Are the effects of psychosocial exposures attributable to confounding? Evidence from a prospective observational study on psychological stress and mortality

J Macleod, G Davey Smith, P Heslop, C Metcalfe, D Carroll, C Hart

Abstract

***Study objectives*—To examine the association between perceived psychological stress and cause specific mortality in a population where perceived stress was not associated with material disadvantage.**

***Design*—Prospective observational study with follow up of 21 years and repeat screening of half the cohort five years from baseline. Measures included perceived psychological stress, coronary risk factors, and indices of lifecourse socioeconomic position.**

***Setting*—27 workplaces in Scotland.**

***Participants*—5388 men (mean age 48 years) at first screening and 2595 men at second screening who had complete data on all measures.**

***Main outcome measures*—Hazard ratios for all cause mortality and mortality from cardiovascular disease (ICD9 390–459), coronary heart disease (ICD9 410–414), smoking related cancers (ICD9 140, 141, 143–9, 150, 157, 160–163, 188 and 189), other cancers (ICD9 140–208 other than smoking related), stroke (ICD9 430–438), respiratory diseases (ICD9 460–519) and alcohol related causes (ICD9 141, 143–6, 148–9, 150, 155, 161, 291, 303, 571 and 800–998).**

***Results*—At first screening behavioural risk (higher smoking and alcohol consumption, lower exercise) was positively associated with stress. This relation was less apparent at second screening. Higher stress at first screening showed an apparent protective relation with all cause mortality and with most categories of cause specific mortality. In general, these estimates were attenuated on adjustment for social position. This pattern was also seen in relation to cumulative stress at first and second screening and with stress that increased between first and second screening. The pattern was most striking with regard to smoking related cancers: relative risk high compared with low stress at first screening, age adjusted 0.64 (95% CI 0.42, 0.96), p for trend 0.016, fully adjusted 0.69 (95% CI 0.45, 1.06), p for trend 0.10; high compared with low cumulative stress, age adjusted 0.69 (95% CI 0.44, 1.09), p for trend 0.12, fully adjusted 0.76 (95% CI 0.48, 1.21), p for trend 0.25; increased compared with decreased stress, age adjusted 0.65 (95% CI 0.40, 1.06), p for trend 0.09, fully adjusted 0.65 (95% CI 0.40, 1.06), p for trend 0.08.**

***Conclusions*—This implausible protective relation between higher levels of stress, which were associated with increased smoking, and mortality from smoking related cancers, was probably a product of confounding. Plausible reported associations between psychosocial exposures and disease, in populations where such exposures are associated with material disadvantage, may be similarly produced by confounding, and of no causal significance.**

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Patterns of human health, for example social inequalities in health, are not fully explicable in terms of established physiological and behavioural disease risk factors. Psychosocial factors, such as stress and job control, are widely held to be important determinants of physical health.[1–3] It has been suggested that such factors are important in the aetiology of socioeconomic health gradients and should be the target of interventions to reduce health inequalities.[4 5] Studies on non-human primates have been cited as suggesting that psychoneuroendocrine mechanisms link psychosocial environment to physical disease.[6 7] In addition, studies on human subjects indicate an association between adverse psychosocial exposure and unhealthy behaviour.[8 9]

Evidence for the importance of psychosocial factors in relation to population health is derived mainly from observational studies. Two recent reviews have interpreted this evidence as suggesting a causal relation between psychosocial exposures and coronary heart disease.[2 3]

Two general issues of observational epidemiology complicate interpretation of this evidence. Firstly, reporting bias is able to generate spurious exposure-outcome associations when both measurements depend on self report, and are inflated by a common reporting tendency.[10] In many recent studies purporting to show a causal association between psychosocial exposures and health outcomes both have been measured via self report or have included a large subjective component.[11–15] We have discussed this issue elsewhere.[16]

However, associations between psychosocial exposures and mortality are difficult to attribute to reporting bias. In most positive studies, heightened psychosocial risk was associated

with adverse social position.[17–20] Any measure associated with social disadvantage will also appear to be associated with poorer health as poorer health is associated with social disadvantage. Furthermore, socioeconomic position is often poorly measured in epidemiological studies and thus considerable residual confounding can exist despite apparent "adjustment" for social position in the analyses.[21 22]

The social patterning of many psychosocial constructs is likely to be influenced by discourse patterns in a particular society at a particular time.[23] Thus, the social patterning of apparent psychosocial adversity, in terms of these exposures, may vary. If a psychosocial exposure has a true causal relation with health, then effects would be expected whatever the social distribution of this exposure. However if "effects" are principally the product of confounding they will only be seen when psychosocial adversity coincides with social disadvantage. Similarly, effects of psychosocial exposures seen in populations where heightened exposure is not associated with social disadvantage are difficult to attribute to confounding.

