



Job insecurity and risk of coronary heart disease: Mediation analyses of health behaviors, sleep problems, physiological and psychological factors

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ABSTRACT

Job insecurity has been linked to increased risk of coronary heart disease (CHD), but underlying mechanisms remain uncertain. Our aim was to assess the extent to which this association is mediated through life style, physiological, or psychological factors. A total of 3917 men and women free from CHD provided data on job insecurity in the Whitehall II cohort study in 1997–1999. The association between job insecurity and CHD was decomposed into a direct and indirect effect mediated through unhealthy behaviors (smoking, high alcohol consumption, physical inactivity), sleep disturbances, ‘allostatic load’, or psychological distress. The counterfactual analyses on psychological distress indicated a marginally significant association between job insecurity and incident CHD (hazard ratio (HR) 1.32; 95 % confidence interval (CI) 1.00–1.75). This association was decomposed into a direct (HR 1.22, 95 %CI 0.92–1.63) and indirect association (1.08, 95 %CI 1.01–1.15), suggesting that about 30 % of the total relationship was mediated by psychological distress. No mediation was indicated via health behaviors, sleep disturbances, or allostatic load, although job insecurity was related to disturbed sleep and C-reactive protein, which, in turn were associated with CHD. In conclusion, our results suggest that psychological distress may play a role in the relation between job insecurity and CHD.

1. Introduction

Perceived job insecurity, defined for example, as “perceived powerlessness to maintain desired continuity in a threatened job situation” (Greenhalgh and Rosenblatt, 1984), has been associated with increased risk of coronary heart disease (Virtanen et al., 2013). Some studies have also found that job insecurity is associated with sleep problems (Linton et al., 2015; Mattiasson et al., 1990; Virtanen et al., 2011), as well as psychological wellbeing (De Witte et al., 2016) and may also be associated with unhealthy behaviors and adverse metabolic and inflammatory biomarkers (Arnetz et al., 1991; Ferrie et al., 2002; Magnusson Hanson et al., 2017; Mattiasson et al., 1990; Siegrist and Li, 2017). All these factors are associated with increased risk for cardiovascular disease or diabetes (Donath and Shoelson, 2011; Piepoli et al., 2016). It has been hypothesized that job insecurity increases the risk of

CHD through unhealthy behaviors (such as increased alcohol consumption, smoking, less physical activity), sleep problems, activation of the physiological stress reaction systems, and psychological processes (Ferrie et al., 2001). Plausible mechanisms may also involve increased coagulation and inflammation which may trigger cardiovascular events in individuals with high atherosclerotic burden (Sara et al., 2018). However, relatively few studies to date have examined the relationship between job insecurity and CHD risk factors (Chazelle et al., 2016; De Witte et al., 2016; Dobson et al., 2018; Ferrie et al., 2002; Virtanen et al., 2011) and the mechanisms that explains the relationship between job insecurity and CHD remain uncertain.

The aim of this study was to examine the role of four potential intermediate factors; health behaviors (smoking, high alcohol consumption, physical inactivity), sleep, physiological (measured by an ‘allostatic load’ index) biomarkers, and psychological distress, in the

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relationship between job insecurity and incident coronary heart disease. In contrast to many previous studies in the field, we assessed the total, direct effect of job insecurity on incident coronary heart disease, and indirect effect via the potential mediators using counterfactual-based mediation analysis.

2. Material and methods

2.1. Study population

The study was based on data from the Whitehall II study, in which employees aged 35–55 years were recruited from 20 London-based Civil Service departments (Marmot and Brunner, 2005). The first data collection took place 1985–1988, when all the civil servants were asked to respond to questionnaires, and to visit a research clinic for clinical measurements. In total, 10,308 individuals (6895 men and 3413 women) responded to the first phase, representing 73 % of the invited employees. Since then, study members have been invited at 5-year intervals to attend a research clinic and complete further questionnaires, and also to complete additional questionnaires distributed in the interim. Informed consent was obtained from all participants, and the University College London Medical School Committee on the Ethics of Human Research approved the protocol.

The study sample for the present analyses consisted of participants who responded to questionnaire data and participated in the clinical examination at phase 5 (1997–1999), with survey data on job insecurity. A total of 6510 individuals provided both questionnaire and screening data at phase 5. Out of these, 4102 were employed at the time and provided data on job insecurity. Those with prevalent CHD at phase 5 ($n = 185$) were excluded from the analyses. The basic dataset for analyses thus consisted of 3917 individuals. Everyone with valid data on all variables of interest were included in analyses on job insecurity at phase 5 and subsequent CHD up to phase 9 (2007–2009) as well as analyses of potential mediators (phase 5) and CHD (up to phase 9). Numbers differed slightly in various analyses due to missing data (see Fig. 1).

2.2. Job insecurity

Data on job insecurity was self-reported and measured with the question ‘How secure is your present job?’ Participants responding that they felt ‘Very secure’ and ‘Secure’, were considered as secure, while those reporting ‘Very insecure’ and ‘Insecure’ were considered as insecure.

