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Abstract

Study objective—To explore whether the observed age related decline in the relative risk of death associated with low employment grade can be explained by the profiles of smoking, blood pressure and plasma cholesterol changing differently with age between the employment grades.

Design—Prospective cohort study with 25 years of mortality follow up.

Setting—Whitehall study.

Participants—There were 16 984 men aged 40 to 69 years at baseline with complete information on smoking, blood pressure and plasma cholesterol.

Main results—The relative risk of death associated with low employment grade decreased from 2.1 at 55–59 years of age to 1.3 at 85–89 years of age. Adjustment for smoking status and blood pressure, attenuated the age related decline of the relative risk by 18% and 3% respectively; adjustment for plasma cholesterol increased the decline by 3%. Taken together, these risk factors explain 20% of the observed age related decline.

Conclusions—A small part of the observed age related decline in the relative risk of death associated with low employment grade can be explained by differential changes in the profiles of smoking, blood pressure and plasma cholesterol with age between the employment grades.

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One such risk factor is smoking.² On average, smokers will die at younger ages than non-smokers in both lower and higher employment grades because of their higher risk of death, and thus disappear from the population at risk. This leaves behind a greater proportion of non-smokers at older ages in both lower and higher grades. Because of the higher mortality risk in the lower employment grades, we might expect this differential mortality attributable to smoking to occur more in this group. Consequently, the average risk of death of survivors in the lower employment grades relative to those in the higher grades will decline with increasing age.

The purpose of this study is to explore whether the observed age related decline in the relative risk of death associated with low employment grade can be explained by the profiles of smoking, blood pressure and plasma cholesterol changing differently with age between the employment grades.

Methods

SUBJECTS AND DEFINITIONS

Between 1967 and January 1970, 19 018 men aged 40–69 were enrolled in the Whitehall study. Each participant filled in a standard questionnaire including age, self reported smoking history, civil servants employment grade and health status. Measurements at baseline included height, weight, blood pressure and plasma cholesterol. Full details regarding design and methods used are described elsewhere.⁶

Records from over 99% of subjects were flagged at the National Health Service Central Registry and we were notified of all deaths up to the end of January 1995. All men have been followed up for a minimum of 25 years. For the purpose of the present analyses we excluded the follow up time before the men reached 55 years of age and beyond age 90 because of relatively small numbers of deaths, which made relative risk estimates unstable. This excluded 77 015 person years. Employment grades were initially categorised, corresponding to their socioeconomic position, into four groups: administrative grades, professional or executive grades, clerical grades and “other grades” (men in messenger and other unskilled manual jobs). We have defined administrative, professional or executive grade as higher grades, and clerical and “other” grades as lower grades. These two groups correspond to social classes I and II

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People at lower socioeconomic position are known to have a higher risk of death, partly explained by a difference in known risk factors.^{1 2} At older ages the relative difference between socioeconomic status groups usually becomes smaller.^{3 4} In the Whitehall study the relative risk of death of those in lower compared with higher employment grades was observed to decline with age.⁵ This age related decline may be the result of changes in the socioeconomic position measure itself. In other words, it may reflect differences in the validity of the employment grade measure with increasing age, especially after retirement, or changing social circumstances over time. Alternatively, the decline may be attributable to changes in other factors with age such as risk factors known to be related to employment grade.

combined and to classes III, IV and V combined. For 886 men from the Diplomatic Service and the British Council, employment grading was different and these men have been excluded from all analyses. Smoking habit at entry to the study was defined in four levels: current cigarette smoking (irrespective of their use of pipe or cigars), pipe or cigar smokers, former smokers and never smokers.

A total of 16 984 men present at baseline had complete information on the variables of interest and contributed person years of observation at some point in time during the 25 years of follow up. The total number of person years of observation was 293 872, during which there were 7413 deaths.

STUDY DESIGN

We investigated age related differences in smoking, diastolic and systolic blood pressure and plasma cholesterol as these are important risk factors for all cause mortality, so that it is likely that any influence will be shown for these risk factors. To estimate the impact of age related differences in these risk factors, we compared the slopes of the age related decline in the mortality rate ratio associated with low employment grade before and after adjustment for age related differences in smoking status, diastolic and systolic blood pressure and plasma cholesterol.

Proportional hazard models were used to calculate crude and adjusted mortality rate ratios associated with low employment grade in every age group.⁷ The employment grade mortality rate ratios were first adjusted for the overall confounding effects of smoking, blood pressure and cholesterol on mortality. In these models it is assumed (probably incorrectly) that the effect of the risk factor on mortality is the same across age groups. Secondly, this assumption is relaxed and the effects of the risk factors on mortality are allowed to change with increasing age by additionally controlling for the interaction of the risk factors with age. This was done as their effects are observed to decline with increasing age⁸ and this may be a real effect, but would also be seen if the risk factors changed over time.

