BMJ Open

Psychosocial factors at work and inflammatory markers: protocol for a systematic review and meta-analysis

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To cite: Eguchi H, Watanabe K, Kawakami N, *et al*. Psychosocial factors at work and inflammatory markers: protocol for a systematic review and meta-analysis. *BMJ Open* 2018;**8**:e022612. doi:10.1136/bmjopen-2018-022612

► Prepublication history and additional material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2018-022612).

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Received 2 March 2018
Revised 20 July 2018
Accepted 24 July 2018

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ABSTRACT

Introduction Chronic inflammation may be a mediator for the development of cardiovascular disease (CVD), metabolic diseases and psychotic and neurodegenerative disorders. Meta-analytic associations between work-related psychosocial factors and inflammatory markers have shown that work-related psychosocial factors could affect the flexibility and balance of the immune system. However, few systematic reviews or meta-analyses have investigated the association between work-related psychosocial factors and inflammatory markers. Based on prospective studies, the present investigation will conduct a comprehensive systematic review and meta-analysis of the association between work-related psychosocial factors and inflammatory markers.

Methods and analysis The systematic review and meta-analysis will include published studies identified from electronic databases (PubMed, EMBASE, PsycINFO, PsycARTICLES, Web of Science and Japan Medical Abstracts Society) according to recommendations of the Meta-analysis of Observational Studies in Epidemiology guideline. Inclusion criteria are studies that: examined associations between work-related psychosocial factors and increased inflammatory markers; used longitudinal or prospective cohort designs; were conducted among workers; provided sufficient data for calculating ORs or relative risk with 95% CIs; were published as original articles in English or Japanese; and were published up to the end of 2017. Study selection, data extraction, quality assessment and statistical syntheses will be conducted by 14 investigators. Any inconsistencies or disagreements will be resolved through discussion. The quality of studies will be evaluated using the Risk of Bias Assessment Tool for Non-randomized Studies.

Ethics and dissemination The investigation study will be based on published studies, so ethics approval is not required. The results of this study will be submitted for publication in a scientific peer-reviewed journal. The findings may be useful for assessing risk factors for increased inflammatory markers in the workplace and determining future approaches for preventing CVD, metabolic diseases and psychotic and neurodegenerative disorders.

PROSPERO registration number CRD42018081553.

Strengths and limitations of this study

- This systematic review and meta-analysis will offer comprehensive understanding of the association between work-related psychosocial factors and inflammatory markers.
- The review will include a range of work-related psychosocial factors and focus on inflammatory markers.
- To ensure stronger evidence, the review will include only prospective studies.
- The findings of this review may be useful for assessing chronic inflammation as a risk factor for cardiovascular disease (CVD), metabolic diseases and psychotic and neurodegenerative disorders in the workplace as well as for determining future approaches for preventing CVD, metabolic diseases and psychotic and neurodegenerative disorders.
- Depending on the results, limitations could be confounding factors that may not have been adjusted for in the selected studies as well as low generalisability.

INTRODUCTION

Most adults spend around half of their waking hours at work, and so the workplace is an important setting to promote health and well-being. Increasing attention is being directed to work-related psychosocial factors, such as job strain,[1–5] effort–reward imbalance,[6] organisational justice[7–9] and workplace social capital[10]; there is a major focus on work stress.[2] These factors may affect cardiovascular disease (CVD), metabolic diseases and psychotic and neurodegenerative disorders through such mechanisms as prolonged overactivation and dysregulation of the autonomic nervous system and the hypothalamic–pituitary–adrenal cortex axis.[11–13]

Chronic inflammation has been suggested as a potential mediator for the development of CVD, metabolic diseases and psychotic and neurodegenerative disorders.[14–18]

Several studies have reported associations between adverse work-related psychosocial factors and increased levels of inflammatory markers. Inflammatory markers, including C reactive protein (CRP),[19–24] interleukin 6 (IL-6)[24 25] and tumour necrosis factor-α (TNF-α), have been implicated in coordinating atherosclerosis.[26] Previous meta-analyses[27 28] have identified the associations between psychosocial factors and inflammatory markers; however, the findings from those studies were not conclusive because of methodological heterogeneity (eg, conceptualisation or measurement of work-related psychosocial factors, sample compositions and statistical approaches).

Meta-analytic associations between work-related psychosocial factors and inflammatory markers indicate that such factors may affect the flexibility and balance of the immune system. Some meta-analyses have investigated inflammatory markers in relation to psychological stress[27–30] and unemployment[31]; however, few systematic reviews or meta-analyses have been conducted regarding the associations between work-related psychosocial factors and inflammatory markers. A systematic review of 56 studies by Nakata[32] suggested that work-related psychosocial factors were related to disrupted immune response. However, that study did not statistically synthesise the associations. To our knowledge, only one meta-analysis of the association between effort–reward imbalance and inflammatory markers (k=7, n=9952) found a negative association with immunity (r=−0.09; CI −0.14 to −0.05; p<0.001).[13] These systematic reviews and meta-analyses included cross-sectional studies. However, pooled associations between work-related psychosocial factors and inflammatory markers derived from prospective studies may provide more reliable evidence.

