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Do Cardiovascular Risk Factors Explain the Relation between Socioeconomic Status, Risk of All-Cause Mortality, Cardiovascular Mortality, and Acute Myocardial Infarction?

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Much remains to be understood about how low socioeconomic status (SES) increases cardiovascular disease and mortality risk. Data from the Kuopio Ischemic Heart Disease Risk Factor Study (1984–1993) were used to estimate the associations between acute myocardial infarction and income, all-cause mortality, and cardiovascular mortality in a population-based sample of 2,272 Finnish men, with adjustment for 23 biologic, behavioral, psychologic, and social risk factors. Compared with the highest income quintile, those in the bottom quintile had age-adjusted relative hazards of 3.14 (95% confidence interval (CI) 1.77–5.56), 2.66 (95% CI 1.25–5.66), and 4.34 (95% CI 1.95–9.66) for all-cause mortality, cardiovascular mortality, and AMI, respectively. After adjustment for risk factors, the relative hazards for the same comparisons were 1.32 (95% CI 0.70–2.49), 0.70 (95% CI 0.29–1.69), and 2.83 (95% CI 1.14–7.00). In the lowest income quintile, adjustment for risk factors reduced the excess relative risk of all-cause mortality by 85%, that of cardiovascular mortality by 118%, and that of acute myocardial infarction by 45%. These data show *how* the association between SES and cardiovascular mortality and all-cause mortality is mediated by known risk factor pathways, but full "explanations" for these associations will need to encompass *why* these biologic, behavioral, psychologic, and social risk factors are differentially distributed by SES. *Am J Epidemiol* 1996;144:934–42.

mortality; myocardial infarction; risk factors; socioeconomic factors

The inverse relation between socioeconomic status (SES) and health has been observed for centuries (1). With few exceptions, this association exists regardless of the measure of SES that is employed or the health outcome studied (2–5). Even though the association between SES and health is a strong and consistent finding, is inversely graded across levels of SES, and has been noted in many countries across varying time periods, much remains to be understood about the ways in which SES affects health.

In 1981, Rose and Marmot (6) showed that statistical adjustment for age, smoking, height, body mass index, systolic blood pressure, cholesterol, and blood glucose had only a moderate impact on reducing the magnitude of the inverse association between social class, as measured by occupational grade, and coronary heart disease risk in British civil servants. Since then, many studies have found that the elevated risks of disease associated with lower SES are not greatly attenuated by adjustment for traditional biologic and behavioral risk factors (7–13). In attempts to explain the persistent association between SES and health, a number of literature reviews on the subject have also pointed to an even wider variety of possible risk factors and have argued their potential importance in helping to understand the relation between lower SES and poorer health (14–17). The proposition that SES impacts health in some way independent of known risk factors, if true, has important implications for both research and public health policy.

We investigated the association between income, all-cause mortality, cardiovascular mortality, and acute myocardial infarction (AMI) in a prospective study of a population-based sample of eastern Finnish men. Extensive information on medical, biologic, behavioral, psychologic, and social risk factors allowed the most comprehensive examination to date of the potential pathways that mediate the relation between SES and cardiovascular mortality, all-cause mortality, and AMI.

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Abbreviations: AMI, acute myocardial infarction; CI, confidence interval; RH, relative hazard; SES, socioeconomic status.

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MATERIALS AND METHODS

Study population

Subjects were participants in the Kuopio Ischemic Heart Disease Risk Factor Study, which was designed to investigate previously unestablished risk factors for ischemic heart disease, carotid atherosclerosis, and other related outcomes in a population-based sample of eastern Finnish men (18). Of the 3,433 eligible men aged 42, 48, 54, or 60 years who resided in the town of Kuopio or its surrounding rural communities, 198 could not be included because of death, serious disease, or migration away from the area, and of the remainder, 2,682 (82.9 percent) agreed to participate in the study. Baseline examinations were conducted between March 1984 and December 1989. No marked sociodemographic differences have been found between participants and nonparticipants (19). Complete information on SES and all risk factors was available for 2,272 men for the mortality analyses. A total of 565 of these men were excluded from the AMI analyses because of a prior history of AMI, angina pectoris, nitroglycerine use, or positive findings of angina from the London School of Hygiene Cardiovascular Questionnaire (20), leaving 1,707 men for the analyses of AMI.

Assessment of socioeconomic status

At the baseline examinations, participants completed detailed questionnaires that included items on personal and household income, education, lifetime occupation, housing tenure, and material living conditions. We report results based on personal income as the measure of SES, since previous analyses revealed that it was the strongest predictor of mortality and AMI in this group of men (21). Furthermore, similar findings were obtained for the other indicators of SES, such as education and occupation. The income distribution was divided into quintiles, and four indicator variables were used in the analyses, with those in the highest 20 percent of income as the reference group.

Assessment of follow-up events

Participants were followed until the end of December 1993 for the mortality analyses, with a mean follow-up of 7.2 years (range, 4.05–9.8 years). For the AMI analyses, men were followed until the end of December 1992, for an average of 6.2 years (range, 3.1–8.8 years). All-cause mortality and cardiovascular mortality were ascertained by linkage to the National Death Registry, which is maintained for all Finnish citizens. Classification of death was based on the underlying cause, reviewed at the National Center of Statistics of Finland. Cardiovascular deaths were classified according to *International Classification of Diseases*, Ninth Revision, codes 390–459. There were 156 deaths, 76 of which were from cardiovascular causes.