Additionally, proportional hazard models were used to estimate the slope of the age related change in the relative risk of death associated with low employment grade (on a logarithmic scale) for each of the above models, assuming that this change is linear across the age groups. This was done by fitting a model that included the effect of employment grade, together with a single age group by employment grade interaction term, where age group was coded and included as a continuous variable. The adequacy of assuming a linear decline of the grade effect with age was assessed by comparing this model, and one where separate grade effects were estimated for each age group, with a model containing a single term for the overall effect of employment grade. This showed that there was considerable heterogeneity in the effect of employment grade across the age groups ($\chi^2=24.37$, 6 df, $p<0.001$). Most of this heterogeneity was

Table 1 Rates of death per 1000 person years from all causes by age group at risk and employment grade (the Whitehall study)

Age group at risk	Employment grade		Rate ratio (low/high)
	High grades Rate (deaths)	Low grades Rate (deaths)	
55-59	6.8 (341)	13.9 (167)	2.05
60-64	11.3 (636)	19.9 (334)	1.76
65-69	17.5 (910)	28.1 (495)	1.61
70-74	30.9 (1118)	47.5 (650)	1.54
75-79	50.6 (904)	70.0 (587)	1.38
80-84	78.3 (515)	107.6 (424)	1.38
85-89	144.3 (166)	181.6 (166)	1.26

explained, however, by a linear trend effect with age ($\chi^2 = 21.00$, 1 df, $p<0.001$), leaving only 3.37 on 5 df as a test for departures from a linear trend effect ($p>0.5$). The decline in the effect of employment grade with age is therefore adequately described by a single linear trend term.

The percentage change between the slopes of the adjusted (as in the second adjusted model) versus crude mortality rate ratios, gives an estimate of the influence of smoking status, blood pressure and plasma cholesterol on the declining employment grade relative risk with increasing age. The age related change in the relative risk of death, together with the 95% confidence intervals, was also expressed as the percentage reduction in the employment grade rate ratios per 5 years of age. All analyses were carried out using the statistical package Stata.⁹

Only baseline data on exposure to risk factors was available. The influence of risk factors, as estimated above, thus includes both differential changes in the profiles of these risk factors attributable to differential mortality, and changes in the strength of the relation of the risk factors on mortality with increasing age. With only baseline data available, these two effects cannot be distinguished, but both effects involve changes in other risk factors with increasing age, as compared with age related changes in the socioeconomic position measure itself.

SENSITIVITY ANALYSES

As we excluded the follow up time before the men reached the age of 55, the information on risk factor status at the start of their follow up will be somewhat dated for the men who were 40 to 54 when they entered the study. The description of risk factors for men aged 55 to 69 at baseline is likely to show more resemblance to risk factors during the time that is the focus of the present analysis. We therefore used the sub-sample of these men to assess the validity of assuming that baseline data on risk factors hold reasonably true for later points in time for the entire study sample.

The age related decline in the relative risk of death associated with low employment grade is a sum of the different cause specific declines with increasing age. With increasing age, other causes of death not as influenced by smoking, blood pressure and plasma cholesterol, may become more important. We therefore examined the distribution of the main causes of death by age group. As cause specific declines

Table 2 Relative risks of death associated with low employment grade by age at risk: crude and adjusted for smoking status, diastolic (DBP) and systolic blood pressure (SBP) and plasma cholesterol (Whitehall study), all cause mortality

Age group at risk	Crude	Smoking status		SBP and DBP		Plasma cholesterol		Smoking, SBP, DBP and plasma cholesterol	
		Adj*	Adj†	Adj*	Adj†	Adj*	Adj†	Adj*	Adj†
55-59	2.06	1.88	1.83	2.04	2.03	2.07	2.09	1.85	1.80
60-64	1.73	1.58	1.55	1.72	1.70	1.74	1.74	1.57	1.53
65-69	1.53	1.41	1.40	1.52	1.53	1.54	1.54	1.40	1.39
70-74	1.46	1.34	1.33	1.44	1.44	1.47	1.47	1.33	1.32
75-79	1.34	1.24	1.25	1.33	1.32	1.35	1.35	1.24	1.25
80-84	1.35	1.25	1.29	1.34	1.35	1.37	1.35	1.25	1.28
85-89	1.25	1.17	1.19	1.23	1.26	1.26	1.25	1.14	1.19
p Value of decline	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Slope‡	-0.0725	-0.0694	-0.0594	-0.0737	-0.0705	-0.0721	-0.0746	-0.0694	-0.0579
% Reduction in rate ratio per 5 years	7.00	6.70	5.77	7.11	6.81	6.96	7.19	6.71	5.62
(95% confidence intervals)	(4.1, 9.8)	(3.8, 9.5)	(2.8, 8.7)	(4.2, 9.9)	(3.9, 9.6)	(4.1, 9.8)	(4.3, 10.0)	(3.8, 9.5)	(2.6, 8.5)

