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Letter to the Editor

Cumulative social risk and risk of death from cardiovascular diseases and all-causes

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Mortality rates for cardiovascular diseases (CVD) have declined steadily over the past few decades in high-income countries. This decline has by far disproportionately favored those with higher income, educational attainment, and social support or those who are members of ethnic majority groups [1–7]. Few studies have examined the cumulative effects of multiple social risk factors on CVD mortality rates [8]. Disparate exposure to multiple social risk factors may contribute to social inequalities in CVD mortality rates.

We used data on 10,035 adults (age ≥ 30 years) with no history of CVD, from the NHANES III Mortality Study (1988–1994 survey data linked to 2006 mortality data), to assess the prospective association between cumulative social risk and CVD deaths, <65-year-old mortality, and all-cause mortality. Linkage with the National Death Index allowed definition of CVD deaths as ICD-9 codes 390–459 or ICD-10 codes I00-I99. Income was assessed using the poverty income ratio (ratio of family income to the federal poverty level) dichotomized into below 1.00 (below the official definition of poverty) vs. 1.00 or greater (income above the poverty level). Education level was dichotomized into low (<12 years, representing < high school diploma) vs. high (≥12 years, representing high school diploma, some college, or college degree) levels. Self-reported race/ethnicity was classified into a minority group (non-Hispanic Black, Mexican-American and Other) vs. non-Hispanic White. Single-living status (proxy for social isolation/low level of social support) was classified into two groups, married/living as married vs. never married, widowed, divorced, or separated. Each of the four social risk factors were assigned a score of 1 for their presence or 0 for absence and were summed to create a cumulative social risk score (range 0 to 4). Cox proportional models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for the association between cumulative social risk and mortality. We evaluated the contribution of biological risk factors (body mass index [BMI], HbA1c, systolic blood pressure [SBP], cholesterol, triglycerides, C-reactive protein [CRP] and estimated glomerular filtration rate [eGFR]) to the association between cumulative social risk and CVD deaths. We hypothesized that these biological factors are on the pathway in the association between exposure to social risk factors and occurrence of CVD deaths, and thus are mediators of this association. HbA1c was measured using a Bio-Rad Diamant ion exchange high-performance liquid chromatography system. Serum total cholesterol and triglycerides were measured enzymatically by a Hitachi 704 Analyzer. eGFR was based on the Modification of Diet in Renal Disease study equation. Serum CRP was measured using the Behring latex-enhanced CRP assay.

A total of 31.7% of adults reported at least one social risk factor; 7.1% reported 3 or more. Over a median 14-year follow-up, there were 2604 deaths (1386 in males and 1218 in females) including 924 deaths related to cardiovascular diseases. Table 1 shows the age-and sex-adjusted associations of each social risk factor with CVD deaths, <65-year-old mortality, and all-cause mortality. Hazard ratios for CVD deaths, <65-year-old mortality and all-cause mortality significantly increased with an increasing number of social risk factors and were greatest in those exposed to 3 or more social risk factors compared with those with 0 (Table 1). Table 2 shows the association between exposure to 3 or more social risk factors and CVD deaths, as well as the contribution of biological risk factors to this association. Biological risk factors accounted for 12% (95% CI: 4% to 18%) of the association between exposure to 3 or more social risk factors and CVD deaths.

Previous studies on social inequalities in CVD mortality have typically operationalized social disadvantage using single measures of socioeconomic status (e.g. manual occupational class, low education level, low income) or a composite of socioeconomic measures in several periods through the life course [8]. However, summing the number of times an individual had been in a lower socioeconomic category as a proxy for cumulative social disadvantage, may erroneously attribute CVD mortality to risks associated with the accumulation of only socioeconomic

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Table 1
Association between social risk factors and cardiovascular disease deaths, < 65-year-old mortality and all-cause mortality. National Health and Nutrition Examination Survey III Mortality Study (1988–1994 to 2006).