2.3. Health behaviors

Based on the questionnaire data, we also assessed whether the participants were current smokers or not, had risky alcohol habits or were physically inactive during leisure time. Participants were considered to have a risky alcohol habit if they consumed more than 21 units (men) or 14 units (women) per week and be physically inactive if they reported less than 1 h of moderate or vigorous physical activity per week (less than recommended by the World Health Organisation). A summary index of all the unhealthy behaviors above was created (range 0–3) representing number of unhealthy behaviors which was used in the main analyses. A higher number of unhealthy behaviors has previously been associated with higher risk for CHD and shorter healthy life expectancy (Kivimäki et al., 2013; Stenholm et al., 2016).

2.4. Sleep

Sleep problems were reported according to the Jenkins scale and covered frequency of trouble falling asleep, staying asleep, repeated awakenings, and feeling tired and worn out at awakening, during the last month (Jenkins et al., 1988). Participants with any of the above problems at least 8 nights in the past month were categorized as having sleep disturbances (Stenholm et al., 2019).

2.5. Allostatic load

The clinical screening included measurements of weight (measured by Soehnle scale to the nearest 0.1 kg) and height (measured to the nearest mm using a stadiometer) assessed by trained nurses. Body mass

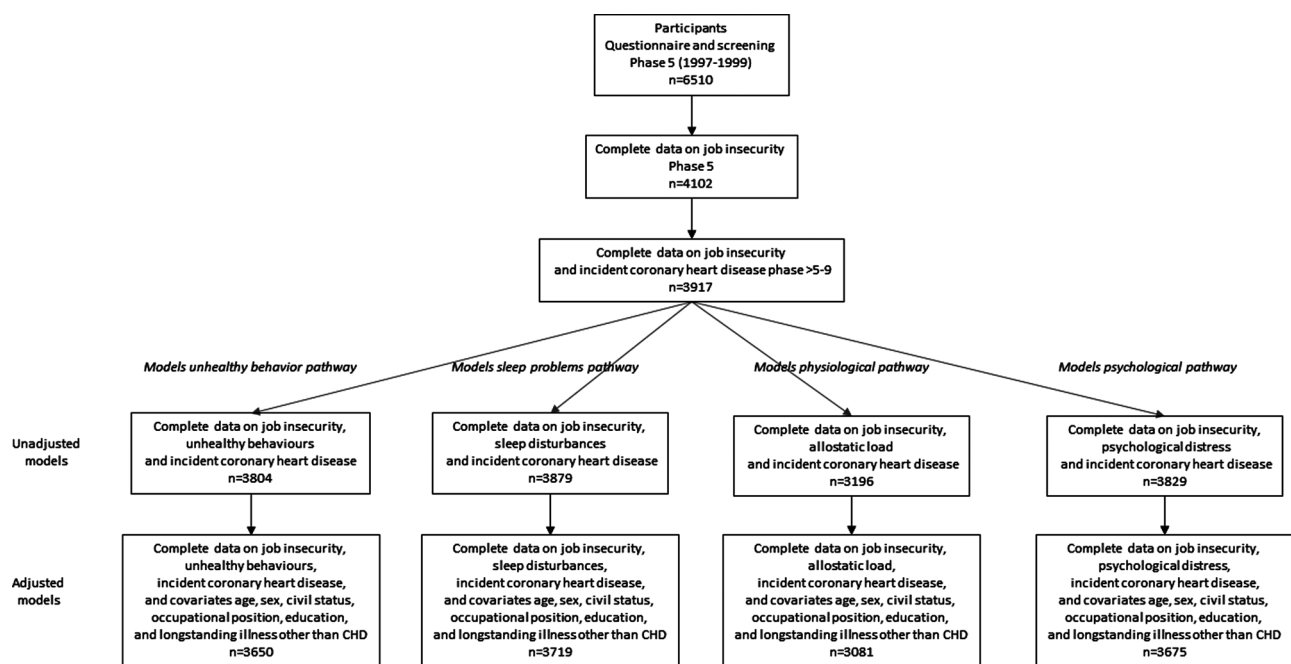


Fig. 1. A flowchart describing selection of participants for inclusion in the overall study sample and in specific analyses focusing on the associations between job insecurity and the potential mediators (exposure-mediator relationship), the potential mediators and coronary heart disease (mediator-outcome relationship), or in the mediation analyses assessing the extent to which the potential mediators may explain the relationship between job insecurity and coronary heart disease (given both a statistically significant exposure-mediator, and mediator-outcome relationship).