We examined the relation between perceived stress and mortality within a workplace recruited cohort of 5388 middle aged Scottish men followed up for 21 years. Approximately half of these men were re-examined five years after initial screening. This gave the opportunity to assess both the effect of stress measured on a single occasion (as previous studies have done) and the effect of stable or changing stress. We have previously reported how perceived stress within this cohort was not related to social disadvantage.[24] Any relation between higher stress and poorer health in this population would therefore be unlikely to be attributable to socioeconomic confounding. Additionally we have reported a positive association between higher stress and unhealthy behaviour in this cohort, suggesting a mechanism through which stress could influence health.[24] To establish whether stress did influence health we examined the relation between different categories of perceived stress and mortality. We also explored how this relation was influenced by social position, established disease risk factors, and by reporting bias.

Methods

This investigation is based on a cohort of men recruited from 27 workplaces in Scotland between 1970 and 1973. Seventy per cent of those invited completed a detailed questionnaire and attended for examination. The final achieved sample was of 5766 men aged 35–64 (mean age at first screening 48) of whom 2655 were re-screened in 1977 (mean screening interval 5.2 years).

Perceived stress was measured using the Reeder Stress Inventory (RSI).[25] The Inventory contains four statements:

- In general I am usually tense or nervous
- There is a great amount of nervous strain connected with my daily activities
- At the end of the day I am completely exhausted mentally and physically
- My daily activities are extremely trying and stressful

Participants indicate the extent to which each statement applies to them using a four point Likert format. In the current cohort, internal consistency was high (Cronbach's α 0.78 at first screening, 0.80 at second screening). Repeatability was acceptable in those screened twice (κ was 0.28 unweighted, 0.45 weighted).

Principal components analysis and maximum likelihood factor analysis yielded a one factor solution. A scoring system was used to derive a summary score ranging from 1 (low perceived stress) to 8 (high perceived stress).[25] Validity of the RSI has previously been suggested by a high degree of correlation with a Dutch stress scale devised by Dirken.[26] In the Framingham study RSI stress was significantly correlated with all other psychosocial measures used, most markedly with Type A behaviour, tension, anger and emotional lability.[27] Higher RSI stress was associated with increased use of tranquilisers in the Los Angeles Heart Study.[28] This, along with the association between higher stress, increased smoking and increased alcohol consumption in the present study suggest, construct validity.[24]

Blood pressure, lung function, height and weight and body mass index (BMI) were measured in standard ways.[29] At first screening, blood samples were taken for measurement of plasma cholesterol concentration. The self completed questionnaire collected information on physical exercise (hours per week), cigarette smoking (ex, current or never smokers; cigarettes smoked daily; age at initiation of smoking, inhalation) and consumption of alcohol. Own occupational social class at time of screening and at entry into the workforce, along with father's social class, were assigned on the basis of the registrar general classification.[30] Participants were also asked whether they owned a car. An area-based measure of deprivation, derived according to the method of Carstairs and Morris,[31] was assigned according to postcode of participants' home address.

In an attempt to quantify tendency to over-report physical symptoms we took five symptoms (polydipsia, polyuria, pruritus, blurred vision and increased skin infections). Participants were asked to report experience of these in the past year. These symptoms showed no relation to mortality over 21 years. We constructed a reporting tendency variable (0–5) based on a count of reports of these. Known diabetics (n=29 at first screening and n=23 at second screening) were excluded on the assumption that their reporting of these hyperglycaemic symptoms was more likely to reflect their diabetes than any reporting tendency.

