American Journal of Epidemiology Advance Access published August 15, 2013

American Journal of Epidemiology

Letter to the Editor

THE AUTHORS REPLY

We are delighted to respond to the points raised by Choi et al. (1) and Landsbergis et al. (2) in their letters regarding our article (3). The commentators suggested that a meta-analysis including previously published studies, in addition to data from the Individual-Participant-Data Meta-analysis of Working Populations (IPD-Work) Consortium (n = 197,473) (4), would be essential to evaluate the association between job strain and coronary heart disease. This meta-analysis has already been published (5). The summary hazard ratio for developing coronary heart disease for job strain versus no job strain based on 26 independent prospective cohort studies from Europe, the United States, and Asia was 1.3 (95% confidence interval: 1.2, 1.5), that is, was consistent with that from the IPD-Work Consortium alone (1.2; 95% confidence interval: 1.1, 1.4) (4).

Our commentators noted that the use of the median split to define job strain in the IPD-Work Study was arbitrary. Although this is certainly true, it is also the case that this measure is the most widely used approach to operationalize job strain in the literature. Landsbergis et al. have previously introduced multiple alternative (though equally arbitrary) measures of job strain: the quotient, the quadrant term, the quadrant term using national means, and linear term formulations (6). However, they do not indicate which measure, in their opinion, should be used.

The lack of standard measures, even after 3 decades of research on the job-strain theory, is indeed a major problem potentially encouraging post hoc decisions, such as selective reporting of findings based on the operationalization that provides the strongest associations. This would lead to an evidence base over-represented by false positive findings. To minimize this bias in the IPD-Work Consortium, we published our harmonized operationalization of job strain before obtaining data on coronary heart disease from the participating studies (7).

The lack of standard definitions for job strain also complicates the interpretation of null findings. In any new publication, a null finding is not necessarily viewed as adding to scientific knowledge, as it may be interpreted as a "false negative" because of the use of nonoptimal measures. It seems that our commentators followed this reasoning, implying that a stronger association with coronary heart disease would have been found if some alternative measures of job strain were used. Our reviewers for the IPD-Work paper (4) requested subsidiary analyses with the quadrant method and separately for job demand and job control components. As reported in the appendix of that article, the associations with coronary heart disease were not stronger for these alternative measures (4).

Our commentators' argument that the use of white-collar cohorts in addition to those from the general working population caused underestimation of the job strain association with coronary heart disease is not supported by the meta-analysis; the hazard ratios for job strain were similar for those in high versus low socioeconomic positions (4). One way of illustrating the relatively modest role of job strain in coronary heart disease etiology is to compare the associations with other risk factors within the same cohort. In the IPD-Work cohort, the population attributable risk for an unhealthy lifestyle (i.e., 2 or more of the following: smoking, heavy alcohol consumption, obesity, and physical inactivity) was 7 times greater (26.4%) than the population attributable risk for job strain (3.8%) (8). That IPD-Work includes some white-collar cohorts cannot explain the relative difference in population attributable risks between job strain and lifestyle factors because the better health of white-collar cohort members is reflected in their having both lower job strain and less unhealthy lifestyle factors. Obviously, these results do not discount the relevance of job strain or other types of work stressors (e.g., rotating shift work, precarious work, work/family balance) as a major problem in terms of quality of life and mental well-being (9, 10).

The commentators suggested that retirement may have created a bias toward the null. However, it is well known that risk ratios associated with many coronary heart disease risk factors, such as smoking, blood pressure, diabetes, and high apolipoprotein B/apolipoprotein A1 ratio, attenuate with age (11). It is therefore uncertain whether age rather than bias due to retirement affects hazard ratios for job strain among older employees. Our age-stratified analysis suggested that, if anything, such associations are likely to be small: Among employees older than 50 years of age, the hazard ratio for job strain was only marginally lower (1.29; 95% confidence interval: 1.08, 1.54) than that among younger employees (1.36; 95% confidence interval: 1.14, 1.62) (4). As the mean follow-up period was 7.5 years, a small proportion of employees in the younger group retired during the study period, whereas a substantial number did so in the older group. The almost identical hazard ratios for these 2 groups suggest that retirement is not a major source of bias.