index (BMI) was calculated as weight divided by height squared, and those with a BMI of 25 or more were considered overweight. Blood pressure was also determined using standard protocols. Systolic (SBP) and diastolic blood pressure (DBP) were measured in the sitting position after 5 min of rest, using an OMRON HEM 907 digital sphygmomanometer. Two measures of SBP and DBP were taken, and their mean was used for calculation of blood pressure. Furthermore, venous blood samples were taken in the morning after over-night fasting, or in the afternoon after no more than a light, fat-free breakfast eaten before 08:00. Blood samples were used to measure cholesterol and triglycerides and high density lipoprotein cholesterol (HDL). The concentration of Low density lipoprotein cholesterol (LDL) was calculated using the Friedewald formula when serum triglycerides were lower than 4.5 mmol/L. A high-sensitivity immunonephelometric assay was used in a BN ProSpec nephelometer (Dade Behring) to assess C-reactive protein (CRP) from serum samples. Plasma Interleukin 6 (IL-6) levels were measured with a high-sensitivity enzyme-linked immunosorbent assay (R&D Systems). According to standard practice, values lower than the detection limit [0.154 mg L⁻¹ for CRP (multiplied by 9524 to express the value in mmol L⁻¹) and 0.08 pg mL⁻¹ for IL-6] were assigned a value equal to half the detection limit. Values of CRP above 20 mg/L that may indicate acute infection were excluded. Fibrinogen was assayed using a modification of the clotting method of Clauss. Finally, glucose was determined in fluoride plasma by an electrochemical glucose oxidase method, and serum insulin was measured by radioimmunoassay using a polyclonal guinea-pig antiserum. The assessment of these physiological parameters have been described in previous studies (Hamer et al., 2012; Tabak et al., 2009).

In line with previous studies, the biomarkers were first dichotomized using previously defined cutpoints; overweight (≥ 25 kg/m²), high blood pressure ($\geq 140/90$ mmHg), high triglycerides (> 1.7 mmol/L), low HDL (< 1.03 mmol/L), high LDL (> 4.9 mmol/L), high CRP (> 3 mg/L), high IL-6 (> 2.06 pg/mL), high fibrinogen (> 4.1 g/L), high glucose (> 5.5 mmol/L) and high insulin values (> 8.6 uIU/mL). For the main analyses we then created an index of allostatic load (range 0–10), representing the number of biomarkers above the cutpoints (Dich et al., 2015; Gallo et al., 2014; Juster et al., 2010). The index consisted of biomarkers used in previous studies based on Whitehall II data (Dich et al., 2015), and fibrinogen commonly used in previous allostatic-load studies (Juster et al., 2010). Allostatic load is assumed to reflect “the wear and tear of the body and brain resulting from chronic overactivity or inactivity of physiological systems that are normally involved in adaption to environmental challenge” (McEwen, 1998), and is regarded a sensitive measure of stress-related effects, capturing adverse levels of a number of physiological markers across multiple biological systems (Gallo et al., 2014; Juster et al., 2010).

2.6. Psychological distress

Self-reported data based on the 30-item General Health Questionnaire (GHQ), was used to assess psychological distress. The GHQ is a likert-scale instrument assessing the likelihood of psychiatric disorder, particularly depression and anxiety (Goldberg, 1972; Stansfeld and Marmot, 1992). People scoring ≥ 4 on the GHQ scale were considered to have psychological distress (Goldberg et al., 1997).

2.7. Follow-up of coronary heart disease

The outcome was incident CHD subsequent to phase 5 and up to phase 9 (8–12 years) including clinically verified myocardial infarction (MI) and angina events. MI included coronary deaths (ICD 9 codes 410–414 or ICD 10 codes I20–I25) or non-fatal MI defined using MONICA criteria (Tunstall-Pedoe et al., 1994). Definite angina was ascertained from clinical records, abnormalities on ECG or coronary angiogram, and nitrate medication use (Rose et al., 1982).

2.8. Covariates

A number of characteristics measured at phase 5 were considered as potential confounders including age, sex and education (linear term). Occupational position was categorized into 3 groups: administrative, professional and executive, and clerical and other (Marmot et al., 1991). Civil status (married/co-habited versus not) and self-reported previous long-standing illness other than CHD (yes versus no), were based on survey responses. Both somatic and mental illnesses were considered including anxious and depressive illnesses.

2.9. Data analysis

Three different sets of analyses were performed to examine the interrelationship between exposure to job insecurity and CHD, and the role of the four potential mediators (allostatic load, unhealthy behaviors, sleep problems and psychological distress). First, the relationship between job insecurity and each of the potential mediators separately was assessed through logistic regression or ordinal logistic regression analyses with the potential mediators at phase 5 as outcomes and job insecurity phase 5 as predictor. Second, to test whether the potential mediators were related to incident CHD, separate Cox regression analyses were fitted for each of the potential mediators with incident CHD as outcome. These analyses were also adjusted for job insecurity. These first two sets of analyses were performed to assess whether some of the standard criteria for mediation were fulfilled, namely whether there was an association between exposure and each potential mediator and between that potential mediator and the outcome, while adjusting for job insecurity (Valeri and Vanderweele, 2013). If these analyses indicated that the criteria for mediation were fulfilled, then a third set of analyses was performed to assess the extent to which the potential mediators explained the relationship between job insecurity and CHD. These mediation analyses were conducted using a mediation macro for counterfactual-based causal mediation analyses (Valeri and Vanderweele, 2013), which was applied separately for each of the potential mediators that fulfilled the criteria for mediation. The macro provides total effect, and effects partitioned into natural direct and indirect effects, irrespective of an interaction between exposure and mediator. The natural direct effect is defined as the change in outcome (CHD) that would be observed if the exposure (job insecurity) could be changed but the mediator (unhealthy behaviors, sleep disturbances, allostatic load, or psychological distress) stayed unchanged. The natural indirect effect is alternatively defined as the change in outcome (CHD) from a change in the mediator (either in unhealthy behaviors, sleep disturbances, allostatic load, or psychological distress) to a value it would naturally take if the exposure (job insecurity) would be changed but when the exposure (job insecurity) is kept unchanged (VanderWeele, 2016). The analyses were based on Cox proportional hazard models, while a logistic regression was specified for the mediator. Since preliminary analyses indicated an interaction between exposure and at least one of the mediators, the analyses allowed for an interaction between job insecurity and the potential mediators.

