

## Associations of job strain and lifestyle risk factors with risk of coronary artery disease: a meta-analysis of individual participant data

Mika Kivimäki PhD, Solja T. Nyberg MSc, Eleonor I. Fransson PhD, Katriina Heikkilä PhD, Lars Alfredsson PhD, Annalisa Casini PhD, Els Clays PhD, Dirk De Bacquer PhD, Nico Dragano PhD, Jane E. Ferrie PhD, Marcel Goldberg MD, Mark Hamer PhD, Markus Jokela PhD, Robert Karasek PhD, France Kittel PhD, Anders Knutsson MD, Markku Koskenvuo MD, Maria Nordin PhD, Tuula Oksanen PhD, Jaana Pentti BSc, Reiner Rugulies PhD, Paula Salo PhD, Johannes Siegrist PhD, Sakari B. Suominen MD, Töres Theorell MD, Jussi Vahtera MD, Marianna Virtanen PhD, Peter J.M. Westerholm MD, Hugo Westerlund PhD, Marie Zins MD, Andrew Steptoe DSc, Archana Singh-Manoux PhD, G. David Batty PhD; for the IPD-Work Consortium

### ABSTRACT

**Background:** It is unclear whether a healthy lifestyle mitigates the adverse effects of job strain on coronary artery disease. We examined the associations of job strain and lifestyle risk factors with the risk of coronary artery disease.

**Methods:** We pooled individual-level data from 7 cohort studies comprising 102 128 men and women who were free of existing coronary artery disease at baseline (1985–2000). Questionnaires were used to measure job strain (yes v. no) and 4 lifestyle risk factors: current smoking, physical inactivity, heavy drinking and obesity. We grouped participants into 3 lifestyle categories: healthy (no lifestyle risk factors), moderately unhealthy (1 risk factor) and unhealthy (2–4 risk factors). The primary outcome was incident coronary artery disease (defined as first nonfatal myocardial infarction or cardiac-related death).

**Results:** There were 1086 incident events in 743 948 person-years at risk during a mean

follow-up of 7.3 years. The risk of coronary artery disease among people who had an unhealthy lifestyle compared with those who had a healthy lifestyle (hazard ratio [HR] 2.55, 95% confidence interval [CI] 2.18–2.98; population attributable risk 26.4%) was higher than the risk among participants who had job strain compared with those who had no job strain (HR 1.25, 95% CI 1.06–1.47; population attributable risk 3.8%). The 10-year incidence of coronary artery disease among participants with job strain and a healthy lifestyle (14.7 per 1000) was 53% lower than the incidence among those with job strain and an unhealthy lifestyle (31.2 per 1000).

**Interpretation:** The risk of coronary artery disease was highest among participants who reported job strain and an unhealthy lifestyle; those with job strain and a healthy lifestyle had half the rate of disease. A healthy lifestyle may substantially reduce disease risk among people with job strain.

**Competing interests:** Töres Theorell receives royalties for books written on various topics, including psychosocial factors; music and health; and Sweden's working life in the 1990s. Hugo Westerlund's institution has received a research grant from Saint-Gobain Ecophon AB, a manufacturer of sound-absorbing materials, to study the effect of such materials on stress, job satisfaction and productivity in open-plan offices. No competing interests declared by the other authors.

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**Correspondence to:** Mika Kivimäki, m.kivimaki@ucl.ac.uk

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Psychosocial work stress, denoted by job strain, is associated with an elevated risk of coronary artery disease.<sup>1–7</sup> This association is apparent across strata of sex, age, socioeconomic status and region, and it does not appear to be completely explained by confounding.<sup>7</sup> For many people, avoidance of stress at work is unrealistic. The absence of strong evidence for effective interventions to reduce job strain therefore raises the challenge of identifying additional approaches for dealing with the health impact of stress in the workplace.