Nonfatal AMIs and coronary deaths were ascertained by linkage to an AMI register established under the World Health Organization Monitoring of Trends and Determinants of Cardiovascular Diseases project (22). If multiple events occurred during follow-up, only the first event for each subject was considered. There were 88 fatal or nonfatal incident AMIs recorded in this group of men.

Assessment of risk factors

Extensive risk factor information was collected as part of the baseline examinations. Risk factors were included in the analyses if they had previously been shown to be associated with mortality or AMI or if they were candidates on theoretical grounds.

Biologic risk factors. Blood samples were drawn after fasting and abstinence from smoking for 12 hours, abstinence from alcohol for 3 days, and abstinence from using analgesics for 7 days. After the subject rested supine for 30 minutes, blood was drawn without a tourniquet, using Terumo Venoject VT-100 PZ vacuum tubes (Terumo Corp., Tokyo, Japan).

Plasma fibrinogen concentration was determined from fresh samples on the basis of clotting of diluted plasma with excess thrombin with the Coagulometer KC4 device (Heinrich Amelung GmbH, Lemgo, Germany) (23). Lipoproteins were separated from unfrozen plasma within 3 days of sampling. High and low density lipoprotein fractions were separated from fresh plasma by using both ultracentrifugation and precipitation. The cholesterol content of all lipoprotein fractions and serum triglycerides was measured enzymatically (CHOD-PAP cholesterol method and GPO-PAP triglyceride method, Boehringer Mannheim, Mannheim, Germany) on the day after the last spin. Serum apolipoprotein B was determined with an immunoturbidimetric method (KONE Corp., Espoo, Finland) by using an antiserum (Orion, Espoo, Finland) (24). Blood hemoglobin was measured photometrically (Gilford Stasar III. Gilford Instrument Laboratories Inc., Oberlin, Ohio) by using the cyanmethemoglobin method within a few hours of blood sampling (25). Blood leukocyte count was measured using the Coulter counter (Coulter Counter Electronics Ltd., Luton, United Kingdom). Serum ferritin was measured with radioimmunoassay (Amersham International, Amersham, United Kingdom) and was based on a double antibody technique (25). Serum copper and hair mercury were determined from frozen serum

specimens by using the 306 Atomic Absorption Spectrometer (Perkin-Elmer, Norwalk, Connecticut) (26, 27). Baseline blood glucose level was derived from venous blood samples taken after a 12-hour fast (28). Blood pressure was measured with a random-zero sphygmomanometer after a supine rest of 5 minutes. Three systolic and diastolic blood pressures were taken while the subject was supine and were averaged. Average systolic pressure was used in this analysis. Body mass index was calculated by dividing the subject's weight by the square of his height (kg/m^2). Cardiorespiratory fitness was measured directly on the basis of respiratory gas exchange during a maximal, symptom-limited exercise tolerance test on a bicycle ergometer (29).

Behavioral risk factors. Alcohol consumption, measured in grams per week, was assessed by dietary recording for a 4-day period and also for the previous 12 months, by self-administered questionnaire (30). The distribution was divided into nondrinkers and quartiles of consumption. Indicator variables were used in the analysis, with the first quartile of consumption as the reference group. Smoking was measured by questionnaire and classified for this analysis as "never smoked," "former smoker," "irregular smoker," and "current smoker" (measured in pack-years). Physical activity was assessed from a 12-month leisure-time history. These analyses used quartiles of the total duration of conditioning physical activity that has been shown to be predictive of AMI in this population (29).

Psychologic risk factors. Depression was assessed from a shortened, 180-item version of the Minnesota Multiphasic Personality Inventory that had been previously used in Finnish populations. Raw scores were converted to T-scores, and the distribution was divided into quartiles. Indicator variables were used in the analyses, with the highest quartile (T-score > 75) as the reference category. Hopelessness was assessed with two questionnaire items, scored on a five-point Likert scale. The distribution of scores was divided into tertiles, and two indicator variables were used in the analyses with the lowest tertile as the reference (31). Cynical hostility was assessed from a shortened version of the Cook-Medley hostility scale. Scores were divided into quartiles, and indicator variables, with the lowest quartile as the reference, were used in the analyses (32).

Social risk factors. The degree of social connectedness of the participants was assessed with a large battery of scales. The number of organizations in which the subject participated and the quality of social support had previously been shown to predict overall mortality in this population (33). The distributions of scores was divided into quartiles, and indicator variables were used in the analyses with the highest quartile as the reference category. Marital status was assessed by questionnaire and categorized as "married," "single," or "divorced/widowed."

Statistical analysis

The association between income, age, risk factors, all-cause mortality, cardiovascular mortality, and AMI was assessed with Cox proportional hazard models (34). The analyses were conducted using the PHREG procedure in SAS version 6.09 on a Sun Sparc Station II (35). To assess the impact of risk factor adjustment on the age-adjusted relative hazard (RH), we calculated the proportion of excess relative risk (hazard) accounted for by risk factor adjustment as:

$$RH_{(\text{age adjusted})} - RH_{(\text{adjusted for age plus risk factors})}/RH_{(\text{age adjusted})} - 1.$$

Risk factors were modeled either continuously or in categories with indicator variables, depending on preliminary analyses of their bivariate associations with the outcomes.