Altogether 5388 men at first screening and 2595 men at second screening had complete information on all measures; analyses are based on these men. A full description of the methods and procedures used has been published elsewhere.[24 29]

Men who died over the 21 years of follow up from first screening were identified through 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*. In addition to all cause mortality several categories of cause specific mortality were examined. These included deaths from cardiovascular causes (ICD9 codes 390–459); coronary heart disease (ICD9 410–414); stroke (ICD9 430–438) and respiratory diseases (ICD9 460–519). Deaths from cancer were taken to be those covered by ICD9 codes 140–208. Smoking related cancers were examined separately and were taken to be covered by ICD9 codes 140, 141, 143–9, 150, 157, 160–163, 188 and 189, as described elsewhere.[32] Alcohol related mortality was also examined separately. Alcohol related deaths were taken to be those covered by ICD9 codes 141, 143–6, 148–9, 150, 155, 161, 291, 303, 571 and 800–998 as described elsewhere.[33]

The distribution of stress scores at first screening showed some clumping around middle values and was positively skewed. Scores were categorised as high (6–8), medium (4–5) and low (1–3). In men screened twice stress scores were summed. This composite score was normally distributed and was divided on the basis of tertiles into high (10–16), medium (7–9) and low (2–6). Finally the difference between stress scores at first and second screening was calculated to allow division of participants into those whose perceived stress increased, decreased or remained stable over the screening interval. Relative risks of all cause and cause specific mortality in relation to different stress exposure categorisations were then calculated.

Survival analysis was undertaken using the proportional hazards method of Cox,[34] hazard ratios were taken to represent relative risk. These are presented adjusted for age, adjusted for age and measures of social position, adjusted for age, social position and risk factors and adjusted for age, social position risk factors and reporting tendency. For models including perceived stress at first screening only, covariates are as measured at first screening. For models including stress measured on two occasions, covariates are as measured at second screening. In all models follow up is censored at 21 years from first screening. All analyses were undertaken using the software package STATA 6.0.[35]

Results

Perceived stress showed a graded association with participants' current occupational social class at both first and second screening (first screening mean stress score for social class I =

Table 1 Relations between perceived stress at first screening and coronary risk factors at first screening

	Perceived stress			
	Low n=1765	*Medium n=2912*	*High n=711*	*p for trend*
Proportion smoking >20 cigarettes daily (%)	18	21	26	<0.001
Proportion consuming >15 units of alcohol weekly (%)	27	29	29	0.020
Proportion taking <3 hours exercise weekly (%)	19	19	26	0.005
Proportion with body mass index >25 kg/m^2 (%)	53	50	46	0.004
Proportion with diastolic blood pressure ⩾ 90 mm Hg (%)	26	25	23	0.10
Proportion with plasma cholesterol >5.5 mmol/l (%)	60	62	60	0.66
Proportion with FEV_1 <90% of predicted value (%)	40	37	37	0.58

Standardisation by the direct method for age and occupational class.

Table 2 Relations between coronary risk factors at second screening and sum of perceived stress scores at first and second screening

	Perceived stress			
	Low n=895	*Medium n=874*	*High n=826*	*p for trend*
Proportion smoking >20 cigarettes daily (%)	21	27	25	0.11
Proportion consuming >15 units of alcohol weekly (%)	35	34	32	0.47
Proportion taking <3 hours exercise weekly (%)	29	26	24	0.37
Proportion with body mass index >25 kg/m^2 (%)	59	58	51	0.006
Proportion with diastolic blood pressure ⩾ 90 mm Hg (%)	29	28	26	0.13
Proportion with FEV_1 <90% of predicted value (%)	43	40	41	0.050

Standardisation by the direct method for age and occupational class.

Table 3 Relations between coronary risk factors at second screening and change in perceived stress score between first and second screening

	Perceived stress			
	Decreased n=828	*Stable n=1085*	*Increased n=682*	*p for trend*
Proportion smoking >20 cigarettes daily (%)	24	25	25	0.60
Proportion consuming >15 units of alcohol weekly (%)	31	33	35	0.17
Proportion taking <3 hours exercise weekly (%)	27	28	23	0.13
Proportion with body mass index >25 kg/m^2 (%)	57	55	57	0.76
Proportion with diastolic blood pressure ⩾ 90 mm Hg (%)	29	27	27	0.31
Proportion with FEV_1 <90% of predicted value (%)	43	41	40	0.08

Standardisation by the direct method for age and occupational class.

