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Long Working Hours and Health in Office Workers:

A Cohort Study of Coronary Heart Disease, Diabetes, Depression and Sleep Disturbances

by Marianna Virtanen

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Department of Epidemiology and Public Health
University College London

Declaration of authorship

I, Marianna Virtanen, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Signature: 
Marianna Virtanen

Date: 23rd February 2012

Abstract

This thesis examined the association between long working hours and health outcomes with high public health relevance; coronary heart disease (CHD), type 2 diabetes, depression and sleep disturbances, in a cohort of middle-aged white-collar British civil servants. Earlier research has shown mixed results on the topic but the evidence relies largely on cross-sectional and case-control studies.

I used data from the longitudinal Whitehall II study where self-reported working hours were assessed at phase 3 (1991-1993) when the employed participants were 39 to 61 years of age. The second assessment of working hours was at phase 5 (1997-1999). CHD was assessed at phases 3, 5, and 7 (2003-04); type 2 diabetes at phases 3 and 7; depression at phases 3 and 5, and sleep disturbances at phases 3, 5, and 7. Analyses of each outcome disorder were based on a cohort free from the specific disorder at baseline. Follow-up time ranged between 6 to 11 years depending on the outcome, and the number of participants in each part of the study ranged between 913 and 6014 depending on the baseline and follow-up data available.

Incidence of CHD was indicated by CHD death, non-fatal myocardial infarction and angina defined on the basis of clinical examinaton, clinical records, and nitrate medication use. Type 2 diabetes was ascertained from high fasting or postload plasma glucose levels, self-reported information on doctor-diagnosed diabetes and use of medication assessed during clinical examinations. Onset of depression was assessed by University of Michigan version of Composite International Diagnostic Interview (UM-CIDI) and onset of sleep disturbances were requested by survey questions on sleep length and four types of sleep disturbances (the Jenkins Scale). Several known confounding and mediating covariates were assessed and included in the analyses.

Working 11-12 hours per day (or >55 hours per week) at baseline, compared with working 7-8 hours per day (or 35-40 per week) was associated with an increased risk of CHD, depression and most types of sleep disturbances at follow-up. Working long hours was not associated with an increased incidence of type 2 diabetes except among prediabetic participants. These findings were robust to adjustments for relevant confounding factors at baseline.

The results of this thesis indicate that long working hours could be recognized as a potential risk marker for the development of CHD, depression, and sleep disturbances. However, the results are generalisable to British white-collar workers only, and as this study is based on observational data it is not known whether the associations are causal.

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Table of contents

List of tables

List of figures

Part of the contents of the following articles is presented with the permission of the publisher:

Virtanen M, Ferrie JE, Singh-Manoux A, Shipley MJ, Vahtera J, Marmot MG, Kivimäki M. Overtime work and incident coronary heart disease: the Whitehall II prospective cohort study. Eur Heart J 2010;31:1737-44.

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Abbreviations

A1C, HbA1C	Glycated hemoglobin
AMI	Acute myocardial infarction
BDI	Beck Depression Inventory
BMI	Body mass index
CA	Cardiac arrest
CAS	Carotid artery stenosis
CEO	Chief executive officer
CES-D	Centre for Epidemiologic Studies Depression Screen
CHD	Coronary heart disease
CI	Confidence interval
CIDI	Composite International Diagnostic Interview
CIS-R	Revised Clinical Interview Schedule
CK-MBm, CK-MB, CK	Creatine kinase
CM	Centimetre
CRH	Corticotropin-releasing hormone
CRP	C-reactive protein
cTn	Troponin
CVD	Cardiovascular disease
DALY	Disability-adjusted life year
DKA	Diabetic ketoacidosis
DL	Decilitre
DSM-III-R	Diagnostic and Statistical Manual of Mental Disorders, 3rd Edition, Revision
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision
ECG	Electrocardiograph
FPG	Fasting plasma glucose
G	Gram
GHQ-30, GHQ-28, GHQ-12	General Health Questionnaire
GTT	Glucose tolerance test
H	Hour
HADS	Hospital Anxiety and Depression Scale
HDL	High-density lipoprotein
HDS	Hamilton Depression Scale
HHS	Hypersmolar hyperglycemic state
HPA	Hypothalamus-pituitary-adrenal
HR	Hazard ratio
HRS	Hours
ICD-9	International Classification of Diseases and Related Health Problems, version 9
ICD-10	International Classification of Diseases and Related Health Problems, version 10
IFG	Impaired fasting glucose
IGT	Impaired glucose tolerance
IHD	Ischemic heart disease
K10, K6	Kessler Psychological Distress Scale
L	Litre
LB	Pound

LDL	Low-density lipoprotein
MBI	Maslach Burnout Inventory
MDE	Major depressive episode
MDD	Major depressive disorder
MG	Milligram
MI	Myocardial infarction
mmHg	Millimetre mercury
MMOL	Millimole
MONICA	Multinational Monitoring of Trends and Determinants of Cardiovascular Disease
MSLT	Multiple Sleep Latency Test
NHS	National Health Service
NS	Non-significant
NSQ	Nordic Sleep Questionnaire
OECD	Organisation for Economic Co-operation and Development
OR	Odds ratio
PG	Plasma glucose
POMS	Profile of Mood States
PSQ	Post-sleep Questionnaire
PSQI	Pittsburgh Sleep Quality Index
RAND	Research and Development Corporation
RAND MHC-12	RAND Mental Health Component scale
RR	Rate ratio
SCL-90	Symptom Checklist
SD	Standard deviation
SDS	Self-rating depression scale
SDQ	Sleep Disorders Questionnaire
SEI	Sleep Effects Index
SEP	Socioeconomic position
SF-36, SF-12	Short Form Health Survey
SMC	Smooth muscle cell
SQAW	Sleep Questionnaire and Assessment of Wakefulness
SRQ	Self-reporting Questionnaire
UM-CIDI	University of Michigan Version of the Composite International Diagnostic Interview
WHO	World Health Organization
WK	Week
WTD	Worktime Directive

Chapter 1

Working hours, disease and health – the general framework

1.1 Introduction

In modern society, working time is no longer limited to hours spent at the workplace - especially in white-collar occupations, work can be done at any time and at any place. An increasingly common opinion is that high demands at work result in insufficient time to get work duties done within standard 7 to 8 hours' workday. For low-wage blue-collar employees, long working hours may comprise of two or more contemporaneus part-time jobs. At the same time, there is a concern that working long hours might be harmful for health. The aim of this thesis is to examine whether this is the case in a sample of white-collar British civil servants.

According to the projections made by the World Health Organization (WHO), the top five leading causes of diseases adversely affecting quality of life in high-income industrialised countries by the year 2030 will be depressive disorders, ischaemic heart disease, Alzheimer's and other dementias, alcohol use disorders, and diabetes mellitus.[1] In addition to human misery, these disorders result in substantial work impairment and costs to society.[1-4] For example, benefits paid to individuals unable to work as a result of mental disorders have been rising in Great Britain in parallel with increases throughout Europe and

North America.[5 6] In addition, sleep disturbances, such as insomnia, is a common problem in adult populations as about 30–50% of adults experience insomnia symptoms occasionally,[7-11] and up to 15% meet the criteria for clinical insomnia.[7 10-12] There is evidence of shortened sleep duration over the past three decades, and recent data suggest an increase in insomnia-related symptoms among middle-aged employees.[8]

Knowledge on the various non-work and work-related risk factors for health and sleep problems has accumulated during the past decades, but less research addressing long working hours as a potential work-related risk factor is available. The main aims of this thesis are to examine the relationship of long working hours for the onset of coronary heart disease, type 2 diabetes mellitus, major depressive disorder, and sleep problems using data from a large prospective occupational cohort, the Whitehall II study. The following section summarises the definition of long working hours and time trends in the prevalence of long working hours in industrialised countries.

1.2 Long working hours

1.2.1 Definition and regulations regarding long working hours

Long working hours can be defined as hours of work that exceed the standard fulltime work week. *Overtime work*, in turn, can also occur in part-time jobs and refers to hours of work that exceed the contracted working hours.

Most countries apply working-time regulations that put restrictions on the maximum number of work hours. According to the 2003 European Worktime Directive (WTD),[13] a worker's working time should not exceed 48 hours (including overtime) per week when averaged over a reference period. This reference period is usually 17 weeks but

it can be increased to 26 in some cases, or up to 52 weeks by agreement. The period cannot include any time off such as holiday, sick or maternity leave and for any such period an equivalent number of working days is added to the reference period. However, in the U.K., employees are entitled voluntarily to work more than 48 hours by signing an individual "opt out" agreement. Employers cannot force or coerce employees to do so, nor can signing such an agreement be made a condition of employment. Some of the rules of the Worktime Directive can be varied by collective agreement between employers and trade unions. In the industrialised countries, the dominant approach is to specify an upper-limit of working hours between 48 and 60 weekly working hours. Exceptions of this are for example Japan, the USA, and New Zealand, by permitting workweeks of more than 60 hours.[14]

1.2.2 Time trends in hours worked

In the early 1800's, the industrial working week covered fourteen to sixteen hours a day, six days a week. Since then, enormous reductions have been taken place in working hours as a result of increased efficiency and productivity, collective bargaining mainly via trade unions, and progressive legislation.[15] Figure 1 presents the mean weekly working hours in 22 European Union countries in 2002.[16] Average weekly working hours in the U.K. are 38.5, ranking very close to the average for all countries (38.2).

However, mean estimates of working hours do not tell a lot about changes in, for example, the number of employees working part-time or those working extremely long hours. The Office for National Statistics[17] presents time series based on the Labour Force Survey of weekly working hours in the U.K. stratified by sex and working hours (part-time, full-time, overtime). Both paid and unpaid overtime working hours among wage earners are included in these statistics. Figure 2 shows the distribution of usual weekly working hours

for salaried men in the UK between 1993 and 2008. The proportion of men working more than 45 hours has decreased from 34.8% to 27.8% and the proportion working 31-45 hours has increased from 58.8% to 61.3%. Thus, a substantial proportion of employed men in the U.K. still work long hours.

Figure 1. Mean weekly working hours per worker in 22 European Union countries in 2002. Source: Organisation for Economic Co-operation and Development (OECD), 2004.[16]

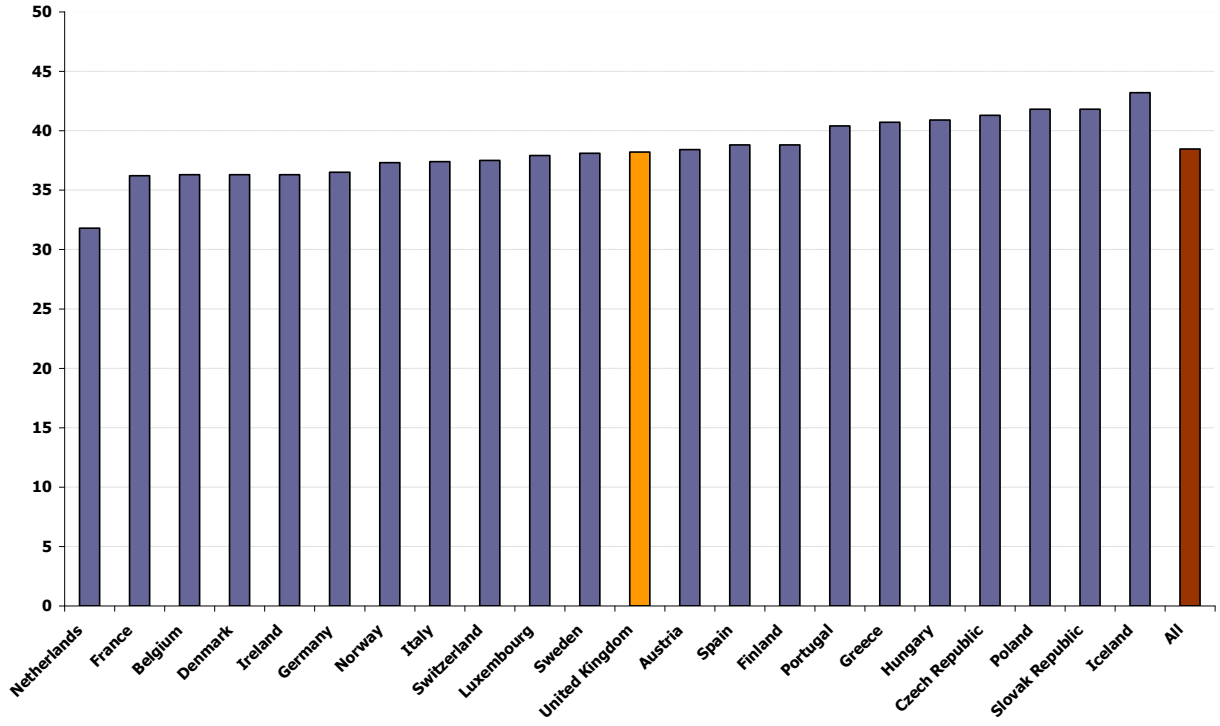
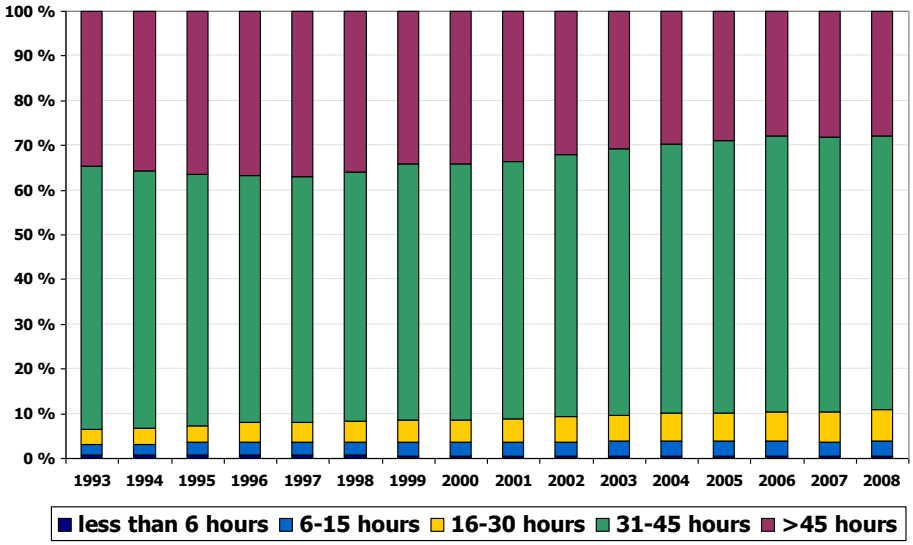


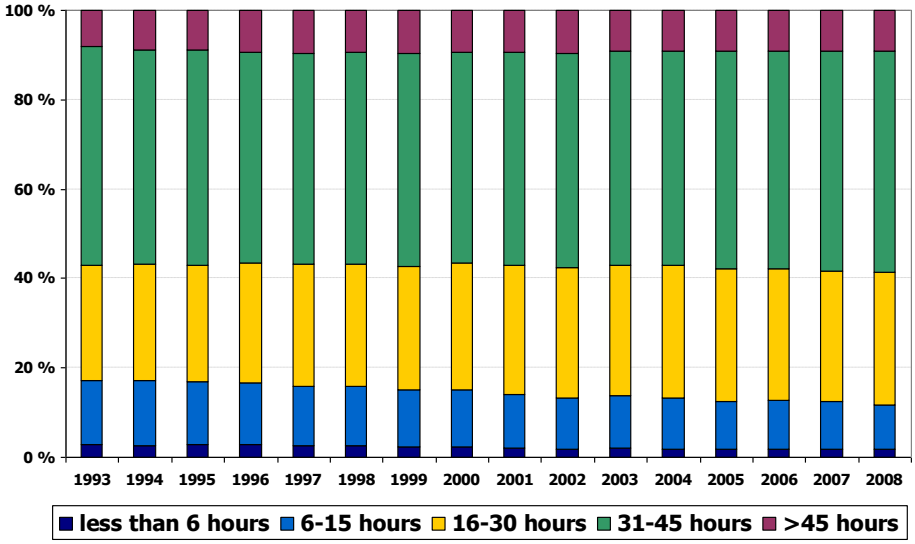
Figure 2. Usual weekly working hours among male wage-earners in the U.K., 1993-2008. Source: The Office for National Statistics[17]



Corresponding figures for women are presented in Figure 3. The proportion of women working more than 45 hours per week is remarkably smaller than that in men. However, the percentage has increased from 8.1% to 9.2% during the follow-up time. The percentage of female employees working 31-45 hours per week has slightly increased (from 48.9% to 49.3%) as well as the proportion of those working 16-30 hours (from 25.9% to 29.7%) while the proportion of female employees working only a few hours a week has decreased.

There is large variation in working hours between occupations. According to a survey done by the U.K. Trades Union Congress,[18] the highest proportion of employees working *unpaid* overtime work is among teaching professionals (56%), followed by corporate managers and senior officials, e.g. senior civil servants and local government officers, directors and CEOs (50%), production managers (47%), and protective service officers (44%).

Figure 3. Usual weekly working hours among female wage-earners in the U.K., 1993-2008. Source: The Office for National Statistics[17]



In the British Civil Service, the following is stated about the working hours: "Hours of work for full-time members of the Senior Civil Service are a minimum of 41 hours in London and 42 hours elsewhere, including daily meal breaks of one hour. Senior civil servants may be required to work such additional extra hours as may from time to time be reasonable and necessary for the efficient performance of their duties. Departments and agencies must not recompense members of the Senior Civil Service for additional hours worked".[19]

Interpretation of the above described statistics needs to be cautious. The comparison between reports from different data sources is complicated by the fact that the sample (e.g. total working population including self-employed vs. wage earners) and definition of working hours (e.g. long working hours, paid overtime work, unpaid overtime work) varies considerably. However, national statistics from the U.K. suggest that among men, excess overtime work has decreased to some degree during the past ten years whereas among women, a slightly increasing trend has been shown. Nevertheless, long working hours seem to be still far more common among men than among women.

1.3 Working hours as a measurement of work-related risk factors

A psychosocial risk factor is defined as a "*measure that potentially relates psychological phenomena to the social environment and to pathophysiological changes*".[20] A major bias in the studies on work-related psychosocial factors and health is *information bias* which refers to the fact that, for example, depressed mood (subclinical state) or early-stage coronary heart disease (CHD) is associated with a person having a negative view of the surroundings, including the working environment. This results in *common method variance,*[21] which means that variance in variables can be attributed to the measurement method rather than to the constructs that are supposed to be measured, such as negative affectivity or tendency of a person to respond in a desirable or consistent way. Even when the study design is longitudinal and cases at baseline are excluded, associations found between perceived stressors and incident diseases may reflect the unmeasured subclinical state and associated negative affect. Furthermore, controlling for these characteristics may not be sufficient to effectively control this type of bias. Bonde[22] highlights in his review the need for independent or more objective measures of workplace exposures and health outcomes.

According to the definition above, working hours can not be strictly classified as work-related psychosocial factors since they do not inherently include the individual's experience of stress or distress. Working hours, as a measure of work exposure, can therefore be considered less sensitive to information bias since the unit of measurement, *an hour*, does not include an affective component, such as perceived discomfort or mental strain.

1.4 A general framework for the association between long working hours and health outcomes

Reviews on the issue of long working hours have suggested adverse effects of long hours on health.[23-34] Figure 4 (p. 24) shows the framework for possible causes and consequences of long working hours, modified from that presented by Caruso et al.[31] The framework may help in understanding the underlying possible causes and consequences of long working hours both at the individual level and community level. Furthermore, the framework provides some insight regarding why long working hours may have adverse effects on health and what are the potential mediators and moderators of the relationship.

One of the mediating mechanisms has been suggested to relate to reduced time available for sleep and recovery from work leading to chronic fatigue, poor health-related behaviours, and eventually, deterioration in health.[24-31] Employees working long hours may also be increasingly exposed to psychosocial and physical workplace hazards, such as high demands (which can also be an underlying cause of extended working hours) and poor working conditions. The hypothesized mediating mechanism between long working hours and cardiovascular health, in particularly, invoves the potential effects associated with psychological over-activation, "stress", and its impacts on the cardiovascular systems[24-28 35] through, for example, chronic elevation of blood pressure and heart rate,[36-41] or through impaired health-related behaviours.[34 42] Similar mechanism can be hypothesised to operate for other outcomes; type 2 diabetes mellitus, depression, and sleep disturbances. Furthermore, social relationships, especially those with close family members, may suffer from long working hours. In such cases, long working hours may affect employee health through exacerbating work-family conflicts.[43-45]

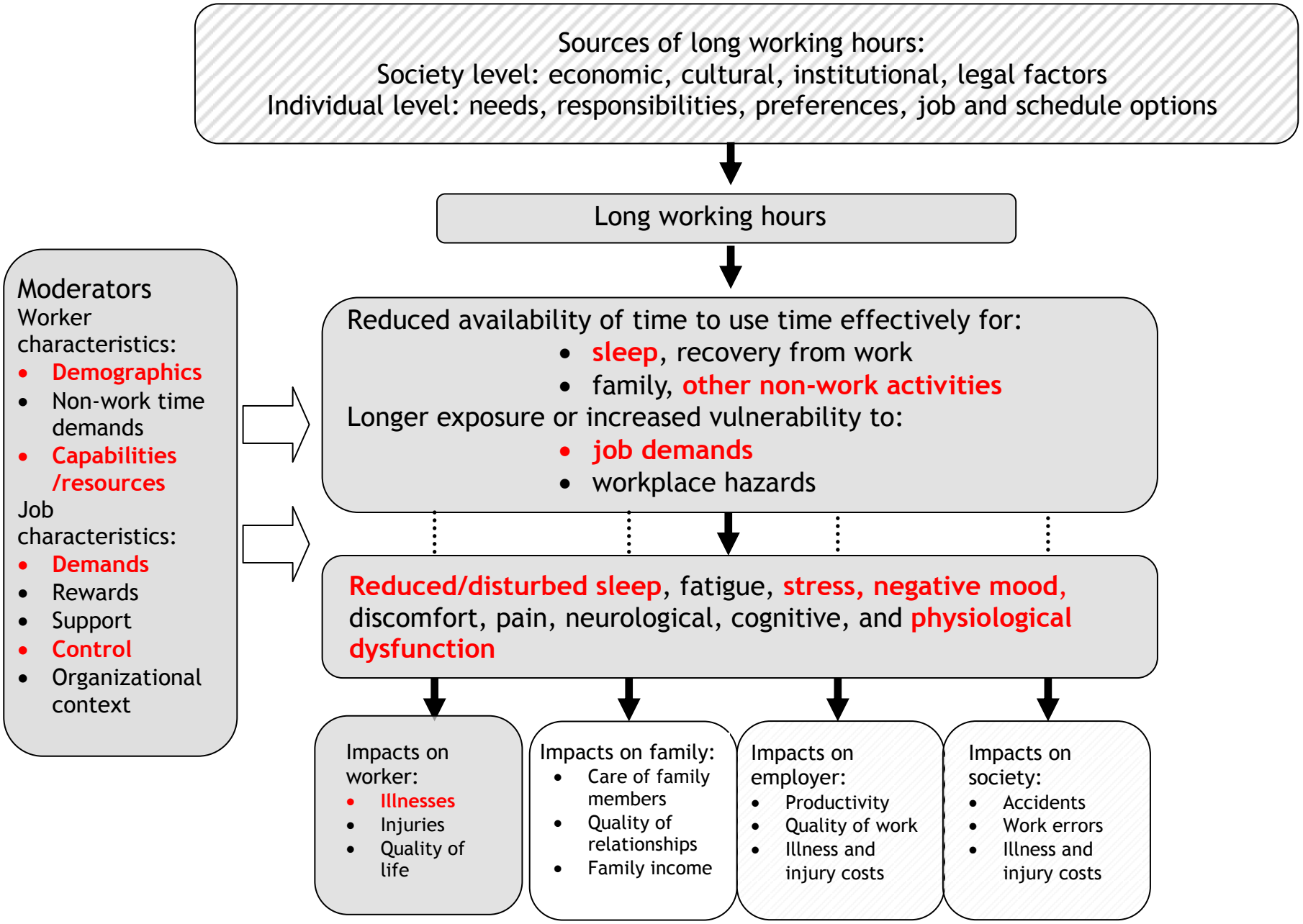
However, there may also be moderators - which can be either buffer or intensify the effects of long working hours - and can include both personal and work-related characteristics. For example, high job control is proposed to moderate the association between long working hours and health so that a combination of long working hours and low job control may have a more adverse effect on health than a combination of long working hours and high job control. Furthermore, physical activity may buffer an individual from the effect of long working hours on physical health, as suggested by a recent study of Holtermann and colleagues.[46]

The boxes with a dark background in Figure 4 indicate those aspects of long working hours that are within the framework of this thesis while the boxes with a light background include aspects that are not included in the scope of the present work. Furthermore, of the outcomes and moderating factors, those printed in *red font* are those included in my thesis.

1.5 Summary

Long working hours are hours of work that exceed the standard fulltime work week, while *overtime work* refers to hours of work that exceed the contracted working hours. Although widespread in industrialised countries, a common definition of long working hours for use in legal matters or statistics is not available. Long working hours are more prevalent among men than women, although recent trends in the U.K. suggest a decline in excessive working hours among men and a slight increase among women. A theoretical perspective suggests that the need to work long hours may arise both from societal and individual level sources. Adverse consequences of long working hours can include individual effects (e.g. health, sleep deprivation, work performance) as well as effects on society, including family members and communities.

Figure 4. Framework for the causes and consequences of long working hours. Modified from Caruso et al., 2006[31]



Chapter 2

Coronary heart disease - definitions, measurements and risk factors

2.1 Introduction

Coronary heart disease (CHD) or ischemic heart disease is the leading cause of death worldwide,[1] and has been projected to keep that rank by 2030, covering a total of 13.4% of all deaths. CHD has also been predicted to rank second in terms of adverse effects on quality of life in high-income industrialised countries.[1] This chapter presents the definition and assessment of CHD, its prevalence, and established and emerging risk factors. These are followed by a literature review on socioeconomic, psychological and psychosocial factors, especially those related to work, associated with the onset of CHD.

2.2 Definition and assessment of coronary heart disease

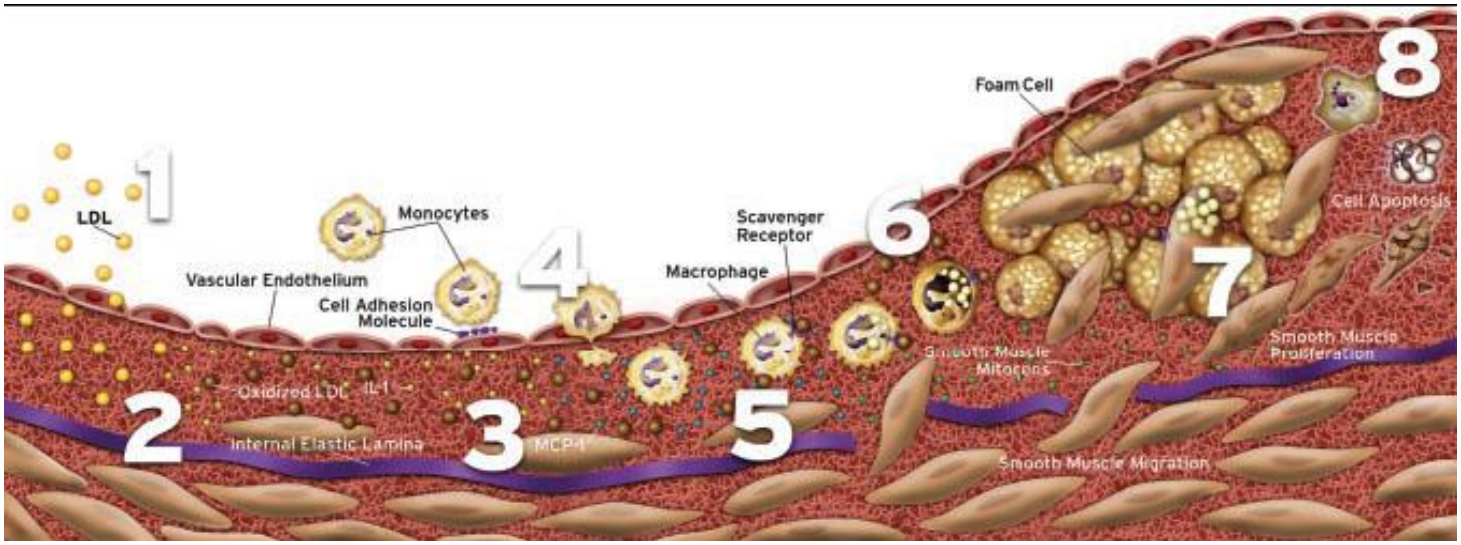
The concept of CHD refers to diseases classified as ischemic heart disease (International Classification of Diseases and Related Health Problems, version 9 [ICD 9[47]] codes 410-414, and version 10 [ICD-10[48]] codes I20-25). The following diagnoses are included in the category: angina pectoris (I20), acute myocardial infarction, AMI (I21), subsequent myocardial infarction (I22), certain current complications following acute myocardial infarction, e.g. haemopericardium, atrial septal defect, rupture of the cardiac wall (I23), other acute ischemic heart diseases, e.g. coronary thrombosis not resulting in myocardial

infarction (I24), and chronic ischaemic heart disease (I25).[48] The symptoms of ischemic heart disease range from non-symptomatic to sudden death. The most common symptom is pain in the centre of the chest with a duration of more than a few minutes. Pain is caused by ischemia, i.e. restriction of blood supply to the heart muscle due to *atherosclerosis* (defined in detail in the following paragraph). Sometimes the pain goes away and comes back and can be described as feeling of uncomfortable pressure, squeezing, or fullness. Other possible symptoms are spread of pain or discomfort into one or both arms, the back, neck, jaw, or stomach, shortness of breath, sweating cold sweat, nausea or lightheadedness.[49] The diagnosis can be verified by electrocardiogram (ECG), a set of biomarkers from blood samples; specifically troponin (cTn), creatine kinase (CK-MBm, CK-MB, CK),[50] and ultrasound or opaque matter imaging.

The pathogenesis of CHD usually includes the development of atherosclerotic plaque within the coronary arteries, i.e. *atherosclerosis*. The earliest stages of the process, fatty streaks, initiate from childhood and the most severe endpoint is myocardial infarction (MI). Progress of the atherosclerotic plaque is illustrated in Figure 5, which is adopted from Faxon et al.[51] The development of the plaque involves various different cell populations and cascade systems, such as macrophages, lymphocytes, platelets and smooth muscle cells (SMCs), as well as an adverse blood lipid profile (e.g. high level of low-density lipoprotein, LDL and low level of high-density lipoprotein, HDL), mechanical stimuli (high blood pressure), inflammatory cell activation, and the haemostatic system. An obstructing atherosclerotic plaque, even in its severe form, may remain stable for years and result in stable angina without progression to complete obstruction, thrombosis. A large body of research shows that inflammation plays a crucial role in atherosclerosis and thrombosis formation.[51-53] In sum, manifestations of CHD are acute coronary syndrome such as unstable

angina, myocardial infarction or sudden cardiac death, caused by blockage of the coronary artery.

Figure 5. The seven stages of development of atherosclerotic plaque. First low-density lipoprotein (LDL) moves into the subendothelium and is oxidized by macrophage and Smooth Muscle Cells (SMCs) (stages 1 and 2). Release of growth factors and cytokines attracts additional monocytes (stages 3 and 4). Foam cell accumulation and SMC proliferation result in growth of the plague (stages 6, 7, and 8). Figure from Faxon et al., 2004.[51]



2.3 Prevalence of coronary heart disease

CHD, or ischemic heart disease, as named in the ICD-10 classification of diseases,[48] will cause a total of 13.4% of all deaths by 2030 which means nearly 10 million deaths each year.[1] CHD is also a leading cause of death among the U.K. population, contributing a total of 16% and 15% of deaths among the total population and the population under 75 years of age, respectively.[54] Fifty-one thousand men and 40 000 women die of CHD each year in the UK. In 2006, lifetime self-reported doctor-diagnosed prevalence of MI in England was 4.1% among men aged 16 years or over and 1.7% among women.[55] Corresponding prevalence of angina was 4.8% and 3.3%, among men and women, respectively. The prevalence increased with age: among men aged 75+ years the prevalence of MI was 16.7% and among women of

that age it was 9.1%. The corresponding figures for angina were 22.7% and 15.9%, respectively.

2.4 General risk factors for coronary heart disease

Hundreds or thousands of risk factors for CHD have been proposed in the scientific literature, some of them presenting risk factors for all cardiovascular diseases (CVD). The European guideline on CVD prevention in clinical practice[56] as well as the one released by the American Heart Association[49] list the following *major risk factors* (with strong evidence): older age, male sex, close relative with CVD (i.e. genetic factors, including race, such as African American, Mexican American, American Indians), smoking, hypertension, dyslipidemia (total cholesterol ≥5 mmol/l, LDL cholesterol ≥3 mmol/l), diabetes (blood glucose ≥6 mmol/l), physical inactivity, and overweight (body mass index, BMI>25 kg/m^2).

Contributing risk factors are those with accumulating evidence but their significance has not yet been precisely determined. Among contributing risk factors are psychological stress, alcohol use and unhealthy diet. However, high alcohol use increases blood pressure, and a healthy diet is highly important in the prevention of overweight and diabetes as well as for controlling cholesterol and blood pressure levels which, in turn, are major risk factors for CHD. The European guideline[56] lists in addition low socioeconomic position (SEP), social isolation and lack of social support, and negative emotions such as depression and hostility. The guideline also specifies sources of psychological stress, such as stress at work and in family life. The evidence for some of these "emerging" risk factors is described in greater detail below.

2.5. Socioeconomic, psychological and psychosocial risk factors for coronary heart disease

The association between low SEP and CHD has been examined for nearly hundred years. A consistent body of research supports an inverse association between SEP, as measured by income, education, or occupational position, and CHD, which is not fully explained by biological, lifestyle or psychosocial factors.[57 58] Recently, various life course approaches have been introduced taking into account the early life socioeconomic circumstances in explaining the association between SEP and CHD in adulthood.[59]

Of the psychological factors, depression is the most frequently researched in association with CHD. The origin of interest in the association between psychological distress and CHD arose from the observations that a sudden trauma or shock may trigger myocardial infarction in a susceptible person and that prolonged stress may be associated with chest pain, breathlessness, and exhaustion.[60] Reviews including meta-analyses on the etiological studies[61 62 63] suggest an independent association between depression and the onset of CHD and in addition, the magnitude of risk was found to be related to the severity of depression. Exposure to an adverse social environment, in terms of e.g. negative life events or lack of social support, has been suggested to explain the association between depression and CHD due to the pathophysiological stress-related changes[64] visible in depression as well as in the progression of CHD; or through unhealthy lifestyle.

Yet, according to the most rigorous definition of a risk factor for CHD, depression has not yet achieved the status of an established major risk factor for CHD and the extent to which the observed associations are causal remains unclear.

Hostility is a form of angry internal rejection or denial in psychology, the concept initially developed by George Kelly.[65] In epidemiology, it was first introduced by Friedman and Rosenman in their classical study of type A behaviour pattern and CHD in 1974.[66] Two components are included in type A behaviour; that is, time urgency and hostility. Since then, hostility rather than type A behaviour has been recognized as a core component of a risk bearing personality trait and independent predictor of CHD.[67] However, two reviews[20 68] and a meta-analysis[69] suggest either a weak relationship or inconclusive association between type A behaviour or hostility and incident CHD.

Lack of social support or social isolation as an etiological factor for CHD has been widely examined, although recent studies on this topic are relatively rare. In their early works Cassell[70] and Cobb[71] observed that patients who were more socially connected seemed to remain more healthy and to have a better prognosis when recovering and two recent meta-analyses suggested a relationship between low social support and the onset of CHD.[72 73]

A growing body of research has examined work-related psychosocial stress as an etiologic factor for CHD.[74] This interest is based on a notion that in general, activation of the stress system in the hypothalamus and the brain stem helps the body to overcome the influence of short-term stressors. However, prolonged overactivity of these systems may cause wear and tear and play a role in the development of CHD.[75] The pathophysiological mechanism through which the physiological stress response increases atherosclerosis may relate to e.g. vascular inflammation,[76] activation of the renin-angiotensin system,[77] and vagal withdrawal.[78 79] The recognition that the physiological reactions to stress can damage the body has provided a basis for epidemiological research on work stress and CHD. One of the leading theoretical models on work-related psychosocial stress factors and health is *the job strain model.*[80 81] The key parameters of the job strain model are high job demands and low

job control, and a combination of high demands and low control is characterised as a strain situation. At least six reviews[68 74 82-85] including one meta-analysis[74] on the relationship between work stress and CHD have been published. The meta-analysis provided a summary estimation of a 1.43-fold risk of CHD associated with high job strain.[74] However, multiple adjustments for potential confounding and mediating factors attenuated the association to 1.16.

2.6. Summary

The pathogenesis of CHD typically involves the development of atherosclerotic plaque within the coronary arteries. Manifestations of CHD are acute coronary syndrome such as unstable angina, myocardial infarction or sudden cardiac death, caused by reduced blood supply in or blockage of the coronary artery. CHD is a leading cause of death worldwide and in the U.K. population, contributing a total of 16% and 15% of deaths among the total population and the population under 75 years of age in the U.K., respectively.

According to clinical guidelines, established major risk factors for CHD are older age, male sex, genetic factors, smoking, hypertension, dyslipidemia, diabetes, physical inactivity, and overweight. Contributing risk factors are alcohol use, unhealthy diet and psychological stress. Low SEP, social isolation and lack of social support, and negative emotions such as depression are also mentioned in the guidelines. Of the psychosocial factors, most support has received depression and social support in empirical studies. Some evidence, although less consistent, has been found for hostility or type A behaviour and work stress factors in relation to the development of CHD.

Chapter 3

Type 2 diabetes mellitus - definitions, measurements and risk factors

3.1 Introduction

The rising incidence of type 2 diabetes mellitus is a serious public health problem. The number of individuals with diabetes has been estimated to be more than 220 million worldwide,[86] and the figure is expected to rise to 366 million by 2030.[87] The increase in type 2 diabetes in industrialized countries is closely associated with the epidemic of obesity. The health and economic burdens of diabetes are considerable for the individual with the diagnosis as well as for society at large. This chapter describes the definition and assessment of type 2 diabetes, its prevalence and incidence, as well as general risk factors. Finally, a literature review on socioeconomic, psychological and psychosocial factors, especially those related to work, associated with the onset of type 2 diabetes is presented.

3.2 Definition and assessment of type 2 diabetes

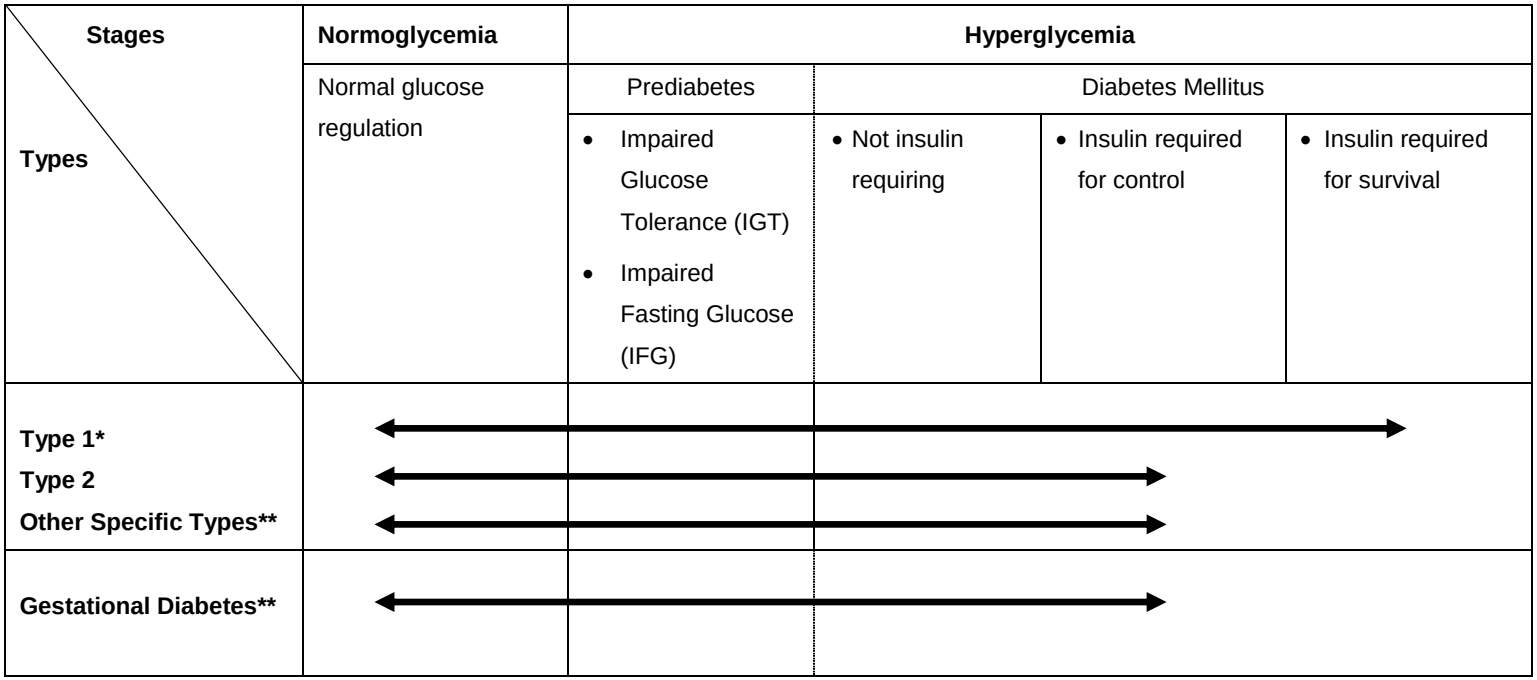
Diabetes is a group of metabolic diseases characterised by hyperglycemia which is caused by defects in insulin secretion of the pancreas, insulin action, or both.[88] Two broad

categories of diabetes have been identified according to etiopathogenesis: type 1 diabetes, also called insulin-dependent diabetes or juvenile-onset diabetes, accounts for 5-10% of diabetes cases. The underlying cause is β-cell destruction in the pancreas, either autoimmune or idiopathic, usually leading to an absolute deficiency of insulin secretion. The cause of type 2 diabetes has been shown to be a combination of resistance to insulin action and an inadequate compensatory insulin secretory response. Other specific types of diabetes include e.g., genetic defects of the β-cell, genetic defects in insulin action, diseases of the exocrine pancreas, endocrinopathies, drug- or chemical-induced diabetes, and infections that cause β-cell destruction, such as congenital rubella, uncommon forms of immune-mediated diabetes, and gestational diabetes mellitus.[88] This thesis concerns the most prevalent category, type 2 diabetes mellitus which covers 90-95% of all diabetes cases.

