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Commentary

Need for More Individual-level Meta-Analyses in Social Epidemiology: Example of Job Strain and Coronary Heart Disease

Mika Kivimäki* and Ichiro Kawachi

* Correspondence to Prof. Mika Kivimäki, Department of Epidemiology and Public Health, University College London, 1-19 Torrington Place, WC1E 6BT London, United Kingdom (e-mail: m.kivimaki@ucl.ac.uk)

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In genetics, major progress was made after pooling of data sets to mega-studies became the norm in the field. In the present commentary, the authors ask whether such an approach would also be worthy of broader application in the field of social epidemiology. Research on job strain and coronary heart disease provides an illustrative example. Over 3 decades, debate has continued as to the relative importance of high psychological demands versus low control—that is, whether one component of job strain is more toxic than the other—and differences by age and sex. Recently, these controversies were largely resolved in an individual-participant meta-analysis of 200,000 participants from 13 cohorts: The combination of both high demands and low control was a greater risk factor than either of the components alone, there were no differences in the associations of job strain with CHD between men and women, between the young and old, or at different levels of socioeconomic position, and the impact was more modest when unpublished data were included but was still robust to all adjustments. The fact that longstanding debates in the job strain literature were resolved by applying an individual-participant data meta-analysis approach suggests that lessons learned in genetics might also apply to social epidemiology.

meta-analysis; research design; social epidemiology

Abbreviation: CHD, coronary heart disease.

Before the era of genetic mega-studies, it was not uncommon for each publication of a genetic variant-disease link to be followed by 3 others that failed to replicate the originally reported association. This sorry state of affairs was resolved by the pooling of genetic studies. Indeed, it could be said that the use of collaborative mega-studies in the field of genetics represents one of the most successful ideas in biomedical research. Associations in genetics typically tend to be small. With the notable exception of socioeconomic status, the same could be said for many risk factor associations in the field of social epidemiology. Would progress be boosted in social epidemiology if pooling of data sets also became the norm in the field? We believe it would.

The story of job strain provides an illustrative example. Robert Karasek, who originated the concept, proposed that a combination of high demands at work and low job control (i.e., "job strain") increased the risk of coronary heart disease (CHD) (1, 2). His theory was well received by both stress researchers and occupational health specialists. The idea is intuitively appealing: Most of us would not want to be stuck in a machine-paced assembly job where there is little variation in the content of work and precious little autonomy over how to manage the demands of the job.

Despite a promising start, however, the empirical replications of Karasek's initial idea mirrored the early genetic research tradition. First, a debate arose as to the relative importance of high psychological demands versus low control—that is, whether one is more toxic than the other. In a narrative review by Rose-Everson and colleagues (3),

it was concluded that job control might be more important. In another narrative review, Eller et al. (4) came to the opposite conclusion: The association of job strain with CHD is likely to be driven by high demands. Second, there has been continuing confusion regarding differences by age and sex. Some authors have suggested that the association between job strain and CHD is more pronounced in men (5), whereas others see women as more vulnerable (6). A further suggestion is that job strain increases CHD risk in younger employees but that the excess risk attenuates at older ages (7). Third, estimates of the magnitude of the association remains heterogeneous, varying from a 9-fold excess risk associated with job strain (6) to a 20% nonsignificant protection against CHD (8). Some critics have suggested that the observed associations are spurious, with job strain being only a marker of other causal risk factors, such as socioeconomic stratification (9).

In 2008, the Individual-Participant Data Meta-Analysis in Working Populations Consortium was established to achieve a more definitive understanding of these debates by using individual-participant meta-analysis of multiple cohort studies. To minimize investigator bias, data were extracted in 2 stages: first, the exposure was harmonized across cohorts in a validation study with investigators masked to outcome information (10), and then the endpoint of interest, CHD, was harmonized across studies.

Data from over 197,000 participants and 2,350 events of incident CHD from 13 cohorts from the United Kingdom, France, Belgium, the Netherlands, Denmark, Sweden, and Finland suggested that the combination of both high demands and low control was a greater risk factor than either of the components alone and that there are no significant differences in the association of job strain and CHD between men and women, between the young and the old, or at different levels of socioeconomic position (11). There was some evidence of publication bias. In the 3 studies that had been published, the hazard ratio for CHD in people reporting job strain relative to those who did not was 1.43 (95% confidence interval: 1.15, 1.77); based on those 10 studies that had not been published but for which the investigators made their raw data available for analyses, the hazard ratio was more than halved (1.16; 95% confidence interval: 1.02, 1.32). The combined hazard ratio was 1.23 (95% confidence interval: 1.10, 1.37). Thus, the study revealed a small 10%–37% excess risk of CHD associated with job strain. This was robust to all adjustments and uniform across subgroups.

Science makes progress through the accumulation of evidence. Three longstanding debates in the job strain literature were answered by applying an individual-participant data meta-analysis approach. Wouldn't such an approach—already proved to be successful in genetics—also be worthy of broader application in the field of social epidemiology?

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Author affiliations: Department of Epidemiology and Public Health, University College London, London, United Kingdom (Mika Kivimäki); and Department of Society, Human Development, and Health, Harvard School of Public Health, Boston, Massachusetts (Ichiro Kawachi).

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