year. "Infective phlegm" was defined as usually bringing up phlegm from the chest first thing in the morning in winter and having had a period of increased cough and phlegm lasting for three weeks or more in the previous three years. Breathlessness was defined as a positive response to the question: "Do you get short of breath walking with people of your own age on level ground?" Bronchitis was defined as having persistent and "infective" phlegm and being breathless.[20]
- Angina was considered present if chest pain or discomfort when walking uphill or hurrying was cited in the sternum or the left chest and arm; caused the subject to stop or slow down; went away when the subject stopped or slowed down; and went away in 10 minutes or less.[20]
- Forced expiratory volume in one second (FEV_1) was taken as the better of two expirations. To estimate impairment the expected value was obtained from linear regression equations of age and height, in which expected $FEV_1 = -278.06 + 4.33 \times \text{height} - 3.06 \times \text{age}$. Age was measured in years and height in centimetres and the value was divided by 100 to give FEV_1 in litres. The coefficients were derived from a healthy subset of the population who had never smoked and answered no to questions on phlegm and breathlessness and to questions asking whether they had wheezy or whistling chest and whether their breathing was affected by the weather. The adjusted FEV_1 was calculated as (actual $FEV_1 \div$ expected $FEV_1) \times 100$
- The electrocardiograms were coded according to the Minnesota system.[20] Any of the codes 1.1-1.3, 4.1-4.4, 5.1-5.3, and 7.1, which encompass diagnoses of definite myocardial infarction, myocardial ischaemia, and left bundle branch block, were considered to be evidence of ischaemia.
- Data on father's, first, or current social class were missing in 199 men, who were excluded from the present analyses, which are therefore based on 5567 participants. The home address at the time of screening was retrospectively given a postcode, enabling an area based deprivation category at the time of the 1981 census as defined by Carstairs and Morris to be ascertained.[22] Deprivation category varies from 1 (least deprived) to 7 (most deprived) and is based on four variables derived from census data at the level of the postcode sector: male unemployment, overcrowding, car ownership, and proportion of residents in social classes IV and V.
- We identified men who had died over the 21 years of follow up by flagging at the NHS Central Registry in Edinburgh, which also provides death certificates coded according to the ninth revision of the *International Classification of Diseases*. We calculated mortality using a person years at risk lifetable approach. These rates have been standardised for age by the direct method, with the total study population as the standard. We tested for trends in age adjusted rates by proportional hazards regression using the PROC PHREG program in the SAS system,[23] with age and the cumulative social class indicator (defined in the Results section) coded as a continuous variable as covariates. We standardised continuous variables for age using the PROC GLM program, with tests for trend for age adjusted means being obtained with the PROC REG program. We standardised categorical variables for age by a direct method and tested for trends with the PROC LOGIST program.
- Proportional hazards coefficients and their standard errors were calculated using Cox's model.[24] Adjustment for age and other risk factors was performed by including terms for these in the proportional hazards models. Exponentiated hazards coefficients were taken as indicators of relative death rates.

Results

Table 1 shows the distribution of social class at different points during the lives of the study population. The largest category consisted of men whose fathers had had manual social class occupations, whose first job had been in a manual social class occupation, and who had a manual social class occupation at the time of screening. The only group that was particularly small consisted of men with fathers who had had a

Table 1 Distribution of social class according to manual or non-manual occupation of study population

	First social class	
Social class at screening	**Non-manual**	**Manual**
Manual		
Father's social class:		
Non-manual	34	177
Manual	247	2319
Non-manual		
Father's social class:		
Non-manual	956	165
Manual	923	746

Table 2 Population characteristics according to cumulative social class. Values are age adjusted means or proportions unless stated otherwise

	Cumulative social class based on occupation					
	All three non-manual (n=956)	Two non-manual, one manual (n=1122)	Two manual, one non-manual (n=1170)	All three manual (n=2319)	Total (n=5567)	P value for trend
Age at screening (years)*	47.5	47.7	48.6	48.6	48.2	<0.0001
Blood pressure (mm Hg):						
Systolic	131.1	132.2	134.1	136.1	134.1	<0.0001
Diastolic	82.4	83.1	84.1	84.7	83.9	<0.0001
Cholesterol (mmol/l)	6.3	6.1	5.8	5.7	5.9	<0.0001
Height (cm)	176.0	174.4	172.6	170.8	172.8	<0.0001
Body mass index	24.7	25.1	25.4	25.3	25.2	<0.0001
FEV_1 (%)	99.4	98.0	94.0	90.3	94.2	<0.0001
Percentage (No) of subjects:						
With angina	4.4 (39)	5.4 (57)	6.5 (77)	7.5 (176)	6.3 (349)	0.0002
With electrocardiographic ischaemia	5.9 (55)	5.2 (57)	6.1 (74)	5.9 (143)	5.9 (329)	0.64
With bronchitis	0.6 (5)	0.5 (6)	2.9 (35)	3.4 (79)	2.2 (125)	<0.0001
Who had never smoked†	20.0 (194)	22.1 (254)	18.1 (209)	14.5 (330)	17.7 (987)	<0.0001
Who were current smokers†	45.4 (435)	46.8 (522)	55.4 (649)	63.5 (1471)	55.3 (3077)	<0.0001
Who were ex-smokers†	30.6 (289)	27.7 (306)	22.9 (270)	20.5 (482)	24.2 (1347)	<0.0001
Average No of cigarettes smoked per day‡	19.6	18.3	19.2	18.9	19.0	0.58
Percentage (No) of subjects:	69.3 (669)	57.5 (646)	54.3 (632)	40.8 (938)	51.8 (2885)	<0.0001
Who drove cars regularly						
Living in area of residence of deprivation category 5-7	18.6 (173)	32.0 (354)	54.3 (638)	66.0 (1539)	48.6 (2704)	<0.0001

*Not age adjusted.
†Excluding 154 men who smoked a pipe or cigars and two men with missing data.
‡For current cigarette smokers only.

non-manual social class occupation, whose first job had been in a non-manual social class occupation, and who had a manual social class occupation at the time of screening.

A cumulative social class indicator was constructed by summing the number of occasions in which each participant's class location was manual or non-manual. In table 2 population characteristics are presented according to this cumulative social class indicator. The men in whom social class was manual on three occasions were on average one year older than the men in whom class was non-manual on all three occasions. After the remaining data on risk factors were adjusted for age we found that moving from the men who had consistently non-manual social class locations to those who had consistently manual social class locations showed trends of increasing systolic and diastolic blood pressure, body mass index, current cigarette smoking, and prevalence of bronchitis and angina and decreasing cholesterol concentration, height, lung function, and prevalence of never having smoked. The men consistently in manual social class locations were less likely than those consistently in non-manual social class locations to be regular drivers. Being a regular car driver is taken to be mainly a marker for ownership of a car, which has been used in various studies as an indicator of available income.[3 4] The men consistently in manual social class locations were also more likely to live in a postcode sector with unfavourable socioeconomic characteristics at the time of the 1981 census.

Over the 21 years of follow up 1580 members of the cohort died. Table 3 shows age adjusted mortality from all causes, cardiovascular disease, cancer, and other causes. Mortality increased with the extent to which the men had had manual social class locations at different times in their life. The trends were most consistent for mortality from all causes and cardiovascular disease; for mortality from cancer the main difference was between men who had had manual social class locations at all three stages of their life compared with the rest.

We fitted proportional hazards models with social class coded as manual or non-manual at the three different stages of life fitted individually and simultaneously. The social class of first occupation was not significantly associated with mortality from all causes or any subcategory of mortality when father's and current social class were taken into account (table 4). Father's social class and current social class were similarly related to mortality from all causes, both when treated singularly and when entered in the model with simultaneous adjustment for all social class measures. Within this general picture mortality from cancer and non-cardiovascular, non-cancer causes seemed to be more strongly associated with social class at the time of screening than with father's social class; the reverse was the case for mortality from cardiovascular disease.

Table 3 Age adjusted death rates (per 1000 person years) over 21 years of follow up according to cumulative social class*

	Cumulative social class based on occupation			
	All three non-manual	Two non-manual, one manual	Two manual, one non-manual	All three manual
All causes				
No of deaths	190	280	339	771
Mortality	100.1	123.4	135.1	153.9
Cardiovascular causes				
No of deaths	84	145	197	388
Mortality	48.3	70.3	84.4	86.6
Cancer				
No of deaths	73	86	95	247
Mortality	41.8	42.4	45.2	58.0
Non-cardiovascular, non-cancer causes				
No of deaths	33	49	47	136
Mortality	19.1	25.7	22.6	34.0

*Significance tests for trend across age adjusted relative rates are given in table 6.

Table 4 Mortality by social class at three different stages of life. Values are age adjusted relative rates (95% confidence intervals), with individual and simultaneous adjustment for each social class indicator

	Father's social class	First social class	Current social class
All causes			
Individual	1.44 (1.27 to 1.64)	1.29 (1.16 to 1.43)	1.40 (1.27 to 1.55)
Simultaneous	1.28 (1.11 to 1.47)	1.01 (0.89 to 1.16)	1.29 (1.14 to 1.47)
Cardiovascular causes			
Individual	1.58 (1.32 to 1.89)	1.35 (1.16 to 1.56)	1.38 (1.20 to 1.59)
Simultaneous	1.41 (1.15 to 1.72)	1.08 (0.90 to 1.30)	1.20 (1.01 to 1.43)
Cancer			
Individual	1.26 (1.02 to 1.56)	1.25 (1.04 to 1.50)	1.35 (1.13 to 1.61)
Simultaneous	1.11 (0.87 to 1.41)	1.04 (0.82 to 1.31)	1.28 (1.03 to 1.60)
Non-cardiovascular, non-cancer causes			
Individual	1.45 (1.07 to 1.98)	1.18 (0.92 to 1.53)	1.59 (1.24 to 2.03)
Simultaneous	1.28 (0.91 to 1.80)	0.80 (0.58 to 1.10)	1.67 (1.22 to 2.28)

Table 5 All cause mortality by cumulative social class, car driving, and deprivation category of area of residence. Values are age adjusted relative rates (95% confidence intervals)

	Cumulative social class			
	All three non-manual	Two non-manual, one manual	Two manual, one non-manual	All three manual
Regular car driver:				
Yes	1	1.28 (1.01 to 1.63)	1.36 (1.08 to 1.73)	1.57 (1.27 to 1.95)
No	1.22 (0.91 to 1.64)	1.52 (1.19 to 1.95)	1.76 (1.40 to 2.21)	2.00 (1.64 to 2.44)
Deprivation category of area of residence:				
1-4	1	1.25 (1.01 to 1.56)	1.37 (1.09 to 1.72)	1.70 (1.39 to 2.09)
5-7	1.06 (0.74 to 1.52)	1.41 (1.10 to 1.82)	1.54 (1.25 to 1.90)	1.74 (1.45 to 2.09)

Two additional indicators of socioeconomic position in adulthood were available: car use and deprivation category of area of residence. Table 5 shows that these indicators are associated with mortality within the strata of cumulative social class. In analyses adjusted only for age not being a regular car driver was associated with a relative rate of mortality of 1.34 (95% confidence interval 1.21 to 1.48); inclusion of the cumulative social class indicator reduced this to 1.25 (1.13 to 1.39). Living in an area in deprivation categories 5-7 was associated with an age adjusted relative rate of mortality of 1.21 (1.10 to 1.34). After inclusion of the cumulative social class indicator this became 1.07 (0.96 to 1.19).

Table 6 shows relative rates of mortality adjusted for age and risk factors. For mortality from cardiovascular disease and all causes the relative rates were adjusted for age, smoking (number of cigarettes smoked, with an additional adjustment for being an ex-smoker), diastolic blood pressure, serum cholesterol concentration, body mass index, adjusted FEV_1, angina, bronchitis, and electrocardiographic ischaemia. For mortality from cancer and from non-cardiovascular, non-cancer causes the relative rates were adjusted for age, smoking, body mass index, adjusted FEV_1, and bronchitis. Such adjustment led to some attenuation in the increased risk of death in relation to social class, although for mortality from all causes, cardiovascular disease, and cancer this attenuation was not great. For mortality from non-cardiovascular, non-cancer causes more considerable attenuation of the trend of increasing risk of death with cumulative social class group was seen, with the association becoming non-significant at conventional levels.

