

HEALTH EVIDENCE NETWORK SYNTHESIS REPORT

The relationship between psychosocial risk factors and health outcomes of chronic diseases: a review of the evidence for cancer and cardiovascular diseases

Hynek Pikhart | Jitka Pikhartova



World Health  
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Health Evidence Network synthesis report

The relationship between psychosocial risk factors and health outcomes of chronic diseases: a review of the evidence for cancer and cardiovascular diseases

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Hynek Pikhart | Jitka Pikhartova



## Abstract

This report summarizes the best available evidence for a link between psychosocial factors and cardiovascular and cancer morbidity and mortality in Europe. A total of 1822 Medline and PubMed articles published in English since January 2000 were searched, identifying 37 systematic reviews and meta-analyses. Among the psychosocial factors repeatedly identified as related to chronic diseases, in and outside work, were high job demand, low autonomy, low control or high effort–reward imbalance, interpersonal conflicts, and low social support or low trust. The evidence suggests that multiple adverse psychosocial factors are independently associated with a range of adverse chronic diseases throughout adulthood. In addition, the social gradient in health observed throughout adulthood may partly operate through psychosocial factors on the pathway between socioeconomic characteristics and health. Psychosocial factors, therefore, might become part of complex total risk-reducing interventions focusing on multiple risk factors.

### Keywords

CANCER, CHRONIC DISEASE, CARDIOVASCULAR DISEASES, EVIDENCE-BASED HEALTH CARE, PSYCHOSOCIAL FACTORS, SOCIAL DETERMINANTS OF HEALTH

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## ABBREVIATIONS

CVD	cardiovascular disease
IPD-Work	Individual-Participant-Data Meta-analysis in Working Populations
NCD	noncommunicable disease



# CONTRIBUTORS

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## SUMMARY

### The issue

The European Region with its 53 Member States is the WHO region with the highest mortality rate from noncommunicable diseases (NCDs) for adults aged 15–59 years (1). A relatively small group of health conditions is responsible for a large part of the disease burden in Europe. Preliminary assessments indicate that chronic diseases (or NCDs) are the leading cause of mortality and morbidity in Europe, accounting for 86% of total premature deaths (2). In order to better understand the main NCDs, it is essential to identify and discuss their risk factors. Among others, psychosocial factors have been proposed as risk factors for NCDs. Despite substantial research, it remains unclear whether psychosocial factors are causally linked with NCDs and whether any interventions focusing on modifying psychosocial factors are effective (in terms of modification of the risk) and might be included in chronic disease prevention and management.

### The synthesis question

The objective of this report is to synthesize research findings from systematic reviews and meta-analyses to address the following question:

What is the evidence for a link between psychosocial factors and morbidity and mortality for chronic diseases?

Based on evidence from the reviews, the report also addresses the issue of whether psychosocial factors might be included in chronic disease prevention and management in Europe.

### Type of evidence used in the review

The evidence comes from 37 systematic reviews and meta-analyses focusing on the role of psychosocial factors at work and outside work in morbidity and mortality from cardiovascular diseases (CVDs) and cancer, including high job demand, low autonomy, low control or high effort–reward imbalance, interpersonal conflicts, low social support, low trust, mastery, depression, anger and hostility.



## Results

- The role of psychosocial factors in development of cardiovascular-related outcomes has been investigated much more extensively than cancer outcomes.
- Only eight identified papers meeting the eligibility criteria include results for cancer outcomes.
- Most studies, particularly for cardiovascular outcomes, focused on work-related psychosocial factors, and in particular the role of job demands, job control and their combination in a job strain model.
- Most psychosocial factors appear to influence cardiovascular outcomes, however, the evidence for an association between psychosocial factors and cancer is weaker than for cardiovascular outcomes.
- There does not seem to be one particular group of reviewed psychosocial factors that would have more importance on development of cardiovascular outcomes or cancer than any other group of factors.

Consistency of findings in most reviews related to social support, social isolation or various measures of stress at work supports the hypothesis that psychosocial factors are causal risk factors for CVDs and cancer.

## Policy considerations

There is only limited evidence related to intervention studies focusing on the role of psychosocial factors in development of CVDs or cancer. However, evidence from observational studies supports the relationship between psychosocial factors and CVDs and, in limited way, with cancer. Although based on results from a relatively low population, attributable risk of psychosocial factors might become part of complex total risk-reducing interventions focusing on multiple risk factors rather than being the focus of single factor interventions.

## GLOSSARY

### Psychosocial factors

Psychosocial factors mean a combination of psychological and social. These are social, cultural or environmental influences affecting health and behaviours of individuals. Although psychosocial factors include acute and chronic stressors, this review focuses on chronic factors. Examples of psychosocial factors used in this review include social support, social networks, social integration, loneliness, social capital, bereavement, social disruption, work environment, psychological distress, depression, anger and hostility. Psychosocial work environment includes high workload, job demands, strict and tight deadlines, lack of control over work, and imbalance between efforts at work and relevant rewards or job satisfaction.

