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Systematic Reviews and Meta- and Pooled Analyses

Long Working Hours and Coronary Heart Disease: A Systematic Review and Meta-Analysis

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The authors aggregated the results of observational studies examining the association between long working hours and coronary heart disease (CHD). Data sources used were MEDLINE (through January 19, 2011) and Web of Science (through March 14, 2011). Two investigators independently extracted results from eligible studies. Heterogeneity between the studies was assessed using the I^2 statistic, and the possibility of publication bias was assessed using the funnel plot and Egger's test for small-study effects. Twelve studies were identified (7 case-control, 4 prospective, and 1 cross-sectional). For a total of 22,518 participants (2,313 CHD cases), the minimally adjusted relative risk of CHD for long working hours was 1.80 (95% confidence interval (CI): 1.42, 2.29), and in the maximally (multivariate-) adjusted analysis the relative risk was 1.59 (95% CI: 1.23, 2.07). The 4 prospective studies produced a relative risk of 1.39 (95% CI: 1.12, 1.72), while the corresponding relative risk in the 7 case-control studies was 2.43 (95% CI: 1.81, 3.26). Little evidence of publication bias but relatively large heterogeneity was observed. Studies varied in size, design, measurement of exposure and outcome, and adjustments. In conclusion, results from prospective observational studies suggest an approximately 40% excess risk of CHD in employees working long hours.

cardiovascular diseases; coronary disease; employment; meta-analysis; myocardial infarction; review; work

Abbreviations: AMI, acute myocardial infarction; CHD, coronary heart disease; CI, confidence interval; SEP, socioeconomic position.

The identification of long working hours as a potential work-related risk factor for ill health has raised interest in the role of working hours in population health (1, 2). Given that persons with longer working hours are more likely to be exposed to high job demands and to have less time for recreational leisure-time activities than their counterparts who work fewer hours, there is a prima facie case that long working hours may be associated with coronary heart disease (CHD) events. CHD is currently a leading cause of death, and projections indicate that this situation will continue for the next several decades (3).

Despite a long research tradition—the first documented study was published in 1958—the association between long working hours and CHD across studies is not well understood. A series of narrative reviews on long working hours and health (4–10) and a meta-analysis on general physical ill health as an outcome (11) have been published, but to the best of our knowledge, there has been no systematic quantification of the link between long working hours and CHD. The purpose of the present study was, for the first time, to conduct a systematic review with a meta-analysis of this relation.

MATERIALS AND METHODS

Data extraction and study searches

The search was conducted according to the Meta-analysis of Observational Studies in Epidemiology (MOOSE) recommendations (12). We used a 4-pronged approach to identifying papers. First, we performed a systematic computerized literature search of MEDLINE (National Library of Medicine) for studies published in English from the inception of the database (1966) until January 19, 2011. The following keywords were used to search study titles and abstracts for exposure to long working hours: "work hours *or* working hours *or* overtime." The following keywords were used to detect the outcome (CHD): "coronary heart disease *or* CHD *or* acute myocardial infarction *or* AMI *or* angina pectoris *or* angina *or* chest pain *or* cardiovascular *or* CVD." Secondly, using Web of Science (Thomson Reuters, New York, New York), we carried out a cited-reference search of these retrieved articles through March 14, 2011, to identify all studies citing the included studies and reviewed their titles and abstracts to determine eligibility. Thirdly, we scrutinized the reference sections of all of the retrieved papers and used a recent book (1) as a potential source of relevant articles. Fourthly, we contacted 4 experts in the field.

Study selection

Two of the investigators (M. V., M. K.) independently assessed the studies identified by the search strategy, to select those that fulfilled the criteria outlined below. Reasons for the exclusion of any study were recorded independently and cross-checked for agreement. All disagreements, which were rare, were resolved by consulting a third investigator (K. H.). Articles were considered for inclusion in the systematic review if: 1) the authors reported data from an original, peer-reviewed study (i.e., not case reports, comments, letters, meeting abstracts, or review articles); 2) the study was a cross-sectional, case-control, or prospective cohort study with a noninstitutionalized adult population (ages ≥18 years); and 3) the authors reported on the association between working hours and a quantitative CHD risk estimate.

