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Is hypertension associated with job strain?
A meta-analysis of observational studies

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ABSTRACT
Job strain results from a combination of high workload and few decision-making opportunities in the workplace. There is inconsistent evidence regarding the association between job strain and hypertension, and methodological shortcomings preclude firm conclusions. Thus, a meta-analysis of observational studies on hypertension among occupational groups was conducted to determine whether job strain was associated with hypertension. In January 2012, we carried out a comprehensive, topic-specific electronic literature search of the Ovid MEDLINE, EMBASE and PsycINFO databases complemented by individual help from non-communicable disease experts. Experimental/interventional studies and studies on personality disorders were excluded. Nine of 894 identified studies met the eligibility criteria and were included in the meta-analysis. The pooled OR of the nine studies was 1.3 (95% CI 1.14 to 1.48; p<0.001), of case–control studies 1.37 (95% CI 1.79 to 5.60; p<0.001) and of cohort studies 1.24 (95% CI 1.09 to 1.41; p<0.001), all of which indicated statistically significant positive associations between job strain and hypertension. In a subgroup analysis, cohort studies of good methodological quality showed significant associations between job strain and hypertension, while those of poor methodological quality showed no association or subgroup differences. We conclude that despite methodological differences, case–control and cohort studies of good methodological quality showed positive associations between hypertension and job strain.

INTRODUCTION
In 2010, cardiovascular and circulatory disorders accounted for 11.8% of the total disability adjusted life years (DALYs) lost worldwide, with ischaemic heart disease (5.2%), haemorrhagic stroke (2.5%), ischaemic stroke (1.6%) and hypertensive heart disease (0.6%) being the most common conditions. Hypertensive heart disease accounted for 15.3 million DALYs lost (3.8%) and 8.7 million deaths (13.5%) in 2010.1 The global prevalence of hypertension is currently increasing and is projected to affect over 500 million people by 2025.2 As blood pressure-related diseases have caused the deaths of over 50 million people, have affected many more and have cost billions of dollars in healthcare,3 reducing the incidence and prevalence of hypertension-related adverse outcomes is a major public health challenge.4

There is strong evidence that modest reductions in hypertension significantly reduce the risk of developing non-communicable diseases such as stroke.5 However, the role of psychosocial and environmental risk factors and their associations with hypertension are still unclear, as the findings from observational studies are largely inconsistent.6 Based on the available literature, it is evident that among working populations, potential biological, psychological, social and environmental contributors are likely to affect the pathogenesis of hypertension.7 Earlier reviews investigated the association between psychological stress and hypertension, but the direction and magnitude of the association was not specifically established.8 9

A previous review of the association between job strain and coronary heart disease (CHD) reported a mild positive association, with job strain slightly increasing the risk of coronary diseases by 3.4% in the general population.10 The authors inferred that the impact of job strain on CHD is lower than that of other established risk factors such as smoking, abdominal obesity and physical inactivity. However, it appears that job strain does not directly result in CHD and affects CHD only by initiating hypertension.11 It is therefore important to determine whether job strain results in hypertension and how this further impacts on the occurrence of CHD. Earlier reviews did not specifically evaluate the role of job strain in the occurrence of hypertension as they included stress factors at home and other places in addition to working environments. Also, earlier reviews included a mix of population-based and workplace-based studies.

It is important to examine this plausible association, and to investigate the role of workplace job strain in the aetiology of hypertension. Therefore, we systematically reviewed studies on hypertension among working populations, synthesised the evidence and performed a meta-analysis to investigate whether hypertension is associated with job strain.

We considered it important to examine this issue as job strain is a modifiable risk factor and amenable to proactive public health interventions.

METHODS
The objective of our study was to estimate the association between job strain and hypertension among adults in occupational settings. A comprehensive meta-analysis was conducted with a predefined protocol developed by the authors for search strategies, inclusion and exclusion criteria, data extraction, study quality rating criteria, evidence summary and analysis.