### Noncommunicable diseases

In line with WHO definition, NCDs are those diseases that are not passed from person to person. In general, they are of long duration and slow progression. The four main groups of NCDs are CVDs, cancers, chronic respiratory diseases and diabetes mellitus. This review focuses only on the first two, CVDs and cancers, as these are responsible for the majority of chronic disease events. For example, it has been estimated that CVDs account globally for 17.3 million deaths annually, followed by cancers (7.6 million), respiratory diseases (4.2 million) and diabetes (1.3 million) (3). These four groups of NCDs thus account for around 80% of all NCD deaths (3). It has been estimated that CVDs alone led to 151 million disability-adjusted life years in 2008 (representing 10% of all disability-adjusted life years in that year) (4). In addition, there were about 12.9 million new cancer cases in 2009 alone and it is projected that this number will further rise to almost 17 million by 2020 (5).



# 1. INTRODUCTION

## 1.1. Background

The European Region with its 53 Member States is the WHO region with the highest mortality rate from NCDs for adults aged 15–59 years (1). A relatively small group of health conditions is responsible for a large part of the disease burden in Europe. Preliminary assessments indicate that chronic (or noncommunicable) disease is responsible for most of the disease and deaths in Europe, accounting for 86% of total premature deaths. CVDs are the number one killer, causing more than half of all deaths across the European Region (2). Data from around the world show that in high-income countries the poor carry a disproportionate amount of the chronic disease burden (6). It has been reported that chronic diseases have significantly influenced economic growth in high-income countries and that every 10% increase in the working age rates of mortality from chronic NCDs decreases economic growth rates by approximately 0.5% (7). At the Sixty-sixth World Health Assembly, countries unanimously adopted and supported a resolution (WHA66.10) on NCDs (8). This marked a major moment for efforts in NCD prevention and control, putting in place the strong foundations of a global NCD framework, through:

- endorsement of the WHO Global Action Plan for the Prevention and Control of NCDs 2013–2020 (9);
- adoption of the Global Monitoring Framework on NCDs, including the 9 global targets and 25 indicators;
- agreement to develop a global coordination mechanism by the end of 2013 to coordinate activities and promote engagement of all actors in the global NCD response; and
- adoption of the Mental Health Action Plan at both global and regional level in Europe.

In addition, all the Member States of the WHO European Region adopted the Health 2020 policy framework in 2012 (10), which included targets to reduce inequalities in Europe and enhance the well-being of the European population. The WHO Regional Office for Europe has launched an initiative to measure subjective and objective well-being in the European population. The European Union's Europe 2020 strategy considers health as a resource for the success of this strategy (11).

Finally, in 2011, the WHO European Region agreed to a European Action Plan for the Implementation of the European Strategy for the Prevention and Control of Noncommunicable Diseases (2012–2016), which has a series of priority actions. The Action Plan included explicit linkage between mental and physical health, and a concern with seeking population- and individual-level interventions that could reduce the burden of NCDs.

In order to better understand the main NCDs, it is essential to improve understanding of, and discuss, their risk factors. In addition to the non-modifiable risk factors such as gender, ethnicity or age, there is whole range of modifiable risk factors such as health behaviours, socioeconomic factors or psychosocial factors that are considered as risk factors for NCDs. A wide range of psychosocial factors have been suggested as risk factors for CVDs, cancer or respiratory diseases in a large number of observational studies (3). Being modifiable, psychosocial conditions are increasingly suggested as a target for interventions. Such interventions are expected to have a relatively strong impact on an individual's life-course health and to achieve higher returns than later interventions. Further research is, however, required to demonstrate that such interventions will indeed will reduce NCD risk.

In recognition of the importance of psychosocial factors, the WHO Commission on Social Determinants of Health report *Closing the gap in a generation* suggested in 2008 that psychosocial factors should play an important role in actions to reduce health inequalities within and between countries and regions (12). The recent WHO Regional Office for Europe review of social determinants and the health divide reinforces this message, suggesting that adverse psychosocial environment both at work and outside work is associated with an increase in stress-related conditions and that unfavourable psychosocial factors can damage health through various mechanisms (13). There are several potential pathways for the effect of psychosocial factors on NCD risk. First, psychosocial factors may be linked with NCDs such as CVDs or cancer through unhealthy behaviours such as lack of exercise and physical activity, eating fatty foods, excessive alcohol drinking or smoking (14). Second, psychosocial factors may influence access and use of health care services and thus indirectly NCD risk. Third, psychosocial distress may be a consequence of unfavourable social position related to increased NCD risk. Psychosocial distress may also have a direct effect on NCDs such as coronary heart disease independent of these other factors (15).

A comprehensive knowledge base detailing which psychosocial factors have the most profound effects on NCDs is, therefore, a fundamental step in structuring



potential interventions. Although a large number of studies exist that have examined the relationship between specific psychosocial factors operating at different levels and specific NCDs, only a few studies to date have attempted to systematically collate and synthesize the overall evidence provided from this considerable, but widely dispersed, evidence base. The existing reviews usually focus on individual psychosocial factor or individual health outcome.

The purpose of this report is to respond to the synthesis question and provide a systematic review of the relevant evidence linking psychosocial factors with two broad groups of NCDs, CVD and cancers, with a focus on the European Region. Such a review will enable identification of the important psychosocial factors operating at various levels, as well as help in evaluation of any important between-country differences. Identifying the range of such factors will facilitate more evidence-informed, clinically relevant and cost-effective interventions in the future. Furthermore, it may help to identify areas that might require more research.