Chronic hyperglycemia is related to long-term complications, dysfunction and failure of several organs, including the eyes (retinopathy), kidneys (nephropathy), nerves (e.g. peripheral neuropathy with risk of foot ulcers, autonomic neuropathy), cardiovascular system (atherosclerotic, cardiovascular, peripherial arterial, cerebrovascular disease, and hypertension).[88 89]

Figure 6 (p.34; adopted from the American Diabetes Association)[88] presents disorders of glycemia according to etiologic types and stages. In type 2 diabetes, patients have insulin resistance and usually have relative (rather than absolute) insulin deficiency. In type 2 diabetes, autoimmune destruction of the β-cells of the pancreas does not occur. Type 2 diabetes may also go undiagnosed for many years because the hyperglycemia develops gradually and at earlier stages no classic symptoms of diabetes such as fatigue, thirst and weight loss are experienced.

Figure 6. Stages of hyperglycemia and types of diabetes (adopted from the American Diabetes Association).[88]



*Even after presenting in ketoacidosis, these patients can briefly return to normoglycemia without requiring continuous therapy.
**In rare instances, patients in these categories may require insulin for survival.

A positive finding on whichever of the three following tests indicates *prediabetes*, that is, an increased risk of later developing diabetes mellitus (for the first two after at least 8 hours' fasting):[88]

- Impaired fasting plasma glucose (IFG): 5.6 to 6.9 mmol/L (100 to 125 mg/dl)
- Impaired glucose tolerance (IGT): 2-hour plasma glucose (PG) in the 75-g oral glucose tolerance test 7.8 to 11.0 mmol/L (140 to 199 mg/dl)
- Glycated hemoglobin (A1C or HbA1C): 5.7 to 6.4%

For all three tests, risk is continuous, extending below the lower limit of the range and becoming disproportionally greater at higher ends of the range. The group of people with prediabetes form an intermediate group of individuals whose glucose levels do not meet the criteria for diabetes, yet are higher than those considered normal. Diagnostic criteria[88] for diabetes mellitus are (for the first two after at least 8 hours' fasting):

- Fasting plasma glucose (FPG) ≥7.0 mmol/l (≥126 mg/dl), or
- 2-hour PG in the 75-g oral glucose tolerance test ≥11.1 mmol/L (≥200 mg/dl), or
- Glycated hemoglobin (A1C or HbA1C) ≥6.5%, or
- In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose (PG) ≥11.1 mmol/L (≥200 mg/dl).

FPG is the amount of glucose in the blood, expressed in millimoles per a litre (mmol/l) or milligrams per a decilitre (mg/dl). The blood sample is taken 8-12 hours after eating. *Oral glucose tolerance test* (OGTT) to determine the prevalence of IGT, is performed in the morning after 8-14 hours' fasting. Blood is sampled before and two hours after intake of fixed amount of glucose, usually 75g dissolved in 250-300 ml water drunk over a period of 5 minutes. *Glycated hemoglobin* (A1C or HbA1C) is used to estimate the

average plasma glucose concentration over prolonged periods of time (2 to 3 months). HbA1C measures the amount of glucose that is being carried by the red blood cells in the body, expressed as a percentage. No fasting is required when sampling blood for HbA1C.

Classic symptoms of hyperglycemia include increased thirst, fatigue, weight loss, frequent urination, headaches, difficulty concentrating, and blurred vision. There are two types of *hyperglycemic crises* in diabetes: diabetic ketoacidosis (DKA) and hypersmolar hyperglycemic state (HHS).[90] DKA is more common in type 1 diabetes while HHS is more often associated with type 2 diabetes. Symptoms of DKA include high PG, (>250 mg/dl), low arterial pH (<7.30), dehydration, and high levels of ketones in urine and serum, among other things. HHS includes among other indicators, severe dehydration and plasma glucose of >600 mg/dl, but not as low arterial pH and not as high levels of ketones as are associated with DKA.[90]

3.3 Prevalence of type 2 diabetes

Type 2 diabetes mellitus is a serious and common metabolic disorder. According to the projections of the WHO[1] diabetes mellitus will be the fourth leading cause of death in high-income countries by the year 2030, covering 4.8% of the total deaths. Worldwide, the ranking is seventh (3% of total deaths). When assessing DALYs (disability-adjusted life years, i.e. years of full health lost due to disease and injury) it is remarkable that in the year 2002 diabetes ranked 20th while the rank projected for 2030 is 11. Among the high-income industrialised countries, the projected rank for diabetes is 5th by the year 2030 (4.5% of total DALYs).

According to the population-based Health Survey for England in 2006[55] the prevalence of self-reported doctor-diagnosed diabetes was 5.6% in men and 4.2% in women

aged 16 or over. The prevalence increased with age: among men and women aged 75 years or more, the prevalence was 13.5% and 10.6%, in men and women, respectively.

3.4 General risk factors for type 2 diabetes

The established risk factors for type 2 diabetes are older age, IFG or IGT, overweight and obesity (BMI> 25 kg/m^2), lack of physical activity, hypertension, dyslipidemia, history of vascular disease,[88 91 92] and increased body fat in the visceral compartment,[93] and among women, gestational diabetes mellitus, delivery of a baby weighing >9 lb, or polycystic ovary syndrome.[88 91 92] It is also associated with ethnic background (e.g. African-American, Latino, Native American, Asian, Pacific Islander, Afro-Caribbean) and has a genetic predisposition, more so than type 1 diabetes.[88 91 92] Thus, having a first-degree relative with type 2 diabetes increases the risk substantially.

3.5. Socioeconomic, psychological and psychosocial risk factors for type 2 diabetes

Of the socio-demographic factors, low SEP have been shown to predict the onset of type 2 diabetes although the association between SEP and type 2 diabetes seems to be mediated by overweight, smoking and physical inactivity.[94-96]

Recently, there has been widespread interest in the relationship between mental health and type 2 diabetes. Some studies suggest an association between depression and incident type 2 diabetes but others have reported null results.[97 98] However, two meta-analyses have been published on this issue, one indicating that depression increases the risk

of type 2 diabetes by 37%[98] and the other one suggesting that the increased risk of incident type 2 diabetes associated with previous depression is as high as 60%.[97] The mechanism between depression and type 2 diabetes may relate e.g., to adverse health behaviours and associated obesity, inflammatory pathways or shared pathophysiological liability that accounts for the co-occurrence of depression and type 2 diabetes.[99]

A growing body of research has investigated associations between psychosocial stress factors and development of type 2 diabetes.[100 101] The idea behind studying this association is exposure to psychosocial stress which has been shown to be associated with a number of pathopshysiological mechanisms that make the association with type 2 diabetes theoretically possible, such as the hypothalamus-pituitary-adrenal (HPA) axis activation during stress, the sympathetic nervous system and inflammatory pathways that are known to adversely affect glucose metabolism.[75 102] In addition, an indirect pathway has been hypothesised, suggesting unhealthy lifestyle to be a mediating factor between stress and type 2 diabetes.[75] However, a meta-analysis of six longitudinal cohort studies found no association between psychosocial factors, such as adverse life events, stress in daily life, poor social support, problems in the family, maladaptive coping, and poor self-efficacy, and the onset of type 2 diabetes.[101] In contrast, a correlation was found with psychosocial stress and poor diabetes control among diabetic individuals.[101]

Regarding work-related stress and incidence of type 2 diabetes, a Swedish study found an association between "passive or tense working situations" and incident type 2 diabetes in women but not in men.[103] In the Whitehall II study of British civil servants, there was a relationship between work stress, as indicated by perceived effort-reward imbalance at work, and incident type 2 diabetes among men but not among women.[96] However, in the same population, high perceived stress at work, when measured as high demands, low control, and low support at work, was related to an increased incidence of type 2 diabetes

among women but not among men during a 15-year follow-up.[104] A null finding was reported between job strain and incident type 2 diabetes in a prospective study of Japanese men.[105] However, a cross-sectional association of job strain and low social support at work with higher levels of glycosylated hemoglobin was found in samples of nondiabetic white collar employees[106] and male manufacturing workers[107] in Japan.

3.6. Summary

Two broad categories of diabetes mellitus have been identified: type 1 diabetes and type 2 diabetes, the latter representing 90-95% of all diabetes cases. Type 2 diabetes is a serious and increasingly prevalent metabolic disorder which is associated with the obesity epidemic in industrialised countries, with increasing number of people predicted to suffer from the condition in the future. In England, the prevalence of self-reported doctor-diagnosed type 2 diabetes in 2006 was slightly higher in men (5.6%) than women (4.2%) and increased with age.

Fasting plasma glucose, oral glucose tolerance test and the proportion of glycated hemoglobin are currently the most important measures in assessing the presence of prediabetes or diabetes mellitus. The established risk factors for type 2 diabetes include older age, impaired fasting glucose or impaired glucose tolerance, overweight, increased body fat in the visceral compartment, lack of physical activity, hypertension, dyslipidemia, history of vascular disease, and genetic factors, and among women, gestational diabetes mellitus, delivery of a baby weighing >9 lb or polycystic ovary syndrome. Although the association of low SEP and depression with the onset of type 2 diabetes has been supported in several studies, research shows an inconclusive relationship between general stress or work stress and the onset of type 2 diabetes.

Chapter 4

Depressive disorders – definitions, measurement and risk factors

4.1 Introduction

Depression is a severe public health concern which has been predicted to be the leading cause of the burden of disease in high-income countries by 2030.[1] In addition to human suffering, depression affects families and communities and is associated with substantial work impairment in terms of lost work days and reduced productivity.[3 4 108] This section reviews some of the key mental health concepts, starting with definitions of depressive disorders and a brief overview of the measurement of these disorders and their symptoms. This is followed by a literature review on risk factors for depressive disorders.

4.2 Definition and assessment of depressive disorders

Depressive disorders have been defined in the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Version (DSM-IV-TR)[109] and ICD-10.[48] The latter system is mostly used in European countries while the former is commonly usedin the U.S. and other non-European countires. *Major depressive disorder* (MDD) is in a category of *mood (affective) disorders* in DSM-IV-TR and in ICD-10. In both systems, the diagnosis of MDD hinges on the presence of single or recurrent *major depressive episodes* (MDE). ICD-10 lists

three symptoms to be required in order to diagnose depression: depressed mood, adhedonia, and reduced energy, of which at least two should be present and which have been persisted for at least two weeks. According to DSM-IV-TR, there are two main symptoms - depressed mood and adhedonia - of which at least one should be present and persisted for at least two weeks. In addition to the presence of at least one of the two *key symptoms* of depression, *associated symptoms* are disturbed sleep (decreased or increased compared to usual), diminished or increased appetite with associated weight change, fatigue or loss of energy, agitation or slowing of movements, poor concentration or indecisiveness, feelings of worthlessness or excessive or inappropriate guilt, and suicidal thoughts or acts. Presence of at least three (with two key symptoms) or four (with one key symptom) associated symptoms are required for a diagnosis of depression. Severity of depression is determined according to the number of symptoms and their effect on functional capacity: mild, moderate, severe, and depression with psychotic features.

If the patient has had an episode of mania or markedly elevated mood, a diagnosis of *bipolar disorder* is made instead of *unipolar* depression. DSM-IV-TR also excludes cases where depressive symptoms are caused by bereavement. MDD tends to be recurrent and the onset of individual episodes is often associated with stressful life events (described in detail in the following chapters). *Dysthymia* is a chronic depression of mood, lasting at least several years, which is not sufficiently severe, or in which individual episodes are not sufficiently prolonged, to justify a diagnosis of at least mild recurrent depressive disorder.

The current British guideline for treatment of depression[110] recommends screening for depression, particularly in people with a past history of depression or a chronic physical health problem with associated functional impairment, by asking the following two questions:[110-112]

- During the last month, have you often been bothered by feeling down, depressed or hopeless?
- During the last month, have you often been bothered by having little interest or pleasure in doing things?

If a person answers 'yes' to either of the depression identification questions, the person's mental state and associated functional, interpersonal and social difficulties should be reviewed. The diagnosis of depression is based on the patient's self-reported experiences, behaviour reported by other people, and a mental status examination by a physician. There is no laboratory test for depression although it is recommended to test for physical conditions that may cause similar symptoms, such as diseases of the thyroid or central nervous system.[113]

Structured diagnostic instruments that correspond to classificatory systems for the diagnosis of mental disorder; such as the Composite International Diagnostic Interview (CIDI)[114 115] or the Revised Clinical Interview Schedule (CIS-R), [115 116] have long been considered the "gold standard" for measuring mental disorders in epidemiological surveys. While these instruments are able to provide specific and differential psychiatric diagnoses, they are lengthy, require trained interviewers, and have complicated scoring algorithms (although to date they are computerised). Therefore, several self-report questionnaires have been developed to be used as screening instruments to identify potential psychopathology, mainly in primary care settings but also in communities and large-scale epidemiological studies.[117]

However, the major limitation in these screening instruments is their inability to detect cases based on psychiatric diagnostic criteria. Thus, they assess presence of *psychological distress*; presence of symptoms (subclinical state) of common mental disorders, such as depressive and anxiety disorders, rather than the disorder itself, as defined

in the diagnostic criteria. The most commonly used self-report instruments for identifying psychological distress, depressive symptoms, or screening depression are (in alphabetical order) as follows:

- Beck Depression Inventory (BDI)[118]
- Centre for Epidemiologic Studies Depression Screen (CES-D)[119]
- General Health Questionnaire (GHQ-30, GHQ-28, GHQ-12)[120-122]
- Hamilton Depression Scale (HDS)[123]
- Hospital Anxiety and Depression Scale (HADS)[124]
- Kessler Psychological Distress Scale (K10, K6)[125]
- RAND Mental Health Component scale (RAND MHC-12)[126]
- Self-rating depression scale (SDS)[127]
- Self-reporting Questionnaire (SRQ)[128]
- Short Form Health Survey (SF-36, SF-12)[129 130]
- Symptom Checklist (SCL-90)[131]
- Two-question Screen[111 112]

4.3 Prevalence of depressive disorders

The median 1-year prevalence of MDD across studies in general populations has been 5.3%.[132] About 75% of patients recover within a year but approximately 60% experience a new episode later in life.[133] The prevalence estimates for psychological distress have not been as widely reported as those for diagnosis-based depressive and anxiety disorders. In a study of the English adult population,[134] high scores for psychological distress, as measured by the 12-item GHQ were reported by 15% of women and 11% of men. In men, the prevalence was highest among those aged 35-44 years and lowest among those aged 65-74

years whereas in women, highest prevalence was found among 16-24 years-olds and 35-44 years-olds, and lowest prevalence among 65-74 years-olds.

4.4 General risk factors for depressive disorders

The exact causes of depressive disorders are not known but it is widely assumed that the etiology is multifactorial involving genetic, biologic, socioeconomic, and psychosocial factors.[135] Established risk factors for depressive disorders in adulthood include female sex, age (early or mid-adulthood), chronic physical disease such as CHD, binge drinking, smoking, low socioeconomic position, and negative stressful life events.[63 113 136]

The genetic epidemiology of common mental disorders, such as depressive and anxiety disorders, shows that they tend to aggregate in families.[137-140] However, twin studies suggest that the estimated heritabilities for MDD (30-50%) is modest, significantly lower than that for schizophrenia (81%) and bipolar disorder (85%). This means that a large proportion of the variance in liability to these disorders may be explained by individual environmental factors.

While familial and twin studies give some support to a genetic basis for common mental disorders, progress towards the identification of specific genes which contribute to illness susceptibility has been relatively limited. By 2006, more than 100 studies had been published and positive associations with MDD were reported for 42 different genes. However, few of them have been confirmed by replication.[141] The most extensively examined association in the field is polymorphism in the promoter of the serotonin transporter genotype (5-HTTLPR) which in several studies has been shown to be associated with a greater risk of adult depressive or anxiety disorder in the presence of either childhood

maltreatment or multiple adverse life events in a 5-year period or shortly before onset.[142-144] However, meta-analyses[145-147] on the effects of 5-HTTLPR and its interaction with stressful life events on the risk of depression have thus far shown inconclusive associations.

4.5 Socioeconomic and psychosocial risk factors for depressive disorders

Of the socioeconomic factors, low SEP and adverse life events (e.g. divorce, widowhood, unemployment) have been shown to predict the onset of depression.[63 113 136] Various other psychological and psychosocial factors have also been suggested to be important contributors to depression.[135 148] Acute negative life events have for a long time been a major focus of the stress-mental disorder literature. Severe acute life events that possess a high degree of threat, negative emotions, and experience of loss have been found consistently to precede the onset of depression (for a review, see Hammen, 2005[149]). These include severe or chronic physical disease, the experience of loss, such as the death of a significant person, separation or divorce, and job loss, as well as work-related events. In 80% of depression cases, onset of depression was preceded by a stressful life event. This finding has been confirmed by including only 'fateful' events such as loss of a close family member or being exposed to a natural disaster that were unlikely to be due to the individual's preceding depression.[150 151]

While stressful negative life events can definitely elicit depression, it is plausible to assume that chronic psychological stress such as work stress may also be of importance through similar mechanistic pathways.[151 152] The 'job strain' model [80 81] has also been tested in the context of mental health. There is some evidence that high demands, low control, and

high strain are associated with common mental health problems.[22 80 81 108 153-156] However, a recent review[22] restricted to clinical MDD suggested that the association is inconclusive. Thus, evidence suggests an association between work-related psychosocial stress factors and symptoms of depression and psychological distress rather than clinical disorder.

4.6 Summary

The core symptoms in depressive disorders are depressed mood, adhedonia, and reduced energy, accompanied by other symptoms such as disturbed sleep (decreased or increased compared to usual), diminished or increased appetite with associated weight change, fatigue or loss of energy, agitation or slowing of movements, poor concentration or indecisiveness, feelings of worthlessness or excessive or inappropriate guilt, and suicidal thoughts or acts. The median 1-year prevalence of MDD across studies in general populations has been 5.3%. Etiology of depression is multifactorial involving genetic, biologic, socioeconomic, and psychosocial factors. Risk factors for depressive disorders in adulthood include female sex, age (early or mid-adulthood), chronic physical disease such as CHD, binge drinking, smoking, low SEP, and severe acute life events during childhood and adulthood that possess a high degree of threat, negative emotions, and experience of loss.

Clinical assessment of depression is rarely feasible in large-scale epidemiologic studies, thus, self-administered surveys are commonly used in large studies. However, with regard to work-related stress factors, the existing evidence suggests an association between work stress and *symptoms* of depression rather than clinically significant disorder. However, to date, research examining the relationship between work exposures and mental health outcomes has been beset by many methodological problems.

Chapter 5

Sleep disturbances – definitions, measurements and risk factors

5.1 Introduction

Insomnia is common in working-age populations and has been shown to be on the increase.[8] Consequences of sleep disturbances at work include reduced productivity, increased rates of accidents at work, health-care use, and work disability.[157 158] Sleep disturbances may predispose towards or be early signs of depression.[159] Sleep deprivation, a common consequence of sleep disturbance, may lead to impairment of neurobehavioral functioning and weaken performance, especially in vigilance tasks,[160] and has even been associated with premature death.[161 162] This chapter presents an introduction to sleep disturbances, their prevalence and risk factors.

5.2 Definition and assessment of sleep disturbances

The term *sleep disorder* rather than sleep disturbance is used in clinical assessment. According to the ICD-10 definition,[48] sleep disorders can be either *organic*, i.e. those that are one of the symptoms of another disorder, either mental or physical, or *non-organic*, those that are independent. Sub-diagnoses include *insomnia*, a condition of unsatisfactory quantity and/or quality of sleep, including difficulty falling asleep, difficulty staying asleep,

or early final wakening; *hypersomnia*, defined as either excessive daytime sleepiness and sleep attacks (not accounted for by an inadequate amount of sleep), or prolonged transition to the fully aroused state upon awakening; *disorder of the sleep-wake schedule* refers to a lack of synchrony between the actual sleep-wake schedule and the desired sleep-wake schedule for the individual's environment, resulting in a complaint of either insomnia or hypersomnia, as well as psychogenic inversion of circadian, nyctohemeral, and sleep rhythms. Other sleep disorders include *sleep apnoea*, *narcolepsy and cataplexy*, *sleepwalking*, *sleep terrors*, *nightmares***,** *other sleep disorders*, and *sleep disorder, unspecified*.

The ICD-10 criteria[48] state that insomnia must be present for at least three nights in seven and have lasted for a considerable amount of time. In addition, the ICD-10 emphasizes the importance of distress and interference by requiring the patient to report ‘preoccupation with the sleeplessness and excessive concern over its consequences at night and during the day'.

Sleep duration, both short and long, has also been shown to be associated with premature death,[162 163] however, evidence on the association between *insomnia* and mortality is mixed.[164] Sleeping problems can also predict the onset of new episode of depression.[159]

There are several ways to assess sleep disorders.[10] In clinical assessments, sleep history, nocturnal symptoms, reports from bed partners, daytime consequences, sleep diaries, Multiple Sleep Latency Test (MSLT), pupillometry assessment, neuropsychological assessment, and polysomnography are among the sources of data leading to a diagnosis of a sleep disorder.[10] However, these instruments are usually not possible to use in large-scale epidemiological studies.

There are several self-report questionnaires available for use as screening instruments to identify potential sleep disorders. However, the same major limitation applies

to these screening instruments as to those screening common mental disorders; they are not able to detect cases based on diagnostic criteria, rather they assess presence of *symptoms* of sleep disorders. The most commonly used self-report instruments of symptoms of sleep disorders (in alphabetical order) are as follows:

- Jenkins Scale[165]
- Karolinska Sleep Questionnaire[166]
- Nordic Sleep Questionnaire (NSQ)[167]
- Pittsburgh Sleep Quality Index (PSQI)[168]
- Post-sleep Inventory[169]
- Post-sleep Questionnaire (PSQ)/ Sleep Effects Index (SEI)[170]
- Sleep Disorders Questionnaire (SDQ)[171]
- Sleep Evaluation Questionnaire[172]
- Sleep Questionnaire and Assessment of Wakefulness (SQAW)[173]
- St. Mary's Hospital Sleep Questionnaire[174]
- Uppsala Sleep Inventory[175]

5.3 Prevalence of sleep disturbances

Insomnia, a condition of unsatisfactory quantity or quality of sleep, is the most common sleep disturbance in adult populations. About 30–50% of adults experience insomnia symptoms occasionally,[7-11] and up to 15% meet the criteria for clinical insomnia.[7 10-12] However, prevalence estimates for insomnia can vary, depending on study methodology and sample. Population-based studies across a number of countries have found that

approximately 30% of individuals report some difficulty in sleeping over the past year and approximately 10% report chronic insomnia.[9] Rates of insomnia in attendees of general medical practices are higher that those of general populations, ranging from 10% to as high as 34%.[176-178].

5.4 General risk factors for sleep disturbances

Epidemiological analyses have demonstrated a high degree of co-morbidity between insomnia and psychiatric illnesses, such as mood (e.g., MDD) and anxiety disorders although the direction of causality is not always easily detected.[10 159 179] Higher rates of insomnia have also been found in women, and those who are separated or divorced, medically ill patients, and those with substance abuse.[10 179 180] Insomnia has been shown to increase with age in both sexes.[9 181]

5.5 Socioeconomic and psychosocial risk factors for sleep disturbances

Low SEP and unemployment have been shown to be associated with the most common form of sleep disturbances, insomnia.[10 179 182] In addition, psychological stress is considered one of the primary causes of persistent primary insomnia.[183] Stress may disturb sleep by causing increased physiological and psychological activation as a response to environmental demands, whereas in order to fall asleep, deactivation of these functions is needed.[184] However, relatively little is known on the role of work-related psychosocial factors

contributing to the onset of sleep disturbances. Most studies on the subject have been cross-sectional or retrospective, showing association, for example, with preceding negative life events and work stress, such as victimization, workplace bullying, or high job strain.[184-186] The anticipation of stress associated with cognitive arousal and worry seems to be a key factor in stress-related insomnia.[184]

5.6 Summary

Insomnia, a condition of unsatisfactory quantity or quality of sleep, is the most common form of sleep disturbances with relatively high prevalence and considered an increasing problem in working-age populations. Population-based studies across a number of countries have found that approximately 30% of individuals report some difficulty in sleeping over the past year and approximately 10% report chronic insomnia. However, the figures include cases of sleep disorders, such as sleep apnoea, in addition to individuals reporting symptoms of insomnia, usually defined by various types of problems in sleep quality and quantity. Consequences of insomnia may be mental disorders such as depression, as well as reduced productivity, increased rates of accidents at work, health-care use, and work disability. There is also evidence on the relationship between short and long hours of sleep and mortality.

Sleep disturbances can be assessed in a clinical setting or using self-reported paper-and-pencil questionnaires. Women, older individuals, people with low SEP, those who are unemployed, separated or divorced, and those with substance abuse or somatic or psychiatric illnesses have insomnia more often than others. Several studies, although many of them cross-sectional, have shown an association between negative life events and work stress, such as victimization of workplace bullying, or high job strain, and sleep disturbances.

Chapter 6

Review of studies on long working hours, chronic diseases and sleep disturbances

6.1 Introduction

In this chapter, an overview is presented of the scientific literature on the association between long working hours and the outcomes presented in the previous chapters. The search strategy using OvidSP Medline tool is presented in Appendix 1. This search resulted in 321 potential studies and was completed by manually searching the bibliographies of retrieved articles, previous reviews, and a recent book.[23-34] The process of cross-referencing was continued until no new references were identified. No specific cut-point for long working hours was required since the definition varies considerably across studies. Only empirical, peer-reviewed studies published in international journals published in English were included. Studies focusing exclusively on extended hours in shift work were excluded because the present study comprised non-shift workers and because in shift work, it is difficult to differentiate the effects of work schedule and the effects of long working hours.

Of all the retrieved studies, 59 were included as eligible (10 studies on long working hours and CHD, three studies on long hours and type 2 diabetes, 30 studies on long hours and depression or psychological distress, and 16 studies on long hours and sleep disturbances).

6.2 Long working hours and coronary heart disease

Studies on the association between long working hours and CHD with individual level information on working hours are presented in Table 1 in chronological order. A couple of ecological studies were not included; for example an early study by Buell and Breslow in 1960[36] where standardised mortality ratios in California, U.S. were examined linking aggregated Census data on working hours to each occupation. The study showed an association between the high proportion of overtime workers in non-farmer occupations and death due to CHD. However, the trend was observed only among men aged 25 to 40 years. A later study with a similar approach was carried out in Sweden by Alfredsson and co-workers.[187] That study showed no association between long working hours by occupation and hospitalization due to myocardial infarction among women. However, in men, a *lower* morbidity rate was found in occupations with long working hours. Another ecological study was carried out in Hungary, showing a correlation between hours worked at the weekend and cardiovascular mortality in men and women.[188] Ecological studies suffer from *the ecological fallacy* which refers to the fact that statistics that accurately describe group characteristics do not necessarily apply to individuals within that group.[189]

Another individual-level study that examined the association between working hours and *overall mortality* in Sweden showed an association among women.[190] Again, a lower mortality rate was found in men who worked overtime, however, no more than five hours a week. However, in that study, the analyses were not adjusted for SEP, a potential confounding factor.

Another early study, not included in Table 1, is a case-control study by Russek and Zohman published in 1958[191] where 91% of the CHD cases but only 20% of the controls, reported more occupational strain (a combination of overtime work, double jobs, job

insecurity, and job stress). In that study, a separate estimate for overtime work was not reported.

Of the 10 studies presented in Table 1, three were prospective studies, six were case-control studies, and one was a cross sectional study. Five were carried out in Japan and one in each of Sweden, Finland and the Netherlands. Two of the three prospective studies indicated no association between long working hours and cardiovascular events in general (including other CVD, such as stroke, in addition to AMI), or insurance claims with diagnoses of overall cardiovascular diseases (ICD-10 codes I00-I99). Holtermann and his colleagues found an excess mortality due to CHD associated with long working hours (≥46 hours a week) among men with low physical fitness but not among men with high physical fitness.[46]

Of the six case-control studies, all but one found an association between long working hours and CHD, indicated by AMI. The exception was a small-scale study (n=133 cases) by Falger and Schouten[192] where the association attenuated after final adjustments. A cross-sectional study by Lallukka et al.[193] reported an association between overtime work and self-reported angina pectoris symptoms in their sample of working women.

In sum, although the evidence suggests an association between long working hours and CHD, the vast majority of studies have been case-control studies. The major problem in case-control studies is the retrospective assessment of working hours, i.e. it is possible that the disease itself, here CHD, influences the patient's work behavior and perception or recall of working hours prior to the onset of illness. A similar problem is related to a cross-sectional study design. The three prospective studies failed to show any consistent relationship, however, the outcome in two of them was nonspecific, including overall CVD. Furthermore, one of the studies had a sample of treated hypertensive patients and the other one used insurance claim records which restricted the follow-up to those who

were employed by the same employer during the follow-up time. In many studies, the reference group included also those who worked part-time. It is problematic since it creates a potential source of reverse causation bias, because part-time work may be a response to health problems rather than a risk factor. Indeed, part-time work has been found to be associated with morbidity and mortality.[39 190]

Table 1. Summary of the studies on the association between long working hours and CHD

Author(s) and year	Sample, location	Study design	Follow-up time	N	Age, sex and distribution by socio-economic position (SEP)	Potential confounders considered	Working hours measure	Outcome measure	Findings
Theorell & Rahe, 1972[194]	Patients admitted to hospital for acute myocardial infarction (AMI), healthy controls from a city service agency, Sweden	Case-control	5-months retrospective	62 cases, 109 controls	100% male, 63% professionals/ managers; non-matched but similar comparison group	Separate analysis among professionals and skilled workers	Self-reported overtime work 4-months prior the event (≥2 h /day) vs. not	Hospital admission due to AMI	Higher prevalence of overtime work among cases (professionals and skilled workers)
Thiel et al., 1972[195]	Patients admitted to hospital, U.S.	Case-control	12-24 months retrospective	50 cases, 50 controls	100% male, aged 40 to 60, 74% non-manual	Matched healthy control group of similar age	Average working hours per week ≥51 vs. less	Hospital admission due to first AMI	66% of cases vs. 52% of controls worked ≥51 hours a week (p<0.05)
Falger & Schouten, 1992[192]	Patients admitted to hospital for AMI, controls from neighbourhoods and hospitals, Netherlands	Case-control	Not reported	133 cases, 133 neighbourhood controls, 192 hospital controls	100% male; non-matched controls, mean age 53, 49, and 51 years among cases and two control groups. 50% of cases, 41% and 47% of controls had primary education only	Age, exhaustion, education, smoking	Prolonged overtime (details not reported)	Hospital admission due to AMI	Overtime associated with AMI in the age-adjusted model (RR 1.94; 1.21-3.12) but not in the full model
Sokejima & Kagamimori, 1998[39]	Patients admitted to hospital for AMI, controls from workplace health examinations, Japan	Case-control	2-months and 1 year retrospective	195 cases, 331 controls	100% male, matched by age and occupation	Age, occupation, hypertension, hypercholesterolemia, diabetes, body mass index, smoking, proportion of sedentary work, burnout index	Self-reported from salary records: daily working hours: 9.01-11, ≥11.01 vs. 7.01-9; increase in daily hours during the year: 1.01-2, 2.01-3, ≥3.01 vs. ≤1.01	Hospital admission due to AMI	≥11.01 hours was associated with AMI: OR=2.94 (1.39-6.25); 2.01-3 hours increase was associated with OR 2.38 (1.08-5.26) and ≥3.01 increase in working hours with OR=2.49 (1.24-4.99)

Table 1 cont.

Liu & Tanaka, 2002[35]	Patients admitted to hospital for AMI with controls from residential registers, Japan	Case-control	1 year, retrospective	260 cases, 445 controls	Matched by age, sex, and residence	Cigarette-year, alcohol use, overweight, hypertension, diabetes, hyperlipidemia, parental CHD, job type, sedentary job	Weekly working hours (past year, past month), 41-60, >60 vs. <41 hours	Hospital admission due to AMI or suspected AMI	Past year >60 hours associated with CHD, OR=1.8 (1.0-3.3); past month >60 hours, OR=1.9 (1.1-3.5)
Tarumi et al., 2003[196]	Office workers, Japan	Pro-spective	1-4 years	453-589	74-79% male, mean age 38-41 years,	Age, sex, type of occupation, BMI, physical exercise	Weekly working hours (≥45 vs. less) at baseline	Insurance claim records of ICD-10 diagnoses I00-I99	No significant association (HR 1.10; 0.53-2.26)
Fukuoka et al., 2005[197]	Hospital sample, controls from heath check-ups, Japan	Case-control	1 month, retrospective	47 cases, 47 controls	Matched by age and sex	None.	Weekly working hours, continuous	AMI	Cases had higher weekly working hours (mean 58.3) than controls (50.7)
Uchiyama et al., 2005[198]	A sample of treated hypertensive patients, Japan	Pro-spective	5.6 years	1615	44% female, mean age 54 years	Age, sex, blood pressure, BMI, total cholesterol, HDL cholesterol, family history of stroke, left ventricular hypertrophy, ischemic ST-T change, atrial fibrillation, smoking	Daily working hours 10 or more vs. less than 10	Cardiovascular event (cerebral haemorrhage /infarction, subaracnoidal hemorrhage, AMI, heart failure, aortic aneurysmal rupture, sudden death)	No association in the total sample (RR= 1.18, 0.57-2.43) or among men (RR= 1.45; 0.67-3.14)
Lallukka et al., 2006[193]	Municipal employees, Finland	Cross-sectional	0	7093	100% female, aged 40, 45, 50, 55, or 60 years, 45% professionals or semiprofessionals	Age, SEP, smoking, alcohol use, BMI, menopause, job demands, job control, work fatigue, mental strain at work, physical strain at work, work-home interface, social support	Weekly working hours >40 vs less	Self-reported angina pectoris symptoms (Rose Questionnaire)	Overtime associated with angina symptoms, OR=1.41 (1.06-1.89)
Holtermann et al., 2010[46]	Employees from 14 companies, Denmark	Pro-spective	30 years	4964	100% male, aged 40-59 years, 55% manual	Baseline healthy cohort. Models adjusted for age.	Weekly working hours 41-45 and ≥46 vs. ≤40	Death due to IHD (ICD-8 diagnoses 410-14, ICD-10 diagnoses I20-I25)	HR 1.59 (1.20-2.11) for 41-45 hours; HR 1.28 (0.91-1.78) for ≥46 hours

6.3 Long working hours and type 2 diabetes

Studies on the association between long working hours and type 2 diabetes are presented in Table 2 in chronological order. Only three studies were found although all of them were prospective. One of them was carried out in the U.S. and two in Japan. A study by Kawakami et al.[105] followed a sample of male industrial workers (n=2194) for eight years and in that study, monthly overtime work of >50 hours was related to incident type 2 diabetes. However, an opposite finding was reported by Nakanishi et al.[199] in their five-year follow-up of male office workers (n=1266): daily working hours of ≥11 were related to lower risk of incident IFG or type 2 diabetes. A study by Kroenke and colleagues[200] in a much larger sample of U.S. female nurses (n=62,574) had a six-year follow-up. Their study showed an association between long working (41 to 60 vs 21-40) and incident type 2 diabetes in the age-adjusted model. However, in the model adjusted for all potential confounding and mediating factors, the association was no longer statistically significant.

In sum, studies on the relationship between long working hours and type 2 diabetes are very scarce. The problem with the Japanese studies is that the outcome was measured at yearly health screenings which restricted the sample followed to those who were employed by the same employer. In two studies, part-time employees were included in the reference group and in the U.S. study, the diagnosis of type 2 diabetes relied on medical records, i.e. it was not possible to identify undiagnosed cases.

None of the studies examined any potential interaction between long working hours and demographic or work-related factors known to be associated with the onset of type 2 diabetes.

Table 2. Summary of the studies on the association between long working hours and type 2 diabetes mellitus

Author(s) and year	Sample, location	Study design	Follow-up time	N	Age, sex and distribution by socio-economic position (SEP)	Potential confounders considered	Working hours measure	Outcome measure	Findings
Kawakami et al., 1999[105]	Industrial workers of an electrical company, Japan	Prospective	8 years	2194	100% men, 18-60 years (78% 18-44 years), 58% machine operators	Age, education, occupation, shift work, job strain, social support, use of technology, BMI, alcohol use, smoking , leisure time physical activity, family history of diabetes	Overtime hours per month (26-50, >50 vs. 0-25 hours)	Yearly screening of diabetes (glucose urine test -> FPG -> 2h OGTT	Monthly overtime of >50 hours associated with incident type 2 diabetes (HR=3.73; 1.41-9.90)
Nakanishi et al., 2001[199]	Office workers, Japan	Prospective	5 years	1266	100% men, aged 35-59 years, 49-70% professionals	Age, occupation, work position, BMI, smoking, alcohol use, eating breakfast, vegetable/fruit consumption, physical exercise, family history of diabetes, blood pressure, fasting plasma glucose, HDL cholesterol, triglycerides	Daily working hours 8-8.9, 9-9.9, 10-10.9, ≥11.0 vs <8 hours	Yearly screening of impaired fasting glucose (IFG), type 2 diabetes	≥11.0 hrs associated with lower risk of incident IFG/type 2 diabetes: RR=0.50 (0.25-0.98) and type 2 diabetes RR=0.30 (0.09-0.94)
Kroenke et al., 2007[200]	A sample of female nurses from 15 states, U.S.	Prospective	6 years	62,574	100% women, aged 29-46 years, all nurses	Age, marital status, number of children, menopausal status, BMI, family history of diabetes, shift work, job strain, work social support, hours at work sitting, hours of work at home, leisure-time physical activity, smoking, alcohol use, trans-unsaturated fat use, glycemic load, caffeine intake, vitamin supplementation, aspirin use	41-60, >60 /week vs. 21-40 /week (ref.)	Self-reported type 2 diabetes verified through medical records	41-60 hours associated with RR 1.24 (0.98-1.57); >60 hours associated with RR 1.14 (0.63-2.07) in the final model

6.4 Long working hours and depression

Studies on the association between long working hours and depression are presented in Table 3 in chronological order. An ecological study by Starrin et al.[201] using macro-aggregated data is not presented in the table. The study reported a positive association between overtime work rate and suicide rate among men and women in Sweden.

The literature search resulted altogether in 30 peer-reviewed empirical studies. Of them, 9 were longitudinal and 21 were cross-sectional. Twelve studies were from Japan, four from Sweden, three from the UK, three from the USA, two from the Netherlands, and one study each from Canada, Denmark, Norway, Australia, Hungary, and Spain. However, in most of the studies, a non-specific *psychological distress* scale was used and in some studies, *psychological burnout* or other correlate of depression which does not directly assess depression or its symptoms, was used.

Of the cross-sectional studies, the majority (13 separate reports) showed a null finding (vs. 9 with a positive finding) between long working hours and depression or its correlates. None of the studies found a negative association. Of the longitudinal studies, the study of Steptoe et al.,[202] had 71 participants and within-subject-analysis of four assessments during six months showed no change in psychological distress in relation to overtime work periods. Shields[42] analysed a random sample of nearly 4000 full time Canadian employees with CIDI interview data and found associations between long (>40) weekly working hours and new-onset major depressive episode among women but not among men. Bildt et al.[203] did not find any association between "frequent overtime work" and incidence of subclinical depressive symptoms or psychological distress in either men or women in their 4-year follow-up study. In their further study[204] with a 24-year follow-up, weekly overtime work was not associated with subsequent depressive disorder either among men or women.

Table 3. Summary of the studies on the association between long working hours and depression and psychological distress

Author(s) and year	Sample, location	Study design	Follow-up time	N	Age, sex and distribution by socio-economic position (SEP)	Potential confounders considered	Working hours measure	Outcome measure	Findings
Oppenheim, 1987[205]	Random sample of music therapists, USA	Cross-sectional	0	239	87% women, mean age 30 years	Number of years at present job	Hours worked per week (continuous)	Burnout (Maslach Burnout Inventory)	No association.
Watanabe et al., 1993[206]	Local government employees working with visual display terminals, Japan	Cross-sectional	0	486	14% female, mean age 33 years,	Not reported.	Hours worked per week (continuous)	Depressive symptoms (SRQ-D)	Depressive employees had longer weekly working hours (61.3 vs. 48.1, $p<0.05$)
Ezoe & Morimoto, 1994[207]	Employees of a manufacturing company. Japan	Cross-sectional	0	2800	24% women, mean age 36 years in men, 31 years in women	Sex-stratified analysis, adjusted for age, marital status, physical health status	Hours worked per day (≥10 vs. less in men, ≥9 vs less in women)	Psychological distress (GHQ-28)	Association among women (β=0.80, $p<0.05$), but not among men
Steptoe et al., 1998[202]	Employees of a department store, UK	Prospective	4 assess-ments in 6 months	71	62% women, mean age 36 years in women, 33 years in men, 52% of women, 41% of men had college education	Not reported.	Working hours during the past week in each assessment	Change in psychological distress (GHQ-28 score) within subject	No association.
Borg & Kristensen, 1999[208]	Random sample of travelling salespeople of the Union of Travelling salespeople, Denmark	Cross-sectional	0	1360	10% female, mean age 42 years, mean number of years of vocational training 4 years	Sex, age, marital status, number of children, education, several work-related factors (e.g. non-day work, nights away home)	Continuous variable (mean hours /week)	Symptoms of psychological distress (derived from SF-36)	Linear association between working hours and psychological distress (β=0.08, $p<.05$). Association attenuated after adjustment for psychosocial work characteristics.