	CVD mortality	< 65-year-old mortality	All-cause mortality
	HR (95% CI)	HR (95% CI)	HR (95% CI)
Individual social risk factors[a]			
Low family income	1.38 (1.02–1.87)	2.60 (2.04–3.33)	1.67 (1.41–1.98)
Low education level	1.17 (0.97–1.41)	1.66 (1.31–2.10)	1.28 (1.11–1.48)
Minority ethnic group	1.14 (0.90–1.43)	1.40 (1.14–1.71)	1.17 (1.02–1.34)
Single living	1.34 (1.06–1.71)	1.49 (1.19–1.88)	1.36 (1.16–1.58)
Cumulative social risk score[a]			
0	–	–	–
1	1.15 (0.88–1.49)	1.45 (1.11–1.90)	1.26 (1.06–1.51)
2	1.34 (0.97–1.85)	1.97 (1.49–2.60)	1.60 (1.32–1.92)
3 or more	1.64 (1.18–2.28)	2.96 (2.22–3.94)	1.86 (1.54–2.23)
Per unit score (trend)	1.17 (1.05–1.31)	1.43 (1.29–1.57)	1.24 (1.16–1.32)

HR = hazard ratio; CI = confidence interval; CVD = cardiovascular disease.
[a] Adjusted for age and sex.

exposures. Studies of social inequalities in health have previously shown that socioeconomic indicators including income and education are not interchangeable as they measure different phenomena related (at least partly) to different causal processes [9,10].

This study had several shortcomings. First, we lacked information on specific CVD endpoints, (e.g., myocardial infarction, stroke, heart failure). Such information would have revealed the drivers of the association between cumulative social risk and CVD mortality. Second, cumulative social risk models were additive, precluding exploration of statistical interactions between social risk factors. However, examining higher order interaction terms requires much larger sample sizes and the interpretation is difficult. Third, while we showed that a particular set of underlying biological mediators explained a small amount of the association between exposure to 3 or more social risk factors and CVD mortality, we did not include mediating constructs such as health behaviors (e.g. smoking), or access/uptake of drug therapies. These factors may exert some of their effect through more proximal biological risk factors included in our mediation analysis. Future studies should however examine these alternative constructs to discern the shared underlying mechanisms capable of explaining how cumulative social risk adversely influences CVD mortality. Fourth, definitions of social risk factors in this study may not be applicable to other countries. Thus, comparative cross-national research is needed to ascertain whether the association between cumulative social risk exposure and CVD mortality is generalizable outside of the US.

In conclusion, we found that exposure to an increasing number of social risk factors significantly increased the risk of CVD deaths, <65-year-old mortality, and all-cause mortality. For segments of the adult US population, strategies aimed at reducing social inequalities in CVD mortality rates should consider cumulative exposure to different social risk factors, as addressing multiple social risk factors may be more beneficial than tackling single social risk factors in isolation.

Table 2
Contribution of baseline biological risk factors in explaining association between exposure to 3 or more social risk factors and cardiovascular disease deaths. National Health and Nutrition Examination Survey III Mortality Study (1988–1994 to 2006).

	CVD mortality	
Baseline risk factors	HR (95% CI)	% difference (95% CI)[a]
Model 1[b]	1.46 (1.08–1.93)	–
Model 1 + BMI	1.42 (1.06–1.91)	2 (0 to 5)
Model 1 + HbA_{1c}	1.37 (1.02–1.84)	5 (2 to 9)
Model 1 + SBP	1.33 (1.00–1.78)	8 (3 to 14)
Model 1 + cholesterol	1.44 (1.08–1.93)	0 (0 to 2)
Model 1: triglycerides	1.45 (1.09–1.95)	−1 (−4 to 2)
Model 1 + eGFR	1.45 (1.09–1.94)	−1 (−3 to 0)
Model 1 + CRP	1.37 (1.02–1.84)	5 (2 to 11)
Model 2: model 1 + all risk factors	1.27 (0.97–1.69)	12 (4 to 18)

BMI = body mass index; SBP = systolic blood pressure; and CRP = C-reactive protein. eGFR = estimated glomerular filtration; CVD = cardiovascular disease; HR = hazard ratio. CI = confidence interval.
[a] Bias-corrected boostrap 95% CI.
[b] Adjusted for age and sex.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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