RESULTS

Each of the 23 risk factors used in these analyses was significantly associated with mortality or AMI. (Detailed tables of the specific age-adjusted bivariate relations for each risk factor and the outcomes are available from the author upon request). The 23 risk factors were grouped into biologic, behavioral, and psychologic and social categories. Analyses were conducted in two phases. The first phase was to examine the relation between SES, mortality, and AMI with separate adjustment for each group of risk factors and age. The psychologic and social risk factors were included as one group and modeled together in this phase. The measure of cynical hostility was not included in the final models because it was not importantly associated with any outcomes when modeled with the other psychosocial risk factors and because it had a relatively large number of missing values. In the second stage, the relation between SES, mortality, and AMI was adjusted for age and all 23 risk factors simultaneously.

SES and all-cause mortality

Table 1 presents the relative hazards for all-cause mortality by quintiles of income, adjusted for age, for age plus each risk factor group separately, and, finally, for age plus all risk factor groups simultaneously. The age-adjusted relative hazards for all-cause mortality

TABLE 1. Age-adjusted relative hazards (RH) and 95% confidence intervals (CI) for the association between income quintiles and all-cause mortality in 2,272 eastern Finnish men aged 42–60 years, by risk factor group, 1984–1993

Income quintile	Adjusted covariates									
	Age		Biologic risk factors*		Behavioral risk factors†		Psychologic and social risk factors‡		All risk factors§	
	RH	95% CI	RH	95% CI	RH	95% CI	RH	95% CI	RH	95% CI
First (lowest)	3.14	1.77–5.56	1.90	1.05–3.44	2.39	1.33–4.28	2.03	1.10–3.74	1.32	0.70–2.49
Second	2.31	1.29–4.14	1.63	0.89–2.98	2.05	1.14–3.70	1.62	0.88–2.98	1.27	0.67–2.39
Third	0.80	0.40–1.62	0.67	0.33–1.37	0.67	0.33–1.37	0.64	0.31–1.32	0.55	0.27–1.15
Fourth	1.10	0.56–2.18	0.93	0.46–1.85	0.99	0.50–1.97	0.95	0.48–1.90	0.83	0.41–1.68
Fifth (highest)	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference

* Biologic risk factors: fibrinogen, high density lipoprotein cholesterol, serum apolipoprotein B, serum ferritin, copper, hair mercury, triglycerides, blood leukocytes, hemoglobin, fasting blood glucose, systolic blood pressure, cardiorespiratory fitness, body mass index, and height.

† Behavioral risk factors: smoking, alcohol consumption, and physical activity.

‡ Psychologic risk factors: depression and hopelessness. Social risk factors: marital status, participation in organizations, and quality of social support.

§ Includes age, biologic, behavioral, psychologic, and social risk factors.

for the lowest to the highest income quintiles were 3.14 (95 percent confidence interval (CI) 1.77–5.56), 2.31 (95 percent CI 1.29–4.14), 0.80 (95 percent CI 0.40–1.62), 1.10 (95 percent CI 0.56–2.18), and 1.0 (reference), respectively. After separate adjustment for biologic, behavioral, and psychologic and social risk factors, the magnitude of the associations was attenuated, but remained inversely graded. For example, the relative hazard for the lowest quintile of income was reduced by 58 percent to 1.90 (95 percent CI 1.05–3.44) after adjustment for biologic risk factors, by 35 percent to 2.39 (95 percent CI 1.33–4.28) after adjustment for behavioral risk factors, and by 52 percent to 2.03 (95 percent CI 1.10–3.74) after adjustment for psychologic and social risk factors. Simultaneous adjustment for all risk factors combined decreased the age-adjusted relative hazard for the lowest income quintile to 1.32 (95 percent CI 0.70–2.49). In this lowest 20 percent of income earners, simultaneous adjustment for all risk factors reduced the age-adjusted excess relative risk of death from any cause by 85 percent. Table 2 presents the results of a regression model simultaneously adjusted for all risk factors. In this model, lower levels of cardiorespiratory fitness; high levels of fibrinogen, body mass index, cigarette smoking, and hopelessness; and being divorced or widowed remained importantly associated with higher risk of all-cause mortality.

SES and cardiovascular mortality

Table 3 presents the relative hazards for cardiovascular mortality by quintiles of income, adjusted for age, for age plus each risk factor group separately, and for age plus all risk factor groups simultaneously. The age-adjusted relative hazards for cardiovascular mortality for the lowest to the highest income quintiles were 2.66 (95 percent CI 1.25–5.66), 1.90 (95 percent CI 0.88–4.14), 0.69 (95 percent CI 0.26–1.78), 0.72 (95 percent CI 0.27–1.93), and 1.0 (reference), respectively. Separate adjustment for groups of biologic, behavioral, and psychologic and social risk factors all reduced the associations between income quintiles and cardiovascular mortality to statistical nonsignificance. Compared with those in the highest 20 percent of income, simultaneous adjustment for all risk factors decreased the associations between SES and cardiovascular mortality to 0.70 (95 percent CI 0.29–1.69), 0.74 (95 percent CI 0.31–1.76), 0.34 (95 percent CI 0.13–0.93), and 0.42 (95 percent CI 0.15–1.16) for the lowest to the next-to-highest quintiles of income, respectively. In the lowest quintile of income earners, simultaneous adjustment for all risk factors reduced the age-adjusted excess relative risk of death from cardiovascular causes by 118 percent. In the model adjusted for all risk factors simultaneously, lower levels of cardiorespiratory fitness; high levels of fibrinogen, body mass index, cigarette smoking, and hopelessness; and being divorced or widowed remained important predictors of higher cardiovascular mortality, while moderate alcohol consumption was related to lower risk of cardiovascular mortality.