Discussion

Cumulative socioeconomic disadvantage and mortality

Most of the numerous studies relating socioeconomic position to mortality have used measures of socioeconomic circumstances in adulthood.[1-5] This in part reflects the view that exposures acting at this time have the most impact on the risk of premature death.[8] However, the risk of premature death may reflect the accumulation of environmental insults or the cumulative effects of unfavourable behavioural or psychological factors, which progressively increase susceptibility to disease.[25 26] The few studies that have assessed socioeconomic position throughout life show the strengths of this notion. Thus in a study based on record linkage of the 1960, 1970, and 1980 censuses in Norway particularly high risks of premature death were seen among men who had had limited education and then worked in manual occupations and lived in poor housing.[27 28] Similar findings have come from the national longitudinal survey of older men in the United States.[18]

Our cohort was recruited from workplaces, but the study was initiated at a time of comparatively low unemployment and recruited men from across the social spectrum. The mortality differentials according to social class in our study are similar to those in men of the same age group in Scotland around 1981, the mid-

Table 6 Relative death rates (95% confidence intervals) by cumulative social class, adjusted for age and risk factors

	Cumulative social class				
	All three non-manual	Two non-manual, one manual	Two manual, one non-manual	All three manual	P value for trend
All causes					
Age	1	1.29 (1.08 to 1.56)	1.45 (1.21 to 1.73)	1.71 (1.46 to 2.01)	<0.0001
Age and risk factor*	1	1.30 (1.08 to 1.57)	1.33 (1.11 to 1.60)	1.57 (1.33 to 1.85)	<0.0001
Cardiovascular causes					
Age	1	1.51 (1.16 to 1.98)	1.90 (1.47 to 2.45)	1.94 (1.53 to 2.45)	<0.0001
Age and risk factor*	1	1.57 (1.20 to 2.05)	1.78 (1.37 to 2.31)	1.92 (1.51 to 2.45)	<0.0001
Cancer					
Age	1	1.04 (0.76 to 1.42)	1.06 (0.78 to 1.44)	1.44 (1.11 to 1.87)	0.001
Age and risk factor†	1	1.04 (0.76 to 1.42)	1.01 (0.74 to 1.37)	1.34 (1.03 to 1.75)	0.009
Non-cardiovascular, non-cancer causes					
Age	1	1.31 (0.84 to 2.03)	1.16 (0.75 to 1.82)	1.75 (1.20 to 2.56)	0.002
Age and risk factor†	1	1.30 (0.83 to 2.02)	1.02 (0.65 to 1.60)	1.42 (0.97 to 2.09)	0.09

*Adjusted for age, smoking, diastolic blood pressure, cholesterol concentration, body mass index, adjusted FEV_1, angina, bronchitis, electrocardiographic ischaemia.
†Adjusted for age, smoking, body mass index, adjusted FEV_1, and bronchitis.

point of the follow up period. For men aged 55 to 64 in the general Scottish population the death rates were 66% higher in social classes IV and V than in social classes I and II.[29] In our study the age adjusted death rate was 61% higher in men of social classes IV and V than in men of social classes I and II. The general population data also show mortality differentials for the main causes of death that are similar in size to those seen in our study. Our workplace sample thus seems to be a reasonable model for studying factors underlying socioeconomic differentials in risk of premature death in the general population, and the non-response rate, which is comparable to that in other such studies, does not seem to have introduced any serious bias. Our findings (*a*) that socioeconomic position in early and later life contribute separately to the risk of premature death and (*b*) that the risk can be further differentiated by adding additional adult socioeconomic indicators (use of a car and area based deprivation category) to the cumulative social class indicator are likely to be generalisable to other populations.

The cumulative social class indicator shows graded associations with most of the risk factors and morbidity measures included in our study. Strong associations with mortality were also evident. Adjustment for risk factors measured in adulthood attenuated the association of social class with mortality from cancer and from non-cancer, non-cardiovascular causes more than it did that with mortality from cardiovascular disease. This may partly reflect the fact that a major risk factor for coronary heart disease—serum cholesterol concentration—was higher in the group with the more favourable socioeconomic experience.

The use of a cumulative social class indicator does not take into account directions of social class change. Thus a participant whose father had had a manual occupation, whose first occupation had been manual, and who had a non-manual occupation at screening would be in the same group as a participant whose father had had a non-manual occupation and who had manual occupations both at first and at screening. Other studies have suggested that social mobility is not an important contributor to overall mortality differentials,[30] and detailed analyses of our data (to be reported elsewhere) show this too. We repeated the mortality analyses using all combinations of social class and found that the associations of mortality with cumulative social class were generally not dependent on the order in which different social classes came (basic tables available from us).

Socioeconomic position in childhood and mortality

There has been particular interest in the association between living conditions in childhood and risk of coronary heart disease in adult life. This follows from the work of Forsdahl, who suggested that early deprivation followed by later affluence increased the risk of coronary heart disease, an effect in part mediated by an increase in blood cholesterol concentrations.[31 32] The attribution of increased risk of coronary heart disease to an interaction between poor socioeconomic circumstances in early life and later affluence has received little support from subsequent studies.[9 10 33] Similarly, the suggestion that the effects of deprivation in early life are mediated through high blood cholesterol concentrations in adulthood has not been substantiated in later investigations.[33] In our cohort men with fathers of a manual social class had lower, rather than higher, serum cholesterol concentrations than men with fathers of a non-manual social class.[34] In contrast to these negative assessments of the Forsdahl hypothesis, the basic notion that unfavourable socioeconomic conditions in childhood predispose to increased risk of coronary heart disease in adulthood has received more support. Most[9 11 13 33 35-37] but not all[10 38] studies have found an association of childhood socioeconomic circumstances with risk of coronary heart disease, which was apparently not purely due to the adverse social conditions in adulthood of those born into poor circumstances. In a Swedish census follow up study men with fathers who had manual occupations had considerably higher risk of dying from coronary heart disease than had those whose fathers had non-manual occupations.[35] For mortality from all causes this was much less evident, mortality being dependent on social class in adulthood much more than social class in childhood. This particular dependence of the risk of coronary heart disease on socioeconomic circumstances in childhood has also been observed in area based studies from Finland.[39 40] Our study had similar findings, father's social class being particularly important for mortality from cardiovascular disease but not for mortality from cancer or non-cardiovascular, non-cancer causes. Analyses of the association between height and cause specific mortality, in which height is taken to be an indicator of childhood circumstances, show similar specificity.[41] These findings are clearly relevant to the hypothesis that fetal development is associated with the risk of cardiovascular disease in later life[42] as parental social class will influence early development. Socioeconomic factors in childhood will also influence growth, and recent evidence suggests that poor growth in childhood is also associated with higher mortality from cardiovascular disease in adulthood.[43] Studies with data covering all stages of development are needed to determine which stages of development most affect the risk of cardiovascular disease in adulthood.

Conclusions

Our data show a clear cumulative effect of socioeconomic circumstances acting over a life time. Combining the cumulative social class index with additional indicators of socioeconomic position in adulthood led to further differentiation of the risk of premature death. This has important implications for studies that try to control for socioeconomic factors when analysing outcomes in relation to socially patterned exposures. Single measures of adult social class, traditionally used in such studies, will not adequately capture the full extent of socioeconomic differentials between groups with different exposures. Statistical adjustment for these single measures will therefore not control for socioeconomic differences, and apparently independent risk relations may remain confounded by factors related to socioeconomic environment.[44]

Specific patterns emerge within the general picture of higher death rates among people with less favourable socioeconomic trajectories during their lives.

Key messages

- Health and risk of premature death are determined by socioeconomic factors acting throughout life
- Socioeconomic influences on particular causes of death may have different critical times
- The risk of premature death from cardiovascular disease is particularly sensitive to socioeconomic influences acting in early life
- Studies with data on socioeconomic circumstances at only one stage of life are inadequate for fully elucidating the contribution of socioeconomic factors to health

Firstly, mortality from cardiovascular disease seems to be more strongly related to cumulative social disadvantage than does that from cancer or non-cardiovascular, non-cancer causes.

Secondly, whereas social class in adulthood is the more important socioeconomic indicator over a life time for differentiating groups with differing risks of mortality from cancer and non-cardiovascular, non-cancer causes, the socioeconomic environment in childhood seems to be particularly important with respect to mortality from cardiovascular disease. These findings should help direct the attention of disease specific aetiological research to influences acting both in childhood and in adult life.

The Department of Health's report *Variations in Health* has directed attention to the accumulation of socially patterned adverse exposures over a life time.[17] Our results add to the as yet limited data that show the necessity of such an approach. Any serious attempt to elucidate the contributions of socially distributed risk factors to the risk of disease in adulthood should aim to collect information covering the entire lifespan of study participants.[14]

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Interaction of workplace demands and cardiovascular reactivity in progression of carotid atherosclerosis: population based study

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Abstract

Objective: To examine the combined influence of workplace demands and changes in blood pressure induced by stress on the progression of carotid atherosclerosis.

Design: Population based follow up study of unestablished as well as traditional risk factors for carotid atherosclerosis, ischaemic heart disease, and other outcomes.

Setting: Eastern Finland.

Subjects: 591 men aged 42-60 who were fully employed at baseline and had complete data on the measures of carotid atherosclerosis, job demands, blood pressure reactivity, and covariates.

Main outcome measures: Change in ultrasonographically assessed intima-media thickness of the right and left common carotid arteries from baseline to 4 year follow up.

Results: Significant interactions between workplace demands and stress induced reactivity were observed for all measures of progression ($P < 0.04$). Men with large changes in systolic blood pressure (20 mm Hg or greater) in anticipation of a maximal exercise test and with high job demands had 10-40% greater progression of mean (0.138 *v* 0.123 mm) and maximum (0.320 *v* 0.261 mm) intima-media thickness and plaque height (0.347 *v* 0.264) than men who were less reactive and had fewer job demands. Similar results were obtained after excluding men with prevalent ischaemic heart disease at baseline. Findings were strongest among men with at least 20% stenosis or non-stenotic plaque at baseline. In this subgroup reactive men with high job demands had more than 46% greater atherosclerotic progression than the others. Adjustment for atherosclerotic risk factors did not alter the results.

Conclusions: Men who showed stress induced blood pressure reactivity and who reported high job demands experienced the greatest atherosclerotic progression, showing the association between dispositional risk characteristics and contextual determinants of disease and suggesting that behaviourally evoked cardiovascular reactivity may have a role in atherogenesis.

Introduction

People's susceptibility to disease varies widely and may be a reflection of differences in biological predispositions, personality, behaviour, and environmental exposures. In addition, psychological stress is commonly believed to play an important part in illness and premature death, particularly with respect to cardiovascular diseases.

One model that may explain why some people under great stress develop cardiovascular diseases or other illnesses and others do not is the diathesis-stress model of disease susceptibility. This model assumes that a biological predisposition to disease will be expressed only if a predisposed individual is exposed to unusual or prolonged stress.[1] One mechanism by which stress may be associated with cardiovascular diseases is hyperreactivity of the sympathetic nervous system, which manifests as exaggerated increases in blood pressure or heart rate in response to psychological or behavioural stressors.[2 3] In the diathesis-stress framework behaviourally evoked reactivity is considered to be a biological predisposition of an individual that is expressed and consequently leads to cardiovascular diseases only under high stress conditions.[1]

Situations in which stress induced reactivity may be elicited differ between people. The work environment is probably an important source of stress for most adults.[4] Furthermore, previous studies indicate that stressful jobs have a role in the illness and death caused by cardiovascular disease.[4-6] We used the diathesis-stress model to examine the interactive effects of blood pressure reactivity to stress and high workplace demands on the progression of carotid atherosclerosis. This report is from the Kuopio ischaemic heart disease risk factor study, an ongoing, population based study of previously unestablished risk factors for carotid atherosclerosis, ischaemic heart disease, mortality, and other outcomes among middle aged men from the Kuopio region in Eastern Finland, an area of high coronary morbidity and mortality.[7 8]

Subjects and methods

A total of 2682 men aged 42, 48, 54, and 60 (82.9% of those eligible) were recruited for the baseline examination, which occurred between March 1984 and December 1989. Follow up examinations were conducted between March 1991 and December 1993 in men who had undergone ultrasound examination of the right and left carotid arteries at baseline. Of the 1229 men who were eligible for the follow up examination, 1038 (88.2%) participated, 107 refused, 52 could not participate because they had died, had severe illness, or had moved, and 32 could not be contacted. Average time to follow up was 4.2 years (range 3.9-5.1 years).

We excluded subjects if they were not fully employed at the time of the baseline examination (348 men), did not participate in the bicycle ergometer test because of scheduling difficulties (72), or had missing data on the covariates at baseline (27). Therefore, the results reported here are based on 591 men who were fully employed and had complete data on the job

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demands scale, the measure of anticipatory blood pressure reactivity, all covariates at baseline, and measurements of intima-media thickness at baseline and follow up. A comparison of the 447 subjects who were excluded with the 591 subjects with complete data found no significant differences in resting systolic blood pressure, body mass index, or mean intima-media thickness at baseline, although the subjects who were excluded were older (55.1 *v* 48.6 years, $P < 0.0001$).