We used broad inclusion criteria for studies, including all definitions of working hours (self-reported, register-based) and CHD (self-reported, clinically validated, register-based). Studies that utilized outcomes with a broader definition of cardiovascular disease were included, in recognition of the fact that most non-CHD events are due to stroke, and stroke and CHD have a partially similar pathophysiology. This was the case in 2 studies (13, 14). We excluded studies with a risk factor as the sole outcome, such as lipid levels or hypertension ($n = 8$) (15–22), carotid intima-media thickness ($n = 1$) (23), and the metabolic syndrome or diabetes ($n = 4$) (24–27). We also excluded studies with no original data—that is, reviews ($n = 22$) (2, 4–11, 28–40), editorials and letters ($n = 3$) (41–43), studies with no control group ($n = 2$) (44, 45), ecologic studies ($n = 4$) (46–49), studies with no relevant effect estimate ($n = 1$) (50), and studies with a nonspecific outcome, such as a single-item question on chest pain ($n = 1$) (51) or nonspecific self-reported cardiovascular symptoms ($n = 1$) (52). We found no overlapping papers from the same study population.

We extracted summary data for prespecified items: for the association between long working hours and CHD, minimally adjusted relative risks with 95% confidence intervals, minimum + socioeconomic position (SEP)-adjusted relative risks with 95% confidence intervals, and maximally (multivariate-) adjusted relative risks with 95% confidence intervals; study location; study design; follow-up time; number of participants; number/percentage of men; distribution of the study sample by age and SEP; potential confounders considered; methods used to measure the exposure; and methods used to measure the outcome.

Statistical analysis

We performed a meta-analysis of observational studies (12). Where possible, we used published estimates of the relative risk of CHD among persons who worked long hours as compared with those who worked "normal" hours. For the studies in which no estimate of relative risk was published, we calculated these estimates based on the reported numbers of participants. Risk estimates (odds ratios, risk ratios, or hazard ratios) and their standard errors were calculated for each study separately. Minimally adjusted, minimally and SEP-adjusted, and maximally adjusted risk estimates and their standard errors were pooled using fixed-effect and random-effects meta-analyses. We quantified heterogeneity in the study-specific effect estimates using the I^2 statistic, which indicates the proportion of the total variation in the estimates that is due to variation between studies rather than to chance (53). Furthermore, we carried out subgroup analyses to examine whether the association differed depending on study design (case-control, prospective), region (United Kingdom/United States, Japan, other countries), cutpoint for the definition of long working hours (>50 hours/week/ >10 hours/day vs. a lower cutpoint), or sex distribution (men only vs. men and women/ women only). We investigated possible publication bias using Egger's test for small-study effects (54) and a funnel plot of the estimates versus their standard errors. All statistical analyses were performed using Stata SE 11.0 (StataCorp LP, College Station, Texas). All statistical tests were 2-sided.

RESULTS

From MEDLINE, we identified 121 studies that included both exposure and outcome keywords (Figure 1). Of those, 7 met the inclusion criteria. An additional 552 articles were found from cross-referencing procedures and citations screened from Web of Science, of which 5 were not identified earlier and met the inclusion criteria, resulting in 12 eligible studies altogether (13, 14, 55–64).

Five studies included Japanese participants (13, 14, 59–61), 2 studies were from the United States (55, 57), and there was 1 study from each of the following countries: Denmark (63), Finland (62), the Netherlands (58), Sweden (56), and the United Kingdom (64) (Table 1). Publication year ranged from 1958 to 2010. Seven studies were case-control studies (55–61) using CHD patients admitted to a hospital and their healthy controls. Four studies were prospective (13, 14, 63, 64), with follow-up times ranging from 3 years to 30 years, and 1 was cross-sectional (62).