SES and AMI

Table 4 shows the relative hazard of AMI for each quintile of income in models adjusted for age, for age plus each risk factor group separately, and for age plus all risk factors simultaneously. The age-adjusted relative hazards of AMI for the lowest to the highest income quintile were 4.34 (95 percent CI 1.95–9.66), 2.25 (95 percent CI 0.97–5.21), 2.25 (95 percent CI

TABLE 2. Relative hazards (RH) and 95% confidence intervals (CI) for the age-adjusted associations between income and all-cause mortality adjusted for all risk factors in 2,272 Finnish men aged 42–60 years, 1984–1993

	RH	95% CI
Income (quintiles)		
First (lowest)	1.32	0.70–2.49
Second	1.27	0.67–2.39
Third	0.55	0.27–1.15
Fourth	0.83	0.41–1.68
Fifth (highest)	1.00	
Plasma fibrinogen (g/liter) (quartiles)		
Second	1.29	0.63–2.65
Third	1.81	0.92–3.53
Fourth (highest)	2.76	1.43–5.31
Serum apolipoprotein B (g/liter) (quartiles)		
Second	1.04	0.98–1.20
Third	0.97	0.59–1.59
Fourth (highest)	0.96	0.58–1.60
Serum high density lipoprotein cholesterol (mmol/liter)	0.94	0.49–1.79
Serum triglycerides (mmol/liter)	1.11	0.92–1.34
Serum ferritin (≥200 μg/liter)	1.08	0.73–1.60
Serum copper (mg/liter)	1.76	0.70–4.45
Blood leukocyte ($\times 10^{-3}$/mm^{-3})	1.08	0.98–1.20
Blood hemoglobin (g/liter)	1.00	0.98–1.01
Blood glucose (mmol/liter)	1.04	0.94–1.16
Mercury (hair) (μg/g)	0.98	0.91–1.05
Systolic blood pressure (mmHg) (quartiles)		
Second	0.77	0.46–1.27
Third	0.77	0.46–1.26
Fourth (highest)	1.19	0.75–1.88
Body mass index (kg/m^2)	1.06	1.01–1.11
Cardiorespiratory fitness (liters/minute)		
First (lowest)	1.98	1.04–3.78
Second	1.35	0.70–2.60
Third	1.21	0.61–2.41
Height (cm) (quartiles)		
Second	0.92	0.59–1.41
Third	1.08	0.70–1.70
Fourth (highest)	1.15	0.72–1.85
Smoking		
Former smokers	1.03	0.60–1.78
Infrequent smokers	2.14	0.83–5.54
Current smokers (pack-years) (tertiles)		
First	1.65	0.82–3.33
Second	2.01	1.03–3.92
Third (highest)	1.84	0.96–3.52
Alcohol consumption (quartiles)		
Nondrinkers	1.18	0.65–2.16
Second	0.80	0.46–1.41
Third	0.94	0.55–1.60
Fourth (highest)	1.28	0.77–2.14
Conditioning physical activity (quartiles)		
First (lowest)	0.89	0.58–1.38
Second	0.90	0.56–1.44
Third	0.92	0.56–1.50
Quality of social relationships (quartiles)		
First (lowest)	1.24	0.75–2.03
Second	1.35	0.83–2.22
Third	1.11	0.66–1.86
Organizational participation (quartiles)		
First (lowest)	1.23	0.72–2.11
Second	1.07	0.66–1.74
Third	1.20	0.74–1.96
Depression (quartiles)		
First (lowest)	1.08	0.64–1.80
Second	1.05	0.68–1.65
Third	1.06	0.69–1.63
Hopelessness (tertiles)		
Second	1.70	1.15–2.52
Third (highest)	1.82	1.12–2.98
Marital status		
Never married	1.10	0.59–2.05
Widowed/divorced	1.65	1.12–3.05

0.98–5.15), 2.18 (95 percent CI 0.94–5.05), and 1.0 (reference), respectively. After separate adjustment for biologic, behavioral, and psychologic and social risk factors, the magnitude of the associations was attenuated and inversely graded. The relative hazard for the lowest quintile of income was reduced by 45 percent to 2.83 (95 percent CI 1.21–6.61) after adjustment for biologic risk factors, by 34 percent to 3.20 (95 percent CI 1.41–7.23) after adjustment for behavioral risk factors, and by 3 percent to 4.25 (95 percent CI 1.83–9.84) after adjustment for psychologic and social risk factors. Simultaneous adjustment for all risk factors reduced the age-adjusted relative hazard for the lowest income quintile to 2.83 (95 percent CI 1.14–7.00). In this lowest 20 percent of income earners, simultaneous adjustment for all risk factors attenuated the age-adjusted excess relative risk of AMI by 45 percent. In the model adjusted for all risk factors simultaneously, lower levels of income and cardiorespiratory fitness and higher levels of systolic pressure, serum apolipoprotein B, body mass index, mercury, and cigarette smoking remained important predictors of increased AMI risk, while high levels of conditioning physical activity and high density lipoprotein cholesterol were related to lower risk of AMI.