Baseline and follow up examinations

Examinations were carried out over two days, one week apart, at both baseline and follow up and consisted of a wide variety of biochemical, physiological, anthropometric, and psychosocial tests, including a questionnaire on workplace demands and characteristics (see job demands scale). In addition, a maximal exercise tolerance test on an upright bicycle ergometer was administered at baseline. Medical history and drug treatment were checked during a medical examination at both baseline and follow up.

Blood pressure measurement

Blood pressure readings were obtained on two occasions by a trained observer using a random zero muddler sphygmomanometer (Hawksley). The protocol on the first examination day was as follows. Subjects rested supine for 15 minutes and blood pressure was measured at 5, 10, and 15 minutes; they then stood at rest and blood pressure was taken once after 1 minute; they finally sat at rest for 10 minutes, and blood pressure was measured at 5 and 10 minutes. Blood pressure while subjects were seated was also measured on the second examination day, one week later, after the subject had been seated on the bicycle ergometer for 5 minutes but before the exercise test protocol was begun. Measurements on both examination days were taken in the mornings.

Cardiovascular reactivity

The measure of reactivity used in this study was change in systolic blood pressure in anticipation of the exercise test (blood pressure after five minutes of seated rest on the bicycle ergometer before the start of the exercise test), which was calculated as the difference between the blood pressure reading while seated before exercise and the average of the two resting blood pressure readings while seated on the first examination day. The anticipation of exercise is characterised by emotional, behavioural, and physiological arousal attendant to the impending challenge. Blood pressure increases during this anticipatory period thus reflect cardiovascular adjustments in response to psychological and behavioural stress. In this study men with a systolic response of 20 mm Hg or greater were considered to be high reactors (45.7%). This measure of reactivity is a significant, independent predictor of incident hypertension in this population.[9]

Job demands scale

As part of the baseline examination participants completed a detailed questionnaire that included items about their work environment. The measure of job demands used in this study was an 11 item scale developed by Lynch *et al*[10] that conformed to important theoretical dimensions of the work environment.[4 5 11] Using a four point Likert response, respondents indicated how much stress they experienced from excessive supervision of time schedules, troublesome supervisors, troublesome coworkers, job responsibilities, poorly defined tasks and responsibilities, risk of accidents, risk of unemployment, and irregular work schedules. They were also asked to indicate how often they had work deadlines and how much stress this caused them and to rate both the mental and physical strenuousness of their work. Individual items were dichotomised such that only men reporting more than average strain or stress for any given item were considered positive for that item. The 11 dichotomised items were then summed to create the job demands scale score, which had a mean of 3.0 and range of 0-11 in the full sample, with Cronbach's α of 0.78. We considered men with a score of 4 or greater on the job demands scale to have high job demands. This cut off point was selected because it represented the upper quartile (26%) of the distribution of job demands scores in this population. Scores on the job demands scale were imputed based on non-missing items for men who had two or fewer items with missing responses (5%); those with more than two missing items were excluded from analyses. This scale predicts mortality and acute myocardial infarction in this population.[10]

Measurement of carotid atherosclerosis

The extent of carotid atherosclerosis was assessed by high resolution B mode ultrasonography of the right and left common carotid arteries in a 1.0-1.5 cm section at the distal end, proximal to the carotid bulb. Images were focused on the posterior wall of the right and left common carotid arteries and recorded on videotape for later analysis. Near wall images were not obtained because of their greater variability in measurement.[12] Ultrasound examinations at baseline and follow up were conducted by one of four sonographers who had been trained for a minimum of six months, and they were performed with the subject lying supine after a 15 minute rest. Details of the scanning protocol, technical aspects of measurement, and their reliability have been described elsewhere.[13]

At baseline arterial images were obtained using the ATL UM4 duplex ultrasound system with a 10 MHz sector transducer (Advanced Technology Laboratories, Bothell, WA). At follow up images were obtained with a Biosound Phase 2 scanner equipped with a 10 MHz annular array probe.[13] Wedge phantom studies of this system, calibrated against a 414B tissue phantom (Radiation Measurement, Middleton, WI), have shown measurement precision of 0.03 mm.[14 15]

Intima-media thicknesses were measured at baseline and follow up by computerised analysis of the videotaped ultrasound images using Prosound software (University of Southern California, Los Angeles, CA). This software uses an edge detection algorithm specifically designed for use with ultrasound imaging and permits automatic detection, tracking, and recording of the interfaces between intima and lumen and media and adventitia.[16] Intima-media thickness, calculated as the mean distance between these interfaces, was estimated at around 100 points in both the right and left common carotid arteries.

We used three measures of intima-media thickness: (*a*) mean intima-media thickness, calculated as the mean of all estimates from the right and left common carotid arteries and considered an overall measure of the atherosclerotic process in the carotid arteries; (*b*) maximum intima-media thickness, the average of the points of maximum thickness from the right and left common carotid arteries and indicative of the depth of intrusion of atherosclerotic thickening into the lumen in this part of the arteries; and (*c*) plaque height, the average of plaque height in the right and left common carotid arteries, calculated as the difference between maximum and minimum thickness, and an assessment of how steeply atherosclerotic lesions protruded into the lumen. Progression of atherosclerosis was estimated as follow up minus baseline values for each of these measures.

Baseline covariates

Biological risk factors—Resting systolic blood pressure was calculated as the average of the last two supine and the two seated blood pressure measurements obtained on the first examination day. Apolipoprotein B concentration was determined by an immunoturbidimetric method (KONE, Espoo, Finland). High density lipoprotein cholesterol-2, the protective subfraction of high density lipoprotein cholesterol, was separated from fresh plasma using ultracentrifugation and precipitation and its concentration measured enzymatically (CHOD-PAP cholesterol method, Boehringer Mannheim, Mannheim, Germany). Blood glucose concentration was measured in whole blood samples after at least 12 hours of overnight fasting by the glucose dehydrogenase method after precipitation of the proteins with trichloroacetic acid (Granutest 100, Merck, Darmstadt, Germany). Body mass index was calculated as weight divided by height squared (kg/m^2).

Behavioural and educational factors—Alcohol consumption was assessed by a questionnaire on drinking behaviour over the previous 12 months and from dietary records over four days. Cigarette smoking was assessed by self report of never, former, and current smoking (measured in pack years). Education was assessed by self report of completed years of schooling.

Drug treatment—The use of drugs to treat hypertension and hyperlipidaemia was assessed at baseline by interview.

History of diabetes—A participant was considered to have a history of diabetes if he reported having taken drugs for or used diet to control diabetes or if he had a fasting blood glucose concentration of 6.7 mmol/l or greater at baseline.

Evaluation of prevalent ischaemic heart disease—Participants were considered to have prevalent ischaemic heart disease at baseline if they had a history of angina or myocardial infarction; if they currently took drugs for angina; or if they had positive findings of angina according to the Rose questionnaire.[17]

Data analyses

We examined the influence of workplace demands and cardiovascular reactivity on the progression of atherosclerosis over four years by estimating the mean change in each measure of intima-media thickness (mean, maximum, plaque height) according to low *v* high job demands and low *v* high reactors. These dichotomous variables and their product interaction term were entered as predictors into our linear regression models. Two sets of regression models were calculated. The initial model included adjustments for age, baseline intima-media thickness, zooming depth of the ultrasound scan, sonographer, and participation in the placebo or treatment arm of an unrelated clinical trial of pravastatin.[18] The second model included all variables in the initial model plus variables representing systolic blood pressure, apolipoprotein B concentration, high density lipoprotein cholesterol-2 concentration, body mass index, cigarette smoking, alcohol consumption, use of antihypertensive or antihyperlipidaemic drugs, and history of diabetes.

Analyses were performed using the general linear models procedure in SAS, version 6.09,[19] installed on a Sun Sparcstation 20. This procedure allowed least square mean values of intima-media thickness to be estimated and contrasted for each job demands/reactor group while simultaneously controlling for age and other covariates.

Table 1 Baseline covariates according to job demands and reactivity. Values are means (SD) unless stated otherwise

	Low job demands		High job demands	
	Low reactors (n=233)	High reactors (n=192)	Low reactors (n=88)	High reactors (n=78)
Job demands scale	1.7 (0.8)	1.8 (0.8)	5.0 (1.3)	5.0 (1.1)
Systolic pressure response (mm Hg)	8.5 (7.2)	31.6 (9.5)	9.3 (7.3)	33.0 (10.5)
Age (years)	47.6 (5.4)	50.7 (5.9)	47.8 (5.4)	51.6 (5.6)
Education (years)	10.9 (3.9)	9.5 (3.4)	9.4 (3.6)	9.3 (4.0)
Intima-media thickness (mm):				
Mean	0.70 (0.13)	0.76 (0.15)	0.73 (0.20)	0.77 (0.21)
Maximum	0.87 (0.17)	0.94 (0.20)	0.91 (0.27)	0.97 (0.29)
Plaque height (mm)	0.35 (0.13)	0.37 (0.14)	0.37 (0.17)	0.41 (0.22)
Resting systolic pressure (mm Hg)	131.2 (16.2)	131.9 (13.5)	132.2 (15.6)	130.8 (12.8)
Apolipoprotein B (mmol/l)	2.58 (0.60)	2.63 (0.53)	2.57 (0.54)	2.62 (0.51)
High density lipoprotein cholesterol 2 (mmol/l)	0.89 (0.30)	0.88 (0.27)	0.87 (0.28)	0.87 (0.28)
Blood glucose (mmol/l)	4.70 (1.08)	4.72 (1.21)	4.57 (0.54)	4.51 (0.46)
Body mass index (kg/m^2)	26.9 (3.6)	26.7 (3.2)	26.2 (2.9)	26.6 (3.1)
No (%) of subjects:				
Drinking alcohol (drinks/day):				
None	21 (9)	22 (12)	8 (9)	8 (10)
>2	61 (26)	37 (19)	18 (21)	15 (19)
Smoking:				
Never	76 (33)	52 (27)	29 (33)	23 (30)
Formerly	80 (34)	70 (37)	31 (35)	32 (41)
Currently	77 (33)	70 (36)	28 (32)	23 (30)
Receiving drug treatment:				
Antihyperlipidaemic agent	0	2 (1)	1 (10)	1 (1)
Antihypertensive agent	24 (10)	25 (13)	10 (11)	13 (17)
With diabetes	10 (4)	5 (3)	1 (1)	2 (3)

Results

Table 1 shows scores on the job demands scale, change in systolic blood pressure in anticipation of exercise, age, intima-media thicknesses at baseline, and other covariates by job demands and reactivity.

Demands, reactivity, and atherosclerotic progression

Table 2 shows age adjusted scores for changes in mean and maximum intima-media thickness and plaque

Table 2 Progression of carotid atherosclerosis over four years according to job demands and reactivity in 591 Finnish men. Values are mean (SE) increases in millimetres

	Low job demands		High job demands		
	Low reactors (n=233)	High reactors (n=192)	Low reactors (n=88)	High reactors (n=78)	P value for interaction
Model 1*					
Intima-media thickness:					
Mean	0.123 (0.008)	0.109 (0.009)	0.099 (0.013)	0.138 (0.013)	<0.014
Maximum	0.261 (0.013)	0.267 (0.013)	0.238 (0.020)	0.320 (0.021)	<0.021
Plaque height	0.264 (0.013)	0.289 (0.013)	0.255 (0.020)	0.347 (0.021)	<0.04
Model 2†					
Intima-media thickness:					
Mean	0.122 (0.008)	0.106 (0.009)	0.093 (0.013)	0.134 (0.013)	<0.008
Maximum	0.261 (0.013)	0.262 (0.013)	0.228 (0.020)	0.312 (0.021)	<0.013
Plaque height	0.264 (0.013)	0.282 (0.013)	0.246 (0.020)	0.340 (0.020)	<0.022

*Adjusted for age, baseline intima-media thickness, ultrasound zooming depth, sonographer, and participation in placebo or treatment arms of Kuopio artherosclerosis prevention study.[18]
†Includes adjustments from model 1 plus covariates representing education, resting systolic blood pressure, apolipoprotein B concentration, high density lipoprotein cholesterol-2 concentration, fasting blood glucose concentration, former and current smoking, body mass index, alcohol consumption, use of antihyperlipidaemic or antihypertensive drugs, and history of diabetes.

