A systematic review of studies in the contributions of the work environment to ischaemic heart disease development

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Background: There is need for an updated systematic review of associations between occupational exposures and ischaemic heart disease (IHD), using the GRADE system. Methods: Inclusion criteria: (i) publication in English in peer-reviewed journal between 1985 and 2014, (ii) quantified relationship between occupational exposure (psychosocial, organizational, physical and other ergonomic job factors) and IHD outcome, (iii) cohort studies with at least 1000 participants or comparable case-control studies with at least 50+50 participants, (iv) assessments of exposure and outcome at baseline as well as at follow-up and (v) gender and age analysis. Relevance and quality were assessed using predefined criteria. Level of evidence was then assessed using the GRADE system. Consistency of findings was examined for a number of confounders. Possible publication bias was discussed. Results: Ninety-six articles of high or medium high scientific quality were finally included. There was moderately strong evidence (grade 3 out of 4) for a relationship between job strain and small decision latitude on one hand and IHD incidence on the other hand. Limited evidence (grade 2) was found for iso-strain, pressing work, effort-reward imbalance, low support, lack of justice, lack of skill discretion, insecure employment, night work, long working week and noise in relation to IHD. No difference between men and women with regard to the effect of adverse job conditions on IHD incidence. Conclusions: There is scientific evidence that employees, both men and women, who report specific occupational exposures, such as low decision latitude, job strain or noise, have an increased incidence of IHD.
Methods

The present review was based upon studies with a prospective design or comparable case control design which enabled a valid and reliable assessment of working conditions preceding illness and is focused on the relationship between working conditions and development of IHD among the employees. We conducted this systematic review within the framework for the Swedish Agency for Health and Technology Assessment and Assessment of Social Services, a public national agency with the charge of providing impartial and scientifically reliable information to decision makers and health care providers (http://www.sbu.se/en/Assessment-and-Evidence/). The review was conducted according to the guidelines stated by PRISMA, i.e. the Preferred Reporting Items for Systematic Reviews and Meta-Analysis.10

Search strategy

Systematic literature search was performed in the following data bases: PubMed, Embase and Psycinfo. A combination of controlled search words (e.g. MeSH) and free-text words was used. The search strategy for the outcome was performed for mesh terms. The whole search strategy is available at http://sbu.se/240E. We only accepted articles in scientific journals with independent peer-reviews.

Inclusion criteria

In the literature search, we accepted a wide range of heart diseases, e.g. IHD, arrhythmia and cardiomyopathy. However, the articles fulfilling our inclusion criteria and meeting the required quality were almost exclusively focused on IHD such as myocardial infarction. Therefore, we present results on IHD specifically.

The inclusion criteria for studies were:

(1) The study should have examined the importance of the work environment (psychosocial, organizational, physical and other ergonomic job factors) for IHD.
(2) The study should be based on people at work and should have been published during the period 1985–2014. Work environments in the whole world were included.
(3) IHD should have been defined according to accepted criteria. Examples were acute myocardial infarction (fatal or non-fatal, ICD codes 8th revision 410–414 and 10th revision 121–122). The outcome should have been certified through diagnostic investigation and with established methods including type of illness onset, enzyme elevation and ECG changes). Other studies (of mortality) have had a wider definition of IHD including ICD codes (according to the 9th edition) 390–459. For more detailed information regarding outcome, see detailed tables of all included studies at http://sbu.se/240E.
(4) Only prospective cohort studies with at least 1000 persons, and case control studies with at least 50 cases (with design equivalent to prospective) were accepted. By case control studies with ‘design equivalent to prospective’ we are referring to studies with strict definition of cases recruited in a representative way in the same population as the control group and with exposure data as well as IHD data from the period before disease onset. The study design should consider age and gender, e.g. by adjustment or stratification.

Multiple publications investigating the same population were systematically identified and only the most relevant publication in a doublet was included in the graded result.

Analyses of relevance and quality

Abstract screening and full-text assessment were conducted by a specialist in occupational medicine and staff with long experience of systematic reviewing procedures.