## 1.2. Methodology

### 1.2.1. Sources for the review

This report is primarily based on searching scientific literature databases (Medline and PubMed). In addition, relevant references and bibliographies were hand searched for additional studies. We developed and followed a standard protocol for this review according to the PRISMA guidelines for systematic reviews, which define a process of study identification, screening, eligibility and inclusion (the PRISMA checklist is given in Annex 1) (16).

### 1.2.2. Eligibility criteria

Studies were considered eligible for inclusion in this review if they were published between 1 January 2000 and 20 June 2014. This is because the role of psychosocial factors has been documented to change over time, and this review aimed to reflect the current situation. Papers were considered eligible only if they were themselves reviews or meta-analyses of observational or interventional studies. This is because psychosocial factors have become the subject of numerous reviews in recent years (see section 2), and systematic reviews on this subject form an extensive body of evidence. All included studies were published in English (although a few non-English studies were identified as they had English abstracts, these were excluded from the report). Only those papers published in national or international peer-reviewed journals were considered.

Additionally, reviews were considered only if they included discussion of quantitative assessments of the associations between psychosocial factors and selected health outcomes. In studies considering more than one health outcome, studies were included in this review if they included at least one of the outcomes of this report. Some studies appear more than once in selected reviews but this will be discussed in later stages of this report. Across studies, a 5% significance level was accepted as evidence of statistical significance.

An initial review of titles and abstracts and, subsequently, a full review of all remaining search results were carried out independently by two reviewers to determine whether they met the criteria for inclusion in this review. All disagreements were resolved via discussion between the two reviewers. Where additional information pertaining to a study was necessary, the respective authors were contacted.

### 1.2.3. Data extraction

Study identification and data extraction were performed using the search terms listed in Annex 1. A flow chart shows the stages of data extraction (Fig. 1). In Medline and PubMed, 1818 potential titles were identified and these were screened based on title and abstract content. Most of these were excluded as they were not relevant to the research questions of this report; 83 papers were identified as potential for inclusion into the review. Among those excluded, in addition to many studies that were irrelevant for the studied topic, there were some studies focusing on psychosocial factors affecting various outcomes such as quality of life after a CVD or cancer event. As the focus of this review was on risk factors for these outcomes, all such papers were excluded. A full-text article review was performed for these remaining 83 articles. Of these, 35 were considered as eligible to be included in the final review. Papers focusing on individual studies were excluded from this synthesis. Reference lists of these identified papers were further screened and four papers were identified as possible additions. These were also obtained and a full-text review performed. Two of these four papers have been classified as eligible and included in the review. This gave a final number of 37 papers to be included in the systematic review (17–52). (The full reference list is included; Table 1 gives a brief description of the included papers.)

Fig. 1. Flow diagram for the systematic review (PRISMA template)