Guidelines for the prevention of heart disease emphasize the importance of a healthy lifestyle — physical activity, a healthy diet (and

healthy weight) and not smoking — in lowering disease risk.<sup>8–11</sup> Whether a healthy lifestyle offsets the deleterious impact of job strain on coronary artery disease remains unclear. A straightforward approach to test this hypothesis would involve comparing the rates of coronary artery disease among people with job strain and an unhealthy lifestyle with the rates among those with job strain and a healthy lifestyle. If a marked difference is apparent, one would consider a healthy lifestyle to be the likely factor contributing to the reduced risk among those with job strain. However, such stratifications require a large, well-characterized dataset, which to date has been lacking. We pooled individual-

level data for more than 100 000 men and women participating in 7 cohort studies to examine the combined associations of job strain and lifestyle with risk of coronary artery disease.

## Methods

### Study population

We used pooled individual-level data from 7 European prospective cohort studies participating in the Individual-participant-data Meta-analysis in Working Populations (IPD-Work) Consortium:<sup>7</sup> the Whitehall II Study in the United Kingdom;<sup>12</sup> the GAZEL Study in France;<sup>13</sup> the Belgian Job Stress Project (Belstress);<sup>14</sup> the Work, Lipids, and Fibrinogen Study in Stockholm (WOLF-S)<sup>15</sup> and in Norrland (WOLF-N),<sup>16</sup> Sweden; the Finnish Public Sector Study;<sup>17</sup> and the Health and Social Support (HeSSup) Study in Finland.<sup>18</sup> Details of the study design and participants have been published previously and are summarized in Appendix 1 (available at [www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121735/-/DC1](http://www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121735/-/DC1)).<sup>12-18</sup>

For our meta-analysis, we included all men and women from the cohort studies who were free of coronary artery disease at baseline (1985–2000 depending on the year recruitment began) and for whom complete data on job strain, lifestyle risk factors and coronary artery disease were available. Mean follow-up for incident coronary artery disease ranged from 3.1 to 15.1 years depending on the study.

### Ethics approval

Each constituent study in the IPD-Work Consortium was approved by the relevant local or national ethics committees, and all participants gave informed consent to take part.

### Measurement of job strain and lifestyle risk factors

Predefined, harmonized measures were used to assess job strain (yes v. no) and 4 lifestyle risk factors at baseline: current smoking (yes v. no),<sup>19</sup> physical inactivity (yes v. no),<sup>20</sup> heavy drinking ( $\geq 21$  and  $\geq 28$  units of alcohol per wk for women and men, respectively),<sup>21</sup> and obesity (body mass index [BMI]  $\geq 30$ ).<sup>22</sup> A detailed description of these measures, including their validation and harmonization, has been published previously.<sup>19,23,24</sup> In brief, questions used to measure job strain were taken from a validated job-content questionnaire and demand-control questionnaire and were included in all studies at baseline (sample statement/question: “My job requires working very hard,” “Do you have the possibility of learning new things through your work?”).<sup>23</sup> All items required responses on a Lik-

ert-type scale (e.g., 1 = “never or very seldom” and 5 = “almost always or very often”).

We calculated job-demand and job-control scales using the mean response scores for individual questions. Job strain was defined as having a job with high demands (a job-demand mean score above the study-specific median) and low control (a job-control mean score below the study-specific median); “no job strain” was denoted by all other combinations of demands and control.<sup>23</sup> In a previous report from the IPD-Work Consortium, the collective measure of job strain rather than its components (demands and job control separately) was found to be associated with risk of coronary artery disease.<sup>7</sup>

Tobacco smoking, alcohol intake and physical inactivity were ascertained from participant-completed questionnaires in all of the studies.<sup>19-21</sup> Enquiries were made about the total number of alcoholic drinks, by type of drink, consumed in a week.<sup>21</sup> “One drink” was defined as the equivalent of about 1 unit or 1 glass of alcoholic drink or 10 g of ethanol. Men who consumed 28 or more drinks per week and women who had 21 or more drinks per week were classified as heavy drinkers.<sup>25</sup> Physical inactivity was defined as no or very little moderate or vigorous leisure-time physical activity or exercise.<sup>20</sup> The data on physical activity varied across studies, with examples of definitions of physical inactivity such as “no weekly leisure-time physical activity” and “no or very little exercise, or only occasional walks.”<sup>20</sup> We calculated BMI using data for height and weight, which were self-reported in 3 studies<sup>13,17,18</sup> and measured directly in 4 studies.<sup>12,14-16</sup> Obesity was defined as a BMI of 30 or greater.<sup>22</sup>