Table 3 cont.

Shields 1999[42]	Random sample of full time workers, Canada	Prospective	2 years	3830	43% women, aged 25-54 years, 42% of men 10% of women blue-collar	Sex-stratified analysis adjusted for age, marital status, education, income, occupation, shift work, work stress	Weekly working hours (35-40, >40)	DSM-IV major depressive episode (MDE), CIDI- interview	Association found among women (OR 2.2) but not among men
Hobson & Beach, 2000[209]	Managers working in two factories, UK	Cross-sectional	0	41	Not reported.	Not reported.	A diary of working hours during a week	Psychological distress (GHQ-30)	No association.
van der Hulst & Geurts, 2001[44]	Sample of postal service employees, Netherlands	Cross-sectional	0	535	5% female, mean age 44 years, 15% in executive position, 62% postmen or drivers	Sex, age, executive position, marital status, parental status	Weekly overtime work (>38h) vs. not	Burnout symptoms (MBI)	No overall association; a combination of overtime with low rewards associated with emotional exhaustion (OR 2.2) and cynicism (OR 3.4).
Bildt et al. 2002[203]	Representative sample of working population in one county, Sweden	Prospective	4 years	420	53% female	Sex-stratified analysis adjusted for age	Overtime work (often vs. not at all /sometimes)	Sub-clinical depression (Nottingham life-quality questionnaire), psychological distress (GHQ-12)	No association with either of the outcome variables.
Tarumi et al., 2002[210]	Office workers of a manufacturing company, Japan	Cross-sectional	0	230	100% male, aged ≥35 years (mean age 45/46 years)	Not reported.	Working hours /week during the last month (35-44, 45-49, ≥50)	Psychological distress (GHQ-12)	No association.
Marchand et al., 2003[211]	Representative sample of residents in Quebec, Canada	Cross-sectional	0	8812	40% female, mean age 36 years, 19% professionals or semi-professionals	Age, sex, shift work, seniority, occupation	Weekly working hours (continuous)	Psychological distress	Association: β=0.007, p<0.01

Table 3 cont.

Michélsen & Bildt 2003[204]	Representative sample of working population in one county, Sweden	Prospective	24 years	367	52% female, 31% of women 33% of men aged 51-58 at follow-up, 55% of women, 69% of men education <9 years	Sex-stratified analysis, age, education, occupation, marital status, children at home, leisure time social life, work stress factors, shift work	Overtime >1 hour /week vs. less	Depressive disorder (DSM-III-R), psychological distress (GHQ-12)	No association found in either sex
Suwazono et al., 2003[212]	Employees of a telecommunication enterprise, Japan	Prospective	4 years	23,837	20% female, age range 20-54 years	Sex-stratified analysis	≤8h, 8-12h, >12h /day	Psychological distress	Association found among men but not among women.
Tarumi et al., 2003[196]	Office workers of a manufacturing company, Japan	Prospective	4 years	453-589	21-26% female, mean age 38-42 years	Sex, age, occupation	≥45 hours vs less	Diagnosis of mental disorder in medical insurance claim records	No association (HR 1.56; .
Tucker & Rutherford, 2005[213]	Train drivers of one train operating company, south of England	Cross-sectional	0	372	100% male, mean age 42 years, all train drivers	Age, length tenure, number of night shifts, smoking, alcohol use, exercise, waist circumference; interaction tested with social support, job maintenance, commitment, pressure to work overtime, worktime control	Weekly working hours (continuous variable)	Psychological distress (GHQ-12)	No main effect, no interaction effects
Nishikitani et al., 2005[214]	Employees of an IT company, Japan	Cross-sectional	0	377	19% women, mean age 28 years (all <40 years), single occupation (IT professionals)	Sex-stratified analysis	Overtime work during a month obtained from employer's records (continuous variable)	Depressive symptoms (HDS), Profile of Mood State; tension-anxiety, anger-hostility (POMS)	Association with depressive symptoms among men and women and anger-hostility among men and women; no association after adjustment for sleep duration and job strain

Table 3 cont.

Table 3 cont.

Dahlgren et al., 2006[215]	Sample of office workers, Sweden	Experi-mental field study, prospective	2 weeks	16	56% women, mean age 46 years, all white-collar	Within subject analysis	a week with 8-hour workdays compared with a week with 12-hour workdays	Exhaustion, irritation	Overtime associated with increased exhaustion and irritation
Grosch et al., 2006[216]	Representative sample of English-speaking adult population, US	Cross-sectional	0	1744	51% female, mean age 41 years, 61% with more than 12 years of education	Sex, age, ethnicity, education	Hours worked within last week (1-34, 35-40, 41-48, 49-69, 70 or more hours)	Poor mental health days in past month (14 or more vs. less than 14)	No association.
Suwazono et al., 2006[217]	Employees of a steel company, Japan	Cross-sectional	0	3 069	100% male	Age, marital status, occupational grade, days off on holidays, living arrangements, health behaviours	Daily working hours as a continuous variable	Irritability, anxiety, depressive feelings	Association with irritability and anxiety but not depressive feelings
Allen et al. 2007[218]	Employees of truck and engine corporations, US	Prospective	4 months	2746	20% female, mean age 46 years, 52% production workers	Age, sex, SEP, baseline mental health, health behaviours	>48 <60 h / ≥60 h vs < 40 h	SF-36 mental health status	No association between long hours and good mental health (β=.12)
De Raeve et al. 2007[219]	Employees from 45 companies, Netherlands	Prospective (transition occurred during the follow-up)	1 year	6271	17% female, Mean age 43 years, 42% highly educated	Sex-stratified analysis adjusted for age, education, functional mobility, psychosocial work characteristics (shift workers excluded)	Transition from 36-40 hours to >40 hours/ week vs. staying in 36-40 hours' group	Psychological distress (GHQ-12)	Transition to long hours not associated with psychological distress either in men (OR 0.79) or in women (OR 1.31)
Nagashima et al., 2007[220]	Employees of a chemical factory, Japan	Cross-sectional	0	715	100% male	Age, marital status, smoking, alcohol use, exercise	Monthly working hours (<199h, 200-219, 220-239, 240-259, 260-279, ≥280)	Self-rated depression scale (SDS), Cumulative Fatigue Symptom Index (subscale of anxiety symptoms)	Working ≥260 and ≥280 hours per month associated with depression (OR 2.75 and 1.43; the latter non-significant), and anxiety (OR 2.28 and 2.51)

Table 3 cont.

Table 3 cont.

Hilton et al., 2008[221]	Employees of 201 large companies, Australia	Cross-sectional	0	60,556	58% female, 39% >45 years, 50% at least graduate degree	Sex-stratified analysis adjusted for age, marital status, no. of children, education, occupation, sector, industry	Expected working hours /week (7 categories) vs. 30-34 hours	Psychological distress (K6)	Expected hours 50-59 and 60+ associated with psychological distress in men (ORs 1.9, 3.9) and women (ORs 1.4, 2.4)
Kleppa et al. 2008[222]	Residents of one county, Norway	Cross-sectional	0	11,541	37% female, age, SEP not reported	Sex-stratified analysis adjusted for education, occupation, income, shiftwork, physical activity	41-48 /49-100 vs. 35-40 in men; 41-100 vs. 32-40 in women	Depression (HADS scale)	Long hours associated with anxiety (OR 1.67, men; 1.44, women) and depression (OR 1.50, men; 1.61, women)
Kopp et al., 2008[223]	Representative sample of economically active population, Hungary	Cross-sectional	0	5863	46% female, aged 18-65	Sex-stratified analysis adjusted for age, education, income, hostility, negative affect, job security, troubles at work, job dissatisfaction	Weekly working hours separately for weekdays and weekend days	Depressive symptoms (BDI-9)	Neither work hours during weekdays nor during weekends was associated with depressive symptoms among men and women
Suwazono et al. 2008[224]	Employees of a steel company, Japan	Cross-sectional	0	3481	12% female, Mean age 45 in men, 37 in women, 40% of men onsite workers, 66% of women office workers	Sex-stratified analysis adjusted for age, occupation, marital status, living arrangements, days off, health behaviours	A continuous variable with 1-hour interval ranging from 7.75 to 12.5	Irritability, anxiety, depressive feelings	Working hours associated with irritability in men (OR 1.22), but not with anxiety or depression in either sex
Artazcoz et al. 2009[225]	Random sample of salaried workers of Catalonia, Spain	Cross-sectional	0	7103	44% female, Mean age 38 years (men), 37 years (women), 60% of men, 45% of women manual workers	Sex-stratified analysis adjusted for age, SEP, marital status, shift work, job contract, domestic work hours, no. of children	41-50 h / 51-60 h vs. 30-40 h	Psychological distress (GHQ-12)	41-50 h OR 1.24 in men, 0.99 in women, both NS; 51-60h OR 2.06 in men, 1.43 (NS) in women

Table 3 cont.

Table 3 cont.

Date et al., 2009[226]	Chinese temporary factory workers in Nagasaki prefecture, Japan	Cross-sectional	0	81	64% female, 36% male, 19-49 years, all factory workers	Multivariate analysis adjusted for significant covariates (age, having an interpreter at the workplace)	Daily and weekly working hours (continuous)	Depressive symptoms (CES-D, 20 items), continuous scale	Daily but not weekly hours associated with depressive symptoms (β=2.59, *p*=0.02)
Otsuka et al. 2009[227]	Random sample of daytime workers, Japan	Cross-sectional	0	1220	40% female, Mean age 42 years (men), 41 years (women)	Sex, age, occupation, employment type, alcohol use	61-65 h/ ≥66 h vs 60 h or less	Negative emotions (4 items: anxious, depressive, restless, irritated; Accumulated Fatigue Checklist)	No association between long hours and negative emotions (estimates not shown)
Takada et al., 2009[228]	Employees from 1509 enterprises, Japan	Cross-sectional	0	4118	31% female, mean age 42 years, 42% managers	Age	Daily working hours: 8-10, >10 vs. ≤8; monthly overtime: 1-45, 46-80, 81-100, >100 vs none; work during holidays (days/month ≥5 vs none)	Depressive symptoms (CES-D self-report scale), suicidal ideation	No associations among men; association between work during holidays and suicidal ideation among women (OR 33.3; 22.4-494.5)

Suwazono and colleagues[212] and Tarumi and colleagues[196] examined Japanese employees using the GHQ-12 score and diagnoses of mental disorders in the records of the employee insurance company. Neither study found an association between long working hours and mental disorders. Dahlgren and her group[215] examined in their experimental field study a sample of Swedish office workers (n=16) and found using within-subject analysis that overtime work (12-hours-a-day workweek) was associated with increased exhaustion and irritation compared with a 8-hours-a-day workweek. De Raeve and others[219] assessed whether a transition from 36-40 hours to >40 hours/ week vs. staying in the 36-40 hour group predicted psychological distress and found no association. However, measurements of transition and change in psychological distress were overlapping.

In sum, the findings are mixed, with some studies showing an association between long working hours and depression or its correlates while others do not. However, considerable heterogeneity in the study samples, assessment of exposure, outcome, and potential confounding factors was revealed in the reviewed studies. The only prospective studies using interview-based clinically verified diagnosis of depression were Shields[42] (association found among women) and Michelsen and Bildt,[203 204] (no association). However, the studies of Michelsen and Bildt included also cases of subclinical depression.

Possible interaction effects between demographic factors and working hours associated with depression were reported in none of the studies, but two studies examined the interaction between working hours and work characteristics. Van der Hulst and Geurts, 2001[44] examined interaction between rewards at work and working hours associated with burnout symptoms and found an association in low-reward-long-hours' jobs compared with high-reward-normal-hours' jobs. Tucker & Rutherford, 2005[213] assessed the interaction between long working hours and social support, job maintenance, commitment, pressure to work overtime, and work time control and found no significant interactions.

6.5 Long working hours and sleep disturbances

Altogether 16 studies were identified on long working hours and sleep disturbances (Table 4). Six were based on Japanese employees, other study countries were Sweden (3 studies), France (2), Finland (2), South Korea (1), Spain (1), and the U.S. (1). One study was prospective with a five-year follow-up,[229] one study was an experimental field study[215] in which a sample of employees was followed for two weeks, and the remaining 14 studies were cross-sectional. The prospective study of Ribet and Derriennic[229] reported that past history, but not baseline overtime work, increased the risk of new-onset sleep disturbance, and the field study of Dahlgren et al.[215] found sleep duration to decrease during a week doing overtime compared with a no overtime week within the same subjects.

Cross-sectional studies focussing on sleep length reported a consistent association between long working hours and *short sleep duration*. However, the evidence on long working hours and *sleep disturbances* seems to be mixed. Studies including Japanese manufacturing employees,[207] Swedish[230] and French[231] private sector employees, and a random sample of the Swedish[232] working population did not find any association between long working hours and sleep disturbances while a study of Japanese civil servants,[233] a study on Finnish information technology professionals[234] and a random sample of Finnish twins[235] found an association. None of the studies reported a negative association between long working hours and sleep disturbances.

However, large heterogeneity in the study samples, assessment of exposure, outcome, and potential confounding factors characterise the reviewed studies. The problem, again, in cross-sectional studies is that direction of causality can not be verified. None of the studies examined any potential interaction between long working hours and demographic or work-related factors associated with sleep disturbances.

Table 4. Summary of the studies on the association between long working hours and sleep disturbances

Author(s) and year	Sample, location	Study design	Follow-up time	N	Age, sex and distribution by socioeconomic position (SEP)	Potential confounders considered	Working hours measure	Outcome measure	Findings
Ezoe & Morimoto, 1994[207]	Employees of a manufacturing company, Japan	Cross-sectional	0	2800	24% women, mean age 36 years (men), 31 years (women)	Sex-stratified analysis, adjusted for age, marital status, physical health status	Hours worked per day (≥10 vs. less in men, ≥9 vs less in women)	Sleep disturbances and anxiety (GHQ-28)	No association.
Maruyama & Morimoto, 1996[236]	Intermediate managers from 110 companies, Japan	Cross-sectional	0	6536	100% men	Stratified analysis in different age groups	≥10 hours / day vs. less	Short sleep (<7 hours)	Association with shorter sleeping hours
Ribet & Derriennic 1999[229]	Random sample of employees listed by occupational physicians, France	Prospective	5 years	16,833	Not reported.	Age, sex, education, physical complaints, leisure-time activity etc.	Work week currently / in the past >48 hours vs. never worked longer than 48 hours	Sleep disturbances (5 items)	Long working hours in the past (OR 1.2) but not at present (OR 0.9) predicted sleep disturbances
Hublin et al., 2001[235]	Representative sample of twins, Finland	Cross-sectional	0	12,423	54% women, age 33-60 years, tertiary education (15% men, 27% women)	Age	Weekly paid working hours <40, ≥40 vs none, weekly paid and at home working hours 25-35, 35-45, 45-54, 55-64, 65-74, ≥75 vs <25	Insufficient sleep (≥1 hour difference between needed and actual sleeping hours)	Paid hours ≥40 associated with insufficient sleep in women (OR 1.24; 1.05-1.46), paid+home work ≥75 hours associated in men (OR 2.49; 1.36-4.57)
Kageyama et al. 2001[237]	Employees of a publishing company, Japan	Cross-sectional	0	283	10% female, 28% 50 years or more, 63% sales persons	Age, workload, commuting time	Overtime work >79 hours vs 0-59 hours in the past 3 months	Required sleep length, actual sleep length, sleep debt (hours)	Association with actual sleep length (β=-0.12) and sleep debt (β=0.12) but not with required sleep length (estimate not reported)
Park et al. 2001[238]	White-collar employees of three electronic companies, South Korea	Cross-sectional	0	238	100% men, mean age 32 years, all white-collar	Age	Weekly working hours (<60, 60-69, ≥70 hours)	Sleep length (mean hours /day)	Association with shorter sleep (6.0 vs 6.4 hours, *p*=0.001)

Table 4 cont.

Liu & Tanaka, 2002[35]	Patients admitted to hospital for acute myocardial infarction with controls from residential registers, Japan	Case-control	1 year, retro-spective	260 cases, 445 controls	Matched by age, sex, and residence	Not reported.	41-60 hours, ≥61 hours / week vs. ≤41 hours	Sleep deprivation (days/week of <5 hours sleep); sleeping hours in workdays	Association with sleep deprivation (p=0.006) and sleeping hours in cases but not in controls
Åkerstedt et al. 2002[232]	Population sample, Sweden	Cross-sectional	0	58,115	48% female, 49% 30-49 years, 34% higher white collar	Sex, age, occupational grade, long-standing illness, shift work	≥ 50 hours/week vs. < 50 hours	Disturbed sleep	No association.
Åkerstedt et al. 2002[230]	Employees of 40 companies, Sweden	Cross-sectional	0	5720	43% female, 44%>45 years, 45% blue collar	Sex, age, occupational grade, work stress, shift work, health behaviours	>15 hours overtime /week vs. 35-40 weekly hours with no overtime	Disturbed sleep, not rested, difficulties awakening	Overtime work neither associated with disturbed sleep (OR 0.64), not rested (OR 1.18) nor difficulties awakening (OR 0.90), crude estimates
Tarumi et al., 2004[239]	Office workers of a manufacturing company, Japan	Cross-sectional	0	286	38% female, mean age 31 years, all white collar	Not reported.	Working hours /day during the past month	Sleeping hours	Association with less sleeping hours (r=-0.18, p<0.01)
Dahlgren et al., 2006[215]	Sample of office workers, Sweden	Experimental field study, prospective	2 weeks	16	56% women, mean age 46 years, all white-collar	Within subject analysis	A week with 8-hour workdays compared with a week with 12-hour workdays	Sleep duration	Overtime associated with shorter sleep duration
Sekine et al. 2006[233]	Civil servants, Japan	Cross-sectional	0	3556	33% female, Mean age 43 years 15% of men and 2% of women managers/ professionals	Sex-stratified analysis adj. for age, occupational grade, work characteristics, shift work, domestic role, family-work conflicts, longstanding illness	> 11 hours/day vs. 7-9 hours	Quality of sleep (PSQI, 17 items)	Long hours associated with poor sleep quality among men (OR 1.49) and women (OR 2.02)

Ansiau et al. 2008[231]	Sample of employees listed by occupational physicians, France	Cross-sectional	0	2337	51% female, 32 years (31%), 42 years (34%), 52 years (31%), 62 years (3%) mean 11 years of education	Sex, age, shift work, workload, type of activity at work	> 10 hours/day vs. < 8 hours	Sleep length, awakenings, difficulty getting back to sleep, sleep dis-satisfaction	Long hours associated with shorter sleeping hours (β= -24.1) but not with other sleep indicators
Kivistö et al., 2008[234]	Sample of information technology professionals, Finland	Cross-sectional	0	2334	29% female, 30% aged 50-69 years, 23% software designers, 23% managers or project managers	Age, sex, early/late-riser type	Working hours / week (continuous)	Sleep debt (differnce between need and actual sleep), insomnia (sleep complaints)	Long hours associated with sleep debt (β= 0.11) and insomnia (β =0.05)
Artazcoz et al 2009[225]	Random sample of salaried workers of Catalonia, Spain	Cross-sectional	0	7103	44% female, Mean age 38 years (men), 37 years (women), 60% of men, 45% of women manual workers	Sex-stratified analysis adjusted for age, SEP, marital status, shift work, job contract, domestic work hours, no. of children	41-50 hours/ 51-60 hours vs. 30-40 hours	Short sleep (6 hours or less)	41-50 hours associated with short sleep in men (OR 1.30) but not in women (OR 1.00); 51-60 hours associated with short sleep in both (OR 1.42 in men, 2.21 in women)
Krueger & Friedman, 2009[240]	Random sample of U.S. adults	Cross-sectional	0	110,441	Sex distribution not reported (mean age 45-50 years)	Age, sex, race, number of children, pregnancy, marital status, education, income, physical activity, smoking, alcohol use, physical health, pain, mental health, BMI, activity limitations	35-40 hours, ≥41 hours /week vs. 1-34 hours	Short sleep (6 hours or ≤5 hours vs 7 hrs) and long sleep ≥9 hrs vs 7 hrs	≥41 hours associated with OR=1.52 (1.34-1.72) of ≤5 hrs vs 7 hrs; OR=1.32 (1.21-1.43) of 6 hrs vs 7 hrs; OR= 0.45 (0.39-0.51) for long sleep, i.e. ≥9 hrs vs 7 hrs

Table 4 cont.

Magee et al., 2009[241]	Random sample of residents of New South Wales aged 45+, Australia	Cross-sectional	0	49,405	53-59% female.	Age, sex, residence, birth country, education, marital status, smoking status, alcohol use, physical activity, BMI, physical disease, hypertension, cholesterol, mental disorder, self-rated health	>40 weekly hours vs. 35-40 hours	Short sleep (6 hours or <6 hours) and long sleep ≥9 hrs vs 7 hrs	>40 hours associated with OR=1.17 (1.08-1.28) of short sleep (6 hrs vs 7 hrs but not <6 hrs vs 7 hrs); OR= 0.65 (0.58-0.73) for long sleep, i.e. ≥9 hrs vs 7 hrs
Knutson et al., 2010[242]	Eight national samples of U.S. adults 1975-2006	Cross-sectional	0	73,072	52 to 56% female, mean age 43 to 50 years, 14 to 28% college graduates	Stratified analysis among full-time and part-time employees adjusted for age, sex, education, year, day of week	Minutes spent at work (one-day diary)	Short sleep < 6 hours	Short sleepers full-time workers spent a mean of 143 minutes more at work than the others (78 minutes more among part-time workers)

6.6 Gaps in the existing evidence

The reviewed evidence is not without limitations. The major gap in previous studies relates to study design: only a minority of the studies were longitudinal with the exception of all three studies with type 2 diabetes as an outcome which were prospective. Studies on CHD were mainly based on a case-control design. The major problem in case-control studies and cross-sectional studies is the assessment of working hours at the time of or retrospectively just prior to the assessment of outcome; that is, it is possible that the disease itself, here CHD, depression or sleeping problems, influences the patient's work behavior (i.e., hours worked) and perception or recall of working hours. Employees with pre-existing health problems may tend to increase their working hours in order to get their tasks done, or decrease their working hours in order to prevent worsening of symptoms. Mixed previous findings may also be due to high heterogeneity in both exposure and outcome measurements. Some of the studies included shift-workers, and in those studies it is difficult to separate effects of the work time schedule from the effect of long working hours. In many studies, the reference group included also those who worked part-time.

The three prospective studies on CHD published so far failed to show any consistent relationship, however, the outcome in two of them was nonspecific, including overall CVD. Furthermore, one of those two studies had a sample of treated hypertensive patients and the other one used insurance claim records which restricted the follow-up to those who were employed with the same employer during the follow-up time. In one study showing no association, the follow-up time was as long as 30 years. Very long follow-up periods are problematic since longer follow-ups tend to increase within-participant variation in work-related exposures (such as working hours) and potentially reduce the precision of the prediction.[82]

Regarding studies with type 2 diabetes as an outcome, only three studies were published to date. The problem in two of them relate to the outcome measured at yearly health screenings which restricted the sample to those who stayed with the same employer. In the third study, part-time employees were included in the reference group and the diagnosis of type 2 diabetes relied on medical records, which does not capture undiagnosed cases.

Studies on depression were mainly cross-sectional and used self-reported symptoms of depression or psychological distress rather than interview-based clinically verified diagnosis of depression. There were only three studies using diagnosis of depression. These found either no association or an association only among women. However, a problem in earlier studies is that long hours were dichotomised by working hours of 40 hours or overtime of >1 hours vs. less, which do not necessarily catch excessive overtime work. In one study, cases of subclinical depression were included in the outcome.

Similarly, studies on sleep disturbances were, with rare exceptions, cross-sectional and none of the previous studies has differentiated specific outcomes of symptoms of insomnia, such as difficulty falling asleep, difficulty staying asleep, early waking and waking without feeling refreshed. Furthermore, no previous studies had addressed this issue using repeat measurements of working hours at two time points, treating them as indicators of long-term or recurrent exposure to long working hours.

Specifically in the British context to date, only studies with small sample sizes (n=41, n=71, n=372) have been published on this issue. Finally, interaction between possible moderators, such as demographic factors and work-related psychosocial factors, was tested only in two cross-sectional studies with relatively small sample sizes (max n=535) and in one study examining physical fitness as a moderator.

6.7 Summary

The vast majority of earlier research on long working hours and health has been cross-sectional. Most of these studies found an association between long working hours and CHD, however, many null findings with symptoms of depression and sleep disturbances have been reported. Only three studies on long working hours and type 2 diabetes have been published, indicating a positive, null, and a negative association. The main shortcomings in previous work are lack of prospective studies, lack of specific outcomes, and lack of studies using clinical assessments. In studies on working hours and CHD, a major shortcoming relates to the lack of prospective studies with a specific outcome, while problems in studies on type 2 diabetes relate to selective drop-out of participants and those with undiagnosed conditions. Studies on depression need prospective designs with a standardised interview-based diagnosis-specific outcome assessment, and studies of sleep disturbances need outcome-specific prospective study designs. There are also major shortcomings in selection of employees (e.g. part-time or shift-workers should not be included) as well as assessment of working hours (scaling of exposure to long working hours is needed). Interactions between possible moderators and working hours have been tested rarely and only using small study samples with relatively limited statistical power.

Chapter 7

The present study

7.1 Study aims and objectives

The principal aim of this study is to extend understanding of the relationship between long working hours and health in office workers using existing data from British civil servants participating in the Whitehall II study. The aim is also to address gaps in previous evidence by using a prospective study design, and validated outcome measures, and assessing, when possible, interaction effects between selected socio-demographic factors, lifestyle factors, and work characteristics and working hours predicting health outcomes, as introduced in the model by Caruso and her colleagues[31] (Figure 4, p. 24). The objectives of the thesis include the following specific study questions:

1.) Are long working hours associated with the onset of CHD, type 2 diabetes, depression, and sleep disturbances?

2.) Do biological risk factors, health behaviours, or work-related psychosocial factors explain (i.e. mediate) the association between long working hours and health outcomes?

3.) Do socio-demographic factors, health behaviours, or work-related psychosocial factors influence (i.e. moderate) the association between long working hours and health?

According to the model by Caruso and her colleagues,[31] three clusters of interactions were tested: socio-demographic factors, health behaviours, and work

characteristics. These can be considered risk-eliciting characteristics that either cause or strengthen the association or resources that act as buffers against the adverse effect of long hours on health. For the study on sleep disturbances, the effect of repeat exposure to long working hours was examined. This was the only study cohort in the present thesis that allowed assessment of working hours at two time points.

Chapter 8

Methods

8.1 Introduction

This chapter presents methods used in the present thesis. First, a general description of the Whitehall II study participants and procedure is presented. After this, methods are presented separately for each outcome; first, methods for Study 1 (long working hours and CHD) are presented, followed by methods for Study 2 (long working hours and type 2 diabetes), methods for Study 3 (long working hours and depression), and finally, methods for Study 4 (long working hours and sleep disturbances).

8.2 Participants and procedures

8.2.1 The Whitehall II study population

The Whitehall II study was set up in the early 1980's to examine reasons for the social gradient in health and disease.[243] The original broad research aim has been much elaborated but remains the central theme 20 years later. The target population for the Whitehall II study was all civil servants (men and women) aged 35–55 years working in the London offices of 20 Whitehall departments in 1985–88. The achieved sample size was 10,308 people: 3413 women and 6895 men. The participants, who were from clerical and office support grades, middle-ranking executive grades, and senior administrative grades, differ widely in salary. The response rate in the baseline assessment was 73%. Since recruitment there have been 9

further data collection phases (Table 5; for details, see Marmot and Brunner[243]). Written informed consent was gained from all participants. The University College London Medical School Committee on the Ethics of Human Research approved the protocol.

Table 5. Data collection phases in the Whitehall II study. Source: Marmot and Brunner, 2005[243]

Phase	Dates	Type	Participants (n)	Response rate (%)
1	1985-88	Screening & questionnaire	10 308	73
2	1989-90	Questionnaire	8 133	79[a]
3	1991-93	Screening & questionnaire	8 637	86[a]
4	1995-96	Questionnaire	8 629	84[a]
5	1997-99	Screening & questionnaire	7 830	76[a]
6	2001	Questionnaire	7 344	71[a]
7	2003-04	Screening & questionnaire	6 967	68[a]
8	2006	Questionnaire	7 173	70[a]
9	2007-09	Screening & questionnaire	6 761	66[a]
10	2011	Questionnaire	Underway	

[a] Response rate of the phase 1 respondents.

8.2.2 The Whitehall II data collection

The Whitehall II cohort is invited to the research clinic at approximately 5-year intervals, and a postal questionnaire is sent to participants between clinic phases (Table 5). A self-administered questionnaire was posted to participants at their place of work at phase 1, and at home in subsequent phases. Ideally, respondents completed the questionnaire and returned it when they attended the screening examination. Questionnaires were checked for completeness and validity during screening by an interviewer who sought missing information or clarification. At phase 7, home visits by nurses were offered for the first time to participants unwilling or unable to travel to the clinic. A brief telephone questionnaire is

administered to those who decline clinic and full questionnaire participation at each phase. Follow-up for mortality through the National Health Services (NHS) Central Registry provides the date and cause of death (99.9% of participants flagged).

In the medical examinations (phases 1, 3, 5, 7, and 9) the following data have been collected from all participants: weight, height, blood pressure, waist-hip ratio, electrocardiogram (ECG), lipids (total cholesterol, HDL-cholesterol, triglycerides, fasting and post-load glucose and insulin (exclusive of phase 1), genotype, fibrinogen, interleukin-6, and C-reactive protein (CRP). However, not all self-reported and all clinical data have been collected at each phase. Some of the measurements (for example CRP) were introduced for the first time at phase 7. Although data on CHD and type 2 diabetes were collected throughout the follow-up, working hours were measured at phases 3 (1991–1993) and 5 (1997–1999), clinically assessed depression was measured at phase 5 only, and sleep disturbances were measured at phases 5 and 7 (2003–04), thus, restricting the study sample of the present thesis to certain phases.

Data quality was ascertained by double entry of questionnaire data, clinical screening data and laboratory test results. All variables were subjected to range and validity checks and in cases where ambiguities could not be resolved were set to missing. However, the number of missing values in responses was low.

Non-respondents to all phases of the Whitehall II study were followed up by two reminder letters and telephone contact when possible. Persistent non-respondents were also mailed by recorded delivery. Invitations to participate in subsequent phases after phase 1 were sent to all 10,308 original participants each time, with the exception of those known to have died or moved abroad (if the address was known). Thus, non-respondents to all phases included also those who had died and those who could not be traced.

8.2.3 The present study populations

As different outcome measures were assessed at different study phases and had different proportions of missing data, the present thesis includes four different study populations according to the four study questions:

1.) Study 1 with CHD outcomes;

2.) Study 2 with type 2 diabetes mellitus outcomes;

3.) Study 3 with major depressive disorder outcome;

4.) Study 4 with sleep disturbances outcomes.

The forthcoming paragraphs will deal each study separately by presenting sample selection, and methods for each study.

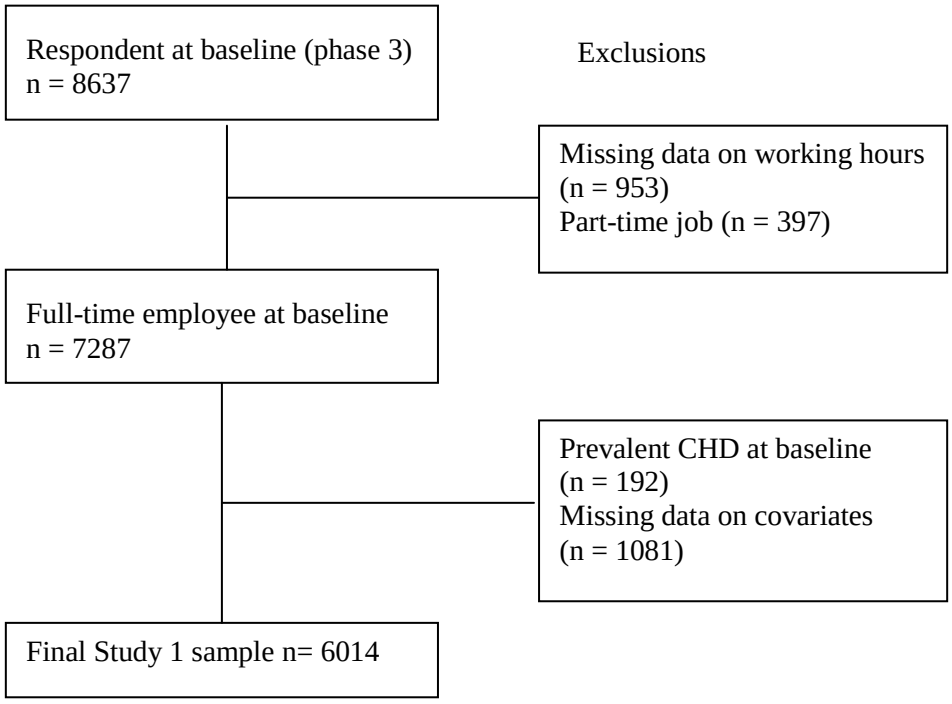
8.3 Study 1: Coronary heart disease

8.3.1 Sample selection

The question on working hours was introduced to the study for the first time at phase 3 (1991-93) which is the baseline for the study on the association between working hours and incident CHD. Of the 8637 participants at that phase, 7684 (89%) were employed and responded to the question on working hours (Figure 7). Of them, 397 (5%) worked part time (less than 7 hours / day) and were excluded from the analysis, leaving a sample of 7287 participants. Out of these, 192 had prevalent CHD at baseline and data were missing on at least one of the covariates for further 1081 participants and were also excluded. Thus, the final sample comprised 6014 participants (4262 men, 1752 women) aged 39 to 61 years

at baseline (phase 3) who were followed until phase 7 (2003-04) which is the most recent phase for which CHD data were available for this thesis.

Figure 7. Sample selection procedure for Study 1 (Long working hours and incidence of CHD)



To assess whether the present study sample at baseline (phase 3) was different from that of the original baseline sample (phase 1), and from the full compliment of phase 3 full time employees (n=7287), Study 1 variables (socio-demographic factors, psychological factors, health behaviours, and working hours at phase 3) were compared according to participation at phase 1, phase 3 full time employment and phase 3 final sample (Table 6). The table shows that dropping out was more common in women, employees with low occupational grade, smokers, those who did not consume fruits and vegetables daily, and those who exercised less than 1.5 hours a week. However, there were no major differences between the phase 3 full-time employed sample and the final phase 3 sample with information of all covariates and exclusion of CHD cases and no difference was found in working hours between phase 3 full-time employees and those in the final phase 3 sample, either.

Table 6. Distribution of the *phase 1 variables* for phase 1 respondents, phase 3 full-time employees, and Study 1 final sample at baseline (phase 3). Figures are n (%)

Variable	(1) Phase 1 respondents (n= 10,308)	(2) Phase 3 full-time employees (n=7287)	(3) Study 1 final sample[a] (n=6014)
Sex			
Men	6895 (67)	5131 (70)	4262 (71)
Women	3413 (33)	2156 (30)	1752 (29)
Occupational grade			
High	3028 (29)	2285 (31)	1924 (32)
Intermediate	4943 (48)	3647 (50)	3055 (51)
Low	2337 (23)	1355 (19)	1035 (17)
Marital status			
Married/cohabited	7608 (74)	5487 (76)	4521 (75)
Non-married/cohabited	2662 (26)	1775 (24)	1478 (25)
Psychological distress			
No	7445 (73)	5296 (73)	4387 (74)
Yes	2744 (27)	1923 (27)	1582 (27)
Type A behaviour			
Low	3116 (31)	2128 (30)	1833 (30)
Moderate	3612 (36)	2559 (36)	2169 (36)
High	3223 (32)	2371 (34)	2012 (33)
Sleeping hours /night			
6 or less	3331 (33)	2317 (32)	1897 (32)
7-8	6832 (67)	4877 (67)	4045 (68)
9 or more	101 (1)	58 (1)	48 (1)
Smoking			
Never	5062 (50)	3690 (51)	3142 (53)
Ex	3274 (32)	2394 (33)	2029 (34)
Current	1883 (18)	1142 (16)	803 (13)
Alcohol use (units/wk)			
0	1873 (18)	1195 (17)	967 (16)
>0 ≤ 14 / 21 (women/men)	6739 (66)	4859 (67)	4047 (68)
> 14 / 21 (women/men)	1602 (16)	1172 (16)	955 (16)
Daily fruit and vegetable consumption			
Yes	5978 (58)	4288 (59)	3594 (60)
No	4297 (42)	2978 (41)	2406 (40)
Moderate / vigorous exercise (hrs /wk)			
<1.5	2713 (28)	1802 (26)	1458 (25)
≥1.5	7083 (72)	5175 (74)	4329 (75)
Working hours /day[b]			
7-8	n.a.	3966 (54)	3256 (54)
9		1490 (20)	1247 (21)
10		1081 (15)	894 (15)
11-12		750 (10)	617 (10)

[a] Participants with no baseline CHD and full data on covariates.
[b] Data derived from phase 3 survey.

8.3.2 Measures

Working hours at baseline (phase 3) were assessed with the following question: "On an average weekday, approximately how many hours do you spend on the following activities (if applicable): Work (daytime and work brought home)?" Response alternatives to be ticked ranged from 1 hour to 12 hours. The following categorical measure of hours worked was formulated: standard hours (7-8); 9 hours; 10 hours; 11-12 hours. The first two categories (7 and 8 hours) were collapsed to form a group of standard hours and the last two categories were collapsed due to relatively low number of respondents working 11 and 12 hours a day (Table 7).

Table 7. Distribution of daily working hours among Study 1 sample at baseline

Daily working hours	n (%)
7	1041 (17)
8	2215 (37)
9	1247 (21)
10	894 (15)
11	318 (5)
12	299 (5)
Total	6014 (100)

The prevalence of CHD was assessed at each phase of the Whitehall II study. For this study, incidence was assessed between phases 3 and 7, a mean follow-up of 11.2 (S.D. 2.7) years. Prevalent cases by phase 3, determined by using a procedure similar to that for incident CHD, were excluded from the analysis. Participants were flagged by the British National Health Service (NHS) Central Registry, who provided the date and cause of all deaths, classified as coronary if ICD-9 (*International Classification of Diseases*, 9th

edition)[47] codes 410–414 or ICD-10 (*International Classification of Diseases*, 10th edition)[48] codes I20–I25 were present on the death certificate. Non-fatal CHD included first nonfatal myocardial infarction (MI) or first definite angina. Non-fatal MI was defined following MONICA (Multinational Monitoring of Trends and Determinants in Cardiovascular Disease) criteria[244] based on study electrocardiograms (ECGs), data obtained from hospital records (acute ECGs, cardiac enzymes) during the acute heart attack (Figure 8, p. 86).

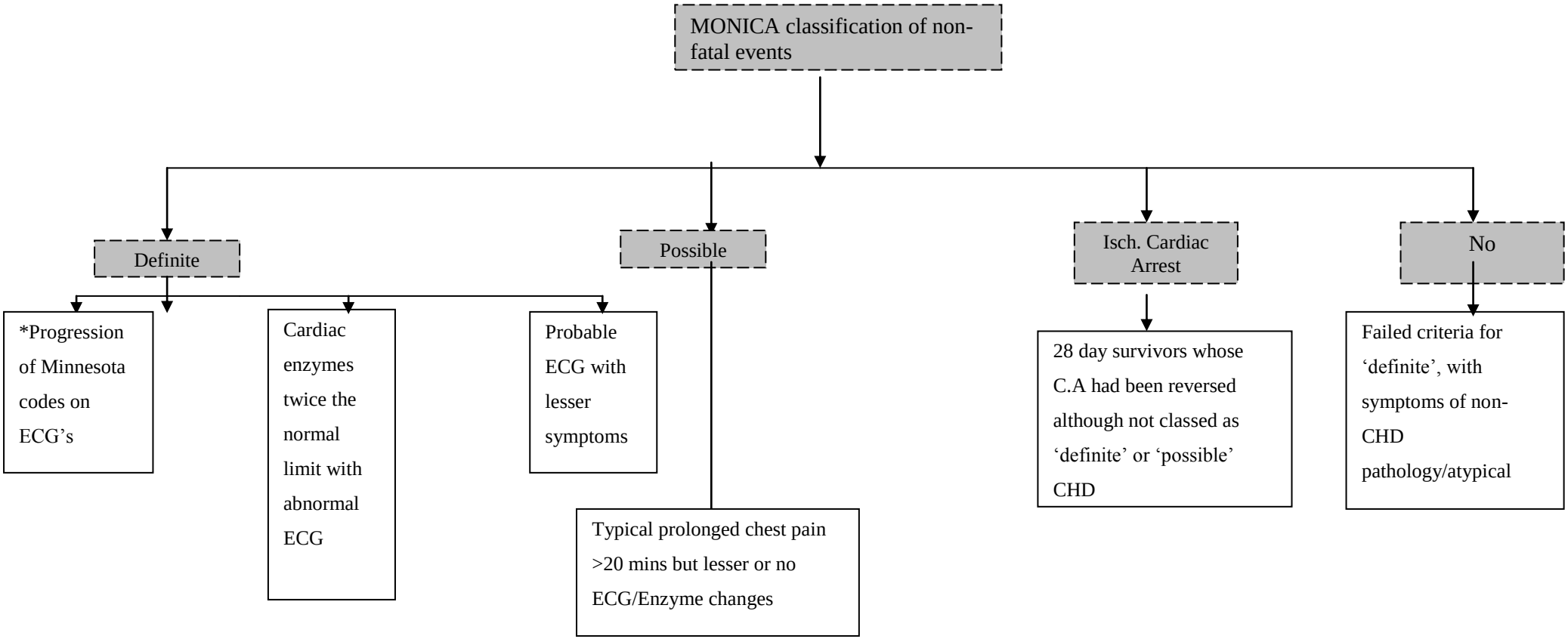
In the study clinic, resting ECGs were recorded onto magnetic tape using a Siemens 'Mingorec' electrocardiograph. Tapes were analysed using Minnesota codes[245] at Professor Peter Macfarlane's laboratory in the Department of Medical Cardiology, University of Glasgow, U.K. Classification was carried out independently by two trained coders, with adjudication in the event of disagreement.