Table 4 Relative risk of mortality (95% CI) associated with perceived stress at first screening

	Perceived stress	*Adjusted for age*	*Adjusted for age and occupational class*	*Adjusted for age and all markers of social position**	*Adjusted, for age, social position, and risk factors†*	*Adjusted for age, social position, risk factors and reporting tendency*
All cause	High	0.88 (0.75, 1.03)	0.95 (0.81, 1.12)	0.95 (0.81, 1.12)	0.94 (0.80, 1.11)	0.97 (0.83, 1.15)
(1528 deaths)	Medium	0.85 (0.76, 0.94)	0.93 (0.83, 1.04)	0.94 (0.84, 1.05)	0.93 (0.83, 1.05)	0.95 (0.84, 1.06)
	Low	1.00	1.00	1.00	1.00	1.00
p for trend		0.020	0.34	0.38	0.33	0.55
All cardiovascular	High	0.84 (0.67, 1.05)	0.90 (0.72, 1.13)	0.90 (0.72, 1.13)	0.92 (0.73, 1.16)	0.94 (0.74, 1.18)
(785 deaths)	Medium	0.83 (0.71, 0.97)	0.91 (0.78, 1.06)	0.92 (0.79, 1.07)	0.92 (0.79, 1.08)	0.93 (0.79, 1.09)
	Low	1.00	1.00	1.00	1.00	1.00
p for trend		0.037	0.26	0.28	0.36	0.44
Coronary heart disease	High	0.86 (0.67, 1.12)	0.93 (0.71, 1.21)	0.93 (0.71, 1.21)	0.96 (0.74, 1.25)	0.97 (0.74, 1.27)
(590 deaths)	Medium	0.86 (0.72, 1.03)	0.94 (0.79, 1.13)	0.95 (0.79, 1.14)	0.97 (0.81, 1.16)	0.97 (0.81, 1.17)
	Low	1.00	1.00	1.00	1.00	1.00
p for trend		0.14	0.50	0.52	0.72	0.78
Smoking related cancers	High	0.64 (0.42, 0.96)	0.71 (0.47, 1.08)	0.71 (0.47, 1.08)	0.66 (0.44, 1.01)	0.69 (0.45, 1.06)
(269 deaths)	Medium	0.79 (0.61, 1.02)	0.91 (0.70, 1.18)	0.91 (0.70, 1.19)	0.89 (0.69, 1.16)	0.90 (0.69, 1.18)
	Low	1.00	1.00	1.00	1.00	1.00
p for trend		0.016	0.13	0.13	0.06	0.10
Other cancers	High	0.91 (0.59, 1.40)	0.91 (0.59, 1.40)	0.93 (0.60, 1.44)	0.94 (0.61, 1.46)	1.00 (0.64, 1.56)
(221 deaths)	Medium	0.93 (0.70, 1.25)	0.93 (0.69, 1.25)	0.94 (0.70, 1.27)	0.94 (0.70, 1.27)	0.96 (0.71, 1.30)
	Low	1.00	1.00	1.00	1.00	1.00
p for trend		0.61	0.60	0.70	0.73	0.93
Stroke	High	0.85 (0.49, 1.48)	0.90 (0.52, 1.58)	0.92 (0.52, 1.60)	0.94 (0.54, 1.65)	0.98 (0.55, 1.72)
(122 deaths)	Medium	0.75 (0.51, 1.10)	0.80 (0.54, 1.19)	0.81 (0.55, 1.20)	0.81 (0.54, 1.21)	0.82 (0.55, 1.23)
	Low	1.00	1.00	1.00	1.00	1.00
p for trend		0.32	0.51	0.54	0.59	0.68
Alcohol related	High	1.13 (0.63, 2.01)	1.29 (0.72, 2.31)	1.26 (0.71, 2.26)	1.22 (0.68, 2.20)	1.30 (0.72, 2.35)
(105 deaths)	Medium	0.86 (0.56, 1.32)	1.01 (0.65, 1.56)	1.01 (0.65, 1.55)	0.97 (0.63, 1.51)	1.00 (0.64, 1.54)
	Low	1.00	1.00	1.00	1.00	1.00
p for trend		0.91	0.51	0.54	0.59	0.68
Respiratory	High	1.23 (0.69, 2.22)	1.39 (0.77, 2.50)	1.36 (0.75, 2.45)	1.22 (0.67, 2.22)	1.38 (0.75, 2.53)
(100 deaths)	Medium	0.94 (0.61, 1.46)	1.09 (0.69, 1.71)	1.11 (0.71, 1.74)	0.96 (0.61, 1.52)	0.99 (0.63, 1.56)
	Low	1.00	1.00	1.00	1.00	1.00
p for trend		0.62	0.31	0.33	0.61	0.40