DISCUSSION

The relation between SES, all-cause mortality, and cardiovascular mortality was eliminated by simultaneous adjustment for age and biologic, behavioral, and psychologic and social risk factors (figure 1). The excess relative risk in the lowest income quintile was reduced by 85 percent for all-cause mortality and by 118 percent for cardiovascular mortality. However, when the relation between SES and AMI was adjusted for the same risk factors, the relative hazards across income groups were diminished but remained inversely graded and elevated (figure 1). While the excess relative risk for the bottom 20 percent of income earners was reduced by 45 percent, those in the lowest income quintile still remained at almost threefold risk of AMI. For both the mortality and AMI outcomes, most of the reduction in excess relative risk was accounted for by adjustment for biologic risk factors. In fact, for AMI, addition of information about behavioral and psychosocial risk factors added nothing to the reduction in excess relative hazard achieved by adjustment for the biologic risk factors alone.

These findings provide compelling evidence that the association between SES, all-cause mortality, and cardiovascular mortality is accounted for by a large number of known risk factors. However, in the case of AMI, similar adjustments failed to account completely

TABLE 3. Age-adjusted relative hazards (RH) and 95% confidence intervals (CI) for the association between income quintiles and cardiovascular mortality in 2,272 eastern Finnish men aged 42–60 years, by risk factor group, 1984–1993

Income quintile	Adjusted covariates									
	Age		Biologic risk factors*		Behavioral risk factors†		Psychologic and social risk factors‡		All risk factors§	
	RH	95% CI	RH	95% CI	RH	95% CI	RH	95% CI	RH	95% CI
First (lowest)	2.66	1.25–5.66	1.24	0.56–2.75	1.83	0.85–3.98	1.71	0.76–3.86	0.70	0.29–1.69
Second	1.90	0.88–4.14	1.15	0.51–2.57	1.55	0.71–3.40	1.29	0.57–2.93	0.74	0.31–1.76
Third	0.69	0.26–1.78	0.48	0.18–1.27	0.53	0.20–1.39	0.52	0.20–1.39	0.34	0.13–0.93
Fourth	0.72	0.27–1.93	0.56	0.21–1.52	0.59	0.22–1.58	0.60	0.22–1.62	0.42	0.15–1.16
Fifth (highest)	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference

* Biologic risk factors: fibrinogen, high density lipoprotein cholesterol, serum apolipoprotein B, serum ferritin, copper, hair mercury, triglycerides, blood leukocytes, hemoglobin, fasting blood glucose, systolic blood pressure, cardiorespiratory fitness, body mass index, and height.

† Behavioral risk factors: smoking, alcohol consumption, and physical activity.

‡ Psychologic risk factors: depression and hopelessness. Social risk factors: marital status, participation in organizations, and quality of social support.

§ Includes age, biologic, behavioral, psychologic, and social risk factors.

TABLE 4. Age-adjusted relative hazards (RH) and 95% confidence intervals (CI) for the association between income quintiles and fatal and nonfatal myocardial infarctions in 1,707 eastern Finnish men aged 42–60 years, by risk factor group, 1984–1993

Income quintile	Adjusted covariates									
	Age		Biologic risk factors*		Behavioral risk factors†		Psychologic and social risk factors‡		All risk factors§	
	RH	95% CI	RH	95% CI	RH	95% CI	RH	95% CI	RH	95% CI
First (lowest)	4.34	1.95–9.66	2.83	1.21–6.61	3.20	1.41–7.23	4.25	1.83–9.84	2.83	1.14–7.00
Second	2.25	0.97–5.21	1.57	0.66–3.74	2.12	0.91–4.95	2.28	0.96–5.44	1.86	0.75–4.63
Third	2.25	0.98–5.15	1.77	0.76–4.13	1.82	0.79–4.21	2.33	1.00–5.43	1.91	0.79–4.63
Fourth	2.18	0.94–5.05	1.93	0.82–4.53	1.95	0.84–4.55	2.32	1.00–5.41	2.12	0.87–5.12
Fifth (highest)	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference

* Biologic risk factors: fibrinogen, high density lipoprotein cholesterol, serum apolipoprotein B, serum ferritin, copper, hair mercury, triglycerides, blood leukocytes, hemoglobin, fasting blood glucose, systolic blood pressure, cardiorespiratory fitness, body mass index, and height.

† Behavioral risk factors: smoking, alcohol consumption, and physical activity.

‡ Psychologic risk factors: depression and hopelessness. Social risk factors: marital status, participation in organizations, and quality of social support.

§ Includes age, biologic, behavioral, psychologic, and social risk factors.

for the elevated risks associated with lower SES, even though the risk factors included in these analyses are strongly associated with this outcome. In analyses not presented here, we examined whether the elevated relative hazards observed after risk factor adjustment were due to differential survival after the acute event, but found no evidence to suggest any relation between income levels and survival after AMI.