Prevalent and incident angina was first identified by the Rose Questionnaire[245] and verified by comparing the information with medical records, nitrate medication use for which data were obtained from the surveys, or abnormal results on a resting ECG, an exercise ECG, or a coronary angiography (the latter data derived from hospital records).

The Rose Questionnaire defines angina according to previously established criteria, i.e. pain that comes on exertion, that causes the person to stop or slow down and goes away within 10 minutes. The pain is located over the sternum or in both left chest and arm. The case identification required an appropriate reply to each part of the questionnaire, i.e. failure to complete any of the first two questions, the presence of pain and its relation exertion, led to a missing value.

Two outcomes were examined: 1) Incident fatal CHD, non-fatal myocardial infarction, or definite angina pectoris (yes/no); 2) Incident fatal CHD or non-fatal myocardial infarction (yes/no).

Figure 8. MONICA classification[244] of non-fatal CHD events



* Progression from no Q wave to definite Q wave.
* Lesser Q wave progression combined with ST segment depression, developing ST segment elevation, or progressive T wave inversion
* Persistent ST elevation with progressive T wave inversion on sequential daily ECG's

Covariates included characteristics that may be either confounding or mediating factors in the association between long working hours and CHD. Age was requested in the questionnaire at phase 1 by asking the date of birth and using that information, age at phase 3 participation date was calculated. Other socio-demographic factors were derived from the survey questionnaires; sex, marital status, and socioeconomic position (SEP) indicated by British civil service occupational grade.[243]

Employment grade in the Whitehall II study is a comprehensive marker of socioeconomic position and is related to salary, social status and level of responsibility at work. The civil service identifies 12 non-industrial grades that, in order of increasing salary, comprise clerical assistant, clerical officer, executive officer, higher executive officer, senior executive officer, and seven 'unified grades'.[243] Other professional and technical staff were assigned to these grades on the basis of salary. For analysis, unified grades 1–6 were combined into one group and the bottom two clerical grades into another, producing six categories; category 1 represents the highest status jobs and category 6 the lowest.

Marital status included altogether five response alternatives: married, cohabiting, widowed, divorced, and single. A dichotomous variable (married/cohabited vs other) was derived from the responses.

In addition to age, sex, occupational grade, and marital status, established conventional risk factors for coronary heart disease[49 56] assessed at baseline (phase 3) included prevalent diabetes, blood pressure, HDL and LDL cholesterol levels, triglycerine level, body mass index (BMI), smoking and physical inactivity. In addition, alcohol consumption,[246] daily fruit and vegetable intake,[247] sleeping hours,[162] psychological distress,[63] type A behavior pattern,[20 68 69] job demands and decision latitude at work, [68 74 82-85] and sickness absence[248] were included as potential risk factors.

The clinical examination at baseline included an examination of impaired fasting glucose (IFG) and a 2-hour 75g oral glucose tolerance test (IGTT) from which presence of different forms of type 2 diabetes was defined (see a more detailed description on page 95):

1.) *Diabetes*: a fasting glucose ≥7.0 mmol/L or a 2-hour postload glucose ≥11.1 mmol/L or self-reported diabetes or use of diabetic medication;

2.) *Prediabetes*, classified as impaired fasting glucose (fasting glucose between 5.6 and 6.9 mmol/L) or impaired glucose tolerance (2-hour postload glucose between 7.8 and 11.0 mmol/L).

During the clinical examination, systolic and diastolic blood pressure was measured twice while seated after a 5 minute rest using the Hawksley random-zero sphygmo-manometer.[249] Readings were tabulated to the nearest 2 mmHg. Means for the two measurements for systolic and for diastolic blood pressure were used in the analyses.

Fasting status (≥8 hours; those who participated in the afternoon had a light fat-free breakfast and fasted ≥5 hours) serum HDL and LDL cholesterol and triglycerides were obtained by venepuncture of the left anticubital vein using a tourniquet. Blood was collected into plain and fluoride Sarstedt (Neumbrecht, Germany) monovettes. Serum for lipid analyses was refrigerated at −4°C and assayed within 72 h.[250] Total cholesterol (to be used for calculation of LDL-cholesterol) was determined by an enzymatic procedure using the CHOD–PAP method (referring to a colorimetric analysis which is a method of determining the concentration of a chemical element or chemical compound in a solution with the aid of a color reagent). Serum HDL cholesterol concentrations were measured from the supernatant after the precipitation of non-HDL-cholesterol with dextran sulphate–magnesium using the CHOD–PAP method.[251] Serum triglyceride was determined by the enzymatic colorimetric method (GPO–PAP). The concentration of LDL-cholesterol was calculated from total cholesterol, HDL-cholesterol and triglycerides (using the Friedewald formula when serum

triglycerides were lower than 4.5 mmol/L).[252] Technical error was estimated by assaying blinded duplicate samples for 5% of subjects. Coefficients of variation were 2.0–6.6%.

Body Mass Index (BMI) was calculated from measurements of weight and height as weight (in kilograms) divided by: height (in metres) multiplied by height (in metres). Height was measured to the nearest 0.5 cm using a standard metal stadiometer with feet together and the head in the Frankfort plane position.[249] Weight was measured to the nearest 0.1 kilograms using a pair of Soehnle digital S electronic scales. Participants were dressed only in underpants and socks while the weight measurement was taken.

The following measures were based on responses to the questionnaire: smoking status, alcohol consumption, exercise level, daily fruit and vegetable consumption, psychological distress, sleeping hours, and sickness absence.

Information on smoking was requested as follows: *"Do you smoke cigarettes now?"*. Information on ex-smoking was derived from previous surveys (i.e. those who reported quitting smoking at phase 1 or phase 2 surveys or who were smokers in either phase but no longer at phase 3 were classified as ex-smokers).

Alcohol consumption was assessed by asking the participants to report the number of alcoholic drinks (spirits, wine, and beer) they had consumed in the last 7 days. This was divided into ‘measures’ of spirits, ‘glasses’ of wine and ‘pints’ of beer. In the United Kingdom a standard measure of spirit and a small glass of wine are considered to contain 8 g of alcohol, while a pint of beer typically contains 16 g of alcohol. The amounts reported were converted to units of alcohol per week which was then classified into three categories: none; >0 to 14 (women) / 21 (men) units; more than 14/21 units).[253]

Exercise level was assesses with the following questions: "*How often do you take part in sports or activities that are mildly energetic, moderately energetic or vigorous?* Then there were descriptions provided for each level of exercise: a) Mildly energetic (e.g. walking, woodwork, weeding, hoeing, bicycle repair, playing darts, general housework); b)

Moderately energetic (e.g. scrubbing, polishing car, dancing, golf, cycling, decorating, lawn mowing, leisurely swimming); c) Vigorous (e.g. running, hard swimming, tennis, squash, digging, cycle racing). Then it was requested: "*Please give average number of hours per week you spend in such sports or activities"*. From the responses, a dichotomous variable ≥1.5 vs less than 1.5 hours of moderate or vigorous exercise per week was formulated.[254]

Daily fruit and vegetable intake was assessed by the following question: *"How often do you eat fresh fruit or vegetables?"* with response alternatives: *seldom or never; less than once a month; 1-3 times a month; 1-2 times a week; 3-4 times a week; 5-6 times a week; daily; 2 or more times a day*. Daily fruit and vegetable intake was derived by collapsing the first six categories to form a "no" category and the last two categories to form a "yes" category.[254]

Sleeping hours were requested using the following question: "*On an average weekday, approximately how many hours do you spend on the following activities (if applicable):..... Sleep?"* Response alternatives to be ticked ranged from 1 hour to 12 hours. Three categories of sleep (short, normal and long sleeping hours) were then calculated: 6 hours or less, 7-8 hours, 9 hours or more), as in a previous study showing associations with mortality.[162]

In each phase of the Whitehall II study, the 30-item General Health Questionnaire (GHQ-30)[121] was used to assess symptoms of psychological distress. Respondents are asked to select one of four answers, typically "*not at all*", "*same as usual*", "*rather more than usual*", or "*much more than usual*" to items such as "*lost much sleep over worry*", "*felt constantly under strain*", "*been losing confidence in yourself*", and "*found at times you couldn't do anything because your nerves were too bad*". A sum score was then calculated from dichotomised items (0 = "*not at all*"/"*same as usual*", 1 = "*rather more than usual"/"much more than usual*"), and a cut-point of 5 or more was used to indicate GHQ-caseness.[255] The GHQ is a well-established scale for the evaluation of psychological distress

in general population samples. In relation to diagnosed mental disorders, especially mood and anxiety disorders, the GHQ has shown good clinical validity.[121 122] The GHQ-30 scale has been specifically validated for this population.[255 256]

Information on sickness absence was requested as follows: "*In the last 12 months how many days were you off work for health reasons?*" The response scale ranged from 0 to 365 and the responses were categorized as 0, 1-7 and >7 days.[248]

Type A behavior pattern (assessed at phase 1 by the Framingham Type A scale[257]). Ten items include e.g. the following questions: "*Are you bossy or dominating?"; "Do you have a strong need to excel (be best) in most things)?; "Are you hard driving and competitive?"; "Have you often felt pressed for time at work?"; "Do you get quite upset when you have to wait for anything?*" with response alternatives *describes me very well, fairly well, somewhat, not at all*. Cronbach's alpha based on standardised items was 0.71, indicating satisfactory internal validity of the scale. A sum score for each respondent was calculated and the scores were then divided into tertiles.

Work characteristics included job demands and decision latitude at work, based on the Job Content Questionnaire by Karasek.[81 258] Three items dealt with job demands: "*Do you have to work very fast; Do you have to work very intensively?; Do you have enough time to do everything?*" with response alternatives *often, sometimes, seldom, never / almost never.* Cronbach's alpha based on standardised items was 0.68. The first two items were reversed and a sum score was calculated, from which the data were divided into tertiles to indicate high, average and low levels of job demands. Fifteen items dealt with decision authority (e.g. "*Do you have a choice in deciding HOW you do your work?; Others take decisions concerning my work"*) and skill discretion (e.g. "*Does your work demand high level of skill or expertise?; Do you have the possibility for learning new things through your work?*), with response alternatives *often, sometimes, seldom, never / almost never.* These were reversed and summed into an index of decision latitude at work.[81 258] Cronbach's alpha

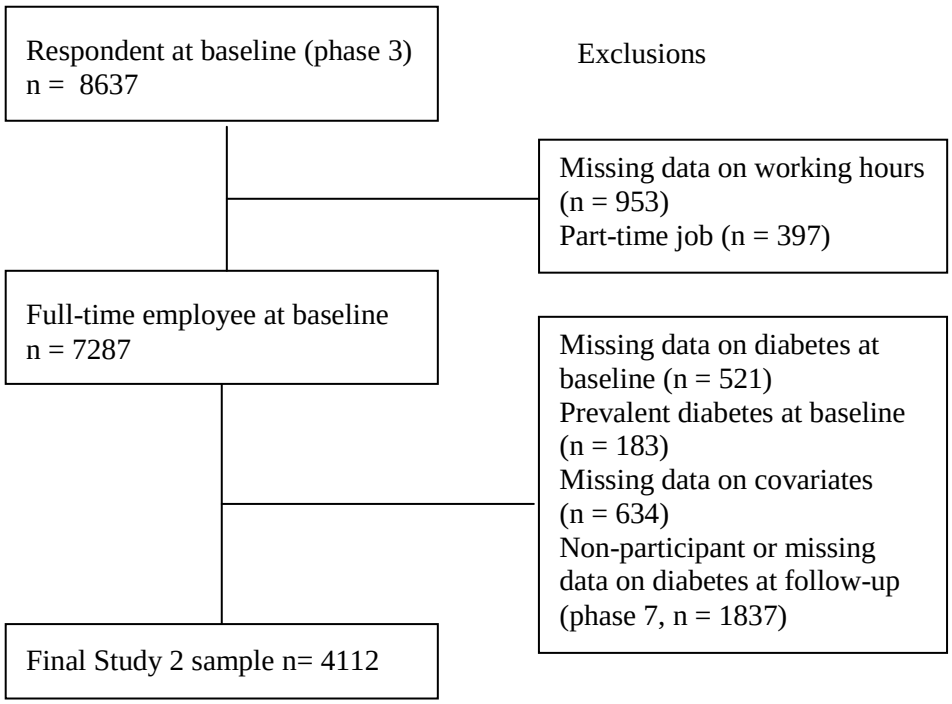
based on standardised items was 0.80. For this measure also, the score was divided into tertiles.

8.4 Study 2: Type 2 diabetes mellitus

8.4.1 Sample selection

As the same baseline sample was used in Study 2 as was used in Study 1, phase 3 forms the baseline for studying the association between working hours and incident type 2 diabetes. Of the 8637 participants at phase 3, 7684 (89%) were employed and responded to the question on working hours (Figure 9). Of them, 397 (5%) worked part time (less than 7 hours / day) and were excluded from the analysis, leaving a sample of 7287 participants. Out of these, data were missing on diabetes (n=521), 183 had prevalent diabetes at baseline and 634 had missing data on at least one of the covariates. A further 1837 were either non-participants or had missing data on type 2 diabetes at follow-up (phase 7) and were also excluded. Thus, the final Study 2 sample comprised 4112 participants (2979 men, 1133 women) aged 39 to 61 years at baseline (mean age 48.5 years) who were followed until phase 7, the most recent phase for which type 2 diabetes data were available for this thesis. The mean follow-up time in Study 2 was 11.3 years (S.D.=0.5, range 9.4 to 12.8 years).

Figure 9. Sample selection procedure for Study 2 (Long working hours and incidence of type 2 diabetes)



To assess whether the final Study 2 sample was different from the original phase 1 sample, a comparison was made according to socio-demographic characteristics and health-related factors measured at phase 1 and working hours measured at phase 3. Table 8 (p. 94) shows the comparisons between the phase 1 sample, phase 3 full-time employees and Study 2 final sample. Women were underrepresented in the final sample, as well as were employees from the lowest occupational grade, those who were smokers, those who exercised little, those who did not had fruits and vegetables daily, and those who did not use alcohol at phase 1. However, the differences were not major. No remarkable difference was found for marital status, psychological distress, type A behaviour pattern, sleeping hours, or working hours between the samples. Regarding differences between phase 3 full-time employees and the final study sample, no remarkable differences were found, exept underrepresentation of low occupational grade employees and those who were teetotals.

Table 8. Distribution of the *phase 1 variables* for phase 1 respondents, phase 3 full-time employees, and Study 2 final sample at baseline (phase 3). Figures are n (%).

Variable	(1) Phase 1 respondents (n= 10,308)	(2) Phase 3 full-time employees (n=7287)	(3) Study 2 final sample[a] (n=4112)
Sex			
Men	6895 (67)	5131 (70)	2979 (72)
Women	3413 (33)	2156 (30)	1133 (28)
Occupational grade			
High	3028 (29)	2285 (31)	1419 (35)
Intermediate	4943 (48)	3647 (50)	2139 (52)
Low	2337 (23)	1355 (19)	554 (13)
Marital status			
Married/cohabited	7608 (74)	5487 (76)	3143 (77)
Non-married/cohabited	2662 (26)	1775 (24)	964 (23)
Psychological distress			
No	7445 (73)	5296 (73)	2979 (73)
Yes	2744 (27)	1923 (27)	1101 (27)
Type A behaviour pattern			
Low	3116 (31)	2128 (30)	1207 (29)
Moderate	3612 (36)	2559 (36)	1494 (36)
High	3223 (32)	2371 (34)	1411 (34)
Sleeping hours /night			
6 or less	3331 (33)	2317 (32)	1257 (31)
7-8	6832 (67)	4877 (67)	2811 (69)
9 or more	101 (1)	58 (1)	29 (1)
Smoking			
Never	5062 (50)	3690 (51)	2227 (54)
Ex	3274 (32)	2394 (33)	1395 (34)
Current	1883 (18)	1142 (16)	465 (11)
Alcohol use (units/wk)			
0	1873 (18)	1195 (17)	580 (14)
>0 ≤ 14 / 21 (women/men)	6739 (66)	4859 (67)	2854 (70)
> 14 / 21 (women/men)	1602 (16)	1172 (16)	649 (16)
Daily fruit and vegetable consumption			
Yes	5978 (58)	4288 (59)	2515 (61)
No	4297 (42)	2978 (41)	1587 (39)
Moderate / vigorous exercise (hrs /wk)			
<1.5	2713 (28)	1802 (26)	954 (24)
≥1.5	7083 (72)	5175 (74)	3037 (76)
Working hours / day[b]			
7-8	n.a.	3966 (54)	2193 (53)
9		1490 (20)	851 (21)
10		1081 (15)	636 (15)
11-12		750 (10)	432 (11)

[a] Participants with full data at baseline and at follow-up.
[b] Data derived from phase 3 survey.

8.4.2 Measures

Study 2 baseline covariates included characteristics that may be either confounding or mediating factors in the association between long working hours and type 2 diabetes.[88 91-98 100 101]

These factors were to a great extent the same as those for CHD, used in Study 1. Therefore they are only listed below with the exception of those which are additional as well as the description of outcome, type 2 diabetes.

The following measures were the same as in Study 1 (see pages 84 to 92): working hours, age, sex, marital status, occupational grade, prevalent CHD, smoking, alcohol use, fruit and vegetable consumption, excercise level, sleeping hours, psychological distress, sickness absence, type A behaviour, job demands, decision latitude at work, BMI, systolic and diastolic blood pressure, LDL and HDL cholesterol, and triglycerines.

In addition, waist circumference[93] was taken during the clinical examination as the smallest circumference at or below the costal margin using a fibreglass tape measure at 600 g tension.

Presence of different forms of diabetes mellitus and prediabetes was determined at the clinical examination and surveys at phases 3 and 7 as follows:

1.) Diabetes: a fasting glucose $\geq$7.0 mmol/L or a 2-hour postload glucose $\geq$11.1 mmol/L, or self-reported doctor-diagnosed diabetes or use of diabetic medication;

2.) Prediabetes: Impaired fasting glucose, IFG (fasting glucose between 5.6 and 6.9 mmol/L) or impaired glucose tolerance, IGT (2-hour postload glucose between 7.8 and 11.0 mmol/L).

Diagnosis of incident type 2 diabetes based on FPG or GTT was based on the current definition of the disease, that is, a fasting plasma glucose of 7.0 mmol/L or more, or

a 2-h postload glucose of 11.1 mmol/L or more.[88 250 259 260] Participants with IFG or IGT but not with clinical diabetes were classified as *prediabetics*.

Because of the relatively old age of the cohort, new cases were very likely to be type 2 diabetes cases rather than type 1 (juvenile-onset) diabetes which accounts for only 5-10% of diabetes cases[88] although it was not differentiated in this study. To obtain comparability across study phases, definition of diabetes was handled during both phases according to similar standard protocols and baseline cases were excluded from the prospective analyses.

Venous blood samples were taken in individuals who were instructed to fast ≥8 hours (those whose sampling was taken in the afternoon had a light fat-free breakfast and they fasted for ≥5 hours) before undergoing a standard 2-h oral glucose tolerance test. Fasting reduces the possibility of false positive cases. Glucose samples were drawn into fluoride monovette tubes and insulin samples into native tubes, which were centrifuged on site within 1 h. Plasma or serum was immediately removed from the monovette tubes, and moved into microtubes and stored at –70°C. Blood glucose was measured with the glucose oxidase method[261] on YSI model 23A glucose analyser[262] and YSI model 2300 STAT PLUS analyser[263] (YSI Corporation, Yellow Springs, OH, USA).

Also in Study 2, the first two categories (7 and 8 hours) were collapsed to form a group of standard hours and the last two categories were collapsed due to relatively low number of respondents working 11 and 12 hours a day (Table 9).

Table 9. Distribution of daily working hours among Study 2 sample at baseline

Daily working hours	n (%)
7	698 (17)
8	1495 (36)
9	851 (21)
10	636 (15)
11	228 (6)
12	204 (5)
Total	4112 (100)

8.5 Study 3: Depression

8.5.1 Sample selection

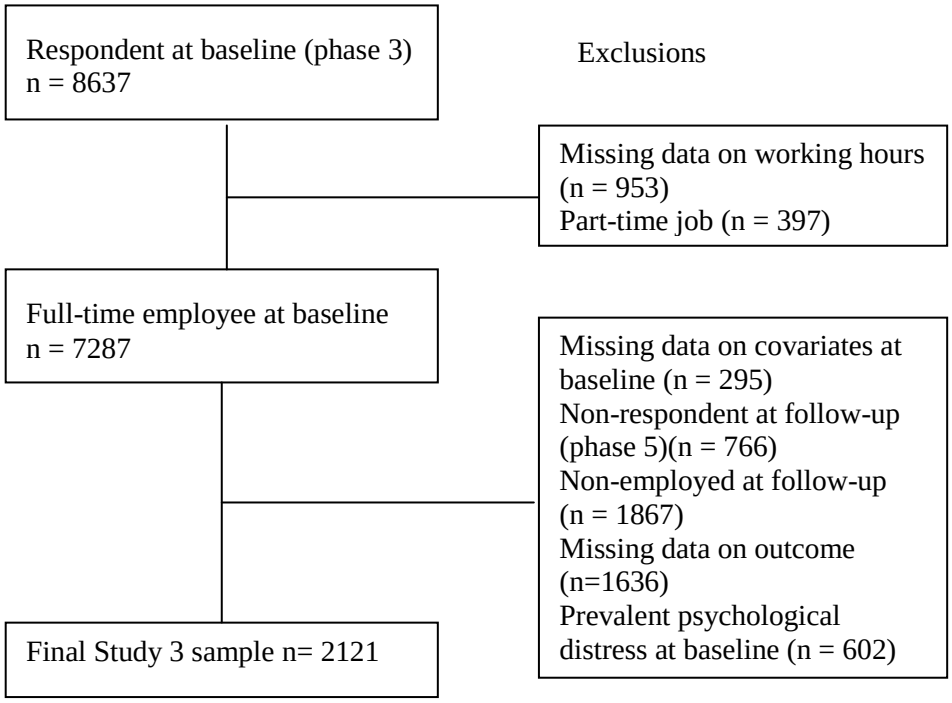
Data for exposure and outcome measures for the study on working hours and depression are drawn from two survey phases; phase 3 (1991-93), the baseline; and phase 5 (1997-99), follow-up, when DSM-III-R MDE was evaluated for the first and only time in the Whitehall II study. The mean follow-up time was 5.8 (S.D. 0.4) years.

Figure 10 (p. 98) presents the sample selection procedure for Study 3. Of the 8637 participants at phase 3, 7684 (89%) were employed and responded to the question on working hours. Of them, 397 (5%) worked part time (less than 7 hours / day) and were excluded from the analysis, leaving a sample of 7287 full time employed participants. Out of these, data were missing on at least one of the covariates for 295 participants and of these, 766 did not respond at follow-up. Of the remaining respondents at follow-up, 1867 were no longer employed.

Those who were employed were selected to reduce misclassification of the work exposure due to retirement during the follow-up. This selection was done for mental health - related outcomes (depression and sleep disturbances) because in these, the course of disease is fluctuating and at retirement, a relapse is unlikely to be associated with work.

A further 1636 did not participate in the CIDI interview. Of the remaining participants, prevalent psychological distress at baseline was identified for 602 who were further excluded from the analysis. Thus, the final sample comprised 2121 participants (1623 men, 498 women) aged 39 to 61 years at baseline.

Figure 10. Sample selection procedure for Study 3 (Long working hours and onset of depression)



To assess selection for health or socio-demographic factors that is, whether the present study sample at baseline (phase 3) was different from that of the original baseline sample (phase 1), as well as that of the phase 3 full time employees, we compared the Study 1 variables (socio-demographic factors, psychological factors, and health behaviours at

phase 1, and working hours at phase 3) according to participation at phase 1, phase 3 full time employment and phase 3 final sample (Table 10). The table shows that in the final sample, men, those with higher occupational grades, married/cohabited, non- or ex-smokers, and those who used moderately alcohol were overrepresented. In addition, those participants who had no psychological distress at phase 1 were more likely to be in the final sample at phase 3 which is understandable because GHQ-30 cases were excluded from the final sample and psychological distress is likely to be recurrent. However, prevalence of psychological distress was equal among phase 1 respondents and phase 3 full-time employees. In addition, the final sample did not remarkably differ from phase 3 full time employees in terms of working hours.

Table 10. Distribution of the *phase 1 variables* for phase 1 respondents, phase 3 full-time employees, and Study 3 final sample at baseline (phase 3). Figures are n (%).

Variable	**(1) Phase 1 respondents (n= 10,308)**	**(2) Phase 3 full-time employees (n=7287)**	**(3) Study 3 final sample[a] (n=2121)**
Sex			
Men	6895 (67)	5131 (70)	1623 (77)
Women	3413 (33)	2156 (30)	498 (23)
Occupational grade			
High	3028 (29)	2285 (31)	706 (33)
Intermediate	4943 (48)	3647 (50)	1099 (52)
Low	2337 (23)	1355 (19)	316 (15)
Marital status			
Married/cohabited	7608 (74)	5487 (76)	1663 (79)
Non-married/cohabited	2662 (26)	1775 (24)	449 (21)
Psychological distress			
No	7445 (73)	5296 (73)	1684 (80)
Yes	2744 (27)	1923 (27)	418 (20)
Smoking			
Never	5062 (50)	3690 (51)	1136 (54)
Ex	3274 (32)	2394 (33)	716 (34)
Current	1883 (18)	1142 (16)	261 (12)
Alcohol use (units/wk)			
0	1873 (18)	1195 (17)	300 (14)
>0 ≤ 14 / 21 (women/men)	6739 (66)	4859 (67)	1455 (69)
> 14 / 21 (women/men)	1602 (16)	1172 (16)	354 (17)
Working hours /day[b]			
7-8	n.a.	3966 (54)	1103 (52)
9		1490 (20)	442 (21)
10		1081 (15)	348 (16)
11-12		750 (10)	228 (11)

[a] Participants with no baseline psychological distress and no missing data on covariates/ outcome depression.
[b] Data derived from phase 3 survey.

8.5.2 Measures

Study 3 baseline covariates included characteristics that may be either confounding or mediating factors in the association between long working hours and depression.[63 113 136] They were derived from baseline (phase 3) data and the following variables were the same as those used in Studies 1 and 2: working hours, age, sex, marital status, occupational grade, alcohol use, smoking, sickness absence, job demands and decision latitude at work.

In addition, chronic disease was indicated by the presence of at least one of the following conditions: report of longstanding illness, disease, or medical condition for which the participant had sought treatment in the 12 months before the baseline survey or presence of CHD (as defined earlier).

Presence of a major depressive episode (MDE) in the preceding 12 months was ascertained during the clinical health examination at phase 5 using the University of Michigan version of the Composite International Diagnostic Interview (UM-CIDI) adapted for self-administered computerised interview.[264 265] The program used operationalized criteria for diagnoses in the Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R).[266] In addition to the criteria for the presence and duration of the DSM-III-R symptoms, the definition of a MDE required that the episode also fulfilled criteria for impairment and change in function, and was not due to organic conditions, bereavement, or mania. The CIDI interview was commenced after the beginning of screening at phase 5: all participants attending the screening clinic were invited to complete the interview.

Exclusion of participants with psychiatric morbidity at baseline was performed according to caseness on the 30-item General Health Questionnaire (GHQ-30 total score $\geq$5).[120] In relation to diagnosed mental disorders, especially mood and anxiety disorders, the GHQ has shown good clinical validity as a screening instrument.[120 122] The GHQ-30 has

been validated specifically against the Clinical Interview Schedule in Whitehall II data, giving a cut-off point of 4/5 for dividing 'non-cases' from 'cases'.[255]

Distribution of working hours in the final Study 3 sample is presented in Table 11. As previously, **t**he first two categories (7 and 8 hours) were collapsed to form a group of standard hours and the last two categories were collapsed due to relatively low number of respondents working 11 and 12 hours a day.

Table 11. Distribution of daily working hours among Study 3 sample at baseline

Daily working hours	n (%)
7	346 (16)
8	757 (36)
9	442 (21)
10	348 (16)
11	122 (6)
12	106 (5)
Total	2121 (100)

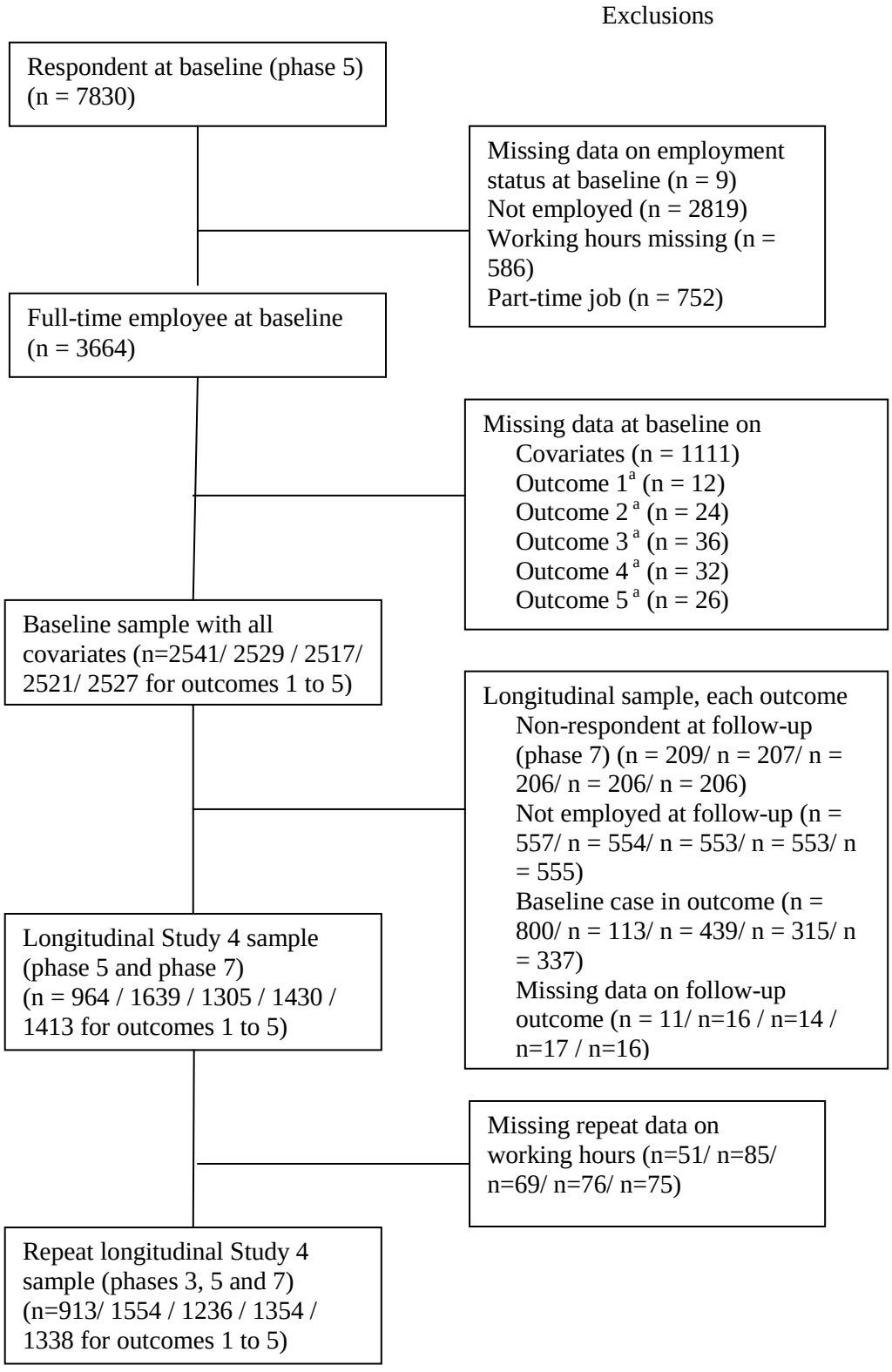
8.6 Study 4: Sleep disturbances

8.6.1 Sample selection

Sample selection procedure for Study 4 is presented in Figure 11. For this study, data were derived from phases 5 (1997-99) and 7 (2003-4). In addition, information on working hours at phase 3 was used to examine the relationship between repeat exposure to long working hours and the onset of sleep disturbances. The final longitudinal sample (participants with full-time work and full data at phase 5 and those employed at phase 7 and responded to each

outcome) resulted in number of participants being 964 to 1639 for the study using one measure of working hours and 913 to 1554 for the study using repeat measures of working hours. The mean follow-up time for Study 4 was 5.5 (S.D. 0.5) years.

Figure 11. Sample selection procedure for Study 4 (Long working hours and onset of sleep disturbances)



[a] Outcome 1 = short sleep; outcome 2 = difficulty in falling asleep; outcome 3 = frequent waking during the night; outcome 4 = early waking; outcome 5 = waking without feeling refreshed.

To assess selection on health or socio-demographic factors, that is, whether the present study sample at baseline (phase 5) was different from that of the original baseline sample (phase 1), as well as that of the phase 5 full time employees, the Study 1 variables (socio-demographic factors, health, and health behaviours at phase 1, and working hours at phase 5) were compared according to participation at phase 1, phase 5 full time employment and Study 4 final sample for outcome 1 (with the smallest n) at phase 5 (Table 12, p. 104). The table shows that again, men, those with higher occupational grade, married or cohabiting, never-smokers, and moderate alcohol users are overrepresented in the final Study 4 sample when comparisons are made with phase 1 respondents. However, no major differences with the exception of occupational grade were found among phase 5 full time employees and those included in the final Study 4 sample. Employees who had worked >55 hours at baseline were slightly unerrepresentated (6% in the final Study 4 sample vs 9% among full time employees at phase 5).

Table 12. Distribution of the *phase 1 variables* for phase 1 respondents, phase 5 full-time employees, and Study 4 final sample at baseline (phase 5). Figures are n (%).

Variable	(1) Phase 1 respondents (n= 10,308)	(2) Phase 5 full-time employees (n=3664)	(3) Study 4 final sample (Outcome 1, (n=964)[a]
Sex			
Men	6895 (67)	2751 (75)	735 (76)
Women	3413 (33)	913 (25)	229 (24)
Occupational grade			
High	3028 (29)	1178 (32)	344 (36)
Intermediate	4943 (48)	1966 (54)	529 (55)
Low	2337 (23)	520 (14)	91 (9)
Marital status			
Married/cohabited	7608 (74)	2814 (77)	767 (80)
Non-married/cohabited	2662 (26)	839 (23)	194 (20)
Psychological distress			
No	7445 (73)	2643 (73)	714 (75)
Yes	2744 (27)	991 (27)	243 (25)
Smoking			
Never	5062 (50)	1944 (53)	545 (57)
Ex	3274 (32)	1163 (32)	298 (31)
Current	1883 (18)	530 (15)	117 (12)
Alcohol use (units/wk)			
0	1873 (18)	524 (14)	112 (12)
>0 ≤ 14 / 21 (women/men)	6739 (66)	2491 (69)	676 (71)
> 14 / 21 (women/men)	1602 (16)	621 (17)	170 (18)
Working hours /week[b]			
35-40	n.a.	1468 (40)	401 (42)
41-48		1000 (27)	282 (29)
49-55		849 (23)	220 (23)
>55		347 (9)	61 (6)

[a] Participants with no baseline psychological distress and no missing data on covariates/ outcome.
[b] Data derived from phase 5 survey.

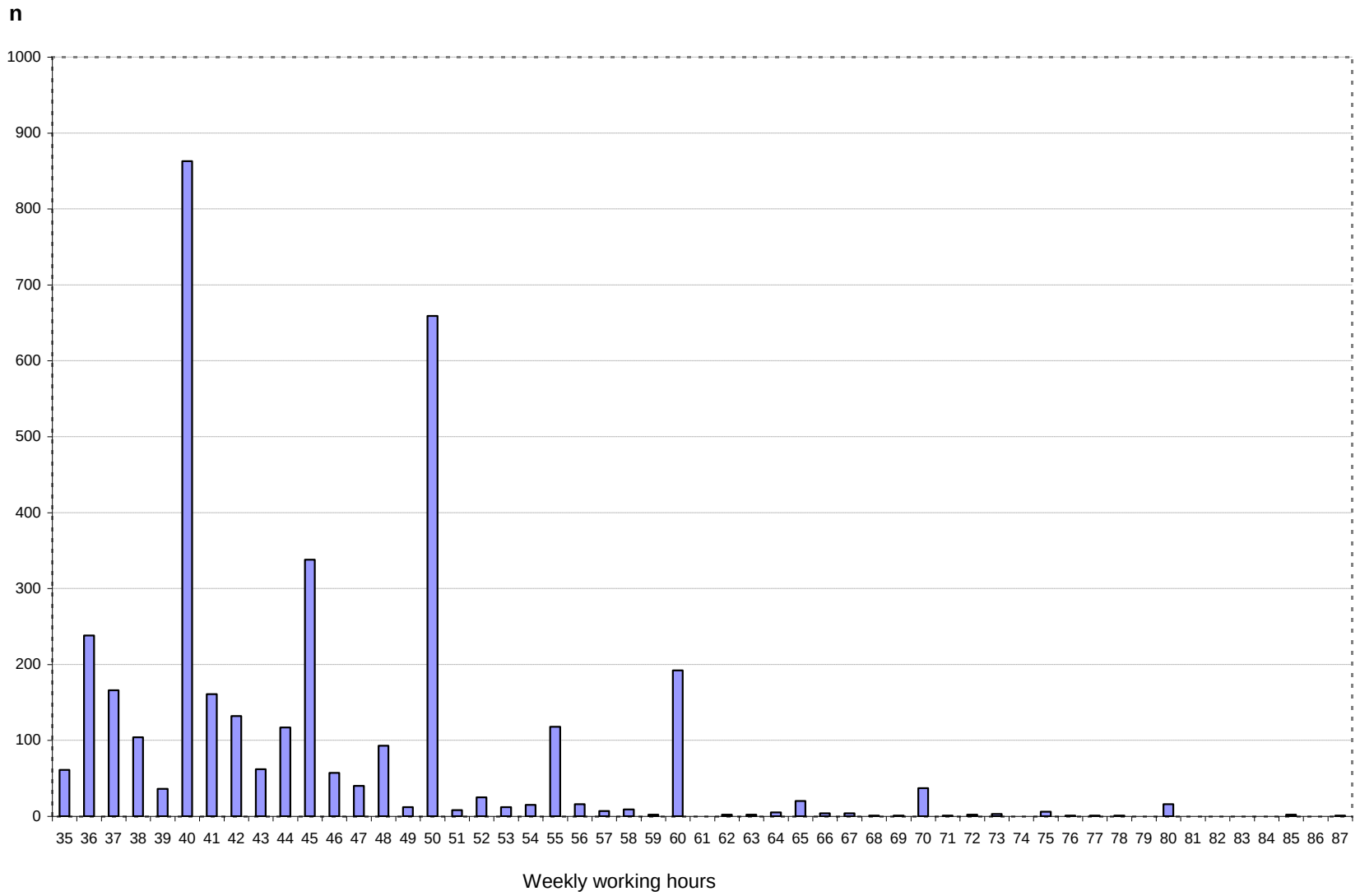
8.6.2 Measures

In Study 4, working hours were measured at phases 3 and 5. At phase 3, working hours were ascertained from the following question: "On an average weekday, approximately how many hours do you spend on the following activities: Work (daytime and work brought home)?" with response alternatives ranging from 1 to 12. At phase 5, working hours were ascertained from the following 2 questions: “How many hours do you work per average week in your main job, including work brought home?”, and (for participants with more than one job) “How many hours do you work in an average week in your additional employment?” with response alternatives ranging from 0 to 100+ and 0 to 99, respectively.

For Study 4, cut-points for the EU Working Time Directive (41-48 hours per week)[13] for long working hours and a definition (>55 hours per week) for very long working hours used in 2 high-quality studies on sleep disturbances[233] and myocardial infarction[39] were chosen. Standard working hours were defined as 35-40 hours per week. Thus, the participants were divided into 4 groups: 1 = 35–40 hours; 2 = 41–48 hours; 3 = 49-55 hours; and 4 = more than 55 hours per week. For the measurement of repeated exposure to long working hours, daily working hours at phase 3 were transformed to weekly hours by multiplying them by 5, and an average of the 2 time points (phase 3 and 5) was calculated. Finally, participants were divided into 4 groups as described above.

Distribution of working hours among the 3664 full-time employees with data on working hours at phase 5 is presented in Figure 12 (employees with >87 hours [n=11] were not included in the figure due to limited space). Descriptive statistics showed mean weekly working hours to be 45.4, median 44.0 hours, (S.D. 8.5, range 35 to 120). The most common reported working hours was 40 hours per week (n=863). For 341 (9%) employees, working hours included the sum of two jobs. Assessment of normality showed skewness of 2.1 and kurtosis of 8.6 for the continuous working hours variable, both acceptable.