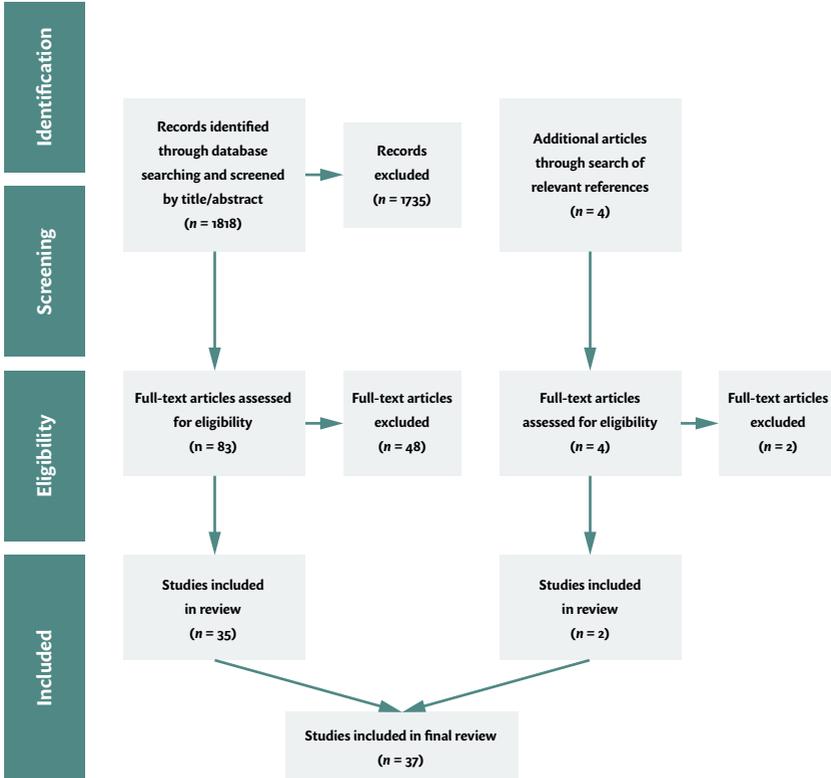


Table 1. Selected papers

Paper	No. studies	Psychosocial factor	Outcome	Period covered	Paper type	Main findings
<b>CVD-related outcomes</b>						
Rugulies, 2002 (17)	11	Depression	CHD	1966–2000	R/M	Pooled estimate RR, 1.64 (95% CI, 1.29–2.08)
Kuper et al., 2009 (18)	11	Depression	CHD	–2007	R/M	Pooled estimate RR, 1.9 (95% CI, 1.5–2.4)
Strike & Steptoe, 2005 (19)		Emotional stress, anger, extreme excitement	Acute coronary syndrome	1970–2004	R	Consistent evidence for triggering syndrome
Kuper et al., 2002 (20)		5 psychosocial factors	CHD	1966–2001	R	Proportion of etiologic studies reporting a strong or moderate association
	18	Type A behaviour and hostility				6/18
	22	Depression				15/22
	8	Anxiety				4/8
	13	Psychosocial work characteristics				10/13
	9	Social support				6/9
Belkic et al., 2004 (21)	34	Job strain	CVDs	1966–2001	R	Job strain related to CVD in most studies (including cohort, case-control and cross-sectional studies); authors suggested most studies biased towards null (underestimating real association)
Kivimäki et al., 2006 (22)	14	Work stress	CHD	–2006	M	Age/sex-adjusted RR Low job strain: RR, 1.16 (95% CI 0.94–1.43) Organizational injustice: RR, 1.47 (95% CI 1.12–1.95) Effort-reward imbalance: RR, 1.58 (95% CI 0.84–2.97)

Table 1. contd

Paper	No. studies	Psychosocial factor	Outcome	Period covered	Paper type	Main findings
Eller et al., 2009 (23)	33	Work-related factors (demand-control, social support at work, effort-reward imbalance, injustice, job insecurity, long working hours)	IHD	-2006	R	High psychologic demands, lack of social support, isostrain: moderate evidence in men Job strain: inconsistent results in men Effort-reward imbalance, injustice, insecurity, long working hours: not sufficient evidence in men No conclusions for women
Pejtersen et al., 2014 (24)	44	Work-related factors (demand-control, social support at work, effort-reward imbalance, injustice, job insecurity, long working hours)	IHD	-2013	R	Update to Eller et al. (23) with 11 additional studies: similar results
Babu et al., 2014 (25)	9	Job strain	Hypertension	-2011	M	OR, 1.3 (95% CI, 1.14-1.48) (OR, 3.17 for case-control studies and 1.24 for cohort studies)
Backé et al., 2012 (26)	26	Work stress	CVD		R	Work stress: 13/20 cohorts show association Demand-control model: 7/13 cohorts Effort-reward imbalance: 3/3 Other models: 3/6 Most results only for men; results for women less clear
Szerencsi et al., 2012 (27)	71	Work stress	CVD		R	Inconsistent results; may related to methodology used in individual studies
Kivimäki et al., 2012 (28)	13	Job strain	CHD	1985-2006	M <sup>a</sup>	RR, 1.23 (95% CI, 1.10-1.37)

Table 1. contd

Paper	No. studies	Psychosocial factor	Outcome	Period covered	Paper type	Main findings
Kivimäki et al., 2013 (29)	7	Job strain	Coronary artery disease	1985–2006	M <sup>a</sup>	RR, 1.25 (95% CI, 1.06–1.47)
Gilbert-Ouimet et al., 2014 (30)	74: 64 DCS, 12 ERI (2 both exposures)	Demand–control–support (DCS) model and effort–reward imbalance (ERI) model	Blood pressure	1979–2010	R	Both models showed a more consistent adverse effect of work stress for men DCS: studies of higher methodological quality observed a more consistent effect than those of lesser quality
Landsbergis et al., 2013 (31)	29	Job strain	Blood pressure	1985–2012	R	Association identified, higher for men than women
Nyberg et al., 2013 (32)	8	Job strain	CVD risk factors		M <sup>a</sup>	Diabetes: OR, 1.29 (95% CI, 1.11–1.51) Smoking: OR, 1.14 (95% CI, 1.08–1.20) Physical inactivity: OR, 1.34 (95% CI, 1.26–1.41) Obesity: OR, 1.12 (95% CI, 1.04–1.20) Elevated Framingham risk score: OR, 1.13 (95% CI, 1.03–1.25) Raised blood pressure or blood lipids: no association
Step toe & Kivimäki, 2013 (33)			CHD	1988–2012	R/M	
	17	Job strain				RR, 1.34-fold (95% CI, 1.18–1.51)
	9	Loneliness and social isolation				RR, 1.51-fold (1.21–1.88)
Rosenthal, 2012 (34)	54	Occupational stress	Hypertension	1977–2011	R	Seemed to be risk factor for elevated blood pressure and hypertension
Hwang & Hong, 2012 (35)	10 (work stress), 3 social support)	Work stress, social support	CVD	1985–2009	R	Both related to CVD