Criteria for study inclusion
Individual studies and previous reviews were assessed. Cohort and case–control studies were included, but cross-sectional studies were excluded.

since they are particularly susceptible to biases such as the healthy worker effect and reverse causation. Only studies published in English and conducted among occupational workforces were included. We also restricted the analysis to studies where: (a) hypertension (blood pressure >140/90) (Stage-1 and stage-2 hypertension according to the seventh report of the Joint National committee, JNC 7) was either reported as a pre-existing condition by the study participants or was diagnosed by a healthcare worker; (b) documentation of job strain was an integral part of the study; and (c) participants were at least 18 years of age. In addition, case–control studies must have compared participants with hypertension with control individuals without hypertension. Further, we excluded studies that measured coping or other strategies for adapting to any type of stress and studies enrolling participants with psychiatric diagnoses. We also excluded papers that involved only physical stress, chemical factors and factors implicated in psychosocial occupational strain. Intervention studies were excluded as all measured transient reductions in BP in experimental settings and not decreases in BP in patients with essential hypertension.

Search strategy
We defined job strain as ‘the combination of high job demands and low job decision latitude that may lead to negative physical health outcomes such as hypertension and cardiovascular disease (CVD)’. Similar definitions have been adopted in developing models for job strain.

We conducted a complete search of the Ovid MEDLINE, EMBASE and PsycholINFO databases for all papers published between 1908 and 20 January 2012 using MeSH (‘Medical Subjects Headings’) terms (see box 1). MeSH is the controlled vocabulary thesaurus developed by the National Library of Medicine and consists of sets of terms and aids to narrow searches to the intended topics. We also screened papers in the public health database maintained by CAB Direct at the biomedical library of the University of California Los Angeles. CAB Direct is a public health database emphasising international health issues and contains the Global Health Current File (1973 to present) and the Global Health Archive (1908–1973), in addition to records from the British Bureau of Hygiene and Tropical Diseases up to 1983.

Data collection and analysis
The review process consisted of four stages.

Stage 1: identification of studies for inclusion
The first two authors independently assessed abstracts retrieved from electronic databases, references and studies identified through personal contact with relevant experts.

Stage 2: selection of relevant studies
Studies found to be relevant in stage 1 were independently assessed against the inclusion criteria. Disagreements between the first two authors were resolved by consulting a third author.

Stage 3: quality assessment
The criteria for assessing the quality of papers included: (a) the appropriateness of the study design; (b) the adequacy of the sample size; (c) documentation of the occupations as well as the characteristics of participants; and (d) the accuracy of the instruments used for measuring job strain and BP. Specific attention was paid to the methods for controlling for confounding, minimising selection bias, reducing reporting errors and minimising measurement errors.

Two authors (GRB and AJT) independently checked the full-text reports for eligibility and then extracted and tabulated all relevant data. Disagreements were resolved by consensus between all authors. If there was more than one report on the same study, that with the information specific to job strain and ambulatory hypertension in occupational settings was included.

Stage 4: data extraction and synthesis of results
Our initial search of the electronic databases retrieved 1014 studies (see figure 1). As a first step, we included papers with a title and abstract fulfilling the inclusion criteria. We also included 20 papers based on consultation with experts and the authors of earlier systematic reviews. We cross-checked with other databases and earlier reviews to identify additional papers. We then downloaded the full texts of the papers for review and extracted the following information: first author, year, country, study setting (such as study design employed), inclusion criteria, whether job strain was measured or not and the measuring instruments used, and the cut-off points for hypertension. Further, we assessed the quality of the studies using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. These guidelines are intended to help authors report a wide array of systematic reviews to assess the benefits and harms of healthcare interventions, and focus on ways in which authors can ensure the transparent and complete reporting of systematic reviews and meta-analyses.

Statistical analysis
We obtained a summary estimate by combining estimates from all included studies. The meta-analysis was performed using RevMan V.5 and STATA V.11. A double-entry procedure was employed. Data were initially entered and analysed using the Cochrane Collaboration’s Review Manager software V.5 for Windows (Cochrane Collaboration, Oxford, England), and subsequently entered into a spreadsheet and re-analysed using the ‘metan’
command of STATA V11 for Mac (STATA, College Station, Texas, USA). Outputs were cross-checked for internal consistency.