Our findings are based on a population of men in eastern Finland, but we believe these results are generalizable beyond the immediate confines of the region. Kuopio is the major provincial center in eastern Finland and has an administrative-, industrial-, and service-based economy dominated by processing of farm, food, metal, and forest products. Most men in this sample resided in the city or suburbs of Kuopio (70 percent) and were evenly employed in white- (40 percent) and blue- (44 percent) collar occupations, with 16 percent engaged in farming. The size of the socioeconomic inequalities in mortality in Finland is comparable with England, but smaller than the differences experienced in the United States (36). Thus, the overall sociodemographic profile of this sample makes it comparable with populations in other industrialized countries. Furthermore, many of the risk factors used in these analyses are importantly related to mortality, cardiovascular disease, and socioeconomic status in population samples from a variety of countries (37, 38). However, because the sample is limited to middle-aged men and there are no studies of women that use such a wide variety of risk factors, it is unclear if these findings can be applied to the socioeconomic inequalities in female mortality and AMI.

There are three issues that should be considered before drawing conclusions from these results. First, while we have demonstrated that risk factor adjustment attenuates the association between SES and AMI, it is possible that a single measurement of these

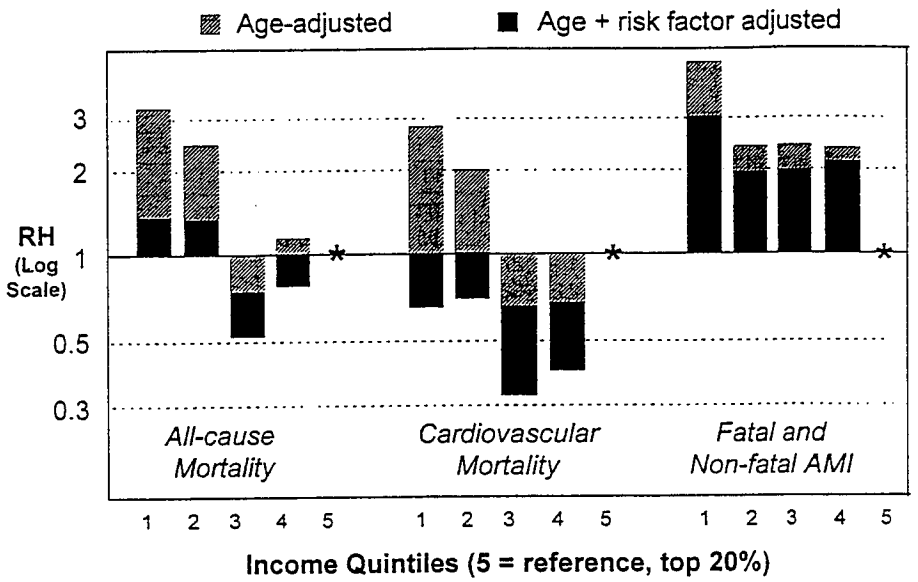

FIGURE 1. Relative hazards (RH), on the log scale, of all-cause mortality, cardiovascular mortality, and acute myocardial infarction (AMI), by quintile of income. Height of the hatched bars reflects RH adjusted for age. Black bars represent relative hazard after adjustment for all risk factors in a population-based sample of 2,272 (mortality analyses) and 1,707 (AMI analyses) eastern Finnish men aged 42–60 years (1984–1993). *, reference category.

risk factors at one point in time does not adequately represent exposure over the life course or that with increased follow-up the risk factors might become even more important correlates of AMI. Given the biologic variability in some risk factors and the errors associated with measurement on one occasion, it is possible that the impact of these risk factors may be even larger than assessed here. Second, it is also possible that there are one or more risk factors for AMI that we have not assessed in this study, such as environmental or other macrosocial forces that may further reduce the association between SES and AMI (39). Third, in attempting to assess the relation between SES and these outcomes, it is important to consider the role that imprecise measurement of correlated risk factors might play in biasing the observed associations with all-cause mortality, cardiovascular mortality, and AMI (40, 41). Dwyer and Feinleib (42) and Liu (43) have shown that the direction and magnitude of such bias is unpredictable in a multivariate context, and so it is possible that the magnitude of the relative hazards for SES observed after adjustment may be at least partly due to imprecise measures of the risk factors. In this light, the common practice of claiming statistical "independence" for a particular risk factor, after adjustment for covariates, should be viewed as potentially misleading unless the degree of bias associated with measurement error can be assessed. Unfortunately, information about the magnitude of such bias is unavailable in most epidemiologic studies.

The premise for this research was whether known biologic, behavioral, and psychosocial risk factors could "explain" the association between SES, all-cause mortality, cardiovascular mortality, and AMI. We have demonstrated that the commonly observed association between SES, mortality, and AMI appears, to a great extent, to be grounded in known biologic, behavioral, and psychosocial risk factor pathways. Our findings suggest that most of the association between SES, cardiovascular outcomes, and total mortality can be accounted for if all known risk factors are considered. The failure of previous studies to show this may be due to a more limited repertoire of risk factors and possibly to higher measurement variability. The Kuopio Ischemic Heart Disease Risk Factor Study was specifically designed to explore both known and suspected biologic mechanisms that mediate the association between ischemic heart disease and social, behavioral, and psychologic factors by assessing large numbers of risk factors in multiple domains with state-of-the-art measurement technology and great attention to quality control (18).

While we have also attempted to point out some limitations in interpreting multivariate models containing large numbers of correlated covariates, we believe that the most important limitation of such analyses is that they are causally uninformative. Given that SES, biologic, behavioral, and psychosocial variables are assessed at the same point in time, it is not possible to disentangle the important temporal relations between these risk factors. To a great extent, we have shown

that a large number of known risk factors appear to act as the mechanisms of *how* SES affects mortality and AMI, but our results do not shed any light on *why* these biologic, behavioral, psychologic, and social risk factors are differentially distributed by SES.