Table 1. contd

Paper	No. studies	Psychosocial factor	Outcome	Period covered	Paper type	Main findings
Virtanen et al., 2013 (36)	17 (13 in individual meta-analysis + 4 published)	Perceived job insecurity	CHD	~2012	R/M <sup>b</sup>	Age-adjusted RR, 1.32 (95% CI, 1.09–1.59) Multivariable-adjusted RR, 1.19 (95% CI, 1.00–1.42)
Barth et al., 2010 (37)	5	Social support	CHD, myocardial infarction	1950–2007	R	Functional social support: 3 studies suggesting some evidence for a negative role Structural social support: 2 studies with low evidence for a negative role
Fortmann & Gallo, 2013 (38)	11	Social support	Nocturnal blood pressure dipping		R	5/7 studies showed association Some preliminary evidence for protective effects of marriage and social contact frequency
Holt-Lunstad et al., 2010 (39)	148	Social relationships	All cause mortality, cause-specific mortality	1900–2007	R/M	50% increased likelihood of survival for participants with stronger social relationships
Tay et al., 2012 (40)		Social relations	CVD			Social relations predictive of CVD
Chida & Steptoe, 2008 (41)	6	Positive psychological well-being	Cardiovascular mortality	1969–2007	M	Combined HR, 0.71 (95% CI, 0.52–0.98)
Russ et al., 2012 (42)	10	Psychological distress	CVD	1994–2008	M <sup>a</sup>	GHQ scores: 1–3: RR, 1.25 (1.08–1.44) 4–6: RR, 1.45 (1.23–1.71) 7–12: RR, 1.72 (1.44–2.06) p < 0.001 for trend
Richardson et al., 2012 (43)	6	Perceived stress	Incident CHD		M	Combined RR, 1.27 (95% CI, 1.12–1.45)
Roepke & Grant, 2011 (44)	32	Mastery	CVD events/mortality, other measures of cardiometabolic health		R	Mastery associated with better cardiometabolic health and reduced risk of disease/death

Table 1. contd

Paper	No. studies	Psychosocial factor	Outcome	Period covered	Paper type	Main findings
Chida & Steptoe, 2009 (45)	25	Anger and hostility	CHD	–2008	M	Combined HR, 1.19 (95% CI, 1.05–1.35)
Koenig, 2012 (46)	19	Religion, spirituality	CVD	–2010	R	Significant inverse relationship: 12 studies Positive relationship: 1 study
Steptoe & Kivimäki, 2013 (33)	5	Emotional stress	Acute coronary syndrome	1995–2012	R/M	RR, 2.48 (1.75–3.51)
Mostofsky et al., 2014 (47)	9	Anger	Acute cardiovascular events	1966–2013	R/M	Higher rate of events in the 2 hours after outbursts of anger
<b>Cancer-related outcomes</b>						
Duijts et al., 2003 (48)	27	Stressful life events, death of spouse, death of relative or friend, personal health difficulties, change in marital status, change in financial status	Breast cancer	1966–2002	M	Stressful life events: OR, 1.77 (95% CI, 1.31–2.40) Death of spouse: OR, 1.37 (95% CI, 1.10–1.71) Death of relative/friend: OR, 1.35 (95% CI, 1.09–1.68)
Chida et al., 2008 (49)	165 (incidence); 53 (mortality)	Stress-related factors (e.g. as acute life events, work stress, personality, coping style, depression)	Cancer incidence	1996–2007	M	Incidence, 1.21 (95% CI, 1.09–1.34) Mortality: 1.29 (95% CI, 1.16–1.44) Cancer-specific estimates also published
Santos et al., 2009 (50)	6	High intensity stress	Breast cancer	1982–2007	M	RR, 1.73 (95% CI, 0.98–3.05)

Table 1. contd

Paper	No. studies	Psychosocial factor	Outcome	Period covered	Paper type	Main findings
Russ et al., 2012 (42)	10	Psychological distress	Cancer deaths	1994–2008	M <sup>a</sup>	GHQ scores 1–3: RR, 0.95 (95% CI, 0.85–1.07) 4–6: RR, 1.05 (95% CI, 0.85–1.30) 7–12: RR, 1.29 (95% CI, 1.04–1.61) p = 0.14 for trend
Koenig, 2012 (46)	29	Religion, spirituality	Cancer	–2010	R	More religious/spiritual had a lower risk of cancer in 16 studies Significantly worse prognosis in 2 studies
Tay et al., 2012 (40)		Social relations	Cancer		R	Mixed evidence for an association
Heikkila et al., 2013 (51)	12	Work stress	Cancer		M <sup>a</sup>	All cancers: HR, 0.97 (95% CI, 0.90–1.04) (no association) Colorectal cancer: HR, 1.16 (95% CI, 0.90–1.48) Lung cancer: HR, 1.17 (95% CI, 0.88–1.54) Breast cancer: HR, 0.97 (95% CI, 0.82–1.14) Prostate cancer: HR, 0.86 (95% CI, 0.68–1.09)
Lin et al., 2013 (52)	7	Stressful life events	Breast cancer	1995–4/2012	M	Striking life events: pooled OR, 1.51 (95% CI, 1.15–1.97) Severe life events: pooled OR, 2.07 (95% CI, 1.06–4.03)

Notes: CHD: coronary heart disease; CI: confidence interval; GHQ: General Health Questionnaire; HR: hazard ratio; IHD: ischaemic heart disease; M: meta-analysis; OR: odds ratio; R: review; RR: relative ratio.

<sup>a</sup> Individual participant's data meta-analysis.

<sup>b</sup> Partial individual participant's data meta-analysis.

## 2. RESULTS

### 2.1. Psychosocial factors and CVDs

Although this review focuses on the period after 1 January 2000, it is important to mention the work by Hemingway & Marmot in 1999 (53). Their work is probably the first extensive systematic review of prospective cohort studies covering a wide range of psychosocial factors including depression, work stress or social support. It was updated in 2002 (20) and concluded based on the existing results that there was evidence for the association between depression, social support and psychosocial work characteristics and etiology of coronary heart disease.