All models were adjusted for a range of covariates, which included age, sex, education, occupational position, civil status and previous longstanding illness. In addition, analyses estimating the extent of mediation separately for each of the plausible mediators (allostatic load, unhealthy behaviors, sleep problems and psychological distress) were conducted controlling for the other potential mediators of interest. We also repeated the main analyses for the specific health behaviors and biomarkers included in the indices for unhealthy behaviors and allostatic load. All analyses were performed with SAS Statistical Software, version 9.4.

3. Results

Among the study participants, 26 % reported perceived job

Table 1
Descriptive Characteristics At Phase 5 (1997-1999) For The 3917 Whitehall II (UK) Study Participants, By Perceived Job Insecurity.

		No job insecurity n (%) or mean (SD)	Job insecurity n (%) or mean (SD)
Sex	Men	2177 (75)	707 (69)
	Women	720 (25)	313 (31)
Age		53.0	53.0
Married or cohabiting	Yes	2277 (80)	762 (76)
	No	582 (20)	245 (24)
Occupational position	Administrative	605 (21)	162 (16)
	Professional/executive	1790 (62)	626 (62)
	Clerical/support	489 (17)	226 (22)
Educational level	No academic qualification	179 (6)	89 (9)
	Ordinary level	631 (23)	243 (25)
	A/S level qualification:Ordinary National Certificate/Higher National Diploma	752 (27)	268 (28)
	Bachelor of Arts /Bacheolor of Science	705 (26)	230 (24)
	Higher degree	497 (18)	132 (14)
Longstanding illness	No	1712 (60)	556 (55)
	Mental illness	54 (2)	21 (2)
	Other	1079 (38)	430 (43)

Table 2
Frequency Of Unhealthy Behaviors, Sleep Problems, Physiological Biomarkers and Psychological Distress Phase 5 (1997-1999) Among The 3917 Whitehall II (UK) Study Participants, By Perceived Job Insecurity.

	All n (%) or Mean (SD)	No job insecurity n (%) or Mean (SD)	Job insecurity n (%) or Mean (SD)	P value, test differences
Unhealthy behaviors (range 0–3)	1.2 (0.7)	1.2 (0.7)	1.2 (0.7)	0.68
Current smoking	383 (10)	267 (9)	116 (11)	0.04
Risky alcohol consumption	1000 (26)	743 (26)	257 (26)	0.75
Physical inactivity	3136 (81)	2340 (82)	796 (79)	0.06
Sleep problems	1453 (37)	997 (35)	456 (45)	< 0.001
Allostatic load (range 0–10)	2.1 (1.7)	2.1 (1.8)	2.1 (1.7)	0.70
Overweight	1956 (50)	160 (50)	496 (49)	0.33
High blood pressure	638 (16)	486 (17)	152 (15)	0.15
High Triglycerides	802 (21)	585 (20)	217 (22)	0.44
Low high density lipoprotein (HDL)	432 (13)	319 (13)	113 (13)	0.96
High low density lipoprotein (LDL)	387 (11)	295 (12)	92 (10)	0.27
High C reactive protein (CRP)	582 (15)	402 (14)	180 (18)	< 0.01
High interleukin 6 (IL-6)	832 (22)	602 (22)	230 (23)	0.23
High glucose	740 (19)	551 (19)	189 (19)	0.73
High insulin	1401 (36)	1042 (36)	359 (35)	0.66
High fibrinogen	166 (5)	118 (4)	48 (5)	0.38
Psychological distress	496 (13)	315 (11)	181 (18)	< 0.001

SD = standard deviation.

insecurity. The overall distribution of sociodemographic characteristics according to job insecurity status is shown in [Table 1](#). [Web Table 1](#) further shows the distribution of sociodemographic characteristics among the study participants and the participants at Phase 5 free from CHD who were excluded from analyses. Women and people with longstanding illness were overrepresented among those with job insecurity, while the proportion of participants with high educational level was lower in this group. The distribution of study variables by job insecurity is presented in [Table 2](#). In total, the study participants were followed for a mean of 11 years (a total of 43,181 person years at risk) during which there were 252 (6.4 %, rate 5.8 per 1000 personyears) incident CHD events.