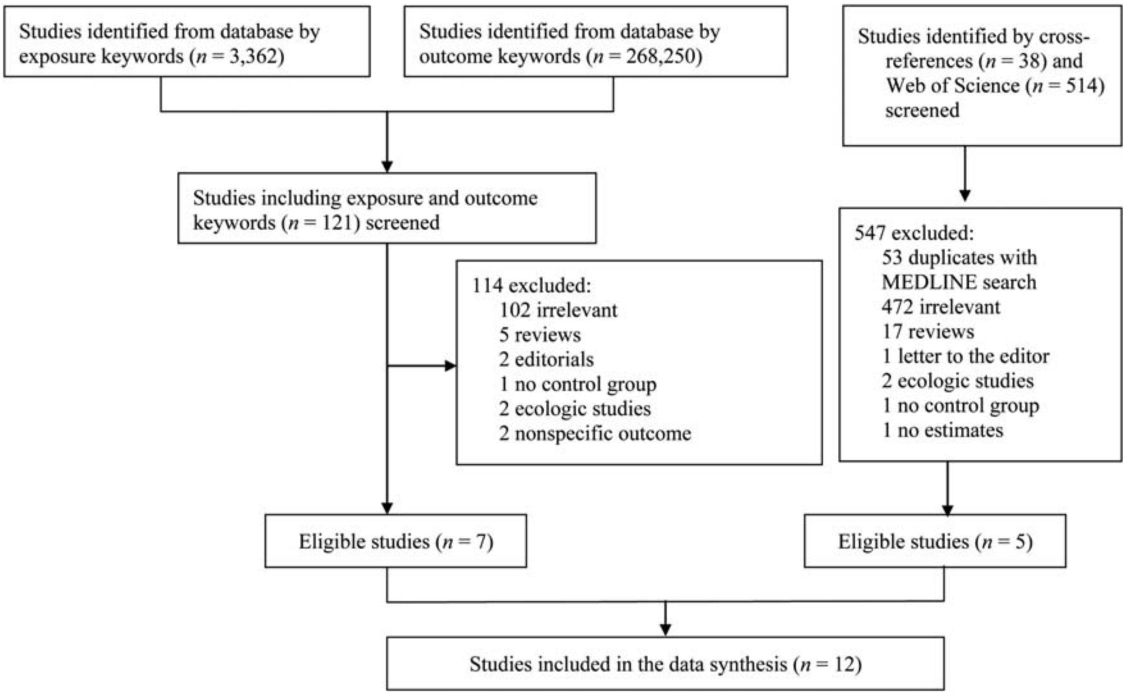

Figure 1. Search strategy for published observational studies on the association between long working hours and coronary heart disease. Data sources used were MEDLINE (through January 19, 2011) and Web of Science (through March 14, 2011).

The total number of participants across the studies was 22,518 (12,827 men (57%), 9,691 women (43%)). A total of 2,313 CHD cases were included in the studies. In most of the studies, participants were middle-aged (>40 years). Exceptions were the study by Russek and Zohman (55), in which the participants were 25–40 years old at the time of the AMI event, and the prospective study by Tarumi et al. (13), which included participants aged 20–60 years at baseline. In 7 studies (13, 56, 57, 59–61, 64), the majority of the participants were nonmanual employees, while in 3 studies (14, 62, 63) the majority were manual employees.

There was large variation in the confounding or mediating factors considered. In 7 studies, SEP had been taken into account (13, 55, 56, 58–60, 64). Only in 5 studies did authors report estimates based on multivariate adjustment for important covariates, such as health behaviors, body mass index, lipid status, blood pressure, diabetes, psychological distress, sleeping hours, and work characteristics (13, 14, 59, 60, 64), and those studies were included in the maximally (multivariate-) adjusted analyses.

There were several ways to assess working hours. Some studies used reported overtime work (56, 58), while others assessed daily working hours (the cutpoint for the definition of long working hours ranged from ≥10 hours to >11 hours) (14, 59, 64) or weekly working hours (the cutpoint for long hours ranged from >40 hours to >65 hours) (13, 55, 57, 60–63).

Of the outcomes, 4 case-control studies used hospital admission due to first myocardial infarction (57–60); 1 study assessed first myocardial infarction or angina (55). In 2 case-control studies, first and recurrent myocardial infarction events were combined into a single outcome (56, 61). The only cross-sectional study (62) used an outcome measure of angina pectoris symptoms measured by the Rose questionnaire (65).

All 4 prospective studies excluded participants with CHD at baseline; however, the study sample of Uchiyama et al. (14) was comprised of participants who had been receiving antihypertensive treatment regularly for at least 1 year. There was variation in the outcomes among the prospective studies: 1 study used insurance claim records including diagnoses of diseases of the circulatory system in *International Classification of Diseases*, Tenth Revision, chapter 9 (diagnostic categories I00–I99) (13); 1 study used patient medical records to identify all cardiovascular events (14); 1 study used a nationwide register of CHD mortality (63); and 1 study used a combination of clinically verified and nationwide register data on fatal CHD, nonfatal myocardial infarction, and definite angina (64).

Summary estimates of CHD risk

A minimally adjusted summary estimate of all 12 studies suggested a relative risk of 1.80 (95% confidence interval (CI): 1.42, 2.29) for long working hours (Figure 2). “Minimum adjustment” refers to age and sex (where relevant) in 5 studies (14, 57, 61–63) and to age, sex (where relevant), and SEP in 7 studies (13, 55, 56, 58–60, 64), plus ethnic origin in 1 study (55). In 7 of these 12 individual studies, the investigators reported a significant positive association between long working hours and CHD (55, 56, 58–61, 64), while 5 studies found a positive but nonsignificant association (13, 14, 57, 62, 63).