Figure 12. Distribution of weekly working hours among full-time employees in Study 4 at baseline



Duration of sleep was assessed at Phases 5 and 7 by asking the number of hours of sleep on an average week night with the following question: *On an average weekday, approximately how many hours do you spend on the following activities:..... Sleep?"* Response alternatives to be ticked ranged from 1 hour to 12 hours. Short sleep was indicated as six hours or less per night.[162 267]

The Jenkins Scale[165] was used to indicate how often the participants had experienced *sleep disturbances* during the past month. This scale includes 4 questions: "having trouble falling asleep," "waking up several times per night," "having trouble staying asleep," and "waking up after the usual amount of sleep feeling tired and worn out" (i.e., waking without feeling refreshed); all items have a 6-point response scale (1 = not at all; 2 = 1–3 days; 3 = 4–7 days; 4 = 8–14 days; 5 = 15–21 days; 6 = 22–31 days). Each category of sleep disturbance was dichotomized as ≥8 days versus <8 days per month. In the present data, this cut-off point (corresponding to at least 2–3.5 times /week) was chosen to approximate to the ICD-10 diagnosis (F51.0)[48] and other guidelines to assess insomnia,[11] in which chronic insomnia is detected if the frequency of complaint is more than 2 times[48] or ≥3[11] times a week.

Study 4 baseline covariates included characteristics that may be either confounding or mediating factors in the association between long working hours and sleep disturbances.[9 10 159 179-181 184-186] Baseline covariates were derived from the phase 5 questionnaire or from the clinical data collected at phase 5. Similar procedure to that used at phase 3 was used, thus, the variables which are identical with those measured in Studies 1, 2, and 3 at phase 3 are only listed below: age, sex, marital status, occupational grade, chronic disease, BMI, alcohol use, smoking, job demands, and decision latitude at work (more detailed descriptions can be found on pages 84 to 91).

In addition, physical activity was requested using 20 items to assess frequency and duration of participation in walking, cycling, sports, gardening, housework, home

maintenance, and other activities. Frequency and duration of each activity were combined to compute hours per week of physical activity, and a compendium of activity energy costs was then used to assign each of the 20 physical activities assessed a metabolic equivalent.[268] High, moderate, and low levels of physical activity were defined based on a sum score of energy utilization as previously.[268]

8.7 Statistical analysis

Already mentioned on pages 91 and 92, Cronbach's α (alpha)[269] was calculated for scale variables that were sum scores of several questions (type A behaviour, job demands and decision latitude at work). Cronbach's α is a coefficient of reliability. It is commonly used as a measure of the internal consistency reliability of a psychometric test score for a sample of participants, i.e. it is suggested to indirectly indicate the degree to which a set of items measures a single unidimensional latent construct (range 0 to 1 where an estimate close to 1 indicates good internal consistency).

In all parts of this thesis, descriptive statistics (freqencies, means and standard deviations) were calculated. Then, analysis of variance and χ^2 tests were carried out to assess heterogeneity between the groups with regard to working hours and covariates. When the study outcome was binary and the follow-up time for the event was about of equal length for all participants, binary logistic regression models were used to calculate the odds ratios (OR) and their 95% confidence intervals (CIs) for prevalent cases for working hours and for incident disease for baseline covariates and for working hours. In Studies 1 to 3, the reference group was 7-8 hours per day while in Study 4, the reference group was 35-40 hours per week. In prospective analyses, only cases with no disease under study at baseline were included to examine incident cases at follow-up.

In the main analysis, the models were serially adjusted for covariates in order to examine the effect of covariates on the association. Test for trend was carried out by fitting the working hours variable as a continuous variable in the models.

In Study 1 (CHD), The Kaplan-Meier Estimator was first calculated and a Kaplan-Meier curve was produced. It is used for estimating the survival function from life-time data. In medical research, it is often used to measure the fraction of patients living for a certain amount of time after treatment. It can take into account some types of censored data, particularly *right-censoring*, which occurs if a patient withdraws from a study, i.e. is lost from the sample before the final outcome is observed. In Study 1 also, Cox proportional hazard models with follow-up period as the time scale were used to calculate hazard ratios and 95% confidence intervals for incident CHD among participants free from CHD at baseline. The time-dependent interaction term between working time and the logarithm of the follow-up period for both outcomes was non-significant confirming that the proportional hazards assumption was not violated (p=0.41 and p=0.35 for the CHD outcomes, respectively). The analyses were repeated using a restricted definition of the outcome variable: only fatal CHD and non-fatal MI.

To examine whether there is a non-random drop-out of individuals due to missing values on covariates, I carried out a sensitivity analysis with the cohort including also those with missing data on covariates (n=7090). In addition, as suggested by Fox and Collier,[270] Fox et al.[271] and Goldblatt et al.[272] there might be health-related selection in employed cohorts. In this case, selection would operate such that employees with pre-existing but undetected illnesses reduce their working hours. "Wearing off of selection" would occur along with the increasing follow-up time. Therefore, in this thesis, sensitivity analyses were carried out to examine a possible effect of health-related selection into shorter (7-8) working hours on the association between working hours and CHD. This was done by excluding CHD cases occurring during the first 1 to 4 years of the follow-up time.

In study 2 (diabetes), there was a possibility to examine different phases of type 2 diabetes separately; therefore an analysis was made with incidence of prediabetes as an outcome and a sub-group analysis assessing the association between working hours and onset of type 2 diabetes was carried out among those participants who were prediabetics at baseline. Sensitivity analyses were carried out by excluding participants who had fasted 5 hours but not 8 hours or more; thus a better fasting status was obtained.

In Study 4 (sleep disturbances), the association between working hours measured at one time point (phase 5) as a predictor of incident sleep disturbances at phase 7 was examined. Then the association between working hours measured at 2 time points (phase 3 and phase 5) and incident sleep disturbances at phase 7 was examined. To examine linear trend in the association between working hours and sleep disturbances, the analysis was repeated treating working hours as a continuous variable.

To examine whether the association of working hours with CHD and type 2 diabetes was dependent on age (dichotomised by the mean, 49 years), sex, socioeconomic position (6 categories collapsed into 3), prevalent diabetes or prediabetes, prevalent psychological distress, exercise level, overweight/ obesity (=BMI≥25kg/m^2), or work characteristics (job demands, decision latitude at work), interaction effects were tested. In addition to the main effects of working hours and the covariate in question, an interaction term 'working hours variable multiplied by the covariate' was entered into the model as suggested by Cohen and Cohen.[273] Interaction tests were not carried out in Studies 3 and 4 because the number of cases was not sufficient to perform reliable analyses.

All p-values are two-tailed, and those below 0.05 were considered to indicate statistical significance. SAS version 9.2 (SAS, Cary, NC, USA) was used for all statistical analyses.

Chapter 9

Results

9.1 Introduction

This chapter presents results for the present study; first, results are presented for Study 1 (long working hours and CHD), then results for Study 2 (long working hours and type 2 diabetes), followed by results for Study 3 (long working hours and depression), and finally, results for Study 4 (long working hours and sleep disturbances).

9.2 Coronary heart disease

9.2.1 Cross-sectional association between working hours and prevalent CHD at baseline

Table 13 shows the cross-sectional association between working hours and prevalent CHD at the baseline sample of Study 1 (n=7279 with baseline socio-demographic covariates). Cases of CHD were those who had non-fatal myocardial infarction or definite angina verified between phases 1 and 3 (n=192). After adjustment for age, sex, marital status and occupational grade, employees who had a usual working day of 9 hours had a lower probability of having CHD than those who worked 7-8 hours a day (OR 0.48, 95% CI 0.30-0.77). Although the odds ratios for employees working 10 and 11-12 hours were also smaller compared to employees working standard hours, the associations were not statistically significant.

Table 13. Association between working hours and prevalence of CHD (definite non-fatal myocardial infarction or angina) at baseline

Daily working hours	n of cases	n of parti-cipants	Prevalence (%)	OR (95% CI)[b]	*P* value
All participants	192	7287	2.6		
All participants with covariates[a]	192	7279	2.6		
7-8	134	3963	3.4	1.00	Ref.
9	21	1487	1.4	0.48 (0.30-0.77)	0.003
10	23	1080	2.1	0.71 (0.44-1.14)	0.16
11-12	14	749	1.9	0.61 (0.34-1.10)	0.10

OR=Odds ratio. CI=Confidence interval.
[a] With information on age, sex, marital status, and occupational grade.
[b] Adjusted for age, sex, marital status, and occupational grade.

9.2.2 Association between working hours and covariates at baseline

In the final cohort for Study 1, participants with prevalent CHD as well as those with missing data on covariates at baseline were excluded from further analyses resulting 6014 participants. In that sample, 3256 (54%) did not usually work overtime, 1247 (21%) worked approximately 9 hours a day, 894 (15%) worked 10 hours a day, and 617 (10%) 11 or 12 hours a day (Table 14, p. 114). Participants working long hours were slightly younger than participants working standard hours. Men, married or cohabitating participants and those in higher occupational grades worked longer hours than women, non-married/co-habiting or lower-grade participants. Absence of pre-existing diabetes, smoking history and alcohol use exceeding recommended limits were also associated with long hours in these unadjusted analyses. More of those working long hours reported more exercise but shorter sleeping hours and less sickness absence days. They also reported higher prevalence of psychological distress and higher scores on measures of type A behaviour, higher job demands, and higher decision latitude at work than individuals working shorter hours. Long working hours were

associated with lower HDL cholesterol levels compared to employees with standard 7-8 hours of work. Working hours were not associated with daily fruit and vegetable consumption, body mass index, systolic blood pressure, diastolic blood pressure, LDL-cholesterol, or triglycerides.

Table 14. Characteristics of the final Study 1 sample participants by daily working hours at baseline

Characteristics	All n (%) / Mean (S.D.)	Daily working hours n (%) / Mean (S.D.)				*P* value[a]
	All (n=6014)	7-8 hours (n=3256)	9 hours (n=1247)	10 hours (n=894)	11-12 hours (n=617)	
Age, years	48.7 (5.7)	49.0 (5.8)	48.5 (5.6)	48.5 (5.4)	48.3 (5.5)	0.004
Sex						<0.001
Male	4262 (71)	2081 (64)	965 (77)	685 (77)	531 (86)	
Female	1752 (29)	1175 (36)	282 (23)	209 (23)	86 (14)	
Marital status						<0.001
Married/cohabitating	4610 (77)	2356 (72)	974 (78)	727 (81)	553 (90)	
Non-married/-cohabitating	1404 (23)	900 (28)	273 (22)	167 (19)	64 (10)	
Occupational grade level						<0.001
1 highest	1056 (18)	223 (7)	291 (23)	289 (32)	253 (41)	
2	1353 (23)	577 (18)	372 (30)	257 (29)	147 (24)	
3	880 (15)	505 (16)	205 (16)	98 (11)	72 (12)	
4	1048 (17)	686 (21)	170 (14)	122 (14)	70 (11)	
5	815 (14)	571 (18)	132 (11)	68 (8)	44 (7)	
6 lowest	862 (14)	694 (21)	77 (6)	60 (7)	31 (5)	
Diabetes						<0.001
No	5278 (88)	2812 (86)	1108 (89)	796 (89)	562 (91)	
Impaired fasting glucose	136 (2)	61 (2)	33 (3)	28 (3)	14 (2)	
Impaired glucose tolerance	459 (8)	292 (9)	77 (6)	55 (6)	35 (6)	
Yes	141 (2)	91 (3)	29 (2)	15 (2)	6 (1)	
Smoking						0.002
Never	3092 (51)	1730 (53)	629 (50)	436 (49)	297 (48)	
Ex	2108 (35)	1073 (33)	478 (38)	324 (36)	233 (38)	
Current	814 (14)	453 (14)	140 (11)	134 (15)	87 (14)	
Alcohol use (units / week)						<0.001
0	1085 (18)	717 (22)	158 (13)	125 (14)	85 (14)	
>0 ≤ 14 / 21 (women/men)	3958 (66)	2073 (64)	871 (70)	605 (68)	409 (66)	
> 14 / 21 (women/men)	971 (16)	466 (14)	218 (18)	164 (18)	123 (20)	
Daily fruit and vegetable consumption						0.20
Yes	3691 (61)	1964 (60)	767 (62)	565 (63)	395 (64)	
No	2323 (39)	1292 (40)	480 (39)	329 (37)	222 (36)	
Moderate / vigorous exercise (hrs / week)						<0.001
≥1.5	4002 (67)	2054 (63)	885 (71)	616 (69)	447 (72)	
<1.5	2012 (33)	1202 (37)	362 (29)	278 (31)	170 (28)	
Sleeping hours / night						0.007
6 or less	1587 (26)	825 (25)	306 (25)	262 (29)	194 (31)	
7-8	4284 (71)	2348 (72)	911 (73)	611 (68)	414 (67)	
9 or more	143 (2)	83 (3)	30 (2)	21 (2)	9 (2)	
Psychological distress						<0.001
No	4680 (78)	2621 (81)	932 (75)	667 (75)	460 (75)	
Yes	1334 (22)	635 (20)	315 (25)	227 (25)	157 (25)	
Type A behaviour						<0.001
Low	1833 (31)	1256 (39)	323 (26)	157 (18)	97 (16)	
Moderate	2169 (36)	1234 (38)	446 (36)	291 (33)	198 (32)	
High	2012 (34)	766 (24)	478 (38)	446 (50)	322 (52)	

Table 14 cont.

Table 14 cont.

Job demands						<0.001
Low	1242 (21)	974 (30)	137 (11)	80 (9)	51 (8)	
Moderate	2751 (46)	1650 (51)	552 (44)	341 (38)	208 (34)	
High	2021 (34)	632 (19)	558 (45)	473 (53)	358 (58)	
Decision latitude at work						<0.001
Low	1528 (25)	1096 (34)	214 (17)	137 (15)	81 (13)	
Moderate	1887 (31)	1149 (35)	379 (30)	217 (24)	142 (23)	
High	2599 (43)	1011 (31)	654 (53)	540 (60)	394 (64)	
Sickness absence days (past year)						<0.001
0	2017 (34)	899 (28)	470 (38)	375 (42)	273 (44)	
1-7	2857 (48)	1589 (49)	595 (48)	403 (45)	270 (44)	
>7	1140 (19)	768 (24)	182 (15)	116 (13)	74 (12)	
Body mass index (kg/m^2)	25.1 (3.6)	25.1 (3.7)	25.1 (3.5)	25.3 (3.8)	25.2 (3.2)	0.48
Systolic blood pressure (mmHg)	120.0 (13.3)	120.1 (13.5)	120.3 (12.9)	119.8 (13.2)	119.7 (12.8)	0.74
Diastolic blood pressure (mmHg)	79.5 (9.3)	79.4 (9.4)	79.6 (9.2)	79.6 (9.2)	79.9 (9.0)	0.47
LDL-cholesterol (mmol/L)	4.37 (1.03)	4.37 (1.05)	4.33 (1.00)	4.38 (1.01)	4.42 (1.02)	0.25
HDL-cholesterol (mmol/L)	1.44 (0.41)	1.45 (0.41)	1.43 (0.40)	1.44 (0.41)	1.38 (0.37)	<0.001
Triglycerides (mmol/L)	1.35 (0.74)	1.36 (0.77)	1.33 (0.71)	1.33 (0.71)	1.38 (0.71)	0.39

[a]*P*-value for the heterogeneity across the working hours' groups.

9.2.3 Association between covariates and incident CHD

Altogether there were 67,544 person-years of follow-up during which 369 new events of CHD occurred, resulting in a rate of 5.46 events per 1000 person-years. Table 15 (p. 117) presents the association between baseline characteristics (covariates) and incident CHD in the final Study 1 sample. In the age-adjusted models, older age, male sex, having definite diabetes, current smoking, being teetotal, having a high level of type A behaviour, and having sickness absenteeism of more than a week during the past year, as well as all the biological risk factors (higher body mass index, systolic and diastolic blood pressure, LDL cholesterol and triglycerides, and lower HDL-cholesterol) were significantly associated with incident CHD. Weaker (non-significant) or no association was found for marital status, socioeconomic position, impaired fasting glucose, impaired glucose tolerance, ex-smoking, heavy alcohol use, fruit and vegetable consumption, exercise level, sleeping hours, psychological distress, job demands, and decision latitude at work.

Table 15. Association between baseline covariates and incident CHD at follow-up, adjusted for age

Covariate	n of events	n of parti-cipants	Person-years	Rate / 1000 person-years	HR (95% CI)	*P* value
Age (years)	-	-	-	-	1.09 (1.07-1.11)	<0.001
Sex						
Female	80	1752	19,610.4	4.08	1.00	ref.
Male	289	4262	47,933.6	6.03	1.61 (1.26-2.07)	<0.001
Marital status						
Non-married/cohabiting	76	1404	15,677.2	4.85	1.00	ref.
Married/-cohabiting	293	4610	51,866.8	5.65	1.14 (0.89-1.47)	0.30
Occupational grade						
1 (highest)	65	1056	12,193.9	5.33	1.00	ref.
2	87	1353	15,371.4	5.66	1.23 (0.89-1.70)	0.21
3	38	880	10,102.6	3.76	0.85 (0.57-1.28)	0.43
4	58	1048	11,871.2	4.89	1.06 (0.74-1.51)	0.75
5	65	815	8964.0	7.25	1.40 (1.00-1.98)	0.05
6 (lowest)	56	862	9040.8	6.19	1.03 (0.72-1.48)	0.85
Diabetes						
No	308	5278	59,558.1	5.17	1.00	ref.
Impaired fasting glucose	13	136	1467.5	8.86	1.45 (0.83-2.52)	0.19
Impaired glucose tolerance	32	459	5061.3	6.32	1.07 (0.75-1.55)	0.71
Yes	16	141	1457.0	10.98	1.78 (1.07-2.94)	0.026
Smoking						
Never	157	3092	35,182.2	4.46	1.00	ref.
Ex	140	2108	23,706.0	5.91	1.23 (0.98-1.54)	0.08
Current	72	814	8655.8	8.32	1.86 (1.41-2.46)	<0.001
Alcohol use (units / week)						
0	84	1085	11,821.5	7.11	1.32 (1.03-1.70)	0.029
>0 ≤ 14 / 21 (women/men)	225	3958	44,841.9	5.02	1.00	ref.
> 14 / 21 (women/men)	60	971	10,880.6	5.51	1.19 (0.89-1.58)	0.24
Daily fruit and vegetable consumption						
Yes	217	3691	41,879.2	5.2	1.00	ref.
No	152	2323	25,664.7	5.9	1.19 (0.97-1.46)	0.10
Moderate / vigorous exercise (hrs / week)						
≥1.5	238	4002	45,313.2	5.3	1.00	ref.
<1.5	131	2012	22,230.8	5.9	1.03 (0.84-1.28)	0.76
Sleeping hours / night						
6 or less	106	1587	17,632.9	6.0	1.11 (0.89-1.39)	0.36
7-8	258	4284	48,332.5	5.3	1.00	ref.
9 or more	5	143	1578.5	3.2	0.61 (0.25-1.48)	0.27
Psychological distress						
No	281	4680	52,594.6	5.3	1.00	ref.
Yes	88	1334	14,949.3	5.9	1.22 (0.96-1.56)	0.10
Type A behaviour						
Low	98	1833	20,581.3	4.8	1.00	ref.
Moderate	134	2169	24,243.6	5.5	1.18 (0.91-1.53)	0.21
High	137	2012	22,719.0	6.0	1.38 (1.06-1.79)	0.016
Job demands						
Low	79	1242	13,688.9	5.8	1.00	ref.
Moderate	177	2751	30,823.3	5.7	1.08 (0.83-1.41)	0.57
High	113	2021	23,031.8	4.9	0.98 (0.73-1.30)	0.87

Table 15 cont.

Table 15 cont.

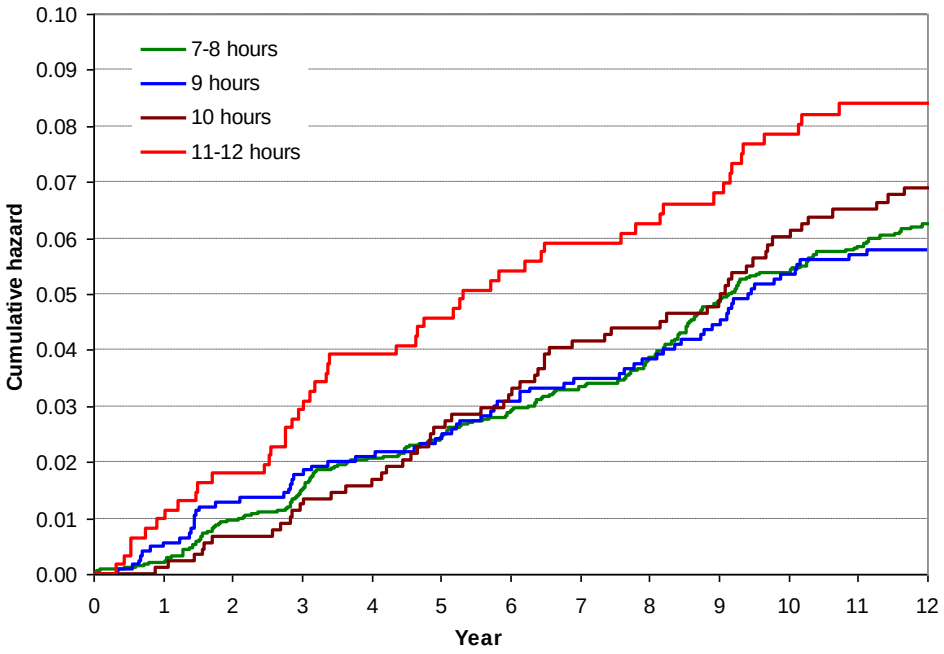
Decision latitude at work						
High	163	2599	29,543.5	5.5	1.00	ref.
Moderate	113	1887	21,290.4	5.3	0.98 (0.77-1.25)	0.89
Low	93	1528	16,710.1	5.6	0.94 (0.73-1.21)	0.63
Sickness absence days (past year)						
0	109	2017	22,990.5	4.7	1.00	ref.
1-7	180	2857	32,205.2	5.6	1.23 (0.97-1.56)	0.09
>7	80	1140	12,348.2	6.5	1.39 (1.04-1.85)	0.026
Body mass index (kg/m^2)	-	-	-	-	1.10 (1.07-1.12)	<0.001
Systolic blood pressure (mmHg)	-	-	-	-	1.02 (1.02-1.03)	<0.001
Diastolic blood pressure (mmHg)	-	-	-	-	1.04 (1.03-1.05)	<0.001
LDL-cholesterol (mmol/L)	-	-	-	-	1.34 (1.22-1.47)	<0.001
HDL-cholesterol (mmol/L)	-	-	-	-	0.32 (0.24-0.43)	<0.001
Triglycerides (mmol/L)	-	-	-	-	1.64 (1.47-1.83)	<0.001

HR=Hazard ratio; CI=Confidence interval.

9.2.4 Association between working hours and incident CHD

The unadjusted Kaplan-Meier curves for cumulative hazard for incident CHD according to hours worked are presented in Figure 13, showing that the time to the onset of CHD was associated with working 11-12 hours a day at baseline. For example, at 7 years' follow-up the cumulative hazard was 0.06 (cumulative incidence 6%) among that group and 0.035 (cumulative incidence 3.5%) among those who worked 7-8 hours per day. The separation of the curves between this group and standard (7-8) hours' group started from the beginning of the follow-up and widened thereafter. Those who worked 9 or 10 hours did not remarkably differ from those who worked 7-8 hours a day.

Figure 13. Kaplan-Meier curves for unadjusted cumulative hazard for incident CHD comparing each group of employees according to hours worked at baseline



Multivariate-adjusted association between working hours at baseline (phase 3) and incident CHD (by phase 7), as indicated by coronary death, incident non-fatal myocardial infarction or incident definite angina pectoris is presented in Table 16 (p. 122). In the model adjusted for sociodemographic factors (Model A), working 11-12 hours (but not 9 or 10 hours) was associated with incident CHD (HR 1.60), compared with no overtime work. The reductions in effect size after adjustments were found to be small, largest being found after adjustment for health behaviors (Model C). Of these, smoking, body mass index and being teatotal were significantly related to incident CHD and of these, smoking history was related to long working hours. In Model E, some effect size reduction was found after adjustment for type A behaviour pattern, also a significant predictor of CHD and associated with long working hours. A significant trend was observed at each step after entering the categorical working hours into the model as continuous, suggesting a dose-response relationship. However, the actual risk seemed not to emerge until 11+ hours of work per day.

The analyses were repeated with the outcome defined as fatal CHD and new non-fatal MI, but excluding definite angina pectoris (Table 17, p. 123). In the model adjusted for

socio-demographic characteristics, working 11-12 hours a day (but not 9 or 10 hours) was associated with incident fatal CHD or non-fatal myocardial infarction (HR 1.90) when compared with employees with no overtime work (Model A). Again, the largest reduction in the hazard ratio was found after adjustment for health behaviors (Model C) and type A behaviour pattern (Model E). A significant trend was observed at each step after entering categorical working hours into the model as continuous, suggesting a dose-response relationship. However, as with the previous outcome, the actual risk seemed not to emerge until 11+ hours of work per day.

Finally, the analyses were repeated by removing three covariates from the models that were associated with the onset of CHD but were *less* prevalent at baseline among employees working long hours, i.e., being teetotal, high sickness absence and type 2 diabetes. This procedure did not affect the findings (HR for incident fatal CHD, non-fatal myocardial infarction, or definite angina for 11-12 hours vs 7-8 hours 1.55 [1.10-2.18]; HR for incident fatal CHD or non-fatal myocardial infarction 1.66 [1.01-2.74]; data not shown in the tables).

Findings of a sensitivity analysis examining the impact of missing data to the association between working hours and CHD are reported in Appendix Table 2. With this larger cohort the association between long working hours and CHD seems slightly weaker.

Appendix Tables 3 to 6 show the association between working hours and CHD after the CHD cases during the first 1, 2, 3, and 4 follow-up years have been excluded. Exclusion of the cases from the first 1 and 2 years suggest a slightly weaker but statistically significant association between 11-12 hours of work and CHD when compared to 7-8 hours (with attenuation after additional adjustments). Further exclusions (3 and 4 years) resulted in a still weaker association which is now non-significant already at the first model. In the analysis with cases excluded from the first 4 years, a significant association between working 10 hours (but not 11-12 hours) at baseline and incident CHD emerges (HRs vary between 1.44 and 1.50 depending on the adjustment, Appendix Table 6). However, in that

analysis, the total number of CHD cases is only 238 and the number of cases in the group working 11-12 hours was 27 while with the full data the corresponding numbers were 369 and 51. Selection of employees with a subclinical CHD state into shorter (7-8) hours would have resulted in a stronger association found between long hours and CHD after exclusion of CHD events that occurred during the first years of follow-up. This sensitivity analysis did not reveal such a selection effect since the associations became weaker rather than stronger after exclusions.

Table 16. Association between working hours at baseline and incident coronary heart disease at follow-up, as indicated by coronary death, incident definite non-fatal myocardial infarction or incident definite angina pectoris

Daily working hours	n of events	n of parti-cipants	Person-years	Rate / 1000 person-years	Model A HR (95% CI)[a]	*P* value	Model B HR (95% CI)[b]	*P* value	Model C HR (95% CI)[c]	*P* value	Model D HR (95% CI)[d]	*P* value	Model E HR (95% CI)[e]	*P* value
All	369	6014	67543.9	5.46										
7-8	189	3256	36331.7	5.20	1.00	ref.	1.00	ref.	1.00	ref.	1.00	ref.	1.00	ref.
9	69	1247	14185.4	4.86	1.01 (0.76-1.34)	0.94	1.06 (0.79-1.40)	0.71	1.04 (0.78-1.39)	0.77	1.06 (0.79-1.41)	0.70	1.04 (0.78-1.39)	0.80
10	60	894	10115.8	5.93	1.28 (0.95-1.74)	0.11	1.32 (0.98-1.79)	0.07	1.24 (0.92-1.69)	0.16	1.29 (0.95-1.76)	0.11	1.23 (0.90-1.69)	0.19
11-12	51	617	6911.0	7.38	1.60 (1.15-2.23)	0.005	1.67 (1.20-2.32)	0.002	1.56 (1.12-2.17)	0.009	1.63 (1.16-2.28)	0.005	1.56 (1.11-2.19)	0.011
P value for trend						0.004		0.002		0.009		0.004		0.012

HR=Hazard ratio. CI=Confidence interval.
[a] Model A: Adjusted for age, sex, marital status, and occupational grade.
[b] Model B: As Model A and additionally adjusted for diabetes, systolic and diastolic blood pressure, LDL and HDL cholesterol, and triglycerides.
[c] Model C: As Model B and additionally adjusted for smoking, alcohol use, fruit and vegetable consumption, exercise level, body mass index, and sleeping hours.
[d] Model D: As Model C and additionally adjusted for sickness absence, psychological distress, job demands, and decision latitude at work.
[e] Model E: As Model D and additionally adjusted for type A behaviour

Table 17. Association between working hours at baseline and incident coronary heart disease at follow-up, as indicated by coronary death or incident non-fatal definite myocardial infarction

Daily working hours	n of events	n of parti-cipants	Person-years	Rate / 1000 person-years	Model A HR (95% CI)[a]	*P* value	Model B HR (95% CI)[b]	*P* value	Model C HR (95% CI)[c]	*P* value	Model D HR (95% CI)[d]	*P* value	Model E HR (95% CI)[e]	*P* value
All	159	6014	68893.0	2.31										
7-8	81	3256	37015.1	2.19	1.00	ref.	1.00	ref.	1.00	ref.	1.00	ref.	1.00	ref.
9	27	1247	14456.5	1.87	0.95 (0.61-1.49)	0.84	1.01 (0.65-1.58)	0.97	0.99 (0.63-1.55)	0.97	0.96 (0.61-1.52)	0.87	0.93 (0.59-1.47)	0.76
10	27	894	10310.7	2.62	1.46 (0.93-2.30)	0.10	1.51 (0.96-2.38)	0.07	1.39 (0.88-2.18)	0.15	1.34 (0.84-2.13)	0.22	1.26 (0.79-2.02)	0.33
11-12	24	617	7110.7	3.38	1.90 (1.17-3.06)	0.009	1.98 (1.22-3.20)	0.005	1.80 (1.11-2.91)	0.017	1.76 (1.07-2.89)	0.025	1.68 (1.02-2.77)	0.041
P value for trend						0.007		0.004		0.014		0.024		0.046

HR=Hazard ratio. CI=Confidence interval.
[a] Model A: Adjusted for age, sex, marital status, and occupational grade.
[b] Model B: As Model A and additionally adjusted for diabetes, systolic and diastolic blood pressure, LDL and HDL cholesterol, and triglycerides.
[c] Model C: As Model B and additionally adjusted for smoking, alcohol use, fruit and vegetable consumption, exercise level, body mass index, and sleeping hours.
[d] Model D: As Model C and additionally adjusted for sickness absence, psychological distress, job demands, and decision latitude at work.
[e] Model E: As Model D and additionally adjusted for type A behaviour.

9.2.5 Analysis of interaction effects

To examine whether the association between long working hours and CHD was dependent on age, sex, socioeconomic position, prevalent diabetes prediabetes, prevalent psychological distress, exercise level, overweight or obesity, or work characteristics (job demands, decision latitude at work), interaction effects were tested. No interaction was found between age (*P*-value=0.33), sex (*P*=0.34), occupational grade (*P*=0.56), prevalent diabetes or prediabetes (*P*=0.14), prevalent psychological distress (*P*=0.34), exercise level (*P*=0.74), overweight or obesity (*P*=0.22), or job demands (*P*=0.41) with working hours predicting coronary death, incident non-fatal MI or definite angina pectoris, but a significant interaction was found for decision latitude at work (*P*=0.025). Sub-group analysis revealed that in low decision latitude jobs (n=1528), working 11-12 hours a day compared to 7-8 hours a day was associated with a hazard ratio of 2.22 (95% CI 1.13-4.37) whereas in intermediate or high decision latitude jobs (n=4486), the corresponding HR was 1.52 (1.04-2.21).

Interaction analyses were replicated using coronary death or incident non-fatal MI as an outcome. No interaction was found for age (*P*=0.26), sex (*P*=0.26), occupational grade (*P*=0.64), prevalent diabetes or prediabetes (*P*=0.45), prevalent psychological distress (*P*=0.64), exercise level (*P*=0.23), overweight or obesity (*P*=0.82), job demands (*P*=0.73), or decision latitude at work (*P*=0.73).

9.2.6 Summary of the results of Study 1 (CHD)

In Study 1, the association between long working hours and incident CHD was examined with an average follow-up period of 11 years. Working 11-12 hours per day was associated with a 1.56-fold risk of CHD, after accounting for the effects of demographic factors and

several known risk factors for CHD. A similar association was found with an outcome comprising only coronary death and non-fatal myocardial infarction (HR 1.68).

The relationship was not dependent on the participant's age, sex, socioeconomic position, health status, lifestyle, or work characteristics, with the exception of decision latitude at work which seemed to provide some protection against the adverse coronary effects associated with long working hours.

9.3 Type 2 diabetes

9.3.1 Cross-sectional association between working hours and prevalent diabetes at baseline

The baseline participants (n=6761 and 6579 with full data on working hours, diabetes and socio-demographic factors at basline) were included in the analysis to examine the cross-sectional association of working hours with diabetes and prediabetes (as indicated by impaired fasting glucose or impaired glucose tolerance). Prevalence of diabetes at baseline was 2.7 and prevalence of prediabetes was 10.5 (Table 18). No association was found between long hours and prevalent diabetes or prediabetes; a borderline association (P=0.05) was found with 11-12 hours of daily work and lower prevalence of diabetes (OR 0.46).

As a sensitivity analysis, I excluded those 45 cases who had fasted 5-7 hours but not 8 hours or more before blood sampling. In this analysis, the odds ratio of having diabetes at basline was 1.15 (0.73-1.82), 1.11 (0.65-1.92) and 0.39 (0.14-1.09) among those who worked 9, 10 and 11+ hours at baseline compared to those who worked 7-8 hours (adjusted for age, sex, marital status and occupational grade). After excluding 306 pre-diabetes cases who had fasted for 5-7 hours but not 8 hours or more, the corresponfig odds ratios for

having prediabetes vs. no diabetes were 1.05 (0.80-1.39), 1.09 (0.79-1.49) and 0.78 (0.51-1.19) for 9, 10 and 11+ hours, respectively (data not shown in the tables).

Table 18. Association between working hours and prevalence of diabetes and prediabetes at baseline

Daily working hours	n of cases	n of participants	Prevalence (%)	OR (95% CI)[b]	*P* value
	Outcome: diabetes				
All participants	183	6766	2.7		
All participants with covariates[a]	182	6761	2.7		
7-8	118	3723	3.2	1.00	ref.
9	34	1373	2.5	1.04 (0.70-1.56)	0.84
10	23	990	2.3	1.01 (0.63-1.62)	0.97
11-12	7	675	1.0	0.46 (0.21-1.00)	0.05
	Outcome: prediabetes				
All participants	692	6583[c]	10.5		
All participants with covariates[a]	690	6579[c]	10.5		
7-8	411	3605	11.4	1.00	ref.
9	126	1339	9.4	0.88 (0.71-1.10)	0.27
10	99	967	10.2	0.99 (0.78-1.27)	0.96
11-12	54	668	8.1	0.78 (0.57-1.06)	0.12

OR=Odds ratio. CI=Confidence interval.
[a] With information on age, sex, marital status, and occupational grade.
[b] Adjusted for age, sex, marital status, and occupational grade.
[c] Participants with diabetes excluded.

9.3.2 Association between working hours and covariates at baseline

Characteristics of the 4112 participants in the final (longitudinal) Study 2 sample by daily working hours at baseline are presented in Table 19. Of them, 2193 (53%) worked standard 7-8 hours, 851 (21%) worked 9 hours, 636 (15%) worked 10 hours and 432 (11%) worked 11-12 hours a day. Similarly with the Study 1 cohort, men, married or cohabiting persons, those with higher occupational grade, those with fewer sickness absence days, ex-smokers,

those who used a lot of alcohol, those with higher exercise hours, daily intake of fruits and vegetables, less sleeping hours, higher level of psychological distress and type A behaviour, high job demands and high decision latitude at work worked longer hours. Of the biological risk factors, employees working long hours had greater waist circumference and lower HDL cholesterol than those working standard hours. However, the table shows unadjusted estimates and waist circumference especially is associated with sex. When adjusted for sex, there was still a difference in waist circumference between 11-12 working hours' and 7-8 working hours' groups (P=0.042).

Table 19. Characteristics of the final Study 2 sample participants by daily working hours at baseline

Characteristics	All n (%) / Mean (S.D.)	Daily working hours n (%) / Mean (S.D.)				
	(n=4112)	7-8 hours (n=2193)	9 hours (n=851)	10 hours (n=636)	11-12 hours (n=432)	*P* value[a]
Age, years	48.5 (5.6)	48.6 (5.7)	48.4 (5.6)	48.5 (5.4)	48.2 (5.5)	0.66
Sex						<0.001
Male	2979 (72)	1455 (66)	660 (78)	492 (77)	372 (86)	
Female	1133 (28)	738 (34)	191 (22)	144 (23)	60 (14)	
Marital status						<0.001
Married/cohabitating	3210 (78)	1624 (74)	668 (79)	529 (83)	389 (90)	
Non-married/-cohabitating	902 (22)	569 (26)	183 (22)	107 (17)	43 (10)	
Occupational grade level						<0.001
1 highest	801 (19)	185 (8)	210 (25)	213 (33)	193 (45)	
2	972 (24)	415 (19)	264 (31)	195 (31)	98 (23)	
3	659 (16)	385 (18)	142 (17)	79 (12)	53 (12)	
4	714 (17)	478 (22)	114 (13)	74 (12)	48 (11)	
5	514 (13)	363 (17)	84 (10)	40 (6)	27 (6)	
6 lowest	452 (11)	367 (17)	37 (4)	35 (6)	13 (3)	
Coronary heart disease						0.06
No	4033 (98)	2139 (98)	840 (99)	627 (99)	427 (99)	
Yes	79 (2)	54 (2)	11 (1)	9 (1)	5 (1)	
Sickness absence days (past year)						<0.001
0	1446 (35)	641 (29)	327 (38)	280 (44)	198 (46)	
1-7	1968 (48)	1068 (49)	416 (49)	287 (45)	197 (46)	
>7	698 (17)	484 (22)	108 (13)	69 (11)	37 (9)	
Smoking						0.015
Never	2197 (53)	1207 (55)	455 (53)	320 (50)	215 (50)	
Ex	1456 (35)	734 (33)	323 (38)	234 (37)	165 (38)	
Current	459 (11)	252 (11)	73 (9)	82 (13)	52 (12)	
Alcohol use (units / week)						<0.001
0	650 (16)	414 (19)	99 (12)	82 (13)	55 (13)	
>0 ≤ 14 / 21 (women/men)	2806 (68)	1455 (66)	615 (72)	443 (70)	293 (68)	
> 14 / 21 (women/men)	656 (16)	324 (15)	137 (16)	111 (17)	84 (19)	
Daily fruit and vegetable consumption						0.50
Yes	2617 (64)	1381 (63)	538 (63)	410 (65)	288 (67)	
No	1495 (36)	812 (37)	313 (37)	226 (36)	144 (33)	
Moderate / vigorous exercise (hrs / week)						<0.001
≥1.5	2792 (68)	1426 (65)	618 (73)	438 (69)	310 (72)	
<1.5	1320 (32)	767 (35)	233 (27)	198 (31)	122 (28)	
Sleeping hours / night						0.029
6 or less	1042 (25)	522 (24)	208 (24)	178 (28)	134 (31)	
7-8	2987 (73)	1622 (74)	628 (74)	445 (70)	292 (68)	
9 or more	83 (2)	49 (2)	15 (2)	13 (2)	6 (1)	
Psychological distress						<0.001
No	3194 (78)	1762 (80)	631 (74)	482 (76)	319 (74)	
Yes	918 (22)	431 (20)	220 (26)	154 (24)	113 (26)	
Type A behaviour						<0.001
Low	1207 (29)	822 (37)	214 (25)	110 (17)	61 (14)	
Moderate	1494 (36)	844 (38)	301 (35)	205 (32)	144 (33)	
High	1411 (34)	527 (24)	336 (39)	321 (50)	227 (53)	

Table 19 cont.

Table 19 cont.

Job demands						<0.001
Low	783 (19)	626 (29)	88 (10)	40 (6)	29 (7)	
Moderate	1888 (46)	1118 (51)	376 (44)	248 (39)	146 (34)	
High	1441 (35)	449 (20)	387 (45)	348 (55)	257 (59)	
Decision latitude at work						<0.001
High	1877 (46)	738 (34)	461 (54)	395 (62)	283 (66)	
Moderate	1293 (31)	792 (36)	250 (29)	157 (25)	94 (22)	
Low	942 (23)	663 (30)	140 (16)	84 (13)	55 (13)	
Body mass index (kg/m^2)	25.0 (3.5)	24.9 (3.6)	24.9 (3.4)	25.2 (3.7)	25.2 (3.1)	0.30
Waist circumference (cm)	85.3 (11.3)	84.3 (11.4)	85.7 (11.0)	86.4 (11.5)	87.7 (10.0)	<0.001
Systolic blood pressure (mmHg)	119.5 (12.9)	119.5 (13.1)	119.6 (12.5)	119.8 (13.0)	119.2 (12.6)	0.86
Diastolic blood pressure (mmHg)	79.2 (9.0)	79.1 (9.1)	78.9 (8.9)	79.5 (9.0)	79.6 (8.7)	0.51
LDL-cholesterol (mmol/L)	4.3 (1.0)	4.3 (1.0)	4.3 (1.0)	4.4 (1.0)	4.4 (1.0)	0.06
HDL-cholesterol (mmol/L)	1.4 (0.4)	1.5 (0.4)	1.4 (0.4)	1.4 (0.4)	1.4 (0.4)	0.003
Triglycerides (mmol/L)	1.3 (0.7)	1.3 (0.7)	1.3 (0.7)	1.3 (0.7)	1.4 (0.7)	0.40

[a] *P*-value for the heterogeneity across the working hours' groups.