After that, the scientific experts started their examination. Pre-set evaluation forms were used. The experts judged relevance and quality of the studies on the basis of the relevance and quality criteria, their experience as researchers and their knowledge of the field. Accordingly they were recruited among Swedish academic high ranking specialists in fields of relevance for the process, namely cardiology, neurology and stroke medicine, epidemiology and occupational medicine. This group was divided into pairs. In the following process, the articles remaining in the process were randomly assigned to the three pairs (with avoidance of author bias). Concordance in judgments of relevance and quality was trained. After the training session, each member of the pair did the assessments separately, and then discordances were discussed within the pair. If disagreement remained another pair was asked to make an independent judgment. If that decision was in disagreement with the first group, we made the decision in the whole group.

In the first expert phase, the group judged relevance. Relevance criteria are presented in http://sbu.se/240E. Second, the scientific experts performed a quality assessment. In the final grading process only studies with at least medium high quality were accepted. No distinction was made between medium high and high quality. Studies on the borderline between low and medium high quality were re-examined by the whole group. A list of relevant articles meeting the inclusion criteria judged to be of low quality is available at http://sbu.se/240E.

The following aspects of quality were considered:

(1) Representativeness of study sample. Ways of defining and recruiting the sample as well as attrition in different steps were considered in the quality rating. Statistical considerations and an insightful discussion of possible consequences of a possible selection bias for findings were required in case of marked drop-out problems.
(2) Confounding. Age and at least some aspect of socioeconomic conditions should have been considered. Gender specific analyses were preferred but when such analyses were not available, adjustment for gender was required. Analyses of life habits such as smoking, overweight and alcohol consumption as confounders contributed to upgrading of quality. Biological risk factors such as blood pressure, serum lipids and in a small number of studies coagulation factors were also considered in this way. Very few studies in the field have taken physical activity into account as a possible confounder.
(3) Prospective data collection. All results of the studies included in this review (apart from case-control studies) are based upon assessments of exposure and degree of IHD at start and of incident (or worsening of) IHD at least 1 year later. Application of robust statistical methods and thorough discussion of longitudinal data rendered higher quality ratings.
(4) For both exposure and outcome assessment, standardized and validated methods were required.
(5) Designs that enable the analysis of a dose response relationship contributed to a high quality rating.

Even between studies of specific work environment factors there were differences with regard to operationalization of exposure. Examples are job strain (combination of high psychological demands and low decision latitude) and effort reward imbalance (combination of high effort and poor reward). Since the overall aim of the present study was to grade total evidence, not to assess magnitude of associations, and because it was impossible to reconstruct operationalizations in such a way that they would match one another, we decided to use the definitions presented by the authors themselves and to abstain from assessment of overall magnitude of the different relationships.

(psychosocial/organizational and physical such as noise, irradiation and vibrations) and near-future development of IHD. Chemical exposures, such as solvents, dust and heavy metals, in the workplaces were not included in this work.
The final list of studies judged to be of high or medium high quality is listed in http://sbu.se/240E.

GRADE procedure: According to the GRADE instructions explicit consideration should be given to each of the GRADE criteria for assessing the quality of evidence (risk of bias/study limitations, directness, consistency of results, precision, publication bias, magnitude of the effect, dose-response gradient, influence of residual plausible confounding, bias and ‘antagonistic bias’). For level 4 (=High), randomized trials are required and there were no such published relevant studies in our search. For observational studies as in the present review, the highest possible grade is Moderate = 3 if there is sufficient reason for an upgrading from the normal level for such studies of 2 (=Limited). Level 1 (=Insufficient) corresponds to evidence based on case reports and case series or on reports with downgraded evidence from observational studies.

We allowed for upgrading the scientific evidence when there was strong coherence of results between studies. Accordingly when there were many published observational studies of medium or high quality with homogenous results (almost all pointing in the same direction although all findings may not have been statistically significant) the evidence was graded on level 3.