Results from the subgroup analyses are shown in Figure 3. SEP-adjusted studies (13, 55, 56, 58–60, 64) provided an overall summary estimate of the relative risk of 2.06 (95% CI: 1.55, 2.74). Restricting the analyses to maximally (multivariate-) adjusted studies (13, 14, 59, 60, 64) resulted in an estimate of 1.59 (95% CI: 1.23, 2.07). The 7 case-control studies (55–61) provided an estimate of 2.43 (95% CI: 1.81, 3.26), whereas the 4 prospective cohort studies (13, 14, 63, 64) suggested a slightly weaker estimate (relative risk = 1.39, 95% CI: 1.12, 1.72). The use of men-only samples and higher cutpoints to define long hours suggested a stronger association between long working hours and CHD than analysis of studies that also included women or included only women and studies that used lower cutpoints for long working hours. No clear differences in estimates were found when the studies were stratified by geographic region. In order to eliminate confounding due to potential shift work, we analyzed the data after restricting the studies to those with known daytime workers (13, 64) and found an estimate of 1.51 (95% confidence interval: 1.12, 2.03; data not shown).

There was some heterogeneity in the minimally adjusted estimates ($I^2 = 61.9\%$, $P = 0.002$ (Figure 2)). However, we observed little evidence of publication bias in our meta-analyses. The funnel plot for minimally adjusted study results appeared symmetric (Figure 4), but there was no evidence of an association between study size and the estimates (Egger's test: $B = 1.69$, 95% CI: −0.79, 4.16; $P = 0.16$).

DISCUSSION

In this meta-analysis of 12 studies including 22,518 participants and 2,313 CHD cases, we found that long working hours were related to an approximately 1.80-fold (95% CI: 1.42, 2.29) increased probability of CHD, and analyses restricted to the 4 prospective studies resulted in an estimate of 1.39 (95% CI: 1.12, 1.72). To our knowledge, this is the first meta-analysis of the available evidence on long working hours and CHD. An advantage of meta-analysis is that it provides a more objective summary of the existing evidence than narrative reviews.

An association between long working hours and hospital admission due to AMI was reported by Russek and Zohman (55) as early as 1958, for 100 male cases and their 100 controls. Using similar but older-age samples, Theorell and Rahe (56), Falger and Schouten (58), Sokejima and Kagamimori (59), Liu and Tanaka (60), and Fukuoka et al. (61) also found a significant relation between long working hours and CHD. The summary estimate for the case-control studies was high: 2.43. A major problem with case-control studies is that the retrospective assessment of working hours potentially introduces recall bias and reverse causation bias—that is, it is possible that the diseases or symptoms themselves (here CHD) influence the patient's work behavior and perception or recall of working hours prior to the onset of illness. However, the study by Sokejima and Kagamimori (59), which was able to address this problem using patients' salary records instead of self-reports to determine working hours, produced an estimate of 2.44 (95% CI: 1.26, 4.73).

Overall, a major limitation of our results is that meta-analyses based on observational studies cannot prove causality. Furthermore, the vast majority of studies were case-control studies (plus 1 cross-sectional study). On the basis of these data, we cannot indicate the direction of the association because the studies are open to bias due to reverse causation. We addressed the problem of reverse causation by performing a sensitivity analysis restricted to the 4 prospective studies (13, 14, 63, 64). Of those studies, a statistically significant association was found in 1: the Whitehall II Study, which included middle-aged white-collar employees followed for 11 years (64). In two of the other prospective studies, the outcome included a large variety of cardiovascular events (13, 14), and in one study, the follow-up period was very long—30 years (63). Nonetheless, the overall estimate was statistically significant, albeit slightly weaker (relative risk = 1.39, 95% CI: 1.12, 1.72). However, even in prospective studies, we cannot exclude the possibility of bias due to preclinical disease or confounding by unmeasured factors linked to both the tendency to work long hours and increased CHD risk.

Adjustment for standard CHD risk factors—both potential mediating factors and confounding factors—was lacking in the majority of studies. When we restricted the analysis to studies with maximum (multivariate) adjustment, the association became attenuated to some degree but was still significant. Because CHD risk factors may be on the causal path between exposure and outcome, multiple adjustments may actually be overzealous if the outcome of interest is the magnitude of the association between long working hours and CHD. On the other hand, CHD risk factors may also represent confounders of the working hours-CHD association. Although the possibility of residual confounding by unmeasured or imprecisely measured predictors of coronary events can never be entirely ruled out in observational studies, our results may represent an overestimation of the association.

We restricted our search to studies published in English. However, our manual search did not reveal any published articles in languages other than English. A problem could appear if the association between long working hours and CHD was different among employees of different nationalities and if results of such studies were reported predominantly in languages other than English. However, because we did not find any strong evidence suggesting regional differences in the association between long hours and CHD, this seems unlikely.