We grouped the participants into 3 lifestyle categories: healthy lifestyle (no lifestyle risk factors), moderately unhealthy lifestyle (1 risk factor) and unhealthy lifestyle (2–4 lifestyle risk factors).

### Outcome measure

The primary outcome was incident coronary artery disease, defined as first nonfatal myocardial infarction or cardiac-related death. Participants were followed from baseline to the earliest occurrence of incident coronary artery disease, death or the end of the registry follow-up.<sup>7</sup> Nonfatal myocardial infarction was identified according to the criteria from the World Health Organization MONICA (Multinational Monitoring of Trends and Determinants in Cardiovascular Disease) Project,<sup>26</sup> the International Classification of Diseases, 9th Revision (ICD-9) code 410, or ICD-10 codes I21–I22. Deaths were classified as cardiac related if either ICD-9 codes 410–414 or ICD-10 codes I20–I25 were cited on the death certificate.

## Statistical analysis

We pooled the data from the participating cohort studies after harmonization of all measures. To examine the absolute difference in risk between groups, we computed age-, sex- and cohort-adjusted 10-year incidence of coronary artery disease by baseline measures of job strain, lifestyle risk factors and combinations of both. Hazard ratios (HRs) and 95% confidence intervals (CIs) were computed using Cox regression. To examine whether the associations of the combinations of job strain and lifestyle risk factors with the risk of coronary artery disease were confounded by social patterning of these characteristics, we adjusted the models for socioeconomic status. To account for differences between countries in which the cohort studies were conducted, the models were adjusted for country. We also entered job strain and lifestyle category in a model simultaneously to ascertain whether they were independently associated with risk of

coronary artery disease. All analyses were performed with the use of SAS 9.2 statistical software (SAS Institute Inc., Cary, North Carolina).

We calculated population attributable risk for 3 exposures: job strain, unhealthy lifestyle and their combination, as described in Appendix 2 (available at [www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121735/-/DC1](http://www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121735/-/DC1)). Population attributable risk is the estimated proportion of all cases of coronary artery disease that are attributable to the exposure; it assumes a causal association between risk factor and disease.

## Results

A total of 102 128 men and women from the cohort studies met the inclusion criteria. The baseline characteristics of the pooled study population are shown in Table 1. The mean age was 44.3 (range 17–70) years; 51.8% of the participants were women. Overall, 15 986 (15.7%) of the participants reported job strain. Cohort-specific figures are provided in Appendix 3 (available at [www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121735/-/DC1](http://www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121735/-/DC1)).

A total of 1086 participants had incident events of coronary artery disease during 743 948 person-years at risk (mean follow-up 7.3 years). The

**Table 1:** Characteristics of 102 128 men and women free of coronary artery disease at baseline in 7 cohort studies

Characteristic	No. (%) of participants* n = 102 128
Age, yr, mean ± SD	44.3 ± 9.0
Sex	
Men	49 219 (48.2)
Women	52 909 (51.8)
Current smoking	
Yes	22 150 (21.7)
No	79 978 (78.3)
Heavy drinking†	
Yes	8 205 (8.0)
No	93 923 (92.0)
Physical inactivity	
Yes	15 655 (15.3)
No	86 473 (84.7)
Obesity‡	
Yes	10 796 (10.6)
No	91 332 (89.4)
Job strain§	
Yes	15 986 (15.7)
No	86 142 (84.3)

Note: SD = standard deviation.  
\*Unless specified otherwise.  
†Consumption of ≥ 21 units (women) or ≥ 28 units (men) of alcohol per wk.  
‡Body mass index ≥ 30.  
§Defined as having a job with high demands (a job-demand mean score above the study-specific median) and low control (a job-control mean score below the study-specific median); “no job strain” was denoted by all other combinations of demands and control.