Meta-analyses/forest plots

We constructed forest plots for visual interpretation, and we chose to illustrate associations calculated by different methods [e.g. hazard ratios (HRs), odds ratios (ORs) and relative risks (RRs)] in the same graph. To assist in illustrating the results, and as a contribution to the overall assessment, these forest plots (meta-analyses) were constructed when in at least two studies the same risk factor was analysed using the Comprehensive Meta-Analysis software package (www.meta-analysis.com/index.php). Since the data in the graphs were not mathematically compatible, we did not calculate a summary OR. The strength of the scientific evidence, using data from all of the included studies (not just those illustrated in the meta-analyses), was determined by the expert pairs and then discussed and confirmed by all experts.

Informal homogeneity tests were performed in order to compare results from studies using general population studies vs. specific occupational cohorts, men vs. women, case-control studies vs. prospective studies, early vs. late publications and geographical origin (North America vs. Nordic and other European countries). In these tests, we conducted sub-analyses of the presented findings and compared results between the sub-categories, e.g. if the association between job exposure and IHD differed according to study design.

Finally, in order to explore possible publication bias, funnel plots were constructed which illustrate the relationship between number of participants and magnitude of association—when there is an overrepresentation of studies with low power and strong association, publication bias is suspected. Such plots were constructed whenever there were at least five studies of sufficient quality examining a given exposure.

Ethics

All studies perused in this review have been approved by the scientific ethical committees in their universities. Accordingly, no additional ethical approval has been required for the present review.

Results

In the literature search, we accepted a wide range of heart diseases, e.g. IHD, arrhythmia and cardiomyopathy. However, the articles fulfilling our inclusion criteria and meeting the required quality were almost exclusively focused on IHD such as myocardial infarction.
There is scientific evidence for an association between exposure and outcome. The result is based on studies of high or moderate quality. The quality of evidence has been upgraded due to consistency of the data (control and job strain) or large magnitude of effect.

It is not possible to determine if there is any association between exposure and outcome. The motivation is that one or several conditions apply: (i) no study fulfilled the inclusion criteria, (ii) none of the studies fulfilling the inclusion criteria were relevant to the quality. The quality of evidence has been upgraded due to consistency of the data (control and job strain) or large magnitude of effect.

Table 1 Degree of scientific evidence for different studied work environment factors

| Work-related factor                              | Participants | Studies | Scientific evidence |
|--------------------------------------------------|--------------|---------|---------------------|
| Relationship between occupational environment and ischaemic heart disease |              |         |                     |
| Low decision latitude                           | 804 086      | 25      | ★★★★★               |
| Job strain (low decision latitude, high job demands) | 237 273      | 18      | ★★★★★               |
| Iso-strain (job strain + low job support)        | 24 645       | 2       | ★★★★                |
| High pressure job                               | 1 024 128    | 7       | ★★★★                |
| Effort reward imbalance                         | 29 917       | 5       | ★★★★                |
| Low support at the work place                   | 167 307      | 11      | ★★★★                |
| Low work place justice                          | 20 296       | 3       | ★★★★                |
| Poor skill discretion                           | 1 012 008    | 5       | ★★★★                |
| Job insecurity                                  | 64 527       | 4       | ★★★★                |
| Night work                                      | 34 413       | 3       | ★★★★                |
| Long working week                               | 1 013 046    | 7       | ★★★★                |
| Noise                                           | 584 735      | 9       | ★★★★                |

The scientific evidence is insufficient (★★★★) to determine if there is a relationship between the following occupational factors and IHD.

Demands at work, Active job (high decision latitude, high job demands), Passive job (low decision latitude, low job demands), Poor social climate at the work place, Bullying at work, Conflicts at work, Shift work, Physically demanding work, Sitting work, Manual handling—lifts, Electromagnetic fields, Radiation (gamma- and ionizing radiation), Radon

judged to have insufficient evidence (grade 1). Chemical exposures were not included in this review.

The number of studies with sufficient quality varied considerably for the different exposures. Low decision latitude had been studied in relation to IHD in 25 studies, and job strain (the combination of high demand and low decision latitude) in 19 studies. Low support had been studied in 11, noise in 9, long working hours in 7, ‘pressing job’ in 7, effort reward imbalance in five and poor skill discretion in five studies respectively. The numbers of study participants were just above 1 000 000 for each of the exposures ‘pressing work’, long working hours and low skill discretion. In the studies of low decision latitude there were 800 000, in the studies of noise almost 600 000 and in the studies of job strain more than 200 000 participants. In the forest plots strength of association has been presented as HR, OR or RR. The diagrams are based upon the least adjusted model in the studies.