Based on published prospective studies, the present investigation will conduct a comprehensive systematic review and meta-analysis of the associations between work-related psychosocial factors and inflammatory markers. Inflammatory markers will include those that were previously investigated in terms of associations with psychosocial factors at work, including CRP, IL-6 and TNF-α. Our hypothesis is that adverse work-related psychosocial factors would increase inflammatory markers. Moreover, we will identify the work-related psychological factors that have the strongest associations with specific inflammatory markers.

METHODS AND ANALYSIS

Study design

This study protocol for a systematic review and meta-analysis of prospective studies follows the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols guideline.[33] Future findings will be reported according to the Meta-analysis of Observational Studies in Epidemiology (MOOSE) reporting guidelines.[34] This study protocol was registered with PROSPERO (CRD42018081553).

Eligibility criteria

Participants, exposures, comparisons and outcomes (PECO) of the studies included in this systematic review and meta-analysis will be defined as follows: (P) inclusion of all workers; (E) presence of adverse psychosocial factors at work; (C) absence of adverse psychosocial factors at work; and (O) increased inflammatory markers. Target participants will all be employees of participating companies. There will be no exclusion criteria related to employment status, job type or shift type. The study exposures (adverse psychosocial factors at work) will include a range of task and organisational characteristics and work conditions,[35] such as job strain,[1–5] low social support, effort–reward imbalance,[6] organisational injustice[7–9] and low workplace social capital.[10] Long working hours and shift work will also be included as target exposures. Inflammatory markers will include those investigated in terms of association with psychosocial factors at work in previous studies, including CRP, IL-6 and TNF-α.

Eligibility criteria for selection are the following studies that (1) were conducted to evaluate associations between psychosocial factors at work and inflammatory markers; (2) used longitudinal or prospective cohort designs; (3) were conducted among workers; (4) provided sufficient data for calculating coefficients of associations between psychosocial factors at work and inflammatory markers (γ, β), ORs, relative risks (RRs) or HRs with SEs or 95% CIs; (5) were published as original articles in English or Japanese; and (6) were published up to the end of 2017.

Information sources, search strategy and data management

A systematic search of published studies will be conducted using electronic databases: PubMed (MEDLINE), EMBASE, PsycINFO, PsycARTICLES, Web of Science and the Japan Medical Abstracts Society. Search terms will include words related to the PECO of eligible published studies. The proposed search strategy appears in online supplementary appendix 1. All identified studies will be managed in a Microsoft Excel file (Washington, USA). Before the study selection process, duplicated citations in the Excel file will be excluded by KW. Decisions on all studies will be recorded.

Study selection process

First, following the eligibility criteria, 14 investigators (HE, KW, EA, HA, YA, AI, RI, MI, KI, YK, NN, YO, ASa and KT) will independently conduct screening of identified titles and abstracts in pairs. Second, we will obtain full texts of all eligible studies. In the full-text review phase, the studies will be examined using a standardised form (see online supplementary appendix 2) to assess eligibility for inclusion in this review. The number of papers examined by each investigator will depend on the investigator's capacity. Any discrepancies in assessment will be recorded and the inter-rater reliability determined; such matters will be discussed among all the investigators until consensus is reached. We will directly contact the corresponding authors

of eligible studies if the results of the publication are unclear and may be related to multiple interpretations or if the reported results did not show data relevant to our study analysis. The reasons for excluding studies will be recorded. A flow chart will be prepared showing the entire review process.

Data extraction

Data will be extracted independently from the included studies by 14 investigators (HE, KW, EA, HA, YA, AI, RI, MI, KI, YK, NN, YO, ASa and KT) working in pairs using a standardised data extraction form. The data will be distributed according to the investigators' capacity. Any discrepancies or inconsistencies in the assessment will be recorded and the inter-rater reliability determined; such matters will be discussed among all the investigators until consensus is reached. The extracted data will include the following: year of publication; country where the study was conducted; number of participants at baseline and in the analysis; sampling framework; participants' demographic characteristics (ie, mean age, sex proportions and employment status); length of follow-up; follow-up rate; exposure and comparison variables (adverse psychosocial factors at work); outcome variables (inflammatory markers); number and proportion of participants with increased levels of inflammatory markers or mean scores and variances or SD of markers; and sufficient data for calculating the coefficients (β, γ), ORs, RRs or HRs with SEs or 95% CIs for the association between adverse psychosocial factors at work and inflammatory markers. If the included studies report multiple measures of association, we will attempt to select measures of association adjusted by demographic variables (eg, age, sex, education and marital status). If the studies report measures of association adjusted by lifestyle variables (eg, smoking, physical activity and sleep), we will as far as possible extract measures both with and without adjustment for lifestyle variables. To avoid overadjustment, measures of association adjusted for other adverse psychosocial factors at work or inflammatory markers will not be adopted. Sex-stratified coefficients will be selected if they are the only reported results. Any missing data from the studies will be obtained by contacting the relevant research team.