9.3.3 Association between covariates and incident type 2 diabetes

Table 20 presents association between baseline covariates and incident type 2 diabetes among the Study 2 final sample of 4112 participants free from diabetes at baseline. Altogether 266 new cases were detected, indicating an incidence rate of 6.5%. Older age, lower occupational grade, prevalent prediabetes, prevalent CHD, higher sickness absence rate, smoking, teetotal, no fruits and vegetables daily, sedentariness, higher body mass index and waist circumference, higher blood pressure, lower HDL cholesterol, and higher triglycerides were all associated with an increased risk of incident type 2 diabetes. The strongest predictor was prediabetes (OR 8.74 compared to no indication of prediabetes). No significant association was found for sex, marital status, ex-smoking, heavy alcohol use, sleeping hours, psychological distress, type A behaviour pattern, or LDL cholesterol and the onset of type 2 diabetes. In addition, high job demands were related to a lower odds (0.61) of diabetes compared to low job demands in this age-adjusted analysis. After adjustment for sex and occupational grade the odds ratio attenuated to 0.91 (95% CI 0.61-1.33).

Table 20. Association between baseline covariates and incident type 2 diabetes at follow-up, adjusted for age

Covariate	n of cases	n of participants	Rate (%)	OR (95% CI)	*P* value
Age (years)	-	-	-	1.05 (1.03-1.08)	<0.001
Sex					
Female	87	1133	6.0	1.00	ref.
Male	179	2979	7.7	0.79 (0.61-1.03)	0.08
Marital status					
Non- married/cohabiting	64	902	7.1	1.00	ref.
Married/-cohabiting	202	3210	6.3	0.86 (0.64-1.15)	0.32
Occupational grade					
1 (highest)	26	801	3.3	1.00	ref.
2	44	972	4.5	1.55 (0.95-2.55)	0.08
3	46	659	7.0	2.53 (1.54-4.15)	<0.001
4	53	714	7.4	2.67 (1.65-4.34)	<0.001
5	46	514	9.0	3.04 (1.85-5.00)	<0.001
6 (lowest)	51	452	11.2	3.65 (2.24-5.95)	<0.001
Prediabetes					
No	149	3694	4.0	1.00	
Yes	117	418	28.0	8.74 (6.66-11.47)	<0.001
Coronary heart disease					
No	255	4033	6.3	1.00	ref.
Yes	11	79	13.9	2.04 (1.06-3.92)	0.034
Sickness absence days (past year)					
0	81	1446	5.6	1.00	ref.
1-7	115	1968	5.8	1.08 (0.80-1.44)	0.62
>7	70	698	10.0	1.94 (1.39-2.72)	<0.001
Smoking					
Never	134	2197	6.1	1.00	ref.
Ex	91	1456	6.3	0.99 (0.75-1.30)	0.92
Current	41	459	8.9	1.52 (1.05-2.19)	0.025
Alcohol use (units / week)					
0	61	650	9.4	1.66 (1.22-2.26)	0.001
>0 ≤ 14 / 21 (women/men)	162	2806	5.8	1.00	ref.
> 14 / 21 (women/men)	43	656	6.6	1.20 (0.84-1.70)	0.31
Daily fruit and vegetable consumption					
Yes	139	2617	5.3	1.00	ref.
No	127	1495	8.5	1.72 (1.34-2.21)	<0.001
Moderate / vigorous exercise (hrs / week)					
≥1.5	161	2792	5.8	1.00	ref.
<1.5	105	1320	8.0	1.36 (1.05-1.76)	0.019
Sleeping hours / night					
<7	80	1042	7.7	1.27 (0.97-1.68)	0.08
7-8	181	2987	6.1	1.00	ref.
>8	5	83	6.0	1.01 (0.40-2.52)	0.99
Psychological distress					
No	206	3194	6.5	1.00	ref.
Yes	60	918	6.5	1.06 (0.78-1.43)	0.72
Type A behaviour					
Low	89	1207	7.4	1.00	ref.
Moderate	95	1494	6.4	0.85 (0.63-1.14)	0.27
High	82	1411	5.8	0.79 (0.58-1.08)	0.15

Table 20 cont.

Table 20 cont.

Job demands					
Low	64	783	8.2	1.00	ref.
Moderate	131	1888	6.9	0.86 (0.63-1.17)	0.34
High	71	1441	4.9	0.61 (0.43-0.87)	0.006
Decision latitude at work					
High	110	1877	5.9	1.00	
Moderate	83	1293	6.4	1.13 (0.84-1.52)	0.42
Low	73	942	7.8	1.32 (0.97-1.80)	0.08
Body mass index (kg/m^2)	-	-	-	1.22 (1.18-1.26)	<0.001
Waist circumference (cm)	-	-	-	1.07 (1.06-1.08)	<0.001
Systolic blood pressure (mmHg)	-	-	-	1.04 (1.03-1.05)	<0.001
Diastolic blood pressure (mmHg)	-	-	-	1.06 (1.04-1.07)	<0.001
LDL-cholesterol (mmol/L)	-	-	-	1.11 (0.98-1.25)	0.11
HDL-cholesterol (mmol/L)	-	-	-	0.26 (0.18-0.38)	<0.001
Triglycerides (mmol/L)	-	-	-	2.14 (1.87-2.45)	<0.001

OR=Odds ratio; CI=Confidence interval.

9.3.4 Association between working hours and incident type 2 diabetes

Separate analyses were made to assess the association between working hours and (1) incident type 2 diabetes; (2) incident prediabetes; and (3) incident type 2 diabetes among participants with prediabetes. Table 21 (p. 133) shows the serially adjusted association between working hours and incident type 2 diabetes among participants free from diabetes at baseline. No association was found in any of the analyses. Excluding those 25 participants whose fasting hours were 5-7 hours but not 8 hours or more did not materially alter this finding: OR 1.18 (0.83-1.68), 1.39 (0.94-2.05), and 1.02 (0.60-1.72) in participants working 9, 10, and 11-12 hours at baseline (model A; data not shown in the tables).

The association between working hours and incident prediabetes among participants with no indication of diabetes or prediabetes at baseline is presented in Table 22 (p. 134). Four-hundred-fifty-two new cases of prediabetes were identified among a sample of participants with no diabetes or prediabetes at baseline (rate 12.9%). The table also shows no evidence on an association with working hours. Excluding those 124 participants whose fasting hours were 5-7 hours but not 8 hours or more did not affect the results: OR 0.85

(0.62-1.16), 0.95 (0.68-1.34), and 0.90 (0.60-1.35) in participants working 9, 10, and 11-12 hours at baseline (model A; data not shown in the tables).

Finally, the sample was restricted to those participants (n=418) in the longitudinal study cohort with prediabetes at baseline (Table 23, p. 135). Participants with longer working hours seemed to be more likely to be definite cases of type 2 diabetes at follow-up (ORs 2.20, 2.18 and 2.13 in the groups working 9, 10 and 11-12 hours, respectively). Although the test of trend was significant, the results suggest equal risk in each group and in the highest working hours' group the association was not statistically significant (probably caused by the low number of cases and participants, 10/36). When the two highest categories of working hours were further collapsed together, the associations were as follows: 9 hours vs 7-8 hours OR 2.20 (1.21-4.00); 10 hours or more vs 7-8 hours OR 2.16 (1.18-3.98). Adjustment for various covariates seemed to strenghten the relationships rather than attenuate them.

A sensitivity analysis excluding those 201 cases whose fasting hours were 5 to 7 hours but not 8 hours or more showed similar relationship: OR 2.23 (1.04-4.82), 2.44 (1.01-5.91), and 2.35 (0.67-8.23) in participants working 9, 10, and 11-12 hours at baseline (model 1); OR 2.24 (1.04-4.83) and 2.42 (1.08-5.41), in participants working 9 and 10+ hours at baseline compared to those working 7-8 hours, respectively (model A; data not shown in the tables).

Table 21. Association between working hours at baseline and incident type 2 diabetes at follow-up

Daily working hours	n of events	n of participants	Rate (%)	Model A OR (95% CI)[a]	*P* value	Model B OR (95% CI)[b]	*P* value	Model C OR (95% CI)[c]	*P* value	Model D OR (95% CI)[d]	*P* value	Model E OR (95% CI)[e]	*P* value
All	266	4112	6.5										
7-8	154	2193	7.0	1.00	ref.	1.00	ref.	1.00	ref.	1.00	ref.	1.00	ref.
9	51	851	6.0	1.12 (0.79-1.57)	0.53	1.18 (0.82-1.71)	0.37	1.16 (0.80-1.69)	0.42	1.21 (0.83-1.76)	0.33	1.19 (0.81-1.74)	0.38
10	41	636	6.5	1.31 (0.90-1.90)	0.16	1.46 (0.97-2.18)	0.07	1.37 (0.91-2.06)	0.13	1.48 (0.97-2.25)	0.07	1.35 (0.87-2.08)	0.18
11-12	20	432	4.6	0.99 (0.60-1.63)	0.96	1.00 (0.59-1.72)	0.99	0.97 (0.57-1.67)	0.92	1.06 (0.61-1.84)	0.85	1.02 (0.58-1.79)	0.95
P value for trend					0.44		0.29		0.42		0.26		0.42

OR=Odds ratio. CI=Confidence interval.
[a] Model A: Adjusted for age, sex, marital status, and occupational grade.
[b] Model B: As Model A and additionally adjusted for prediabetes, CHD, systolic and diastolic blood pressure, LDL and HDL cholesterol, and triglycerides.
[c] Model C: As Model B and additionally adjusted for smoking, alcohol use, fruit and vegetable consumption, exercise level, and sleeping hours.
[d] Model D: As Model C and additionally adjusted for psychological distress, sickness absence, type A behaviour, job demands, decision latitude at work.
[e] Model E: As Model D and additionally adjusted for body mass index and waist circumference.

Table 22. Association between working hours at baseline and incident prediabetes at follow-up

Daily working hours	n of events	n of participants	Rate (%)	Model A OR (95% CI)[a]	*P* value	Model B OR (95% CI)[b]	*P* value	Model C OR (95% CI)[c]	*P* value	Model D OR (95% CI)[d]	*P* value	Model E OR (95% CI)[e]	*P* value
All	452	3515	12.9										
7-8	248	1841	13.5	1.00	ref.	1.00	ref.	1.00	ref.	1.00	ref.	1.00	ref.
9	92	741	12.4	0.90 (0.69-1.18)	0.44	0.92 (0.70-1.20)	0.53	0.92 (0.70-1.21)	0.55	0.91 (0.69-1.20)	0.50	0.90 (0.69-1.19)	0.47
10	67	548	12.2	0.89 (0.65-1.20)	0.44	0.89 (0.66-1.21)	0.45	0.90 (0.66-1.22)	0.49	0.88 (0.64-1.21)	0.45	0.88 (0.64-1.21)	0.44
11-12	45	385	11.7	0.86 (0.60-1.23)	0.41	0.86 (0.60-1.23)	0.41	0.86 (0.60-1.23)	0.40	0.85 (0.58-1.23)	0.38	0.84 (0.58-1.22)	0.37
P value for trend					0.30		0.31		0.33		0.30		0.29

OR=Odds ratio. CI=Confidence interval.
[a] Model A: Adjusted for age, sex, marital status, and occupational grade.
[b] Model B: As Model A and additionally adjusted for CHD, systolic and diastolic blood pressure, LDL and HDL cholesterol, and triglycerides.
[c] Model C: As Model B and additionally adjusted for smoking, alcohol use, fruit and vegetable consumption, exercise level, and sleeping hours.
[d] Model D: As Model C and additionally adjusted for psychological distress, sickness absence, type A behaviour, job demands, and decision latitude at work.
[e] Model E: As Model D and additionally adjusted for body mass index and waist circumference.

Table 23. Association between working hours at baseline and incident type 2 diabetes at follow-up among participants with prediabetes at baseline

Daily working hours	n of events	n of participants	Rate (%)	Model A OR (95% CI)[a]	*P* value	Model B OR (95% CI)[b]	*P* value	Model C OR (95% CI)[c]	*P* value	Model D OR (95% CI)[d]	*P* value	Model E OR (95% CI)[e]	*P* value
All	117	418	28.0										
7-8	61	238	25.6	1.00	ref.	1.00	ref.	1.00	ref.	1.00	ref.	1.00	ref.
9	27	83	32.5	2.20 (1.21-4.00)	0.009	2.24 (1.19-4.22)	0.013	2.31 (1.21-4.40)	0.011	2.55 (1.28-5.11)	0.009	2.69 (1.30-5.58)	0.008
10	19	61	31.2	2.18 (1.09-4.36)	0.027	2.67 (1.27-5.60)	0.009	2.69 (1.26-5.73)	0.010	3.22 (1.45-7.14)	0.005	2.95 (1.24-6.98)	0.014
11-12	10	36	27.8	2.13 (0.88-5.14)	0.09	1.68 (0.65-4.34)	0.29	1.85 (0.68-5.00)	0.23	2.13 (0.75-6.07)	0.17	2.54 (0.85-7.60)	0.10
P value for trend					0.010		0.017		0.013		0.008		0.009

OR=Odds ratio. CI=Confidence interval.
[a] Model A: Adjusted for age, sex, marital status, and occupational grade.
[b] Model B: As Model A and additionally adjusted for CHD, systolic and diastolic blood pressure, LDL and HDL cholesterol, and triglycerides.
[c] Model C: As Model B and additionally adjusted for smoking, alcohol use, fruit and vegetable consumption, exercise level, and sleeping hours.
[d] Model D: As Model C and additionally adjusted for psychological distress, sickness absence, type A behaviour, job demands, and decision latitude at work.
[e] Model E: As Model D and additionally adjusted for body mass index and waist circumference.

9.3.5 Analysis of interaction effects

To examine whether the association between long working hours and incident type 2 diabetes was dependent on age, sex, socioeconomic position, prevalent psychological distress, exercise level, overweight/obesity, high waist circumference, or work characteristics (job demands, decision latitude at work), interaction effects were tested. No interaction was found between age (P=0.17), sex (P=0.52), occupational grade (P=0.87), smoking (P=0.33), exercise level (P=0.60), overweight or obesity (P=0.098), high waist circumference (P=0.57), job demands (P=0.40), or decision latitude at work (P=0.69) with working hours predicting type 2 diabetes.

No interaction was found between age (P=0.48), sex (P=0.23), occupational grade (P=0.84), smoking (P=0.44), exercise level (P=0.97), overweight or obesity (P=0.35), high waist circumference (P=0.80), or decision latitude at work (P=0.49) with working hours predicting prediabetes. Interaction with job demands was significant (P=0.045), but sub-group analysis for high demands (n=1262) and low/intermediate demands (n=2253) did not reveal any meaningful associations with working hours (ORs for high demands group 1.09 [95%CI 0.71-1.69], 0.77 [0.48-1.26], 0.68 [0.39-1.18] and for low/intermediate demands group 0.72 [0.50-1.04], 1.03 [0.58-1.55] and 1.12 [0.68-1.83], in participants working 9, 10, and 11-12 hours, respectively). Interaction analyses were not performed among the sub-group of prediabetic participants due to a low number of participants with prediabetes.

9.3.6 Summary of the results of Study 2 (diabetes)

Study 2 examined associations between working hours and diabetes using information on different phases of the development of diabetes, that is, prediabetes, when the criteria for

clinical diabetes are not fulfilled but the participant has either impaired fasting glucose or impaired glucose tolerance, and clinical type 2 diabetes when the criteria are fulfilled. The third phase is the development of clinical type 2 diabetes from prediabetes. No evidence was found of an association between working hours and incidence of type 2 diabetes or prediabetes among healthy participants. However, when the sample was restricted to those who were prediabetics at baseline, participants with longer working hours seemed to be more likely to develop type 2 diabetes at follow-up (ORs 2.20, 2.18 and 2.13 in the groups working 9, 10 and 11-12 hours, respectively). However, numbers were probably too small to confirm that these associations are significant. This study suggests no interaction effects; that is, the association between working hours and the development of type 2 diabetes or prediabetes was not dependent on socio-demographic factors, behavioural characteristics, or work characteristics.

9.4 Depression

9.4.1 Cross-sectional association between working hours and prevalent psychological distress at baseline

At the baseline sample of 7276 participants, psychological distress measured by GHQ-30-caseness was used as an indicator of depressive symptoms. Table 24 shows associations between working hours and psychological distress at baseline. Overall prevalence of psychological distress was 22.4%. Working 11-12 hours a day was related to higher prevalence (26.1%) compared to working 7-8 hours (20.1%) and the logistic regression analysis indicated an odds ratio of 1.49 after adjustment for socio-demographic factors. Working 9 hours and 10 hours were also related to an incresed odds of psychological distress (1.31 and 1.35, respectively), when compared to 7-8 hours a day. *P*-value for trend was significant which suggests a dose-response relationship.

Table 24. Association between working hours and prevalence of psychological distress (GHQ-30-caseness) at baseline

Daily working hours	n of cases	n of parti-cipants	Prevalence (%)	OR (95% CI)[c]	*P* value
All participants[a]	1630	7283	22.4		
All participants with data[b]	1629	7276	22.4		
7-8	797	3963	20.1	1.00	ref.
9	366	1486	24.6	1.31 (1.13-1.52)	<0.001
10	271	1080	25.1	1.35 (1.14-1.60)	<0.001
11-12	195	747	26.1	1.49 (1.23-1.81)	<0.001
P value for trend					<0.001

OR=Odds ratio. CI=Confidence interval.
[a] With information on working hours and psychological distress.
[b] With information on age, sex, marital status, occupational grade, psychological distress and working hours.
[c] Adjusted for age, sex, marital status, and occupational grade.

9.4.2 Association between working hours and covariates at baseline

Table 25 presents associations between working hours and covariates at baseline among the final Study 3 sample (n=2121). Age and chronic disease were not related to working hours while long hours were more common in men, married or co-habited employees, those with high occupational grade, those having less sickness absence days, those using alcohol over the recommended limits, those with high job demands and high decision latitude. Employees who worked long hours were also more likely to have a history of smoking than those who worked standard 7 to 8 hours a day.

Table 25. Characteristics of the final Study 3 sample participants by daily working hours at baseline

Characteristics	Daily working hours n (%) / Mean (S.D.)					
	All (n=2121)	7-8 hours (n=1103)	9 hours (n=442)	10 hours (n=348)	11-12 hours (n=228)	*P* value[a]
Age	46.7 (4.8)	46.6 (4.8)	46.6 (4.6)	47.3 (4.8)	46.7 (4.8)	0.17
Sex						<0.001
Male	1623 (77)	778 (71)	364 (82)	276 (79)	205 (90)	
Female	498 (23)	325 (29)	78 (18)	72 (21)	23 (10)	
Marital status						<0.001
Married/cohabiting	1714 (81)	847 (77)	363 (82)	291 (84)	213 (93)	
Non-married/-cohabiting	407 (19)	256 (23)	79 (18)	57 (16)	15 (7)	
Occupational grade						<0.001
1 (highest)	385 (18)	67 (6)	103 (23)	109 (31)	106 (46)	
2	527 (25)	216 (20)	145 (33)	111 (32)	55 (24)	
3	349 (16)	202 (18)	79 (18)	43 (12)	25 (11)	
4	333 (16)	225 (20)	48 (11)	35 (10)	25 (11)	
5	278 (13)	193 (18)	46 (10)	26 (7)	13 (6)	
6 (lowest)	249 (12)	200 (18)	21 (5)	24 (7)	4 (2)	
Chronic disease						0.98
No	1452 (68)	756 (69)	299 (68)	240 (69)	157 (69)	
Yes	669 (32)	347 (31)	143 (32)	108 (31)	71 (31)	
Sickness absence days (past year)						<0.001
0	814 (38)	334 (30)	189 (43)	175 (50)	116 (51)	
1-7	987 (47)	545 (49)	210 (48)	141 (41)	91 (40)	
>7	320 (15)	224 (20)	43 (10)	32 (9)	21 (9)	
Alcohol use						<0.001
No	331 (16)	207 (19)	56 (13)	44 (13)	24 (11)	
Moderate	1431 (67)	731 (66)	313 (71)	234 (67)	153 (67)	
High	359 (17)	165 (15)	73 (17)	70 (20)	51 (22)	
Smoking						0.003
Never	1106 (52)	610 (55)	230 (52)	164 (47)	102 (45)	
Ex	756 (36)	351 (32)	165 (37)	138 (40)	102 (45)	
Current	259 (12)	142 (13)	47 (11)	46 (13)	24 (11)	
Job demands						<0.001
Low	438 (21)	340 (31)	57 (13)	30 (9)	11 (5)	
Moderate	1025 (48)	568 (52)	209 (47)	161 (46)	87 (38)	
High	658 (31)	195 (18)	176 (40)	157 (45)	130 (57)	
Decision latitude at work						<0.001
High	1045 (49)	384 (35)	266 (60)	235 (68)	160 (70)	
Moderate	632 (30)	390 (35)	121 (27)	71 (20)	50 (22)	
Low	444 (21)	329 (30)	55 (12)	42 (12)	18 (8)	

[a] *P*-value for the heterogeneity across the working hours' groups.

9.4.3 Association between covariates and onset of depression

Among the 2121 participants, 66 new-onset cases of major depressive episode (MDE) were identified, indicating a rate of 3.1%. Table 26 presents the relationship between baseline covariates and new-onset MDE at follow-up. Predictors of the onset of MDE were female sex, lower occupational grade, chronic disease, sickness absence, and moderate decision latitude at work compared to high decision latitude. In addition, the odds ratio for MDE for participants who used alcohol was increased in the expected direction but not statistically significant at conventional levels. In this sample there were no robust associations between marital status, smoking, job demands, or low decision latitude at work predicting the onset of MDE.

Table 26. Association between baseline covariates and onset of depression at follow-up, adjusted for age

Covariate	n of events	n of participants	Rate (%)	OR (95% CI)	*P* value
Age (years)	-	-	-	0.95 (0.90-1.00)	0.06
Sex					
Male	41	1623	2.5	1.00	ref.
Female	25	498	5.0	2.06 (1.24-3.43)	0.005
Marital status					
Married/cohabiting	49	1714	2.9	1.00	ref.
Non-married/-cohabiting	17	407	4.2	1.41 (0.80-2.49)	0.23
Occupational grade					
1 (highest)	4	385	1.0	1.00	ref.
2	16	527	3.0	2.78 (0.92-8.40)	0.07
3	9	349	2.6	2.30 (0.70-7.59)	0.17
4	13	333	3.9	3.46 (1.11-10.79)	0.033
5	15	278	5.4	5.05 (1.65-15.43)	0.005
6 (lowest)	9	249	3.6	3.58 (1.09-11.76)	0.036
Chronic disease					
No	32	1452	2.2	1.00	ref.
Yes	34	669	5.1	2.44 (1.49-3.99)	<0.001
Sickness absence days (past year)					
0	12	814	1.5	1.00	ref.
1-7	37	987	3.8	2.52 (1.31-4.88)	0.006
>7	17	320	5.3	3.66 (1.73-7.77)	<0.001
Alcohol use					
No	5	331	1.5	1.00	ref.
Moderate	51	1431	3.6	2.36 (0.93-5.95)	0.07
High	10	359	2.8	1.80 (0.61-5.33)	0.29
Smoking					
Never	29	1106	2.6	1.00	ref.
Ex	27	756	3.6	1.41 (0.82-2.40)	0.21
Current	10	259	3.9	1.47 (0.71-3.06)	0.30
Job demands					
Low	16	438	3.7	1.00	ref.
Moderate	29	1025	2.8	0.77 (0.42-1.44)	0.42
High	21	658	3.2	0.86 (0.44-1.67)	0.66
Decision latitude at work					
High	24	1045	2.3	1.00	ref.
Moderate	27	632	4.3	1.85 (1.06-3.24)	0.031
Low	15	444	3.4	1.51 (0.78-2.90)	0.22

OR=Odds ratio; CI=Confidence interval.

Table 27. Associations between working hours at baseline and onset of depression at follow-up

Daily working hours	n of events	n of partici-pants	Rate (%)	Model A OR (95% CI)[a]	*P* value	Model B OR (95% CI)[b]	*P* value	Model C OR (95% CI) [c]	*P* value	Model D OR (95% CI)[d]	*P* value
All	66	2121	3.1								
7-8	37	1103	3.4	1.00		1.00		1.00		1.00	
9	9	442	2.0	0.78 (0.37-1.67)	0.52	0.80 (0.37-1.73)	0.58	0.77 (0.35-1.66)	0.50	0.78 (0.35-1.70)	0.53
10	10	348	2.9	1.23 (0.59-2.58)	0.59	1.36 (0.64-2.87)	0.43	1.33 (0.62-2.83)	0.47	1.37 (0.63-2.96)	0.43
11-12	10	228	4.4	2.42 (1.11-5.27)	0.026	2.61 (1.19-5.73)	0.017	2.52 (1.14-5.55)	0.022	2.57 (1.14 to 5.78)	0.023
P for trend				0.07		0.042		0.05		0.047	

[A]Model A: Adjusted for age, sex, occupational grade, and marital status.
[b]Model B: As model A and additionally adjusted for chronic disease and sickness absence.
[c]Model C: As model B and additionally adjusted for smoking and alcohol use.
[d]Model D: As model C and additionally adjusted for job demands and decision latitude at work.
OR=Odds ratio; CI=Confidence interval.

9.4.4 Association between working hours and onset of depression

Working 11-12 hours a day was related to a 2.42-fold odds of MDE compared to working 7-8 hours a day in an analysis adjusted for socio-demographic characteristics (Table 27, p. 143, Model A). Further adjustment for chronic disease and sickness absence (Model B), health behaviours (Model C) and work characteristics (Model D) made little change to the association (OR 2.57 in Model D). An additional analysis removing protective factors from the adjustments (sickness absence and decision latitude which were more favourable in the long-hours' group) showed an odds ratio of 2.26 (1.02-5.05) in the employees working 11-12 hours compared to those working 7-8 hours. The trend was statistically significant only in Models B, C, and D which may be due to the finding that working 9 hours was related to a slightly lower odds of MDE; 0.77 to 0.80 when compared to 7-8 hours.

9.4.5 Summary of the results of Study 3 (depression)

In study 3, long working hours were associated with psychological distress at baseline. During the mean of nearly six years' follow-up, long working hours also predicted the onset of a clinically significant major depressive episode among employees who had no symptoms of psychological distress at baseline. Several baseline characteristics predicted the onset of MDE, including female sex, low SEP, prevalent chronic disease and high sickness absenteeism. Working 11 or more hours a day was associated with a 2.4- to 2.6-fold risk of an MDE when compared with working a standard 7-8 hours a day. Although the number of cases was relatively low, this association was robust to adjustment for a range of socio-demographic, life-style, health, and work-related factors at baseline.

9.5 Sleep disturbances

9.5.1 Cross-sectional association between working hours and prevalent sleep disturbances at baseline

At baseline, the prevalence of sleep disturbances was as follows: short sleep 46%, frequent waking 27%, early waking and waking without feeling refreshed 20% each, and difficulty falling asleep 7%. Cross-sectional analyses were carried out in those full-time employees who had complete data on working hours, socio-demographic factors, and a sleep outcome under study (n ranging from 3535 to 3565). Long weekly working hours were strongly related to the probability of sleeping 6 hours or less per night (Table 28, p. 146). The association followed a dose-response pattern so that increasing hours of work were related to increasing probability of short sleeping hours. Working 49-55 hours but not >55 hours a week was associated with difficulty falling asleep (OR 1.63). Working hours were not associated with frequent waking during the night. However, long hours were associated with early waking (OR 1.38 for >55 hours and OR 1.33 for 49-55 hours compared to 35-40 weekly hours, Table 29, p. 146). Long hours were also associated with waking without feeling refreshed (OR 1.38 for >55 hours and OR 1.36 for 49-55 hours).

Table 28. Cross-sectional association between working hours and sleep disturbances at baseline

Weekly working hours	Outcome variable at baseline											
	Short sleep[a]				Difficulty falling in sleep[a]				Frequent waking[a]			
	n of cases	N of partici-pants (%)	OR (95% CI)[b]	*P* value	n of cases	n of partici-pants (%)	OR (95% CI)[b]	*P* value	n of cases	n of partici-pants (%)	OR (95% CI)[b]	*P* value
All	1655	3565 (46)			242	3550 (7)			951	3536 (27)		
35-40	597	1425 (42)	1.00		97	1414 (7)	1.00		386	1413 (27)	1.00	
41-48	445	979 (45)	1.29 (1.09-1.53)	0.003	59	976 (6)	1.01 (0.72-1.42)	0.96	252	967 (26)	0.97 (0.80-1.18)	0.78
49-55	415	830 (50)	1.77 (1.47-2.14)	<0.001	67	827 (8)	1.63 (1.14-2.32)	0.007	226	824 (27)	1.03 (0.84-1.27)	0.77
>55	198	331 (60)	2.72 (2.10-3.53)	<0.001	19	333 (6)	1.12 (0.66-1.90)	0.68	87	332 (26)	0.94 (0.70-1.25)	0.65
P for trend				<0.001				0.07				0.89

[a] Participants with data on working hours, age, sex, marital status, occupational grade and outcome measure at baseline.
[b] Adjusted for age, sex, marital status, and occupational grade.

Table 29. Cross-sectional association between working hours and sleep disturbances at baseline

Weekly working hours	Outcome variable at baseline							
	Early waking[a]				Waking without feeling refreshed[a]			
	n of cases	n of partici-pants (%)	OR (95% CI)[b]	*P* value	n of cases	n of partici-pants (%)	OR (95% CI)[b]	*P* value
All	702	3535 (20)			696	3544 (20)		
35-40	259	1408 (18)	1.00		265	1413 (19)	1.00	
41-48	197	973 (20)	1.21 (0.98-1.49)	0.08	192	975 (20)	1.17 (0.94-1.44)	0.16
49-55	174	824 (21)	1.33 (1.06-1.68)	0.015	172	825 (21)	1.36 (1.07-1.71)	0.011
>55	72	330 (22)	1.38 (1.01-1.88)	0.042	67	331 (20)	1.38 (1.00-1.89)	0.049
P for trend				0.008				0.007

[a] Participants with data on working hours, age, sex, marital status, occupational grade and outcome measure at baseline.
[b] Adjusted for age, sex, marital status, and occupational grade.

9.5.2 Association between working hours and covariates at baseline

Table 30 shows associations between working hours, categorized into 4 groups, and study covariates at baseline (phase 5) among the longitudinal Study 4 sample (participants with phase 5 characteristics and data on at least one of the sleep outcomes at phase 7, n=1782). Anova and χ^2 tests of heterogeneity suggest some heterogeneity in sex, marital status, occupational grade, physical activity, alcohol use, job demands and decision latitude between groups with different working hours. The means and percentages indicate that long hours' groups include more men, more married or cohabiting people, those with high occupational grades and those who use alcohol over recommended limits, as well as those with high job demands and high decision latitude. With regard to physical activity, employees with standard (35-40) and very long (>55) working hours seem to be less active than those who worked 41-48 or 49-55 hours per week. No heterogeieity was found in age, chronic disease, smoking, or body mass index between the groups of working hours.

Table 30. Characteristics of the final Study 4 sample participants by weekly working hours at baseline

Characteristics	All n (%) / Mean (S.D.)	Weekly working hours n (%) / Mean (S.D.)				
	All (n=1782)	35-40 (n=672)	41-48 (n=507)	49-55 (n=446)	>55 (n=157)	*P* value[a]
Age (years)	51.1 (3.5)	51.1 (3.6)	51.0 (3.4)	50.9 (3.4)	51.5 (3.6)	0.28
Sex						<0.001
Men	1378 (77)	486 (72)	400 (79)	361 (81)	131 (83)	
Women	404 (23)	186 (28)	107 (21)	85 (19)	26 (17)	
Marital status						<0.001
Married/cohabited	1422 (80)	493 (73)	418 (82)	378 (85)	133 (85)	
Non-married/ cohabited	360 (20)	179 (27)	89 (18)	68 (15)	24 (15)	
Occupational grade						<0.001
1 (highest)	418 (23)	54 (8)	112 (22)	171 (38)	81 (52)	
2	449 (25)	120 (18)	138 (27)	150 (34)	41 (26)	
3	277 (16)	126 (19)	87 (17)	50 (11)	14 (9)	
4	330 (19)	192 (29)	78 (15)	51 (11)	9 (6)	
5	178 (10)	104 (15)	51(10)	14 (3)	9 (6)	
6 (lowest)	130 (7)	76 (11)	41 (8)	10 (2)	3 (2)	
Chronic disease						0.06
No	966 (54)	343 (51)	299 (59)	238 (53)	86 (55)	
Yes	816 (46)	329 (49)	208 (41)	208 (47)	71 (45)	
Body Mass Index (BMI)	26.1 (4.3)	26.0 (4.7)	26.0 (3.8)	26.3 (4.3)	26.4 (3.3)	0.47
Physical activity						<0.001
Low	269 (15)	126 (19)	62 (12)	52 (12)	29 (18)	
Intermediate	635 (36)	263 (39)	163 (32)	154 (35)	55 (35)	
High	878 (49)	283 (42)	282 (56)	240 (54)	73 (47)	
Alcohol use (units/wk)						0.011
0	203 (11)	93 (14)	64 (13)	32 (7)	14 (9)	
>0 ≤ 14 / 21 (women/men)	1115 (63)	424 (63)	305 (60)	288 (65)	98 (62)	
> 14 / 21 (women/men)	464 (26)	155 (23)	138 (27)	126 (28)	45 (29)	
Smoking						0.07
No	1611 (90)	599 (89)	473 (93)	397 (89)	142 (90)	
Yes	171 (10)	73 (11)	34 (7)	49 (11)	15 (10)	
Job demands						<0.001
Low	261 (15)	162 (24)	68 (13)	29 (7)	2 (1)	
Moderate	792 (44)	348 (52)	240 (47)	159 (36)	45 (29)	
High	729 (41)	162 (24)	199 (39)	158 (58)	110 (70)	
Decision latitude at work						<0.001
High	847 (48)	216 (32)	244 (48)	281 (63)	106 (68)	
Moderate	585 (33)	256 (38)	172 (34)	116 (26)	41 (26)	
Low	350 (20)	200 (30)	91 (18)	49 (11)	10 (6)	

[a]*P*-value for the heterogeneity across the working hours' groups.

9.5.3 Association between covariates and onset of sleep disturbances

Tables 31 and 32 show the association between covariates measured at baseline and new-onset sleep disturbances by sleep category at follow-up. Rates of onset in different sleep disturbances were as follows: short sleeping hours 21%, frequent waking 21%, early waking 14%, waking without feeling refreshed 10%, and difficulty falling asleep 4%. Age was inversely associated with "waking without feeling refreshed" but not with other outcomes. Female sex was associated with shortened sleeping hours (OR 1.9 compared with male sex), difficulty falling asleep (OR 2.5), early waking (OR 1.7), and waking without feeling refreshed (OR 2.1) but not with frequent waking during the night. Marital status was not related to sleep outcomes. A strong inverse association was found between occupational grade and difficulty falling asleep (OR 2.7 for the lowest vs. highest occupational grade). A similar albeit less strong relationship was found for waking without feeling refreshed (OR 1.8 for the lowest vs. highest grade). Occupational grade was not related to shortened sleep, frequent waking, or early waking.

Chronic disease was associated with new-onset of difficulty falling asleep (OR 2.3 compared to not having a disease) and early waking (OR 1.6) but not with shortened sleep, frequent waking, or waking without feeling refreshed. Each unit's increase in body mass index predicted an increased frequency of onset of difficulty falling asleep of 5% and onset of frequent waking of 4% but it was not related to shortened sleeping hours, early waking, or waking without feeling refreshed. Physical activity was not significantly associated with any of the outcomes whereas heavy alcohol use was related to lower odds of new-onset shortened sleep and difficulties falling asleep when compared with being teetotal. Moderate alcohol consumption predicted lower probability of future difficulties falling asleep, but alcohol use was not related to frequent waking during the night, early waking, or waking

without feeling refreshed. In contrast, smoking predicted the onset of non-refreshing sleep (OR 1.8 compared to non-smoking).

High job demands were related to shortened hours of sleep (OR 1.7 compared to low demands, frequent waking (OR 1.6), and they were marginally associated with feelings of non-refreshing sleep (OR 1.8 [NS] for high demans, OR 1.8 for moderate demands). Low decision latitude at work predicted the onset of difficulty falling asleep (OR 2.1 compared to high decision latitude), early waking (OR 1.6), and waking without feeling refreshed (OR 2.3). It was marginally related to reduced sleeping hours (OR 1.5 [NS] for low decision latitude, OR 1.8 for moderate decision latitude).

In sum, of the covariates, female sex was strongly related to the study outcomes while age and marital status were not. For low versus high occupational grade, the strongest association was found with difficulty falling asleep. Associations between physical health and health behaviours were mixed indicating effect on some outcomes but not with others, and alcohol use seemed to protect against difficulties falling asleep. Work stress factors showed some consistency by indicating high demands and low decision latitude to predict various sleep outcomes studied.

Table 31. Association between covariates at baseline and onset of sleep disturbances at follow-up, adjusted for age

Covariate	Outcome variable at follow-up											
	Short sleep				Difficulty falling in sleep				Frequent waking			
	n of cases	n of partici-pants (%)	OR (95% CI)	*P* value	n of cases	n of partici-pants (%)	OR (95% CI)	*P* value	n of cases	n of partici-pants (%)	OR (95% CI)	*P* value
Age (years)	-	-	0.98 (0.94-1.03)	0.38	-	-	0.98 (0.91-1.05)	0.58	-	-	1.02 (0.98-1.06)	0.39
Sex												
Men	133	735 (18)	1.00		40	1294 (3)	1.00		213	1045 (20)	1.00	
Women	67	229 (29)	1.86 (1.32-2.62)	<0.001	26	345 (8)	2.54 (1.53-4.23)	<0.001	64	260 (25)	1.28 (0.93-1.76)	0.13
Marital status												
Married/cohabited	155	780 (20)	1.00		50	1318 (4)	1.00		220	1040 (21)	1.00	
Non-married/ cohabited	45	184 (24)	1.29 (0.88-1.89)	0.19	16	321 (5)	1.32 (0.74-2.35)	0.35	57	265 (22)	1.03 (0.74-1.44)	0.84
Occupational grade												
1 (highest)	49	241 (20)	1.00		9	391 (2)	1.00		70	295 (24)	1.00	
2	54	259 (21)	1.01 (0.66-1.57)	0.95	13	420 (3)	1.35 (0.57-3.19)	0.50	76	351 (22)	0.90 (0.62-1.30)	0.58
3	29	138 (21)	1.02 (0.60-1.71)	0.95	6	254 (2)	1.02 (0.36-2.90)	0.98	45	209 (22)	0.90 (0.59-1.38)	0.63
4	38	164 (23)	1.14 (0.70-1.86)	0.59	22	303 (7)	3.28 (1.48-7.30)	0.004	49	238 (21)	0.85 (0.56-1.29)	0.45
5 to 6 (lowest)[a]	30	162 (19)	0.88 (0.53-1.46)	0.61	16	271 (6)	2.65 (1.15-6.09)	0.022	37	212 (17)	0.69 (0.44-1.07)	0.10
Chronic disease												
No	109	540 (20)	1.00		24	920 (3)	1.00		150	765 (20)	1.00	
Yes	91	424 (21)	1.09 (0.79-1.48)	0.61	42	719 (6)	2.32 (1.39-3.87)	0.001	127	540 (24)	1.26 (0.96-1.65)	0.09
Body Mass Index (BMI)	-	-	1.03 (0.99-1.06)	0.12	-	-	1.05 (1.00-1.10)	0.035	-	-	1.04 (1.01-1.08)	0.007
Physical activity												
High	93	496 (19)	1.00		26	817 (3)	1.00		137	653 (21)	1.00	
Intermediate	68	312 (22)	1.21 (0.85-1.72)	0.29	27	572 (5)	1.50 (0.87-2.61)	0.15	96	449 (21)	1.03 (0.77-1.38)	0.86
Low	39	156 (25)	1.44 (0.94-2.20)	0.10	13	250 (5)	1.67 (0.84-3.30)	0.14	44	203 (22)	1.04 (0.71-1.53)	0.84
Alcohol use (units/wk)												
0	29	114 (25)	1.00		15	183 (8)	1.00		32	157 (20)	1.00	
>0 ≤ 14 / 21 (women/men)	129	589 (22)	0.82 (0.51-1.30)	0.39	39	1019 (4)	0.44 (0.24-0.82)	0.010	183	817 (22)	1.13 (0.74-1.72)	0.57
> 14 / 21 (women/men)	42	261 (16)	0.56 (0.33-0.96)	0.033	12	437 (3)	0.32 (0.15-0.69)	0.004	62	331 (19)	0.90 (0.56-1.44)	0.65

Table 31 cont.

Table 31 cont.

Smoking												
No	180	876 (21)	1.00		60	1495 (4)	1.00		252	1177 (21)	1.00	
Yes	20	88 (23)	1.13 (0.67-1.90)	0.66	6	144 (4)	1.03 (0.44-2.44)	0.94	25	128 (20)	0.89 (0.57-1.42)	0.63
Job demands												
Low	23	159 (14)	1.00		9	248 (4)	1.00		32	197 (16)	1.00	
Intermediate	95	439 (22)	1.61 (0.98-2.66)	0.06	32	735 (4)	1.19 (0.56-2.53)	0.66	128	604 (21)	1.41 (0.92-2.16)	0.12
High	82	366 (22)	1.69 (1.02-2.80)	0.043	25	656 (4)	1.03 (0.47-2.25)	0.93	117	504 (23)	1.59 (1.03-2.45)	0.036
Decision latitude at work												
High	82	473 (17)	1.00		25	791 (3)	1.00		125	645 (19)	1.00	
Intermediate	76	313 (24)	1.51 (1.06-2.15)	0.023	21	536 (4)	1.23 (0.68-2.23)	0.49	101	423 (24)	1.33 (0.98-1.79)	0.06
Low	42	178 (24)	1.47 (0.96-2.23)	0.07	20	312 (6)	2.09 (1.14-3.82)	0.017	151	237 (22)	1.15 (0.80-1.66)	0.45

[a] Due to low numbers, grades 5 and 6 were collapsed together.