**Table 2:** Age-, sex- and cohort-adjusted 10-year incidence of coronary artery disease by job strain, lifestyle risk factors and their combinations at baseline

Variable	No. of participants	No. of events of coronary artery disease	10-yr incidence per 1000*	Difference in incidence
<b>Job strain†</b>				
No	86 142	921	14.7	0 (ref)
Yes	15 986	165	18.4	3.7
<b>No. of lifestyle risk factors‡</b>				
0	55 090	437	12.0	0 (ref)
1	33 347	382	17.8	5.8
2–4	13 691	267	30.6	18.6
<b>No. of lifestyle risk factors‡ and job strain</b>				
0 – No	47 154	375	11.6	0 (ref)
0 – Yes	7 936	62	14.7	3.1
1 – No	27 815	319	17.1	5.5
1 – Yes	5 532	63	21.7	10.1
≥ 2 – No	11 173	227	30.4	18.8
≥ 2 – Yes	2 518	40	31.2	19.6

Note: ref = reference group.  
\*Adjusted for age, sex and cohort.  
†Defined as having a job with high demands (a job-demand mean score above the study-specific median) and low control (a job-control mean score below the study-specific median); “no job strain” was denoted by all other combinations of demands and control.  
‡Smoking, heavy drinking, physical inactivity and obesity. 0 lifestyle risk factors = healthy lifestyle, 1 risk factor = moderately unhealthy lifestyle, 2–4 risk factors = unhealthy lifestyle.

crude 10-year incidence of coronary artery disease was 14.6 per 1000 people. The 10-year rates by job strain and lifestyle risk factors, adjusted for age, sex and cohort, are shown in Table 2. The rate was 18.4 per 1000 among participants with job strain and 14.7 per 1000 among those without job strain, for a difference of 3.7 events per 1000. The corresponding HR was 1.25 (95% CI 1.06–1.47) and population attributable risk 3.8%. The 10-year incidence was 30.6 per 1000 among participants with an unhealthy lifestyle, 17.8 per 1000 among those with a moderately unhealthy lifestyle and 12.0 per 1000 among those with a healthy lifestyle. Participants with an unhealthy lifestyle had 18.6 more events per 1000 than those

with a healthy lifestyle (HR 2.55, 95% CI 2.18–2.98). The population attributable risk for unhealthy and moderately unhealthy lifestyles versus a healthy lifestyle was 26.4%. Relative to the group in which the risk factor was absent, age-, sex- and cohort-adjusted HRs for single lifestyle risk factors were 2.14 (95% CI 1.89–2.44) for current smoking, 1.19 (95% CI 0.98–1.44) for heavy drinking, 1.52 (95% CI 1.32–1.74) for physical inactivity and 1.67 (95% CI 1.41–1.98) for obesity.

The risk of coronary artery disease associated with combinations of job strain and individual lifestyle risk factors, adjusted for age, sex and cohort, is shown in Figure 1. Having any of the lifestyle risk factors of smoking, physical inactiv-

