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Low Socioeconomic Status and Depression: A Double Jeopardy for Cardiovascular Disease?

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Few population-based cohort studies have examined the combined association of low socioeconomic status (SES) and depression with the incidence of cardiovascular disease (CVD) despite growing evidence on the importance of these two risk factors. The recognition that traditional health and lifestyle factors do not entirely explain CVD risk is growing, with the acknowledgement that treatment and prevention strategies for CVD should also emphasize the role of psychosocial factors (e.g. depression) and social determinants of health (e.g. SES). While these factors have not yet been incorporated in cardiovascular risk scoring systems, there have been several calls for the recognition of SES and depression on CVD risk [1–3].

Many studies have shown that depression is associated with an increased risk of CVD in initially healthy subjects and an increased risk of mortality among patients with underlying coronary heart disease, which are summarized and supported by several meta-analyses [4,5]. The precise mechanisms through which depression and psychosocial stress may increase the risk for adverse cardiovascular outcomes are not completely understood. However, it is increasingly recognized that changes in neurobiology in depressed patients may alter cardiovascular function and structure, and that dysregulation of stress-response pathways (e.g., the sympathetic nervous system, neurohormonal stress responses, and alterations in central brain function) may also contribute to disease in vulnerable individuals [3].

Similarly, low SES at the individual and contextual (neighborhood) level has been associated with adverse cardiovascular outcomes, particularly among patients with underlying coronary heart disease [6,7]. Studies have shown disparities in treatment of low vs. high SES patients or those in low vs. high income areas, such as cardiac rehabilitation and administration of statin medications [8,9]. SES is a complex and multidimensional construct that has important implications on health beyond access to care and treatment. Lower SES individuals are exposed to more stress, social challenges, and adversity, but also have fewer interpersonal and intrapersonal resources to cope with these stressful events [10,11]. Several emerging studies have linked low SES at the individual and even at the contextual level with

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the body's stress response through the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system [12,13] suggesting that low SES can also be considered a psychosocial stressor with physiological implications. Therefore, socioeconomic disadvantage can lead to disparities in access, treatment, and care, but may also increase cardiovascular risk through shared stress pathophysiology with depression.

In this issue of the *Journal of Psychosomatic Research*, Cho et al. [14] test the separate and combined associations of SES and depression with the incidence of acute myocardial infarction (AMI) and stroke. To test their hypothesis that the risk of CVD is compounded by the simultaneous presence of low SES and depression, they used nationwide health insurance claims data from 2004–2005 of 2.7 million adults in South Korea with a median follow-up of 11.6 years.

Hospital visits for depression as well as the main outcomes in the study, including AMI and stroke, were defined using ICD-10 codes from the insurance claims data. SES was based on health insurance premiums that were set according to the income status reported to the government. Patients were classified into 1 of 6 risk groups of SES and depression: 1) a high SES without depression (reference), 2) a medium SES without depression; 3) a low SES without depression; 4) a high SES with depression; 5) a medium SES with depression; and 6) a low SES with depression.

Using Cox proportional hazards regression, Cho et al. [14] found that both low SES and depression were independently associated with increased risk of AMI and stroke. Specifically, a low SES was associated with an increased risk of AMI (HR: 1.16; 95% CI: 1.14, 1.19) and stroke (HR: 1.13; 95% CI: 1.11, 1.14). Depression was also associated with an increased risk of AMI (HR: 1.26; 95% CI: 1.21, 1.31) and stroke (HR: 1.24; 95% CI: 1.21, 1.27). When the authors examined the risk associated with the combination of SES and depression, patients with both depressive symptoms *and* low SES had the greatest risk of developing AMI (HR: 1.47; 95% CI: 1.36, 1.60) and stroke (HR: 1.37; 95% CI: 1.30, 1.44) compared to patients with a high SES without depression. The authors concluded that SES and depression exerted positive effect modification on the additive scale for MI and negative effect modification on the additive scale for stroke.

Cho et al. [14] also formally tested the product term of SES-by-depression and then estimated specific HRs for linear combinations of SES and depression on each outcome of interest, but with alternating reference groups (contrasts). The overall p-values for the interaction term of SES-by-depression were not statistically significant at an alpha level of 0.05, for either AMI (p=0.09) or stroke incidence (p=0.09) among this sample of 2.7 million individuals, suggesting a non-significant departure from homogeneity of effects, or that risks were not significantly different across subgroups of exposures on AMI and stroke. However, it would have been interesting to see these results if a common reference group were applied.

The overall significance of these results by Cho et al. [14] would have also been strengthened by presenting more detailed methods and results with calculations that led to their conclusions regarding effect modification, especially because recommendations on how

to interpret and present such data are well established [15]. The discussion would also have been enhanced by addressing the public health implications of these findings and how they may influence future interventions given the authors' contrasting findings of positive effect modification on the additive scale for MI and negative effect modification on the additive scale for stroke.

Despite these limitations in the interpretation of results presented, there are a number of strengths in this study. First, it utilized a nationwide population-based study with an enormous sample size that included both men and women. Second, the authors were also able to merge national health data with health insurance claims data to obtain information on potential confounding factors. Importantly, significant associations were found between the confluent role of low SES and depression on increased risk for AMI and stroke after adjusting for demographic, behavioral, and lifestyle risk factors.

We should, however, also recognize limitations in this study inherent with using health insurance claims data, which have been previously pointed out [16]. Some of these are acknowledged by the authors (misclassification, unmeasured confounding, residual confounding) and may have biased results towards the null given that the effect sizes for AMI and stroke were quite small. In addition, the clinical diagnosis of depression (2.4% of patients) in this study may have been under-reported in the medical records due to culture and stigma in Korea for psychiatric care. Further, competing events due to non-cardiovascular deaths were not considered. Whether data on mortality and cause of death out of the hospital were available in the claims data or were linked from other sources is unclear from this paper, although, the authors did mention that participants with missing mortality data were excluded from the analysis. Previously published studies using other health insurance data in South Korea were linked to mortality data [17,18]; however, it is unclear if a similar strategy was adopted here.

The paper by Cho et al. [14] brings needed attention to the combined risk of SES and depression on CVD. The results presented by the authors suggest a cumulative effect of SES and depression on risk of AMI and stroke and that having both low SES and depression is worse than having one risk factor or none. These results add to the growing recognition on the importance of depression and SES and cardiovascular outcomes. Future studies should confirm these findings with rigorous study protocols and analyses of effect modification and interaction. Potentially, these results may illuminate future avenues for improving individual and population health.

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