We found large variation in the assessment of working hours, ranging from nonspecific definition of "overtime" (56, 58) to more specific inquiry about daily working hours (cutpoints for long hours ranged from ≥10 hours to >11 hours) (14, 59, 64) or weekly working hours (cutpoints for long hours ranged from >40 hours to >65 hours) (13, 55, 57, 60–63). However, in only 2 studies (59, 64) was the reference group comprised of employees with a definite standard workday of 7–8 or 9 hours. Use of dichotomous categorizations may affect the resulting associations, since

Table 1. Characteristics of Published Studies on the Association Between Long Working Hours and Coronary Heart Disease

First Author, Year (Reference No.)	Study Location	Sample	Study Design	Follow-Up Time	No. of Participants	% Male	Age, years	Distribution by SEP	Potential Confounders Considered	Measure of Working Hours	Outcome Measure
Russek, 1958 (55)	United States	Patients admitted to the hospital	Case-control	N/A	100 cases, 100 controls	97	25–40	No information available	Nonmatched healthy control group of similar age, occupation, and ethnic origin	Evening job in addition to main job (yes/no) or ≥60 working hours per week vs. less	Hospital admission due to first AMI or angina
Theorell, 1972 (56)	Sweden	Patients admitted to the hospital	Case-control	5 months, retrospective	62 cases, 109 controls	100	Mean = 56	65% professionals/managers, 35% skilled workers/lower managerial positions	Matched healthy control group of similar age and occupation	Self-reported overtime work 4 months prior to the event (≥2 hours/day) vs. not	Hospital admission due to AMI
Thiel, 1973 (57)	United States	Patients admitted to the hospital	Case-control	12–24 months, retrospective	50 cases, 50 controls	100	40–60	74% nonmanual workers	Matched healthy control group of similar age	Average working hours per week: ≥51 vs. less	Hospital admission due to first AMI
Falger, 1992 (58)	The Netherlands	Patients admitted to the hospital	Case-control	N/A	133 cases, 133 neighborhood controls, 192 hospital controls	100	Mean = 53	50% had more than a primary school education	Nonmatched healthy control group of similar age and area of residence	Prolonged overtime (details not reported)	Hospital admission due to first AMI
Sokejima, 1998 (59)	Japan	Patients admitted to the hospital	Case-control	2 months and 1 year, retrospective	195 cases, 331 controls	100	Mean = 55.5	51% managers and officials	Healthy controls matched by age and occupation; models adjusted for age, occupation, hypertension, hypercholesterolemia, diabetes, BMI, smoking, proportion of sedentary work, and burnout index	Self-reported from salary records; daily working hours: 9.01–11 or ≥11.01 vs. 7.01–9; increase in daily hours during the year: 1.01–2, 2.01–3, or ≥3.01 vs. ≤1.01	Hospital admission due to first AMI
Liu, 2002 (60)	Japan	Patients admitted to the hospital	Case-control	1 year, retrospective	260 cases, 445 controls	100	40–79	64% nonmanual	Matched healthy control group of similar age, sex, and residence; models adjusted for smoking, alcohol use, overweight, hypertension, diabetes, hyperlipidemia, parental CHD, SEP, and sedentary job	Weekly working hours (past year, past month): 41–60 or >60 vs. ≤40	Hospital admission due to first AMI
Tarumi, 2003 (13)	Japan	Office workers	Prospective	3 years	824	74–79	20–60	100% nonmanual workers	Baseline healthy cohort; models adjusted for age, sex, type of occupation, BMI, and physical exercise	Weekly working hours: ≥45 vs. less	Insurance claim records of diseases of the circulatory system (ICD-10 diagnoses I00–I99)