Table 32. Association between covariates at baseline and onset of sleep disturbances at follow-up, adjusted for age

Covariate	Outcome variable at follow-up							
	Early waking				Waking without feeling refreshed			
	n of cases	n of partici-pants (%)	OR (95% CI)	*P* value	n of cases	n of partici-pants (%)	OR (95% CI)	*P* value
Age (years)	-	-	0.98 (0.94-1.03)	0.47	-	-	0.91 (0.86-0.96)	0.001
Sex								
Men	147	1141 (13)	1.00		99	1135 (9)	1.00	
Women	57	289 (20)	1.66 (1.18-2.32)	0.003	48	278 (17)	2.13 (1.46-3.10)	<0.001
Marital status								
Married/cohabited	157	1154 (14)	1.00		117	1144 (10)	1.00	
Non-married/ cohabited	47	276 (17)	1.29 (0.90-1.85)	0.16	30	269 (11)	1.05 (0.68-1.61)	0.83
Occupational grade								
1 (highest)	42	344 (12)	1.00		28	350 (8)	1.00	
2	57	375 (15)	1.28 (0.83-1.96)	0.27	33	364 (9)	1.07 (0.63-1.82)	0.79
3	29	229 (13)	1.03 (0.62-1.71)	0.92	21	211 (10)	1.15 (0.63-2.09)	0.65
4	44	255 (17)	1.47 (0.93-2.34)	0.10	33	260 (13)	1.49 (0.87-2.55)	0.15
5 to 6 (lowest)[a]	32	227 (14)	1.17 (0.71-1.92)	0.54	32	228 (14)	1.78 (1.04-3.05)	0.037
Chronic disease								
No	95	811 (12)	1.00		78	817 (10)	1.00	
Yes	109	619 (18)	1.61 (1.20-2.17)	0.002	69	596 (12)	1.24 (0.88-1.75)	0.21
Body Mass Index (BMI)	-	-	1.01 (0.98-1.05)	0.51			0.97 (0.93-1.02)	0.23
Physical activity								
High	94	714 (13)	1.00		69	714 (10)	1.00	
Intermediate	74	503 (15)	1.13 (0.82-1.58)	0.45	56	495 (11)	1.18 (0.81-1.71)	0.40
Low	36	213 (17)	1.34 (0.88-2.04)	0.17	22	204 (11)	1.12 (0.67-1.87)	0.66
Alcohol use (units/wk)								
0	22	166 (13)	1.00		17	158 (11)	1.00	
>0 ≤ 14 / 21 (women/men)	135	895 (15)	1.16 (0.71-1.88)	0.55	102	880 (12)	1.10 (0.64-1.90)	0.73
> 14 / 21 (women/men)	47	369 (13)	0.96 (0.56-1.65)	0.87	28	375 (7)	0.69 (0.37-1.31)	0.26

Table 32 cont.

Table 32 cont.

Smoking								
No	184	1290 (14)	1.00		126	1283 (10)	1.00	
Yes	20	140 (14)	1.00 (0.61-1.64)	0.99	21	130 (16)	1.75 (1.06-2.90)	0.030
Job demands								
Low	26	218 (12)	1.00		14	223 (6)	1.00	
Intermediate	83	645 (13)	1.08 (0.67-1.73)	0.75	74	653 (11)	1.81 (1.00-3.27)	0.05
High	95	567 (17)	1.47 (0.92-2.34)	0.11	59	537 (11)	1.75 (0.95-3.21)	0.07
Decision latitude at work								
High	83	708 (12)	1.00		49	701 (7)	1.00	
Intermediate	76	462 (16)	1.47 (1.05-2.06)	0.026	61	461 (13)	1.91 (1.28-2.85)	0.002
Low	45	260 (17)	1.57 (1.06-2.33)	0.025	37	251 (15)	2.25 (1.42-3.55)	<0.001

[a] Due to low numbers, grades 5 and 6 were collapsed together.

9.5.4 Association between working hours and onset of sleep disturbances

Associations between working hours and the new-onset sleep disturbances between phases 5 and 7 are shown in Table 33 (p. 156). Long working hours (>55 hours a week) were not associated with shortened sleeping hours. However, when a continuous working hours variable was entered in the model, each 10-hour increase was related to a 1.30-fold increase in the probability of sleeping 6 hours or less at follow-up among those who slept at least 7 hours at baseline. A strong relationship was found for difficulty falling asleep (OR 4.90 for >55 hours when compared to 35-40 hours). With serial adjustments, the association strengthened to 5.84. Again, a strong linear association was found with a continuous working hours variable indicating a 10-hour increase (OR 1.63). Working hours did not predict the onset of frequent waking during the night at follow-up. An association was found for early waking (OR 1.74 for >55 hours, OR 1.26 for each 10-hour increase) and for waking without feeling refreshed (OR 2.27 for >55 hours, OR 1.34 for each 10-hour increase).

When Model D was adjusted for job demands but not with decision latitude at work, the results were not changed: a 10-hour increase in working hours was related to an OR of 1.26 (0.98-1.62) for short sleep; the OR for >55 hours for difficulty in falling asleep was 5.45 (2.26-13.15; 1.64 [1.26-2.13] for each 10-hour increase); the OR for >55 hours for early waking was 1.61 (0.90-2.87; 1.24 [1.02-1.50] for each 10-hour increase); and the OR for >55 hours for waking without feeling refreshed was 2.11 (1.09-4.06; 1.30 [1.05-1.62] for each 10-hour increase).

Interaction effects were not tested due to relatively small number of cases.

Table 33. Associations between weekly working hours at baseline and onset of sleep disturbances at follow-up

Weekly working hours	Outcome variable at follow-up							
	Short sleep							
	n of cases / n (%)	**Model A OR (95% CI)[a]**	***P* value**	**Model B OR (95% CI)[b]**	***P* value**	**Model C OR (95% CI)[c]**	***P* value**	**Model D OR (95% CI)[d]**	***P* value**
All	200/964 (21)								
35–40	80/401 (20)	1.00		1.00		1.00		1.00	
41–48	60/282 (21)	1.17 (0.78-1.73)	0.45	1.17 (0.79-1.74)	0.45	1.16 (0.78-1.73)	0.47	1.16 (0.77-1.75)	0.47
49-55	42/220 (19)	0.98 (0.62-1.56)	0.93	0.98 (0.62-1.56)	0.94	0.96 (0.60-1.54)	0.87	0.98 (0.60-1.59)	0.92
> 55	18/61 (30)	1.83 (0.95-3.50)	0.07	1.83 (0.96-3.51)	0.07	1.77 (0.92-3.42)	0.09	1.82 (0.92-3.62)	0.09
P for trend			0.29		0.29		0.35		0.33
For each 10h increase		1.30 (1.02-1.65)	0.032	1.30 (1.02-1.65)	0.033	1.28 (1.01-1.63)	0.044	1.31 (1.02-1.69)	0.038
	Difficulty in falling asleep							
	n of cases / n (%)	**Model A OR (95% CI)[a]**	***P* value**	**Model B OR (95% CI)[b]**	***P* value**	**Model C OR (95% CI)[c]**	***P* value**	**Model D OR (95% CI)[d]**	***P* value**
All	66/1639 (4)								
35–40	21/615 (3)	1.00		1.00		1.00		1.00	
41–48	23/475 (5)	1.93 (1.03-3.60)	0.039	2.05 (1.09-3.84)	0.025	2.11 (1.12-3.98)	0.022	2.20 (1.16-4.19)	0.016
49-55	11/405 (3)	1.36 (0.62-3.00)	0.45	1.37 (0.62-3.03)	0.44	1.39 (0.63-3.10)	0.41	1.47 (0.65-3.34)	0.35
> 55	11/144 (8)	4.90 (2.11-11.38)	<0.001	5.15 (2.20-12.03)	<0.001	5.15 (2.18-12.18)	<0.001	5.84 (2.38-14.34)	<0.001
P for trend			0.004		0.004		0.004		0.003
For each 10h increase		1.63 (1.27-2.09)	<0.001	1.65 (1.28-2.12)	<0.001	1.62 (1.26-2.10)	<0.001	1.67 (1.29-2.18)	<0.001
	Frequent waking							
	n of cases / n (%)	**Model A OR (95% CI)[a]**	***P* value**	**Model B OR (95% CI)[b]**	***P* value**	**Model C OR (95% CI)[c]**	***P* value**	**Model D OR (95% CI)[d]**	***P* value**
All	277/1305 (21)								
35–40	106/491 (22)	1.00		1.00		1.00		1.00	
41–48	79/380 (21)	0.90 (0.64-1.27)	0.56	0.91 (0.65-1.28)	0.60	0.90 (0.64-1.28)	0.57	0.88 (0.62-1.25)	0.49
49-55	69/324 (21)	0.87 (0.60-1.27)	0.48	0.87 (0.59-1.26)	0.45	0.85 (0.58-1.24)	0.40	0.83 (0.56-1.24)	0.36
> 55	23/110 (21)	0.84 (0.48-1.44)	0.52	0.83 (0.48-1.43)	0.49	0.80 (0.46-1.38)	0.42	0.79 (0.45-1.39)	0.41
P for trend			0.42		0.39		0.32		0.31
For each 10h increase		1.00 (0.83-1.21)	0.98	1.00 (0.83-1.20)	0.99	0.99 (0.82-1.19)	0.88	0.98 (0.81-1.20)	0.87

Table 33 cont.

Table 33 cont.

	Early waking								
	n of cases / n (%)	**Model A OR (95% CI)[a]**	***P* value**	**Model B OR (95% CI)[b]**	***P* value**	**Model C OR (95% CI)[c]**	***P* value**	**Model D OR (95% CI)[d]**	***P* value**
All	204/1430 (14)								
35–40	78/546 (14)	1.00		1.00		1.00		1.00	
41–48	49/404 (12)	0.89 (0.60-1.33)	0.57	0.92 (0.62-1.37)	0.70	0.94 (0.63-1.40)	0.75	0.92 (0.61-1.38)	0.69
49-55	54/358 (15)	1.21 (0.80-1.82)	0.37	1.22 (0.81-1.85)	0.35	1.23 (0.81-1.87)	0.33	1.21 (0.79-1.87)	0.38
> 55	23/122 (19)	1.74 (1.00-3.05)	0.05	1.77 (1.01-3.10)	0.047	1.78 (1.01-3.12)	0.045	1.76 (0.98-3.16)	0.06
P for trend			0.07		0.07		0.06		0.08
For each 10h increase		1.26 (1.05-1.51)	0.015	1.26 (1.05-1.52)	0.016	1.28 (1.06-1.54)	0.011	1.28 (1.05-1.56)	0.017
	Waking without feeling refreshed								
	n of cases / n (%)	**Model A OR (95% CI)[a]**	***P* value**	**Model B OR (95% CI)[b]**	***P* value**	**Model C OR (95% CI)[c]**	***P* value**	**Model D OR (95% CI)[d]**	***P* value**
All	147/1413 (10)								
35–40	55/538 (10)	1.00		1.00		1.00		1.00	
41–48	39/406 (10)	1.08 (0.69-1.70)	0.72	1.10 (0.69-1.70)	0.68	1.12 (0.71-1.77)	0.61	1.12 (0.70-1.77)	0.64
49-55	35/343 (10)	1.33 (0.81-2.18)	0.25	1.34 (0.81-2.18)	0.25	1.29 (0.78-2.13)	0.31	1.37 (0.82-2.29)	0.23
> 55	18/126 (14)	2.27 (1.20-4.30)	0.011	2.29 (1.21-4.32)	0.011	2.29 (1.20-4.35)	0.012	2.43 (1.24-4.75)	0.010
P for trend			0.023		0.022		0.030		0.022
For each 10h increase		1.34 (1.08-1.65)	0.007	1.34 (1.09-1.66)	0.006	1.34 (1.08-1.66)	0.007	1.37 (1.10-1.70)	0.005

[a]Model A: Adjusted for age, sex, marital status, and occupational grade.
[b]Model B: As model A and additionally adjusted for chronic disease.
[c]Model C: As model B and additionally adjusted for exercise level, body mass index, smoking, and alcohol use.
[d]Model D: As model C and additionally adjusted for job demands and decision latitude at workl.

9.5.5 Association between repeat working hours and onset of sleep disturbances

Table 34 (p. 159) presents association between mean working hours measured at two time points (phase 3 and phase 5) and new-onset sleep disturbances at phase 7 among those free of sleep disturbances at phase 5. Long working hours predicted shortened sleep (OR 2.50 for >55 hours compared to 35-40 hours, OR 1.51 for each 10-hour increase). A particularly strong association was found between long working hours and the onset of difficulty falling asleep (OR 8.94 for >55 hours, OR 2.09 for each 10-hour increase) although the number of cases tended to be small. Again, long working hours were not associated with frequent waking during the night. Long hours predicted onset of early waking (OR 2.41 for >55 hours compared to 35-40 hours, OR 1.32 for each 10-hour increase). Association between long working hours and waking without feeling refreshed did not reach statistical significance when using working hours as a categorical variable. However, each 10-hour increase in working hours was related to an odds ratio of 1.43 for waking without feeling refreshed. The significant associations were little affected by serial adjustment for covariates.

When Model D was adjusted for job demands but not with decision latitude at work, the results were not materially changed: OR for >55 hours for short sleep was 2.27 (0.97-5.29); a 10-hour increase hours was related to an OR of 1.25 (0.96-1.62) for short sleep; the OR for >55 hours for difficulty in falling asleep was 10.22 (3.83-27.26; 2.17 [1.45-3.23] for each 10-hour increase); the OR for >55 hours for early waking was 2.25 (1.13-4.48; 1.27 [0.97-1.67] for each 10-hour increase); and the OR for each 10-hour increase in working hours for waking without feeling refreshed was 1.36 (1.00-1.86).

Interaction effects were not tested due to relatively small number of cases.

Table 34. Associations between repeat weekly working hours measured at two time points and new-onset sleep disturbances at follow-up

Mean repeat working hours	Outcome variable at follow-up								
	Short sleep								
	n of cases / n (%)	**Model A OR (95% CI)[a]**	***P* value**	**Model B OR (95% CI)[b]**	***P* value**	**Model C OR (95% CI)[c]**	***P* value**	**Model D OR (95% CI)[d]**	***P* value**
All	193/913 (21)								
35–40	62/339 (18)	1.00		1.00		1.00		1.00	
41–48	84/382 (22)	1.37 (0.93-2.03)	0.11	1.37 (0.93-2.03)	0.11	1.38 (0.93-2.05)	0.11	1.35 (0.90-2.03)	0.15
49-55	36/156 (23)	1.58 (0.93-2.67)	0.09	1.58 (0.94-2.67)	0.09	1.56 (0.91-2.65)	0.10	1.63 (0.94-2.83)	0.08
> 55	11/36 (31)	2.50 (1.11-5.65)	0.027	2.51 (1.11-5.67)	0.027	2.42 (1.06-5.54)	0.036	2.40 (1.02-5.62)	0.045
P for trend			0.017		0.016		0.023		0.023
For each 10h increase		1.51 (1.11-2.06)	0.008	1.51 (1.11-2.06)	0.008	1.50 (1.10-2.05)	0.011	1.55 (1.12-2.15)	0.009
	Difficulty in falling asleep								
	n of cases / n (%)	**Model A OR (95% CI)[a]**	***P* value**	**Model B OR (95% CI)[b]**	***P* value**	**Model C OR (95% CI)[c]**	***P* value**	**Model D OR (95% CI)[d]**	***P* value**
All	65/1554 (4)								
35–40	18/508 (4)	1.00		1.00		1.00		1.00	
41–48	29/651 (4)	1.80 (0.96-3.36)	0.07	1.84 (0.98-3.46)	0.06	1.92 (1.01-3.63)	0.045	1.98 (1.04-3.78)	0.038
49-55	8/310 (3)	1.54 (0.61-3.86)	0.36	1.57 (0.62-3.96)	0.34	1.58 (0.62-4.06)	0.34	1.58 (0.63-4.30)	0.31
> 55	10/85 (12)	8.94 (3.55-22.55)	<0.001	9.77 (3.83-24.93)	<0.001	9.41 (3.63-24.39)	<0.001	9.96 (3.73-26.57)	<0.001
P for trend			<0.001		<0.001		<0.001		<0.001
For each 10h increase		2.09 (1.44-3.06)	<0.001	2.14 (1.46-3.15)	<0.001	2.10 (1.42-3.11)	<0.001	2.21 (1.48-3.30)	<0.001
	Frequent waking								
	n of cases / n (%)	**Model A OR (95% CI)[a]**	***P* value**	**Model B OR (95% CI)[b]**	***P* value**	**Model C OR (95% CI)[c]**	***P* value**	**Model D OR (95% CI)[d]**	***P* value**
All	263/1236 (21)								
35–40	81/405 (20)	1.00		1.00		1.00		1.00	
41–48	116/519 (22)	1.09 (0.78-1.53)	0.60	1.09 (0.78-1.52)	0.61	1.06 (0.76-1.49)	0.73	1.02 (0.72-1.45)	0.89
49-55	51/250 (20)	0.92 (0.60-1.43)	0.72	0.91 (0.59-1.41)	0.68	0.88 (0.57-1.37)	0.58	0.89 (0.56-1.40)	0.62
> 55	15/62 (24)	1.14 (0.58-2.22)	0.70	1.13 (0.58-2.21)	0.72	1.07 (0.54-2.09)	0.85	1.05 (0.53-2.08)	0.90
P for trend			1.00		0.96		0.81		0.81
For each 10h increase		1.02 (0.80-1.31)	0.87	1.01 (0.79-1.30)	0.92	0.99 (0.77-1.28)	0.94	1.00 (0.77-1.29)	0.97

Table 34 cont.

Table 34 cont.

	Early waking								
	n of cases / n (%)	**Model A OR (95% CI)[a]**	***P* value**	**Model B OR (95% CI)[b]**	***P* value**	**Model C OR (95% CI)[c]**	***P* value**	**Model D OR (95% CI)[d]**	***P* value**
All	194/1354 (14)								
35–40	57/440 (13)	1.00		1.00		1.00		1.00	
41–48	87/561 (16)	1.34 (0.92-1.96)	0.13	1.34 (0.92-1.96)	0.13	1.35 (0.92-1.98)	0.12	1.32 (0.89-1.95)	0.16
49-55	34/280 (12)	1.13 (0.68-1.87)	0.64	1.12 (0.67-1.85)	0.67	1.13 (0.68-1.87)	0.64	1.13 (0.67-1.91)	0.65
> 55	16/73 (22)	2.41 (1.23-4.69)	0.010	2.46 (1.26-4.82)	0.008	2.49 (1.27-4.90)	0.008	2.41 (1.20-4.84)	0.013
P for trend			0.07		0.07		0.06		0.08
For each 10h increase		1.32 (1.01-1.71)	0.042	1.32 (1.01-1.72)	0.040	1.33 (1.02-1.74)	0.035	1.33 (1.01-1.76)	0.047
	Waking without feeling refreshed								
	n of cases / n (%)	**Model A OR (95% CI)[a]**	***P* value**	**Model B OR (95% CI)[b]**	***P* value**	**Model C OR (95% CI)[c]**	***P* value**	**Model D OR (95% CI)[d]**	***P* value**
All	140/1338 (10)								
35–40	41/442 (9)	1.00		1.00		1.00		1.00	
41–48	65/552 (12)	1.61 (1.04-2.49)	0.032	1.61 (1.04-2.49)	0.032	1.59 (1.02-2.47)	0.040	1.52 (0.97-2.39)	0.07
49-55	25/269 (9)	1.53 (0.85-2.74)	0.16	1.52 (0.85-2.73)	0.16	1.49 (0.82-2.69)	0.19	1.56 (0.85-2.87)	0.15
> 55	9/75 (12)	2.19 (0.95-5.00)	0.06	2.21 (0.97-5.07)	0.06	2.16 (0.94-4.98)	0.07	2.11 (0.90-4.96)	0.09
P for trend			0.043		0.043		0.06		0.06
For each 10h increase		1.43 (1.06-1.93)	0.020	1.43 (1.06-1.94)	0.019	1.43 (1.05-1.94)	0.023	1.46 (1.06-2.01)	0.019

[a]Model A: Adjusted for age, sex, marital status, and occupational grade.
[b]Model B: As model A and additionally adjusted for chronic disease.
[c]Model C: As model B and additionally adjusted for exercise level, body mass index, smoking, and alcohol use.
[d]Model D: As model C and additionally adjusted for job demands and decision latitude at work.

9.5.6 Summary of the results of Study 4 (sleep disturbances)

Study 4 examined associations between long working hours and disturbed sleep. At baseline, working >55 hours per week was associated with various forms of sleep disturbance, that is, short sleeping hours, early waking and waking without feeling refreshed. In the prospective analysis, long working hours predicted incident sleep disturbances, especially difficulty falling asleep, among employees free from such disturbance at baseline. The effects were slightly stronger for working hours measured repeatedly than at only one point in time suggesting a dose-response association. All the analyses were repeated with working hours treated as a continuous variable. The results were robust and not totally explained by known risk factors such as health behaviors or baseline health status. However, some adjustments suggested that high job demands may partially explain the association between long working hours and sleep disturbances.

Chapter 10

Discussion

10.1 Introduction

This thesis was motivated by the lack of robust prospective evidence on the potential adverse health effects of long working hours, a common concern in the general public. The longitudinal study design and wide range of measurements on background characteristics, lifestyle factors and health in the Whitehall II study of British civil servants provided a rare opportunity to explore this question in a U.K. context. This chapter critically discusses the findings of the present thesis. First, general findings for each outcome are discussed, followed by an assessment of study strengths and limitations. Finally, implications and suggestions for future research are presented.

10.2 Synopsis of findings and comparison with previous studies

In this sample of British white-collar employees, the prevalence of men and women working 10 hours or more was 29% and 17% at the baseline of the study (1991-1993), respectively. Although not fully comparable, corresponding percentages for male and and female wage-earners in the U.K. during the same time period (35% and 8% worked >45 hours per week,

respectively)[17] indicate that in the Whitehall II study, men worked slightly less and women more often long hours than the British wage earners in general.

10.2.1 Coronary heart disease

In this study, the prevalence of CHD among full-time employed participants at baseline was 2.6. Corresponding prevalence in the U.K. population has been higher: lifetime self-reported doctor-diagnosed prevalence of MI in England was 4.1% among men aged 16 years or over and 1.7% among women[55] while the prevalence of angina was 4.8% and 3.3%, among men and women, respectively. This discrepancy may be due to the relatively young age of the cohort and the 'healthy worker effect'[274] resulting in the healthier individuals to remain employed.

In the present thesis, majority of the listed major risk factors[49 56] were predictive of CHD: older age, male sex, smoking, hypertension, dyslipidemia, diabetes, and body mass index. The only exception was physical inactivity. Of the contributing risk factors, the only significant association was found for type A behaviour. This study therefore gives some support to the fact that the contributing risk factors are not yet established as having strong evidence as predictors of CHD and may not predict CHD in all populations. However, it is also possible that part of the measures were not sensitive enough, for example GHQ-30 as an indicator of mental health.

Long working hours and incident CHD was examined in a sample followed up for an average of 11 years. When compared to a standard 7-8 hours per day, working 11-12 hours was associated with a 1.56-fold risk of CHD, after accounting for the effects of demographic factors and several known risk factors for CHD. Similar association was

found with an outcome comprising only coronary death and non-fatal myocardial infarction.

The findings are in accordance with several previous case-control studies on this topic.[35 39 191 192 194 197] A major problem of case-control studies is the retrospective assessment of working hours potentially introducing reverse causation bias, i.e. it is possible that the diseases itself, here CHD, influences either patient's work behavior or perception or recall of working hours prior to the onset of illness. However, Sokejima and Kagamimori,[39] using patients' salary records rather than self-reports to determine working hours, were able to overcome this problem and their findings confirm those of other case-control studies in the field which showed a positive association between working hours and CHD.

At least five studies have reported a positive but non-significant association.[46 193 195 196 198] One of these was reported in a prospective study which, unlike many other studies with middle-aged samples aged 40 years or more, included participants aged 20 to 60 years, and follow-up time in that study was only three years.[196] Another non-significant association was reported in the study of Thiel and colleagues[195] which included only 50 cases and 50 controls and therefore probably had limited statistical power to detect any association. Uchiyama et al.[198] also reported a positive but non-significant finding in their prospective study, however, their sample included hypertensive patients, and the outcome included all cardiovascular events rather than CHD only. A cross-sectional study by Lallukka and colleagues[193] was based on self-reported angina pectoris symptoms. A prospective study by Holtermann and others,[46] in turn, had a 30-year follow-up time which may have diluted the association between long working hours and CHD.

This thesis found some evidence of associations of long working hours with smoking history and lower concentration of HDL cholesterol, both well-established risk factors for CHD.[49 56] Although these risk factors might be potential mechanisms explaining

the association between long hours and CHD, adjustment for biological factors and health behaviours had no major effect on the association found in the present study. Thus, differences in these risk factors do not seem to be strong mediators of the observed relationship.

In their case-control study of Japanese men,[39] Sokejima and Kagamimori suggested that the relationship between extended working hours and acute myocardial infarction may be explained by changes in the activity of the autonomic nervous system; through increases in sympathetic nervous activity and increased blood pressure levels; and through reduced parasympathetic nervous system which is also a risk factor for CHD. Earlier studies on the possible mechanisms, such as hypertension, show mixed results,[26] and our baseline assessment does not support hypertension as being on the pathway between overtime work and cardiovascular disease. However, ambulatory blood pressure monitoring might be the best way of assessing whether masked, or "hidden" hypertension[275] is a possible mediator. Work-related stress has been shown to be associated with hidden hypertension,[275] and there is indeed some evidence showing long working hours to be related to elevated ambulatory blood pressure.[276]

Krause and colleagues found longer hours worked to be positively associated with progression of carotid atherosclerosis in middle-aged Finnish men.[277] A stronger association was found among men with pre-existing ischemic heart disease (IHD) or carotid artery stenosis (CAS) than among men without these conditions. The authors concluded that the findings were consistent with the hypothesis of hemodynamic factors contributing to atherosclerosis. More specifically, mental arousal, emotional reactivity, and physical activities on the job may increase average heart rate, which leads to changes in blood flow which in turn cause arterial wall injury and inflammation and, finally, atherosclerosis. This suggested causal pathway needs to be directly examined in the future.

This thesis showed long working hours to be related to some of the other suggested risk factors for CHD, namely type A behavior pattern, psychological distress - a correlate for depression and anxiety symptoms - and short sleeping hours. Negative emotions, such as depression and anxiety,[61 62 63] and reduced sleeping hours,[162] have been found to be independent predictors of CHD and mortality. However, adjustment for these factors had little effect on the association between long working hours and CHD. In contrast, adjustment for type A behavior pattern, which also predicted incident CHD, attenuated the hazard ratios by 11-12%, suggesting that part of the association may be explained by such behaviors. Type A behaviour pattern is viewed to represent a specific adverse behavioural style in response to environmental stress and can as such be a risk factor for CHD.[20 68] Type A behavior is also characterized by a chronic, incessant struggle to achieve more and more in less and less time, and is also characterised by aggressiveness and irritability.[66]

However, although the association between long working hours and CHD was not totally explained by risk factors measured in this study, there might be several other factors that were not measured and may underlie the association between long working hours and CHD. For example, even though the association was not explained by adjustment for sleeping hours in the present analyses, insufficient time for recovery in spite of increased need,[278] or difficulties in unwinding after work remain possible contributing mechanisms.[279] Employees who work long hours may also be more likely to work while ill, i.e. be reluctant to be absent from work despite illness. Indeed, the present study showed lower sickness absenteeism among employees working long hours although presenteeism was not directly measured. Presenteeism has been found to be associated with increased risk of myocardial infarction in men in the Whitehall II study cohort.[280]

Although long hours workers in this study were more likely to be in higher occupational grades which suggests better resources e.g. for health-promoting activities,

such as diet, exercise, and medical care, long working hours work may also be a part of a lifestyle in which symptoms of ill health are ignored and medical care not sought. This possibility is supported by the findings reported by Fukuoka and colleagues showing that long working hours are associated with a delay in seeking care in acute coronary events among Japanese men.[281]

In this thesis, interaction of demographic factors (age, sex, occupational grade), behavioural factors, and work characteristics with working hours predicting CHD was tested, but the findings suggest no interaction effects except for decision latitude at work. Thus, it seems that the association is similar in older and younger workers, both sexes and each socioeconomic category, that is, it is not dependent on participant's specific characteristics.

Although there is a large body of research on work stress and CHD,[74 82 83] it is not known whether work stress, as indicated by high job demands and low decision latitude at work, modifies the association between long working hours and CHD. In an earlier study, Tucker & Rutherford, 2005[213] assessed the interaction between long working hours and social support, job maintenance, commitment, pressure to work overtime, and work time control associated with self-reported health and found no significant interactions. In the present study, interactions were tested between long working hours and job demands, but none was found. In contrast, there was some indication that decision latitude at work may modify the effect of long working hours on CHD. The excess risk of CHD was smaller for employees with high decision latitude than for those with lower levels of decision latitude. However, this interaction was not significant when the angina pectoris cases were excluded from the outcome. Further research is therefore needed to determine whether factors, such as high decision latitude or working long hours through choice, would reduce the excess risk of CHD associated with long hours.

Holtermann and colleagues found in their 30-year follow-up study of Danish men that long working hours were associated with ischemic heart disease mortality only among participants with low levels of physical activity.[46] In the present study, lifestyle resources (physical activity, smoking, and obesity) were examined as potential effect modifiers but no support was found for any of the lifestyle characteristics acting as a modifier. However, as the number of participants and cases in some of the sub-groups was relatively small, more research is needed with larger datasets before any firm conclusions can be made about effect modification in this area of research.

In sum, this study indicates that working long hours is associated with approximately a 1.6-fold risk of CHD, after accounting for the effects of demographic factors and several known risk factors for CHD. The findings are in line with previous research on this topic although the vast majority of the studies have been case-control studies. This study also suggests that high decision latitude at work may protect the employee against the adverse coronary effects associated with long working hours. However, replication of these findings with other populations and larger samples for interaction analyses are needed.

10.2.2 Type 2 diabetes

In this study, the prevalence of diabetes at baseline was 2.7. It is higher in the general population of England since according to the Health Survey for England in 2006[55] the prevalence of self-reported doctor-diagnosed diabetes was 5.6% in adult men and 4.2% in adult women. Again, the present cohort was relatively young and it is also possible that chronic diseases such as diabetes are among the factors that predict early exit from the

labour force, thus, the present employed cohort at baseline may be healthier than the English population in general.

Of the covariates assessed at baseline, older age, lower occupational grade, prevalent prediabetes and CHD, smoking, teetotal, no fruits and vegetables daily, low level of physical activity, higher body mass index and waist line, higher blood pressure, lower HDL cholesterol, and higher triglycerides were all associated with an increased risk of incident type 2 diabetes. Unsurprisingly, the strongest predictor was prediabetes (OR 8.7 compared to no indication of prediabetes). These findings were well in line with the list of established risk factors for type 2 diabetes, that is, older age, IFG or IGT (prediabetes), overweight and obesity, lack of physical activity, hypertension, dyslipidemia, history of vascular disease,[88 91 92] and increased body fat in the visceral compartment, as indicated by a bigger waist circumference.[93] In line with a previous study, smoking was also associated with incident type 2 diabetes.[95] The present findings also correspond with earlier research suggesting older age and lower SEP to predict the onset of type 2 diabetes[94-96]

As predictors of onset of type 2 diabetes in this thesis, no significant association was found for sex, marital status, heavy alcohol use, sleeping hours, psychological distress, type A behaviour, or LDL cholesterol. Of these, all but LDL cholesterol level are not included in the list of established risk factors for type 2 diabetes.[88 91 92] However, although some studies suggest an association between depression and incident type 2 diabetes, null findings have also been reported.[97 98] In this thesis, psychological distress was measured, instead of depression, using the GHQ-30 scale; thus it remains unclear whether clinical depression would have predicted incident type 2 diabetes in the present sample. In addition, a meta-analysis of six longitudinal cohort studies on the association between psychosocial stress factors (such as stressful life events, maladaptive coping and poor self-efficacy) and the onset of type 2 diabetes[101] suggests no association.

The measure of type A behaviour in the present study is a correlate of "maladaptive coping" and thus the null finding in the present study is in line with earlier studies. However, the association between psychosocial stress and the onset of type 2 diabetes is not yet established since another review suggests an association between emotional stress and the onset of type 2 diabetes.[100] In the present study, high job demands were related to a lower odds (0.61) of diabetes compared to low job demands in the age-adjusted analysis. After adjustment for sex and occupational grade the odds ratio attenuated to non-significant. This finding is in line with previous research which has shown mixed relationships between work stress and incident type 2 diabetes.[96 101 103-105]

In this thesis, genetic factors were not assessed although type 2 diabetes has been suggested to have a genetic predisposition more so than has type 1 diabetes.[88 91 92] However, genetic factors would have introduced a major bias to the study only if they were associated with both the exposure (working hours) and the outcome (type 2 diabetes).

In the cross-sectional analysis, no significant association was found between long working hours and prevalent diabetes or prediabetes; however, a borderline association (P=0.05) was found with 11-12 hours of daily work compared to standard hours, and lower prevalence of diabetes (OR 0.46). Because the baseline analysis was cross-sectional conclusions regarding the direction of causality cannot be made. It is possible that employees with diabetes shorten their working hours because of the disease; however, from the cross-sectional analysis it cannot be ruled out that working long hours can protect employees from developing type 2 diabetes. The protective assumption was supported by the study of Nakanishi and others[199] who in their five-year follow-up of male office workers found that daily working hours of ≥11 were related to lower risk of IFG or type 2 diabetes. The authors suggest that the finding may relate to the characteristics of the study cohort (highly educated men of whom 60% were architects and researchers). They also found that

employees with longest working hours had highest 24 hour energy expenditure; thus, they seemed to be physically more active during their waking time than employees who worked normal hours. In the present study, overtime workers reported more leisure-time exercise than employees working standard hours. However, this may be due to their higher socioeconomic position.

The reference group in the study of Nakanishi and colleagues[199] included employees who worked 8 hours or less, thus, part-time workers were in the reference group. The outcome was measured at yearly health screenings which restricted the sample followed to those who stayed with the same employer the study seriously risk a bias due to the 'healthy worker effect'.[274] However, in the present study, no association between working hours and incident diabetes or prediabetes was found in the prospective analyses, thus, a protective effect of long hours on type 2 diabetes was not supported.

The present findings contradict an earlier study by Kawakami et al.[105] in which a sample of male industrial workers was followed for eight years showing that monthly overtime work of >50 hours was related to incident type 2 diabetes. The exposure in that study corresponds to >12 hours overtime per week and 2-3 hours per day which is close to the long hours exposure assessed in the present study. However, that study included mainly blue-collar workers whereas the Whitehall II study comprises white-collar workers. Keeping also in mind the study of Nakanishi and colleagues[199] which included highly educated men and suggested lower risk of type 2 diabetes among those with long hours, it remains to be investigated in the future whether long working hours are a risk factor for type 2 diabetes in manual or blue-collar occupations only. It is also not known whether the association is sex-specific. A U.S. study by Kroenke and colleagues[200] found an association between long working hours and incident type 2 diabetes although the adjusted model was not statistically

significant. However, a serious limitation in the U.S. study was that the diagnosis of type 2 diabetes relied on medical records. Thus, non-diagnosed cases were not able to be detected.

The present study suggests that among prediabetics (n=418), participants with longer working hours were more than two times more likely to be definite cases of type 2 diabetes at follow-up. Although the test of trend was significant, it seems that there was an equal risk in each group of working hours compared to standard hours, and no dose-response effect was found. In addition, in the highest working hours' group (11-12 hours a day), the association was not statistically significant. This might have been due to the low number of cases and participants (10/36), making the analysis underpowered.

If replicated in larger datasets, this finding may indicate that long hours pose a type 2 diabetes risk when a person is already in the progress of developing diabetes, in this case, a prediabetic. People with prediabetes are usually advised to pay attention to their lifestyle, such as maintaining healthy diet and exercise and avoiding overweight and excess alcohol use. It is possible that individuals who spend longer hours at work are not able to be as dedicated in their adherence to advices as their colleagues working standard hours. In the present study, participants with overtime used more alcohol and had greater waist circumference than those working standard hours. Greater waist circumference indicates increased body fat in the visceral compartment and thus is a risk factor for type 2 diabetes.[93] An earlier study found an association between long working hours and overweight.[282] In this study, however, in the unadjusted model, overtime workers exercised more than those with standard working hours. However, adjustment for all lifestyle factors, including waist circumference, had no effect on the association.

Another hypothesis relates to stress as a contributing factor. Longer working hours correlate with psychological stress, and psychosocial stress has earlier been found to predict poor diabetes control among diabetic individuals.[101] Similarly, stress factors may lead to a

poor prognosis in individuals with prediabetes. However, adjustment for any of the stress-related factors, such as psychological distress, type A behaviour pattern, or work stress did not affect the relationship between overtime work and incident diabetes among prediabetics.

A dose-response relationship between working hours and incident type 2 diabetes among prediabetics would have been expected but instead, each category of overtime was equally associated with risk of type 2 diabetes. However, according to the Bradford Hill's criteria of causation,[283] demonstrating a dose-response relationship (5^{th} criterion) strengthens the argument for cause and effect, but its absence is weak evidence against causation because not all causal associations exhibit a dose-response relationship. Whichever is the case, the present findings should be interpreted cautiously and more research with larger samples of prediabetics is needed to examine whether the association found in the present study is robust.

In the present study, socio-demographic factors, lifestyle characteristics (physical activity, smoking, and obesity), and work characteristics were examined as potential effect modifiers for the association between working hours and the onset of type 2 diabetes but no support was found for any of the characteristics acting as such a modifier. In sum, this study found no evidence of an association between long working hours and incidence of type 2 diabetes or prediabetes. Thus far the research on this topic remains inconclusive. However, although the study sample was small, long working hours seemed to be associated with an increased risk of type 2 diabetes in participants with prediabetes. Further research with different populations and larger samples for interaction analyses is still needed.

10.2.3 Depression

In this thesis, the onset of depression at follow-up was 3.1%. The median 1-year prevalence of depression across studies in general populations has been higher, 5.3%.[132] This might be due to the prospective study design and difference in the study populations: the Whitehall II study comprised a working population which has been shown to have lower prevalence of MDD than the general population,[284] and in the present thesis, 'healthy' participants at baseline were selected for follow-up. The prevalence of psychological distress at baseline was 22% in the present sample, using the GHQ-30 score. A study of the English adult population,[134] found high scores for psychological distress, as measured by the 12-item GHQ in 15% of women and 11% of men. This difference might be due to different GHQ scores (GHQ-30 vs GHQ-12) used. In agreement with the present middle-aged working sample, higher distress in English adults was found among middle-aged (i.e. working-age) participants while lower scores were found among those who had already passed the retirement age.

Of the covariates examined in the present study, predictors of the onset of MDE were female sex, lower occupational grade, chronic disease and moderate decision latitude at work compared to high decision latitude. In addition, the odds ratio for MDE for participants who used alcohol was increased in the expected direction but not statistically significant at conventional levels. The findings are in line with earlier studies suggesting established risk factors for depressive disorders in adulthood to be female sex, chronic disease such as CHD, binge drinking, and low socioeconomic position.[63 113 136]

Stressful negative life events have also been strong predictors of depression.[149] These include severe or chronic disease, the experience of loss, such as the death of a significant person, separation or divorce, and job loss and often work-related events. In the

Whitehall II study phases used in the present thesis, stressful negative life events were not separately examined. However, chronic disease was included and as a covariate and it was found to predict the onset of MDE. No significant association was found between marital status and depression although divorce and widowhood have been shown to predispose to depression.[113] However, onset of depression is more likely shortly after the event and as date of divorce was not collected it was not possible to examine this in the present thesis.

Smoking was not related to the onset of MDE which is in contrast with previous studies.[113] The reasons for this discrepancy are not easy to see but may be related to low prevalence of 'heavy smokers' among white-collar employees. However, more detailed research on this issue is needed in the future. Work-related psychosocial stress factors, that is, job demands and job control were not associated with the onset of MDE, either. This is in line with earlier studies which suggest an inconsistent association between work stress and mental disorders when the outcome is clinical depression instead of symptom scores such as the GHQ.[22 80 81 153-156]

Regarding working hours, this study showed an association between long working hours and the onset of a MDE during a mean 5.8-year follow-up. Working 11 or more hours a day was associated with a 2.3- to 2.5-fold risk of an MDE when compared with working a standard 7-8 hours a day. The association was robust to adjustment for a range of socio-demographic, life-style, and work-related factors at baseline.

Of the earlier cross-sectional studies, the majority (13 separate reports) showed a null finding (vs. 9 with a positive finding) between long working hours and depressive symptoms or its correlates. None of the studies found a negative association. The present study, using the GHQ-30 psychological distress as an outcome, showed a significant cross-sectional association between long working hours and distress at baseline.

Of the earlier prospective studies, the study of Steptoe et al.,[202] had 71 participants and within subjects analysis of four assessments during six months showed no change in psychological distress in relation to overtime work periods while Dahlgren et al., 2006[215] in a similar experimental study using within-subject analysis found that overtime work was associated with increased exhaustion and irritation compared with an 8-hours-a-day workweek. Shields,[42] using the CIDI interview method, found an association between long (>40) weekly working hours and new-onset MDE among women but not among men. Bildt et al.[203 204] did not find any association between overtime work and incidence of subclinical depressive symptoms or psychological distress in either men or women in their 4-year or 24-year follow-up studies. A null finding was also reported by Suwazono et al., 2003[212] and Tarumi et al., 2003[196] in Japan using the GHQ-12 score and diagnoses of mental disorders in the records of the employee insurance company. De Raeve et al.[219] assessed whether a transition from 36-40 hours to >40 hours/ week vs. staying in the 36-40 hour group predicted psychological distress and found no association. However, measurement of transition and change in psychological distress were overlapping in that study. In sum, earlier cross-sectional and prospective studies show mixed findings regarding long working hours and mental health.