It is important to identify the mechanisms through which SES affects mortality and AMI, but it is only part of providing an "explanation" for these associations (44, 45). Increased understanding of why SES is related to all-cause mortality, cardiovascular mortality, and AMI might be gained by considering the causal pathways through which SES affects health (37). If lower SES acts as a powerful force in the adoption of poor dietary habits or influences behaviors such as smoking and physical activity or if poorer people are more likely to be hopeless or depressed, then the explanation of the relation between SES and these outcomes must include more than an estimate of how much of its effect is mediated by known biologic, behavioral, psychologic, and social pathways (46). A more complete explanation would require an understanding of why poorer people are more likely to possess the constellation of biologic risk factors, behaviors, and psychosocial characteristics that increase their risk of mortality and AMI.

Ideally, long-term studies are needed that can examine the development and maintenance of behavior, psychosocial, and biologic risk factors over the life course. While it is well established that lower SES groups have poorer adult risk factor profiles, we have shown in other analyses that a large constellation of adult behavioral and psychosocial characteristics is strongly associated with socioeconomic conditions during childhood (47). Analyses such as these cannot show which specific factors are responsible for the differences in behavior and psychosocial orientation, but they suggest that adult risk factor profiles have SES roots early in life.

Our findings imply that efforts to reduce the disease burden associated with low SES can legitimately focus on the behavior, psychosocial, and biologic risk factors that mediate the relation. Reductions in this inequitable distribution of disease could come from interventions that "target" low SES groups for modification of risk factors. However, if the influence of SES in childhood is important in the development of behavioral and psychosocial characteristics and these characteristics are differentially reinforced, constrained, and maintained by socioeconomic influences throughout the life course, then a great potential exists for the primary prevention of socioeconomic health inequalities by improving the social, environmental, material, and economic circumstances that may generate and mold adult risk factors over time.

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REFERENCES

1. Antonovsky A. Social class, life expectancy and overall mortality. Milbank Mem Fund Q 1967;45:31–73.
2. Lynch JW. Social position and health. (Editorial). Ann Epidemiol 1996;6:21–3.
3. Haan MN, Kaplan GA, Syme SL. Socioeconomic status and health: old observations and new thoughts. In: Bunker JP, Gomby DS, Kehrer BH, eds. Pathways to health: the role of social factors. Menlo Park, CA: H. J. Kaiser Family Foundation, 1989:76–135.
4. Gunning-Schepers LJ, Spruit IP, Krijnen JH, eds. Socioeconomic inequalities in health. The Hague, the Netherlands: Netherlands Ministry of Welfare, Health, and Cultural Affairs, 1989.
5. Lahelma E, Manderbacka K, Rahkonen O, et al. Ill-health and its social patterning in Finland, Norway and Sweden. Helsinki, Finland: National Research and Development Center for Welfare and Health, 1993.
6. Rose G, Marmot MG. Social class and coronary heart disease. Br Heart J 1981;45:13–19.
7. Salonen JT. Socioeconomic status and risk of cancer, cerebral stroke, and death due to coronary heart disease and any disease: a longitudinal study in eastern Finland. J Epidemiol Community Health 1982;36:294–7.
8. Markowe HLJ, Marmot MG, Shipley MJ, et al. Fibrinogen: a possible link between social class and coronary heart disease. Br Med J (Clin Res Ed) 1985;291:1312–14.
9. Pocock SJ, Shaper AG, Cook DG, et al. Social class differences in ischaemic heart disease in British men. Lancet 1987; 2:197–201.
10. Davey Smith G, Shipley MJ, Rose G. Magnitude and causes of socioeconomic differentials in mortality: further evidence from the Whitehall Study. J Epidemiol Community Health 1990;44:265–70.
11. Lundberg O. Causal explanations for class inequality in health—an empirical analysis. Soc Sci Med 1991;32:385–93.
12. North F, Syme SL, Feeney A, et al. Explaining socioeconomic differences in sickness absence: the Whitehall II Study. BMJ 1993;306:361–6.
13. Dennis BH, Zhukovsky GS, Shestov DB, et al. The association of education with coronary heart disease mortality in the USSR Lipid Research Clinics Study. Int J Epidemiol 1993; 22:420–7.
14. Marmot M, Theorell T. Social class and cardiovascular disease: the contribution of work. Int J Health Serv 1988;18: 659–74.
15. Williams DR. Socioeconomic differentials in health: a review and redirection. Soc Psychol Q 1990;53:81–99.
16. Syme SL. Social determinants of disease. In: Last JM, Wallace RB, eds. Maxcy-Rosenau public health and preventive medicine. Norwalk, CT: Appleton and Lange, 1992: 678–700.
17. Adler NE, Boyce T, Chesney MA, et al. Socioeconomic status and health. The challenge of the gradient. Am Psychol 1994; 49:15–24.
18. Salonen JT. Is there a continuing need for longitudinal epidemiologic research? The Kuopio Ischaemic Heart Disease Risk Factor Study. Ann Clin Res 1988;20:46–50.
19. Lakka TA, Salonen JT. Physical activity and serum lipids: a cross-sectional population study in eastern Finnish men. Am J Epidemiol 1992;136:806–18.
20. Rose GA, Blackburn H, Gillum RF, et al. Cardiovascular survey methods. Geneva, Switzerland: World Health Organi-