Table continues

Table 1. Continued

First Author, Year (Reference No.)	Study Location	Sample	Study Design	Follow-Up Time	No. of Participants	% Male	Age, years	Distribution by SEP	Potential Confounders Considered	Measure of Working Hours	Outcome Measure
Uchiyama, 2005 (14)	Japan (Hypertension Follow-up Group Study)	Treated hypertensive workers	Prospective	5.6 years	1,615	56	Mean = 54	35% nonmanual workers	Baseline healthy cohort; models adjusted for age, sex, blood pressure, BMI, total cholesterol, high density lipoprotein cholesterol, family history of stroke, left ventricular hypertrophy, ischemic ST-T change, atrial fibrillation, and smoking	Daily working hours: ≥10 vs. less	New cardiovascular event (cerebral hemorrhage/ infarction, subarachnoidal hemorrhage, AMI, heart failure, aortic aneurysmal rupture, or sudden death)
Fukuoka, 2005 (61)	Japan	Patients admitted to the hospital	Case-control	1 month, retrospective	47 cases, 47 controls	98	Mean = 52	83% nonmanual	Matched healthy control group of similar age and sex	Weekly working hours: >65 vs. less	Hospital admission due to AMI
Lallukka, 2006 (62)	Finland (Helsinki Health Study)	Municipal employees	Cross-sectional	N/A	7,060	N/A	40, 45, 50, 55, or 60	45% professionals or semi-professionals	Models adjusted for age, job demands, job control, work fatigue, mental strain at work, physical strain at work, work-home interface, and social support	Weekly working hours: >40 vs. less	Self-reported angina pectoris symptoms (Rose questionnaire)
Holtermann, 2010 (63)	Denmark (Copenhagen Male Study)	Employees from 14 companies	Prospective	30 years	4,943	100	40–59	55% manual workers	Baseline healthy cohort; models adjusted for age	Weekly working hours: ≥46 vs. ≤40	Death due to ischemic heart disease (ICD-8 diagnoses 410–414, ICD-10 diagnoses I20–I25)
Virtanen, 2010 (64)	United Kingdom (Whitehall II Study)	Employees from the civil service	Prospective	11 years	6,014	71	Mean = 49	100% nonmanual workers	Baseline healthy cohort; models adjusted for age, sex, marital status, occupational grade, diabetes, blood pressure, cholesterol, triglycerides, smoking, alcohol use, fruit and vegetable consumption, exercise level, BMI, sleeping hours, sickness absence, psychological distress, job demands, decision latitude, and type A behavior pattern	Daily working hours: 11–12 vs. 7–8	Clinically verified and register data on fatal CHD, nonfatal myocardial infarction, and definite angina

Abbreviations: AMI, acute myocardial infarction; BMI, body mass index; CHD, coronary heart disease; ICD-8, *International Classification of Diseases*, Eighth Revision; ICD-10, *International Classification of Diseases*, Tenth Revision; N/A, not applicable; SEP, socioeconomic position.