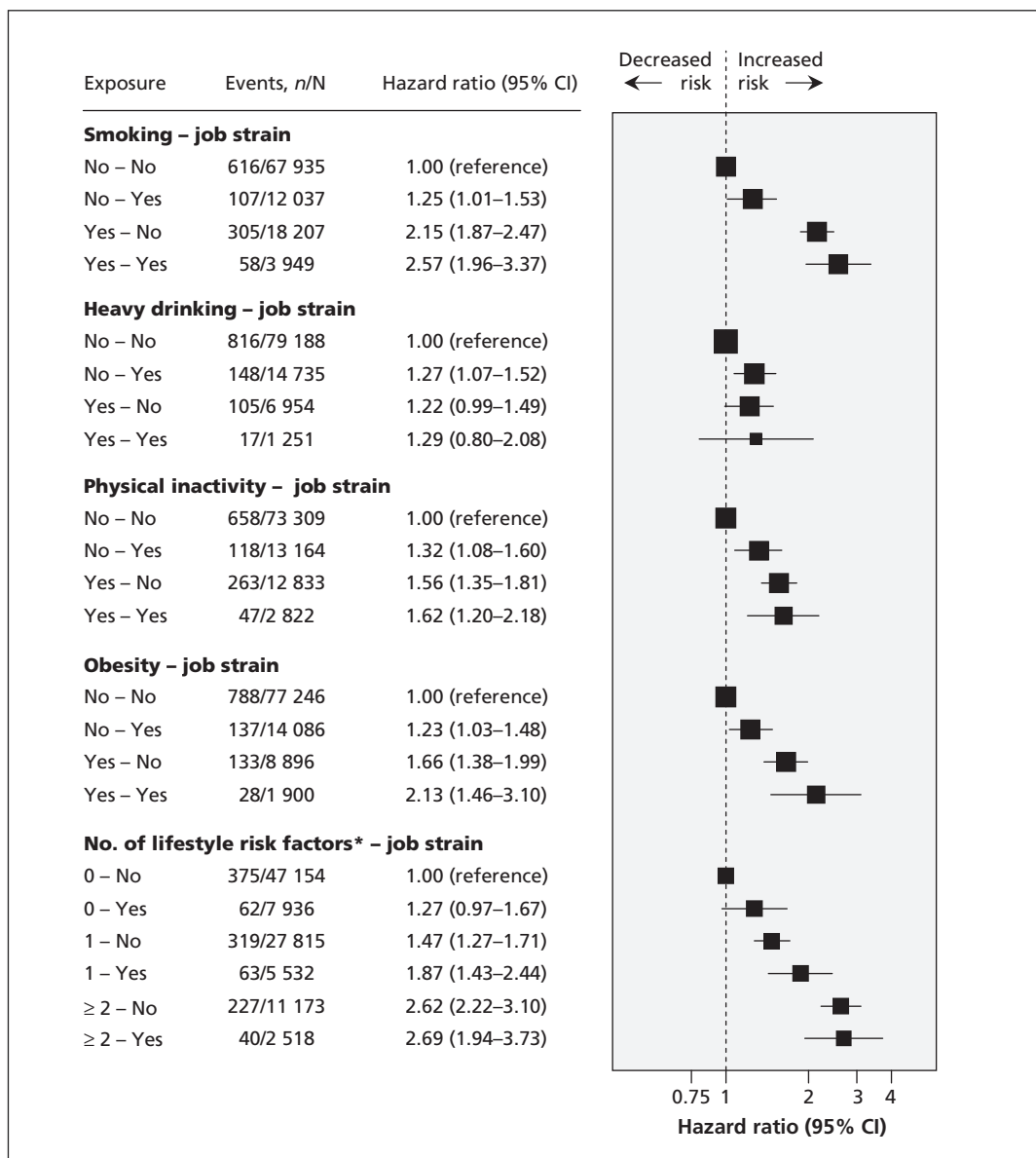


Figure 1: Associations of lifestyle risk factors and job strain with risk of coronary artery disease after adjustment for age, sex and cohort. Values greater than 1.0 indicate an increased risk of incident coronary artery disease. CI = confidence interval. \*0 risk factors = healthy lifestyle, 1 risk factor = moderately unhealthy lifestyle and  $\geq 2$  risk factors = unhealthy lifestyle.

ity or obesity but no job strain was associated with an increased risk of coronary artery disease. The addition of job strain to obesity increased the risk of coronary artery disease, but the risk did not increase appreciably when job strain was added to smoking, heavy drinking or physical inactivity.