*Adjusted for the overall effect of the risk factor on mortality. †Adjusted for the overall effect of the risk factor and the interaction of the risk factor with age. ‡The estimated slope gives the change in the log relative risk of death for low versus high employment grade for an increase in 5 year age groups.

will, in turn, have different dependencies on smoking, blood pressure and plasma cholesterol, we repeated the analyses using cardiovascular mortality, as it is known that these three risk factors are important risk factors for cardiovascular disease even at older ages.

Results

Table 1 shows the age specific death rates for men in lower and higher grades in our study. The rate ratio associated with low employment grade is shown to decline with increasing age.

Table 2 presents crude and adjusted mortality rate ratios associated with low employment grade in every age group and the estimated slope of the mortality rate ratios with increasing age. The reduction in the mortality rate ratio with increasing age is, statistically, highly significant ($p < 0.001$). The first column of table 2 shows the crude mortality rate ratios for all cause mortality associated with low employment grade. The second column shows the mortality rate ratios adjusted for the overall confounding effect of smoking, resulting in smaller relative risks in all age groups at risk, and decreasing the estimated slope of the log relative risks with increasing age by 4.3%. The percentage reduction of the rate ratios per 5 years changes from 7.0% to 6.7%. Allowing the effect of smoking to change with age, results in a further decrease of the slope (third column of table 2). The difference between the slopes in the first and the third column gives an estimate of the influence of smoking (a reduction of 18%). Similarly, the fourth and the fifth column of table 2 show the effect of adjusting the mortality rate ratios for diastolic and systolic blood pressure, which reduces the mortality rate ratios in all age groups, but to a smaller extent than adjustment for smoking. Compar-

ing the slopes in the first and the fifth column gives a reduction of 3% as the estimated influence of diastolic and systolic blood pressure. Adjustment for plasma cholesterol does not have much effect on the mortality rate ratios and results in a 3% increase of the slope (comparing the first and the seventh column of table 2). Adjusting the mortality rate ratios for the combined effect of these three risk factors, results in a 20% decrease of the slope (comparing the first and the last column of table 2).

SENSITIVITY ANALYSES

Including only the men aged 55 to 69 years at entry gave similar results. Adjustment for smoking reduced the slope by 18%, adjustment for diastolic and systolic blood pressure by 2% and adjustment for plasma cholesterol increased the slope by 2% (data not shown). The combined effect of the risk factors resulted in a 17% decrease of the slope (data not shown).

Table 3 shows the main causes of death by age group at death. In all age groups cardiovascular diseases are the main cause of death, followed by cancers, although the contribution to the total number of deaths decreases with increasing age. The proportion of deaths from respiratory causes, strongly related to smoking, increases markedly with increasing age. Therefore, the overall effects of the risk factors are likely to remain important even into older ages. Repeating the analyses for cardiovascular mortality gave the following results: adjustment for smoking and blood pressure reduced the slope by 31% and 6% respectively and adjustment for plasma cholesterol increased the slope by 5% (data not shown). The combined effect of

Table 3 Main causes of death by age group at death (the Whitehall study, 25 years of follow up)

Age group at death	Cause of death					Total n (%)
	Cardiovascular diseases n (%)	Cancers n (%)	Respiratory diseases n (%)	Accidents/suicide n (%)	Other causes n (%)	
55-59	280 (55.5)	164 (32.5)	27 (5.4)	15 (3.0)	19 (3.8)	505 (100)
60-64	505 (52.3)	325 (33.6)	55 (5.7)	29 (3.0)	52 (5.4)	966 (100)
65-69	722 (51.5)	459 (32.7)	108 (7.7)	23 (1.6)	91 (6.5)	1403 (100)
70-74	900 (51.0)	546 (31.0)	179 (10.2)	25 (1.4)	114 (6.5)	1764 (100)
75-79	745 (50.0)	407 (27.3)	198 (13.3)	14 (0.9)	125 (8.4)	1489 (100)
80-84	447 (47.7)	221 (23.6)	159 (17.0)	7 (0.8)	104 (11.1)	938 (100)
85-89	159 (48.0)	74 (22.4)	58 (17.5)	5 (1.5)	35 (10.6)	331 (100)
Total	3758 (50.8)	2196 (29.7)	784 (10.6)	118 (1.6)	540 (7.3)	7396 (100)

these risk factors resulted in a 35% reduction of the slope (data not shown).