Table 3 Progression of carotid atherosclerosis over four years according to job demands and reactivity in 518 men without prevalent ischaemic heart disease. Values are mean (SE) increases in millimetres*

	Low job demands		High job demands		
	Low reactors (n=216)	High reactors (n=168)	Low reactors (n=77)	High reactors (n=57)	P value for interaction
Intima-media thickness:					
Mean	0.122 (0.008)	0.110 (0.008)	0.112 (0.012)	0.126 (0.014)	<0.15
Maximum	0.256 (0.012)	0.255 (0.012)	0.252 (0.019)	0.290 (0.021)	<0.20
Plaque height	0.262 (0.013)	0.276 (0.013)	0.257 (0.020)	0.324 (0.022)	<0.12

*Adjusted for age, baseline intima-media thickness, ultrasound zooming depth, sonographer, and participation in placebo or treatment arms of Kuopio artherosclerosis prevention study.[18]

Table 4 Progression of carotid atherosclerosis over four years according to job demands and reactivity and degree of stenosis at baseline. Values are mean (SE) increases in millimetres*

	Low job demands		High job demands		P value for interaction
	Low reactors	High reactors	Low reactors	High reactors	
Carotid stenosis ≥20% or presence of non-stenotic atherosclerotic plaque					
No of subjects	34	54	13	20	
Intima-media thickness:					
Mean	0.118 (0.026)	0.097 (0.021)	0.004 (0.044)	0.173 (0.034)	<0.003
Maximum	0.250 (0.044)	0.252 (0.037)	0.134 (0.074)	0.420 (0.059)	<0.0095
Plaque height	0.255 (0.040)	0.272 (0.035)	0.280 (0.070)	0.418 (0.056)	<0.24
Carotid stenosis <20%					
No of subjects	199	138	75	58	
Intima-media thickness:					
Mean	0.123 (0.009)	0.113 (0.010)	0.112 (0.013)	0.120 (0.014)	<0.40
Maximum	0.262 (0.013)	0.276 (0.015)	0.254 (0.020)	0.279 (0.021)	<0.71
Plaque height	0.257 (0.014)	0.296 (0.014)	0.253 (0.019)	0.310 (0.021)	<0.56

*Adjusted for age, baseline intima-media thickness, ultrasound zooming depth, sonographer, and participation in placebo or treatment arms of Kuopio artherosclerosis prevention study.[18]

height for the four groups from both the initial and fully adjusted models. Significant interactions between self reported job demands and reactivity were noted for progression of mean intima-media thickness ($\beta = 0.052$, 95% confidence interval 0.011 to 0.093, SE 0.021, $P < 0.014$), maximum intima-media thickness ($\beta = 0.076$, 0.012 to 0.141, SE 0.033, $P < 0.021$), and plaque height ($\beta = 0.067$, 0.003 to 0.131, SE 0.033, $P < 0.04$). Men who reported high job demands and who were high reactors had the largest increases in mean and maximum intima-media thickness and plaque height over the four years of follow up (table 2). Results were essentially unchanged after including adjustments for education, resting systolic blood pressure, apolipoprotein B concentration, high density lipoprotein cholesterol-2 concentration, body mass index, former and current smoking, alcohol consumption, use of drugs for hypertension or hyperlipidaemia, and history of diabetes. Indeed, the group with high demands and high reactivity showed 10-40% greater atherosclerotic progression than the other groups, even after adjustment for the various risk factors.

Demands, reactivity, and atherosclerotic progression in men without prevalent ischaemic heart disease

Table 3 shows mean (SE) changes in mean and maximum intima-media thickness and plaque height for the four groups, excluding 73 men with prevalent ischaemic heart disease at baseline. The pattern of findings was similar, albeit slightly weaker, to that in the full sample, with interactions between job demands and reactivity noted for each measure of atherosclerotic progression ($\beta = 0.03$, -0.011 to 0.070, SE 0.021, $P < 0.15$ for mean intima-media thickness; $\beta = 0.04$, -0.021 to 0.100, SE 0.031, $P < 0.20$ for maximum intima-media thickness; and $\beta = 0.052$, -0.013 to 0.117, SE 0.033, $P < 0.12$ for plaque height). Men with high job demands and high reactivity had a 13-15% greater increase in maximum intima-media thickness and a 17-26% greater increase in plaque height relative to the other groups. Adjustment for atherosclerotic risk factors in this subgroup did not alter the size of these differences (data not shown).

Demands, reactivity, and atherosclerotic progression by degree of stenosis at baseline

Table 4 shows the mean values of the three measures of atherosclerotic progression for the four groups according to the presence of carotid stenosis or non-stenotic atherosclerotic plaque at baseline.

Among the 121 men with at least 20% carotid stenosis or evidence of non-stenotic atherosclerotic plaque at baseline there were significant interactions between job demands and reactivity for progression of mean and maximum media-intima thickness ($\beta = 0.189$, 0.065 to 0.313, SE 0.063, $P < 0.003$ and $\beta = 0.284$, 0.073 to 0.495, SE 0.108, $P < 0.0095$ respectively); the interaction for plaque height was almost significant ($\beta = 0.121$, -0.080 to 0.323, SE 0.103, $P < 0.24$). Men with high job demands and reactivity showed the greatest increases in mean and maximum intima-media thickness and plaque height from baseline to follow up, being more than 46% larger than those in the other groups. Models that included adjustments for atherosclerotic risk factors produced essentially the same patterns of results for both strata (data not shown). No interactions between job demands and reactivity were seen in the men without advanced thickening at baseline. However, high reactors showed greater progression of plaque height than low reactors (0.303 *v* 0.255 mm, $P < 0.037$). No differences were noted for mean or maximum intima-media thickness in this subgroup.

Discussion

We found a significant interaction between cardiovascular reactivity and reported job demands such that men who showed a heightened increase in systolic blood pressure before an exercise stress test and who reported a highly demanding work environment experienced greater progression of carotid atherosclerosis than men who were less reactive or had fewer job demands, or both. This interaction was observed for the measures of mean and maximum intima-media thickness and plaque height and was largely unaffected by adjustment for known atherosclerotic risk factors. A similar, albeit slightly weaker, pattern of findings was seen in the subset of healthy men without prevalent ischaemic heart disease at baseline. However, the strongest associations were seen among men with early evidence of atherosclerosis, suggesting that the combined effects of stress induced reactivity and high job demands may be more pronounced once atherosclerotic plaque or measurable stenosis has occurred.

Support for diathesis-stress model of disease

Our data clearly show that dispositional characteristics of the individual, in combination with the work environment, are importantly related to disease progression. These findings support the diathesis-stress model of disease susceptibility, which emphasises the synergistic relation between dispositional risk characteristics and contextual determinants of diseases. Moreover, our results provide some of the clearest human evidence to date that stress induced cardiovascular reactivity may play a part in atherogenesis. Additional support for this hypothesis comes from research in cynomolgus macaques which has shown that heightened sympathetic nervous system arousal and endothelial injury induced by psychosocial stressors (threat of capture, social disruption, and reorganisation) potentiate diet induced coronary and carotid atherosclerosis.[20-22] Interestingly, these psychosocially mediated effects are abolished after administration of β adrenergic antagonists.[3 22]

Interpretation of results

Our consistent results across the measures of mean and maximum intima-media thickness and plaque height suggest that the interactive effects of heightened blood pressure responses and high job demands influence the overall atherosclerotic process and contribute to the development or progression of focal lesions of the common carotid arteries. Increased arterial wall roughness with steeply projecting lesions may lead to greater shear stress and flow turbulence on the vessel walls, thereby increasing the likelihood of plaque rupture and thrombus formation.[22] Furthermore, although the differential pathological and clinical significance of the three measures of carotid atherosclerosis used in this study remains to be determined, cross sectional data from the entire Kuopio ischaemic heart disease risk factor study sample showed that each 0.10 mm difference in maximum thickness was associated with an 11% increase in risk of acute myocardial infarction ($P < 0.001$).[13]

The relations between behaviourally evoked reactivity and high job demands and atherosclerotic progression identified in our study were essentially unchanged after adjustments for known atherosclerotic risk factors, including resting blood pressure, lipoprotein concentrations, alcohol and cigarette consumption, body mass index, and education. This relative lack of confounding is somewhat surprising because of the strength of the known associations between these risk factors and atherosclerosis.[24 25] However, the cumulative effect of these variables on atherosclerosis may be accounted for by their associations with baseline intima-media thickness, which is a highly significant covariate in all models.

Key messages

- Psychological stress plays an important part in the illness and premature death associated with cardiovascular disease, but individual susceptibility to disease varies according to biological predispositions, personality, behaviour, and environmental exposures
- This study found that a demanding work environment in combination with a predisposition to exaggerated blood pressure reactivity to stress was significantly related to progression of carotid atherosclerosis over four years among employed middle aged men and was independent of known atherosclerotic risk factors
- These findings support the role of stress induced reactivity in human atherogenesis
- Future research needs to confirm these findings in other populations and to examine the influence of other risk factors and environments on the progression of disease

Conclusions

Our findings are limited to employed, middle aged white men. Additional research is needed to determine if these relations are also evident in non-white or female populations or among other age groups. Given that men and women are often employed in different occupational sectors and may perceive and experience workplace demands and job stress differently from one another, it is particularly important to examine the influence of sex differences on these associations. Furthermore, work is only one aspect of life. Therefore, it is important to consider a variety of social and interpersonal contexts that may be potential sources of stress in individuals' daily lives. The diathesis-stress model offers a valuable framework within which future research may be conducted and for examining the relations between various dispositional traits and work or other environments in relation to cardiovascular diseases and other illnesses.

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Low job control and risk of coronary heart disease in Whitehall II (prospective cohort) study

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See editorial by Haines and Smith and pp 541, 547, 553, 591

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Abstract

Objective: To determine the association between adverse psychosocial characteristics at work and risk of coronary heart disease among male and female civil servants.

Design: Prospective cohort study (Whitehall II study). At the baseline examination (1985-8) and twice during follow up a self report questionnaire provided information on psychosocial factors of the work environment and coronary heart disease. Independent assessments of the work environment were obtained from personnel managers at baseline. Mean length of follow up was 5.3 years.

Setting: London based office staff in 20 civil service departments.

Subjects: 10 308 civil servants aged 35-55 were examined—6895 men (67%) and 3413 women (33%).

Main outcome measures: New cases of angina (Rose questionnaire), severe pain across the chest, diagnosed ischaemic heart disease, and any coronary event.

Results: Men and women with low job control, either self reported or independently assessed, had a higher risk of newly reported coronary heart disease during follow up. Job control assessed on two occasions three years apart, although intercorrelated, had cumulative effects on newly reported disease. Subjects with low job control on both occasions had an odds ratio for any subsequent coronary event of 1.93 (95% confidence interval 1.34 to 2.77) compared with subjects with high job control at both occasions. This association could not be explained by employment grade, negative affectivity, or classic coronary risk factors. Job demands and social support at work were not related to the risk of coronary heart disease.

Conclusions: Low control in the work environment is associated with an increased risk of future coronary heart disease among men and women employed in government offices. The cumulative effect of low job control assessed on two occasions indicates that giving employees more variety in tasks and a stronger say in decisions about work may decrease the risk of coronary heart disease.

Introduction

In the first Whitehall study men in the lower grades of the British civil service had nearly three times the 10 year risk of mortality from coronary heart disease compared with men in the higher grades.[1] Less than half of this gradient could be explained by accepted coronary risk factors, and we speculated that psychosocial factors may provide some of the missing predictive power. As we examined differences in employment grade with coronary heart disease,

psychosocial work characteristics became a logical subject to study.[2]

Studies using Karasek's job strain model have shown higher cardiovascular risk in jobs characterised by high demands and low control.[3-5] An analysis of British occupational mortality suggested that high demands were less important predictors of mortality than low control.[2] In the Whitehall II study people in the high grades, who have lower coronary risk, have higher demands than the low grades. Low control therefore seemed to be more promising.[6 7]

The longitudinal phase of the Whitehall II study allowed us to examine the relation between the psychosocial work environment and newly reported cases of coronary heart disease. In particular, it enabled us to test whether low control is more strongly related to coronary heart disease than is the full job strain model. Furthermore, this study allowed us to examine both men and women[5]; the possible role of reporting bias (using a measure of negative affectivity)[8-11]; and the cumulative effects of adverse work characteristics by using measures of low control assessed on two occasions.[12 13] A methodological advance is the use of an independent measure of control. By having an independent assessment as well as a self report of the work environment, the study could address the question of whether job stress is influenced by (subjective) perceptions or by more objective appraisals of the work, or by both.[14]

Subjects and methods

Study population

The Whitehall II study is the sequel to the first Whitehall study, which began in 1967.[1 15] The Whitehall II study was set up primarily to investigate the degree and causes of the social gradient in illness rates; to study work characteristics, social support, and additional factors related to the gradient in mortality; and, importantly, to include women. In the study a new cohort of civil servants was established between 1985 and 1988 (phase 1). All male and female civil servants aged between 35 and 55 in 20 London based civil service departments were sent an introductory letter and screening questionnaire and were offered a screening examination for cardiovascular diseases. The response rate was 73%. The true response rate would probably have been higher, however, because about 4% of the civil servants on the lists provided by the civil service had moved before the study and were therefore not eligible for inclusion. In total, 10 308 civil servants were examined—6895 men (67%) and 3413 women (33%).