3.1. Unhealthy behaviors as mediators

The results from analyses examining the relationship between job insecurity and the potential mediators are illustrated in [Fig. 2](#). After adjustment for all covariates (sex, age, civil status, occupational position, education and previous longstanding illness other than CHD), job insecurity was not any more related to the number of unhealthy behaviors (OR 0.97; 95 % CI 0.83, 1.12), nor was unhealthy behaviors associated with incident CHD (OR 1.00; 95 % CI 0.83, 1.22). In corresponding analyses focusing on specific health behaviors, job

insecurity was weakly but not statistically significantly associated with smoking, and smoking was weakly but not statistically significantly associated with CHD ([Web Tables 2–3](#)). Job insecurity was on the other hand associated with a lower odds of physical inactivity, but we found no relationship between physical inactivity and incident CHD, nor between job insecurity and risky alcohol consumption or between risky alcohol consumption and incident CHD. The analyses therefore indicated no major role of unhealthy behaviors as mediator in the relationship between job insecurity and CHD.

3.2. Sleep problems as mediator

Job insecurity was associated with sleep disturbances (OR 1.47; 95 % CI 1.26, 1.71) and there appeared to be a relationship between sleep disturbances and CHD, though the risk estimate was not statistically significant. Furthermore, there appeared to be a relationship between sleep disturbances and CHD, though the risk estimate was not statistically significant. As job insecurity was associated with sleep disturbances and the analyses indicated a probable association with CHD, we ran a mediation model with CHD as outcome, job insecurity as exposure, and sleep disturbances as the potential mediator, including the covariates:sex, age, civil status, occupational position, education and previous longstanding illness other than CHD. These analyses showed

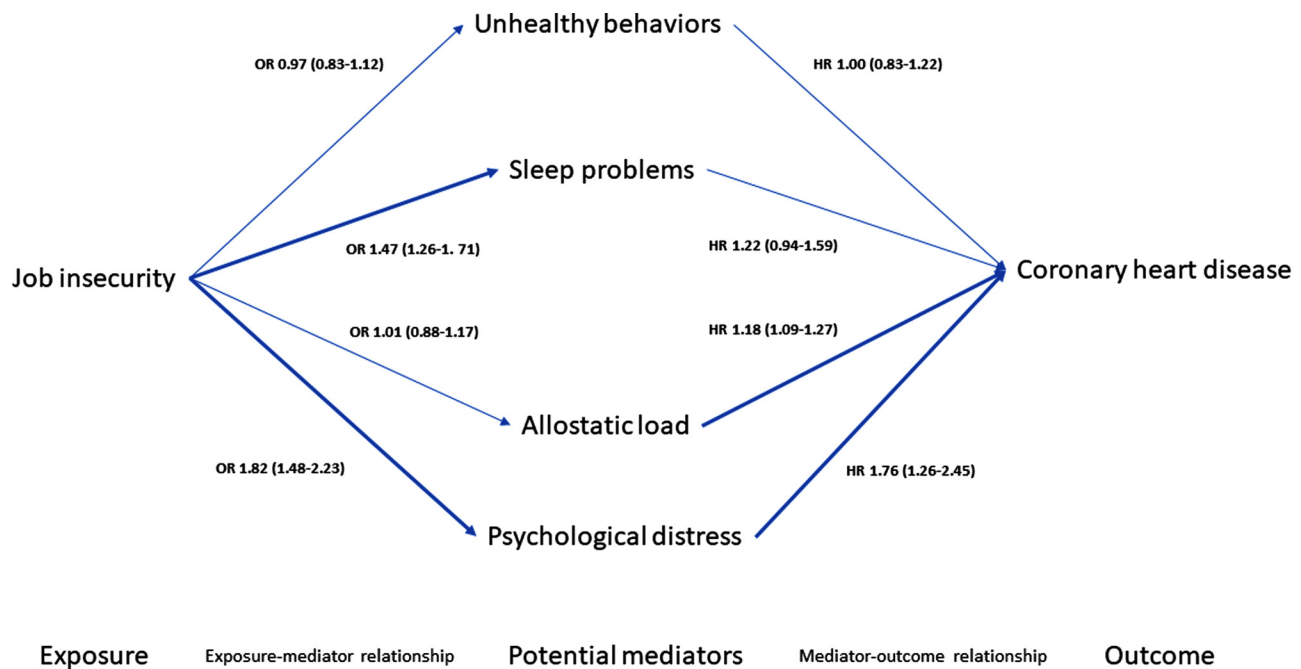


Fig. 2. An illustration of the relationships between exposure and potential mediators (left hand side) estimated through logistic regression and between potential mediators and outcome (right hand side) through proportional hazard regression. Presents risk estimates with 95 % confidence intervals within parenthesis from the regression models. The models were assessing the relationship between job insecurity and potential mediators were adjusted for sex, age, education, occupational position, civil status, previous longstanding illness other than CHD, while the models assessing the relationship between potential mediator and coronary heart disease were also adjusted for job insecurity.