Figure 2a shows the forest plot for job strain that was judged with evidence grade 3 to be related to incidence of IHD. For this exposure there is data from 19 studies. Three of these studies have included women and in these studies data are presented separately for men and women. In addition, one study presented separate data for blue collar and white collar workers. These data are also presented separately in the diagram. Accordingly, the diagram includes 23 estimates with 95% confidence limits. All estimates except one are above 1. Twelve of the confidence limits are above 1. This was judged as a homogenous finding across the studies that motivated an upgrading from evidence level 2 to level 3.

Supplementary Figure S2b shows the forest diagram for noise; the evidence was judged to be limited (grade 2) because the number of studies was more limited than for job strain and low decision latitude.

Homogeneity tests were performed for all exposures for which we could conclude that there was an association to IHD. The tests showed that results were comparable for men and women, for general population vs. specific occupation cohorts and for prospective studies vs. case control studies. Job strain in relation to IHD in prospective (lower half) studies vs. case control (upper half) studies is displayed as an example of these homogeneity tests in figure 2a.

For job strain, the homogeneity tests showed that the findings were similar for participants with low and high socioeconomic status. For low decision latitude, however, when socioeconomic group was taken into account the association had a lower magnitude for white collar workers than for blue collar workers. For both exposures, adjustment for lifestyle factors such as smoking and physical activity during leisure time had small effects on the associations with IHD. The homogeneity tests also showed that the association between job strain and IHD was stronger during recent years than previously.

Figure 3 exemplifies funnel plots. It illustrates the relationship between the logarithm of the estimated magnitude of the association (HR, OR or RR) and the standard error of this association. The graph shows that there is no indirect evidence of positive publication bias.

Discussion

Main findings and recent developments in the field

The results provide evidence for several work conditions being linked to IHD. Scientific evidence of grade 3 out of 4 (moderately strong) was shown for job strain (high psychological demands and low decision latitude) and low decision latitude. Furthermore, limited evidence (grade 2) was found for the combination of job strain and poor support at work = iso-strain, ‘pressing job’, effort reward imbalance, low support at work, low work place justice, poor skill discretion, insecure employment, night work, long working week and noise.

The systematic search ended in December 2014. It was not possible to re-start the full procedure. A large study based upon the IPD Work collaboration examining the relationship between long working hours and incidence of coronary heart disease was published in August 2015. This study was based upon five published and 17 hitherto unpublished prospective studies of the relationship between long working hours and coronary heart disease. The general conclusion was that there is a weak relationship...
Figure 2 (a) Association between job strain and development of ischaemic heart disease. The graph is based on data from the least adjusted model in studies expressing the strength of the association either as HR, OR or RR. The figure also provides an informal homogeneity test. Case control studies (above blue line) are compared with prospective cohort studies (below blue line). (b) Association between occupational noise and development of ischaemic heart disease. The graph is based on data from the least adjusted model in studies expressing the strength of the association either as hazard ratios (HR), OR or RR.

Figure 3 Funnel plot illustrating possible publication bias based upon data on job strain in relation to IHD.
between long working hours and IHD but that this may be mediated or confounded by other risk factors. 11

Job strain has been a commonly examined exposure in the epidemiological literature, and our conclusion is that it is associated with IHD risk. This conclusion differs from the review by Eller et al. 4 who concluded that there was insufficient evidence for a relationship between job strain and coronary heart disease. Our present conclusion is consistent with the large IPD study published more recently. 5,6,12 In the IPD study exposure and outcome data were standardized in a number of European cohort studies. This enabled an individual prospective study of almost 200,000 individuals who were followed for an average of 7 years. The findings showed a clear relationship that was consistent across gender, geographical region, socioeconomic status, publication status (published/unpublished) and lifestyle. The findings also showed that there was an interaction between high psychological demands and low decision latitude—i.e., that the combination had worse effect on risk than a merely additive one. 13