After the initial participation in phase 1 the participants were approached again in 1989-90 (phase 2: postal questionnaire) and in 1991-3 (phase 3: postal questionnaire and screening examination). The participation rates at these two phases were 79% and 83% respectively; 7372 subjects (72%) participated in all three phases and 9302 subjects (90.2%) participated in either phase 2 or 3. Furthermore, although still eligible for participation, 1286 subjects (12.5%) had left the civil service before phase 3. The length of follow up was 5.3 years on average, with a range of 3.7 to 7.6 years. Full details of the screening examinations are reported elsewhere.[7 16]

Coronary heart disease

Four indicators of coronary heart disease were analysed: angina, severe pain across the chest, diagnosed ischaemic heart disease, and any coronary event. Angina was measured by the Rose questionnaire and defined as pain located over the sternum or in both the left chest and the left arm that is precipitated by exertion, that causes the person to stop, and that goes away in 10 minutes or less.[17] Severe pain across the chest was defined as having ever had a severe pain across the front of the chest lasting half an hour or more. Diagnosed ischaemic heart disease depended on whether the subject reported that a general practitioner or hospital doctor had ever suspected or confirmed myocardial infarction or angina. Subjects could report more than one of these outcomes. Reports of any of these three outcomes were coded as any coronary event. The outcomes were assessed at all three phases.

Work characteristics

Two methods were used to assess the psychosocial work environment: self reports by the civil servants and ratings by personnel managers (independent assessments). The self report items were derived from well known questionnaires for the central components of the job strain model—that is, job demands, job control, and social support (appendix).[3 4 18 19] As the results with specific subconstructs, such as skill discretion and social support from colleagues, did not differ from the results with the three main constructs, we focused on the main constructs (job control, job demands, social support). After all items were recoded in the same direction scores for each scale were calculated as the sum of the item scores. Subjects who did not answer one item in a scale were assigned an average score based on the items that they did answer. Self reported work characteristics were available at all three phases. In addition, at phase 1 personnel managers assessed each job in terms of work pace, the importance of not making mistakes, conflicting demands, and the degree of control (appendix). In 18 out of 20 departments 140 well informed personnel managers undertook these ratings. Detailed information was obtained on individual jobs because 5766 different jobs were filled by 8838 subjects.

Statistical analysis

The logistic regression model was used to estimate the strength of the association between the psychosocial work characteristics in thirds at phase 1 and the occurrence of newly reported coronary heart disease at phase 2 or 3. Tests for trends were also performed by modelling the group scores of each work characteristic (1, 2, 3) as one variable. The corresponding odds ratio reflects the increase in the odds of new coronary heart disease per unit increase in this variable. To examine their independent impact on new coronary heart disease, self reported and independently assessed work characteristics were simultaneously controlled. By using both phase 1 and 2 self reported work characteristics as predictive factors, further insight was obtained into their cumulative effects on coronary heart disease reports at phase 3 (phase 1 and 2 were about three years apart). Several multivariate logistic regression models provided further insight into the extent to

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Table 1 Numbers (percentages) of baseline and new cases of angina, severe chest pain, diagnosed ischaemic heart disease, and any coronary event among 6895 men and 3413 women

	Phase 1	Phase 2 or 3*
Angina:		
Men	164 (2.4)	177 (3.7)
Women	134 (4.0)	151 (7.0)
Severe chest pain:		
Men	433 (6.3)	258 (5.5)
Women	193 (5.7)	145 (6.8)
Diagnosed ischaemic heart disease:		
Men	84 (1.2)	124 (2.5)
Women	15 (0.4)	42 (1.8)
Any coronary event:		
Men	595 (8.7)	401 (8.8)
Women	319 (9.5)	253 (12.3)

*Excluding baseline cases at phase 1 and non-participants at phase 2 or 3.

Table 2 Mean self reported job control by sex and employment grade at phase 1

	Men		Women	
	No	Mean (SD) score*	No	Mean (SD) score*
Employment grade:				
1 (High)	1007	78.3 (9.9)	117	77.3 (10.6)
2	1627	73.8 (11.1)	261	73.4 (11.6)
3	1223	71.5 (11.1)	197	71.8 (11.8)
4	1490	66.6 (12.3)	475	67.2 (12.5)
5	879	61.2 (13.8)	655	59.5 (14.0)
6 (Low)	634	46.5 (17.0)	1635	47.7 (16.1)
Total	6860	68.4 (15.0)	3340	57.2 (18.0)

*Continuous self reported job control was rescaled to variable ranging from 0 (low) to 100 (high).

which adverse work characteristics affected the future reporting of coronary heart disease, independent of employment grade, negative affectivity, and classic coronary risk factors.

Negative affectivity is the disposition to respond negatively to questionnaires and may inflate correlations between self reported work characteristics and self reported disease.[8-11] Negative affectivity was measured with the negative affect subscale of the affect balance scale.[20 21]

Coronary risk factors included smoking (never smoked, stopped smoking, smoked 1-10, 11-20, or 21 or more cigarettes daily), cholesterol concentration (mmol/l), diastolic blood pressure (mm Hg), drug treatment for high blood pressure, and body mass index (kg/m^2). Ordinal variables, such as employment grade, were represented by dummy indicators in the analyses. All logistic regression analyses were adjusted for age and length of follow up. Baseline cases were excluded in all analyses. In the analyses using work characteristics during phases 1 and 2 cases of coronary heart disease at both phase 1 and 2 were excluded.

Results

Table 1 presents the number of baseline and new cases of all four outcomes. Women reported angina and any coronary event more often than men. Men more often reported that a doctor had confirmed coronary heart disease. Women reported severe chest pain less often than men at phase 1. During follow up they reported severe chest pain more often than men.

Job demands and social support were not related to any of the outcomes. The odds ratio of any coronary

Table 3 Odds ratios (95% confidence intervals)* of newly reported coronary heart disease at phase 2 or 3 by self reported and independently assessed job control at phase 1 in men and women

	Angina	Severe chest pain	Diagnosed ischaemic heart disease	Any coronary event
Self report				
Men:				
High	1.00	1.00	1.00	1.00
Intermediate	1.16 (0.81 to 1.68)	0.89 (0.65 to 1.20)	1.37 (0.89 to 2.11)	1.05 (0.81 to 1.34)
Low	1.54 (1.05 to 2.26)	1.33 (0.97 to 1.82)	1.60 (1.01 to 2.55)	1.55 (1.20 to 2.01)
Test for trend†	1.24 (1.02 to 1.50)	1.13 (0.96 to 1.33)	1.27 (1.01 to 1.60)	1.23 (1.08 to 1.41)
No of men (events)	4812 (168)	4683 (250)	5021 (118)	4522 (384)
Women:				
High	1.00	1.00	1.00	1.00
Intermediate	1.16 (0.70 to 1.94)	2.01 (1.12 to 3.61)	0.35 (0.11 to 1.04)	1.80 (1.16 to 2.79)
Low	1.20 (0.74 to 1.92)	1.80 (1.02 to 3.16)	0.85 (0.38 to 1.87)	1.74 (1.15 to 2.64)
Test for trend†	1.08 (0.86 to 1.36)	1.23 (0.96 to 1.56)	1.03 (0.67 to 1.59)	1.23 (1.03 to 1.49)
No of women (events)	2107 (138)	2093 (123)	2240 (36)	2001 (225)
Independent assessment				
Men:				
High	1.00	1.00	1.00	1.00
Intermediate	1.43 (0.94 to 2.18)	0.87 (0.61 to 1.24)	1.15 (0.70 to 1.89)	1.16 (0.87 to 1.55)
Low	1.50 (1.00 to 2.25)	1.10 (0.79 to 1.53)	1.33 (0.83 to 2.12)	1.43 (1.09 to 1.88)
Test for trend†	1.21 (0.99 to 1.48)	1.05 (0.89 to 1.24)	1.15 (0.91 to 1.45)	1.20 (1.04 to 1.37)
No of men (events)	4165 (149)	4054 (212)	4347 (106)	3913 (331)
Women:				
High	1.00	1.00	1.00	1.00
Intermediate	1.08 (0.58 to 1.99)	1.03 (0.53 to 1.99)	0.68 (0.18 to 2.56)	1.15 (0.70 to 1.88)
Low	1.46 (0.87 to 2.43)	1.70 (0.98 to 2.93)	1.43 (0.53 to 3.85)	1.73 (1.14 to 2.62)
Test for trend†	1.23 (0.96 to 1.57)	1.36 (1.04 to 1.78)	1.31 (0.79 to 2.17)	1.35 (1.10 to 1.65)
No of women (events)	1838 (122)	1833 (107)	1956 (31)	1756 (200)

*Adjusted for age and length of period between phase 1 and 3; baseline cases at phase 1 were excluded.
†Group scores of job control (1, 2, 3) were modelled as one (ordinal) variable; odds ratio reflects increase in odds of new coronary heart disease per unit increase in this variable.

event (trend test) for job demands (low, intermediate, high) was 0.97 (95% confidence interval 0.85 to 1.12) and 1.17 (0.98 to 1.41) for men and women, respectively. The independent assessments of job demands showed similar negative findings. Work support (high, intermediate, low) had the following odds ratios: 1.11 (0.96 to 1.28) and 1.15 (0.95 to 1.38). Furthermore, there was no consistent pattern across the outcomes. Multiplicative interactions between job demands, job control, and social support did not add to the prediction of new coronary heart disease. Therefore, only the results for job control are presented.

Table 2 shows that there were striking grade related differences in job control. The mean self reported job control was 47 and 78 for the lowest and highest employment grade, respectively. Men had higher scores on self reported job control than women. However, within employment grades there were hardly any differences between men and women. Similar findings were found for independently assessed job control.

The odds ratios indicated about 50% higher risks of any new report of coronary heart disease report at phase 2 or 3 for men with low job control compared with men with high job control at phase 1 (table 3). The odds ratio for women was about 1.70. The odds ratio of low self reported job control and doctor diagnosed ischaemia among women (odds ratio 0.85) was an exception to the general inverse association. This may reflect the small number of newly reported diagnosed ischaemic heart disease among women (n = 36). The associations of self reported job control and independently assessed job control with reported coronary heart disease were about equally strong.

Because the odds ratios for men and women did not differ significantly, further analyses were based on the total sample (sex was controlled for in each model). Self reported job control and independently assessed job control were not highly correlated (Pearson correlation coefficient 0.41). The associations of self reported and independently assessed job control at phase 1 with future reported coronary heart disease seemed to be independent from each other (table 4). Furthermore, both assessment instruments had similarly strong associations with the outcomes. Simultaneously adjusted, the odds ratios of any new coronary event for subjects with low self reported job control or low independently assessed job control were both 1.40. There was no indication that subjects with discrepancies between self reported and independently assessed job control had any particular excess risk. The presented odds ratios may be underestimated because both measurements probably reflected the same work characteristic.

Self reported job control at phase 1 and 2 were independently associated with newly reported coronary heart disease at phase 3 (table 5). Although the odds ratios were not significant, the findings indicate that job control in phases 1 and 2 had cumulative effects on new coronary heart disease. This implies that subjects with low job control on both occasions had the highest risks of new coronary heart disease, whereas subjects with high job control on both occasions had the lowest risks. Subjects with stable

Table 4 Odds ratios (95% confidence intervals)* of newly reported coronary heart disease at phase 2 or 3 by self reported and independently assessed job control at phase 1 in whole sample (men and women combined), unadjusted (model I) and adjusted for other assessment instrument (model II)

	Angina	Severe chest pain	Diagnosed ischaemic heart disease	Any coronary event
Self report				
Model I:				
High	1.00	1.00	1.00	1.00
Intermediate	1.16 (0.87 to 1.56)	1.07 (0.82 to 1.39)	1.13 (0.75 to 1.68)	1.21 (0.98 to 1.49)
Low	1.33 (0.99 to 1.79)	1.32 (1.02 to 1.72)	1.48 (0.99 to 2.22)	1.50 (1.21 to 1.85)
Test for trend†	1.15 (1.00 to 1.34)	1.15 (1.01 to 1.32)	1.22 (0.99 to 1.49)	1.22 (1.10 to 1.36)
No of subjects (events)	6919 (306)	6776 (373)	7261 (154)	6523 (609)
Model II:				
High	1.00	1.00	1.00	1.00
Intermediate	1.18 (0.86 to 1.63)	1.08 (0.81 to 1.44)	0.99 (0.54 to 1.53)	1.19 (0.95 to 1.50)
Low	1.24 (0.89 to 1.73)	1.27 (0.94 to 1.71)	1.28 (0.82 to 2.00)	1.39 (1.10 to 1.77)
Test for trend†	1.11 (0.94 to 1.30)	1.14 (0.98 to 1.32)	1.14 (0.91 to 1.42)	1.18 (1.05 to 1.33)
No of subjects (events)	5952 (266)	5838 (315)	6247 (136)	5620 (523)
Independent assessment				
Model I:				
High	1.00	1.00	1.00	1.00
Intermediate	1.28 (0.91 to 1.81)	0.91 (0.67 to 1.24)	1.08 (0.68 to 1.71)	1.15 (0.89 to 1.47)
Low	1.47 (1.07 to 2.02)	1.23 (0.94 to 1.62)	1.38 (0.91 to 2.09)	1.51 (1.21 to 1.89)
Test for trend†	1.21 (1.03 to 1.41)	1.12 (0.98 to 1.29)	1.18 (0.96 to 1.46)	1.24 (1.11 to 1.38)
No of subjects (events)	6003 (271)	5887 (319)	6303 (137)	5669 (531)
Model II:				
High	1.00	1.00	1.00	1.00
Intermediate	1.26 (0.89 to 1.78)	0.90 (0.66 to 1.23)	1.06 (0.67 to 1.69)	1.14 (0.88 to 1.46)
Low	1.38 (1.00 to 1.92)	1.18 (0.89 to 1.56)	1.27 (0.82 to 1.96)	1.40 (1.11 to 1.76)
Test for trend†	1.17 (1.00 to 1.37)	1.09 (0.95 to 1.27)	1.13 (0.91 to 1.41)	1.18 (1.05 to 1.33)
No of subjects (events)	5952 (266)	5838 (315)	6247 (136)	5620 (523)

*Adjusted for age, sex, and length of period between phase 1 and 3; baseline cases at phase 1 were excluded.
†Group scores of job control (1, 2, 3) were modelled as one (ordinal) variable; odds ratio reflects increase in odds of new coronary heart disease per unit increase in this variable.