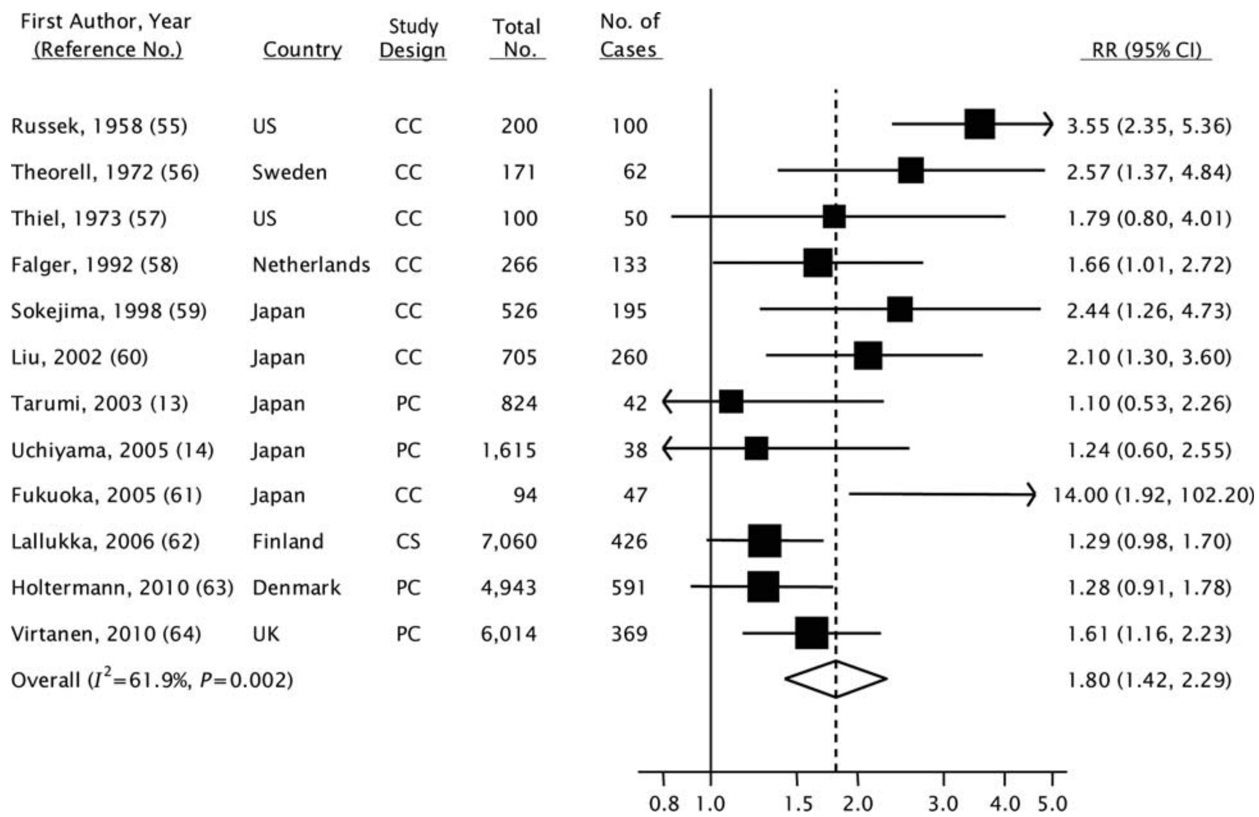

Figure 2. Minimally adjusted relative risk (RR) of coronary heart disease in employees working long hours among studies published through spring 2011. Bars, 95% confidence interval (CI). (CC, case-control; CS, cross-sectional; PC, prospective cohort; UK, United Kingdom; US, United States).

employees with relatively long working hours are included in the exposure group or the reference group depending on the cutoff point chosen. Indeed, our subgroup analysis revealed that the association may be stronger when higher cutpoints are used—that is, when the exposed group consists of employees with rather excessive working hours. We also found stronger associations in men-only samples, which may indicate either that men have a higher susceptibility to CHD at working age or that men who engage in overtime work more hours than women who work overtime. Furthermore, many studies included part-time employees in the reference group. This is also problematic because of the elevated CHD risk found among part-time employees (59). In addition, poor health is a possible reason for working reduced hours (66). In future studies, a reference group with a standard workday of approximately 8 hours would be preferable.

The increased onset of CHD associated with long working hours could be related to chronic exposure to extensive working hours and/or a temporary increase in hours acting as a trigger for serious coronary events. However, none of the prospective studies in this review assessed whether the number of working hours reported by participants at baseline was stable over the duration of follow-up. One study examined whether a change in working hours had occurred during the year preceding the AMI and found that men who experienced a >3-hours' increase in average working hours had a 2.5-fold higher risk of AMI compared with men who experienced little change in their working hours (59).

The most common outcomes were AMI and angina, diagnosed by a physician during hospital treatment, in the study clinic, or based on diagnoses in national mortality registers. Although the outcome assessment can be considered rather reliable in the majority of the studies in the present meta-analysis, more specific CHD endpoints (67–70), such as stable angina, nonstable angina, first myocardial infarction with elevation of the ST segment on electrocardiogram (STEMI), and first myocardial infarction without such elevation (non-STEMI) would be preferable in future studies to increase understanding of the potential adverse consequences of long working hours.

There are several potential mechanisms that may underlie the association between long working hours and CHD. One candidate is prolonged exposure to psychological stress and related dysregulation of the hypothalamic-pituitary-adrenal and sympatho-adrenomedullary axes, which are the primary biologic systems activated during the stress response (71–73). Such dysregulation, which is often marked by cortisol and catecholamine hypersecretion, may contribute to a variety of endocrine, metabolic, autoimmune, and psychiatric disorders, which in turn are risk factors for CHD (71, 73). There are some studies that suggest associations between long working hours and increased cortisol levels