OR = Odds ratio HR = Hazard ratio.

Table 3

Results From The Mediation Analyses Assessing To What Extent The Association Between Job Insecurity And Incident CHD May Be Mediated By Unhealthy Behaviors, Sleep Problems, Allostatic load Or Psychological distress. The Analyses Were Based on Whitehall II (UK) Study Participants With Complete Data on Job Insecurity and Potential Mediator Phase 5 (1997-1999) And Incident Coronary Heart Disease > Phase 5-9 And Provides Hazard Ratios (HRs) And 2-sided 95 % Confidence Intervals (CI).

Potential mediator	Total effect		Natural direct effect		Natural indirect effect through mediator		Proportion mediated
	HR	95 % CI	HR	95 % CI	HR	95 % CI	
Unhealthy behaviors ^a	1.34	1.03 – 1.77					
Sleep problems	1.37	1.04, 1.80	1.39	1.05, 1.83	0.99	0.95, 1.03	0
Allostatic load ^b	1.25	0.91 – 1.71					
Psychological distress	1.32	1.00, 1.75	1.22	0.92, 1.63	1.08	1.01, 1.15	0.31

^a Only total effect reported since no association was observed between exposure and mediator and between mediator and outcome while adjusting for exposure. Hence, the criteria for mediation were not fulfilled.

^b Only total effect reported since no association was observed between exposure and mediator. Hence, the criteria for mediation was not fulfilled. Analyses based on fewer number of participants because of missing data on allostatic load biomarkers.

that the total effect of job insecurity on CHD (HR 1.37; 95 % CI 1.04, 1.80) was not mediated by sleep disturbances. The HR for indirect effect was 0.99 (95 % CI 0.95, 1.03) and for direct effect 1.39 (95 % CI 1.05, 1.83) as presented in Table 3. Further adjustment for number of unhealthy behaviors, allostatic load, and psychological distress did not notably affect the risk estimates (data not shown).

3.3. Allostatic load as mediator

No clear relationship was noted between job insecurity and the allostatic load index considering all 10 physiological biomarkers jointly (Fig. 2). On the other hand, we found that allostatic load was related to incident CHD, when adjusting for sex, age, occupational position, education, civil status, longstanding illness other than CHD and job insecurity (Fig. 2). The analyses therefore indicated no major role of allostatic load as mediator in the relationship between job insecurity and CHD. Corresponding analyses of the specific biomarkers of the

allostatic load index yielded similar findings (Web Tables 2–3). Job insecurity was not clearly related to any of the biomarkers, with exception for CRP. CRP and most of the other biomarkers were in turn associated with incident CHD. A mediation analysis was therefore performed with CHD as outcome, job insecurity as exposure, and high CRP as the potential mediator, with adjustment for age, sex, civil status, occupational position, education and previous long-standing illness other than CHD (Web Table 4). This analyses supported a statistically significant total effect (HR 1.34; 95 % CI 1.01–1.76), of which the major part appeared to be direct (HR 1.33; 95 % CI 1.01–1.76) and only a negligible, statistically insignificant part (2%) indirect (HR 1.01; 95 % CI 0.99–1.02). For triglycerides which tended to be associated with both job insecurity and CHD, a mediation model also showed a negligible and statistically insignificant indirect effect (HR 1.00; 95 % CI 0.99–1.01, out of a total effect of HR 1.34; 1.01–1.76, corresponding to a proportion mediated of 1 %).

3.4. Psychological distress as mediator

Finally, job insecurity was strongly associated with psychological distress (OR 1.77; 95 % CI 1.28, 2.45) after adjustment for sex, age, occupational position, education, civil status and previous longstanding illness including previous mental illnesses such as anxious and depressive illnesses (Fig. 2). Psychological distress was also related to incident CHD after confounder adjustment and job insecurity. In this analytic sample, the total effect of job insecurity on CHD was of marginal significance (HR 1.32; 95 % CI 1.00, 1.75). The mediation analyses further showed a direct effect of 1.22 (95 % CI 0.92, 1.63) and indirect effect of 1.08 (95 % CI 1.01, 1.15) suggesting that 33 % of the association was explained by an indirect effect through psychological distress (Table 3). In a corresponding model additionally adjusting for the measures on unhealthy behaviors, sleep problems and allostatic load, the total effect of job insecurity was reduced to 1.22 (95 % CI 0.88, 1.68), but this model supported a statistically significant indirect effect (1.06; 95 % CI 1.00, 1.13) (data not shown).

4. Discussion

In this longitudinal study using counterfactual-based mediation analysis, job insecurity was associated with sleep disturbances and psychological distress, but only psychological distress was indicated to mediate the relationship between job insecurity and CHD. There was no evidence to support allostatic load or lifestyle factors, such as smoking, high alcohol consumption or physical inactivity, as mediators of this association.