Following these reviews, a number of other systematic reviews have been conducted to investigate the adverse effect of a range of psychosocial factors. Among these, the role of work-related psychosocial factors on CVDs was investigated most frequently (e.g. 21,22,23,26). The evidence related to the role of work-related psychosocial factors is not entirely consistent. Most reviews concluded that work-related psychosocial factors play an important role in development of CVDs. Most of these reviews also concluded that negative effects of work-related factors were more consistently identified in men than women (e.g. 22,26). Two reviews (31,34) published recently have showed that adverse work-related psychosocial factors may increase the risk of elevated blood pressure. However, they also showed results that were not entirely consistent. For example, Landsbergis et al. (31) reported that more than half of published studies found nonsignificant effects.

Most recently, the Individual-Participant-Data Meta-analysis in Working Populations (IPD-Work) consortium published a series of papers reporting the associations between work-related psychosocial factors and a range of outcomes, including coronary heart disease, coronary artery disease or cardiovascular risk factors (28,29,32,36). The advantage of this collaboration is that it is using original data and allowing uniform analysis including the same covariates and thus is able to prepare directly comparable results. This collaboration has brought extensive new evidence on the association between work-related stress (and other psychosocial factors, as mentioned below) and CVD-related outcomes; however, it is based on the same set of cohort studies, all originating from western and northern European countries (including Finland, Sweden, Denmark, the Netherlands, Belgium, France, Germany and the United Kingdom). Some of these studies are occupational cohorts (such as studies from the United Kingdom and France) and do not represent the



whole population. No countries from other regions, such as Asia, northern America, south Europe or eastern Europe, are represented.

The role of other psychosocial factors on risk of CVDs has not been investigated to the extent seen with work stress. Among these, the most consistent results can be found for the association between depression and coronary heart disease. While Hemingway & Marmot (53) reported that depression was associated with coronary heart disease in 11 out of 11 identified studies, Kuper, Marmot & Hemingway (20) in the updated review reported the same in 15 out of 22 identified studies. In two meta-analyses, Rugulies (17) and Kuper et al. (18), respectively, reported 64% and 90% increased risk of coronary heart disease associated with depression.

Social support was studied as one of the psychosocial factors of interest by Kuper, Marmot & Hemingway (20), who reported its relationship with coronary heart disease in six out of nine identified studies. Hwang & Hong (35) identified three studies focusing on the relationship between social support and CVDs and reported that social support was likely to be related to CVDs. In more detailed review, Barth, Schneider & von Känel (37) identified three studies suggesting some evidence for a negative role of low functional support on coronary heart disease and myocardial infarction, and two studies giving weak evidence of the negative role of low structural social support on coronary heart disease. In another two reviews Tay et al. (40) and Steptoe & Kivimäki (33) focused on social relations and social isolation, respectively, and also concluded that these psychosocial factors might be related to CVDs and coronary heart disease. Fortmann & Gallo (38) focused on the role of social support on the nocturnal dip in blood pressure that had previously been shown as a risk factor for coronary heart disease and found that five out of seven identified studies showed the association between functional social support and studied outcome.

Further reviews focused either on more general psychosocial constructs such as positive psychological well-being (41), psychological distress (42) or perceived stress (43). Other reviews focused on a range of more specific psychosocial outcomes such as personal mastery (44), anger and hostility (45,46), religion and spirituality (46) or emotional stress (33). Most studies in these reviews were longitudinal, thus allowing assessment of the temporality of the association, but no interventional research was included. Although the magnitude of identified associations was not very large in most reviews and meta-analyses, most results showed a negative role for psychosocial disadvantage in development of CVDs or coronary heart disease.

## 2.2. Psychosocial factors and cancer

Compared with cardiovascular outcomes, fewer systematic reviews and meta-analyses have been identified for cancer outcomes (either all cancers combined or site-specific cancers). Duijts et al. (48), Lin et al. (52) and Chida et al. (49) focused on stressful life events and concluded that stressful events increase risk of breast cancer (48,52), cancer incidence and cancer mortality (49). In addition to stressful events, Chida et al. (49) included work stress, personality, coping style and depression among investigated psychosocial factors and their relationship with cancer incidence and mortality. Psychosocial distress was investigated also by Russ et al. (42), who found only weak evidence for its association with cancer mortality. Heikkilä et al. (51), in a meta-analysis of the association between work stress and risk of cancer, found no association with all-cancer risk or risk of colorectal, lung, breast and prostate cancer. Tay et al. (40) found mixed evidence for the association between social relations and cancer risk. Finally, Santos et al. (50) found only weak borderline association between high-intensity stress and breast cancer. Results of cancer reviews suggest that except for stressful life events the evidence for an association between psychosocial factors and cancer is much weaker than that for cardiovascular outcomes.