*Current occupational class, occupational class of first employment, father's occupational class, car ownership, deprivation category of area of residence. †Cigarettes smoked daily, ex, current, never smokers, age at initiation of smoking, inhalation, alcohol consumption (0, >0–15, >15 units weekly), hours of exercise weekly, diastolic blood pressure (mm Hg), plasma cholesterol (mmol/l), body mass index (kg/m^2), FEV$_1$%.

4.4, social class V = 2.8, p for trend <0.001; second screening mean stress score social class I = 4.5, social class V =2.9 p for trend <0.001).

Table 1 shows the distribution of risk factors by stress score category at first screening. After standardisation for age and social class, greater stress at first screening is associated with an adverse pattern of behavioural risk (more smoking, less exercise, greater alcohol consumption) but shows no clear relation with physiological risk factors (blood pressure, blood cholesterol and lung function). Greater

Table 5 All cause and cause specific mortality according to the sum of perceived stress at first and second screening

	Perceived stress	*Adjusted for age*	*Adjusted for age and occupational class*	*Adjusted, for age, occupational class and risk factors**	*Adjusted for age, occupational class, risk factors and reporting tendency*
All cause	High	0.92 (0.76, 1.11)	1.00 (0.83, 1.23)	0.98 (0.81, 1.19)	1.00 (0.82, 1.22)
(642 deaths)	Medium	0.93 (0.77, 1.11)	1.00 (0.82, 1.20)	0.98 (0.81, 1.19)	0.99 (0.82, 1.20)
	Low	1.00	1.00	1.00	1.00
p for trend		0.38	0.93	0.85	0.98
All cardiovascular	High	1.02 (0.79, 1.33)	1.13 (0.85, 1.47)	1.12 (0.85, 1.46)	1.16 (0.88, 1.53)
(335 deaths)	Medium	1.02 (0.79, 1.33)	1.11 (0.85, 1.44)	1.10 (0.84, 1.43)	1.11 (0.85, 1.45)
	Low	1.00	1.00	1.00	1.00
p for trend		0.86	0.36	0.42	0.28
Coronary heart disease	High	1.00 (0.75, 1.36)	1.11 (0.82, 1.51)	1.11 (0.82, 1.51)	1.16 (0.84, 1.58)
(258 deaths)	Medium	0.99 (0.73, 1.33)	1.07 (0.79, 1.44)	1.07 (0.79, 1.44)	1.08 (0.80, 1.46)
	Low	1.00	1.00	1.00	1.00
p for trend		0.97	0.51	0.50	0.36
Smoking related cancers	High	0.69 (0.44, 1.09)	0.78 (0.50, 1.24)	0.76 (0.48, 1.20)	0.76 (0.48, 1.21)
(126 deaths)	Medium	0.91 (0.61, 1.37)	1.00 (0.67, 1.52)	0.99 (0.65, 1.50)	0.97 (0.64, 1.47)
	Low	1.00	1.00	1.00	1.00
p for trend		0.12	0.32	0.26	0.25
Other cancers	High	0.90 (0.53, 1.52)	0.90 (0.53, 1.55)	0.90 (0.52, 1.54)	0.91 (0.52, 1.57)
(89 deaths)	Medium	1.09 (0.67, 1.78)	1.10 (0.66, 1.81)	1.10 (0.67, 1.83)	1.11 (0.67, 1.84)
	Low	1.00	1.00	1.00	1.00
p for trend		0.71	0.73	0.71	0.73
Stroke	High	1.63 (0.77, 3.46)	1.67 (0.77, 3.60)	1.55 (0.72, 3.34)	1.64 (0.75, 3.58)
(42 deaths)	Medium	1.35 (0.62, 2.92)	1.37 (0.63, 3.02)	1.35 (0.62, 2.96)	1.37 (0.63, 3.02)
	Low	1.00	1.00	1.00	1.00
p for trend		0.20	0.19	0.27	0.21
Respiratory	High	0.97 (0.50, 1.88)	1.05 (0.53, 2.06)	0.87 (0.44, 1.70)	0.91 (0.46, 1.81)
(45 deaths)	Medium	0.52 (0.24, 1.14)	0.55 (0.25, 1.23)	0.54 (0.24, 1.20)	0.55 (0.25, 1.24)
	Low	1.00	1.00	1.00	1.00
p for trend		0.85	0.96	0.64	0.77
Alcohol related	High	0.96 (0.46, 2.25)	1.01 (0.45, 2.24)	0.97 (0.43, 2.16)	1.05 (0.46, 2.39)
(37 deaths)	Medium	0.83 (0.38, 1.84)	0.87 (0.39, 1.94)	0.83 (0.37, 1.86)	0.85 (0.38, 1.92)
	Low	1.00	1.00	1.00	1.00
p for trend		0.91	0.98	0.93	0.92