The IPD Work study could not be included in the present review since it is a combination of published studies (which are included in the present review) and a few unpublished studies (which could not be included). The present review also includes studies of sufficiently high quality that have been published after the IPD study. Our results are entirely consistent with the IPD conclusion—with the interesting addition that case control studies show findings that are very similar to the prospective studies. Our conclusions are also consistent with the conclusions made by Kivimäki and Kawachi 12 in their recent review. That review, however, only included three exposures, namely job strain, long working hours and job insecurity. For all of those the authors concluded that there is convincing evidence for an association although intervention studies are lacking which makes it impossible to use grade 4 for the evidence.

Our own review includes more risk factors than the Kivimäki–Kawachi review. First of all we note that low decision latitude in itself is a risk factor with evidence of the same grade as job strain—albeit with lower ORs. Low decision latitude at work is correlated with social class, and accordingly adjustment for social class reduces the magnitude of the association. Subjects who grow up in poor socioeconomic conditions, particularly those maintaining poor conditions as adults are more likely to be exposed to adverse working conditions than other people. Such adverse conditions partly explain why socioeconomic status is related to higher illness risk. Therefore, adjusting for social class may lead to over-adjustment. There is no ideal solution to this theoretical problem—we need information about associations both adjusted and non-adjusted for social class. Some of the excess risk associated with low social class may also be due the associations between social class and biological risk factors.

Job insecurity and long working hours are less established than job strain and poor decision latitude (grade 2). Because they are important potential risk factors in the modern working world more studies—in particular intervention studies—are recommended. The same statement relates to effort reward imbalance, low support, unfavourable social climate, lack of procedural and relational justice, conflicts with superiors and colleagues and limited skill discretion. Effort reward imbalance is probably of the same importance as job strain but it has not been examined to the same extent as job strain. Recent reviews have discussed and emphasized its importance in relation to cardiovascular disease as well as recurrent episodes of IHD. 14 Social support that was introduced in the empirical studies by Johnson and Hall 15 is in the same group.

There has been a debate regarding the magnitude of the association between job strain and acute coronary heart disease. The most frequently used operationalization of job strain (‘median split’) is the self-reported combination of a score for psychological demand above median and at the same time a score for decision latitude below the median. The most frequently used standardized questionnaire has been the Job Content Questionnaire (JCQ) or the shorter Swedish version (DCQ)—which are comparable. With these questionnaires and the mentioned operational definition the OR for myocardial infarction (comparing those with ‘job strain’ with all the others) is in the order of 1.3. Critics have commented that the crude median split definition of job strain leads to underestimation of the true magnitude of the association because there is too little contrast in the comparison. 7,8

Since job strain has been examined more extensively than the other factors it is of interest to discuss some of the theoretical and empirical problems that have been discussed in relation to job strain. The role of life style factors in the association between job strain and cardiovascular disease has been discussed. Researchers agree that the magnitude of the job strain association with coronary heart disease is relatively unaffected when adjusted for life style factors. In the IPD Work study 6 there was very little added IHD risk among those 14% who had at least two life style (smoking, overweight, etc.) risk factors. However among participants (32%) with one such risk factor job strain added 40% to the IHD risk (OR from 1.5 to 1.9). The OR among those with no life style risk factors was 1.3. Sorensen et al. 16 have argued that the effects of individual life style health promotion in the work site will have much better effects if it is combined with work organizational work.

The adverse conditions discussed in this review show some overlap but are also partly unrelated to one another. It has been shown for instance that a combination of poor effort reward imbalance and low decision latitude 27 or a combination of poor effort reward imbalance and poor control at work 18 are associated with more pronounced augmentation of risk than each one alone. The implications of this are important since it means that the total effect of adverse working conditions is much greater than each one of the relatively small ORs indicate. The population attributable risk for job strain in relation to acute IHD is in the order of 5% if we assume a RR of 1.3 and a prevalence of job strain of 22%. If the risks related to all the other job factors are added, the effects on a societal level are substantial despite the fact that each one of the excess risks are moderate or small. There is also increasing evidence showing that a similar set of adverse working conditions is associated with increased incidence of stroke 11,19 and with the onset of diabetes 2,20.