ORs reported in selected studies were pooled using generic inverse variance for overall estimates. All procedures conformed to the guidelines for the meta-analysis of observational studies in epidemiology. We used RevMan for developing flow charts, assessing the methodological quality of studies and calculating unadjusted ORs with 95% CIs, using a random effects model for all analyses. Small-study bias and publication bias were assessed with funnel plot analysis (see figure 2). The OR for each individual study was calculated from the data cell values of the corresponding study. The pooled OR was calculated using the individual unadjusted ORs of each study within each subgroup of case–control and cohort studies. Hence, the pooled OR was also unadjusted. We measured heterogeneity using the $I^2$ statistic, which describes the percentage of total variation across studies that is due to heterogeneity rather than chance. $I^2$ can be readily calculated from basic results obtained from a typical meta-analysis as $I^2 = 100\% \times \frac{(Q - df)}{Q}$, where $Q$ is Cochran’s heterogeneity statistic and df is degrees of freedom. An advantage of $I^2$ is that it does not depend on the number of studies included in the meta-analysis.

In order to minimise heterogeneity within the case–control and cohort study subgroups, the included reviews were divided into those with higher and with lower methodological quality.
based on: (a) study characteristics such as study setting, study design, sample size and inclusion criteria; (b) the methods used to measure job strain and hypertension; and (c) minimising bias due to confounding, selection bias and measurement error. Each of these parameters was assigned a score of 2, giving a maximum score of 20 (See-appendix 1). Studies with a score above 15 were considered to have higher methodological quality and studies with score equal to or less than 15 were considered to have lower methodological quality. Subsequently, the association between job strain and hypertension was measured using pooled ORs within the groups with higher and lower methodological quality for both case–control and cohort studies.

RESULTS
Search results
The initial search identified 1014 studies. We cross-checked for earlier systematic reviews, and included additional studies which were not identified through our initial search. After checking for duplicates, we assessed 894 studies and excluded 738 of these as not relevant. Thus, 156 of 894 were included for full text review and 147 of these were then excluded from the meta-analysis (see figure 1). Among the 147 excluded papers, 29 were written in languages other than English and 23 were not traceable due to accessibility issues. After careful review, we rejected another 95 papers: 14 had insufficient information and 81 were not eligible. The ineligible studies were rejected for the following reasons: (a) the occupational group was not defined in 18 studies; (b) BP reactivity was defined as a physiological response to stimuli being measured instead of a direct measure in 15 studies; (c) 10 studies either targeted an intervention or were carried out in a clinical setting; (d) 10 studies were editorials or reviews; (e) job strain was not the exposure of interest in eight studies; (f) hypertension was not an outcome in six studies; (g) it was difficult to interpret the measure of association used for outcome in five studies; (h) there was no mention of psychosocial stress in two studies; (i) job strain was not directly assessed in two studies; (j) two studies involved coping; and (k) one study was written in a language other than English. Seven papers were excluded for more than one reason. We also considered another seven papers for qualitative review but could not include them because they lacked estimates that could be used in the meta-analysis. Finally, nine studies satisfying the review criteria were included in the meta-analysis.

Characteristics of included studies
Three case–control31–33 and six cohort studies were included in the meta-analysis.34–39 The participants ranged from 15 to 65 years of age. Karasek’s job strain questionnaire was used in two case–control studies and one cohort study31 32 34 (see table 1).

Methodological quality of included studies
All included studies reported information on confounding factors. Selection bias was discussed in three studies.37–39 All studies mentioned the possibility of measurement error, but only one study discussed it in detail (see online supplementary appendix 1 and figure 2 for details).31

The funnel plot depicting publication bias had an inverted funnel shape with studies of higher precision relatively closer to the pooled OR, indicating that publication bias was minimal (see online supplementary appendix 2).

Overall combined effect of job strain on BP
The pooled estimate from all studies showed a statistically significant association between job strain and hypertension (OR 1.3; 95% CI 1.14 to 1.48) (see figure 3). The pooled estimate from case–control studies showed a positive association between hypertension and job strain (OR 3.17; 95% CI 1.79 to 5.60) (see figure 4). The heterogeneity around this estimate (I² statistic) was 0%, indicating low variability among the included case–control studies (see figure 4). The pooled OR from cohort studies was 1.24 (95% CI 1.09 to 1.41). However, we observed considerable heterogeneity among the estimates of cohort studies, with the I² statistic being 80% (see figure 3). The observed heterogeneity was further explored in subgroup analysis and heterogeneity was reduced to zero (I²=0%, p=0.15) among studies with good methodological quality while the association between hypertension and job strain still remained (I² for good methodological quality was 0% compared to 86% for poor quality studies) (see figure 5). Among the cohort studies, a positive association was seen only among studies with good methodological quality (OR 1.49; 95% CI 1.23 to 1.77) (see online supplementary appendix 3).