Table 5 Odds ratios (95% confidence intervals)* of newly reported coronary heart disease at phase 3 by self reported job control at phase 1 and phase 2 (simultaneously controlled) and by average job control at phase 1 and 2 in total sample (men and women combined)

	Angina	Severe chest pain	Diagnosed ischaemic heart disease	Any coronary event
Job control at phase 1:				
High	1.00	1.00	1.00	1.00
Intermediate	1.29 (0.78 to 2.15)	0.90 (0.57 to 1.42)	1.09 (0.59 to 2.02)	1.22 (0.84 to 1.75)
Low	1.48 (0.83 to 2.64)	1.20 (0.70 to 2.04)	1.16 (0.54 to 2.48)	1.40 (0.92 to 2.13)
Test for trend†	1.21 (0.91 to 1.61)	1.09 (0.83 to 1.43)	1.08 (0.74 to 1.57)	1.18 (0.95 to 1.46)
Job control at phase 2:				
High	1.00	1.00	1.00	1.00
Intermediate	1.27 (0.78 to 2.08)	1.34 (0.86 to 2.09)	1.09 (0.59 to 2.02)	1.57 (1.10 to 2.24)
Low	1.45 (0.82 to 2.56)	1.18 (0.67 to 2.08)	1.41 (0.54 to 2.48)	1.36 (0.88 to 2.10)
Test for trend†	1.20 (0.90 to 1.59)	1.10 (0.84 to 1.45)	1.18 (0.81 to 1.73)	1.16 (0.94 to 1.44)
Average job control at phases 1 and 2‡:				
High	1.00	1.00	1.00	1.00
Intermediate	1.36 (0.83 to 2.23)	1.36 (0.88 to 2.10)	1.39 (0.79 to 2.45)	1.71 (1.20 to 2.43)
Low	2.09 (1.29 to 3.37)	1.52 (0.96 to 2.38)	1.49 (0.81 to 2.74)	1.93 (1.34 to 2.77)
Test for trend†	1.46 (1.15 to 1.85)	1.23 (0.98 to 1.53)	1.22 (0.91 to 1.65)	1.36 (1.15 to 1.62)
No of subjects (events)	6565 (132)	6372 (136)	6982 (73)	5999 (231)

*Adjusted for age, sex, and length of period between phase 1 and 3; baseline cases at phase 1 and phase 2 were excluded.
†Group scores of job control (1, 2, 3) were modelled as one (ordinal) variable; odds ratio reflects increase in odds of new coronary heart disease per unit increase in this variable.
‡Sum of continuous job control scales at phase 1 and 2, with resulting score divided into thirds.

Table 6 Odds ratios (95% confidence intervals)* of newly reported coronary heart disease at phase 3 by average self reported job control at phase 1 and 2† in total sample (men and women combined) adjusted for age, sex, and length of period between phase 1 and phase 3 (model I), and separately adjusted for employment grade (model II), negative affectivity (model III), and coronary risk factors (model IV)

	Model I	Model II	Model III	Model IV
Angina:				
High	1.00	1.00	1.00	1.00
Intermediate	1.36 (0.83 to 2.23)	1.20 (0.71 to 2.03)	1.33 (0.81 to 2.18)	1.44 (0.86 to 2.39)
Low	2.09 (1.29 to 3.37)	1.80 (1.03 to 3.14)	2.02 (1.25 to 3.27)	2.02 (1.22 to 3.34)
Test for trend‡	1.46 (1.15 to 1.85)	1.36 (1.03 to 1.80)	1.44 (1.13 to 1.82)	1.42 (1.11 to 1.82)
No of subjects (events)	6565 (132)	6565 (132)	6565 (132)	6228 (123)
Severe chest pain:				
High	1.00	1.00	1.00	1.00
Intermediate	1.36 (0.88 to 2.10)	1.31 (0.83 to 2.06)	1.28 (0.83 to 1.98)	1.48 (0.94 to 2.31)
Low	1.52 (0.96 to 2.38)	1.38 (0.81 to 2.34)	1.38 (0.87 to 2.17)	1.52 (0.95 to 2.45)
Test for trend‡	1.23 (0.98 to 1.53)	1.17 (0.90 to 1.53)	1.17 (0.94 to 1.46)	1.23 (0.97 to 1.54)
No of subjects (events)	6372 (136)	6372 (136)	6372 (136)	6028 (128)
Diagnosed ischaemic heart disease:				
High	1.00	1.00	1.00	1.00
Intermediate	1.39 (0.79 to 2.45)	1.42 (0.78 to 2.56)	1.35 (0.76 to 2.38)	1.36 (0.77 to 2.41)
Low	1.49 (0.81 to 2.74)	1.39 (0.67 to 2.86)	1.42 (0.77 to 2.62)	1.26 (0.67 to 2.39)
Test for trend‡	1.22 (0.91 to 1.65)	1.19 (0.84 to 1.69)	1.19 (0.88 to 1.61)	1.13 (0.83 to 1.54)
No of subjects (events)	6982 (73)	6982 (73)	6982 (73)	6617 (69)
Any coronary event:				
High	1.00	1.00	1.00	1.00
Intermediate	1.71 (1.20 to 2.43)	1.59 (1.10 to 2.30)	1.64 (1.15 to 2.34)	1.81 (1.26 to 2.60)
Low	1.93 (1.34 to 2.77)	1.81 (1.18 to 2.73)	1.82 (1.26 to 2.63)	1.99 (1.36 to 2.91)
Test for trend‡	1.36 (1.15 to 1.62)	1.32 (1.08 to 1.62)	1.33 (1.11 to 1.58)	1.38 (1.15 to 1.65)
No of subjects (events)	5999 (231)	5999 (231)	5999 (231)	5681 (218)

*Cases of coronary heart disease at phase 1 and 2 were excluded.
†Sum of continuous job control scales at phase 1 and 2, with resulting score divided into thirds.
‡Group scores of job control (1, 2, 3) were modelled as one (ordinal) variable; odds ratio reflects increase in odds of new coronary heart disease per unit increase in this variable.

intermediate job control or subjects who changed from low to high job control or vice versa generally had intermediate risks of coronary heart disease.

The continuous job control scales at phase 1 and 2 were summed and divided into thirds to reflect the cumulative effects of low job control during phases 1 and 2. Subjects with low job control on average had an odds ratio for any subsequent coronary event of 1.93 (1.34 to 2.77) compared with subjects with high job control on average. This is primarily caused by the high odds ratios for angina. The odds ratios for severe chest pain and diagnosed ischaemic heart disease were smaller (about 1.50).

The odds ratios for average job control slightly decreased after adjustment for employment grade, negative affectivity, and classic coronary risk factors, but they continued to be significant for angina and any coronary event (table 6). The decrease in the odds

ratios for diagnosed ischaemic heart disease when the coronary risk factors were taken into account (odds ratio 1.26) was primarily caused by the higher prevalence of subjects having drug treatment for hypertension in the group reporting low job control. When employment grade at phase 2 was additionally controlled for in the model already controlling for employment grade at phase 1 the odds ratios did not change substantially.

Discussion

The results of the Whitehall II study provide evidence that particular psychosocial factors may account for some of the missing predictive power for coronary heart disease. Excess risks of coronary heart disease were found for male and female British civil servants in jobs characterised by low control. Self reported and independently assessed job control showed roughly similar associations with coronary heart disease. Self reported job control assessed on two occasions had cumulative effects on new coronary heart disease. The association was independent of employment grade, negative affectivity, and conventional coronary risk factors. Although small numbers did not permit extensive analyses of the associations between employment grade, job control, and coronary heart disease, the findings showed that low job control had adverse effects in all employment grades (data not shown). This implies that the association between job control and coronary heart disease was not confounded by employment grade. The relative contribution of work and other factors to the association between grade and coronary heart disease will be investigated in future analyses.

High job demands, low social support, and the interactions between work characteristics (job strain) were not related to the coronary outcomes. The findings correspond to the review by Schnall *et al*, in which 17 out of 25 studies found significant associations between job control and cardiovascular outcome, whereas associations with job demands were significant in only eight out of 23 studies.[5] The importance of job control was further elaborated by several other investigators.[22-24] Specific characteristics of our sample of white collar workers may have contributed to the negative findings for high job demands and high job strain. High job demands were more common in the higher employment grades, and high job demands and high job control were positively associated, resulting in comparatively few high strain jobs.

The similar associations between job control and coronary heart disease in men and women support the conclusion by Schnall *et al* that psychosocial work characteristics as yet seem to have no sex specific effects on coronary heart disease.[5] However, this should be interpreted cautiously because angina and severe chest pain reported with the Rose questionnaire may be differently related to underlying coronary heart disease in men and women.[25 26] Given that people with low job control, angina, severe chest pain, or diagnosed ischaemic heart disease at phase 1 had lower participation rates at phase 2 or 3, the impact of job control on newly reported coronary heart disease is probably somewhat underestimated in the analyses. Controlling for whether people had left the civil service did not affect the results.

Changing job control

It is still unclear how long, with what intensity, and how frequently subjects have to be exposed to stress at work before their health becomes damaged.[12] Whether previous exposure to adverse work environments is mitigated when people move to positive work environments is not known. The Whitehall II study provides evidence that the risk profile may change during individual job trajectories. In general, subjects who changed from a work environment characterised by high job control to a work environment with low job control or vice versa had intermediate risks of coronary heart disease. Subjects who had stable work environments with low job control had the highest risks, while subjects with stable high job control tended to have the lowest risk. These findings may point to the usefulness of measuring job stress as a function of intensity, frequency, and possibly duration of adverse work characteristics during the whole occupational career.[12]

Methodological issues

Given the known variability in reporting of angina,[27] which has been replicated in our data set, the use of new reports of angina or severe chest pain as an indicator of incident coronary disease may be problematic. The underlying condition may not have altered but the tendency to report might have changed. A new report of a diagnosed disease is likely to be a better indicator of new disease, although other factors may also influence both recall of diagnosis or access to medical care. Preliminary results show that 87% of the 188 subjects reporting a myocardial infarction at phase 3 had documented coronary heart disease. Furthermore, the classic coronary risk factors were related to all four outcomes, suggesting that the outcomes reflect coronary heart disease and not only reporting bias. Despite the different sensitivity and specificity of the outcomes, job control shows consistent effects. This supports an aetiological hypothesis. The credibility of this hypothesis is further strengthened by the finding in baseline data of the Whitehall II study that fibrinogen concentrations were raised in men and women with independently assessed low job control.[28] This finding points to a possible psychophysiological mechanism relating low job control to coronary heart disease. Future analyses will examine the effects of low job control on fatal and non-fatal myocardial infarction.