Mixed findings in this field of research may relate to considerable heterogeneity in the study samples, assessment of exposure, outcome, and potential confounding factors in the earlier studies. The only studies using interview-based clinically verified diagnosis of depression were Shields[42] (association found among women) and Michelsen and Bildt,[203 204] (no association). However, the studies of Michelsen and Bildt included also cases of subclinical depression. There is also substantial heterogeneity in the operationalisation of long working hours, that is, in some studies the cut-point has been 40 hours, in some studies

45 hours or even more, while some studies used "overtime work", defined as any amount of hours exceeding the normal hours, as an indicator of long working hours.

Plausible explanations of why long working hours were associated with the onset of MDE in the present study cannot directly be drawn. Serial adjustment for socio-demographic factors and several potential confounding or mediating factors had little effect on the association or even strengthened it. However, long working hours may in part affect mental health through factors not measured in the present study, such as work-family conflicts,[45] insufficient time for recovery in spite of increased need,[278] difficulties in relaxing after work,[279] or prolonged increased cortisol levels caused by excess activity due to long hours at work.[285] The hypothalamic-pituitary-adrenal (HPA) axis has been shown to be hyperactive in depression, and that glucocorticoids, especially corticotropin-releasing hormone (CRH) which is released in the stress response, have a direct involvement in the etiology of depression.[286] Cortisol, in turn, is the hormonal endpoint of the HPA-axis activation and has been found to be elevated among depressed individuals.[286 287] However, one cross-sectional study addressing this issue found that men (but not women) who worked long hours actually had lower cortisol secretion than those who worked shorter hours.[288]

In sum, this study suggests an association between long working hours and the onset of major depressive episode which is in line with some but not all earlier findings on this issue. Mixed findings may relate to the large heterogeieneity in both exposure and outcome measures. Furthermore, more research is needed to explain the mechanisms linking long working hours to depression.

10.2.4 Sleep disturbances

In this study, the most prevalent sleep disturbance was short sleep (46%) followed by frequent waking (27%), early waking (20%) and waking without feeling refreshed (20%), whereas lowest prevalence was in difficulty falling asleep (7%). Short sleep can not be considered a problem in all cases because some people are 'natural' short sleepers and do not experience any discomfort relating to their amount of sleep. In addition, female sex was strongly related to the majority of study outcomes. The results for women are in line with earlier research showing higher rates of insomnia in women.[10 179 180] Zhang and colleagues ask in their meta-analysis of sex differences in insomnia[180] whether the excess insomnia among women is just a proxy for underlying mental health problems, such as anxiety or depression, or whether it represents genuine sex-specific changes in sleep physiology and the contribution of, for example, hormonal differences[289] and their changes during the life course. This issue remains to be investigated in the future studies.

In contrast, no consistent association was found for marital status predicting sleep disturbances. However, in the present study, non-married included also people who were single or widowed while other studies have reported insomnia among those non-married persons who were separated or divorced.[10 179] In this study it was not possible to further differentiate the participants by marital status due to the relatively low number of non-married persons.

The present study indicates no association between age and onset of sleep disturbances, except waking without feeling refreshed which was associated with younger age. The findings contradict with earlier reports suggesting that insomnia increases with age.[9 181] The contradicting findings may relate to the insomnia outcomes used in different studies. Several sleep-related disorders, such as sleep disordered breathing, periodic limb

movement disorder, and restless legs syndrome tend to increase with age.[290] However, these objective sleep disorders have been found to correlate with subjective sleep complaints only moderately,[291] and the present study used subjective complaints as indicators of sleep disturbances. In studies including participants who retire during the follow-up, a reduction of sleep disturbances shortly after retirement is likely and may have affected the results.[292]

The present findings are in agreement with earlier studies suggesting low socioeconomic position to be associated with insomnia.[10 179 182] For occupational grade, an inverse association was found with difficulty falling asleep and waking without feeling refreshed, but no association was found with shortened hours of sleep, frequent waking, or early waking. However, earlier studies using occupational grade as an indicator of SEP have been inconsistent.[182] Lallukka and her colleagues argue in their paper that economic difficulties is the SEP indicator that is most consistently associated with sleep complaints. They also show that economic difficulties experienced already in childhood are strongly associated with sleep complaints in adulthood.[182] It would be therefore important to assess economic difficulties when examining the association between SEP and sleep disturbances.

Associations of chronic disease and health risk behaviours with sleep disturbances were mixed indicating effect on some outcomes but not with others, and in addition, heavy alcohol use seemed to protect against difficulties falling asleep. Having a chronic disease was strongly associated with difficulty falling asleep and early waking but not with other sleep outcomes.

Work stress factors showed more consistency in the present study by indicating that high demands and low decision latitude predict various sleep outcomes. High job demands were related to shortened hours of sleep, frequent waking, and marginally to feelings of non-refreshed sleep while low decision latitude at work predicted the onset of difficulty falling asleep, early waking, and waking without feeling refreshed and it was marginally related to

shortened sleeping hours. One would have anticipated high demands at work to predict difficulty falling asleep due to physiological and psychological arousal which prevents an individual from falling asleep.[184] In fact, low decision latitude at work seemed to act as such a stressor in the present study. The results on work stress are in line with earlier, mostly cross-sectional studies on the topic.[184-186]

Regarding working hours, the cross-sectional analysis showed that working >55 hours per week was related to short hours of sleep, early waking and waking without feeling refreshed. Unlike prospective analysis, this analysis did not reveal a consistent association between long (>55) working hours and difficulty in falling asleep while the association was found in employees working 49-55 hours compared to those working 35-40 hours. It is possible that some employees have been forced to shorten their working hours because of sleeping problems, and this may have diluted the associations in a cross-sectional analysis.

The results from prospective analysis suggest the onset of various sleep disturbances among employees who were free from such disturbance but worked long hours at baseline. In the prospective analysis, the strongest effect was found for difficulty falling asleep (ORs ranging from 4.90 to 9.96 for >55 hours compared to 35-40 hours), waking without feeling refreshed (ORs ranging from 2.27 to 2.43), early waking (ORs ranging from 1.74 to 2.49), and shortened hours of sleep (ORs ranging from 2.40 to 2.50). The associations seemed mainly to be driven by the group of longest hours (>55 hours) although entering working hours as a continuous variable resulted in an effect of linear trend.

This study was probably the first prospective cohort study to examine the association between repeat exposure, i.e., long working hours measured at two time points, and subsequent sleep disturbances, taking into account several known risk factors. The effects were slightly stronger for working hours measured repeatedly than at only one point

in time suggesting a dose-response association between long work hours, incident shortened sleep, difficulty in falling asleep, and early waking.

The results on long working hours and sleep disturbances were robust and not totally explained by known risk factors such as health behaviours or health status. However, adjustments suggested that high job demands may partially explain the association between long working hours and sleep disturbances.

The findings correspond with earlier cross-sectional studies on sleep length which have reported a consistent association between long working hours and *short sleep duration*.[35 215 225 231 236-240] However, earlier research has shown mixed findings on the association between long working hours and *sleep disturbances*. Null findings have been reported in some studies[207 230-232] while a study of Japanese civil servants,[233] a study carried out among Finnish information technology professionals[234] and a random sample of Finnish twins[235] found an association between long working hours and sleep disturbances. All these studies were cross-sectional and therefore the direction of causality can not be established.

At least two previous studies have examined working hours and sleep longitudinally. Ribet and Derriennic[229] followed middle-aged French employees for 5 years and found that long working hours at baseline did not predict incident sleep disorders. However, participants who reported that they had worked overtime at some time in the past, but not at the time of the baseline survey, were at an increased risk of sleep disorder. Dahlgren and her colleagues[215] followed 16 employees for two weeks in their field study and found that a week of overtime resulted in a decrease in sleeping hours as well as increased feelings of exhaustion.

A specific strength of the Study 4 was the possibility to use non-overlapping measurements of working hours and sleep disturbances. Furthermore, examination of five distinct measures of sleep disturbances offered the opportunity to consider whether long

working hours are uniformly and equally strongly associated with sleep disturbances. This was the case in the majority of outcomes, however, the strongest effect was found for difficulty falling asleep, with even stronger evidence generated by repeated or prolonged exposure to long working hours as opposed to working hours measured at one time point only.

A plausible causal pathway between long working hours and sleep disturbances may be, again, poor recovery after work reflecting a lack of leisure time. At the end of a day at work, a certain time may be needed for recovery as a natural consequence of the fatigue resulting from efforts expended at work. Recovery after work may not only include sleep but also relaxation, such as spending time with family members and friends, resting, or reading. Relaxation has been recognized as an important prerequisite in the prevention of sleep-onset insomnia,[293] which correlates with "difficulty falling asleep" measured in the present study. As long working hours have been found to be associated with increased need of recovery after work,[278] employees working long hours would actually need more time to recover than workers with workdays of normal length. In this study, high job demands attenuated to some degree, but did not fully explain, the associations between long working hours and sleep disturbances. Indeed, adjustment for job demands might lead to overcontrolling because high demands and long hours may represent two indicators of the same stressful work environment rather than two distinct risk factors.

It is possible that sleep disturbances in the present study reflect an underlying disease, particularly a mental disorder. Even though sleep disturbances are associated with physical illnesses, they have been shown to be a symptom of a mental disorder 10 times as often as a physical illness.[179 294] The most common diagnoses to which insomnia symptoms are related are the mood-, anxiety-, and substance-related disorders.[294] Keeping in mind this viewpoint and the fact that there was an association between long working hours and mental

ill health, and because insomnia is a major symptom in depressive and anxiety disorders, the possibility that the sleep disturbances in the present study reflect symptoms of these disorders can not be ruled out. Assessment of comorbidity between sleep disturbances and incidence of psychiatric disorders was beyond the resources of this analysis because depressive disorders were assessed only at phase 5 and the number of cases was quite low. However, comorbidity should be considered as an important topic for future research. Further research should also clarify whether long working hours predict primary insomnia or organic sleep disorders such as somatic disease or sleep apnea, or whether insomnia is mainly a symptom of a mental disorder.

In this thesis, little evidence was found for the relationship between long working hours and frequent waking during the night. Behavioral, psychiatric, and circadian disorders have been associated with trouble falling asleep and early awakening, whereas primary sleep disorders (such as sleep apnea) and other medical conditions have been more closely associated with frequent waking during the night.[179 293 295]

Although there was no cross-sectional association between long working hours and prevalent chronic disease in the present study and there is little evidence of that association in earlier studies,[24 26] it is still possible that the association between long working hours and sleep complaints is partially accounted for by comorbid organic disorders not assessed in the present study, or by behavioral correlates of insomnia, e.g., caffeine use. Although for the effects of several confounding or mediating factors were controlled, it was not possible to differentiate between sleep disturbances resulting from nonorganic insomnia and those related to organic sleep disorders, such as periodic limb movements, restless legs syndrome, or narcolepsy.[296] However, the significant associations remained after body mass index, a correlate of obstructive sleep apnea, was controlled for. However, measurements of organic sleep disorders would be needed in the future to further investigate these issues.

In summary, the findings indicate that long working hours predict onset of various forms of new sleep disturbances. Sleep disturbances can have a significant negative effect on an individual's quality of life, and the consequences associated with sleeping disturbances are serious including, for example, a higher risk of accidents due to fatigue, increased risk of all-cause mortality, cardiovascular diseases and mental disorders, increased sickness absence rates, and substantial medical care costs.[157 158 162 297-299] The findings also suggest that continued overtime work should be recognized as a risk marker for the development of sleep disturbances.

10.3 Strengths and limitations

The main strengths of the present thesis are its large sample size and longitudinal design where the exposure and outcome were measured at different time points and baseline cases were excluded; thus the potential for reversed causality, that is, health as a predictor of working hours, was reduced. Furthermore, the outcome measures of CHD and type 2 diabetes were based on clinical examinations instead of sole self-reported data and the assessment of depression was carried out using standardised clinical interview method.

However, a common feature in all prospective cohort studies followed for many years is loss of participants between baseline and follow-up (see Table 5).[243] There was also considerable non-participation at baseline (response rate 73%). However, in the Whitehall II study, attrition at subsequent phases has been minimized by careful tracing those lost to postal contact. For participants who were lost at follow-up screenings and questionnaire surveys, health information was obtained from hospitalization records (from the NHS-Wide Clearing Service) and death certificates. Thus, data on CHD death can be considered reliable. Data quality was ascertained by double entry of questionnaire data, clinical

screening data and laboratory test results. All variables were subjected to range and validity checks and in cases where ambiguities could not be resolved were set to missing.

Selection bias was examined in two ways. First, the impact of missing data on the association between working hours and CHD was examined using a dataset including also those participants who had missing data on covariates. This examination did not suggest any selection bias due to missing data. Second, selection into shorter working hours due to pre-existing ill-health was examined by sequentially excluding CHD events that occurred during the first 1, 2, 3, and 4 years of follow-up. Selection of employees with a subclinical CHD state into shorter (7-8) hours would have resulted in a stronger association between long working hours and CHD after exclusion of cases at the beginning of follow-up. This sensitivity analysis did not reveal such a selection effect since the associations became weaker after exclusions.

Regarding the other outcomes, the present study relied on participation in clinical examinations and surveys. Considerable loss to follow-up was seen in participants with certain socio-demographic characteristics, such as female sex and low SEP, as well as some of the characteristics related to health and health behaviours. Low participation rate was also observed in the CIDI interview. Cohorts like the Whitehall II study that follow the same individuals over an extended time period are subject to a 'healthy survivor' or 'healthy worker' effect as participants with severe illnesses are more prone to drop out of the study over time.[274] However, work exposures such as working hours cannot be examined among participants who are no longer exposed to work. The issue of attrition was analysed in Tables 6, 8, 10, and 12 which suggested no major loss to follow-up due to ill health, health risk behaviours, or working hours. However, a strong attrition was found among participants with low SEP who seemed to be more likely to be non-participants at follow-up than those

with high SEP. However, this would be a problem only if the thesis topic was to study the association between SEP and health outcomes.

The Civil Service represents white-collar employment in a public sector workplace and the participants were middle-aged (35-55 years) already at the first phase of the study. Therefore the results can not be generalised to the general working population of the UK. In addition, the Whitehall II study has demographic features that reflect the composition of the Civil Service at study baseline in the mid-1980s. At that time, one-third of the baseline cohort was women, and of them, half were in the clerical and office support grade. The proportion of women decreased during the follow-up. Due to a small number of women working long hours, sex-stratified analyses were not possible to perform in the present study.

An important potential bias relates to *common method variance* or *information bias* which means that variance in variables can be attributed to the measurement method rather than to the constructs that are supposed to be measured, such as negative affectivity or a tendency of a person to respond in a desirable or consistent way.[21] Common method variance is especially strong when the exposure (e.g. work stress) and the outcome (e.g. depression) are likely to reflect, for example, the unmeasured subclinical mental health state and associated negative affect. Potential bias due to common method variance is especially problematic when both the exposure and outcome are based on self-reports. In the present study, ascertainment of CHD relied on clinical and register data, and diabetes was based on a combination of self-report and clinical data, whereas depression was assessed by a structured interview and sleep disturbances were based on self-report paper-and-pencil scales. Thus, the probability for bias due to common method variance was most pronounced in the studies on depression and sleep disturbances. However, if common method variance was a major bias in the present study, it should have inflated all associations, which was not

the case, for example, as associations were heterogenous for the different sleep outcomes studied.

However, this study has other important limitations and the findings should be interpreted within the context of those. First, as in all observational studies, the possibility of residual confounding by other, unmeasured or imprecisely measured predictors of coronary events, type 2 diabetes, depression and sleep disturbances can never be entirely ruled out. Covariates were measured as time independent which means that they were assessed only at baseline. This should be acknowledged as a potential limitation when investigating mediating effects or mechanisms as it does not take into account the impact of possible changes in these factors on the risk of incident health problems.

Furthermore, although the aim was to examine interaction effects, the present study was not well powered for subgroup analyses. Interaction effects were possible to carry out only regarding CHD and type 2 diabetes outcomes. Even in these analyses, the findings should be interpreted cautiously and replicated in studies with larger sample sizes.

10.4 Methodological issues

10.4.1 Definition and validation of working hours

In this thesis, working hours were measured by self-reports. At phase 3, working hours were ascertained from the following question: "On an average weekday, approximately how many hours do you spend on the following activities: Work (daytime and work brought home)?" with response alternatives ranging from 1 to 12. The advantage of this question is that the respondent reports an average day and he/she does not need to calculate or sum up weekly working hours which may result in inaccurate estimates. However, work during weekend

was not requested which may cause an underestimate of working hours. This may, however, introduce a bias in the study only if weekend working hours were distributed differently from weekday working hours among the respondents.

At phase 5, working hours were ascertained from the following two questions: “How many hours do you work per average week in your main job, including work brought home?”, and (for participants with more than one job) “How many hours do you work in an average week in your additional employment?” with response alternatives ranging from 0 to 100+ and 0 to 99, respectively. The latter assessment can be considered a more accurate way to ascertain hours worked since additional jobs as well as weekend jobs / hours worked during the weekend were included in the estimate. At phase 3, employees who worked in their main job during the weekend and those who worked longer than 12 hour per day were therefore inaccurately classified. This misclassification could have produced bias only if there were many respondents with a full-time job in the civil service and an additional weekend job somewhere else or if many respondents worked 'normal' hours during weekdays and extra hours during weekends.

In the analyses of sleep outcomes (Study 4) using working hours measured at two time points, the phase 3 assessment was daily hours for weekdays (transformed into weekly) while the phase 5 assessment included average number of work hours for the entire week, including weekends. Therefore the averaged measurement across these 2 time points cannot be considered as accurate as if exactly the same measures had been used at both phases.

Vast majority of studies on long working hours and health rely on self-reports of working hours. Self-reported working hours may involve *recall bias* which refers to inability of the employees to accurately remember their hours worked. However, some investigators have noted that self-reported work hours are the most reliable item in occupational activity questionnaires (eg, 2-week test-retest intraclass correlation coefficient of 0.91).[277] However,

a bias could only exist if inaccuracy in the reporting of working hours was associated with actual hours worked as well as with the onset of the outcome under study. Sokejima and Kagamimori,[39] overcame this problem by using patients' salary records instead of self-reports to determine working hours in their study, and found a 2.4-fold risk for myocardial infarction among employees who worked 11 hours or more a week, in line with findings for the self-reported hours in the same study. Thus, it seems that self-reported working hours and those derived from salary records give rather similar associations with CHD. There are limitations in using company records as well, because in many cases, overtime hours are not registered and therefore company records would result in an underestimation of hours worked. For large epidemiologic cohorts as the Whitehall II study is, fine-grained data collection, such as keeping diaries, is not feasible, or at least it is possible to carry out only in a limited number of participants.

In addition, it is not clear whether the number of working hours reported by participants at baseline was stable over the longer follow-up. This could be a potential source of misclassification of the exposure measure or represent an actual change in hours worked. However, data on working hours were measured twice (at phases 3 and 5). Although the first version of the question had been modified and requested weekly working hours rather than daily working hours, it was possible to explore the stability among the 2013 phase 3 overtime (>8 hours / day) workers who were still in employment at phase 5. Of them 33% worked a maximum of 40 hours per week at follow-up, 24% worked 41-48 hours and 43% worked more than 48 hours per week. Thus in the Whitehall II data, working long hours appears to be a relatively stable characteristic.

Regarding bias caused by common method variance, working hours can not be strictly be classified as a "stressor" since the unit of measurement, *an hour*, does not inherently include the individual's experience of stress or distress. Therefore, working hours

can be considered less sensitive to this bias than work exposures including a strong affective component.

10.4.2 Definition and validation of CHD

In Study 1, two outcomes were examined: 1) Fatal CHD, non-fatal myocardial infarction, or definite angina pectoris; 2) Fatal CHD or non-fatal myocardial infarction. Prevalent cases by phase 3, determined by using a procedure similar to that for incident CHD, were excluded from the analysis. Classification was carried out independently by two trained coders, with adjudication in the event of disagreement.

For fatal CHD, participants were flagged by the British National Health Service (NHS) Central Registry, who provided information on the date and cause of all deaths, classified as coronary if ICD-9 (*International Classification of Diseases*, 9th edition)[47] codes 410–414 or ICD-10 (*International Classification of Diseases*, 10th edition)[48] codes I20–I25 were present on the death certificate. Regarding the NHS Central registry which covers all deaths in the U.K., fatal CHD can be considered an accurate measure if the cause of death had been diagnosed accurately. Individuals who died abroad were included in the cohort if their death certificate was able to be obtained.

Non-fatal CHD included first nonfatal myocardial infarction (MI) or first definite angina. Non-fatal MI was defined following MONICA criteria[244] based on study electrocardiograms, hospital acute ECGs, and cardiac enzymes, and biochemical markers (see Figure 8, p.86). The need for a standard protocol to identify nonfatal cases originally rose from the fact that not all nonfatal cases come to medical attention and thus are undiagnosed and misclassified. MONICA criteria has shown good agreement with clinical expert diagnoses (see e.g. Kavsak et al.[300]) suggesting good validity. Later, in 2000,

redefinition of AMI has been published by the European Society of Cardiology and the American College of Cardiology (ESC/ACC), in which there is a rising and falling concentration of troponin that elevates to >99th percentile of a reference population in the presence of symptoms of ischemia.[301] Inclusion of troponin assays in the criteria resulted in a remarkable increase in the frequency of diagnosed AMI.[300] From phase 7 the Whitehall II study criteria included also troponin level as a marker of AMI.

Incident angina was first identified by the Rose Questionnaire[245] and corroborated by medical records, nitrate medication use, or abnormal results on a resting ECG, an exercise ECG, or a coronary angiography. Thus, only screening was relied on self-report.

10.4.3 Definition and validation of type 2 diabetes

Diagnosis of incident diabetes from venous blood samples was based on the current definition of the disease, that is, a fasting glucose of 7.0 mmol/L or more, or a 2-h postload glucose of 11.1 mmol/L or more,[250 259] and self-reported doctor-diagnosed diabetes or use of diabetes medication. To obtain comparability across study phases, type 2 diabetes was handled during both phases according to similar standard protocols and baseline cases were excluded from the prospective analyses.

To reduce false positive cases, blood samples were taken in individuals who were instructed to fast ≥5 hours before blood sampling and undergoing a standard 2-h oral glucose tolerance test. Fasting hours were also requested and recorded in the clinical examination. To ensure a high standard, glucose samples were handled according to guidelines and standard protocols were followed in the analyses.[261-263] Sensitivity analyses were made among participants who fasted ≥8 hours.

A proportion of the diabetes cases in the Whitehall II study is ascertained from information on self-reported doctor-diagnosed diabetes (35%) and self-reported use of diabetic medication (15%).[260] However, validation studies have suggested self-reported diabetes to be satisfactorily concordant with other diagnostic evidence of diabetes, such as OGT[302 303] or diagnosis obtained from medical files.[303] In fact, self-reported use of oral antidiabetic agents has been proved to be 99-100% concordant with information on the prevalence of diabetes obtained from medical files.[303]

10.4.4 Definition and validation of depression

Presence of an MDE was ascertained during the clinical health examination at phase 5 using the University of Michigan version of the Composite International Diagnostic Interview (UM-CIDI) adapted for self-administered computerised interview.[264 265] The program used operationalized criteria for diagnoses in the Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R).[266] The CIDI interview has shown good validity as a measure of DSM-III-R non-psychotic disorders.[264]

However, as a limitation, the CIDI was only available at follow-up so baseline cases had to be excluded based on GHQ-30 caseness. However, the GHQ is a well-established scale for the evaluation of psychological morbidity in general population samples. In relation to diagnosed mental disorders, especially mood and anxiety disorders, the GHQ has shown good clinical validity.[120 122 255] However, as the GHQ-30 also detects a range of minor psychiatric disorders such as subclinical depression it is possible that the baseline exclusion of GHQ-30 cases is over zealous. Another limitation related to the CIDI interview in the present study is that only the present clinical status, not the severity of MDE was taken into account.

10.4.5 Definition and validation of sleep disturbances

The data on sleep length and sleep disturbances are limited by the fact that they were collected via self-reports (see discussion of this limitation in the paragraph 10.4.1; "Definition and validation of working hours", p. 186).

The present study used the Jenkins scale to determine sleep disturbances which is validated against psychological symptoms[165] and widely used in epidemiological studies.[304] [305] However, it is not validated against insomnia, which is a limitation, although the items are in accordance with the diagnostic criteria for insomnia, that is, difficulty falling asleep or maintaining sleep during the night, too early morning awakenings, and non-restorative sleep with a duration of at least one month.[109] In the present data, the cut-off point (corresponding at least 2–3.5 times /week) was chosen to approximate to the ICD-10 diagnosis (F51.0)[48] and other guidelines to assess insomnia,[11] in which chronic insomnia is detected if the frequency of complaint is more than 2 times[48] or ≥3[11] times a week.

Sleep duration was based on self-reports and used hourly categories as responses and did not explicitly ask participants to differentiate time asleep from time in bed. In large epidemiologic studies, it is not feasible to collect more objective data on sleep, such as sleep diaries, actrigraphs, or polysomnography. However, earlier smaller studies have shown that self-reports and actigraph-measured sleep duration appear to be moderately correlated, averagely providing an overestimation of sleep duration.[306] [307] Concordance between self-reported sleep duration and polysomnography, the gold standard, has found to be low to moderate.[308] However, as self-reported sleep duration is associated with various health outcomes it can be a useful indicator of sleep.[162] [163]

10.5 Implications

Results of this prospective study suggest long working hours to predict an increased risk of CHD, depression, and sleep disturbances. However, no robust association was found with the onset of type 2 diabetes, although the findings cannot exclude the possibility that long working hours might increase the further risk of developing type 2 diabetes among prediabetic individuals. Therefore findings of the present study suggest that long working hours should be recognized as a potential risk marker for the development of these health problems.

As this study is based on observational data it is not known whether the associations found are causal, even though the study design was prospective. However, long working hours may at least represent a risk marker - indeed, convincing additional evidence comes from a recent investigation which found that information on working hours improved prediction of CHD risk based on the Framingham risk score in the Whitehall II study.[309] Nonetheless, as the Whitehall II study is of white-collar public sector employees, any implications should be considered only to apply similar populations until other prospective studies in general working populations, as well as different occupational groups confirm the findings. Best possible evidence comes from large-scale intervention studies designed to reduce working hours and test whether the intervention would alter health risk in working populations.

It is known that some employees work long hours because they enjoy their work whereas others are required to work long hours or do so because they are forced to do so or they need the money. However, not all employees extra working hours are paid overtime. Different types of 'overtime' workers in terms of underlying motivation have been distinguished; one type is a constructive, highly committed achievement-oriented

employee.[310] Some individuals work long hours in order to get an advantage over the competition in working life or in the hope for rewards. Alternatively, working long hours may relate to employer demands or work overload. In the present study, participants who worked long hours were usually in higher occupational positions and had high decision latitude at work but they can also be characterised as competitive because they scored high in type A behaviour. However, what is not known is whether the adverse effects of long working hours are contingent on these or other factors, such as sex, negative spill-over to leisure time and family relations, or the level of domestic responsibilities.

Finally, as one of the primary motivations for working longer hours is to increase productivity, paradoxically, the effect of extended workdays on health may result in increased mistakes and accidents as well as impairing work performance by diminishing attention and arousal and by impairing memory consolidation and insight formation, which, in turn, block learning and creativity.[28 34 311] Furthermore, negative effects of long working hours may spread to family members. These are important implications to be considered and examined in future studies.

10.6 Future work and unanswered questions

In the literature on long working hours and health, there was large variation in the assessment of working hours, ranging from non-specific definition of "overtime" to more specific inquiry about daily working hours (cut point for long hours ranging from ≥10 to >11 hours), or weekly working hours (cut point for long hours ranging from >40 to >65 hours). In addition, very rarely the reference group comprised employees with a standard 7-8/9 hours' workday. Use of dichotomous categorisation with a high cut-off point defining long

hours in some studies may have led to an underestimation of the association, as employees with relatively long working hours are included in the reference group.

Furthermore, many studies included part-time employees in the reference group. This is also problematic because of the elevated health risk among part-time employees;[39] indeed, poor health is a possible reason for working reduced hours.[312] In future studies, a reference group with a standard work day, approximately eight hours would be preferable.

The effects of 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 health problems. It is thus important to establish the *length of exposure* to long working hours which is likely to cause health problems (ie, is the threshold weeks, months or years) as well as *change in exposure* to working hours. Very rarely the prospective studies examined whether the number of working hours reported by participants at baseline was stable over the follow-up. However, one study examined whether a change in working hours had occurred during the year preceding the AMI and found that men who experienced a more than 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.[39] Thus, more evidence on the amount of exposure needed for adverse health effects and on the nature of the exposure (e.g. trigger) is needed to increase understanding of the relationship between long working hours and health.

Regarding studies on CHD, the most common outcomes in previous studies were AMI and angina, diagnosed by a physician during hospital treatment, in the study clinic, or based on diagnoses in national registers. Although the outcome assessment of the present study can be considered rather reliable, more specific CHD endpoints,[313-316] such as stable angina, non-stable angina, first MI with elevation of the ST segment on ECG (STEMI) and first MI without such elevation (non-STEMI) would be preferable in future studies to increase understanding of the potential adverse consequences of long working hours.

To date, very little is known on the association between long working hours and type 2 diabetes, and the findings thus far are contradictory. Future research should examine whether the discrepancy is due to methodological shortcomings or whether there are certain circumstances where long hours are associated with the onset of diabetes.

Although the present study used a validated CIDI interview to ascertain depression, the sample size was relatively small and baseline cases were excluded using caseness of the GHQ-30. Future studies with larger datasets and repeat measurements of depressive disorders are therefore needed to confirm the robustness of the present findings. In addition, as depressive disorders usually initiate at young age,[113] childhood and pre-employment mental health should be taken into account to remove bias due to reverse causality.

Future research on the association between long working hours and sleep disturbances should employ clinical assessment of sleep disorders to differentiate symptoms of sleep disturbances from clinically significant sleep disorders, and further to differentiate clinically significant organic sleep disorders, i.e. those that are one of the symptoms of another disorder, either mental or physical, from non-organic sleep disorders that could be consequence of work-related exposures.

Although several possible factors that may mediate the association between long working hours and health were controlled in the present study, they did not seeem to emerge as important mediating factors. In the future, other biological and behavioural pathways should be examined in detail, new potential pathways should be explored and mediators should be examined as time-dependent.

According to the model by Caruso and others,[31]there might be effect modifiers between long working hours and health outcomes (see Figure 4, page 24). Although the possibility of finding several effect modifiers was tested in this thesis, the results regarding moderation were very modest. It is possible that: 1) there are actually no effect modifiers; 2)

there are no effect modifiers in this particular sample; 3) effect modifiers are different from those assessed in this study; 4) the present study was not large enough to reliably test effect modification. Indeed, it was not possible to carry the tests out with regard to depression and sleep disturbances. It is possible that there are, for example, sex differences in the association between long working hours associated with mental health and sleep disturbances, so further studies with larger sample sizes are needed to examine these possible interaction effects. Furthermore, it would be important to include new aspects of effect modification, such as voluntary versus involuntary nature of long hours or the number of hours worked due to domestic responsibilities. Further support for causality would be obtained from studies where interventions designed to reduce working hours would alter disease risk in working populations.

10.7 Conclusions

The results of this thesis indicate that long working hours could be recognized as a potential risk marker for the development of CHD, depression, and sleep disturbances. However, the results are generalisable to British white-collar workers only, and as this study is based on observational data it is not known whether the associations are causal.

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APPENDIX TABLE 1. Search strategy (OvidSP Medline) for the literature of long working hours and study outcomes.

	Searches	**Result (n)**
1	Work hours.mp.	1093
2	exp Diabetes Mellitus, Type 2/ or exp Cardiovascular Diseases	1647583
3	overtime.mp.	963
4	working hours.mp.	1956
5	1 or 3 or 4	3882
6	2 and 5	203
7	exp Depression/	57567
8	5 and 7	31
9	from 6 keep 1-203	203
10	exp Sleep Disorders/	47177
11	5 and 10	167
12	exp Mental Disorders/ or psychological distress.mp.	790778
13	5 and 12	321

APPENDIX TABLE 2. Association between working hours at baseline and incident coronary heart disease at follow-up, as indicated by coronary death, incident definite non-fatal myocardial infarction or incident definite angina pectoris, participants with missing covariates included

Daily working hours	n of events	n of participants	Person-years	Rate / 1000 person-years	HR (95% CI)[a]	*P* value
All	442	7090	78760.7	5.61		
7-8	232	3831	42244.9	5.49	1.00	ref.
9	77	1466	16551.3	4.65	0.91 (0.70-1.19)	0.49
10	76	1058	11828.9	6.42	1.29 (0.98-1.69)	0.07
11-12	57	735	8135.6	7.01	1.40 (1.03-1.90)	0.032
P value for trend						0.015

[a]Adjusted for age, sex and occupational grade (missing values in age & sex, n=0; occupational grade, n=5).

APPENDIX TABLE 3. Association between working hours at baseline and incident coronary heart disease at follow-up, as indicated by coronary death OR incident definite non-fatal myocardial infarction, with exclusion of cases during the first year of follow-up

Daily working hours	n of events	n of parti-cipants	Person-years	Rate / 1000 person-years	Model A HR (95% CI)[a]	*P* value	Model B HR (95% CI)[b]	*P* value	Model C HR (95% CI)[c]	*P* value	Model D HR (95% CI)[d]	*P* value	Model E HR (95% CI)[e]	*P* value
All	349	5994	67533.0	5.17										
7-8	182	3249	36328.9	5.01	1.00	ref.	1.00	ref.	1.00	ref.	1.00	ref.	1.00	ref.
9	63	1241	14181.7	4.44	0.95 (0.71-1.28)	0.73	0.99 (0.74-1.34)	0.97	0.98 (0.73-1.32)	0.90	1.00 (0.74-1.35)	0.98	0.98 (0.72-1.32)	0.88
10	59	893	10114.9	5.83	1.30 (0.95-1.76)	0.10	1.34 (0.99-1.83)	0.06	1.26 (0.93-1.72)	0.14	1.32 (0.96-1.81)	0.09	1.26 (0.92-1.74)	0.15
11-12	45	611	6907.5	6.51	1.45 (1.02-2.05)	0.036	1.50 (1.06-2.13)	0.021	1.41 (0.99-1.99)	0.05	1.47 (1.03-2.10)	0.034	1.41 (0.99-2.02)	0.06
P value for trend						0.021		0.010		0.034		0.018		0.039

HR=Hazard ratio. CI=Confidence interval.
[a] Model A: Adjusted for age, sex, marital status, and occupational grade.
[b] Model B: As Model A and additionally adjusted for diabetes, systolic and diastolic blood pressure, LDL and HDL cholesterol, and triglycerides.
[c] Model C: As Model B and additionally adjusted for smoking, alcohol use, fruit and vegetable consumption, exercise level, body mass index, and sleeping hours.
[d] Model D: As Model C and additionally adjusted for sickness absence, psychological distress, job demands, and decision latitude at work.
[e] Model E: As Model D and additionally adjusted for type A behaviour.

APPENDIX TABLE 4. Association between working hours at baseline and incident coronary heart disease at follow-up, as indicated by coronary death, incident definite non-fatal myocardial infarction or incident definite angina pectoris, with exclusion of cases during the first 2 years of follow-up

Daily working hours	n of events	n of parti-cipants	Person-years	Rate / 1000 person-years	Model A HR (95% CI)[a]	*P* value	Model B HR (95% CI)[b]	*P* value	Model C HR (95% CI)[c]	*P* value	Model D HR (95% CI)[d]	*P* value	Model E HR (95% CI)[e]	*P* value
All	305	5950	67468.8	4.52										
7-8	158	3225	36293.2	4.35	1.00	ref.	1.00	ref.	1.00	ref.	1.00	ref.	1.00	ref.
9	53	1231	14167.5	3.74	0.92 (0.66-1.26)	0.59	0.96 (0.69-1.32)	0.79	0.95 (0.69-1.31)	0.74	0.96 (0.69-1.33)	0.80	0.95 (0.68-1.31)	0.74
10	54	888	10107.6	5.34	1.35 (0.98-1.87)	0.07	1.40 (1.01-1.94)	0.043	1.32 (0.95-1.83)	0.10	1.36 (0.98-1.90)	0.07	1.32 (0.94-1.85)	0.11
11-12	40	606	6900.6	5.80	1.46 (1.01-2.18)	0.043	1.51 (1.04-2.18)	0.029	1.41 (0.97-2.04)	0.07	1.46 (1.00-2.14)	0.0495	1.42 (0.97-2.08)	0.07
P value for trend						0.019		0.011		0.035		0.022		0.038

HR=Hazard ratio. CI=Confidence interval.
[a] Model A: Adjusted for age, sex, marital status, and occupational grade.
[b] Model B: As Model A and additionally adjusted for diabetes, systolic and diastolic blood pressure, LDL and HDL cholesterol, and triglycerides.
[c] Model C: As Model B and additionally adjusted for smoking, alcohol use, fruit and vegetable consumption, exercise level, body mass index, and sleeping hours.
[d] Model D: As Model C and additionally adjusted for sickness absence, psychological distress, job demands, and decision latitude at work.
[e] Model E: As Model D and additionally adjusted for type A behaviour.

APPENDIX TABLE 5. Association between working hours at baseline and incident coronary heart disease at follow-up, as indicated by coronary death, incident definite non-fatal myocardial infarction or incident definite angina pectoris, with exclusion of cases during the first 3 years of follow-up

Daily working hours	n of events	n of parti-cipants	Person-years	Rate / 1000 person-years	Model A HR (95% CI)[a]	*P* value	Model B HR (95% CI)[b]	*P* value	Model C HR (95% CI)[c]	*P* value	Model D HR (95% CI)[d]	*P* value	Model E HR (95% CI)[e]	*P* value
All	270	5915	67374.4	4.01										
7-8	141	3208	36247.8	3.89	1.00	ref.	1.00	ref.	1.00	ref.	1.00	ref.	1.00	ref.
9	47	1225	14151.3	3.32	0.91 (0.65-1.28)	0.59	0.95 (0.68-1.34)	0.78	0.94 (0.67-1.33)	0.73	0.94 (0.67-1.33)	0.72	0.93 (0.66-1.31)	0.67
10	49	883	10093.6	4.85	1.38 (0.98-1.94)	0.07	1.43 (1.01-2.01)	0.042	1.35 (0.96-1.91)	0.08	1.37 (0.97-1.95)	0.08	1.33 (0.93-1.89)	0.12
11-12	33	599	6881.7	4.80	1.35 (0.90-2.02)	0.14	1.39 (0.93-2.08)	0.11	1.30 (0.87-1.96)	0.20	1.33 (0.88-2.01)	0.17	1.29 (0.85-1.95)	0.23
P value for trend						0.05		0.033		0.08		0.07		0.11

HR=Hazard ratio. CI=Confidence interval.
[a] Model A: Adjusted for age, sex, marital status, and occupational grade.
[b] Model B: As Model A and additionally adjusted for diabetes, systolic and diastolic blood pressure, LDL and HDL cholesterol, and triglycerides.
[c] Model C: As Model B and additionally adjusted for smoking, alcohol use, fruit and vegetable consumption, exercise level, body mass index, and sleeping hours.
[d] Model D: As Model C and additionally adjusted for sickness absence, psychological distress, job demands, and decision latitude at work.
[e] Model E: As Model D and additionally adjusted for type A behaviour.

APPENDIX TABLE 6. Association between working hours at baseline and incident coronary heart disease at follow-up, as indicated by coronary death, incident definite non-fatal myocardial infarction or incident definite angina pectoris, with exclusion of cases during the first 4 years of follow-up

Daily working hours	n of events	n of parti-cipants	Person-years	Rate / 1000 person-years	Model A HR (95% CI)[a]	*P* value	Model B HR (95% CI)[b]	*P* value	Model C HR (95% CI)[c]	*P* value	Model D HR (95% CI)[d]	*P* value	Model E HR (95% CI)[e]	*P* value
All	238	5883	67268.9	3.54										
7-8	122	3189	36185.3	3.37	1.00	ref.	1.00	ref.	1.00	ref.	1.00	ref.	1.00	ref.
9	43	1221	14137.9	3.04	0.96 (0.67-1.38)	0.83	1.01 (0.70-1.44)	0.98	1.00 (0.70-1.43)	0.99	0.99 (0.80-1.98)	0.96	0.98 (0.68-1.41)	0.91
10	46	880	10083.5	4.56	1.50 (1.05-2.14)	0.026	1.54 (1.08-2.21)	0.017	1.47 (1.03-2.10)	0.036	1.49 (1.03-2.15)	0.035	1.44 (0.99-2.08)	0.05
11-12	27	593	6862.2	3.93	1.30 (0.84-2.02)	0.24	1.33 (0.85-2.06)	0.21	1.24 (0.79-1.93)	0.35	1.26 (1.16-2.28)	0.32	1.22 (0.78-1.92)	0.38
P value for trend						0.06		0.039		0.09		0.09		0.13

HR=Hazard ratio. CI=Confidence interval.
[a] Model A: Adjusted for age, sex, marital status, and occupational grade.
[b] Model B: As Model A and additionally adjusted for diabetes, systolic and diastolic blood pressure, LDL and HDL cholesterol, and triglycerides.
[c] Model C: As Model B and additionally adjusted for smoking, alcohol use, fruit and vegetable consumption, exercise level, body mass index, and sleeping hours.
[d] Model D: As Model C and additionally adjusted for sickness absence, psychological distress, job demands, and decision latitude at work.
[e] Model E: As Model D and additionally adjusted for type A behaviour.