DISCUSSION
Measurement of exposure and outcome
Many theoretical models and concepts have been developed in job strain research, but the dominant model during the last few decades has been the job demand and control model of Karasek and Theorell.7 This model is based on two dimensions: job demands and job control or decision latitude. The authors in one included paper mentioned that “decision latitude is determined to a great extent by the content of work in the occupation, whereas the demands and social support to a greater extent reflect local work site conditions and individual perception”.

This model assesses job strain from the perspective of worker perceptions of the environment. The validity, operationalisation and understanding of the theoretical conceptual framework of this model have been tested and validated across several occupations and regions.41

We observed statistically significant associations between job strain and hypertension for both case–control studies and cohort studies. Since heterogeneity was high for the cohort studies, subgroup analysis was performed taking methodological quality into account; we observed a statistically significant increased risk of hypertension among participants identified as experiencing job strain in the cohort studies with good methodological quality, and heterogeneity was reduced to 0% in this analysis.

The discrepancy between the various pooled estimates may be explained as follows. First, several different constructs and operationalised definitions of job strain are described in the literature.42 An exhaustive but not exclusive list of such constructs would include Karasek and Theorell’s model combining job demands and control,43 the Occupational Stress Index (OSI)44 integrating several paradigms of stress-related cardiovascular dysfunction, Hockey’s construct of ‘resources’ or total burden on the human operator,45 the ‘Effort-Distress Model’ of Folkow,46 Job Content Questionnaire (JCQ) paradigms,47 Demand-Control Questionnaire (DCQ) constructs,48 the Work Organisation Matrix (WOM) for imputing job title averages of job characteristics to study subjects49 and the effort-reward imbalance (ERI) model of work stress.50

Second, BP measurements were heterogeneous, with several studies relying on readings in the clinic,51 on point estimates of BP alone52 or only on ambulatory BP,53 54 while several other studies considered change in BP over time as the main outcome.