Among the exposures included in this review there are some that are more objectively assessed, such as number of working hours and noise, whereas the assessments of others are more subjectively flavoured. Conflicts, lack of justice and social support are examples of psychosocial dimensions that are difficult to assess by means of objective assessments. For decision latitude it has been shown that self-reported levels correlate highly with expert ratings and job exposure matrix measures of decision latitude. 21 Psychological demands could be divided into several kinds of demands such as quantitative, cognitive and emotional. 22 In the demand control model the five questions about psychological demands mainly reflect quantitative demands. Correlations with expert ratings and job exposure matrix assessments are lower for psychological demands than for decision latitude.

Decision latitude also has two components 23 namely decision authority (which corresponds to everyday workplace democracy) and skill discretion (which corresponds to possibility to develop skills which are needed for decision latitude) which are mostly added to one another. In some studies (for instance in the British Whitehall II studies of British state employees) decision latitude only includes decision authority. This does not seem to have any importance for the job strain findings.

Shields, 24 Stansfeld et al. 25 and De Lange et al. 26 have examined possible effects of exposure to job strain two or more times in the follow-up survey waves. Their findings indicate that accumulated or increasing job strain has a stronger adverse statistical effect on risk of experiencing increased ratings of depressive symptoms during follow-up than decreasing job strain. These studies show that two
or more assessments of the job situation provide more precise information regarding risk than only one measurement. Similar observations have been made on the relationship between psychosocial working conditions and coronary heart disease. Therefore stronger evidence regarding the influence of working conditions on poor health may be expected in future research with a growing body of studies with such methodology.

Gender

Our results showed that similar work conditions were related to a similar relative increase in incidence of IHD among men and women. However, although there is no gender difference in relative excess risk associated with adverse work conditions, studies have shown that women actually have higher levels of job strain than men. Thus, despite the gender difference in absolute IHD prevalence and incidence, the relative increase is the same in men as in women for a given work exposure.

Technical issues

In this review, we have not reviewed evidence whether there is interaction or not between high psychological demands and low decision latitude (as discussed for instance in Karasek and Theorell). As recommended in the epidemiological literature we produced funnel plots to investigate possible publication bias. When there is pronounced publication bias, studies reporting ‘confirmed’ associations, e.g. ORs, with wide confidence intervals are more common than studies reporting ‘rejected’ associations with wide confidence intervals. Such an analysis cannot replace a real analysis of publication bias—the best analysis would be to contact researchers asking for unpublished studies. But according to our exploration, there was no such evidence of publication bias.

Limitations

We may have underestimated the importance of work environmental factors that have been subjected to few empirical studies. This illustrates the need for more detailed studies of different aspects of demands, and of effort reward imbalance.

Societal relevance

The work environment factors for which we found scientific evidence for an association to IHD development are possible to influence by means of work organization changes. For instance, it has been shown that decision latitude for employees can be improved by analysis of the work organization with subsequent goal-directed organization intervention or by a year-long education of managers about psychosocial factors. Reviews of natural experiments designed to reduce psychosocial risks in the work environment have shown that such interventions may result in reduced biological stress and improved health in that group. The present results suggest that in assessment and treatment plans of IHD, work environment should be taken into account.

Conclusions

There is scientific empirical evidence that employees, both men and women, who report adverse occupational exposure, especially lack of decision latitude or job strain, have an increased risk of IHD.

Many of the work environmental factors can be favourably influenced by effective organizational interventions. An important step in this research field would be the launching of good evaluations of psychosocial interventions. For some kinds of working conditions that are developing in the modern working world, new research on IHD will be needed.

Supplementary data

Supplementary data are available at EURPUB online.

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Conflicts of interest: None declared.

Key points

- Several psychosocial job factors are associated with IHD risk
- Many of those can be favourably influenced by effective organizational interventions.
- For some kinds of working conditions that are developing in the modern working world, new research on IHD will be needed.

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