Assessment of study quality

Fourteen investigators (HE, KW, EA, HA, YA, AI, RI, MI, KI, YK, NN, YO, ASa and KT) will independently assess in pairs the quality of each included study using the internationally recognised Risk of Bias Assessment Tool for Non-randomized Studies (RoBANS).[36 37] The RoBANS was developed to determine the risk of bias of non-randomised studies; it comprises six domains: selection of participants; confounding variables; measurement of exposure; blinding of outcomes; incomplete outcome data; and selective outcome reporting. The risk of bias for each domain is classified as low, high or unclear risk. The number of papers assessed by each investigator will depend on their capacity. Any discrepancies in quality assessment among the investigators will be recorded and the inter-rater reliability determined; such matters will be discussed among all the investigators until consensus is reached.

Data synthesis and statistical methods

The included studies will be statistically synthesised in a meta-analysis to estimate pooled coefficients and 95% CIs, stratified by types of measures of association (β, γ, OR, RR and HR). If the included studies report ORs, RRs or HRs, we will calculate log-transformed ORs, RRs or HRs and determine SEs based on 95% CIs. These parameters will be used in the meta-analysis and for examining publication bias by means of a funnel plot and Egger's test with statistical software, R V.3.4.1.[38 39] We will employ a random-effects model[40] to summarise the results using R V.3.4.1 with the 'meta' and 'metafor' packages.[41]

For the main analysis, we will synthesise all types of psychosocial factors at work in the random-effects model. The results will be presented in a narrative format if a meta-analysis is not appropriate or possible, for example, if only two or fewer studies are eligible and included in the study. Heterogeneity will be assessed using the χ^2 test with Cochran's Q statistic, which is calculated by I^2 values,[42] assuming that I^2 values of 25%, 50% and 75% indicate low, medium and high heterogeneity, respectively.

Subgroup and sensitivity analyses will be conducted to compare the results across subgroups or under specific conditions when sufficient heterogeneity is detected. Major possible grouping characteristics will include types of exposure and outcome, participants' demographic characteristics (eg, sex, age, employment status, occupational groups) and study quality. Any subgroup differences will be reported, and our findings will be explained by considering these differences. Results with and without adjustment for lifestyle variables will be compared in another sensitivity analysis. If trends are observed between pooled associations and any grouping characteristics, meta-regression will be conducted using the 'metareg' function of R. A sensitivity analysis may be conducted for included studies where the RoBANS is classified as low risk. All extracted data and analysed results will be deposited by the corresponding author and made available for external reviewers and readers on request.

Patient and public involvement statement

This study will not involve any patients or study participants: this study protocol is for a systematic review and meta-analysis.

Ethics and dissemination

This study does not require ethical approval because the systematic review and meta-analysis will be based on previously published studies. The results will be

submitted for publication in a scientific peer-reviewed journal, according to the MOOSE guideline.[34]

Strengths and limitations

This systematic review and meta-analysis will be based on prospective studies and show the strongest evidence for the associations between psychosocial factors at work and inflammatory markers. The findings will highlight potential mediators and underlying mechanisms for the development of CVD owing to adverse psychosocial factors.

There are several likely limitations in this study, including confounding bias and low generalisability. If selected studies do not report demographic-adjusted associations, the findings will be distorted by the unobserved characteristics among the population. In addition, the findings will not be generalisable to populations not included in the selected studies.

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Acknowledgements We thank Audrey Holmes, MA, from Edanz Group (www.edanzediting.com/ac) for editing a draft of this manuscript.

Contributors HE, KW, NK, EA, HA, YA, AI, RI, MI, KI, YK, NN, YO, ASa, KT, ASh and AT made substantial contributions to the conception and design of the study, writing the protocol and revising it critically for important intellectual content and approving the final version to be published. All authors were involved in the entire study process (ie, data extraction, assessment and synthesis).

Funding This work is supported by the Work-related Diseases Clinical Research Grant 2016 (160701-01) and 2018 (180701-01) from the Ministry of Health, Labour and Welfare, Japan.

Competing interests None declared.

Patient consent Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

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