Discussion

In this study among men aged 40 years and older we found that only 20% of the observed age related decline in the relative risk of death associated with low employment grade is explained by age related differences in smoking, diastolic and systolic blood pressure and plasma cholesterol.

The effect of adjustment was largest for smoking and smaller for blood pressure and plasma cholesterol. Although all three factors are related to mortality, the relation with employment grade differs. Smoking is strongly related to employment grade, with many more smokers in the lower than in the higher grades (56% versus 36% respectively). Blood pressure and plasma cholesterol on the other hand, are less strongly related to employment grade.

In this study, only baseline risk factor information was available and we assumed that no changes occurred in the risk factor status during follow up. Although for some risk factors, like plasma cholesterol, baseline information may predict mortality as well or even better,¹⁰ this may not be true for other risk factors like smoking. It is probably that with increased duration of follow up (and thus at the older ages), changes in smoking status will occur for instance because people quit smoking, and more so in the higher grades (differential quitting).¹¹ In that case, using baseline smoking status results in more misclassification in the higher than in the lower grades at higher ages, so that we will have overestimated the employment grade mortality rate ratio adjusted for smoking in the older age groups, and thus will have underestimated the change with increasing age (that is, that the slope is in fact stronger). Consequently, the reduction in the slope attributable to adjustment for smoking will have been overestimated in this study, so that the estimated influence of smoking of 18% is a maximum and likely to be smaller. Evidence for differential quitting could already be seen at the baseline examination in the Whitehall study. Of those men who had ever smoked, 52% in the higher employment grades claimed to have quit smoking compared with 34% in the lower grades. Data from the National Health Interview Survey in the United States show that 22% of those aged 45 to 64 tried to quit in the past year and 26% of those aged 65 years and older.¹² Therefore, it seems probable that a large proportion of smokers beyond age 40 quit smoking and that this is greater in the higher, compared with the lower, employment grades. However, we are not aware of any study that has looked specifically at quitting activity in men beyond age 40 by socioeconomic status to support this impression.

One of the explanations for our finding that only a small part of the age related decline in the relative risk of death is explained by these risk factors, might be that with increasing age other causes of death less strongly associated with smoking, blood pressure and plasma

KEY POINTS

- The relative risk of death of those in lower compared with those in higher employment grades declines with age.
- A small part of the observed decline is explained by the profiles of smoking, blood pressure and plasma cholesterol changing differently with age between the employment grades.
- A large part of the decline remained unexplained and may reflect differences in the validity of the socioeconomic position measure with increasing age or changing social circumstances over time.

cholesterol become more important. This is supported by the analysis of cardiovascular mortality, showing a greater influence of the three risk factors. We showed that the contribution of "other causes of death" became more important with increasing age, in line with the above explanation. However, the contribution of respiratory causes, strongly related to smoking, also increased with age, and cardiovascular diseases are still the main cause of death at older ages. This would argue against the above. An alternative explanation could be that it is the effect of the three risk factors on mortality that decreases with age.

Our findings can be generalised to populations with similar smoking, blood pressure and plasma profiles as the British population enrolled in the Whitehall study. Given the different smoking behaviour and the different age dependency of blood pressure and plasma cholesterol in women, these findings will not necessarily apply to women.

A large part of the age related decline in the mortality rate ratios associated with low employment grade seems to remain after adjustment for smoking, blood pressure and plasma cholesterol. Of course, age related differences in other risk factors may be responsible for this remaining decline, but these risk factors need to be strongly related to both mortality and employment grade to explain much of the remaining decline. Given the results of this study, in which only smoking accounted for much of the age related decline (and the presented estimates are a maximum), we feel that it is not likely that the effect of adjustment for other known risk factors would have a strong influence on the age related decline. However, there may be additional differential mortality because of genetic susceptibility. Alternative explanations for the remaining age related decline in mortality rate ratios may have to be sought in changes in the socioeconomic position measure itself. One may be that employment grade, being a work-based measure, is not as good a predictor for mortality after retirement. However, the age related decline in mortality rate ratios is also seen for other measures of socioeconomic position,^{3 4 13 14} so that this is not likely to be the entire explanation. Another possibility is that it is attributable to changes in circumstances, for

example that social circumstances are more similar after retirement than before because of greater similarity in income. To investigate the importance of these explanations may be the subject of further studies.

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