*Cigarettes smoked daily, ex, current, never smokers, alcohol consumption (0, >0–15, >15 units weekly), hours of exercise weekly, diastolic blood pressure (mm Hg), body mass index (kg/m^2), FEV$_1$%.

Table 6 All cause and cause specific mortality according to the difference between perceived stress at first and second screening

	Perceived stress	*Adjusted for age*	*Adjusted for age and occupational class*	*Adjusted, for age, occupational class, and risk factors**	*Adjusted for age, occupational class, risk factors and reporting tendency*
All cause	Increased	0.97 (0.79, 1.18)	0.97 (0.80, 1.19)	0.98 (0.80, 1.21)	0.99 (0.80, 1.21)
(642 deaths)	Stable	0.95 (0.79, 1.15)	0.95 (0.79, 1.14)	0.99 (0.81, 1.17)	0.97 (0.80, 1.16)
	Decreased	1.00	1.00	1.00	1.00
p for trend		0.73	0.78	0.91	0.88
All cardiovascular	Increased	1.04 (0.78, 1.37)	1.04 (0.79, 1.38)	1.06 (0.80, 1.40)	1.05 (0.80, 1.39)
(335 deaths)	Stable	0.95 (0.73, 1.22)	0.95 (0.73, 1.22)	0.97 (0.75, 1.25)	0.96 (0.74, 1.23)
	Decreased	1.00	1.00	1.00	1.00
p for trend		0.83	0.79	0.71	0.75
Coronary heart disease	Increased	1.08 (0.79, 1.48)	1.09 (0.80, 1.49)	1.11 (0.81, 1.52)	1.10 (0.80, 1.51)
(258 deaths)	Stable	0.91 (0.68, 1.21)	0.91 (0.68, 1.21)	0.92 (0.69, 1.24)	0.91 (0.68, 1.23)
	Decreased	1.00	1.00	1.00	1.00
p for trend		0.65	0.62	0.55	0.57
Smoking related cancers	Increased	0.65 (0.40, 1.06)	0.66 (0.41, 1.07)	0.65 (0.40, 1.06)	0.65 (0.40, 1.06)
(126 deaths)	Stable	0.87 (0.58, 1.28)	0.86 (0.58, 1.28)	0.87 (0.58, 1.29)	0.86 (0.58, 1.28)
	Decreased	1.00	1.00	1.00	1.00
p for trend		0.09	0.09	0.09	0.08
Other cancers	Increased	0.86 (0.49, 1.48)	0.86 (0.49, 1.49)	0.88 (0.51, 1.53)	0.88 (0.51, 1.53)
(89 deaths)	Stable	0.92 (0.57, 1.49)	0.92 (0.57, 1.49)	0.93 (0.57, 1.51)	0.93 (0.57, 1.50)
	Decreased	1.00	1.00	1.00	1.00
p for trend		0.58	0.58	0.65	0.64
Stroke	Increased	0.91 (0.41, 2.01)	0.91 (0.41, 2.01)	0.92 (0.42, 2.04)	0.92 (0.42, 2.03)
(42 deaths)	Stable	0.90 (0.44, 1.82)	0.90 (0.44, 1.82)	0.91 (0.45, 1.85)	0.90 (0.44, 1.83)
	Decreased	1.00	1.00	1.00	1.00
p for trend		0.81	0.81	0.83	0.83
Respiratory	Increased	1.65 (0.79, 3.45)	1.66 (0.79, 3.48)	1.99 (0.94, 4.22)	1.92 (0.90, 4.08)
(45 deaths)	Stable	0.99 (0.47, 2.09)	0.99 (0.47, 2.09)	1.04 (0.49, 2.21)	0.99 (0.46, 2.13)
	Decreased	1.00	1.00	1.00	1.00
p for trend		0.17	0.17	0.07	0.08
Alcohol related	Increased	1.10 (0.52, 2.34)	1.10 (0.52, 2.35)	1.14 (0.53, 2.45)	1.13 (0.53, 2.42)
(37 deaths)	Stable	0.54 (0.24, 1.21)	0.54 (0.24, 1.21)	0.58 (0.26, 1.31)	0.57 (0.25, 1.29)
	Decreased	1.00	1.00	1.00	1.00
p for trend		0.86	0.85	0.79	0.81

