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The association between study characteristics and outcome in the relation between job stress and cardiovascular disease – a multilevel meta-regression analysis [1]

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[1] Appendix: categorization of the variables; random effect model; model construction for the study feature "correction for confounders within a study"

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Appendix

A. Categorization of the variables

Outcome assessment was classified into three categories: (i) questionnaires in which people were asked whether they had CVD, (ii) questionnaires in which people were asked whether they had a *doctor confirmed* CVD, and (iii) the use of diagnostics (review of medical dossier, hospital and death registers, diagnostic criteria).

Three types of exposure questionnaires were included: (i) original JCQ (defined as 9 items for control and 5 items for demands and an answer category 'disagree-agree'), (ii) JCQ-like (defined as 6–15 JCQ comparable items for control, 4–7 JCQ comparable items for demands and/or a different answer category than disagree-agree), and (iii) "different"' (the number of items is different from the number of items defined under JCQ-like and/or the items were different altogether but they still needed to be comparable to what the demand–control model intends to measure).

In the individual studies exploring the job strain and CVD association, adjustment for confounders is performed. Which confounders are included and the manner of adjustment differs: some studies analyze in different steps to explore the effect of adjustment for a confounder. The reason for this is differences in theories about whether some confounders are actually intermediates and therefore should not be included in the model, but also because of differences in the (lack of) availability of data about these confounding factors. For each confounder a dichotomized variable was made ("yes" versus "no" adjustment).

The exposure level for decision latitude and job demands is mostly presented as tertiles and quartiles in the published studies. To standardize these exposure categories and thereby to enhance the comparability of the various exposure levels among studies, we dichotomized all these categories into two exposure levels: above and below the median value. The procedure that was used to standardize the exposure levels will be clarified by means of the two following examples: (i) if a study presented the CVD risk for employees exposed to the fourth quartile of job demands compared to employees exposed to the first quartile, the difference between the two exposure groups was calculated by: 7/8 minus 1/8 = 6/8 = 0.75; (ii) if a study presented the CVD risk for employees exposed to the highest tertile of job demands compared to employees exposed to the lowest tertile, the difference between the two groups was calculated by: 1/6 minus 5/6 = 4/6 = 0.67. This was done for all categories; finally this new variable was divided by two.

For job strain, we used the categories as they were presented in the studies, which are (most often) conform to the theory of Karasek (1). These were grouped into three categories: (i) high strain versus the other three quadrants (low strain, passive and active), (ii) high strain versus low strain, and (iii) high strain defined as alternative formulations than based on median value.

The quality of the included studies was categorized into "good" (the "very good" and "good" studies) and "poor" ("moderate", "poor", "very poor" studies).

B. The random effects model

The model used for the analyses is given by

$$\begin{bmatrix} y_{11} \\ y_{12} \\ y_{21} \\ y_{31} \\ y_{32} \\ y_{33} \\ \ldots \end{bmatrix} = \mathbf{X\beta} + \mathbf{u} + \boldsymbol{\varepsilon}$$

where y_{ij} denotes the j^{th} observed effect in the i^{th} study (eg, study 1 provided two effects), $\mathbf{X}$ is the design matrix including the values of moderators (i.e., study characteristics), and $\boldsymbol{\beta}$ denotes the vector of regression coefficients. The vector $\mathbf{u}$ denotes random effects to model (residual) heterogeneity in the study-specific true effects. We assume that the variance-covariance matrix of $\mathbf{u}$ has a compound symmetric structure with constant variance τ^2 and ρ denoting the correlation of the true effects within the same study:

$$Var[\mathbf{u}] = \begin{bmatrix} \rho\tau^2 & \tau^2 & & & & & \\ & & \tau^2 & & & & \\ & & & \tau^2 & \rho\tau^2 & \rho\tau^2 & \\ & & & \rho\tau^2 & \tau^2 & \rho\tau^2 & \\ & & & \rho\tau^2 & \rho\tau^2 & \tau^2 & \\ & & & & & & \ldots \end{bmatrix}$$

The variance-covariance matrix of the vector of sampling errors, **ε**, is assumed to take on a structure of the form:

$$Var[\boldsymbol{\varepsilon}] = \begin{bmatrix} v_{11} & \lambda\sqrt{v_{11}}\sqrt{v_{12}} & & & & & & \\ \lambda\sqrt{v_{11}}\sqrt{v_{12}} & v_{12} & & & & & & \\ & & v_{21} & & & & & \\ & & & v_{31} & \lambda\sqrt{v_{31}}\sqrt{v_{32}} & \lambda\sqrt{v_{31}}\sqrt{v_{33}} & & \\ & & & \lambda\sqrt{v_{31}}\sqrt{v_{32}} & v_{32} & \lambda\sqrt{v_{32}}\sqrt{v_{33}} & & \\ & & & \lambda\sqrt{v_{31}}\sqrt{v_{33}} & \lambda\sqrt{v_{32}}\sqrt{v_{33}} & v_{33} & & \\ & & & & & & \ddots & \end{bmatrix}$$

where v_{ij} is the (approximately) known sampling variance of the observed effect y_{ij} and λ denotes the unknown correlation between the errors within the same study. We assume that λ is constant across all studies. For a given value of λ, $Var\boldsymbol{\varepsilon}]$ can be computed and then τ^2, ρ, and the coefficients in **β** can be estimated with restricted maximum-likelihood estimation (assuming normality of the distribution of **u** and **ε**) as described by van Houwelingen et al (2). We therefore estimated λ by repeatedly fitting the model above using various assumed values for λ to determine which value maximizes the restricted likelihood. Using this approach, we estimated correlations of 0.86, 0.35, and 0.55 for job strain, demands, and control, respectively. The results provided in the text are those obtained using these maximum likelihood estimates for λ.

C. Model construction for the study feature "correction for confounders within a study"

The impact of studies that adjust for possible confounders (eg, age, body mass index, socioeconomic status etc) compared to studies that do not adjust for these confounders on the reported effect size had to be assessed in such a manner that all these confounders were included simultaneously in the model. The reason for this is that these confounders are highly correlated and the issue is not whether adjustment has taken place, but rather for which ones. However, the multitude of study characteristics (confounders and factors such as design, outcome assessment etc) restricted us from including all these variables in the model at once because over-fitting of the model had to be prevented.

Thus, all the confounders were simultaneously included in one model to quantify the effect of adjusting for a specific confounder compared to not adjusting for that specific confounder, adjusted for the impact of adjusting for other confounders.

If adjustment for a specific confounder was significantly associated with the CVD risk estimate (judged on the magnitude of the association in combination with the width of the confidence interval), the other selected study features (such as country, type of questionnaire etc) were included into the model to assess whether the association between adjustment for a confounder and the CVD risk still remained after inclusion of other study features.

References

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