Our analyses of the combinations of job strain and lifestyle categories (unhealthy, moderately unhealthy and healthy) associated with risk of coronary artery disease are also shown in Figure 1. The adjusted HR for a combination of job strain and an unhealthy lifestyle compared with no job strain and a healthy lifestyle was 2.69 (95% CI 1.94–3.73). Among participants who reported job strain, the 10-year incidence of coronary artery disease was 31.2 per 1000 people for those with an unhealthy lifestyle and 14.7 per 1000 for those with a healthy lifestyle, for a difference of 16.5 events per 1000 (Table 2). Among participants with a healthy lifestyle but no job strain, the corresponding incidence was 11.6 per 1000 (3.1 events lower than the rate among those with a healthy lifestyle and job strain).

In multivariable analyses, job strain and lifestyle were independently associated with risk of coronary artery disease. In a multivariable model including age, sex and cohort, mutual adjustment for job strain and lifestyle yielded a HR of 1.21 (95% CI 1.03–1.43) for job strain relative to no job strain, and 1.77 (95% CI 1.57–2.00) for an unhealthy versus healthy lifestyle. There was no evidence of an interaction between job strain and lifestyle on coronary artery disease ( $p = 0.6$ ).

Results from the analyses in which we adjusted for socioeconomic status in addition to age, sex and cohort are shown in Appendix 4 (available at [www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121735/-/DC1](http://www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121735/-/DC1)). This additional adjustment had little effect on estimates shown in Figure 1. For example, the adjusted HR for a combination of job strain and an unhealthy lifestyle compared with no job strain and a healthy lifestyle was 2.47 (95% CI 1.77–3.44). In a model adjusted for age, sex and country, the corresponding HR was 2.50 (95% CI 1.80–3.46). There was no evidence of an interaction between sex and job strain–lifestyle combinations ( $p = 0.5$ ), between country and job strain–lifestyle combinations ( $p = 0.2$ ) or between cohort and job strain–lifestyle combinations ( $p = 0.9$ ).

## Interpretation

In our meta-analysis of individual-level data for more than 100 000 participants in 7 prospective cohort studies, we found that the risk of coronary artery disease was highest among those who reported job strain and an unhealthy lifestyle at baseline. Participants who reported job strain but

who had a healthy lifestyle had about half the rate of disease. These findings suggest that a healthy lifestyle is associated with a reduced risk of coronary artery disease among people with job strain. Our findings were robust to adjustment for socioeconomic status, and there was no evidence of heterogeneity of effects according to sex, cohort or country.

We assume that the difference in the 10-year incidence of coronary artery disease between the participants with a healthy lifestyle and those with an unhealthy lifestyle was due to the favourable effects of healthy behaviours. This assumption is justified because evidence from randomized controlled trials have shown that lifestyle changes can reduce disease risk. In trials of weight reduction interventions, for example, weight loss resulted in reduced blood pressure and hypertension<sup>27,28</sup> and improved high-density lipoprotein cholesterol levels among overweight and obese individuals.<sup>29</sup> In a trial with an extended 15-year follow-up, an intensive smoking cessation program followed by 5 years of reinforcement reduced mortality among individuals with airway obstruction.<sup>30</sup> Other randomized controlled trials have been based on short-term interventions (e.g., smoking advice) or have targeted patients with prevalent cardiovascular disease.<sup>31,32</sup> Evidence for the beneficial effects of physical activity<sup>33,34</sup> and the adverse effects of high alcohol consumption<sup>25,35,36</sup> and job strain<sup>7,37</sup> on heart disease is mostly limited to observational studies. Nevertheless, the findings obtained are robust and demonstrate dose–response associations even after adjustment for other relevant risk factors.

Numerous studies have examined the associations of lifestyle-related factors<sup>27–30,33–36,38</sup> and work stress<sup>6</sup> with coronary artery disease, but few have had sufficient power to examine their combined effects. One exception is the INTERHEART case–control study, which recruited about 11 000 patients with incident myocardial infarction and more than 11 000 controls from 52 countries.<sup>2,38</sup> The investigators found that work stress was associated with a doubling of the odds of myocardial infarction<sup>38</sup> — a stronger association than in our study (1.25-fold excess risk of incident coronary artery disease). Because the INTERHEART study assessed risk factors after disease ascertainment, the disease event may have affected perceptions of stress levels, thus leading to reverse causality. This is a less likely explanation for our findings, which are based on a prospective study design.