*Cigarettes smoked daily, ex, current, never smokers, alcohol consumption (0, >0–15, >15 units weekly), hours of exercise weekly, diastolic blood pressure (mm Hg), body mass index (kg/m^2), FEV_1%.

stress is strongly related to lower BMI. High cumulative stress at first and second screening (table 2) was strongly related to lower BMI and less strongly to better lung function. Change in stress over the screening interval (table 3) shows no clear relation with established behavioural and physiological risk factors. Change in stress was not related to change in risk factors (not shown).

Table 4 shows relative risk of all cause and cause specific mortality associated with high and medium reported stress (compared with low stress as baseline) at initial screening. The general pattern apparent is of an ostensibly protective relation, particularly in the case of cancers associated with smoking, which is attenuated and weakened on adjustment for social position. Further adjustment for risk factors and reporting tendency has little effect on all estimates. The exception to this pattern is a weak suggestion of an increased relative risk of respiratory mortality and mortality related to alcohol consumption, particularly after adjustment for current occupational class. Adjustment for other indices of life course social position has little additional influence. The estimate is only moderately attenuated on adjustment for risk factors including alcohol consumption and smoking. Adjustment for these risk factors individually did not substantially change this pattern (not shown).

Measures of social position other than current occupational class and age at initiation and inhalation for smokers were not included in models using second screening data.

Table 5, mortality by the sum of stress scores at first and second screening, shows broadly the same pattern as table 4. There is a weak suggestion of a small protective effect of higher stress in relation to all cause mortality and a slightly stronger suggestion of a larger protective effect with mortality from smoking related cancers. Both these estimates are considerably attenuated on adjustment for current occupational class. There was a weak suggestion of an increased risk of stroke with higher cumulative stress. Adjustment for risk factors and reporting tendency had little influence on any effect estimates most of which were close to the null value. The increased relative risk of respiratory and alcohol related mortality apparent at first screening was not seen in relation to cumulative stress.

These patterns are repeated in table 6 showing mortality by change in stress score. Few of these estimates are markedly different from the null value. Again there is a moderately strong suggestion of a protective effect of increasing stress in relation to smoking related cancers. Conversely, respiratory mortality is positively associated with increasing stress.

Discussion

It seems unlikely that stress, which is associated with increased smoking,[24] is protective against smoking related cancers. It is similarly unlikely that the suggestion of a protective effect of higher stress, in relation to all cause and cardiovascular mortality, is genuine. Rather, our results reflect the influence of confounding in observational epidemiology.[36]

The association between adverse lifetime material circumstances and poorer health in this population has been described previously.[37] The apparent protective relation between higher stress and better health was attributable

to the association between higher stress and material advantage in this population. The relation was weakened on adjustment for current occupational class, one indicator of material circumstances. Adjustment for additional indices of social position had little additional influence on the model containing current occupational class. Adjustment for established disease risk factors made, in most instances, little difference.