Third, there was heterogeneity among the studied populations. Most of the studies included occupational groups with
<table>
<thead>
<tr>
<th>No.</th>
<th>Author et al</th>
<th>Year</th>
<th>Age, years</th>
<th>Sex</th>
<th>Occupation</th>
<th>Setting</th>
<th>Study design</th>
<th>Sample size</th>
<th>Inclusion criteria</th>
<th>Exposures</th>
<th>Outcome</th>
<th>Methodological quality of study</th>
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<tr>
<td>1</td>
<td>Odahara</td>
<td>2010</td>
<td>42.9 ±6.76</td>
<td>Male only</td>
<td>Employees at Hitachi health care centre</td>
<td>Workplace</td>
<td>Cohort</td>
<td>815</td>
<td>Workers attending the Hitachi health centre</td>
<td>Work hours, over-time worked</td>
<td>LOPS protocol</td>
<td>No selection bias, no measurement error</td>
</tr>
<tr>
<td>2</td>
<td>Guimont</td>
<td>2006</td>
<td>18–65</td>
<td>Male and female</td>
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<td>White-collar workers working over 20 h</td>
<td>Karasek’s job strain</td>
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<td>Mentioned and discussed</td>
</tr>
<tr>
<td>3</td>
<td>Markovitz</td>
<td>2004</td>
<td>18–30</td>
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<td>3 recordings after 5 min rest</td>
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</tr>
<tr>
<td>4</td>
<td>Levenstein</td>
<td>2001</td>
<td>Adult age group*</td>
<td>Male and female</td>
<td>Population-based study in Alameda County</td>
<td>Alameda County</td>
<td>Cohort</td>
<td>2357</td>
<td>Random sample of Alameda County subjects</td>
<td>Psychological and low work status</td>
<td>Treated hypertension</td>
<td>Mentioned and discussed</td>
</tr>
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<td>5</td>
<td>Nakanishi</td>
<td>2007</td>
<td>35–54</td>
<td>Male only</td>
<td>Japanese white collar workers</td>
<td>T Corporation</td>
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<td>Participants in annual health examination for all employees</td>
<td>Job level, working hours</td>
<td>Mean arterial BP, WHO criteria</td>
<td>Mentioned and discussed</td>
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<tr>
<td>6</td>
<td>Peter</td>
<td>1998</td>
<td>19–70</td>
<td>Male and female</td>
<td>Employees of 40 companies in Stockholm</td>
<td>Workplace</td>
<td>Cohort</td>
<td>5720</td>
<td>Different companies in Stockholm</td>
<td>Effort–reward imbalance</td>
<td>2 recordings 1 min apart</td>
<td>Mentioned and discussed</td>
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<td>7</td>
<td>Radi</td>
<td>2005</td>
<td>41.5 male 43.5 female</td>
<td>Male and female</td>
<td>Workers within the IHPAF study</td>
<td>Nested case–control</td>
<td>609</td>
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<td>Standardised BP measures, automatic BP, OMRON instrument</td>
<td>Mentioned and discussed</td>
<td>Not rated</td>
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<td>8</td>
<td>Landsbergis</td>
<td>2003</td>
<td>30–60</td>
<td>Male</td>
<td>Various occupations</td>
<td>Several occupations</td>
<td>Case–control</td>
<td>264: 88 cases; 176 controls</td>
<td>Karasek job strain</td>
<td>Average of 2 or 3 readings</td>
<td>Excellent</td>
<td>Good discussion</td>
</tr>
<tr>
<td>9</td>
<td>Schnall</td>
<td>1990</td>
<td>30–60</td>
<td>Male</td>
<td>Working men in 7 locations in New York</td>
<td>Several occupations</td>
<td>Case–control</td>
<td>215: 128 cases; 87 controls</td>
<td>Job Content Questionnaire</td>
<td>Ambulatory BP</td>
<td>Race, education, smoking, type A behaviour, exercise, 24 h urine sodium, work site</td>
<td>Discussed</td>
</tr>
</tbody>
</table>

*BMI, body mass index; BP, blood pressure; CHD, coronary heart disease; FBS, fasting blood sugar; HDL, high density lipoprotein; LOPS protocol, Laboratory of Physical Science protocol; SBP, systolic blood pressure; SES, socioeconomic status; TG, triglycerides.
varying exposure to high levels of job strain. For example, information technology professionals are expected to experience high levels of job strain but were less studied.54 Earlier reviews have detailed the role of anxiety, anger control, social support and psychosocial stress in hypertension.8 However, the findings of these reviews remain inconclusive.91 92 0 Our review included four studies which were also reviewed in an earlier report.9 In contrast with earlier reviews, the inclusion criterion in our study was job strain as the exposure of interest. Furthermore, the use of heterogeneous job strain instruments has complicated assessment of the stress-hypertension association in work settings. Despite several theories for elucidating this mechanism, there is very little research on contextually relevant stress factors and individual perception of job strain in different workforces. Compared to earlier reviews, we conducted our analyses using a different method by considering cohort and case-control studies separately in the analysis.9 19 20 A previous review also supports a positive association between job strain and ambulatory BP. The study involved quantitative meta-analysis of 23 cross-sectional studies and systematic review of three cross-sectional studies of cumulative exposures to job strain, one case-control study and one longitudinal study. The authors found that associations were stronger in men compared to women and in populations with limited occupational variance compared to broadly based populations.55

The positive associations found in both the cohort and case-control studies have two important implications. First, this result strengthens the evidence that job strain is an important risk factor for hypertension and thereby an important distal determinant of CHD. Second, the meta-analysis provides guidance towards exploring better exposure and outcome assessment to examine whether job strain influences hypertension. Studies have found associations between job strain and certain biomarkers such as IgA, amylase and cortisol in saliva, and C-reactive protein in blood.56

Hypertension is a strong and consistent risk factor in the aetiology of CHD, stroke, transient ischaemic attack and congestive heart failure, and carries a three to fourfold higher risk compared to normal BP.57 Due to the role of hypertension in premature CHD, this higher risk may result in increased morbidity and mortality.15 8 The results from an earlier review indicate that job strain may not have a direct role in increasing CHD.10 The evidence from our meta-analysis indicates that job strain might only have an indirect effect on CHD through hypertension. Although this indirect association warrants further examination, we suggest job strain should be considered as having a role in CHD. Further investigation of biomarkers such as IgA, amylase and cortisol in saliva, and C-reactive protein should be carried out to elucidate the precise mediation mechanism.56 More research is needed to confirm the correlation between job strain and hypertension.