## 3. DISCUSSION

### 3.1. Linkages with CVDs and cancer

Overall, the results of the analysis of the 37 reviews and meta-analyses published since the beginning of 2000 provide evidence that psychosocial factors are associated with these two groups of outcomes: CVDs and cancers. These 37 reviews and meta-analyses included results from several hundred individual studies originating in wide range of countries. The role of psychosocial factors in development of cardiovascular-related outcomes has been investigated much more extensively than cancer outcomes. Only eight identified papers included results for cancer outcomes. Most studies, particularly for cardiovascular outcomes, focused on work-related psychosocial factors, and especially the role of job demands, job control and their combination in a job strain model. As instruments for measurement of psychosocial outcomes have been developed relatively recently, and have been included in cohort studies more commonly only from 1990s, most results of individual studies have been published after 2000; consequently, many systematic reviews and meta-analyses have been published in last three or four years and have added substantial new evidence to the existing knowledge base.

Although a large range of countries are represented in these meta-analyses and systematic reviews, it is important to note that most reported results originate from small number of countries, and in particular from the United Kingdom, the Scandinavian countries, Germany, Belgium, the Netherlands, France and the United States. Other countries are represented substantially less and there is a very limited number of studies included in these systematic reviews and meta-analyses originating from whole regions such as eastern Europe, Asian countries or Latin America. Almost no results exist for African countries.

Nevertheless, findings in most reviews related to social support, social isolation or, to some extent, various measures of stress at work support the hypothesis that psychosocial factors are causal risk factors for CVDs and cancer. In particular, detailed analysis by the IPD-Work consortium showing that the relationship between job stress and coronary heart disease remains similar after excluding events from the first five years after assessing psychosocial measures (28) support arguments of causality of the association.

## 3.2. Strengths and limitations of the review

This review provides the largest systematic synthesis of existing systematic reviews and meta-analyses on psychosocial factors and their role on two large groups of NCD-related outcomes. It has a number of strengths.

1. Inclusion of only contemporary and, therefore, relevant and timely evidence (only reviews published after 2000 were considered) reduced the possibility of a cohort effect (although it did not removing it entirely).
2. Inclusion only of reviews published in peer-reviewed journals ensured quality of the data.
3. A definition of psychosocial factors was used to reflect the full spectrum of (potential) psychosocial disadvantage.
4. Inclusion of a wide range of health outcomes in these two groups of NCDs similarly allowed reflection of the spectrum of potential outcomes.

Conversely, there are some limitations in this synthesis.

1. Although evidence comes from a wide range of countries, most of this evidence is derived primarily from the United States, the United Kingdom and northern and western European countries.
2. Only English written publications were considered.
3. Only reviews and meta-analyses were considered. Consequently, psychosocial factors that have not been previously a focus of reviews were omitted. Similarly, studies that have never been included in reviews were omitted. It is likely that only a very limited number of such individual studies have been omitted as a large number of reviews were identified. Nevertheless, it is possible that some studies not published in English language were omitted because most of the systematic reviews included in this synthesis also looked only into publications written in English language.
4. The proportion of studies reporting significant associations between psychosocial factors and selected outcomes may be an overestimate because of underreporting of nonsignificant findings (i.e. publication bias).

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5. Some individual studies appear in several of the systematic reviews and meta-analyses included in this synthesis, and therefore they artificially strengthen the evidence showing the association between psychosocial factors and these two groups of NCDs.
  6. Most evidence originates from observational studies while evidence originating from intervention studies is very limited. The proportion of observation studies included in the reviews is cross-sectional, thus allowing assessment only of an association between psychosocial factors and reported health outcomes rather than evaluating causality.

### 3.3. Policy options and implications for research, scientific knowledge, policy and practice

The findings of this study carry important implications for scientific knowledge, policy and practice: (1) most psychosocial factors identified appear to be associated with cardiovascular outcomes but less so with cancer outcomes; (2) there does not seem to be one particular group of psychosocial factors that would have more importance on development of CVD outcomes or cancer compared with other factors, although the association with depression and social isolation is more consistent than with work-related factors; (3) there are some gender differences repeatedly reported in individual studies and systematic reviews, suggesting that these psychosocial factors may operate differently in men and women.

There is only limited evidence related to intervention studies focusing on the role of psychosocial factors in development of CVD or cancer. No systematic reviews focusing on intervention studies have been identified so far, perhaps with the exception of that of Schneider et al. (54), who reported results combining two randomized control trials of long-term effects on mortality of stress reduction using transcendental meditation. They showed that mortality from CVDs decreased by 30% and cancer mortality by 49% in an intervention group. These large effects must, however, be considered in the light of small sample size: even when the two studies were combined the sample size was just 202 subjects. Some individual intervention studies have been reported in recent years, and focusing a systematic review on such studies may be one direction of research that should be developed in the future.

The findings from the above-mentioned observational studies might also have implications for policy and practice, although caution should be exercised because of the limited results from interventions. We have identified three policy options.

1. The finding that multiple psychosocial factors, operating in different environments (at work and outside work), affect a range of different, often related, health outcomes highlights the complex nature of psychosocial disadvantage. It also indicates the multiplicity of targets that potential interventions could, and should, consider in order to be maximally effective. Although findings related to work stress, social support or social isolation may form a basis for interventions, it must be taken into account that recently published estimates of population attributable risk are relatively low (28), around 4% for coronary heart disease, and lower than estimates for smoking or physical activity. Therefore, funders may decide to focus on behavioural interventions when focusing specifically on coronary heart disease or cancer. When arguing for psychosocial intervention, a wider range of health outcomes or general well-being must be considered.
2. Psychosocial interventions on CVDs or cancer have focused mostly on patients with advanced disease, while primary prevention needs more attention. The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention recommended in 2012 that psychosocial factors should be assessed by clinical interview and tailored management is recommended for individuals with high CVD risk (55). This might be an important step towards moving interventions from those already ill towards primary prevention of chronic disease. Psychosocial factors, therefore, might become part of complex total risk-reducing interventions focusing on multiple risk factors rather than single risk factor interventions.
3. The Health 2020 policy framework (10) promotes development of national (and subnational) health policies, preparing comprehensive health and well-being plans and strategies. Recent evidence related to the role of psychosocial factors on chronic disease outcomes should inform those developing such strategies and highlight areas for effective use of resources with the aim of improving health and well-being across the life-course as well as reducing health inequalities within the societies.