This study extends previous research regarding potential mechanisms linking job insecurity with CHD. A large body of literature suggests an association between job insecurity and development of mental ill health (De Witte et al., 2016) and the results of this study supported this observation. However, findings regarding the relationship between job insecurity and health behaviors have generally been inconsistent and we found no clear indication in support of a behavioural pathway. Instead, our results support some previous studies suggesting an increase in sleep disturbances among men (Mattiasson et al., 1990) and women (Arnetz et al., 1988) and increased risk for suboptimal sleep quality (Virtanen et al., 2011) among people who experience job insecurity. It has also been found that organizational downsizing, a potential source of job insecurity, is associated with the use of hypnotics and sedatives, often used to treat sleep problems, during the anticipation phase before downsizing (Blomqvist et al., 2018). However, not all studies observed an association between job insecurity and sleep disturbances (Chazelle et al., 2016).

This work also extends earlier research on biological CHD risk markers. Some previous work on organizational change among civil servants participating in the Whitehall II study found adverse changes in blood pressure among women anticipating transition from secure to insecure job situation (Ferrie et al., 2002). Other studies have also noted increases in serum cholesterol (Arnetz et al., 1991; Mattiasson et al., 1990), although levels of cholesterol were not affected in civil servants (2002) (Ferrie et al., 2002). A study by Arnetz et al. (1991) found lower HDL-cholesterol connected to anticipation of unemployment (Arnetz et al., 1991). Our study is apparently the first on job insecurity and a range of biomarkers including inflammatory markers such as CRP and IL-6. The results did not suggest a relationship between job insecurity and allostatic load. There was also little evidence of a relationship between job insecurity and specific biomarkers, only between job insecurity and CRP, although we cannot exclude a relationship between job insecurity and specific physiological responses not captured in this study.

Our findings are in line with a previous study, which found no clear indications that health behaviors play an important role as intermediate factors in the relationship between job insecurity and health (Ferrie et al., 2001). On the other hand, our findings suggest that psychological

distress mediated the relationship between job insecurity and CHD, and this is in line with the findings by Ferrie et al. (2013) that the relationship between job insecurity and CHD in civil servants was reduced when adjustment was made for mental health (Ferrie et al., 2013). However, in contrast to Ferrie et al. (2013) we performed formal mediation analyses based on the counterfactual framework avoiding the limitation of non-collapsability of hazard ratios and inability to validly assess indirect effects in presence of exposure-mediator interaction (Valeri and Vanderweele, 2013).

The formal mediation analyses allowed for effect decomposition of a total effect irrespective of interactions and nonlinearities, which was an issue in the present work (Valeri and Vanderweele, 2013). This is contrast to classic approaches to mediation analyses which do not allow for effect decomposition of a total effect in situations with interactions and nonlinearities. The study also has a number of other strengths. The study was based on analyses of clinical measures of CHD measured subsequent to exposure/mediators. The study also investigated a large range of physiological markers measured in the study clinic according to standard protocol.

A limitation is that several measures were obtained using standard questionnaires rather than objective measurements. Self-reports may be subject to reporting bias. We assessed job insecurity based on self-report, an operationalisation that is close to the affective component of job insecurity (feeling threat) and in agreement with the widely-used definition of job insecurity as a perceived likelihood of involuntary job loss (De Witte et al., 2016). A recent meta-analysis found that the association between job insecurity and coronary heart disease was similar when job insecurity was assessed by a score that concerned different aspects of insecurity in the present job to when it was measured by means of fear of lay-off or unemployment, suggesting that this association is not dependent on a particular operationalization of job insecurity (Virtanen et al., 2013). However, our assessment of job insecurity was based on a single-item measure which necessarily has a more limited variation than multi-item scales and thus might have contributed to an underestimation of the relationship with coronary heart disease. We lacked objective data on job changes, which prevented us to validate our measure of job insecurity against an external criterion. However, other findings support the construct validity of our job insecurity measurement. First, we found an association between self-reported job insecurity and self-reported experience or expectancy of undesirable changes in the respondent's work situation. As expected, however, a relatively large proportion of people experiencing no past or expected undesirable changes experienced job insecurity (14 %), and similarly a relatively large group of people reporting job insecurity reported no past or expected undesirable changes to their work situation (34 %). This indicate that threats of changes do not necessarily lead to perceived job insecurity and that fear of job loss and negative job changes are distinct albeit partially overlapping concepts. Second, we also found an association between job insecurity and psychological distress which provides further support for construct validity and is in accordance with a number of previous studies that found a link between job insecurity and reduced wellbeing or health (De Witte et al., 2016) and a longitudinal study observing an association between the affective component of job insecurity and purchases of psychotropic drugs ascertained from administrative data drugs (Blomqvist et al., 2020).