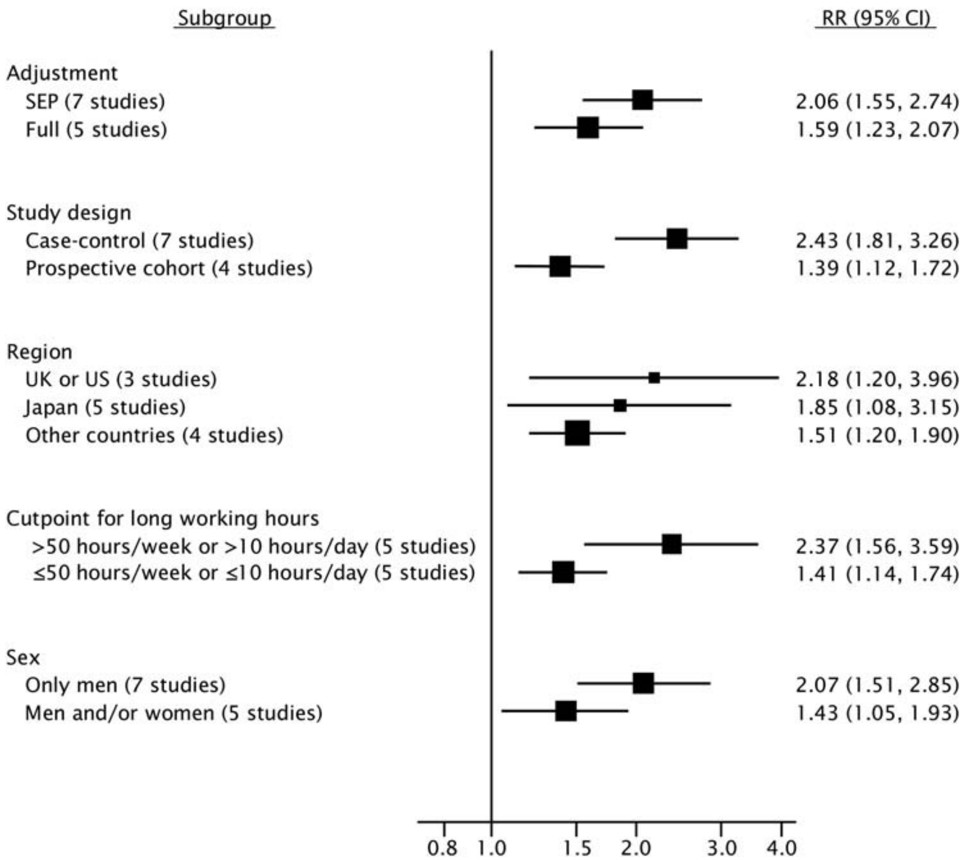

Figure 3. Relative risk (RR) of coronary heart disease in employees working long hours among studies published through spring 2011, according to type of statistical adjustment, study design, region, cutpoint used to define long hours, and sex. Bars, 95% confidence interval (CI). (SEP, socioeconomic position; UK, United Kingdom; US, United States).

(74), elevated blood pressure (15, 20), carotid intima-media thickness (23), anxiety and depression (75–77), type 2 diabetes (27), overweight (22, 78–80), unhealthy dietary habits (78, 81), smoking (80), and lower physical activity (21, 80, 81), although other studies found no association between long working hours and cardiovascular risk factors (6, 16, 18, 19, 21, 22, 25, 26, 79).

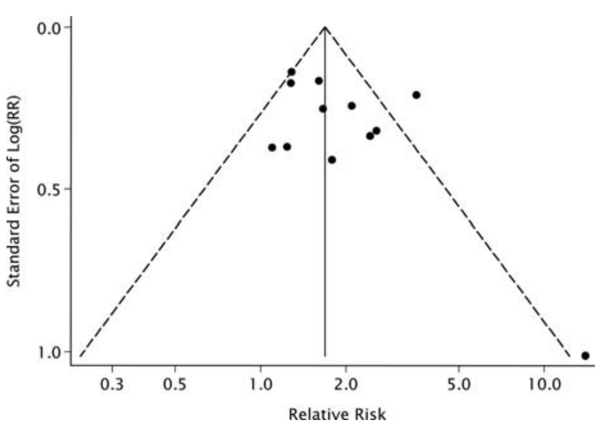

Figure 4. Funnel plot of the relative risk (RR) of coronary heart disease according to long working hours, with pseudo-95% confidence intervals (dashed lines).

Other contributing factors in the development of CHD may be related to the lack of rest and poor unwinding (82, 83), as well as sleep deprivation, which has been shown to be associated with both long working hours (84) and CHD (85). Furthermore, there is an association between shift work and CHD (86), raising the possibility that the association between long working hours and CHD may be attributable to confounding by shift work. However, this seems an unlikely explanation for the present findings, because restricting the meta-analysis to studies targeting daytime workers only did not affect the association. It is still possible that the combination of shift work *and* long working hours is related to a particularly high health risk, as Violanti et al. (24) demonstrated in their study of the metabolic syndrome among police officers. Excess hazard may also be branch-specific; for example, employees in transportation may be especially vulnerable, since overtime work and lack of sleep and rest are also likely to compromise safety at work (87), a problem which has been addressed by government regulations (88, 89). These are important hypotheses to be examined in future studies.

In addition, employees who work overtime may be reluctant to be absent from work despite illness. In a study of British civil servants, such sickness presenteeism was found to be associated with increased risk of myocardial infarction in men (90). In one study, Japanese overtime workers had a delay in seeking care during an acute coronary event (91).

In summary, this study overall suggests an approximately 1.8-fold increased probability of CHD associated with long working hours, with a somewhat reduced estimate of a 1.4-fold increased risk when analyses are restricted to the 4 prospective studies. We observed little evidence of publication bias in our meta-analyses; however, there was some heterogeneity in the effect estimates. Because the meta-analysis from which this estimate is derived was based on observational data, it is not known whether this association is causal.

Despite the limitations noted above, the results of this meta-analysis represent the most precise and accurate estimate of the strength of the relation between long working hours and CHD currently available. A recent investigation found that information on working hours may improve prediction of CHD risk based on the Framingham risk score in a low-risk working population (92). To further evaluate the clinical value of the measurement of working hours, it is important to clarify whether long hours at work are a causal risk factor or only a marker of increased CHD risk.

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