## 4. CONCLUSIONS

In the largest systematic review of psychosocial factors on CVDs and cancer to date, we indirectly included several hundred individual, mostly observational, studies in reported reviews and meta-analyses. As such, this report provides evidence that psychosocial factors play an important role in explaining CVD and cancer outcomes (although the evidence of the relationship between psychosocial factors and cancer is not as strong as for CVDs), and that these factors act independently as risks for these groups of NCDs. In particular for CVDs, the evidence for the association with depression and social isolation is both strong and consistent. These findings suggest that psychosocial factors may provide multiple opportunities for prevention, intervention and possible intersectoral approaches to tackle the social inequalities in health observed in middle and older ages. These findings also support the Health 2020 policy framework and strategy, which aims to reduce health inequalities and focuses on actions that would improve health, including improving psychosocial conditions to reduce stress through measures such as job control, adequate social protection or improved job security (10).

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## ANNEX 1. PRISMA GUIDELINES FOR SYSTEMATIC REVIEWS

The PRISMA guidelines for systematic reviews define a process of study identification, screening, eligibility and inclusion and are outlined in Table A1.

Table A1. PRISMA systematic review reporting checklist

Section/topic	No.	Checklist item
<b>TITLE</b>		
Title	1	Identify the report as a systematic review, meta-analysis, or both
<b>ABSTRACT</b>		
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number
<b>INTRODUCTION</b>		
Rationale	3	Describe the rationale for the review in the context of what is already known
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes and study design (PICOS)
<b>METHODS</b>		
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g. web address), and, if available, provide registration information including registration number
Eligibility criteria	6	Specify study characteristics (e.g. PICOS, length of follow-up) and report characteristics (e.g. years considered, language, publication status) used as criteria for eligibility, giving rationale
Information sources	7	Describe all information sources (e.g. databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched

Table A1. contd

Section/topic	No.	Checklist item
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated
Study selection	9	State the process for selecting studies (i.e. screening, eligibility, included in systematic review and, if applicable, included in the meta-analysis)
Data collection process	10	Describe method of data extraction from reports (e.g. piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators
Data items	11	List and define all variables for which data were sought (e.g. PICOS, funding sources) and any assumptions and simplifications made
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis
Summary measures	13	State the principal summary measures (e.g. risk ratio, difference in means)
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g. I <sup>2</sup> ) for each meta-analysis
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g. publication bias, selective reporting within studies)
Additional analyses	16	Describe methods of additional analyses (e.g. sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified
<b>RESULTS</b>		
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g. study size, PICOS, follow-up period) and provide the citations

Table A1. contd

Section/topic	No.	Checklist item
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see Item 12)
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15)
Additional analysis	23	Give results of additional analyses, if done (e.g. sensitivity or subgroup analyses, meta-regression [see Item 16])
<b>DISCUSSION</b>		
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g. health care providers, users and policy-makers)
Limitations	25	Discuss limitations at study and outcome level (e.g. risk of bias) and at review level (e.g. incomplete retrieval of identified research, reporting bias)
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research
<b>FUNDING</b>		
Funding	27	Describe sources of funding for the systematic review and other support (e.g. supply of data); role of funders for the systematic review



## ANNEX 2. SEARCH STRATEGY

The present review was based upon a bibliographic search of databases, concluded on 23 June 2014.

### Databases

The PubMed and Medline databases were searched, using keywords as set out in the search terms below.

### Search terms

1. psychosocial OR “psycho-social” OR “PS factor” OR “PS factors” OR stress OR “job demand” OR “job demands” OR “job strain” OR “work demand” OR “work demands” OR “job control” OR “perceived control” OR “ERI” OR effort OR reward OR trust OR “social capital” OR “social support” OR “social network” OR “social disruption” OR “loneliness” OR bereavement” OR “psychological work environment” OR “social integration” OR “self esteem” OR “self-esteem” OR “social esteem” OR happiness
2. “systematic review” OR “metaanalysis” OR “meta-analysis”
3. “chronic disease” OR “NCD” OR “non-communicable disease” OR “noncommunicable disease” OR “non-communicable mortality” OR “noncommunicable mortality” OR “cancer” OR “neoplasm” OR “neoplasma” OR “tumour” OR “malignancy” OR “melanoma” OR “CVD” OR “CHD” OR “MI” OR “heart attack” OR “stroke” OR “AMI” OR “myocardial infarction” OR “cardiovascular” OR “coronary heart”
4. “2000/01/01”[Date - Publication] : “3000”[Date - Publication]
5. 1 AND 2 AND 3 AND 4

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