zation, 1982.
21. Lynch JW, Kaplan GA, Cohen RD, et al. Childhood and adult socioeconomic status as predictors of mortality in Finland. Lancet 1994;343:524–7.
22. Tuomilehto J, Arstila M, Kaarsalo E, et al. Acute myocardial infarction (AMI) in Finland—baseline data from the FINMONICA AMI register in 1983–1985. Eur Heart J 1992; 13:577–87.
23. Wilson TW, Kaplan GA, Kauhanen J, et al. Association between plasma fibrinogen concentration and five socioeconomic indices in the Kuopio Ischemic Heart Disease Risk Factor Study. Am J Epidemiol 1993;137:292–300.
24. Salonen JT, Salonen R, Seppänen K, et al. HDL, HDL_2 and HDL_3 subfractions and the risk of acute myocardial infarction. A prospective population study in eastern Finnish men. Circulation 1991;84:129–39.
25. Salonen JT, Nyyssönen K, Korpela H, et al. High stored iron levels are associated with excess risk of myocardial infarction in eastern Finnish men. Circulation 1992;86:803–11.
26. Salonen JT, Salonen R, Korpela H, et al. Serum copper and the risk of acute myocardial infarction: a prospective study in men in eastern Finland. Am J Epidemiol 1991;134:268–76.
27. Salonen JT, Seppänen K, Nyyssönen K, et al. Intake of mercury from fish, lipid peroxidation, and the risk of myocardial infarction and coronary, cardiovascular, and any death in eastern Finnish men. Circulation 1995;91:645–55.
28. Lynch JW, Helmrich SP, Lakka TA, et al. Moderately intense physical activity and high levels of cardiorespiratory fitness reduce the risk of non-insulin-dependent diabetes mellitus in middle-aged men. Arch Intern Med 1996;156:1307–14.
29. Lakka T, Venäläinen JM, Rauramaa R, et al. Relation of leisure-time physical activity and cardiorespiratory fitness to the risk of acute myocardial infarction. N Engl J Med 1994; 330:1549–54.
30. Ihanainen M, Salonen R, Seppänen R, et al. Nutrition data collection in the Kuopio Ischaemic Heart Disease Risk Factor Study: nutrient intake of middle-aged Finnish men. Nutr Res 1989;9:597–604.
31. Everson SA, Goldberg DE, Kaplan GA, et al. Hopelessness and risk of mortality, myocardial infarction and cancer incidence. Psychosom Med 1996;58:113–21.
32. Julkunen J, Salonen R, Kaplan GA, et al. Hostility and the progression of carotid atherosclerosis. Psychosom Med 1994; 56:519–25.
33. Kaplan GA, Wilson TW, Cohen RD, et al. Social functioning and overall mortality: prospective evidence from the Kuopio Ischemic Heart Disease Risk Factor Study. Epidemiology 1994;5:495–500.
34. Cox DR, Oakes D. Analysis of survival data. New York, NY: Chapman Hall, 1984.
35. SAS Institute. SAS user's guide: statistics. Version 6.09. Cary, NC: SAS Institute, Inc., 1990.
36. Kunst AE, Mackenbach JP. The size of mortality differences associated with educational level in nine industrialized countries. Am J Public Health 1994;84:932–7.
37. Kaplan GA, Keil JE. Socioeconomic factors and cardiovascular disease: a review of the literature. Circulation 1993;88: 1973–98.
38. Stamler J. Established major coronary risk factors. In: Marmot M, Elliot P, eds. Coronary heart disease epidemiology. Oxford, England: Oxford University Press, 1992:35–66.
39. Haan M, Kaplan GA, Camacho T. Poverty and health: prospective evidence from the Alameda County Study. Am J Epidemiol 1987;125:989–98.
40. Phillips AN, Davey Smith G. Bias in relative odds estimation owing to imprecise measurement of correlated exposures. Stat Med 1992;11:953–61.
41. Salonen JT. Statistical correction for measurement imprecision. (Letter). Lancet 1992;339:1116.
42. Dwyer JH, Feinleib M. Introduction to statistical models for longitudinal observation. In: Dwyer JH, Feinleib M, Lippert P, et al., eds. Statistical models of longitudinal studies of health. New York, NY: Oxford University Press, 1990:3–48.
43. Liu K. Measurement error and its impact on partial correlation and multiple linear regression analyses. Am J Epidemiol 1988; 127:864–74.
44. Lynch J, Kaplan GA, Salonen R, et al. Socioeconomic status and carotid atherosclerosis. Circulation 1995;92:1786–92.
45. Krieger N, Rowley DL, Herman AA, et al. Racism, sexism, and social class: implications for studies of health, disease, and well-being. Am J Prev Med 1993;9 (Suppl. 6):82–122.
46. Lynch JW, Kaplan GA, Cohen RD, et al. Socioeconomic status and progression of carotid atherosclerosis: prospective evidence from the Kuopio Ischemic Heart Disease Risk Factor Study. Arterioscler Thromb Vasc Biol 1996 (In press).
47. Lynch JW, Kaplan GA, Salonen JT. Why do poor people behave poorly? Soc Sci Med 1996 (In press).