Information bias is a potential source of bias in our study, because information on both job control and coronary heart disease was obtained from self reports.[29-32] This bias may have caused overestimated odds ratios because a complaining attitude towards work and health (negative affectivity) may have resulted in negative reports about both job control and coronary heart disease. However, because baseline cases were excluded in the longitudinal study and a measure of negative affectivity was controlled for, negative affectivity was unlikely to have biased the results for the participants' reports.[8-11] Furthermore, the association between the independent assessment of job control and newly reported coronary heart disease

Key messages

- Low job control in the work environment contributes to the development of coronary heart disease among British male and female civil servants
- The risk of heart disease is associated with both objective low job control and perceived low job control.
- Increase in job control over time decreases the risk of coronary heart disease. This suggests that policies giving people a stronger say in decisions about their work or providing them with more variety in work tasks may contribute to better cardiovascular health

was of about equal strength. The only partial agreement between self reported and independently assessed job control suggests that these assessment instruments provide partially complementary information on objective job control. However, the possibility that perceived job control was influenced by need for control or indicators of low status control, such as job insecurity, cannot be excluded.[33 34]

Conclusion

Low control in the work environment is associated with an increased risk of coronary heart disease among men and women employed in government offices. The fact that independently assessed low job control is as important as self reported low job control points to the relevance of objective low job control, not just appraisal or perception of low job control. The cumulative effect of low job control assessed on two occasions implies that giving subjects more variety in tasks and a stronger say in decisions related to work could have benefits for public health. The results add to the body of work linking psychosocial work characteristics to the risk of coronary heart disease.

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Conflict of interest: None.

Appendix

Self reports of the work environment

Three characteristics of the work environment—job control, job demands, and social support—were assessed by means of 25 items. Response categories ranged from 1 (often) to 4 (never).

Job control—Nine of the 15 items for job control covered decision authority and six covered skill discretion; these subscales were equally weighted. Cronbach's $\alpha = 0.84$ (measure of internal consistency). The nine items for decision authority were Do you have a choice in deciding how you do your job? Do you have a choice in deciding what you do at work? Others take decisions concerning my work; I have a good deal of say in decisions about work; I have a say in my own work speed; my working time can be flexible; I can decide when to take a break; I have a say in choosing with whom I work; and I have a great deal of say in planning my work environment. The six items for skill discretion were Do you have to do the same thing over and over again? Does your job provide you with a variety of interesting things? Is your job boring? Do you have the possibility of learning new things through your work? Does your work demand a high level of skill or expertise? Does your job require you to take the initiative?

Job demands—Cronbach's $\alpha = 0.67$ for job demands, which had four items: Do you have to work very fast? Do you have to work very intensively? Do you have enough time to do everything? Do different groups at work demand things from you that you think are hard to combine?

Social support—Cronbach's $\alpha = 0.79$ for social support, which had six items: How often do you get help and support from your colleagues? How often are your colleagues willing to listen to your work related problems? How often do you get help and support from your immediate superior? How often is your immediate superior willing to listen to your problems? Do you get sufficient information from line management (your superiors)? Do you get consistent information from line management (your superiors)?

Independent assessments of the work environment

Response categories for independent assessments of the work environment ranged from 1 (often) to 12 (never). There were four items: How often does the job involve working very fast? How often is it extremely important to do the work without mistakes? How often do different groups at work demand things which are difficult to combine? How often does the job permit complete discretion and independence in determining how, and when, the work is to be done?

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Randomised double blind controlled study of recurrence of gastric ulcer after treatment for eradication of *Helicobacter pylori* infection

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Abstract

Objective: To determine whether eradication of *Helicobacter pylori* infection reduces recurrence of benign gastric ulceration.
Design: Randomised, double blind, controlled study. Patients were randomised in a 1:2 ratio to either omeprazole 40 mg once daily for eight weeks or the same treatment plus amoxycillin 750 mg twice daily for weeks 7 and 8. A 12 month untreated follow up ensued.
Setting: Teaching and district general hospitals between 1991 and 1994.
Subjects: 107 patients with benign gastric ulcer associated with *H pylori*.
Main outcome measures: Endoscopically confirmed relapse with gastric ulcer (analysed with life table methods), *H pylori* eradication, and healing of gastric ulcers (Mantel-Haenszel test).
Results: 172 patients were enrolled. Malignancy was diagnosed in 19; 24 were not infected with *H pylori*; four withdrew because of adverse events; and 18 failed to attend for start of treatment, leaving 107 patients eligible for analysis (35 omeprazole alone; 72 omeprazole plus amoxycillin). In the omeprazole/amoxycillin group 93% (67/72; 95% confidence interval 84% to 98%) of gastric ulcers healed and 83% (29/35; 66% to 94%) in the omeprazole group ($P = 0.103$). Eradication of *H pylori* was 58% (42/72; 46% to 70%) and 6% (2/35; 1% to 19%) ($P < 0.001$) and relapse after treatment was 22% (16/72) and 49% (17/35) (life table analysis, $P < 0.001$), in the two groups, respectively. The recurrence rates were 7% (3/44) after successful *H pylori* eradication and 48% (30/63) in those who continued to be infected ($P < 0.001$).
Conclusions: Eradication of *H pylori* reduces relapse with gastric ulcer over one year. Eradication rates achieved with this regimen, however, are too low for it to be recommended for routine use.

Introduction

There is a strong association between the risk of developing peptic ulcers and infection of the gastric and duodenal mucosa by *Helicobacter pylori*.[1 2] Over 90% of duodenal ulcers are associated with *H pylori* infection, but only about 70% of gastric ulcers exhibit this association.[3] The remainder are caused mainly by treatment with non-steroidal anti-inflammatory drugs. Although most gastric ulcers can be healed by antisecretory treatment, many will relapse when treatment is stopped. Therefore, continuous antisecretory treatment is taken by those with relapsing ulcers. Eradication of *H pylori* infection in patients with duodenal ulcer greatly reduces the rate of relapse.[3] At the time we started this study (1991), however, there were no data on the effect of eradication treatment on gastric ulcer relapse. Therefore, we set out to determine whether recurrence could be reduced after such treatment.

Amoxycillin treatment in combination with omeprazole eradicates *H pylori* in a substantial proportion of patients with minimal side effects and without the development of antibiotic resistance, and so this dual treatment was chosen as the eradication treatment.

Patients and methods

The study was approved by the ethics committees of all participating centres. Consecutive patients with gastric ulcers confirmed endoscopically were invited to enter the study. Patients with a benign gastric ulcer at least 5 mm in diameter but without other active upper gastrointestinal disease or relevant cardiovascular, renal, or liver disease were included. Intake of bismuth

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compounds or antibiotics within the previous month or regular intake of non-steroidal anti-inflammatory drugs within the past two months were exclusion criteria.

The study was a double blind, double dummy design of eight weeks' healing with omeprazole and *H pylori* eradication treatment followed by one year of untreated follow up. *H pylori* status was assessed at the first and subsequent endoscopy visits by histology and culture. Patients who were infected with *H pylori* were randomised so that two thirds received omeprazole 40 mg once daily for eight weeks with amoxycillin 750 mg twice daily for weeks 7 and 8 and one third received omeprazole 40 mg once daily for eight weeks with dummy for weeks 7 and 8 (see fig 1). Randomisation was performed at each centre by allocating consecutive patients to the next available treatment pack from a computer generated randomisation list. Randomisation was performed on entry to the study rather than immediately before eradication treatment to ensure an even randomisation as some but not all patients would have had healed ulcers after six weeks of antisecretory treatment. Relapse was defined as an endoscopically verified gastric ulcer, and this resulted in withdrawal from the study.

H pylori was considered to have been eradicated if both histology and culture yielded negative results one month after the end of the initial treatment. *H pylori* status was also assessed at six and 12 months of follow up or on ulcer relapse. If either histology or culture yielded positive results at any visit the patient was considered to be positive for *H pylori*.

Biopsies for assessment of *H pylori* and ulcer malignancy

Biopsy samples were taken from the ulcer edge to exclude malignancy. Two antral samples were taken and frozen at −70°C or in liquid nitrogen for microbiological assessment at the microbiology department, Bradford Royal Infirmary. They were ground and a homogenate made which was inoculated on Columbia agar with 7% saponin-lysed horse blood, 1% Vitox and selective antibiotics (SR147, Oxoid), and on non-selective blood agar. Plates were incubated microaerobically at 37°C in a variable atmosphere incubator for up to seven days.

One sample was taken from each of the anterior wall and roof of the duodenum, posterior and anterior walls of the antrum 2 cm proximal to the pylorus, and posterior and anterior walls of the mid-part of the corpus. They were placed in 10% neutral buffered formalin and analysed at the pathology department, Leeds General Infirmary. The samples were sectioned at three levels and assessed by the modified Giemsa technique for *H pylori*.

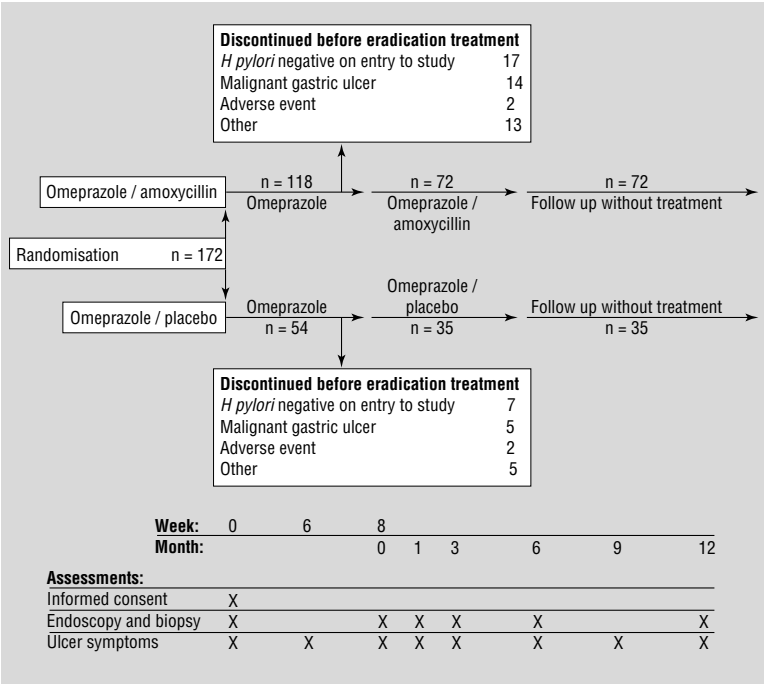

Fig 1 Study design and numbers of patients recruited

Statistical methods

To calculate the number of patients required it was assumed that *H pylori* eradication would be 65% in the omeprazole/amoxycillin treatment group and 5% in the omeprazole treatment group and, additionally, that the risk of relapse by 12 months would be 70% in patients who were infected with *H pylori* and 20% those who were not. This gave risks of 0.675 and 0.375 for the omeprazole alone and omeprazole/amoxycillin group, respectively. With a sample size of 45 and 90 (135 total) and a two sided significance test at the 5% significance level, the test power of the null hypothesis would be 80% in the survival analysis. A total of 172 patients were to be recruited to allow for those lost to follow up during the assessment period. The test power for comparison of risks of relapse in patients with or without *H pylori* would be about 99%.

Data were analysed on an all patients treated basis because the primary objective of the study was to establish whether the eradication of *H pylori* infection reduced the recurrence of benign gastric ulceration rather than to compare the effectiveness of two treatments in ulcer healing and *H pylori* eradication. Nevertheless, for the sake of completeness an intention to treat analysis was also done for gastric ulcer healing and *H pylori* eradication.

Ulcer healing and *H pylori* eradication were analysed by a Mantel-Haenszel test stratified by centre. Patients were excluded from these analyses if they did not have a gastric ulcer, if they had a malignant gastric ulcer, if the intake of the trial drug could not be confirmed, or if they were not infected with *H pylori* at baseline. All patients with data from the visit one month after stopping treatment and those in whom *H pylori* status could not be confirmed were also included in the analysis of *H pylori* eradication rates. The latter patients were included in the analysis as not eradicated.

The main end points of the study—verified ulcer relapse or remission at the one year visit—were analysed by survival analysis with time in remission compared by log rank test. Patients were excluded from the survival analysis if they were not infected with *H pylori* at the baseline endoscopy, when the outcome of healing treatment could not be confirmed, or if they withdrew at the end of treatment with a healed ulcer. When ulcers were unhealed at the end of treatment patients were included in the survival analysis as relapses at day zero.