The ability of confounding to generate apparently robust, independent, yet spurious associations in observational epidemiology is well established,[38] indeed the phenomenon is the mainstay of submissions to the traditionally light hearted Christmas edition of the *British Medical Journal*.[39–41] Essentially, all that separates these latter associations from those presented as meaningful is plausibility. Apparent plausibility is, arguably, the weakest criterion for causality.[38] Plausibility of an association between stress, and other psychosocial exposures, and health is well established.[7] Nevertheless it is probable that many, apparently plausible associations between psychosocial exposures and health, reported in the literature are as much the product of confounding, and therefore equally spurious, as those we have reported here.

The RSI has been superseded by more elaborate stress measures in some more recent studies.[42] Conversely, evidence of a positive relation between stress and health has often rested on simpler measures of stress.[17] The main points of this paper do not relate to the status of the RSI among psychometric instruments (though it appears as reliable as many,[42–45] and we have argued its validity above). The issues we have highlighted are pertinent to any situation where the construct under study is socially patterned. Indeed the consistent relation between certain psychosocial constructs—those indexing different aspects of personal autonomy for example,[46]—and health seems likely to be attributable to the fact that such constructs are consistently related to social position (even to the extent that they are incorporated as measures of this in contemporary social classifications[47]).

It could be argued that our instrument was differentially sensitive to stress in different social groups. Repeating analyses for men in manual and non-manual occupations separately revealed that a "protective" effect was essentially confined to the latter (age adjusted hazard ratio for all cause mortality high versus low stress manual 1.02 (95% CI 0.83, 1.25), non-manual 0.79 (95% CI 0.60, 1.02); for smoking-related cancers manual 0.95 (95% CI 0.59, 1.51), non-manual 0.29 (95% CI 0.11, 0.74)). Some under-reporting of stress may have occurred, suggesting that self report may be problematic in this context. Conversely, more objective measures that ignore the dimension of individual perception and coping, central to all the proposed mechanisms through which stress may influence health, may be inappropriate.

Prevalent disease may increase perception, and hence reporting of stress. Ideally all subjects with significant morbidity at recruitment should have been excluded from mortality analyses. As we did not have complete information on all significant morbidity at recruitment it was not possible to do this. Two considerations are important in this regard. Firstly, a "healthy worker" effect would suggest that the prevalence of significant morbidity would be lower in this cohort than in the general population. Secondly, the effect of prevalent morbidity would be to generate a spurious, *positive* relation between stress and mortality. The confounded *negative* relation we found was, therefore, despite this effect. This can be seen in relation to CHD. If prevalent cases of CHD (Rose angina positive, n=336) are excluded from mortality analyses the confounded "protective" effect of stress is accentuated (age adjusted hazard ratio for all cause mortality medium versus low stress 0.82 (95% CI 0.73, 0.92), high versus low stress 0.82 (95% CI 0.69, 0.97)).

We have illustrated difficulties caused by confounding, in the interpretation of observed associations between psychosocial exposures and health. We have also shown how the traditional approach to this issue, adjustment for the confounding factor by including a measure of it in multivariate models, may not be fully successful. Specificity of association between exposure and outcome can be sought as evidence against confounding. "Blanket" associations between various unrelated psychosocial exposures and similarly distinct health outcomes are strongly suggestive of confounding.[48–50] Though interest has focused on psychosocial factors as potential determinants of health inequality it may be more valuable to study them in populations where they are not associated with material adversity as a positive association with health in this circumstance is difficult to attribute to confounding.

It could be argued that reducing the stressfulness of modern life, creating fairer workplaces and generally being nicer to each other are ethical imperatives in little need of further epidemiological justification.[51] We strongly agree with this, but believe current evidence does not support the suggestion that population health is amenable to improvement

KEY POINTS
- Various indicators of "psychosocial adversity", such as increased psychological stress, have been shown to be associated with increased mortality.
- In studies showing these associations, psychosocial adversity was also associated with socioeconomic disadvantage.
- In a population where increased stress was associated with socioeconomic *advantage* psychosocial adversity appeared to reduce mortality.
- This "effect" was probably the product of socioeconomic confounding.
- Many reported "effects" of psychosocial exposures may be attributable to confounding and of no causal significance.

through psychosocial interventions. Rather, health improvements and reductions in health inequalities are more likely to result from interventions aimed at reducing material disadvantage and at improving behavioural and physiological risk profiles.

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