THREE AUTHORS AND
DR. KUBZANSKY REPLY

We read the letter by Drs. Macleod and Davey Smith (1) with great interest and thank them for their interest in our study (2). The authors of the letter suggest that stress is not an important explanatory factor in the disease process and cite as evidence a lack of association between Karasek’s measure of job stress and two health outcomes in the Nurses’ Health Study. We disagree with the authors’ assessment. The two reports from the Nurses’ Health Study (2, 3) cited by the authors comprised tests of a specific type of stress (job stress) in relation to breast cancer and coronary heart disease incidence. The null findings in these two reports do not amount to a wholesale rejection of the “psychosocial hypothesis” as the authors seem to suggest.

The authors of the letter suggest, “We are not aware of any instance of a robust positive association between stress and objective physical disease being reported from a population where either stress was associated with social advantage (but disease was not) or disease was associated with social advantage (but stress was not)” (1, p. 1134). Because of the narrow range of socioeconomic status in the Nurses’ Health Study, we have a unique data set in which to examine associations of stress with health outcomes, without the strong potential influence of residual confounding by socioeconomic status. We would therefore like to call attention to other work we have done in the Nurses’ Health Study. For example, we have examined stress from caregiving in relation to coronary heart disease, as well as breast cancer. Stress from caregiving was associated with an elevated risk of coronary heart disease but not with breast cancer (4–6). Given these findings, we would agree that it is unlikely that job stress is related to breast cancer, but not because stress is unrelated to all disease, but because in previous work psychosocial factors have been related to lower levels of sex steroid hormones, intermediate variables on the exposure-disease pathway for breast cancer. However, if what the authors suggest is correct, that socioeconomic status explains associations between stress and health, then given the narrow range of socioeconomic status in the Nurses’ Health Study cohort, we would expect to find that stress would not be related to coronary heart disease. However, that is not the case. Indeed, stress has regularly been related to cardiovascular disease in prior work (7). This does not take account of the stress associated with low socioeconomic status or other ways of evaluating distress. In fact, studies in this cohort have consistently found other measures of distress to be prospectively associated with increased risk for coronary heart disease.
Psychosocial factors may be linked to a variety of diseases on the basis of similar underlying mechanisms. Evidence of an association will likely depend on the relevance of the mechanism for a given disease. For example, we predict that psychosocial factors may be positively related to certain cancers (e.g., colon cancer) with similar underlying mechanisms to those of cardiovascular disease. We recently found support for this hypothesis in a study of depression and colon cancer in this cohort (9). Macleod and Davey Smith (10) have argued against making generalizations about the relation between stress and general susceptibility to disease, instead calling for tests of associations between specific exposures and specific disease outcomes. We suggest that a symmetric logic should be applied in the case of general-exposures and specific disease outcomes. We suggest that a symmetric logic should be applied in the case of general-exposures and specific disease outcomes. We suggest that a symmetric logic should be applied in the case of general-exposures and specific disease outcomes. We suggest that a symmetric logic should be applied in the case of general-exposures and specific disease outcomes. We suggest that a symmetric logic should be applied in the case of general-exposures and specific disease outcomes.

We interpret the null association between job stress and breast cancer as a call to refine the quality of psychosocial research. Researchers need to test different ways of conceptualizing and measuring stress, as well as to think more in depth about the range of known biologic as well as nonbiologic mechanisms when proposing studies of stress-disease links. Job stress may not be linked to breast cancer incidence, but it may still be associated with disease progression. Careful delineation of these mechanisms is needed not just in the area of psychosocial factors but also with regard to socioeconomic circumstances. For instance, the authors of the letter suggest that socioeconomic disadvantage has not been associated with breast cancer in North America. This is not completely accurate. Women of higher socioeconomic status have a higher incidence of breast cancer, but women of lower socioeconomic status have a lower rate of survival after diagnosis (11, 12).

Because psychosocial stressors are distal on the pathway to disease, there are both a greater challenge inherent in demonstrating links between stress and health outcomes and a greater potential for understanding the reasons behind disease.

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REFERENCES


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