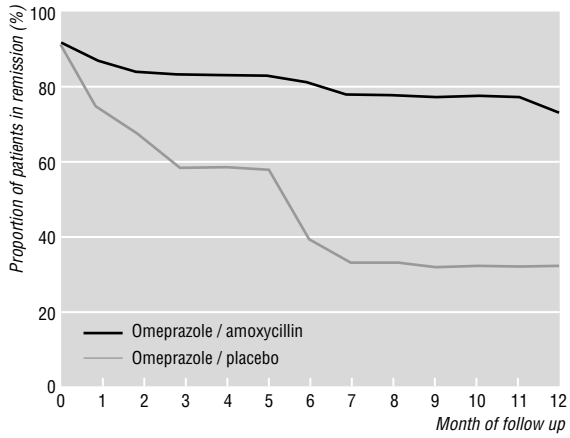

Fig 2 Life table remission curves according to treatment group

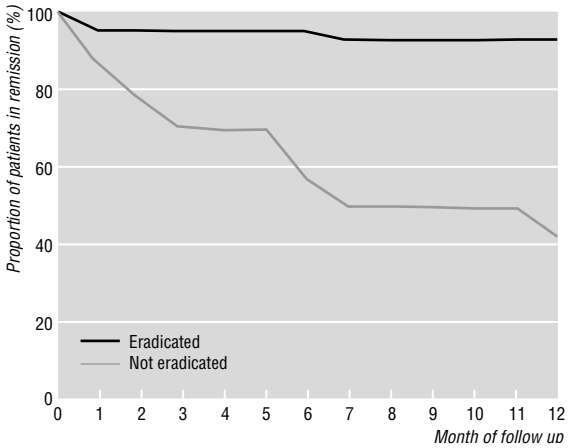

Fig 3 Life table remission curves according to *H pylori* status

Results

A total of 172 patients entered the study. Figure 1 shows the numbers of patients enrolled and randomised, including reasons for exclusion. Of those who entered the study 107 were included in the all patients treated analysis, 72 having received omeprazole and amoxycillin and 35 omeprazole and dummy. The only notable difference in the baseline characteristics was a predominance of men in the omeprazole/amoxycillin group (table 1).

Gastric ulcer healing and *H pylori* eradication

Tables 2 and 3 show the results of the intention to treat analyses of gastric ulcer healing and *H pylori* eradication. These data do not include randomised individuals who were found to have malignancy or who did not have *H pylori* infection at baseline as there was never any intention to treat them with antibiotics.

Gastric ulcer healing—all patients treated analysis

Data were not available for five patients (three omeprazole/amoxycillin and two omeprazole) at the end of healing treatment, and they are included as treatment failures. Overall, healing of gastric ulcer was 88%, and there was no significant difference (P = 0.103) between the groups (table 2).

Table 1 Baseline characteristics of patients according to treatment

Characteristics	Omeprazole/amoxycillin	Omeprazole
No of patients	72	35
Mean age (years)	55	52
Sex (men:women)	47:25	17:18
Duration (months) of gastric ulcer disease (No (%) of patients):		
<6	24 (33)	12 (34)
6-11	11 (15)	5 (14)
12-60	17 (24)	5 (14)
>60	20 (28)	13 (37)
Site of gastric ulcer (No of patients):		
Cardia	4	1
Body	70	31
Antrum	14	10
Prepyloric	22	9
Pyloric	0	1
Not specified	7	1
Smoking (yes:no)	47:25	22:13
Alcohol use (yes:no)	52:20	24:11

Table 2 Healing rates for gastric ulcer according to treatment group

Treatment	No of ulcers healed	Healing rate (%) (95% CI)
All patients treated analysis		
Omeprazole/amoxycillin (n=72)	67	93 (84 to 98)
Omeprazole/placebo (n=35)	29	83 (66 to 94)
Difference		10 (–3 to 23)
Intention to treat analysis		
Omeprazole/amoxycillin (n=87)	67	77 (66 to 86)
Omeprazole/placebo (n=42)	29	69 (52 to 83)
Difference		8 (–8 to 24)

Table 3 Eradication rates for *Helicobacter pylori* according to treatment group

Treatment	No of patients with *H pylori* eradicated	Eradication rate (%) (95% CI)
All patients treated analysis		
Omeprazole/amoxycillin (n=72)	42	58 (46 to 70)
Omeprazole/placebo (n=35)	2	6 (1 to 19)
Difference		42 (32 to 72)
Intention to treat analysis		
Omeprazole/amoxycillin (n=87)	42	48 (37 to 60)
Omeprazole/placebo (n=42)	2	5 (0 to 17)
Difference		43 (25 to 61)

H pylori eradication—intention to treat analysis

H pylori status could not be confirmed at the visit one month after treatment in 24 patients (11 were lost to follow up, six were unhealed, three had symptoms of ulcer and were withdrawn, two had complications of their ulcer disease and were withdrawn, one had an adverse event, and one violated the protocol). These patients are included in the analysis as not eradicated. *H pylori* eradication was confirmed in 42 (58%) patients who received omeprazole/amoxycillin and in 2 (6%) who received only omeprazole (table 3).

Gastric ulcer recurrence

Twenty two per cent (16/72) of patients who received omeprazole/amoxycillin relapsed during the one year follow up period compared with 49% (17/35) of patients who received omeprazole alone. Patients who received eradication treatment were more likely to be in remission than those who received omeprazole alone. The life table curves for the probability of relapse were significantly different (fig 2; P < 0.001).

Recurrence of gastric ulcers was compared in patients in whom eradication of *H pylori* was successful

with those who remained infected with *H pylori*, regardless of the treatment given. Ulcer relapse was 7% (3/44) versus 48% (30/63) in the two groups, respectively. Once again, there was a highly significant difference when the life table curves were compared (fig 3; $P < 0.001$). None of the three patients in whom *H pylori* was eradicated and who later relapsed were reinfected at the time of their relapse.

The treatments were well tolerated, there being only one serious adverse event—a myocardial infarction in a patient taking omeprazole alone.

Discussion

In this study the recruitment criteria excluded patients taking non-steroidal anti-inflammatory drugs. Nineteen of the 172 (11%) patients recruited were eventually found to have malignancy, but of the 153 remaining, 129 (84%) were infected with *H pylori*. These patients were randomised to eradication treatment or simple acid suppression. The eradication treatment chosen was expected to be successful in around two thirds, and for that reason, to complete the study with about equal numbers of patients with and without *H pylori* infection, randomisation was undertaken in a 1:2 ratio.

When we consider those patients in whom we had definite evidence of either eradication or non-eradication the numbers were 44 and 63 respectively. The recurrence of ulcers over the next 12 months in these groups was 7% versus 48%. The Mantel-Haenszel assessment (see figure 3) indicates that there was a substantially better prognosis in those in whom *H pylori* eradication had been achieved compared with those in whom the organism persisted. These data suggest that the eradication of *H pylori* from patients with gastric ulcer is associated with a lower rate of relapse over the next 12 months. This implies that the eradication of *H pylori* changes the natural history of gastric ulcer and that it is, in part, responsible for the disease in most patients with this condition.

The major statistical comparison was between those patients treated with an eradication regimen and one designed simply to reduce acid secretion. Statistically this is appropriate because it compares patient groups that have been independently randomised as opposed to groups of patients that have been selected on the basis of their eradication status. With this analysis there was a significant advantage for the eradication treatment (see table 3 and fig 2). These data therefore confirm that the use of a regimen that eradicates *H pylori* is more effective in the prevention of ulcer relapse than one designed merely to heal the ulcer by acid suppression.

Other studies

There have been two recent reports of the effect of eradication treatment on gastric ulcer recurrence.[4 5] In 1995 Seppala *et al* obtained similar results to our own over a 12 month period with 7% of ulcer relapses in those who were not infected with *H pylori* and 47% in those who were.[4] In their study the eradication of *H pylori* improved healing of gastric ulcers as well as relapse. Their eradication regimen utilised colloidal bismuth subcitrate, however, which has a cytoprotective effect on gastric mucosa, and there is evidence that bismuth may accumulate and be slowly eliminated. The difference in relapse rates in that study, therefore, might have been the result of factors other than *H pylori* eradication.

Key messages

- The occurrence of gastric ulcer is positively associated with *H pylori* infection
- Treatment to eradicate *H pylori* (omeprazole 40 mg once daily and amoxycillin 750 mg twice daily) reduces recurrence of gastric ulcers compared with omeprazole treatment alone
- Regardless of the treatment given, rates of recurrence of gastric ulcers were lower in patients with successful *H pylori* eradication compared with those who continued to be infected
- The rate of eradication of *H pylori* was 58% in the omeprazole/amoxycillin treatment group
- Rates of healing of gastric ulcers were not significantly higher in those patients who received eradication treatment

In the second study, from Hong Kong, results were similar to ours for eradicated versus non-eradicated patients but were better than those we report within treatment groups. This may reflect the high eradication results achieved in their study.[5]

Conclusions

The data presented in this paper show that the eradication of *H pylori* from patients with gastric ulcer substantially improves their long term prognosis. The *H pylori* eradication regimen in use at the start of this study was not as effective as the current regimens. The combination of an acid pump inhibitor combined with two antibiotics (from clarithromycin, amoxycillin, or metronidazole) provides around 90% eradication after only a seven day course. The use of these eradication regimens in combination with ulcer healing treatment should lead not only to better rates of ulcer healing and lower rates of relapse but to a reduction in the long term complications associated with gastric ulceration. Nevertheless, of the 172 patients with apparently benign ulcers recruited to this study 19 were found on biopsy to have gastric cancers. It remains essential, therefore, that in all patients with gastric ulcer, whether or not they are treated for *H pylori* eradication, a further endoscopy is done to ensure ulcer healing and to take biopsies from the area of the ulcer scar so that potentially curable cancers are not missed.

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Conflict of interest: J H Baron previously undertook consultancy work for Astra.

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Controlled trial of weight bearing exercise in older women in relation to bone density and falls

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Studies of the effects of different exercise programmes on bone in postmenopausal women have produced different conclusions, but few have targeted elderly women specifically.[1] We report a controlled trial of weight bearing exercise in this clinically important population.

Methods and results

The study was approved by the local ethics committee. We recruited volunteers by advertising in the local press. After excluding subjects with conditions or drug treatment likely to affect bone, we randomly allocated 118 volunteers (mean age 64.5 (range 60-73) years) to either a group taking calcium supplementation (1000 mg calcium daily, as calcium carbonate) or to an exercise group taking the same calcium supplementation. We monitored compliance with calcium by a tablet count every six months.

We asked volunteers in the calcium group taking exercise to attend the University of Dundee's exercise class for people aged over 60 three times weekly for each of three 10 week terms a year for the two years of the study. Each session lasted for 45 minutes and involved weight bearing exercise to music.[2]

The bone mineral content of the non-dominant distal forearm was measured with a Molsgaard single photon absorptiometer, and lumbar vertebral bone mineral density was measured by quantitative computed tomography both at entry to the study and at two years.

We found no significant differences between the groups at baseline. In all, 12 subjects dropped out from the calcium group and 14 from the calcium group taking exercise, leaving 92 subjects (78%) who completed the two year project. Attendance at the exercise classes for the two years of the study ranged from 46% to 100%, with a mean of 76% of classes attended. The average compliance, based on tablet counts, was 96.9% (range 80% to 100%) in both groups. The range of drug treatment, alcohol intake, total energy intake, and dietary calcium intake was similar in both groups and stable during the study.

The percentage change in bone mineral content and bone mineral density in two years was calculated for each individual; in the ultradistal forearm the change in bone mineral content showed a modest significant increase in the calcium group taking exercise compared with a decline in the calcium group (table 1). Only two fractures were recorded during the two year study, both in the calcium group.

Twenty one women in the calcium group had falls (31 falls in all), compared with 13 women in the calcium group taking exercise (15 falls in all). The difference between the groups in the number of women falling during the whole two year period was not significant ($P = 0.158$), but between 12 months and 18 months into the study the difference was significant ($P = 0.011$).

Comment

We found a modest additional effect of exercise on the bone density of the ultradistal forearm among women aged 60 years and over taking regular weight bearing exercise and dietary calcium supplementation for two years. The ultradistal region of the forearm is predominantly composed of trabecular bone. No significant effect was shown in the lumbar spine, also trabecular bone, but this may reflect the poorer precision for these measurements and the large intersubject variation in our study sample. The distal site of the forearm is predominantly cortical bone, and the lack of response may reflect the lower turnover at this site.

The calcium group taking exercise experienced fewer falls than the calcium group. This finding supports the view that improving balance, strength, and flexibility through exercise might make falls less likely.[3] This study provides a reminder that to focus on improving bone density is to address only part of the problem; prevention of falls might contribute substantially to reducing fracture rates. The association observed in this study between exercise and a reduced tendency to fall may be of considerable importance in fracture prevention and merits further study.

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Conflict of interest: METMcM is codirector of D D Developments, a University of Dundee company whose mission is to provide exercise classes for older people, and whose profits support research into aging and health.

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Table 1 Change in bone mineral content and density over two years of study

Site	Mean % change (95% confidence interval)		P value
	Calcium group (n=48)	Calcium group taking exercise (n=44)	
Ultradistal forearm	−2.6 (−4.6 to −0.6)	1.14 (−0.8 to 3.1)	0.009
Distal forearm	−1.38 (−2.2 to −0.6)	−2.18 (−3.0 to −1.4)	0.16
Lumbar spine	−2.65 (−5.7 to 0.4)	−0.91 (−6.8 to 5.0)	0.60

P=*t* tests for independent samples.