To conclude, given the evidence already available, it seems that continued examination of the points raised by Choi et al. (1) and Landsbergis et al. (2) may not be an optimal use of research resources. The current scientific excitement is elsewhere on more fundamental questions involving chronic stress mediation and interventions, for example: What is the long-term pathological process that follows acute stress reactions and over time leads to the development of coronary heart disease? Is it possible to develop randomized controlled trials to examine whether a reduction in job strain can reduce the risk of coronary heart disease? What genetic variants or epigenetic alterations might identify groups particularly vulnerable to the

adverse effects of stress? (12) Answers to these questions are more likely to contribute to practicable interventions than are endless iterations of job strain measures, methodological refinements to adjust for (minor) retirement effects, or calls to collect yet more observational data to pin down whether the hazard ratio is 1.23 or 1.32.

ACKNOWLEDGMENTS

Dr. Kivimäki was supported by an Economic and Social Research Council professorial fellowship, the Medical Research Council of the United Kingdom (grant K013351), and the National Heart, Lung, and Blood Institute (grant R01 HL036310).

Conflict of interest: none declared.

REFERENCES

1. Landsbergis PA, Dobson M, Schnall P. Re: "need for more individual-level meta-analyses in social epidemiology: example of job strain and coronary heart disease" [letter]. *Am J Epidemiol*. 2013;000(00):000–000.
2. Choi B, Dobson M, Landsbergis PA, et al. Re: "need for more individual-level meta-analyses in social epidemiology: example of job strain and coronary heart disease" [letter]. *Am J Epidemiol*. 2013;000(00):000–000.
3. Kivimäki M, Kawachi I. Need for more individual-level meta-analyses in social epidemiology: example of job strain and coronary heart disease. *Am J Epidemiol*. 2013;177(1):1–2.
4. Kivimäki M, Nyberg ST, Batty GD, et al. Job strain as a risk factor for coronary heart disease: a collaborative meta-analysis of individual participant data. *Lancet*. 2012;380(9852):1491–1497.
5. Steptoe A, Kivimäki M. Stress and cardiovascular disease: An update on current knowledge. *Annu Rev Public Health*. 2013;34:337–354.
6. Landsbergis PA, Schnall PL, Warren K, et al. Association between ambulatory blood pressure and alternative formulations of job strain. *Scand J Work Environ Health*. 1994;20(5):349–363.
7. Fransson EI, Nyberg ST, Heikkila K, et al. Comparison of alternative versions of the job demand-control scales in 17 European cohort studies: the IPD-Work consortium. *BMC Public Health*. 2012;12:62.
8. Kivimäki M, Nyberg ST, Fransson EI, et al. Associations of job strain and lifestyle risk factors with the risk of coronary artery disease: a meta-analysis of individual participant data. [published online ahead of print May 13, 2013]. *CMAJ*. (doi:10.1503/cmaj.121735).
9. Netterstrom B, Conrad N, Bech P, et al. The relation between work-related psychosocial factors and the development of depression. *Epidemiol Rev*. 2008;30:118–132.
10. Virtanen M, Pentti J, Vahtera J, et al. Overcrowding in hospital wards as a predictor of antidepressant treatment among hospital staff. *Am J Psychiatry*. 2008;165(11):1482–1486.
11. Yusuf S, Hawken S, Ounpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART Sstudy): case-control study. *Lancet*. 2004;364(9438):937–952.
12. Steptoe A, Kivimaki M. Stress and cardiovascular disease. *Nat Rev Cardiol*. 2012;9(6):360–370.

Mika Kivimäki[1] and Ichiro Kawachi[2]
(e-mail: m.kivimaki@ucl.ac.uk)
[1] *Department of Epidemiology and Public Health, University College London, London WC1E 6BT, United Kingdom*
[2] *Department of Society, Human Development, and Health, Harvard School of Public Health, Boston, MA 02115*

DOI: 10.1093/aje/kwt194.