Figure 3  Meta-analysis of all studies: association between hypertension and job strain.

Figure 4  Association between hypertension and job strain: meta-analysis of case-control studies.
these biomarkers and job strain to minimise measurement errors arising out of variations in exposure assessment methods.

The strength of this paper is that it is a systematic review. However, because it is based on non-randomised observational studies, it does not provide decisive causal inferences. Also, we tried to obtain information on additional studies from authors, but this was not always possible as the studies were published in other languages. We also could not run meta-regression as this requires a minimum of 10 studies for each study level variable. Given that less than 10 studies were included in this review, analysis by potential effect measure modifiers such as gender or sex, or grouping them by methodological quality and by study design (cohort/case-control), results in relatively small numbers of studies and/or participants. Hence, we were unable to assess heterogeneity.

Conclusion
We detected an association between job strain and hypertension and its direction and magnitude. This emphasises the need to pursue research on job strain and other stress factors which increase morbidity among working populations. The size of the working population, the relatively high prevalence of stress and the increased number of participants in new economic classes all support the need to examine the health profiles of working professionals. Our study has found that job strain and hypertension were positively associated in studies judged to have better methodological quality, which depended heavily on the methods of exposure and outcome ascertainment. This indicates that it might be useful to develop consensus among researchers on assessments for job exposure and health outcomes across nations and industries, after rigorous evaluation of the validity of several instruments to obtain clear scientific guidance for improving health outcomes among occupational groups.

Contributors
GRB was involved in the conception and design, data extraction, data tabulation, help with analysis, maintenance of all the papers, interpretation of data, drafting the article and revising it critically for important intellectual content and final approval of the version to be published. AJT was involved in the conception and design, data extraction, data tabulation, did the analysis, interpretation of data, reviewing the article and revising it critically for important intellectual content and final approval of the version to be published. WM was involved as third author for reference in terms of divergent opinions, revising the content each time for critical and important intellectual content and final approval of the version to be published. SM was involved in help with analysis and interpretation of data, revising it critically for important intellectual content and final approval of the version to be published. RD was involved in guidance towards conception and design, revising it critically for important intellectual content and final approval of the version to be published. NP was involved in guidance towards revising it critically for important intellectual content and final approval of the version to be published.

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Competing interests
None.

Provenance and peer review
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Figure 5 Subgroup analysis: Cohort studies with better methodological quality vs. poor methodological quality.
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Correction

Authors have noted that the correct pooled OR of the nine studies was incorrect. The corrected sentence in Abstract is as follows:

“The pooled OR of the nine studies was 1.29 (95% CI 1.14 to 1.47; p<0.001), of case–control studies 2.88 (95% CI 1.63 to 5.09; p<0.001) and of cohort studies 1.24 (95% CI 1.09 to 1.41; p<0.001), all of which indicated statistically significant positive associations between job strain and hypertension.”

Also the pooled estimate from all studies in Results section under “Overall combined effect of job strain on hypertension” should be as follows “The pooled estimate from all studies showed a statistically significant association between job strain and hypertension (OR 1.29; 95% CI 1.14 to 1.47) (see figure 3). The pooled estimate from case–control studies showed a positive association between hypertension and job strain (OR 2.88; 95% CI 1.63 to 5.09) (see figure 4).” Authors have supplied a modified figure 3, 4 and 5 as the result (See online supplementary 1, 2 and 3.)

Finally, the year of study number 8, Landsbergis et al, in table 1 should be 1994 instead of 2003. Similarly, the year of publication in the paper by Landsbergis should be 1994 instead of 2003. (see modified online Appendix 1).

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