Common method variance, referring to variance attributed to the measurement method rather than the constructs of interest, may also arise in analyses based solely on self-reports (Podsakoff et al., 2003). Common-method bias is an unlikely explanation for the associations between job insecurity and CHD which was ascertained by electronic health records and measured components of allostatic load, but it could have inflated associations between job insecurity, psychological distress and behavioural factors, all assessed using self-administered questionnaire instruments. Furthermore, we were not able to determine the time order between the exposure and mediators, as both job insecurity and psychological distress were measured at baseline. It is possible that

psychological distress also predicts job insecurity and that reverse causation influenced our findings. A number of previous studies have on the other hand supported an influence of job insecurity on well-being/health and only few studies have found wellbeing/health to precede job insecurity (De Witte et al., 2016). We also adjusted for previous long-standing mental illness which should reduce the risk that reverse causality explain the relationship between job insecurity and psychological distress. A previous study based on Whitehall II data examining changes in job security also suggested that previous job insecurity was associated with depression scores and that a relief from job insecurity may not completely reverse health effects (Ferrie et al., 2002). Another previous study also found an association between affective job insecurity and purchases of psychotropic drugs ascertained from administrative data (Blomqvist et al., 2020). This further support a prospective relationship between job insecurity and clinically diagnosed poor mental health, and suggest that there is an association between job insecurity and mental disorders which is not merely driven by common method bias. Some further hypothesize that job insecurity is endogenous, meaning that pessimistic traits may underlie the associations with health. We were unfortunately unable to account for personality traits such as neuroticism, but this hypothesis was not supported by previous work based on Whitehall II study which showed that the association between job insecurity and CHD was unaffected after adjustment for negative affect (Ferrie et al., 2002). Still, future mediation analyses also allowing for time to elapse between job insecurity and psychological distress and accounting for personality traits may be valuable to confirm that psychological distress is one of the true pathways through which job insecurity leads to CHD.

Another possible limitation is that the results for each potential pathway separately do not take into account that the mediating pathways may be intertwined and affect each other. The estimates of the indirect effects for each single pathway may not be correct as some pathways may be counted several times. However, methods for analyzing mediation with multiple mediators based on Cox regression allowing for estimation of path-specific effects, especially when the causal order of mediators is unknown, are not well developed (Fasanelli et al., 2019). Moreover, additional adjustment for the other pathways did not seem to markedly affect the estimates. Another limitation is that the main analyses of different health behaviors and biomarkers collectively may have masked associations for specific health behaviors or biomarkers. However, additional analyses of specific health behaviors and biomarkers did not lead to different conclusions. The allostatic load measure consisted of a number of immune-, metabolic-, cardiovascular-, and anthropometric biomarkers commonly used in allostatic load studies, but no neuroendocrine biomarkers (Juster et al., 2010). The biomarkers thereby primarily included “secondary outcomes” likely resulting from a more long-term stress response, rather than “primary mediators” activated by a more acute stress response. This may reduce the generalizability and comparability to other studies. However, there is substantial variability in the specific indicators chosen in different studies, a lack of gold standard assessment, and some results have shown similar associations between different allostatic load measures and health outcomes (Beckie, 2012). Another study suggested that it may be important to distinguish primary mediators and secondary outcomes (Seeman et al., 2001) and that secondary outcomes may be of particular relevance in relation to CVD (Seeman et al., 2001). A measure consisting of secondary outcomes is also consistent with the allostatic load theory about long-term effects on physical dysregulation (McEwen, 1998) and have been most frequently assessed in studies conducted in occupational settings (Mauss et al., 2015). Although the analyses accounted for many covariates, there may also be other confounders that we were unable to account for of the exposure-outcome relationship, the exposure-mediator association, mediator-outcome association, or mediator-outcome relationship affected by the exposure (exposure dependent confounders). This may have lead to an overestimation of associations. For instance, major life events may be an exposure-

dependent mediator-outcome confounder. Job conditions such as low control and support may also be partial explanations for an associations between job insecurity and health/health related factors. However, such job conditions could also act as exposure-dependent confounders, and adjustment for such factors would require complex modelling for which methods and software capabilities are not well developed yet. Finally, it should be acknowledged that despite a relatively large sample size, the power for estimation associations and mediation may have been somewhat limited. Hence, we cannot exclude that some of the potential mediators are also interrelated with job insecurity and CHD and may partially explain the job insecurity – CHD association.

5. Conclusions

We conclude that psychological distress may play a role in the relation between job insecurity and CHD, whereas health behaviors, sleep and physiological factors seemed of little importance as explanatory mechanisms.

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Declaration of conflicting interest

None declared.

CRediT authorship contribution statement

Linda L. Magnusson Hanson: Conceptualization, Methodology, Formal analysis, Writing - original draft. **Naja H. Rod:** Conceptualization, Methodology, Writing - review & editing. **Jussi Vahtera:** Conceptualization, Methodology, Writing - review & editing. **Marianna Virtanen:** Writing - review & editing. **Jane Ferrie:** Writing - review & editing. **Martin Shipley:** Writing - review & editing. **Mika Kivimäki:** Conceptualization, Investigation, Writing - review & editing, Funding acquisition. **Hugo Westerlund:** Conceptualization, Methodology, Writing - review & editing.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.psyneuen.2020.104706>.

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