## Strengths and limitations

Our study has some notable strengths. We extracted data from studies in 2 stages: the exposure was defined and harmonized across cohorts, with investigators masked to the health outcome;

outcome data were obtained after this stage to minimize investigator bias.<sup>24</sup> We calculated population attributable risk and absolute differences in incidence rates between groups, in addition to HRs, because absolute differences in disease risk are considered to be particularly useful for planning public health policy.

Our results also have limitations. Job strain, as well as smoking status, alcohol intake and physical activity, were self-reported by participants; therefore, some misclassification of these lifestyle indicators may have occurred. Our study was based on observational data; thus, conclusions about causal associations with coronary artery disease are precluded because we cannot rule out residual or unmeasured confounding. However, because no large-scale randomized controlled trials have examined job strain and lifestyle risk factors in relation to heart disease incidence, observational studies provide the best available evidence for clinical practice.

## Conclusion

In our meta-analysis of pooled data from prospective cohort studies, the risk of coronary artery disease was highest among participants who reported job strain and an unhealthy lifestyle; those with job strain and a healthy lifestyle had about half the rate of this disease. These observational data suggest that a healthy lifestyle could substantially reduce the risk of coronary artery disease among people with job strain. In addition to stress counselling, clinicians might consider paying closer attention to lifestyle risk factors in patients who report job strain.

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**Affiliations:** From the Department of Epidemiology and Public Health (Kivimäki, Ferrie, Hamer, Steptoe, Singh-Manoux, Batty), University College London, London, UK; the Centre of Expertise for the Development of Work and Organizations (Nyberg, Heikkilä, Oksanen, Pentti, Salo, Vahtera, Virtanen), Finnish Institute of Occupational Health, Helsinki, Finland; the School of Health Sciences (Fransson), Jönköping University, Jönköping, Sweden; the Institute of Environmental Medicine (Fransson, Alfredsson), Karolinska Institutet, Stockholm, Sweden; the Centre for Occupational and Environmental Medicine (Alfredsson), Stockholm County Council, Stockholm, Sweden; the Stress Research Institute (Fransson, Theorell, Westerlund), Stockholm University, Stockholm, Sweden; the School of Public Health (Casini, Kittel), Université Libre de Bruxelles, Brussels, Belgium; the Department of Public Health (Clays, De Bacquer), Ghent University, Ghent, Belgium; the Department of Medical Sociology (Dragano, Siegrist), University of Düsseldorf, Düsseldorf, Germany; the School of Community and Social Medicine (Ferrie), University of Bristol, Bristol, UK; Inserm U1018 (Goldberg, Singh-Manoux, Zins), Institut national de la santé et de la recherche médicale, Villejuif Cedex, France; Versailles-Saint Quentin University (Goldberg, Zins), Versailles, France; the Institute of Behavioral Sciences (Jokela) and the Department of Public Health (Koskenvuo), University of Helsinki, Helsinki, Finland; the Department of Work Environment (Karasek), University of Massachusetts, Lowell,

Mass.; the Department of Health Sciences (Knutsson), Mid Sweden University, Sundsvall, Sweden; the Department of Psychology (Nordin), Umeå University, Umeå, Sweden; the National Research Centre for the Working Environment (Rugulies), Copenhagen, Denmark; the Departments of Public Health and Psychology (Rugulies), University of Copenhagen, Copenhagen, Denmark; the Department of Psychology (Salo) and the Department of Public Health (Suominen, Vahtera), University of Turku, Turku, Finland; the Folkhälsan Research Center (Suominen), Helsinki, Finland; the Nordic School of Public Health, (Suominen), University of Gothenburg, Gothenburg, Sweden; Turku University Hospital (Vahtera), Turku, Finland; Occupational and Environmental Medicine (Westerholm), Uppsala University, Uppsala, Sweden; and the Centre for Cognitive Ageing and Cognitive Epidemiology (Batty), University of Edinburgh, Edinburgh, UK

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